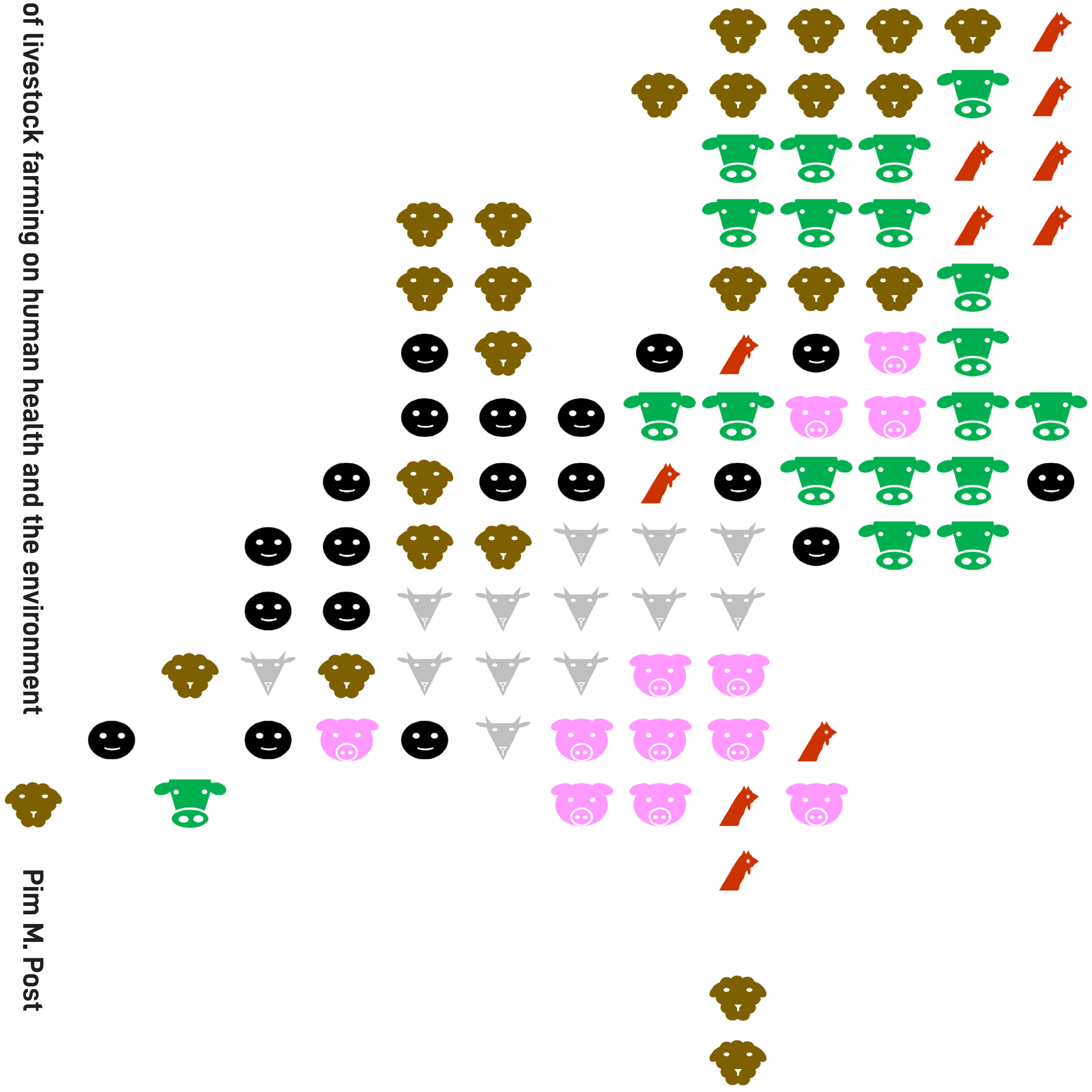
Characterizing effects of livestock farming on human health and the environment

Pim M. Post



Characterizing effects of livestock farming on human health and the environment

Pim M. Post

Characterizing effects of livestock farming on human health and the environment

Colofon
Characterizing effects of livestock farming on human health and the environment – Pim M. Post

Thesis, Utrecht University
ISBN: 978-94-6332-775-6

Printing: GVO drukkers & vormgevers B.V.

Characterizing effects of livestock farming on human health and the environment

Het karakteriseren van effecten van de veehouderij op volksgezondheid en milieu
(met een samenvatting in het Nederlands)

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de
Universiteit Utrecht
op gezag van de rector magnificus, prof.dr. H.R.B.M. Kummeling,
ingevolge het besluit van het college voor promoties in het openbaar te
verdedigen op dinsdag 19 oktober 2021 des middags te 4.15 uur

door
Pim Martijn Post

geboren op 10 januari 1991
te Amsterdam

Promotoren:

Prof. dr. ir. E. Lebret
Prof. dr. L. Posthuma

Copromotor:

Dr. L. Hogerwerf

Dit promotieonderzoek is uitgevoerd binnen het Strategisch Programma RIVM (SPR), een programma voor onderzoek, innovatie en kennisontwikkeling. Zo blijft het RIVM voorbereid op de vragen van morgen.

Contents

Chapter 1

General introduction

This thesis is about the integrated assessment of effects of Dutch livestock production on human health and the environment. Why such integrated assessment is desirable is described in the following sections by providing a short historic perspective on the development of livestock production in the Netherlands, the increasing societal concerns regarding human health and environment, and the need for integrated approaches. This historic perspective is followed by an outline of the scope of this thesis and the contents of subsequent chapters.

A short historic perspective

The current Dutch livestock sector is highly productive. In fact, in terms of economic value the Netherlands is the second largest exporter of agricultural products in the world after only the United States (Dolman et al., 2019), despite being 270 times as small in land surface area. Next to horticulture products, a large part of the export consists of dairy products, eggs, and meat from intensively kept pigs, poultry and veal calves. This high productivity can be traced back to the historical nutrition transition, described by de Bakker and Dagevos (2010;2012) . This transition started with the government promoting increased production and consumption of animal products since the 19th century, to provide the population with a protein rich diet, which contributed to the cultural embedding of meat consumption in the Dutch diet. At the same time, the profits of livestock production for export stimulated innovation, particularly in terms of breeding, feeding and housing systems. Since 1960, the production of animal products in the Netherlands vastly increased, while the number of farms and farmers decreased, indicating high productivity (Figures 1,2). In addition, where traditional farms produced both crops and animals, nowadays most farms are specialized in one form of production (WRR, 2014). The number of poultry, cattle and pigs remains approximately at the same level since 1980, while the number of goats dramatically increased in this period (Figure 3).

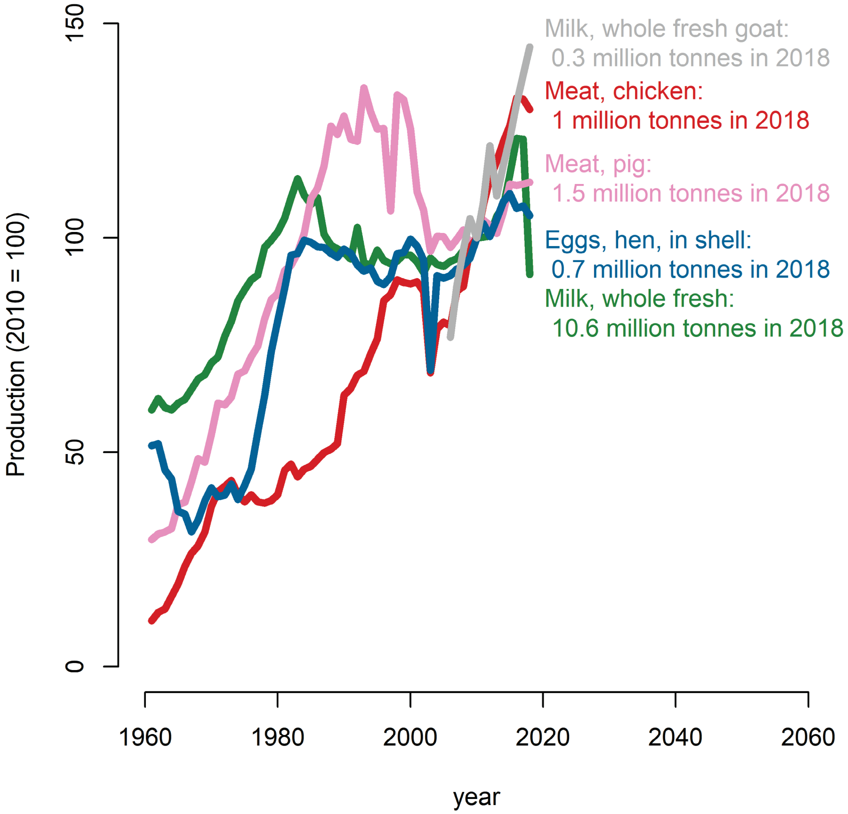


Figure 1. Trend in total production of animal products in the Netherlands since 1960. Source: Faostat.

In the past half century, the increasing productivity and specialization in the livestock sector, and in other sectors, was accompanied by increasing concerns about the environment, human health and other issues, such as animal welfare. Environmental concerns are characterized by key publications such as *Silent Spring,* on the adverse effects of indiscriminate pesticide use (Carson, 2002); *the limits to growth,* warning for inevitable societal challenges with increasing population growth and resource use (Meadows et al., 1972); the Brundtland report, calling for sustainable development (Brundtland, 1987); the Dutch report *Zorgen voor morgen* and subsequent National Environmental Outlooks to advice environmental policy in the Netherlands (Langeweg, 1988); and a series of IPCC reports reporting "scientific, technical and socio-economic information relevant to understanding the scientific basis of risk of humaninduced climate change, its potential impacts and options for adaptation and mitigation" (IPCC, 2013). In addition, in the past half century technology to measure and manage a wide range of pollutants vastly increased, along with efforts to for example reduce air pollution, regulate the use of chemicals, and improve water quality (European Commission, 2000; European Commission, 2006; European Commission, 2008; Lebret, 2015). Furthermore, many diseases that emerged in the past decades, such as human immunodeficiency virus 1 (HIV-1), bovine spongiform encephalopathy (BSE), severe acute respiratory syndrome (SARS), novel influenza viruses and possibly the recent SARS coronavirus 2, can be traced to human consumption of meat of wild and kept animals or other contact with animals (Andersen et al., 2020; FAO, 2013; Jones et al., 2013; Rohr et al., 2019).

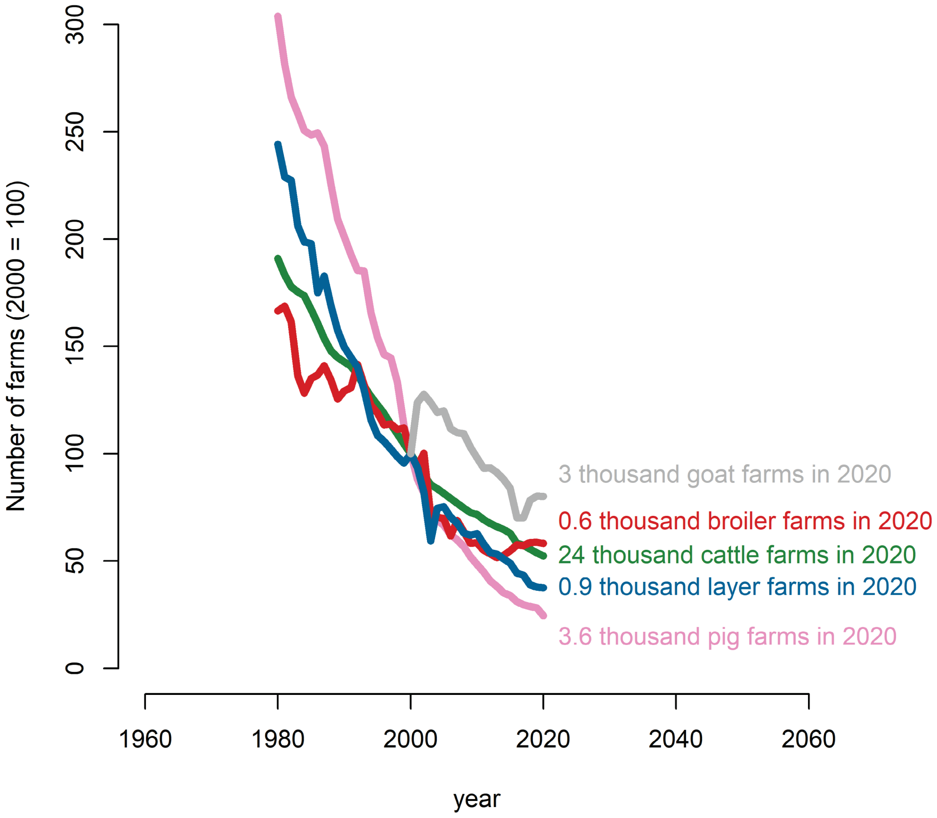


Figure 2. Trend in number of livestock farms in the Netherlands since 1980. Source: CBS Statline.

In the Netherlands, and other parts of Europe, the growth in production led to an excess production of dairy products and milk quota were established to control the production with a guaranteed price. Besides this excess in dairy products, excess in nutrients emissions, caused by the increasing use of artificial fertilizers and import of animal feed, led to European policy to regulate water quality levels, which translated in national production permits for pigs and poultry (van Grinsven et al., 2017; Willems and van Grinsven, 2011). At the same time, European and national regulations, as well as consumer concerns regarding animal welfare, resulted in changes in housing systems for poultry, pigs and veal calves (PBL, 2010; van Zeijts et al., 2007). The Dutch Q-fever epidemic of 2007-2010 may have further elicited public concerns on human health in relation to livestock farming.

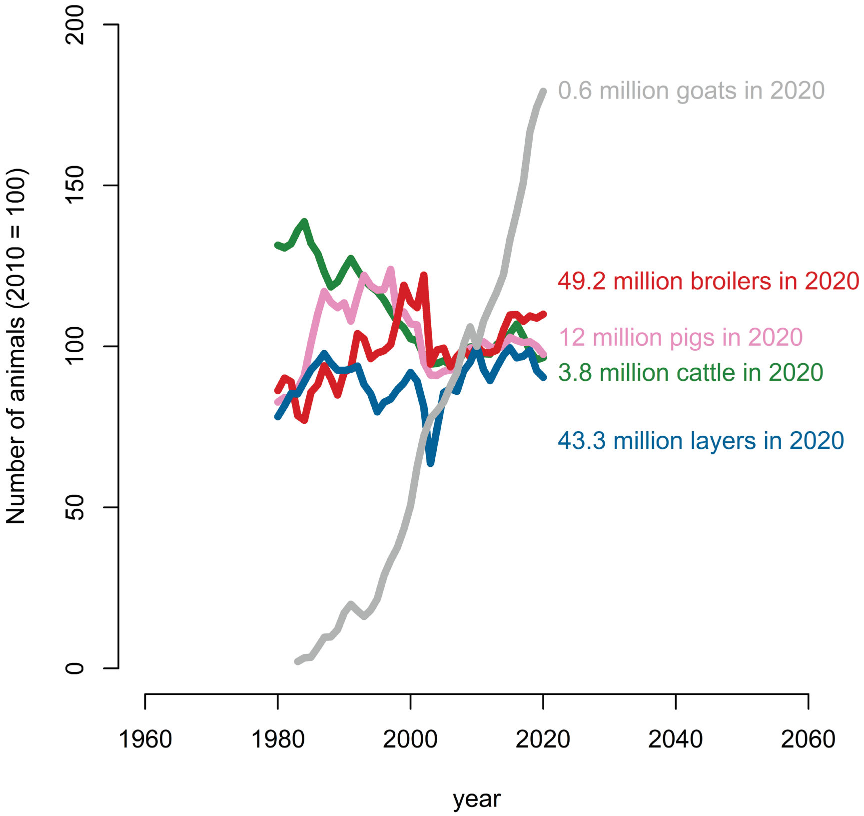


Figure 3. Trend in the total number of animals in the Netherlands since 1980. Source: CBS Statline.

Along with increasingly clear environmental effects, awareness grew that some societal problems require interdisciplinary research and integrated assessments, because these problems can be defined and analyzed in multiple adequate ways where single disciplines would only provide a limited perspective (Gough et al., 1998; Klein, 2004; Rittel and Webber, 1973; Rotmans and Van Asselt, 1996). These so-called “wicked problems” have no definitive or objective optimal solutions, they are unique but interconnect to other problems, and they are real-world problems that not allow for large-scale experimentation.

These characteristics are clearly applicable to developments in the livestock sector, where the historic increase in productivity in some cases conflicted with environmental, human health or other concerns, with no definitive or objective answer to what would be a desirable balance between these benefits and burdens. Even if burdens would have been valued more than benefits, a narrow focus on specific concerns could lead to undesirable trade-offs when attempting to solve those. An example of an unforeseen trade-off is the ban on battery cages for laying hens in order to promote animal welfare. The resulting shift in housing systems is thought to have led to increases in particulate matter emissions, nitrogen emissions and carbon emissions (Dekker et al., 2011; Takai et al., 1998; Winkel et al., 2016).

The importance of interdisciplinary and integrated approaches is now widely recognized, as for example illustrated in the One Health concept, focusing on the intersection between human health, animal health and ecosystem health (Gibbs, 2014; Zinsstag et al., 2011), and in the water-energy-food nexus research field (Hoff, 2011; Leck et al., 2015). Yet even in the context of these intersections bridging existing silo structures proves difficult (Giampietro, 2018; Manlove et al., 2016).

Aim

Given the multi-facetted nature of many societal problems, there is a general need for learning about integrated approaches and improving interdisciplinary cooperation. The multiple concerns of livestock production is one area in which such approaches are required, to describe, understand, and eventually manage the concerns. Such integration involves many disciplines, with hence a multitude of disciplinary concepts, models, practices and types and amounts of data. This thesis is such an interdisciplinary effort, yet with a focus on a limited number of disciplines, in order to make the effort manageable. The focus is on human health and the environment, which already entails a diverse set of concerns, disciplines and information, and can provide lessons for future integrative attempts. As a case study, the thesis focuses on the livestock sector in the Netherlands, because its high density of both humans and animals, as well as the vast changes in productivity shown in Figures 1-3, makes that several human health and environmental impacts co-occur. The overall aim underlying the work in this thesis is hence to integrally assess the effects of Dutch livestock production on human health and environment. The outcomes of this may serve as input in the societal dialogue about the future of animal production in the Netherlands.

Tools for integration

Two main tools have been used that help the integration in this thesis. These are the definition of system boundaries and the use of the *Drivers-Pressures-States-Impacts-Responses* framework. Both are depicted in Figure 4.

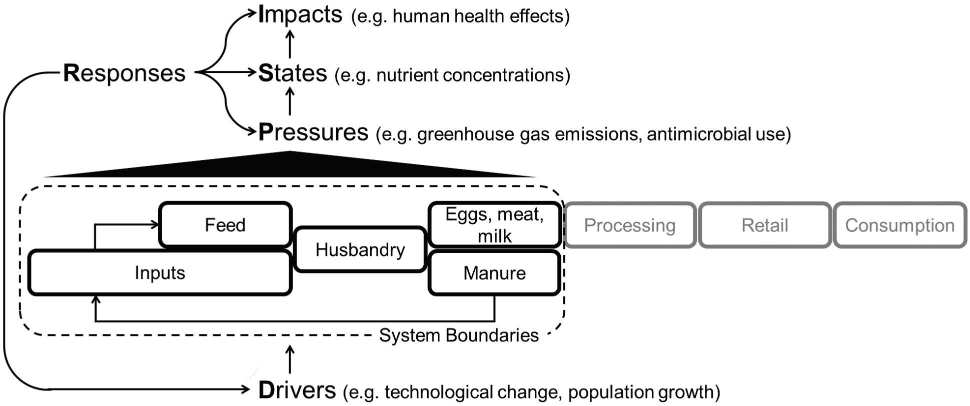


Figure 4. Schematic overview of livestock production chain, system boundaries, and related *Drivers, Pressures, States, Impacts and Responses*.

The system boundaries illustrated in Figure 4 show that this thesis focuses on human health and environmental impacts related to livestock production in the Netherlands, including feed production and production of other inputs, but excluding consumption of animal products. Distinguishing between such production and consumption by Dutch consumers is important because the Dutch diet not only includes imported livestock products but livestock products produced in the Netherlands are also exported, with more pork, poultry, veal and eggs exported than are domestically consumed (Product

Board Poultry & Eggs and Product Board Livestock & Meat, 2013). This means that the livestock products produced in the Netherlands are only for a part consumed by Dutch consumers. Earlier assessment at RIVM took such consumption effects into account, including diet-related health effects and foodborne diseases (Ocké et al., 2017). The focus here is on human health effects related to environmental and for a small part occupational exposure related to livestock production.

The *Drivers-Pressures-States-Impacts-Responses* framework (EEA, 2005; Smeets and Weterings, 1999; Thomas, 1995) has been used as a relational framework that helps to characterize the indicators that have been used to assess human health and environmental impacts. In the DPSIR chain, the *Impacts* expresses the actual impact, i.e. how human health or ecosystems are affected, while *States* (e.g. nutrient concentrations) or *Pressures* (e.g. greenhouse gas emissions) give a more indirect indication of impact (Figure 4). *Drivers* can refer to both the livestock production itself and the (societal) forces that influence livestock production. *Responses* to reduce the impact can be targeted at all elements in the DPSIR chain.

Outline

The body of this thesis consists of an integrated assessment of the current impacts, two specific more in-depth studies on health effects of persons living close to livestock farms, and an *ex ante* integrated assessment of expected future developments towards the policy ambition of a circular livestock production. **Chapter 2** focusses on current livestock production in the Netherlands and provides insights in the broad variety of related human health and environmental impacts, by for a large part quantitatively assessing effects on 17 different impact categories related to the total livestock production of the Netherlands. The third and fourth chapter zoom in on the effects of living in the vicinity of livestock farms on pneumonia, asthma and Chronic Obstructive Pulmonary Disease (COPD), which is one of the impact categories distinguished in chapter 2. **Chapter 3** addresses the risk of pneumonia in relation to living close to goat and poultry farms, by analyzing General-Practitioner data on over 90,000 persons living in the south-east of the Netherlands. **Chapter 4** concerns the apparently decreased risk of asthma and/or COPD among persons living close to livestock farms, by analyzing data on medication dispenses for asthma and COPD that covers the entire Netherlands. Adding to these assessments of current effects, **chapter 5** contains an integrated assessment of future changes in livestock farming practices in the context of the policy ambition of a transition towards circular farming. The expected effects of these changes on human health and environmental impacts were assessed by experts. In the general discussion (**chapter 6**) the main results of chapter 2 to 5 are discussed as well as overarching findings and their contribution to a societal dialogue about the future of animal production in the Netherlands.

References

Andersen K.G., Rambaut A., Lipkin W.I., Holmes E.C., Garry R.F., 2020. The proximal origin of SARS-CoV-2. Nat. Med. 26, 450-452. https://doi.org/10.1038/s41591-020-0820-9.

Brundtland G.H., 1987. Our common future—Call for action. Environmental Conservation. 14, 291-294.

Carson R., 2002. Silent spring. Houghton Mifflin Harcourt.

de Bakker E., Dagevos H., 2010. Vleesminnaars, vleesminderaars en vleesmijders: Duurzame eiwitconsumptie in een carnivore eetcultuur [Meat lovers, meat lessers and meat avoiders: Sustainable protein consumption in a carnivorous food culture]. 2010-003. LEI, Den Haag.

de Bakker E., Dagevos H., 2012. Reducing Meat Consumption in Today's Consumer Society: Questioning the Citizen-Consumer Gap. Journal of Agricultural and Environmental Ethics. 25, 877-894. https://doi.org/10.1007/s10806-011-9345-z.

Dekker S.E.M., de Boer I.J.M., Vermeij I., Aarnink A.J.A., Groot Koerkamp P.W.G., 2011. Ecological and economic evaluation of Dutch egg production systems. Livest. Sci. 139, 109-121. https://doi.org/10.1016/j.livsci.2011.03.011.

Dolman M., Jukema G., Ramaekers P., 2019. De Nederlandse landbouwexport 2018 in breder perspectief [The Dutch agricultural export 2018 in broader perspective]. Wageningen Economic Research, Den Haag.

EEA, 2005. The European environment: state and outlook 2005. Office for Official Publications of the European Communities, Copenhagen.

European Commission, 2000. Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy. L 327. Official Journal of the European Communities

European Commission, 2006. REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC L 396. Official Journal of the European Union.

European Commission, 2008. Directive 2008/50/EC of the European Parliament and of the Council of 21 May 2008 on ambient air quality and cleaner air for Europe. L 152. Official Journal of the European Union.

FAO, 2013. World Livestock 2013- changing disease landscapes. Food and Agriculture Organization of the United Nations (FAO), Rome.

Giampietro M., 2018. Perception and representation of the resource nexus at the interface between society and the natural environment. Sustainability. 10, 2545. https://doi.org/10.3390/su10072545.

Gibbs E.P., 2014. The evolution of One Health: a decade of progress and challenges for the future. The Veterinary record. 174, 85-91. https://doi.org/10.1136/vr.g143 [doi].

Gough C., Castells N., Funtowicz S., 1998. Integrated Assessment: an emerging methodology for complex issues. Environmental Modeling & Assessment. 3, 19-29. https://doi.org/10.1023/A:1019042201713.

Hoff H., 2011. Understanding the Nexus. Background paper for the Bonn2011 Nexus conference: The Water, Energy and Food Security Nexus.

IPCC, 2013. Principles governing IPCC work. https://www.ipcc.ch/site/assets/uploads/2018/09/ipcc-principles.pdf (accessed 06/12 2020).

Jones B.A., Grace D., Kock R., Alonso S., Rushton J., Said M.Y., et al., 2013. Zoonosis emergence linked to agricultural intensification and environmental change. Proceedings of the National Academy of Sciences of the United States of America. 110, 8399-8404. https://doi.org/10.1073/pnas.1208059110.

Klein J.T., 2004. Interdisciplinarity and complexity: An evolving relationship. E:CO. 6, 2-10.

Langeweg F., 1988. Zorgen voor morgen. Nationale milieuverkenning 1985-2010 [Concern for tomorrow. National environmental outlook 1985-2010]. RIVM (National Institute for Public Health and the Environment), Bilthoven.

Lebret E., 2015. Integrated Environmental Health Impact Assessment for Risk Governance Purposes; Across What Do We Integrate? International journal of environmental research public health. 13, 71. https://doi.org/10.3390/ijerph13010071.

Leck H., Conway D., Bradshaw M., Rees J., 2015. Tracing the water–energy–food nexus: Description, theory and practice. Geography Compass. 9, 445-460. https://doi.org/10.1111/gec3.12222.

Manlove K.R., Walker J.G., Craft M.E., Huyvaert K.P., Joseph M.B., Miller R.S., et al., 2016. “One Health” or three? Publication silos among the One Health disciplines. PLoS Biology. 14, e1002448. https://doi.org/10.1371/journal.pbio.1002448.

Meadows D.H., Meadows D.L., Randers J., Behrens W.W., 1972. The limits to growth. New York. 102, 27.

Ocké M., Toxopeus I., Geurts M., Mengelers M., Temme E., Hoeymans N., 2017. Wat ligt er op ons bord? [What is on our plate?]. 24. RIVM (National Institute for Public Health and the Envrionment), Bilthoven.

PBL, 2010. Op weg naar een duurzame veehouderij: Ontwikkelingen tussen 2000 en 2010 [Towards sustainable livestock farming: Developments between 2000 and 2010]. 500139004. Planbureau voor de Leefomgeving (Netherlands Environmental Assessment Agency), Den Haag/Bilthoven.

Product Board Poultry & Eggs, Product Board Livestock & Meat, 2013. Vee, vlees en eieren in Nederland: Kengetallen 2012 [Livestock, meat and eggs in the Netherlands: Key figures 2012]. Productschap Pluimvee & Eieren (Product Board Poultry & Eggs) and Productschap Vee & Vlees (Product Board Livestock & Meat), Zoetermeer.

Rittel H.W., Webber M.M., 1973. Dilemmas in a general theory of planning. Policy sciences. 4, 155-169. https://doi.org/10.1007/BF01405730.

Rohr J.R., Barrett C.B., Civitello D.J., Craft M.E., Delius B., DeLeo G.A., et al., 2019. Emerging human infectious diseases and the links to global food production. Nature Sustainability. 2, 445-456. https://doi.org/10.1038/s41893-019-0293-3.

Rotmans J., Van Asselt M., 1996. Integrated assessment: A growing child on its way to maturity. Climatic Change. 34, 327-336. https://doi.org/10.1007/BF00139296.

Smeets E., Weterings R., 1999. Environmental indicators: Typology and overview. European Environment Agency Copenhagen.

Takai H., Pedersen S., Johnsen J.O., Metz J.H.M., Koerkamp P.W.G.G., Uenk G.H., et al., 1998. Concentrations and emissions of airborne dust in livestock buildings in Northern Europe. J. Agric. Eng. Res. 70, 59-77. https://doi.org/10.1006/jaer.1997.0280.

Thomas R., 1995. A general strategy for integrated environmental assessment at the European Environment Agency. RIVM (National Institute for Public Health and the Envrionment), Bilthoven.

van Grinsven H., Bleeker A., van der Sluis S., van Schijndel M., van Dam J., Tiktak A., et al., 2017. Evaluatie Meststoffenwet 2016: syntheserapport [Evaluation Manure and Fertilisers Acts 2016: Synthesis Report]. PBL (Netherlands Environmental Assessment Agency), Den Haag.

van Zeijts H., van Eerdt M., van der Kolk J., Poot E., 2007. Duurzame ontwikkeling van de landbouw in cijfers en ambities: Veranderingen tussen 2001 en 2006 [Sustainable development of agriculture in numbers and ambitions: Changes between 2001 and 2006]. Milieu en Natuur Planbureau (Netherlands Environmental Assessment Agency), Bilthoven.

Willems J., van Grinsven H., 2011. Afschaffen van productierechten in de veehouderij in 2015: gevolgen voor veehouderij en leefomgeving [Abolition of production rights in livestock farming in 2015: consequences for livestock farming and the environment]. Planbureau voor de Leefomgeving (Netherlands Environmental Assessment Agency), Bilthoven.

Winkel A., van Riel J.W., van Emous R.A., Aarnink A.J., Groot Koerkamp P.W., Ogink N.W., 2016. Abatement of particulate matter emission from experimental aviary housings for laying hens by spraying rapeseed oil. Poultry science. 95, 2836-2848. https://doi.org/10.3382/ps/pew261

WRR, 2014. Naar een voedselbeleid [Towards a food policy]. Wetenschappelijke Raad voor het Regeringsbeleid [The Netherlands Scientific Council for Government Policy], Amsterdam.

Zinsstag J., Schelling E., Waltner-Toews D., Tanner M., 2011. From “one medicine” to “one health” and systemic approaches to health and well-being. Preventive veterinary medicine. 101, 148-156. https://doi.org/10.1016/j.prevetmed.2010.07.003.

Chapter 2

Effects of Dutch livestock production on human health and the environment

Pim M. Post[ab], Lenny Hogerwerf[a], Eddie A.M. Bokkers[c], Bert Baumann[a#], Paul Fischer[a#†], Susanna Rutledge-Jonker[a#], Henk Hilderink[a#], Anne Hollander[a#], Martine J.J. Hoogsteen[a#], Alex Liebman[de#], Marie-Josée J. Mangen[a#], Henk Jan Manuel[a#], Lapo Mughini-Gras[ab#], Ric van Poll[a#], Leo Posthuma[af#], Addo van Pul[a#], Michiel Rutgers[a#], Heike Schmitt[a#], Jim van Steenbergen[a#], Hendrika A.M. Sterk[a#], Anja Verschoor[a#], Wilco de Vries[a#], Robert G. Wallace[eg#], Roy Wichink Kruit[a#], Erik Lebret[ab], Imke J.M. de Boer[c]

[a] *National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands;*
[b] *Institute of Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, the Netherlands;*
[c] *Animal Production Systems group, Wageningen University & Research, Wageningen, the Netherlands;*
[d] *Department of Geography, Rutgers University, USA;*
[e] *Agroecology and Rural Economics Research Corps, St Paul, USA;*
[f] *Department of Environmental Science, Radboud University, Nijmegen, the Netherlands;*
[g] *Institute for Global Studies, University of Minnesota, Minneapolis, USA;*

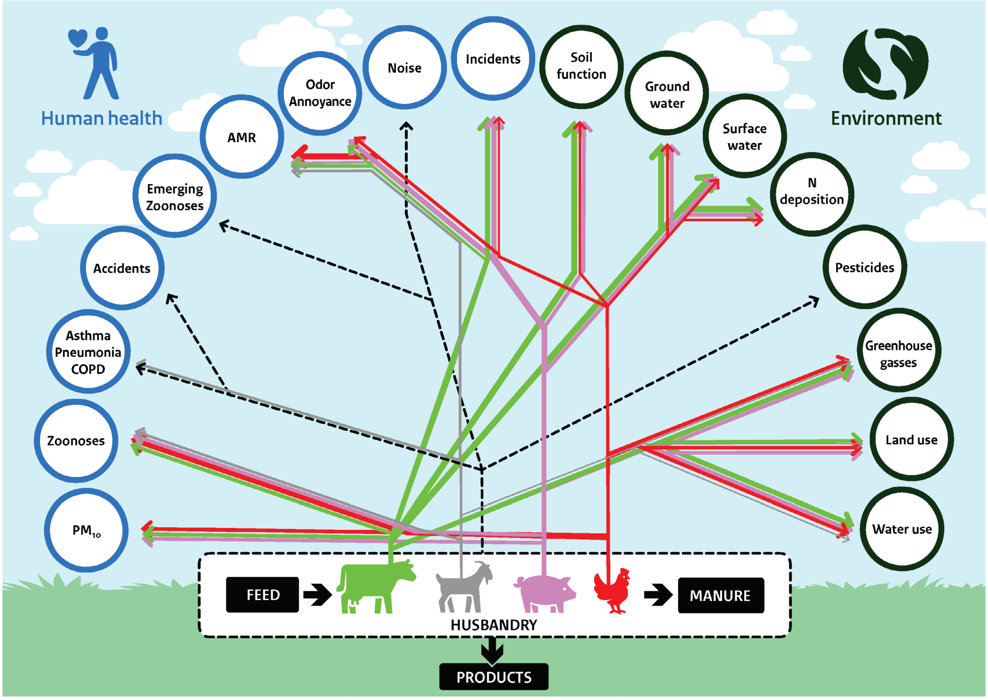
[#] *Alphabetic order*
[†] *Deceased March 17, 2020*

Published in *Science of the Total Environment* 737 (2020), 139702
DOI:10.1016/j.scitotenv.2020.139702

ABSTRACT

Observed multiple adverse effects of livestock production have led to increasing calls for more sustainable livestock production. Quantitative analysis of adverse effects, which can guide public debate and policy development in this area, is limited and generally scattered across environmental, human health, and other science domains. The aim of this study was to bring together and, where possible, quantify and aggregate the effects of national-scale livestock production on 17 impact categories, ranging from impacts of particulate matter, emerging infectious diseases and odor annoyance to airborne nitrogen deposition on terrestrial nature areas and greenhouse gas emissions. Effects were estimated and scaled to total Dutch livestock production, with system boundaries including feed production, manure management and transport, but excluding slaughtering, retail and consumption. Effects were expressed using eight indicators that directly express Impact in the sense of the Drivers-Pressures-State-Impact-Response framework, while the remaining 14 express Pressures or States. Results show that livestock production may contribute both positively and negatively to human health with a human disease burden (expressed in disability-adjusted life years) of up to 4% for three different health effects: those related to particulate matter, zoonoses, and occupational accidents. The contribution to environmental impact ranges from 2% for consumptive water use in the Netherlands to 95% for phosphorus transfer to soils, and extends beyond Dutch borders. While some aggregation across impact categories was possible, notably for burden of disease estimates, further aggregation of disparate indicators would require normative value judgement. Despite difficulty of aggregation, the assessment shows that impacts receive a different contribution of different animal sectors. While some of our results are country-specific, the overall approach is generic and can be adapted and tuned according to specific contexts and information needs in other regions, to allow informed decision making across a broad range of impact categories.

GRAPHICAL ABSTRACT



1 Introduction

Livestock production imposes several environmental and public health effects. At the global level, livestock production contributes to greenhouse gas emissions (Gerber et al., 2013; Herrero et al., 2011); overuse of finite resources such as land, water, and phosphorus (Herrero et al., 2015; Leip et al., 2015); the development of antimicrobial resistance (Chantziaras et al., 2014; Marshall and Levy, 2011; Silbergeld et al., 2008); and the threat of emerging diseases, such as pandemic influenza (FAO, 2013; Jones et al., 2013; WHO, 2017b). Locally, livestock production contributes to nutrient surpluses affecting soil and water quality (Oenema et al., 2007; Sutton et al., 2011); eco-toxicological effects of pesticide application (Nordborg et al., 2017); odor annoyance (Hooiveld et al., 2015); and human health effects from exposure to particulate matter, endotoxins and pathogens (Casey et al., 2015; Douglas et al., 2018; Smit and Heederik, 2017). In addition, there are safety concerns regarding occupational hazards associated with livestock production (Berkhout et al., 2015) and regarding explosions and biogas leaks in manure fermentation systems (Dutch safety board, 2014; Dutch safety board, 2016).

Many of these concerns are especially relevant in areas with large animal and human population densities, found in countries such as the Netherlands, Belgium, Denmark, France, Germany, the USA, and China (Robinson et al., 2011). The Netherlands (41.543 km^2 total area, including water bodies) was chosen as a case region with average densities of 14 goats, 93 cattle, 298 pigs and 2372 poultry per km^2 and of 414 persons per km^2 in 2018 (CBS, 2019a). Over the past decade the public debate about livestock production and consumption intensified in the Netherlands (Kraaij-Dirkzwager et al., 2017), with the globally recognized Q-fever epidemic of 2007-2010

Abbreviations
AMR = Antimicrobial Resistance
BoD = Burden of Disease
COPD = Chronic Obstructive Pulmonary Disease
DALY = Disability-Adjusted Life Year
$DDDA_{NAT}$ = Defined Daily Doses Animal, National
DPSIR = Drivers-Pressures-State-Impact-Response
EIU = Environmental Indicator Unit
ESBL= Extended Spectrum Beta-Lactamase
GHG = Greenhouse Gasses
NL = the Netherlands
PM = Particulate Matter
YLD = Years Lost due to Disability
YLL = Years of Life Lost

occurring in one of the country's most densely populated livestock areas (Roest et al., 2011). Public awareness appears also fueled by other infectious disease outbreaks, such as mad cow disease (BSE) in Europe in the early 1990s, classical swine fever in the Netherlands in 1997-1998, foot-and-mouth disease in the UK and in the Netherlands in 2001 and the global threat of avian influenza since the late 1990s (Mangen and Burrell, 2001; OIE, 2016). Other developments that may have sharpened the public debate include the Paris Agreement to tackle climate change (Klimaatberaad, 2019; United Nations, 2015a), and national policy programs to stop the decline in biodiversity such as the Integrated Approach to Nitrogen (PAS). The latter agreement was a national policy superimposed on the Dutch implementation of the European Habitat Directive and recently led to renewed debate about measures to cut emissions of nitrogen oxides and ammonia when the Dutch Council of State judged that the approach was not compliant with the European directive. The greater attention on sustainable livestock production in the Netherlands is reflected in the initiation of large studies on the human health effects related to living in the vicinity of livestock farms (Heederik and Yzermans, 2011; Maassen et al., 2016) and the formulation of 15 ambitions around a shift toward more sustainable livestock production by multiple Dutch governmental and non-governmental actors (Bos et al., 2017; UDV, 2013). More recently, several policy-oriented publications have called for a new, sustainable orientation to intensive animal husbandry (Ministry of Agriculture, 2018; RLI, 2018; SER, 2016; Vink and Boezeman, 2018).

The public debate on the future of livestock production systems could benefit from an evidence-based overview of the environmental and human health effects of livestock production. Knowledge about such effects, however, is scattered across research domains, and have so far been assessed together to only a limited extent (Aequator Groen en Ruimte et al., 2008; Boone and Dolman, 2010; Bos et al., 2017; Hu et al., 2017; Westhoek et al., 2011). A simultaneous rather than separate assessment of environmental and human health impacts may provide more thorough insight into the challenges that arise when responding to them. The importance of such an integrated approach becomes clear in the example of the historic ban on battery cages for laying hens, with the focus on animal welfare, but concurrent increases in particulate matter emissions, nitrogen emissions, and carbon emissions (Dekker et al., 2011; Takai et al., 1998; Winkel et al., 2016). Another example is the increase in the number of goat farms, which appears to have been driven by introduction of the European milk quotation system for dairy cattle farmers in 1984, as well as by the classical swine fever and foot-and-mouth disease outbreaks of the 1990s and earlier 2000s. The resulting 50-fold increase of goat farms between

1983 and 2009 in turn contributed to the Q-fever epidemic in the Netherlands between 2007 and 2010, mirroring situations in Bulgaria and Canada: an increase in dairy goat farming appears to have driven Q-fever outbreaks there as well (Hatchette et al., 2001; Roest et al., 2011). A broad assessment may thus offer insight into both the variety of responses that are required, and the possible unintended consequences and trade-offs of such responses in relation to other impacts.

The main aim of this study therefore was to assess the multiple human health and environmental impacts of Dutch livestock production, and assess differences between animal sectors.

2 Methods

2.1 General approach

We cover 17 different themes in the human health and environmental domains, associated with livestock production that we refer to as *impact categories*. The selected impact categories have been extensively studied, have been recognized as sources of particular concern by citizens, or are already subject of regular monitoring (Table 1). For each impact category, we selected one or a set of indicators, using the Driver-Pressure-State-Impact-Response (DPSIR) framework (EEA, 2005; Smeets and Weterings, 1999) as a useful conceptual 'Level 2 Relational framework' (Knol et al., 2010), with a focus on P-S-I indicators and preference for indicators representing an Impact (the D for Driving Force and R for Response from DPSIR are outside the scope of this study). The ability to link the indicator to livestock production was another important selection criterium for indicators. Other criteria that were adopted for selecting indicators, corresponding to guidelines for selecting and developing indicators (Corvalán et al., 1996; Harger and Meyer, 1996; Niemeijer and de Groot, 2008) were availability of data, interpretability, sensitivity to changes over time, validity with respect to the representation of the impact category, objectivity, and specificity. Each indicator provides a proxy or direct indication for the impact of the entire Dutch livestock production within a specific impact category and is quantitative where possible. When (data on) suitable Impact indicators were not available, selected indicators are a more indirect indication of Impact by expressing a Pressure (such as greenhouse gas emissions) or a State (such as nutrient concentration; Table 1). Such Pressure and State indicators were mostly used in the environmental domain, thereby in some cases relating both to ecosystem integrity and human health, whereas for the human health domain, mostly Impact indicators were used.

Table 1. Domains, impact categories and indicators for analysis of human health and environmental impacts of Dutch livestock production, representing impacts or proxies of impacts (according to the DPSIR causal chain).

Domain	#	Impact category	Indicator (unit)	PSI[a]
Human Health	1	Particulate Matter	Burden of disease (BoD[b]) related to particulate matter emissions from livestock production, expressed as disability-adjusted life years (DALY[c])	I
	2	Zoonoses	BoD related to livestock-related zoonoses transmitted through direct contact with livestock or through indirect transmission via the environment (DALY)	I
	3	Pneumonia, asthma and COPD[d]	BoD related to pneumonia, asthma and COPD among residents living in the vicinity of livestock farms (DALY)	I
	4	Accidents	BoD related to occupational accidents in the livestock sector (DALY)	I
	5	Emerging zoonotic disease risks	Impact and probability of an emerging zoonotic disease (descriptive)	I
	6	Antimicrobial resistance		
		a. ESBL/pAmpC source attribution	Persons carrying Beta-Lactamase-producing (ESBL/pAmpC) *E. coli* attributed to direct contact or environmental transmission from animal husbandry (%)	S
		b. Antimicrobial use	Use of antimicrobials in livestock (DDDA_{NAT}[e])	P
	7	Odor annoyance	Persons severely annoyed by odors from livestock production processes (%)	I
	8	Noise	Persons severely annoyed by noise from livestock production processes (%)	I
	9	Incidents manure fermentation systems	Buildings within a safety distance of 30 m from a manure fermentation system (number)	P
	10[f]	Nutrient-related impacts on soil functioning		
		a. Nitrogen transfer	Transfer of nitrogen to soil related to livestock production (tonnes per year)	P
		b. Phosphorus transfer	Transfer of phosphorus to soil related to livestock production (tonnes per year)	P
		c. Phosphorus saturation	Level of P saturation expressed as share of the P saturated area over the total available area for agriculture at the level of a farm or region (%).	S

Environment		d. Relative crop and grass production area	Percentage of area for crop production in total area for livestock feed production (%)	P
	11[f]	Nitrate pollution of groundwater	Average nitrate concentration in the shallow groundwater layer under agricultural land (mg/L as NO_3^- per region)	S
	12[f]	Surface water eutrophication		
		a. chemical water quality standard exceedance	Percentage of agricultural water bodies exceeding nutrient standards for N and P (%)	S
		b. biological water quality standard exceedance	Percentage of regional water bodies with insufficient biological water quality (in one of lowest 3/5 classes; %)	S
	13	Nitrogen deposition in terrestrial nature	Percentage of nature areas in which the critical loads are exceeded (% of surface area)	S
	14	Environmental impacts of pesticides application	Environmental impact related to pesticide use for livestock feed production in the Netherlands (Environmental Indicator Units: EIUs)	I
	15	Greenhouse gas emissions	Greenhouse gas emissions from production processes related to livestock production (kg CO_2-equivalents)	P
	16	Land use	Agricultural land use area required for livestock-feed production for livestock production (km^2)	P
	17	Water use	Blue water required for production processes related to livestock production (m^3)	P

[a]PSI: P = Pressure, S = State, I = Impact; [b]BoD: Burden of Disease; [c]DALY: Disability-Adjusted Life Year; [c]COPD: Chronic Obstructive Pulmonary Disease; [e]$DDDA_{NAT}$: Defined Daily Doses Animal, National; [f]overlap in impact

Aggregation and integration of different indicators were performed only to the extent that the resulting sets of indicators were still practical, meaningful and in line with the meaning in the relevant knowledge domains. To facilitate interpreting the indicator estimates, we compare them, where possible, to a value for comparison. These values for comparison are either the total impact related to all sources (*e.g.*, total burden of disease related to particulate matter emissions) or other sources of impact or data that provide a context for the estimate (*e.g.*, odor annoyance related to livestock production is compared to odor annoyance related to sewage systems).

To allow impact estimation, we defined system boundaries, which included feed production both within and outside the Netherlands, manure management and transport, but excluded slaughtering, retail, and consumption. Transboundary effects were assessed only for impact categories concerning resource use and for greenhouse-gas (GHG) emissions, for which data were sufficiently available. Data used to quantify indicators were retrieved directly from the literature or existing databases, or calculated specifically for this study. In principle, data from 2015 were used to quantify indicators. When data from 2015 were not available, data for years closest to 2015 were used. In the absence of suitable quantitative data, a qualitative, more narrative approach was adopted. Wherever possible and appropriate, estimates were derived across different animal categories, impact sources, diseases, or regions. The methods used to provide estimates for each indicator are described briefly below and in more detail in the Supplement (Supp1-17). The latter also includes a description of the main sources of uncertainty for each indicator.

2.2 Human health indicators

A common Impact indicator to express the burden of disease (BoD) from mortality and morbidity is the disability-adjusted life year (DALY). This metric consists of the total estimated years of life lost (YLL) due to premature death and the years of life lived with disability (YLD), calculated separately across diseases (Gold et al., 2002; Murray and Lopez, 1997; Murray et al., 2012). The DALY indicator was used in this study to express the BoD related to *particulate matter, zoonoses, pneumonia, asthma, COPD* and *accidents.*

The BoD associated with *particulate matter* emissions was estimated by first calculating the population-averaged exposure to livestock-related particulate matter (PM) based on an atmospheric dispersion model (Sauter et al., 2018). This particulate matter includes both a primary and a secondary fraction. Primary PM is dust emitted directly from animal production facilities and can affect nearby communities. Secondary PM originates from reactions of ammonia (NH_3), nitrogen oxides (NO_x) and sulfur dioxide (SO_2) in the atmosphere and can affect communities over greater distances. The numbers of deaths and cases of respiratory and cardiovascular diseases attributable to livestock-related PM_{10} exposure for five-year age-groups were estimated based on published relations between PM_{10} exposure and mortality and morbidity. From these numbers, the BoD expressed as DALYs was calculated, using age-group-specific life expectancy to calculate YLL and using YLD estimates per case for non-fatal diseases (Supp1). The BoD associated with livestock-related *zoonoses* (*i.e.,* infectious diseases infecting both animals and humans), was limited to those transmitted either by direct livestock animal contacts or indirect transmission via the environment. The associated BoD estimates, expressed as DALYs, were based on the total BoD estimates for all relevant pathogens from several data sources, and on the attributable fractions per animal and per transmission route, using expert elicitation (Supp2). These estimates do not include the potential future BoD of emerging zoonoses or incremental BoD due to antibiotic resistance. DALYs for *pneumonia, asthma, and COPD* due to living in close proximity to livestock farms were estimated using the same approach as for the BoD associated with particulate matter. These BoDs were estimated by first calculating the number of persons living within specific distances of livestock farms, and subsequently using odds-ratios from several studies to estimate attributive cases and calculating DALYs based on these cases (Supp3). The BoD associated with *accidents* involving persons working in the livestock sector was estimated based on the number of notified cases among employees, whereby distinguishing between fatal cases for estimating YLLs, and non-fatal cases with either permanent or non-permanent lesion for estimating YLDs. The BoD for employees was extrapolated to the total population of persons working in the livestock sector by assuming that the rate of accidents is similar among employers and employees (Supp4).

The DALY metric is not suitable for all impact categories selected here. For example, because they concern impacts that have a low probability of occurrence (less than once every few years), but a potentially high impact (e.g. a Q fever outbreak), or because the health effects involved are not considered as a diagnosable ‘disease’ per se in the medical community, e.g. carriership of antimicrobial resistance (from antibiotic use), hypertension (from noise exposures), or for odor annoyance. While in some cases, ‘translation’ to a DALY is in principle possible, the results would lose meaning to the public health community as well is to the societal and political debate. The potential Impact for *emerging zoonotic disease risk* is expressed in two separate metrics, i.e. the probability and the potential impact of an outbreak of a specific zoonotic disease. These have been determined based on expert judgement, in the context of several other potential future risks in the national security profile (Analistennetwerk Nationale Veiligheid, 2016; Supp5). The Impact of *antimicrobial use* in livestock production and the potential incremental BoD associated with antimicrobial resistant infection is currently hard to quantify. As an example, the attribution of Extended Spectrum Beta-Lactamases (ESBLs) to animal husbandry based on the results of the ESBLAT study (Mevius et al., 2018) and related work (Mughini-Gras et al., 2019) is presented here as State indicator, i.e. prevalence of carriership. In addition, the current use of antimicrobials in livestock is presented as a Pressure indicator (SDa, 2017; Veldman et al., 2016; Supp6). *Odor and noise annoyance* were expressed as Impact indicators in terms of the percentage of severely annoyed persons based on several surveys (Supp7, Supp8). The potential health Impact of *incidents with manure fermentation systems*, such as explosions and leaks of toxic gasses, was expressed as a Pressure indicator: the number of homes in the proximity of such systems (Supp9), which is generally used as a safety measure in the process of issuing building permits for such systems.

2.3 Environmental indicators

Some of the chosen environmental indicators only concern the impacts that occur within the Netherlands. Other indicators concern impacts that occur both in the Netherlands and abroad. We distinguish these here as national environmental indicators and global environmental indicators.

2.3.1 National environmental indicators

The effect of livestock production on national environmental impacts was specified for four environmental compartments: agricultural soils, groundwater, surface water and terrestrial nature. We distinguished four nutrient-related impact categories (Table 1: 10-13), and one impact category that addresses the effects of pesticides on groundwater and surface water compartments (Table 1: 14). The indicators used to quantify each impact category are presented below.

Four indicators were selected to quantify *nutrient-related impacts on soil functioning*, where soil functioning refers to the ability of soils to provide a range of soil functions, including primary production, carbon sequestration, nutrient retention, water retention and natural attenuation. The first two indicators are the total transfer of nitrogen and phosphorus to soils, related to livestock production. These Pressure indicators are derived from national nutrient budgets, as published by Statistics Netherlands (CBS, 2019b;

Supp10a,b), which include input of nutrients, in the form of artificial fertilizer and natural deposition, and outputs in the form of crop-harvest and flows of nutrients to the environment. These budgets contain information on several input sources and output fates, allowing the attribution of nutrient flows to soils and any subsequent flows to groundwater and surface waters (impact categories 11 and 12), to livestock production. The third indicator for *nutrient-related impacts on soil functioning* is the State of phosphorus saturation, based on soil measurements (CBS, 2008; Supp10c). The fourth is the percentage of maize land in the total area of feed production (maize + grass) reflecting a Pressure on the ability of soils to retain nutrients (Supp10d).

The second national environmental impact category is *nitrate pollution of groundwater* and is quantified as nitrate concentration in groundwater under agricultural fields (i.e. mg NO_3^-/L). This State indicator is quantified using measurements of water that leaches from the rootzone of a sample of representative farms in sandy soil, clay, loess, and peat regions in the Netherlands between 2012 and 2015 (Supp11). The percentage of farms at which the acceptable limit of50 mg NO_3^-/L (European Commission, 1991) is exceeded is presented. The contribution of livestock production to the nitrate concentration, relative to other contributing sources, could not be precisely determined based on readily available data, but to provide some insight in this contribution, estimates specifically for dairy farms are reported in addition to estimates for all (also non-livestock) farms (Supp11).

The third national environmental impact category describes the effects of nutrient transfers on *surface water eutrophication*, and is quantified using two State indicators. The first is the percentage of agricultural water bodies exceeding waterbody-specific water quality standards for nitrogen and phosphorus. The second is the percentage of regional water bodies exceeding ecological standards, based on samples taken in several representative water bodies (Klein and Rozemeijer, 2015; van Grinsven et al., 2017; Supp12). The contribution of livestock production to the percentage of agricultural water bodies exceeding water quality standards could not specifically be determined. The contribution of livestock production to the water quality of regional waters is determined based on a modelling study (Groenendijk et al., 2016; Supp 12).

Another national environmental impact category is the *nitrogen deposition on nature areas*, which entails direct nitrogen deposition from the air. Nitrogen deposition was determined using a combination of modelled data and measurements and was subsequently compared to critical loads (deposition loads below which no observable effects on biodiversity occur) to obtain exceedances of the critical loads (Supp13). To assess the contribution of livestock production to such deposition, we present model results of nitrogen deposition with and without emissions from animal husbandry.

A final national environmental impact category is the *environmental impacts of pesticide application* on maize and grass, which represent the most important agricultural land uses for livestock production in the Netherlands. The indicator used to quantify this Impact is Environmental Indicator Units, which indicate the pesticide concentrations in several environmental compartments relative to reference values; legal maximum permissible concentrations for chronic effects on water organisms for the surface water compartment, and a drinking water quality criterion for the groundwater compartment (Verschoor et al., 2019; Supp14).

2.3.2 Global environmental indicators

For the impact categories *greenhouse gas emissions*, *land use,* and *water use,* we were able to make a global estimate and a national estimate of Pressures. The global estimate concerns processes related to the entire life cycle, including, for example, production processes abroad for the production of livestock feed that is consumed by Dutch livestock. For this global estimate, we first determined the total amount of livestock products produced in the Netherlands using several data sources (Appendix of Supplement). Subsequently, we multiplied these production volumes with the greenhouse gas emissions, land use, and blue water use related to single products, derived from the Agri-footprint database (Duringer et al., 2017; Supp15-17). These estimates are complemented by national estimates, concerning greenhouse gas emissions, land use, and water use within the Netherlands. Estimates of livestock-related greenhouse gas emissions within the Netherlands were based on the National Emission Inventory (Coenen et al., 2018; Supp15). Estimates for land use in the Netherlands were based on agricultural land used for livestock feed production (Supp16). Estimates of water use for livestock production in the Netherlands were based on van der Meer (2018; Supp17).

3 Results

Estimates for all 17 impact categories (Table 1) are expressed in eight Impact, six State and eight Pressure indicators and presented in Tables 2-5. Where possible, these are broken down by different animal sectors and compared to values for comparison. We present a summary of the overall impact in the table, followed by an explanation for each impact category.

3.1 Burden of disease estimates

The four human health impacts that could be expressed in Impact indicators for burden of disease (BoD), i.e. in disability-adjusted life years (DALYs) are presented in Table 2 and include both estimated beneficial and adverse effects on human health. The beneficial effects pertain to asthma and COPD in association with living close to livestock farms. The specific mechanisms underlying these associations are not fully understood, yet a lower prevalence of atopic asthma and allergies has been frequently observed in children and adults that have lived in farming areas and finds some biological plausibility in the "hygiene-hypothesis" (Borlée et al., 2015; Ege et al., 2011; Kauffmann et al., 2002; Riedler et al., 2001; Smit et al., 2014; von Mutius, 2016; von Mutius and Vercelli, 2010). Although direct comparison is not straightforward due to methodological differences, under the current assumptions, the estimated beneficial effects appear similar in magnitude to the estimated burden from adverse effects.

Impact category 1: Particulate Matter

The population-averaged concentration of particulate matter that is smaller than 10 µm in diameter (PM_{10}) that can be attributed to Dutch livestock production was 0.75 µg/m^3 in 2015, which is about 4% of the total population-averaged PM_{10} concentration from all sources (Supp1). Exposure to PM causes premature mortality and several respiratory and cardiovascular diseases (Supp1). Assuming the same relation between morbidity and mortality of livestock-related PM, compared to other PM sources, leads to an estimated burden of disease of about 6,300 DALYs (Table 2). The main contributors to this BoD are primary PM emissions from poultry farms and secondary PM related to ammonia emissions from cattle farms, whereas primary PM emissions from cattle farms contribute relatively little (Table 2). The primary PM emissions lead to peak PM_{10} levels in the vicinity of poultry farms, as indicated by higher concentrations in livestock-dense provinces. The secondary PM_{10} fraction shows a more wide spread pattern contributing more equally to the exposure of the population across the Netherlands (Supp1).

Table 2. Point estimates of indicators for selected livestock-related human health impact categories that could be expressed in DALYs[a]

Impact category	Indicator[b]	Estimate[c]	Comparison[d]	Cattle[e]	S Rum[e]	Pigs[e]	Poultry[e]
1. Particulate Matter	Burden of disease (I)	6,300 DALYs per year	4% of total DALYs related to air pollution	31%		19%	30%
Primary[f]		*28 %*		*2%*		*5%*	*21%*
Secondary[f]		*72 %*		*30%*		*14%*	*9%*
2. Zoonoses	Burden of disease (I)	2,400 DALYs per year	4% of a total of 38 infectious diseases	23%	4%	20%	53%
3. Pneumonia, asthma and COPD	Burden of disease (I)	Pneumonia: 300 DALYs per year	1 % of total LRI[h] DALYs		100%		
		COPD: -10,000 DALYs per year[g]	5% of total COPD DALYs	*Not attributed*			
		Asthma: -600 DALYs per year[g]	2% of total asthma DALYs				
		COPD exacerbations: 1,500 DALYs per year					
4. Accidents	Burden of disease (I)	300 DALYs per year	4% of total occupational accident DALYs	*No data available*			

a. A more comprehensive description of indicators can be found in Table 1 and more information on their calculation and sources of uncertainty are presented in the Supplement.

b. A more comprehensive description of the indicator can be found in Table 1 and in the Supplement; I refers to Impact indicator.

c. Trailing zeros do not represent significant numbers; hence DALY estimates have either 1 or 2 significant numbers.

d. Value for comparison to provide context for the estimate in the light of other sources of impact or other comparisons, see text and Supplement for background.

e. S Rum= Small Ruminants; When contributions of animal sectors do not add up to 100%, part of the impact cannot be attributed to a specific animal sector (see Supplement). Cattle includes dairy cattle and beef cattle. Poultry includes laying hens, broilers, and other poultry.
f. Primary particulate matter is directly emitted from livestock farms. Secondary particulate matter originates from reactions of substances in the atmosphere, i.e. from ammonia emissions originating from livestock farms (see Supplement).
g. A negative burden represents a beneficial effect
h. Lower Respiratory tract Infections

Impact category 2: Zoonoses

The BoD related to direct animal contact and indirect transmission via the environment is estimated at 2,400 DALYs in 2016 (Table 2; Supp2). This is about 4% of the total burden of 38 communicable diseases (including Influenza and i. pneumococcal disease) in the Netherlands and about 36% of the total BoD of the considered zoonoses, which are for a large part transmitted via the food-transmission route, which are outside our specified system boundaries (Supp2). The highest contributions to this BoD come from poultry (53%) and cattle (23%, Table 2) and can be largely attributed to *Campylobacter* spp. The contribution of pigs (20%, Table 2) is mainly attributed to Hepatitis E virus and non-typhoidal *Salmonella* spp. (Supp2).

Impact category 3: Pneumonia, asthma and COPD

Recent studies have shown an increased risk of pneumonia among residents living within up to 2000 m from goat farms (Freidl et al., 2017; Kalkowska et al., 2018; Post et al., 2019). In addition, a decreased prevalence of asthma and COPD has been reported among residents living within 500 m of livestock farms (Borlée et al., 2015; Smit et al., 2014). At the same time, among the persons that do live in the vicinity of livestock farms and do have COPD, disease exacerbation is thought to be more frequent (Borlée et al., 2015; van Dijk et al., 2016). Mechanisms underlying most of these associations are only limitedly understood, yet if associations would be causal, the number of persons affected could be high as about 87% of Dutch residents lives within 2000 m and about 21% within 500 m from a livestock farm (Figure 1; Supp3). Under the assumption of causality, disease burden due to pneumonia and the increased burden of exacerbations are weighted against fewer COPD and asthma cases, and hence the overall health effect would be beneficial, and would equal about 9,000 DALYs (Table 2).

Impact category 4: Accidents

Occupational accidents in the livestock sector are estimated to account for 280 DALYs per year (average over 1999-2013), which can mainly be attributed to lethal accidents (Supp4). This is about 4% of the total burden of occupational accidents in the Netherlands (Table 2; Supp4). The average number of accidents in the agricultural sector is 85 per 100.000 work years, which makes agriculture the sector with the third most frequent accidents and is higher than the average of 28 per 100.000 work years (Inspectie SZW, 2018). The estimate cannot be further specified to the level of animal sectors based on the available data.

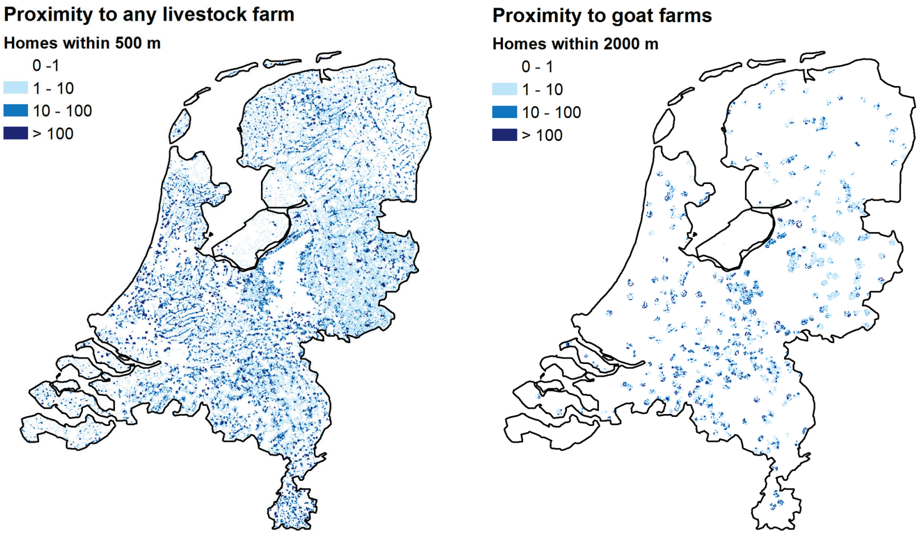


Figure 1. Proximity to farm-types distinguished in the burden of disease calculation for pneumonia, asthma and COPD, the Netherlands, 2015, for homes within 500 m from any livestock farm and within 2000 m from goat farms.

3.2 Other human health impacts

The estimates for five human health impact categories for which the Impact could not be expressed in DALYs are presented in Table 3. For these impact categories, BoD estimates are not appropriate, e.g. because of ‘low probability of occurrence with uncertain impact’, or because the effect on health is not considered a ‘disease’ per se. The estimates include (1) a somewhat probable emerging infectious disease outbreak with a severe impact; (2) an attribution of ESBL/pAmpc antimicrobial resistance to livestock farming of about 6% and markers of use of antimicrobials in livestock that has reduced in all animal sectors since 2009; (3) a percentage of Dutch inhabitants severely annoyed by odors from livestock production processes of <2.5%; (4) an unknown percentage of persons severely annoyed by noise related to livestock production processes; (5) and 100 homes within 30 m of a manure fermentation system.

Table 3. Point estimates of indicators for selected livestock-related human health impact categories for which the impact could not be expressed in DALYs[a]

Impact category	Indicator[b]	Estimate	Comparison[c]	Cattle[d]	S Rum[d]	Pigs[d]	Poultry[d]
5. Emerging zoonoses	Probability	Somewhat probable	0.5-5% probable, no actual indications; imaginable	*No attribution possible*			
	Potential impact (I)	Severe	Several hundreds of deaths, more than 4000 severe illnesses				
6. Antimicrobial resistance							
a. ESBL attribution	Persons with livestock-attributable ESBL/pAmpCs (S)	6% of 5% ESBL/pAmpC carriers	Person to person: 67% Foodborne: 19%	27%	4%	7%	61%
b. Antimicrobial use	Use of antimicrobials in livestock (P)	Broilers: 9.4 DDDA_{NAT} in 2015 Pigs: 8.7 DDDA_{NAT} in 2015 Dairy cattle: 3.1 DDDA_{NAT} in 2015 Veal calves: 20.1 DDDA_{NAT} in 2015	27.4 DDDA_{NAT} reduction since 2009 11.8 DDDA_{NAT} reduction since 2009 2.7 DDDA_{NAT} reduction since 2009 13.7 DDDA_{NAT} reduction since 2009[e]				

7. Odor annoyance	Percentage of persons reporting severe annoyance (I)	< 2.5% of all Dutch inhabitants and up to 8% in some municipalities in the south-east of the Netherlands	Industry: 1.3% Sewage: 2.4%	20%	?	80%	40%
8. Noise	Percentage of persons reporting severe annoyance (I)	*Unknown*	Road traffic: 9.3% Air planes: 2.6%	*No data available*			
9. Incidents manure fermentation systems	Homes within 30 m (P)	100 homes	*Not applicable*	40%[f]		55%[f]	1% [f]

---

a. A more comprehensive description of indicators can be found in Table 1 and more information on their calculation and sources of uncertainty are presented in the Supplement.

b. A more comprehensive description of the indicator can be found in Table 1 and in the Supplement; P, S and I respectively refer to Pressure, State and Impact indicators.

c. Value for comparison to provide context for the estimate in the light of other sources of impact or other comparisons (see text and Supplement for background).

d. S Rum = Small ruminants. When contributions of animal sectors do not add up to 100%, part of the impact cannot be attributed to a specific animal sector (see Supplement). Cattle includes dairy cattle and beef cattle. Poultry includes laying hens, broilers and other poultry.

e. Decrease in antimicrobial use between 2009 and 2014 led to a decrease of 8-79% of AMR in animals, indirectly leading to less human resistance, particularly in farmers (see text and Supplement).

f. Based on contribution to manure processed in manure fermentation systems (see Supplement).

Impact category 5: Emerging zoonotic disease risk

Besides zoonoses that are currently seen (described above), new zoonoses may emerge and existing zoonoses may flare up (re-emerge) when pathogens appear in a new host, evolve novel traits or settle in a new area (Engering et al., 2013). An example of such a re-emerging zoonosis is Q-fever, which was low-endemic in the Netherlands for a long period (20 cases reported/annum) before it caused a major epidemic among persons living up to 5 km from goat farms (De Rooij et al., 2019; van der Hoek et al., 2011), resulting in >4000 notified cases in 2007-2010 and 95 officially estimated deaths as of 2019. Although factors contributing to emerging zoonoses, such as the increase in farm animal populations, have been identified (Engering et al., 2013; Liverani et al., 2013; Mori and Roest, 2018), predicting or modelling zoonosis emergence remains difficult.

Despite the difficulties inherent in predicting emerging zoonotic disease outbreaks, a qualitative indication of emerging zoonotic disease risk has been provided in the national security profile of the Netherlands (Analistennetwerk Nationale Veiligheid, 2016), in which potential national disasters, crises, or threats are identified, and their probability and impact are described in qualitative terms. An example is avian influenza, of which the occurrence of an outbreak in the next 5 years has been judged as somewhat probable and the impact as severe, leading to severe infections and deaths, entailing costs and affecting the accessibility of certain areas, daily life and the societal debate (Table 3; Supp5; Analistennetwerk Nationale Veiligheid, 2016). However, inferring from such example the pressure of different animal sectors on zoonotic disease emergence is impossible. Better insight into factors driving pathogen emergence and disease-specific knowledge such as the reservoir, pathogen prevalence and traits, and human exposure and internal barriers is required (Engering et al., 2013; Plowright et al., 2017).

Impact category 6: Antimicrobial resistance

There is increasing evidence for an association between antibiotic use in livestock and antimicrobial resistance (AMR) in humans (Supp6), even as the attribution of AMR in humans to different sources, such as proximity to or contact with farm animals, is methodologically very challenging. According to recent estimates based on an extensive national project, about 6% of the carriage of Extended Spectrum Beta-Lactamase (ESBL) and plasmid-encoded AmpC (pAmpC)-producing *E. coli* in humans can be attributed to non-foodborne transmission from farm animal and environmental reservoirs, most of which can be attributed to poultry and cattle as a whole (Table 3; Mughini-Gras et al., 2019). In contrast, 19% is attributable to food-borne transmission and 67% to person-to-person transmission (Mughini-Gras et al., 2019). For other types of antimicrobial resistance such attribution has not been made but an indication of the link between, for example, Methicillin-resistant *Staphylococcus aureus* (MRSA) and livestock is that 28% surveillance samples in 2015 were of a livestock-associated strain (Veldman et al., 2016). Besides complicating the treatment of human infections, this carriage of resistant microorganisms has additional consequences, such as the requirement of isolation nursing in Dutch hospitals of farmers with a high likelihood of carrying antimicrobial resistant microorganisms (Werkgroep Infectiepreventie, 2012).

Compared to the recent source-attribution effort indicating the State of antimicrobial resistance, the use of various antimicrobials is as Pressure indicator more indirectly related to human health effects, but it does give an indication of a wider spectrum of resistance patterns and it becomes increasingly clear that reducing antimicrobial use leads to a decrease in microbial resistance against antibiotics in animals (Dorado-García et al., 2016; Tang et al., 2017). For example, in the Netherlands between 2009 and 2017, antimicrobial use declined in broilers from 36.8 defined daily dosages per animalyear ($DDDA_{NAT}$) to 9.4, in pigs from 20.5 to 8.7 $DDDA_{NAT}$, in veal calves from 33.8 to 20.1 $DDDA_{NAT}$ and from 5.8 to 3.1 $DDDA_{NAT}$, in dairy cattle (Table 3; Supp6). The reduction between 2009 and 2014 seems to have led to a reduction in antimicrobial resistance in animals ranging from 8% in broilers to 79% in dairy cattle (Dorado-García et al., 2016).

Impact category 7: Odor annoyance

In 2016, the percentage of the Dutch population that is severely annoyed by odors from agricultural activities was estimated to be 2.5% (Table 3; Supp7), and is assumed to relate mainly to livestock production processes. This percentage is comparable to annoyance related to sewage systems (2.4%), lower than the percentage of persons severely annoyed by odors from barbeques and recreational open fires (4.4%) or fireplaces (3.9%), but higher than the percentage of persons severely annoyed by odors from industry (1.3%) or restaurants (1.1%) (Poll et al., 2018; Supp7). The percentage reporting severe annoyance related to agricultural activities differed across regions, with the highest percentage (4.8%) in the north and the lowest percentage (1.7%) in the west. In the south, which has several livestock dense areas, the percentage of severe annoyance related to all agricultural activities is about 3.1%, while the odor annoyance specifically related to animal housing in the livestock-dense regions in the south, according to a different survey, is estimated to be about 2%, but in certain municipalities up to 8% (Supp7). Odor annoyance is thought to mainly relate to pig farms and much less to cattle farms (Table 3; Supp7).

Impact category 8: Noise

Noise annoyance related to livestock production processes is mainly associated with the transport of animals, feed and manure. Traffic in general is also the main source of noise annoyance in the Netherlands, with about 9.3% of the population reporting severe annoyance with road traffic. Annoyance is lower for main roads (2.5% for a maximum speed of 80 km/h) than for roads with lower speed limits (4.1% for roads with a maximum speed of 30 km/h, 5.6% for a maximum speed of 50 km/h) (Poll et al., 2018; Supp8). No data is available for noise related to traffic specifically due to livestock production processes, nor can differences between animal sectors be inferred, but differences are expected, since between sectors there are large differences in the frequency of animal replacement, milk collection (dairy farms only), deliveries and manure removal.

Impact category 9: Incidents manure fermentation systems

Manure fermentation systems, which convert manure to biogas and re-usable digestate, may pose a risk of gas leaks or explosions, potentially affecting the health of persons living near these systems. Two recent local incidents exemplary of the risk were the release of flammable and toxic biogas, in 2014, which could have but did not cause accidents; and the death of three persons performing cleaning in a manure fermentation system in 2013 (Dutch safety board, 2014; Dutch safety board, 2016). For explosion risk the safety target distance between manure fermentation systems and living areas is declared at 30 m by the Association of Netherlands Municipalities (VNG) as the competent authority for manure fermentation systems. In the Netherlands about 100 homes (mainly those of farmers exploiting the manure fermentation systems) are situated within this distance (Supp9). Legally, binding distances to vulnerable objects, such as homes, are only found for very large manure fermentation systems falling under the Seveso III directive (2012/18/EU). Most manure that is processed by manure fermentation systems comes from pigs (55%) and cattle (40%) (Table 3; Supp9).

3.3 National environmental impacts

Estimates of national environmental impact are presented in Table 4. Indicators describing the nutrient-related effects on soil, groundwater, and terrestrial nature indicate that livestock production contributes significantly to the Pressure of nitrogen and phosphorus transfers to the soil, and nitrogen deposition. The maximum acceptable nitrate concentration per L of upper groundwater, furthermore, is exceeded in most regions. Pesticides applied for the purpose of livestock production appear to have a relatively low Impact on the surface water ecosystem but the Impact of livestock-related pesticide application on drinking water quality are comparable to the average Impact on drinking water quality of pesticides use in the Netherlands.

Impact category 10: Nutrient-related impacts on soil functioning

Soil functioning is the ability of soils to provide a variety of functions, such as primary production, carbon sequestration, nutrient retention, water retention and natural attenuation. It is affected by several processes related to intensive agriculture, for example by soil compaction through the use of heavy machines, but also by a higher supply of nutrients than can be taken up by plants (Supp 10). The high supply of nutrients can be traced to Dutch livestock production via two overlapping routes. First, Dutch livestock produces manure containing nitrogen and phosphorus (497 million kg of nitrogen (N) and 79 million kg of phosphorus (P) in 2015)(CBS, 2019a), which is mainly applied to arable land and grasslands. Second, for the production of livestock feed, nutrients are applied. A large fraction is applied in the form of livestock manure and a smaller part in the form of artificial fertilizer. All nutrients in animal manure, and the part of other fertilizers that are used for the production of livestock feed, can thus be attributed to livestock production (Supp 10).

Table 4. Point estimates of indicators for selected livestock-related impact categories concerning national environmental impacts[a]

Impact category	Indicator[b]	Estimate	Comparison[c]	Cattle[d]	S Rum[d]	Pigs[d]	Poultry[d]
10. Nutrient-related impacts on soil functioning	Nitrogen transfer (P)	225×10^{6} kg N year^{-1}	66% of total N transfer	64%		20%	12%
	Phosphorus transfer (P)	7.8×10^{6} kg P year^{-1}	95% of total P transfer	57%		22%	15%
	Phosphorus saturation (S)	56%					
	Percentage crop-land (P)	30%	max. 20% for derogation[e]				
11. Nitrate pollution of groundwater	Average nitrate concentration (S)	Sand-region: 55 mg/L	47% exceedance of 50mg/L	*No attribution possible*			
		Clay-region: 20 mg/L	8% exceedance of 50mg/L				
		Loess-region: 69 mg/L	60% exceedance of 50mg/L				
		Peat-region: 8 mg/L	0% exceedance of 50mg/L				
12. Surface water eutrophication	Chemical water quality standard exceedance (S)	Sand-region: N 50-70%; P 38-54% Clay-region: N 43-58%; P 37-48% Peat-region: N 50-80%; P 58-92%		*No attribution possible*			
	Biological water quality standards exceedance (S)	95%					

13. Nitrogen deposition in terrestrial nature	Nature areas with excess nitrogen deposition (S)	45% of the surface area in all nature areas is exceeded due to livestock production	75% of the exceeded surface area of all nature areas	63%	21%	11%
14. Environmental impacts of pesticide application	Environmental Indicator Units (EIUs) (I)	Groundwater: 902 EIUs/ha Surface water: 0.9 EIUs/ha	104% of total EIUs/ha in agriculture 5% of total EIUs/ha in agriculture	*No attribution possible*		

a. A more comprehensive description of indicators can be found in Table 1 and more information on their calculation and sources of uncertainty are presented in the Supplement.

b. A more comprehensive description of the indicator can be found in Table 1 and in the Supplement; P, S and I respectively refer to Pressure, State and Impact indicators.

c. Value for comparison to provide context for the estimate in the light of other sources of impact or other comparisons, see text and Supplement for background.

d. S Rum = Small ruminants. When contributions of animal sectors do not add up to 100%, part of the impact cannot be attributed to a specific animal sector (see Supplement). Cattle includes dairy cattle and beef cattle. Poultry includes laying hens, broilers and other poultry.

e. The derogation allows farmers to apply more nitrogen in the form of ruminant manure than is normally allowed under the European Nitrates directive, if they fulfill certain requirements.

The fraction of nutrients not taken up by crops or emitted to air is considered to be transferred to soils, which is used here as a Pressure indicator of soil-functioning but is also a Pressure for run-off and leaching of nutrients into groundwater and surface water (impact categories 11 and 12). Transfers of 225 million kg of N (66% of total) and 7.8 million kg (95% of total) of P to soils may be attributed to livestock production in 2015 (Table 4), although total transfers of N (transfer in 2015 was 68% of transfer in 2000) and P (transfer in 2015 was 17% of transfer in 2000) are declining. For both nutrients, cattle contribute most (Table 4; Supp10). Approximately 56% of the soils to which the nutrients are transferred was found to be phosphate-saturated in 1992-1998, indicating the sensitivity of soils to such transfers (Supp10). Further, about 30% of the land use for feed production in the Netherlands consists of cropland, which is less able to sequester nutrients than grassland (Supp10). This percentage of cropland is higher than the maximum percentage allowed for deviating from the restriction on the amount of nitrogen that may be normally applied under the European Nitrates directive. This restriction is expanded if farmers have a minimum of 80% grassland (maximum 20% cropland) and fulfill several other criteria, such as measuring soil nutrient concentrations and drafting a fertilization plan.

Impact category 11: Nitrate pollution of groundwater

In addition to the unwanted impacts upon soil functioning, nitrogen in the soil, which is largely attributable to livestock production (Supp10), leaches to groundwater mainly in the form of nitrate (NO_3^-). In the Netherlands, the nitrate concentration in the upper groundwater varies among areas with different soil types, with on average 55 mg/L in the sandy soil region, 20 mg/L in the clay region, 69 mg/L in the loess-region and 8 mg/L in the peat region (Table 4; Supp11). In 2012-2015 this led to exceedance of the standard (50 mg nitrate/L) in 47% in the sandy soil region, 8% in the clay region, 60% of the farms in the loess region and none of the farms in the peat region (Table 4; Supp11). The exceedance of standards influences drinking water production and surface water quality. The percentage of farms with exceedance of the standard was different specifically on dairy farms (36% in the sandy soil region, 6% in the clay region, and 41% in the loess region). A precise contribution of livestock production to nitrate leaching, including leaching related to animal manure application on cropland and related to artificial fertilizer application for feed production, was not determined.

Impact category 12: Surface water eutrophication

Run-off and leaching of nutrients from soils and groundwater can increase nutrient concentrations in surface waters, contributing to eutrophication. Such eutrophication is indicated by the concentrations of nitrogen and phosphorus in agriculture-specific surface waters (N and P input dominated by agricultural sources), as well as by biological indicators in regional surface waters (as opposed to large, nationally governed waters). Nutrient concentrations in agriculture-specific surface water are expected to be largely attributable to livestock production as most of the nutrients applied to agricultural soils are attributable to livestock production (Supp 10). Between 2011 and 2014, nitrogen and phosphorus concentrations in such waters exceeded the nitrogen standard at about 50-65% of the measuring points in the sand region and in about 40-60% in the clay region, and exceeded the phosphorus standard at about 40-55% of the measuring points in the sand and clay regions (van Grinsven et al., 2017; Table 4; Supp12).

In regional surface waters, the concentrations of nutrients only partly originate from current fertilizer application (35% for nitrogen, 10% for phosphorus), with other sources including main water systems, sewage treatment system effluent, postponed runoff from agricultural land (not related to manure application), and runoff from nature areas (Groenendijk et al., 2016; Supp12). The biological water quality of such waterbodies, in terms of the presence of algae, water plants, macro fauna, and fish in comparison to reference water type-specific minimally disturbed conditions, was considered good in only 5% of the waterbodies (van Grinsven et al., 2017; Table 4, Supp12).

Impact category 13: Nitrogen deposition in terrestrial nature

The atmospheric deposition of nitrogen compounds can affect terrestrial ecosystems through acidification and eutrophication (Bobbink et al., 1998). Internationally recognized critical nitrogen deposition loads, below which no harmful effects to specific nature target types occur, have been defined (Van Dobben et al., 2012) and form the basis of the indicator we used. We estimate that about 60% of the surface in nature areas is exposed to higher nitrogen deposition than the critical load values for the specific nature target types (Table 4; Supp13). This excess deposition takes place particularly in the eastern and southern parts of the Netherlands (Figure 2). Livestock production in the Netherlands contributes roughly 40% to the total nitrogen deposition, mainly through the emissions of ammonia. The largest contribution to the ammonia emissions is from cattle with 63%, followed by pigs with 21%, and poultry with 11% (Supp13). Changes in total nitrogen deposition do not proportionally affect changes in critical load exceedance. When zero emissions from animal husbandry are assumed, the exceedance drops from about 60% to about 15% (Supp13; Figure 2).

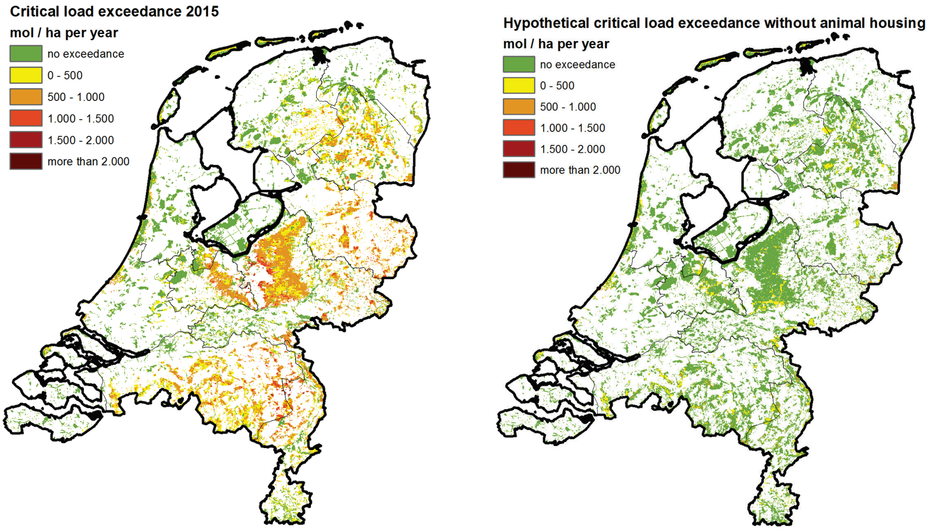


Figure 2. Critical load exceedance of nitrogen in nature areas in the Netherlands (mol/ha) for 2015 and for a hypothetical situation without animal housing, to illustrate the maximally feasible reduction with respect to livestock production.

Impact category 14: Environmental impacts of pesticides application

About 679 × 10^3 kg (7% of total) pesticides are annually applied to land used for livestock feed production (Supp14) in the Netherlands. The ecotoxicological effects of this application are expressed in Environmental Indicator Units (EIUs), which accounts for differences in toxicity of different pesticides and the spatial pattern of application, and expresses the effects relative to legal standards and derived toxicity criteria, which are different for each environmental compartment. In the groundwater compartment, with drinking water criteria as reference, pesticide application on grass and maize accounted for 902 EIUs/ha in 2016 (Verschoor et al., 2019). This value is comparable to the average for all agricultural sectors and considerably higher than 1, indicating that drinking water criteria are likely exceeded in several areas, but not necessarily in each area (Table 4). In the surface water compartment, with standards for the effects on water organisms as a reference, pesticide application accounted for 0.9 EIUs/ha in 2016 which is 95% lower than the agricultural average (Table 4; Verschoor et al., 2019). Note that this latter value is likely an underestimation, because of omitting pesticide application for other feed sources than grass and maize.

3.4 Global environmental impacts

Table 5 shows global Pressures associated with livestock production in the Netherlands. The global land use and GHG emissions are about twice as large as the national land use and GHG emissions, whereas the global blue water use is about three times greater than the national blue water use.

Impact category 15: Greenhouse gas emissions

The contribution of livestock production to emission of greenhouse gases (GHG) has been described extensively (de Boer et al., 2011; Gerber et al., 2013; Herrero et al., 2011; Rojas-Downing et al., 2017). Dutch livestock production is responsible for national emissions of 18 × 10^9 kg CO_2-equivalents in 2015 (Supp15b), 9% of total national emissions (Supp15b). GHG emissions attributable to livestock production mainly originate from feed production, enteric fermentation, manure management and fossil energy use (de Boer et al., 2011; Gerber et al., 2013). Due to the imported feed, a large part of these emissions occur outside the Netherlands. The total GHG emissions related to Dutch livestock production, both within and outside the country, were estimated at 42 ×10^9 kg CO_2-equivalents in 2015, more than twice the national livestock-related emissions (Table 5; Supp15a). The majority of the total GHG emissions (62%) can be attributed to the cattle sector (Table 5; Supp15a).

Impact category 16: Land use

The feed produced for Dutch livestock mainly consists of grass, maize, cereals and protein-rich crops such as soy bean. While most of the grass and maize are produced in the Netherlands, most of the cereals and protein-rich crops are imported from other countries within and outside Europe, resulting in a total estimated 2015 land use of 14 × 10^3 km^2 within the Netherlands and a global land use of 26 × 10^3 km^2 (Table 5; Supp16). This land use puts a Pressure on habitat loss and on the globally available land for food production. The dairy cattle sector contributes most to the global land use (44%). Most of this land is grassland and maize land in the Netherlands (Supp16). Pigs and poultry production contribute more to land use in countries from which their food (cereals and protein-rich crops) is sourced. In the Netherlands, land used for the production of livestock feed accounts for about 70% of all agricultural land.

Table 5. Point estimates of indicators for selected livestock-related impact categories concerning global environmental impacts[a]

Impact category	Indicator[b]	Estimate	Comparison[c]	Cattle[d]	S Rum[d]	Pigs[d]	Poultry[d]
15. Greenhouse gas emissions	Greenhouse gas emissions (P)	Global: 42×10^9 kg CO_2-eq NL: 18×10^9 kg CO_2-eq	9% of total emissions occurring in NL	62%	1%	22%	15%
16. Land use	Area (P)	Global: 26×10^3 km^2 NL: 14×10^3 km^2	70% of Dutch agricultural land use	44%	1%	34%	21%
17. Water use	Blue water use (P)	Global: 28×10^7 m^3 NL: 1×10^8 m^3	2% of Dutch water use	54%	1%	20%	25%

a. A more comprehensive description of indicators can be found in Table 1 and more information on their calculation and sources of uncertainty are presented in the Supplement.

b. A more comprehensive description of the indicator can be found in Table 1 and in the Supplement; P refers to Pressure indicator.

c. Value for comparison to provide context for the estimate in the light of other sources of impact or other comparisons (see text and Supplement for background).

d. S Rum = Small ruminants. When contributions of animal sectors do not add up to 100%, part of the impact cannot be attributed to a specific animal sector (see Supplement). Cattle includes dairy cattle and beef cattle. Poultry includes laying hens, broilers and other poultry.

Impact category 17: Water use

Water for livestock production is mainly required for irrigation of grassland and feed crops, while a smaller share is required for drinking water and cleaning (van der Meer, 2018). Since a large share of the livestock feed is imported, much of this water use takes place outside the Netherlands. In 2015, total water use was an estimated 28×10^7 m^3, which is likely an overestimation because the data for water use per unit of product used are assumed to be overestimated as well (Supp17). About half of this can be attributed to the dairy cattle sector, with pigs and poultry contributing near-equally to the remaining half. Domestically, about 1×10^8 m^3 was used in 2015 for livestock production, or about 2% of total consumption. 31-53 $\times 10^6$ m^3 was used for irrigation and about 50×10^6 m^3 was used for drinking (Supp17; van der Meer, 2018). The tap water use for Dutch livestock production is over 3% of the total tap water use (Supp 17). The national demand for fresh-water is currently only occasionally higher than the supply, but such periodical shortages are expected to increase (Ministry of Infrastructure and Environment and Ministry of Economic Affairs, 2015).

4 Discussion

4.1 Human health and environmental impacts

In this study, we provided quantitative estimates of the human health and environmental impacts of the Dutch livestock production system, including feed production and manure management, but excluding slaughtering, retail, and consumption. We collated available information for 17 different impact categories, based on information from a variety of research and policy traditions, and using eight Impact indicators, six State indicators and eight Pressure indicators along the Driver-Pressure-State-Impact chain of the DPSIR framework. For human health impacts, half of the impact categories could be captured in a burden of disease (Bod) measure, i.e. DALYs. These DALYs show that Impacts from livestock-related particulate matter and zoonotic diseases are generally higher than from pneumonia due to proximity to livestock farms and occupational accidents in the livestock sector. A comparatively large beneficial Impact for asthma and COPD may be present due to reduced incidence in the proximity to livestock farms. Estimated contributions ranged from a beneficial effect of 5% of the current BoD for COPD to an adverse effect of about 4% of the BoD for three different health effects: those related to particulate matter, zoonoses, and accidents.

The contribution of livestock production to environmental impacts in the Netherlands ranges from about 2% of the consumptive water use to about 95% of the phosphorus loss. Moreover, the global area of land required for feed production for livestock production in the Netherlands exceeds the area dedicated to all agricultural land use in the Netherlands, necessitating substantial feed imports. Such imports also contribute to global greenhouse gas emissions and water use in a major way.

The national estimates differ across regions and animal sectors. For example up to 8% of residents experience severe odor annoyance in some livestock-dense municipalities, compared with about 2.5% nationally. Different animal sectors had different relative contributions to human health and environmental impacts for most impact categories (Tables 2-5). Cattle contribute most to greenhouse gas emissions, eutrophication, nitrogen deposition, secondary PM_{10}, and land use domestically, whereas pigs and poultry contribute more to land use abroad. Poultry contributes most to the human disease burden related to primary PM_{10} and zoonoses. For some of the other impacts, a quantitative attribution to animal sectors was not obtained, but differences are still expected: for example, in the pressure on the development of antimicrobial resistance due to differences in use of antimicrobials, which is highest in veal calves. In addition to differences across animal sectors, differences within animal sectors may also be considerable due to a variety of adopted farming practices, which were not considered here.

4.2 Strengths and limitations

To our knowledge, this is the first integrated assessment of livestock production effects on human health and the environment at the national level. Such national level assessment adds a novel perspective to previous overviews focussing on farm level or product level, or not quantified at such uniform scale (Aequator Groen en Ruimte et al., 2008; Boone and Dolman, 2010; Bos et al., 2017; Hu et al., 2017). A national level assessment offers insight on the relative contributions of the entire cattle, poultry, and pig sectors rather than just the relative impact of a kg of beef, poultry or pig meat, for example. Such an analysis takes differences in production volume into account. Moreover, a national level assessment allows comparisons with impacts of other economic sectors or the livestock sectors of other countries.

Another distinctive aspect of our approach is the broad and diverse set of 17 impact categories with 22 indicators that were collated. These reflect different classes of risk problems, with differences in probability of occurrence, in extent of damage and in incertitude of the estimates (Klinke and Renn, 2002; Renn, 2006). Such diversity may come at a cost of uniform presentation across impact categories, as illustrated below.

Ideally, all used indicators would express an Impact. However, we only used eight such Impact indicators, among a total of 22, due to limitations in our current knowledge, in availability of data and lack of operational models. These limitations currently preclude operational modelling with integration across the DPSIR causal chain. Thus, while the DPSIR Framework is a very useful conceptual 'Level 2 Relational framework', it cannot act as a ' Level 3 Operational framework' in an integrated assessment (Knol et al., 2010). The difficulty of using Impact indicators can be illustrated for antimicrobial resistance. For this impact category, the presented data on antibiotics use represents a Pressure on antimicrobial resistance in humans and is relevant in existing monitoring programs but currently the relation with resistance cannot be quantified. The additionally presented results from an attribution-study of a specific type of antimicrobial resistance are closer to the Impact, but generalization to other types of antimicrobial resistance is not possible yet, and even that indicator does not indicate the associated disease burden.

Even where Impact indicators were used to express Impact, they were not uniform across impact categories, not even within the same domain. Here we used the DALY metric for four out of the nine human health impact categories, as burden of disease (BoD) measure of human health impact. The DALY is appropriate for health impacts with multiple occurrences per year. Yet, for risk classes characterised by high incertitude in both probability and in impact, e.g. emerging zoonoses, the DALY metric is less appropriate (Klinke and Renn, 2002; Renn, 2006). A BoD measure such as the DALY is also not appropriate to capture odor and noise annoyance which can be considered adverse health effects but do not constitute 'disease' in the medical sense. Forcing such adverse health effects into the DALY metric would devaluate the DALY metric for public health and medical communities. Moreover, in the societal debate and policy arena, prevalence of severe annoyance is the common well-established metric of choice.

Even though a common DALY metric could be assigned to four impact categories, the calculation of DALYs were quite different; some were exposure-driven, while others were disease incidence-driven. For particulate matter, for instance, the estimate is derived from exposure levels, number of people exposed, disease prevalence, and the exposure-response function from the literature. For infectious disease, the estimate is derived from incidence data of the reported diseases, corrected for under-diagnosis and under-reporting, and attributed to specific exposures by expert judgement. Thus, even for this common metric, the nature and size of uncertainties may vary across factors.

Of course our estimates need to be interpreted with some caution and 'ceteris paribus' comparisons may not always be warranted. The different constructs described by the indicators as well as the different research and policy traditions from which the estimates originate affect the location, nature and range of uncertainty (Knol et al., 2009); these vary considerably across indicators. The main sources of uncertainty for each indicator are described in the Supplement. These include uncertainties in model structure, in parameters and in input data of the models. Also, some are epistemic in nature due to incomplete knowledge leading to incertitude, while others are caused by natural (e.g. ecosystem impacts) and societal variability (e.g. demographics affecting disease burden, or annoyance) (Knol et al., 2009). More specifically, for some indicators, uncertainty is related to data availability, as in the case for accidents, for which the only data available included farm employees but not self-employed farmers (Supp4). For the zoonoses indicator, the relative contributions of transmission routes or animals are not precisely known (Supp2). For the particulate matter indicator, little is known about the difference in Impacts of particulate matter from livestock farms compared to other sources, primarily combustion sources of fossil fuels (Supp1). For the asthma, pneumonia and COPD impact category, for which several positive and negative associations with proximity to livestock have been reported, mechanisms are not well understood. This makes it difficult to disentangle the several health effects around livestock farms (including those caused by livestock-related particulate matter). These different knowledge gaps illustrate that the extent to which estimates are backed-up by scientific evidence differs considerably between impact categories. There may also be inherent uncertainty associated with impacts such as with manure fermentation systems wherein the probability of an incident occurring is difficult to estimate (Supp9), or with emerging zoonotic diseases in the future, where the probability, severity, and the specific pathogen that emerges will be inherently uncertain (WHO, 2017a; Supp5). The diversity in location, nature and range of uncertainties preclude uniform consolidation in a uniform index.

Given the diverse nature of effects of livestock production on human health and the environment, further integration across the impact categories is, in our opinion, currently not warranted. Further integration would involve entering multiple normative judgements. For instance about how disease burden compares to biodiversity impacts, or perception issues, or potential climate impacts of greenhouse gas emissions. Or how commonly and frequently occurring impacts compare to rare but potentially high impact events.

Integrating disparate indicators is possible, by for example using multi-criteria analysis, but would require subjectively weighing indicators, by users of such analysis. Normative weighing and integration would thus be context dependent and would vary from one situation or country to the next.

Even though including 17 different impact categories, our assessment is not complete and offers an underestimation of the total impact of Dutch livestock production. Some impact categories, such as ecotoxicological effects of heavy metals or non-productive ecosystem services such as the influence of landscape on human well-being, have not been taken into account. Human health impacts and some environmental impacts in other countries, such as those related to ammonia that crosses the Dutch borders, have not been taken into account either. Moreover, other aspects, not related to environment and health impacts, such as the economic viability of the sector (including at the farmer level), agroecosystemic resilience and animal welfare, are relevant in considering policy interventions.

4.3 Implications

Current livestock production with its broad and substantial effects on human health and environment is generally no longer considered sustainable and transition to more sustainable productions systems is a political priority (European Comission, 2018; European Comission, 2019; Ministry of Agriculture, 2018; SER, 2016; United Nations, 2015b). Such transition may be guided by integrated assessments about human health and environmental impacts. Ours shows, to the degree possible, the relative contributions of different animal sectors across different impact categories, and thereby consequences of possible shifts between animal sectors, thus highlighting the possible synergies and trade-offs for alternative policies toward sustainability. It also highlights where more research is needed to reduce major uncertainties that affect decision making.

This assessment took a national perspective, while encompassing transboundary impacts. The national perspective is characterised by high animal density, combined with high human population density, with land use for feed production exceeding the available areal. Similar animal densities, and in some cases also human population densities are also present in regions in Germany (Nordrhein-Westfalen), Belgium (parts of Flanders), France (Brittany), Spain (Catalunia), Italy (Po Valley), the USA and Asia, with hence potentially similar human health impacts. A similarly large import of feed can be found in countries such as Japan (Wang et al., 2018), with related impacts across national or regional borders, as well as a high pressure on the local environment in terms of nutrients. The methodology, impact categories and indicators used in our assessment, as well as methodological lessons-learned are therefore considered useful for broader application elsewhere. Thus, application of similar integrated assessments can be informative at the regional, national and international level elsewhere. For instance, it may help to develop strategic plans regarding new regulations for the European common agricultural policy (European Comission, 2018) or for bringing the European Green Deal into practice (European Comission, 2019).

The differences in impacts across animal sectors that we indicated not only imply that a tailoring of mitigation measures to each sector may help to target specific impacts, but also that other impacts not directly addressed by intervention may suddenly become relevant if shifts in production across sectors occur. In the past, such shifts have occurred following the introduction of European regulations such as the milk quotation system, and large animal disease outbreaks. Such possible shifts illustrate the need of evaluating a wide set of impact categories before introducing large policy programs.

The spatial differentiation of impacts has additional implications. One implication is that municipal, provincial, and national governments are likely to assign different priorities to the impacts distinguished here. Another implication is the relevance of spatial organization of farms in regional planning. Such spatial organization is fundamental for responding to particulate matter-related health impacts, odor annoyance, and nitrogen deposition in terrestrial nature areas, as for example becomes clear from the reduction in external costs that might be obtained by relocating pig production between regions in the European Union (van Grinsven et al., 2018). The distribution of farms in the landscape also affects the spread and emergence of zoonotic diseases and evolution of virulence in pathogens (Boender et al., 2007; Lion and Gandon, 2015; Lion and Gandon, 2016; Messinger and Ostling, 2009).

The difficulty of integrating information from a variety of impact categories illustrates a reality in which impacts may be complex, uncertain or ambiguous and requires alternatives for traditional decision-making, such as scenario construction, precautionary approaches, resilience building and stakeholder involvement (Renn, 2006). To further the quality of integrated assessments toward sustainable livestock production systems, we distil several avenues forward from the lessons-learned from this exercise. One avenue is reducing uncertainties around indicators with potentially substantial impacts, for example regarding mechanisms underlying health effects in the proximity of livestock farms. Another avenue is the development of operational models to better link Pressures, States and Impacts across the causal chain, for example for antimicrobial resistance and ecosystem integrity impacts. In addition, more integrated assessments may benefit from the development and application of approaches to involve stakeholders in assessing specific societal goals or policy-directed questions, and for weighing disparate indicators. These may for example be applied in 'ex ante' evaluations of projected policies toward sustainable livestock production.

5 Conclusions

We were able to describe the effects of livestock production on human health and the environment across 17 impact categories, using eight actual Impact indicators and also approximating Impact with six State and eight Pressure indicators. Livestock production may contribute to up to 4% to the burden of disease related to air pollution, infectious diseases and occupational accidents. Additional types of health effects are annoyance and low-probability, high impact events. Livestock production contributes considerably to many environmental impacts as well, with an estimated contribution of up to 95% for phosphorus transfer to soil, and a considerable contribution of Dutch livestock production to impacts abroad due to imports of feed. Moreover, the impacts of livestock production vary widely across animal sectors. For further guidance of the public debate, additional methods for integration of indicators need to be developed and applied, with stakeholder involvement as a vital part.

A supplement containing methodological underpinning to the estimates is available online at
https://ars.els-cdn.com/content/image/1-s2.0-S0048969720332228-mmc1.pdf

Acknowledgements

Peter Teunis (Emory University, Atlanta, GA, USA) contributed in an early stage to the quantification of human health impacts. Kitty Maassen, Joke van der Giessen, Titia Kortbeek and Wilfrid van Pelt (National Institute for Public Health and the Environment: RIVM, Bilthoven, The Netherlands) have made valuable contributions to the calculations for the "Zoonoses" indicator. Annemieke van der Wal (RIVM) contributed to the indicators "Nutrient-related impacts on soil functioning" and "Nitrate pollution of groundwater"; Richard van Duijnen (RIVM) provided data for the latter. Dirk-Jan van der Hoek and Arjen van Hinsberg (Netherlands Environmental Assessment Agency, The Hague, The Netherlands) provided the critical load map used to estimate the nitrogen deposition in terrestrial nature indicator. Ton van der Linden, who passed away unexpectedly on January 25th, 2018, contributed to earlier versions of the pesticide application indicator. Pieter Bos, Lars van de Bovenkamp and Theo Viets (Wageningen University and Research, Wageningen, The Netherlands) provided the basis for the calculation of total livestock production estimates, which have been used for the greenhouse gas emissions, land use and water use indicators. Bram Bos (Wageningen Livestock Research, Wageningen, The Netherlands) contributed to discussions in an early stage of the study. Jan Slingenbergh (Food and Agriculture Organization of the United Nations, Rome, Italy) contributed to the design of the study. Linda McPhee (Linda McPhee consulting) checked English language. Finally, we thank two anonymous reviewers for their extensive and constructive feedback on our work.

References

Aequator Groen en Ruimte, Ecorys Nederland B. V., Witteveen+Bos, 2008. Maatschappelijke effecten van de intensieve veehouderij: een vergelijking van productiesystemen [Societal effects of intensive livestock farming: a comparison of productionsystems]. https://www.rijksoverheid.nl/documenten/rapporten/2008/05/22/maatschappelijke-effecten-van-de-intensieve-veehouderij (accessed Web Page 2016).

Analistennetwerk Nationale Veiligheid, 2016. Nationaal veiligheidsprofiel 2016 [National security profile 2016]. RIVM (National Institute of Public Health and the Environment), Bilthoven.

Berkhout P., Damen M., Ameling C., Sol V., 2015. Ernstige arbeidsongevallen 1999-2011: Trends en ontwikkelingen [Severe occupational accidents 1999-2011: Trends and developments]. RIVM (National Institute of Public Health and the Environment), Bilthoven.

Bobbink R., Hornung M., Roelofs J.G., 1998. The effects of air-borne nitrogen pollutants on species diversity in natural and semi-natural European vegetation. Journal of Ecology. 86, 717-738. https://doi.org/10.1046/j.1365-2745.1998.8650717.x.

Boender G.J., Hagenaars T.J., Bouma A., Nodelijk G., Elbers A.R., de Jong M.C., et al., 2007. Risk maps for the spread of highly pathogenic avian influenza in poultry. PLoS computational biology. 3, e71. https://doi.org/10.1371/journal.pcbi.0030071.

Boone J.A., Dolman M.A., 2010. Duurzame Landbouw in Beeld 2010; resultaten van de Nederlandse land-en tuinbouw op het gebied van People, Planet en Profit [Sustainable Agriculture 2010; Performance of Dutch agriculture and horticulture in terms of People, Planet and Profit]. 105. Wettelijke Onderzoekstaken Natuur & Milieu [Wageningen, Statutory Research Tasks Unit for Nature and the Environment], Wageningen.

Borlée F., Yzermans C.J., van Dijk C.E., Heederik D., Smit L.A.M., 2015. Increased respiratory symptoms in COPD patients living in the vicinity of livestock farms. Eur. Respir. J. 46, 1605-1614. https://doi.org/10.1183/13993003.00265-2015.

Bos A., Puente-Rodríguez D., Reijs J.W., van der Peet G., Koerkamp P.W.G., 2017. Monitoring verduurzaming veehouderij 1.0: een eerste proeve van een Monitorings-systematiek voor de 15 ambities van de Uitvoeringsagenda Duurzame Veehouderij, met initiële resultaten voor drie diersectoren en een aantal keteninitiatieven [Monitoring sustainable development of livestock 1.0]. Wageningen Livestock Research.

Casey J.A., Kim B.F., Larsen J., Price L.B., Nachman K.E., 2015. Industrial Food Animal Production and Community Health. Curr. Environ. Health Rep. 2, 259-271. https://doi.org/10.1007/s40572-015-0061-0.

CBS, 2019a. StatLine. http://statline.cbs.nl/Statweb/ (accessed 02/01 2019).

CBS, 2019b. StatLine: Mineralenbalans landbouw. https://opendata.cbs.nl/statline/#/CBS/nl/dataset/83475NED/table?ts=1556803868297 (accessed 05/02 2019).

CBS, PBL, RIVM, WUR, 2008. Fosfaatverzadiging landbouwgronden (indicator 0267, versie 04 , 20 juni 2008) [Phosphorus saturation agricultural soils]. https://www.clo.nl/indicatoren/nl0267-fosfaatverzadiging-van-landbouwgronden (accessed 04/10 2019).

Chantziaras I., Boyen F., Callens B., Dewulf J., 2014. Correlation between veterinary antimicrobial use and antimicrobial resistance in food-producing animals: a report on seven countries. J. Antimicrob. Chemother. 69, 827-834. https://doi.org/10.1093/jac/dkt443.

Coenen P.W.H.G., Zanten M.C.v., Zijlema P.J., Arets E.J.M.M., Baas K., Berghe A.C.W.M.v.d., et al., 2018. Greenhouse gas emissions in the netherlands 1990-2016. RIVM (National Institute for Public Health and the Environment), Bilthoven.

de Boer I., Cederberg C., Eady S., Gollnow S., Kristensen T., Macleod M., et al., 2011. Greenhouse gas mitigation in animal production: towards an integrated life cycle sustainability assessment. Curr. Opin. Environ. Sustainability. 3, 423-431. https://doi.org/10.1016/j.cosust.2011.08.007.

De Rooij M.M., Van Leuken J.P., Swart A., Kretzschmar M.E., Nielen M., De Koeijer A.A., et al., 2019. A systematic knowledge synthesis on the spatial dimensions of Q fever epidemics. Zoonoses Public Health. 66, 14-25. https://doi.org/10.1111/zph.12534.

Dekker S.E.M., de Boer I.J.M., Vermeij I., Aarnink A.J.A., Groot Koerkamp P.W.G., 2011. Ecological and economic evaluation of Dutch egg production systems. Livest. Sci. 139, 109-121. https://doi.org/10.1016/j.livsci.2011.03.011.

Dorado-García A., Mevius D.J., Jacobs J.J.H., Van Geijlswijk I.M., Mouton J.W., Wagenaar J.A., et al., 2016. Quantitative assessment of antimicrobial resistance in livestock during the course of a nationwide antimicrobial use reduction in the Netherlands. J. Antimicrob. Chemother. 71, 3607-3619. https://doi.org/10.1093/jac/dkw308.

Douglas P., Robertson S., Gay R., Hansell A.L., Gant T.W., 2018. A systematic review of the public health risks of bioaerosols from intensive farming. International Journal of Hygiene and Environmental Health. 221, 134-173. https://doi.org/10.1016/j.ijheh.2017.10.019.

Duringer B., Koukouma E., Broekema R., Paassen M.v., Scholten J., 2017. Agri-footprint 4.0. Blonk Consultants, Gouda.

Dutch safety board, 2014. Dodelijk ongeval in mestsilo te Makkinga [Accident fatalities in manure silo Makkinga] Onderzoeksraad voor Veiligheid (Dutch safety board), Den Haag.

Dutch safety board, 2016. Biogasemissie bij Ecoson, te Son, 7 november 2015 [Biogasemission at Ecoson, Son, november 7th, 2015]. Onderzoeksraad voor Veiligheid (Duch Safety Board), Den Haag.

EEA, 2005. The European environment: state and outlook 2005. Office for Official Publications of the European Communities, Copenhagen.

Ege M.J., Mayer M., Normand A.-C., Genuneit J., Cookson W.O., Braun-Fahrländer C., et al., 2011. Exposure to environmental microorganisms and childhood asthma. New England Journal of Medicine. 364, 701-709. https://doi.org/10.1056/NEJMoa1007302.

Engering A., Hogerwerf L., Slingenbergh J., 2013. Pathogen–host–environment interplay and disease emergence. Emerg. Microbes Infect. 2, e5. https://doi.org/10.1038/emi.2013.5.

European Comission, 2018. Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL establishing rules on support for strategic plans to be drawn up by Member States under the Common agricultural policy (CAP Strategic Plans) and financed by the European Agricultural Guarantee Fund (EAGF) and by the European Agricultural Fund for Rural Development (EAFRD) and repealing Regulation (EU) No 1305/2013 of the European Parliament and of the Council and Regulation (EU) No 1307/2013 of the European Parliament and of the Council, Brussels.

European Comission, 2019. The European Green Deal, Brussels.

European Commission, 1991. Council Directive 91/676/EEC of 12 December 1991 concerning the protection of waters against pollution caused by nitrates from agricultural sources Official Journal, L 375.

FAO, 2013. World Livestock 2013- changing disease landscapes. Food and Agriculture Organization of the United Nations (FAO), Rome.

Freidl G.S., Spruijt I.T., Borlee F., Smit L.A., van Gageldonk-Lafeber A.B., Heederik D.J., et al., 2017. Livestock-associated risk factors for pneumonia in an area of intensive animal farming in the Netherlands. PLoS One. 12, e0174796. https://doi.org/10.1371/journal.pone.0174796.

Gerber P., Steinfeld H., Henderson B., Mottet A., Opio C., Dijkman J., et al., 2013. Tackling climate change through livestock. Food and Agriculture Organization of the United Nations (FAO), Rome.

Gold M.R., Stevenson D., Fryback D.G., 2002. HALYS and QALYS and DALYS, Oh My: similarities and differences in summary measures of population Health. Annu. Rev. Public Health. 23, 115-34. https://doi.org/10.1146/annurev.publhealth.23.100901.140513.

Groenendijk P., van Boekel E., Renaud L., Greijdanus A., Michels R., de Koeijer T., 2016. Landbouw en de KRW-opgave voor nutriënten in regionale wateren: het aandeel van landbouw in de KRW-opgave, de kosten van enkele maatregelen en de effecten ervan op de uit-en afspoeling uit landbouwgronden [Agriculture and the water framework directive obligations for nutrients in regional waters: the share of agriculture in the water framework directive obligations, the costs of some of the measures and the effects of these on run-off and leaching from agricultural soils]. Wageningen Environmental Research, Wageningen.

Hatchette T.F., Hudson R.C., Schlech W.F., Campbell N.A., Hatchette J.E., Ratnam S., et al., 2001. Goat-associated Q fever: a new disease in Newfoundland. Emerging infectious diseases. 7, 413-419. https://doi.org/10.3201/eid0703.010308.

Heederik D., Yzermans C., 2011. Mogelijke effecten van intensieve veehouderij op de gezondheid van omwonenden: onderzoek naar potentiële blootstelling en gezondheidsproblemen [Possible effects of intensive livestock on the health of local residents: a study to investigate potential exposure and health problems]. https://www.rijksoverheid.nl/documenten/rapporten/2011/06/21/mogelijke-effecten-intensieve-veehouderij-op-gezondheid-omwonenden (accessed 13/04 2017).

Herrero M., Gerber P., Vellinga T., Garnett T., Leip A., Opio C., et al., 2011. Livestock and greenhouse gas emissions: The importance of getting the numbers right. Anim. Feed Sci. Technol. 166, 779-782. https://doi.org/10.1016/j.anifeedsci.2011.04.083.

Herrero M., Wirsenius S., Henderson B., Rigolot C., Thornton P., Havlík P., et al., 2015. Livestock and the environment: what have we learned in the past decade? Annu. Rev. Environ. Resour. 40, 177-202. https://doi.org/10.1146/annurev-environ-031113-093503.

Hooiveld M., van Dijk C., van der Sman-de Beer F., Smit L.A., Vogelaar M., Wouters I.M., et al., 2015. Odour annoyance in the neighbourhood of livestock farming - perceived health and health care seeking behaviour. Ann Agric Environ Med. 22, 55-61. https://doi.org/10.5604/12321966.1141369.

Hu Y., Cheng H., Tao S., 2017. Environmental and human health challenges of industrial livestock and poultry farming in China and their mitigation. Environment international. 107, 111-130. https://doi.org/10.1016/j.envint.2017.07.003.

Inspectie SZW, 2018. Monitor arbeidsongevallen en klachten arbeidsomstandigheden 2013-2017 [Monitor occupational accidents and complaints working conditions 2013-2017]. Inspectie SZW (Inspectorate SZW).

Jones B.A., Grace D., Kock R., Alonso S., Rushton J., Said M.Y., et al., 2013. Zoonosis emergence linked to agricultural intensification and environmental change. Proceedings of the National Academy of Sciences of the United States of America. 110, 8399-8404. https://doi.org/10.1073/pnas.1208059110.

Kalkowska D.A., Boender G.J., Smit L.A.M., Baliatsas C., Yzermans J., Heederik D.J.J., et al., 2018. Associations between pneumonia and residential distance to livestock farms over a five-year period in a large population-based study. PLoS One. 13, e0200813. https://doi.org/10.1371/journal.pone.0200813.

Kauffmann F., Oryszczyn M.P., Maccario J., 2002. The protective role of country living on skin prick tests, immunoglobulin E and asthma in adults from the Epidemiological study on the Genetics and Environment of Asthma, bronchial hyper-responsiveness and atopy. Clin. Exp. Allergy. 32, 379-386. https://doi.org/10.1046/j.1365-2222.2002.01325.x.

Klein J., Rozemeijer J., 2015. Meetnet Nutriënten Landbouw Specifiek Oppervlaktewater; Update toestand en trends tot en met 2014 [Monitoring netwok Nutrients Agriculture Specific Surface water; Update on state and trends until 2014]. http://edepot.wur.nl/366462 (accessed 07/11 2018).

Klimaatberaad, 2019. Klimaatakkoord [Climate agreement]. https://www.klimaatakkoord.nl/klimaatakkoord/documenten/publicaties/2019/06/28/klimaatakkoord (accessed 07/17 2019).

Klinke A., Renn O., 2002. A New Approach to Risk Evaluation and Management: Risk-Based, Precaution-Based, and Discourse-Based Strategies. Risk Anal. 22, 1071-1094. https://doi.org/10.1111/1539-6924.00274.

Knol A.B., Briggs D.J., Lebret E., 2010. Assessment of complex environmental health problems: Framing the structures and structuring the frameworks. Science of the Total Environment. 408, 2785-2794.

Knol A.B., Petersen A.C., van der Sluijs J.P., Lebret E., 2009. Dealing with uncertainties in environmental burden of disease assessment. Environ. Health. 8, 21. https://doi.org/10.1186/1476-069X-8-21.

Kraaij-Dirkzwager M., van der Ree J., Lebret E., 2017. Rapid Assessment of Stakeholder Concerns about Public Health. An Introduction to a Fast and Inexpensive Approach Applied on

Health Concerns about Intensive Animal Production Systems. International journal of environmental research and public health. 14, 1534. https://doi.org/10.3390/ijerph14121534.

Leip A., Billen G., Garnier J., Grizzetti B., Lassaletta L., Reis S., et al., 2015. Impacts of European livestock production: nitrogen, sulphur, phosphorus and greenhouse gas emissions, land-use, water eutrophication and biodiversity. Environ. Res. Lett. 10, 115004. https://doi.org/10.1088/1748-9326/10/11/115004.

Lion S., Gandon S., 2015. Evolution of spatially structured host–parasite interactions. Journal of Evolutionary Biology. 28, 10-28. https://doi.org/10.1111/jeb.12551.

Lion S., Gandon S., 2016. Spatial evolutionary epidemiology of spreading epidemics. Proceedings of the Royal Society B: Biological Sciences. 283, 20161170. https://doi.org/10.1098/rspb.2016.1170.

Liverani M., Waage J., Barnett T., Pfeiffer D.U., Rushton J., Rudge J.W., et al., 2013. Understanding and managing zoonotic risk in the new livestock industries. Environmental Health Perspectives (Online). 121, 873. https://doi.org/10.1289/ehp.1206001.

Maassen K., Smit L., Wouters I., van Duijkeren E., Janse I., Hagenaars T., et al., 2016. Veehouderij en gezondheid omwonenden [livestock farming and the health of local residents]. RIVM (National Institute for Public Health and the Environment), Bilthoven.

Mangen M.-J.J., Burrell A.M., 2001. Decomposing Preference Shifts for Meat and Fish in the Netherlands. J. Agric. Econ. 52, 16-28. https://doi.org/10.1111/j.1477-9552.2001.tb00922.x.

Marshall B.M., Levy S.B., 2011. Food animals and antimicrobials: impacts on human health. Clin. Microbiol. Rev. 24, 718-733. https://doi.org/10.1128/CMR.00002-11.

Messinger S.M., Ostling A., 2009. The consequences of spatial structure for the evolution of pathogen transmission rate and virulence. American Naturalist. 174, 441-454. https://doi.org/10.1086/605375.

Mevius D., Heederik D., Duijkeren E., Veldman K., van Essen A., Kant A., et al., 2018. Rapport ESBL-Attributieanalyse (ESBLAT) [Report ESBL-Attribution analysis]. De Stichting TKI Agri&Food (TKI).

Ministry of Agriculture, 2018. Landbouw, natuur en voedsel: waardevol en verbonden - Nederland als koploper in kringlooplandbouw [Agriculture, nature and food: valuable and connected - The Netherlands as a leader in circular agriculture]. Ministerie van Landbouw, Natuur en Voedselkwaliteit [Ministry of Agriculture, Nature and Food Quality], Den Haag.

Ministry of Infrastructure and Environment, Ministry of Economic Affairs, 2015. Nationaal Waterplan 2016-2021 [National waterplan 2016-2021]. Ministerie van Infrastructuur en Milieu en Ministerie van Economische Zaken [Ministry fof Infrastructure and Environment and Ministry of Economic Affairs], Den Haag.

Mori M., Roest H.-J., 2018. Farming, Q fever and public health: agricultural practices and beyond. Arch. Public health. 76, 2. https://doi.org/10.1186/s13690-017-0248-y.

Mughini-Gras L., Dorado-García A., van Duijkeren E., van den Bunt G., Dierikx C.M., Bonten M.J.M., et al., 2019. Attributable sources of community-acquired carriage of Escherichia coli containing β-lactam antibiotic resistance genes: a population-based modelling study. Lancet Planet Health. 3, e357-e369. https://doi.org/10.1016/S2542-5196(19)30130-5.

Murray C.J., Lopez A.D., 1997. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. Lancet. 349, 1436-42. https://doi.org/10.1016/S0140-6736(96)07495-8.

Murray C.J., Vos T., Lozano R., Naghavi M., Flaxman A.D., Michaud C., et al., 2012. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 380, 2197-223. https://doi.org/10.1016/S0140-6736(12)61689-4.

Nordborg M., Davis J., Cederberg C., Woodhouse A., 2017. Freshwater ecotoxicity impacts from pesticide use in animal and vegetable foods produced in Sweden. Science of The Total Environment. https://doi.org/10.1016/j.scitotenv.2016.12.153.

Oenema O., Oudendag D., Velthof G.L., 2007. Nutrient losses from manure management in the European Union. Livest. Sci. 112, 261-272. https://doi.org/10.1016/j.livsci.2007.09.007.

OIE, 2016. HANDISTATUS II. http://web.oie.int/hs2/report.asp (accessed 05/27 2019).

Plowright R.K., Parrish C.R., McCallum H., Hudson P.J., Ko A.I., Graham A.L., et al., 2017. Pathways to zoonotic spillover. Nat. Rev. Microbiol. 15, 502. https://doi.org/10.1038/nrmicro.2017.45.

Poll R.v., Breugelmans O., Houthuijs D., Kamp I.v., 2018. Beleving Woonomgeving in Nederland: Inventarisatie Verstoringen 2016 [Perceiving the physical living environment in the Netherlands: Annoyance inventory 2016]. RIVM (National Institute for Public Health and the Environment), Bilthoven.

Post P.M., Hogerwerf L., Huss A., Petie R., Boender G.J., Baliatsas C., et al., 2019. Risk of pneumonia among residents living near goat and poultry farms during 2014-2016. PLoS One. 14, e0223601. https://doi.org/10.1371/journal.pone.0223601.

Renn O., 2006. White Paper on Risk Governance: Towards and Integrative Approach. International Risk Governance Council (IRGC), Geneva.

Riedler J., Braun-Fahrländer C., Eder W., Schreuer M., Waser M., Maisch S., et al., 2001. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. The Lancet. 358, 1129-1133. https://doi.org/10.1016/S0140-6736(01)06252-3

RLI, 2018. Sustanable and Healthy: working together towards a sustainable food system. RLI (Council for the Environment and Infrastructure).

Robinson T.P., Thornton P.K., Franceschini G., Kruska R., Chiozza F., Notenbaert A.M.O., et al., 2011. Global livestock production systems. Food and Agriculture Organization of the United Nations (FAO) and International Livestock Research Institute (ILRI), Rome.

Roest H., Tilburg J., Van der Hoek W., Vellema P., Van Zijderveld F., Klaassen C., et al., 2011. The Q fever epidemic in The Netherlands: history, onset, response and reflection. Epidemiol. Infect. 139, 1-12. https://doi.org/10.1017/S0950268810002268.

Rojas-Downing M.M., Nejadhashemi A.P., Harrigan T., Woznicki S.A., 2017. Climate change and livestock: Impacts, adaptation, and mitigation. Clim. Risk Manag. 16, 145-163. https://doi.org/10.1016/j.crm.2017.02.001.

Sauter F., Van Zanten M., Van der Swaluw E., Aben J., De Leeuw F., Van Jaarsveld H., 2018. The OPS-model. Description of OPS 4.5. 2. RIVM (National Institute for Public Health and the Environment), Bilthoven.

SDa, 2017. Het gebruik van antibiotica bij landbouwhuisdieren in 2016 [Usage of antibiotics in agricultural livestock in the Netherlands in 2016] SDa (Autoriteit Diergeneesmiddelen), Utrecht.

SER, 2016. Versnelling Duurzame Veehouderij [Acceleration Sustainable Livestock]. 2016. SER (Social and Economic Council), Den Haag.

Silbergeld E.K., Graham J., Price L.B., 2008. Industrial food animal production, antimicrobial resistance, and human health. Annu. Rev. Public Health. 29, 151-169. https://doi.org/10.1146/annurev.publhealth.29.020907.090904.

Smeets E., Weterings R., 1999. Environmental indicators: Typology and overview. European Environment Agency Copenhagen.

Smit L.A.M., Heederik D., 2017. Impacts of Intensive Livestock Production on Human Health in Densely Populated Regions. GeoHealth. 1, 272-277. https://doi.org/10.1002/2017GH000103.

Smit L.A.M., Hooiveld M., van der Sman-de Beer F., Opstal-van Winden A.W.J., Beekhuizen J., Wouters I.M., et al., 2014. Air pollution from livestock farms, and asthma, allergic rhinitis and COPD among neighbouring residents. Occup Environ Med, 134-140. https://doi.org/10.1136/oemed-2013-101485.

Sutton M.A., Oenema O., Erisman J.W., Leip A., van Grinsven H., Winiwarter W., 2011. Too much of a good thing. Nature. 472, 159-161. https://doi.org/10.1038/472159a.

Takai H., Pedersen S., Johnsen J.O., Metz J.H.M., Koerkamp P.W.G.G., Uenk G.H., et al., 1998. Concentrations and emissions of airborne dust in livestock buildings in Northern Europe. J. Agric. Eng. Res. 70, 59-77. https://doi.org/10.1006/jaer.1997.0280.

Tang K.L., Caffrey N.P., Nóbrega D.B., Cork S.C., Ronksley P.E., Barkema H.W., et al., 2017. Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis. Lancet Planet Health. 1, e316-e327. https://doi.org/10.1016/S2542-5196(17)30141-9.

UDV, 2013. Uitvoeringsagenda Duurzame Veehouderij 2023: 4e Voortgangsrapportage [implementation agenda sustainable livestock 2023: 4th progress report]. http://www.uitvoeringsagendaduurzameveehouderij.nl/files/1013/8268/5066/UDV-voortgangsrapportage-2013.pdf (accessed 11/06 2017).

United Nations, 2015a. Paris Agreement. http://unfccc.int/files/essential_background/convention/application/pdf/english_paris_agreement.pdf

United Nations, 2015b. Transforming our world: the 2030 agenda for sustainable development. https://sustainabledevelopment.un.org/content/documents/21252030%20Agenda%20for%20Sustainable%20Development%20web.pdf (accessed 08/24 2017).

van der Hoek W., Hunink J., Vellema P., Droogers P., 2011. Q fever in The Netherlands: the role of local environmental conditions. International Journal of Environmental Health Research. 21, 441-451. https://doi.org/10.1080/09603123.2011.574270.

van der Meer R., 2014. Watergebruik in de agrarische sector 2012 [Water use in the agricultural sector 2012] LEI Wageningen UR, Wageningen.

van der Meer R.W., 2018. Watergebruik in de land- en tuinbouw, 2015 en 2016. Wageningen Economic Research, Wageningen.

van Dijk C.E., Garcia-Aymerich J., Carsin A.-E., Smit L.A.M., Borlée F., Heederik D.J., et al., 2016. 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. 219, 278-287. https://doi.org/10.1016/j.ijheh.2016.01.002.

Van Dobben H., Bobbink R., Bal D., Van Hinsberg A., 2012. Overzicht van kritische depositiewaarden voor stikstof, toegepast op habitattypen en leefgebieden van Natura 2000 [Overview of critical load values for nitrogen, applied to habitat types and sites of Natura 2000]. Alterra Wageningen UR, Wageningen.

van Grinsven H., Bleeker A., van der Sluis S., van Schijndel M., van Dam J., Tiktak A., et al., 2017. Evaluatie Meststoffenwet 2016: syntheserapport [Evaluation Manure and Fertilisers Acts 2016: Synthesis Report]. PBL (Netherlands Environmental Assessment Agency), Den Haag.

van Grinsven H.J.M., van Dam J.D., Lesschen J.P., Timmers M.H.G., Velthof G.L., Lassaletta L., 2018. Reducing external costs of nitrogen pollution by relocation of pig production between regions in the European Union. Reg. Environ. Change. 18, 2403-2415. https://doi.org/10.1007/s10113-018-1335-5.

Veldman K.T., Mevius D.J., Wit B., Pelt W.v., Heederik D., 2016. MARAN 2016: Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands in 2015. Central Veterinary Institute of Wageningen University and Research Centre, Food and Consumer Product Safety Authority (NVWA), National Insititute for Public Health and the Environment (RIVM), Netherlands Veterinary Medicines Authority (SDa),.

Verschoor A., Zwartkruis J., Hoogsteen M., Scheepmaken J., de Jong F., van der Knaap Y., et al., 2019. Tussenevaluatie van de nota Gezonde Groei, Duurzame Oogst. Deelrapport Milieu [Interim evaluation of the memorandum Health Growth, Sustainable Harvest. Subreport Environment] RIVM (National Institute for Public Health and the Environment), Bilthoven.

Vink M., Boezeman D., 2018. Naar een wenkend perspectief voor de Nederlandse Landbouw. Voorwaarden voor verandering [Towards an inviting perspective for the Dutch agricultural sector. Requirements for change]. PBL (Netherlands Environmental Assessment Agency), Den Haag.

von Mutius E., 2016. The microbial environment and its influence on asthma prevention in early life. J. Allergy Clin. Immunol. 137, 680-689. https://doi.org/10.1016/j.jaci.2015.12.1301

von Mutius E., Vercelli D., 2010. Farm living: effects on childhood asthma and allergy. Nature Reviews Immunology. 10, 861. https://doi.org/10.1038/nri2871.

Wang J., Liu Q., Hou Y., Qin W., Lesschen J.P., Zhang F., et al., 2018. International trade of animal feed: its relationships with livestock density and N and P balances at country level. Nutr. Cycl. Agroecosys. 110, 197-211. https://doi.org/10.1007/s10705-017-9885-3.

Werkgroep Infectiepreventie, 2012. WIP-richtlijn MRSA [ZKH] [Hospital guidelines for MRSA of the working group for infection prevention]. http://www.rivm.nl/Documenten_en_publicaties/Professioneel_Praktisch/Richtlijnen/Infectieziekten/WIP_Richtlijnen/WIP_Richtlijnen/Ziekenhuizen/WIP_richtlijn_MRSA_ZKH (accessed 09/15 2017).

Westhoek H., Rood T., Van den Berg M., Janse J., Nijdam D., Reudink M., et al., 2011. The protein puzzle. 500166001. PBL (Netherlands Environmental Assessment Agency), Den Haag, The Netherlands.

WHO, 2017a. Annual review of diseases prioritized under the Research and Development Blueprint. Workshop on Prioritization of Pathogens.

WHO, 2017b. Pandemic influenza risk management: a WHO guide to inform and harmonize national and international pandemic preparedness and response. World Health Organization, Geneva.

Winkel A., van Riel J.W., van Emous R.A., Aarnink A.J., Groot Koerkamp P.W., Ogink N.W., 2016. Abatement of particulate matter emission from experimental aviary housings for laying hens by spraying rapeseed oil. Poultry science. 95, 2836-2848. https://doi.org/10.3382/ps/pew261

Chapter 3

Risk of pneumonia among residents living near goat and poultry farms during 2014-2016

Pim M. Post[abc], Lenny Hogerwerf[a], Anke Huss[b], Ronald Petie[d],
Gert Jan Boender[d], Christos Baliatsas[c], Erik Lebret[ab], Dick Heederik[b],
Thomas J. Hagenaars[d], C. Joris IJzermans[c], Lidwien A.M. Smit[b]

[a] *National Institute for Public Health and the Environment, Bilthoven, the Netherlands;*
[b] *Institute for Risk Assessment Sciences, Utrecht University, Utrecht, the Netherlands;*
[c] *Netherlands Institute for Health Services Research, Utrecht, the Netherlands;*
[d] *Wageningen Bioveterinary Research, Lelystad, the Netherlands*

Published in *PLoS ONE* (2019), 14 (10): e0223601
DOI:10.1371/journal.pone.0223601

ABSTRACT

In the Netherlands, an association was found between the prevalence of pneumonia and living near goat and poultry farms in 2007-2013. This association then led to regulatory decisions to restrict the building of new goat farms and to reduce emissions of poultry farms. Confirmation of these results, however, is required because the period of previous analyses overlapped a Q-fever epidemic in 2007-2010. To confirm the association, we performed a population-based study during 2014-2016 based on general practitioner (GP) data. Electronic medical records of 90,183 persons were used to analyze the association between pneumonia and the population living in the proximity (within 500-2000 m distance) of goat and poultry farms. Data were analyzed with three types of logistic regression (with and without GP practice as a random intercept and with stratified analyses per GP practice) and a kernel model to discern the influence of different statistical methods on the outcomes. In all regression analyses involving adults, a statistically significant association between pneumonia and residence within 500 meters of goat farms was found (odds ratio [OR] range over all analyses types: 1.33-1.60), with a decreasing OR for increasing distances. In kernel analyses (including all ages), a population-attributable risk between 6.0 and 7.8% was found for a distance of 2000 meters in 2014-2016. The associations were consistent across all years and robust for mutual adjustment for proximity to other animals and for several other sensitivity analyses. However, associations with proximity to poultry farms are not supported by the present study. As the causes of the elevated pneumonia incidence in persons living close to goat farms remain unknown, further research into potential mechanisms is required for adequate prevention.

1 Introduction

The evidence regarding the influence of livestock farming on the health of persons living near such farms is mounting (Casey et al., 2015; Douglas et al., 2018; Maassen et al., 2016; Smit and Heederik, 2017; van Dijk et al., 2017). Several health effects have been reported, ranging from an increased risk for zoonotic infections like Q fever and methicillin resistant *Staphylococcus aureus* (MRSA) to a lower prevalence of asthma and chronic obstructive pulmonary disease (COPD) (Borlée et al., 2015; Casey et al., 2015; Smit and Heederik, 2017; Smit et al., 2014). Conversely, persons that have COPD and live close to livestock farms were found to have increased COPD exacerbation (Borlée et al., 2015; van Dijk et al., 2016). Recently, an increased risk of pneumonia was observed in the Netherlands among residents living close to goat and poultry farms (Freidl et al., 2017; Kalkowska et al., 2018; Smit et al., 2017; Smit et al., 2012).

The evidence for this association resulted from several analyses on a large dataset of electronic medical records (2007-2013) of general practitioners' (GP) patients living in the Dutch provinces Noord-Brabant and Limburg and on a subset of 2,500 of those patients that participated in a medical examination and completed a questionnaire (Freidl et al., 2017; Kalkowska et al., 2018; Klous et al., 2018; Smit et al., 2017; Smit et al., 2012; van Dijk et al., 2017). In this area, a major outbreak of Q fever, a zoonosis caused by *Coxiella burnetii*, occurred among goats in 2007-2010 (Roest et al., 2011) and had a significant public health impact on the nearby human population. Residential proximity to goat farms was associated with an increased incidence of Q fever-related pneumonia (Smit et al., 2012). In the years after the epidemic, the association between pneumonia and residence close to goat and other livestock farms was examined in several studies, which mostly indicated that the pneumonia incidence was still elevated among those living near goat farms (Freidl et al., 2017; Kalkowska et al., 2018; Klous et al., 2018). Potential causes of such elevation remain unclear and it has no clear trace to a single pathogen, as the evidence that microorganisms other than *C. burnetii* that can both be found in goats and cause pulmonary complications in humans through indirect transmission is limited to case reports (Meijer et al., 2004).

In two studies investigating cases of pneumonia in relation to proximity to goat farms, a significantly elevated incidence of the disease was also found near poultry farms (Kalkowska et al., 2018; Smit et al., 2012). A similar association between pneumonia and proximity to poultry was recently reported in Pennsylvania, USA (Poulsen et al., 2018), yet in two other studies in the Netherlands, those associations were not significant and positive in only some of the analyses (Freidl et al., 2017; van Dijk et al., 2017). The associations found in some of the studies were hypothesized to be caused by organic dust emissions from poultry farms, causing a disruption of the upper respiratory tract microbiome (Poulsen et al., 2018; Smit et al., 2017). Thus, the elevated incidences of pneumonia were not necessarily caused by zoonotic pathogens. Yet, elevations of pneumonia incidence in residents close to goat and poultry farms may not share that cause, as organic dust emissions from poultry housing are generally much higher than dust emissions from goat farms. In addition, goat farms in the Netherlands generally have natural ventilation and no outdoor access for goats. Such housing may affect potential spread of microorganisms differently than poultry housing, which is generally closed, with mechanical ventilation and, increasingly, with techniques to reduce particulate matter and other pollutants. Exceptions to such closed farms are a minority of free-range farms, where laying hens can freely roam outdoors.

Although causal mechanisms remain to be elucidated, the apparent association between pneumonia and proximity to poultry farms has contributed to policy objectives for halving particulate-matter emissions of Dutch poultry farms within 10 years (van Dam and Dijksma, 2017). Furthermore, the apparent association between pneumonia and proximity to goat farms caused most Dutch provinces to temporarily stop issuing building permits for such new and existing farms (ANP, 2018), indicating that a confirmation of results for more recent years is urgent and relevant. Moreover, the data used for previous analyses are from a period partly overlapping the Q-fever epidemic, thus potentially interfering with the associations. Hence, repeating analyses when an outbreak is not occurring is necessary. Therefore, the main aim of this study was to assess the relation between GP diagnoses of pneumonia and several measures of residential proximity to goat and poultry farms in 2014-2016. In addition to focusing on more recent data, we used four types of statistical analyses that were previously used in separate studies to assess the possible influence of these methods on the outcomes.

2 Materials and methods

2.1 Study design and study population

A population-based study was performed to analyze the relation between GP diagnoses of pneumonia and living near goat and poultry farms in 2014-2016. The study was conducted in the region where previous research provided evidence of an association between pneumonia and residence close to goat and poultry farms (Borlée et al., 2019; Freidl et al., 2017; Heederik and Yzermans, 2011; Kalkowska et al., 2018; Maassen et al., 2016; Smit et al., 2012; van Dijk et al., 2017). Using the same registration criteria for participation as previous studies (Smit et al., 2012), we collected data from 94,295 unique patients registered with 23 GP practices in the area at the time of the study. The selection of these practices, which were all in towns and villages with less than 30,000 inhabitants, varied slightly from earlier studies, because over time, different practices fulfilled quality criteria. Persons living at the same address as a farm location with any livestock (n= 4,081; 4.3%) were excluded from analyses, because these persons were assumed to have an occupational exposure, rather than a residential exposure that is the focus of this study. Persons working on a farm but not living there could not be excluded because occupational data was unavailable, but the percentage of persons excluded was higher than the 1% to 2% of persons working in the agricultural sector in the provinces of Noord-Brabant and Limburg, which comprised the study area. Patients who had multiple home addresses (n=31) were also excluded. Finally, 90,183 residents were included in this study: 73,510 adults (older than 18 years in 2016) and 16,673 children (18 years or younger in 2016).

2.2 Pneumonia data

The health outcome used in this study was defined as the occurrence of at least one event of GP diagnosed pneumonia during 2014-2016, coded as R81 according to the International Classification of Primary Care (ICPC) (Lamberts and Wood, 1987). The classification does not allow further specification of R81 to diseases related to pneumonia, like Q fever, with the exception of R81.01 (*Legionella*). In addition, GP diagnoses are generally based on clinical criteria only. Data on pneumonia diagnoses and patients' age and gender were collected from electronic medical records (EMR). The data provide a complete picture of the registered health status of patients, since in the Netherlands each individual is required to register with one general practice, and GPs then operate as gatekeepers for more specialized health care, usually receiving notification of hospitalization.

2.3 Exposure variables

The proximity of residents to goat farms (n=95, S1 Table) and poultry farms (n=881, S1 Table) was quantified in terms of the distance to the nearest farm (m) and the presence or absence of a farm within buffers of 500, 1000, 1500 or 2000 meters from a resident's home address. Proximity to farms with cattle, pigs, sheep and mink, was also quantified (S1 Table) for use in specific analyses, which are detailed below. Patients' home addresses were obtained from the EMR data and geocoded with high-resolution Dutch cadastral data from 2015 in which geocodes generally represented coordinates that fell within the building footprint. Farm location and additional information regarding the animal type and numbers were collected from provincial databases on compulsory environmental licenses in 2015 (Bestand Veehouderij Bedrijven of Noord-Brabant and Limburg). Goat and poultry farms, as well as other types of farms, were defined on the basis of definitions described in S1 Table. Exposure variables were calculated using the sf-package in R (Pebesma et al., 2018).

In some analyses, a distinction was made between chicken farms and other types of poultry farms. Among chicken farms, a further distinction was made between farms with broilers, where chickens are usually raised in all-in all-out systems in 5 to 10 weeks, and those with laying hens or parent stock (S1 Table), since different farming practices may lead to different pollutant emissions.

2.4 Ethical aspects

The protocol used for the study (number 13/533) has been approved by the Medical Ethical Committee of the University Medical Centre of Utrecht, and the NIVEL Primary Care Database (PCD) complies with the regulations of the Dutch Data Protection Authority and the Dutch law regarding use of health data for epidemiological research purposes (Dutch Civil Law, Article 7:458). According to this law, neither medical ethical approval nor informed consent is required to use EMR data for observational studies on the condition that it contains no directly identifiable data. Medical information and address records were kept separate at all times by use of a Trusted Third Party (Stichting Informatie Voorziening Zorg, Houten).

2.5 Statistical analyses

To evaluate exposure-response relationships between pneumonia and the presence of a specific animal farm within a given distance, we used four different types of statistical analyses that are referred to as single-level and multilevel regression analyses, regression meta-analyses and kernel analyses.

2.5.1 Single-level analyses

Single-level logistic regression analyses were performed with the presence of a livestock farm within a buffer of 500, 1000, 1500 or 2000 meters as an exposure proxy, with the glm function in R (R Core Team). The analyses focused on goat and poultry farms, with for poultry a further specification to chicken farms, farms with laying hens or parental stock, broiler farms and farms with other poultry. In addition to these regression analyses with buffers, the effect of the distance to the nearest farm was analyzed by fixed-distance intervals of 500 meters (max 2000 m) in logistic regression analyses. The association between pneumonia and distance to a farm was also visualized in spline plots through generalized additive modeling, with the gam function of the mgcv package in R (Wood, 2018). Analyses were performed separately for adults and children; all analyses were adjusted for age (linear) and gender and performed for individual years, as well as for the entire period 2014-2016.

2.5.2 Multilevel and meta-analyses

Multilevel analyses and meta-analyses were performed to account for potential differences in registration practices between general practitioners. In multilevel regression analyses (glmer function of the lme4 package (Bates et al., 2017)), GP practice was included as a random intercept and for the remaining part resembled single-level logistic regression analyses. Both multilevel and single-level analyses were performed because although the multilevel analyses may account for differences in the registration of pneumonia between GP practices, they may also lead to over-adjustment of the effect of proximity to livestock farms, as farm types may be clustered close to some GP practices.

Meta-analyses were performed to explore potential differences between GP practices. For each GP practice, logistic regression analyses were performed and the results of these separate analyses were combined in a random effects meta-analysis, via the rma function of the metafor package (Viechtbauer, 2010), including only those practices for which there was sufficient exposure; assumed to be indicated by standard errors less than 10.

2.5.3 Kernel model

In addition to regression models, a spatial kernel model was used as a complementary approach for analyzing the associations between pneumonia and proximity to livestock farms. A kernel model effectively accounts for the influence of multiple farms because the distance between a home address and all surrounding farms is considered in the analysis. Also, a kernel model provides a relatively simple way to determine a population attributable risk (PAR) (Kalkowska et al., 2018; Smit et al., 2017), which makes results comparable. The model is based on assigning to each type of livestock farm a distance-dependent probability of causing pneumonia in a resident living in the vicinity. This probability is then compared with a uniform background probability through a likelihood ratio test. Further methodological background can be found in Kalkowska et al. (Kalkowska et al., 2018) and Smit et al. (Smit et al., 2017).

For the current application, the kernel model was defined on the basis of fixed distances that varied between 500 and 2000 meters with increments of 500 meters. The model was applied to cases of pneumonia in all age groups, without distinguishing between adults and children. In measuring exposure, we delineated six farm types: cattle, goats, mink, pigs, poultry and sheep. For each year, each farm type that gave $\alpha < 0.05$ in the likelihood ratio test for at least one distance was included in a multivariate kernel model, with independent hazards for proximity to each type of farm. This model provided an indication of the risk increase of living within a certain distance of a livestock farm of a specific type, as well as the PAR.

2.5.4 Sensitivity analyses

Three types of sensitivity analyses were performed. First, the effect of changing several assumptions regarding selection criteria and model formulation were tested. In the second type of sensitivity analysis, the effect of leaving out single GP practices from the analyses was assessed. Third, the effect of mutual adjustment for multiple farm types (goats, poultry, pigs, cattle, mink and sheep) in regression analyses was assessed.

3 Results

3.1 Study population

In total, 3,610 (4.0%, 3,079 adults, 531 children) residents had at least one GP diagnosed pneumonia episode during 2014-2016 (incidence per 1,000: 15.9 in 2014, 20.2 in 2015, 18.7 in 2016). Among adults, the odds of being diagnosed with pneumonia increased with age (OR 1.05 per year; 95% CI 1.04-1.05; S2 Table), whereas among children this association was reversed (OR 0.90 per year, 95% CI 0.88-0.91; S2 Table). Females were less likely to be diagnosed with pneumonia than males (female adults: OR 0.90, 95% CI 0.84-0.97, female children: OR 0.79, 95% CI 0.66-0.94; S2 Table).

3.2 Single-level analyses

In single-level logistic regression analyses, the association between pneumonia and residence within specified distances to goat farms among adults was statistically significant for all buffers and decreased from 1.60 (95% CI 1.25-2.03) for the presence of a goat farm within 500 meters (reference >500 m) to 1.17 (95% CI 1.09-1.27) for a buffer of 2000 meters (reference >2000 m; Table 1). Pneumonia risk decreased with increasing distance from goat farms until approximately 4 km (Figure 1A, S3 Table). The association between pneumonia and living within a specified distance from any poultry farm was not statistically significant and relatively close to 1 for any buffer in single-level analyses (Table 1); the association did not significantly decrease with distance in spline analyses (not shown). However, odds ratios were higher for proximity to chicken farms and significantly higher than 1 for the presence of broiler farms within buffers of 1500 and 2000 meters (Table 1), with a decreasing pneumonia risk for increasing distances from chicken or broiler farms (Table S3). Inverse associations with poultry other than chickens were found (Table 1).

Table 1. Associations in adults, between the occurrence of a registered pneumonia episode in 2014-2016 and the presence of goat and poultry farms within buffers from the home address (odds ratios, 95% confidence interval).

Buffer	500 meters	1000 meters	1500 meters	2000 meters
Goat farm				
n=73,510[a]	1.51%	8.47%	19.05%	32.90%
Single-level[b]	1.60 (1.25-2.03)***	1.36 (1.21-1.53)***	1.25 (1.14-1.37)***	1.17 (1.09-1.27)***
Multilevel[c]	1.33 (1.03-1.71)*	1.11 (0.97-1.28).	1.08 (0.97-1.20)	1.07 (0.98-1.18)
Meta-analysis[d]	1.58 (1.10-2.27)*	1.22 (0.97-1.55).	1.08 (0.96-1.22)	1.07 (0.97-1.18)
Poultry farm				
n=73,510[a]	10.78%	46.76%	79.79%	92.22%
Single-level[b]	1.03 (0.92-1.16)	1.02 (0.95-1.10)	1.00 (0.91-1.09)	0.95 (0.83-1.09)
Multilevel[c]	1.01 (0.89-1.15)	0.98 (0.90-1.07)	1.02 (0.92-1.14)	0.91 (0.77-1.06)
Meta-analysis[d]	1.04 (0.92-1.18)	0.99 (0.89-1.10)	1.00 (0.88-1.14)	0.87 (0.73-1.02).
Chicken farm				
n=73,510[a]	10.07%	43.13%	74.37%	90.62%
Single-level[b]	1.06 (0.94-1.20)	1.05 (0.97-1.13)	1.06 (0.97-1.15)	1.04 (0.92-1.18)
Multilevel[c]	1.02 (0.90-1.16)	0.98 (0.90-1.07)	1.03 (0.94-1.14)	0.96 (0.82-1.12)
Meta-analysis[d]	1.05 (0.92-1.20)	0.99 (0.89-1.10)	1.02 (0.91-1.15)	0.91 (0.76-1.08)

Farm with laying hens or parent stock				
n=73,510[a]	8.08%	36.73%	62.29%	83.65%
Single-level[b]	1.08 (0.94-1.23)	1.06 (0.98-1.14)	1.01 (0.94-1.09)	0.95 (0.86-1.05)
Multilevel[c]	1.02 (0.88-1.18)	0.98 (0.90-1.08)	1.02 (0.93-1.11)	0.99 (0.88-1.11)
Meta-analysis[d]	1.08 (0.93-1.25)	1.01 (0.90-1.14)	1.02 (0.93-1.12)	0.97 (0.86-1.10)
Farm with broilers				
n=73,510[a]	2.51%	12.19%	33.60%	52.55%
Single-level[b]	1.11 (0.87-1.40)	1.11 (0.99-1.24).	1.13 (1.04-1.21)**	1.11 (1.03-1.20)**
Multilevel[c]	1.12 (0.88-1.41)	1.03 (0.92-1.15)	0.98 (0.90-1.07)	0.98 (0.90-1.07)
Meta-analysis[d]	1.23 (0.96-1.56).	1.04 (0.93-1.16)	0.96 (0.86-1.07)	0.96 (0.87-1.06)
Farm with other poultry				
n=73,510[a]	0.63%	5.27%	14.54%	24.34%
Single-level[b]	0.75 (0.42-1.24)	0.86 (0.71-1.03).	0.82 (0.73-0.92)***	0.90 (0.82-0.98)*
Multilevel[c]	0.88 (0.51-1.51)	0.98 (0.81-1.19)	0.93 (0.82-1.06)	1.10 (0.97-1.23).
Meta-analysis[d]	1.13 (0.66-1.95)	1.05 (0.86-1.28)	0.96 (0.84-1.09)	1.13 (0.99-1.29).

Each odds ratio indicates the outcome of a different regression model.

.p<0.15, *p<0.05, **p<0.01, ***p<0.001

[a] Percentages indicate the percentage of residents living within a buffer

[b] adjusted for age (linear) and gender

[c] adjusted for age (linear), gender and including GP practice as random intercept

[d] meta-analysis of logistic regression estimates (adjusted for age and gender) for individual GP practices

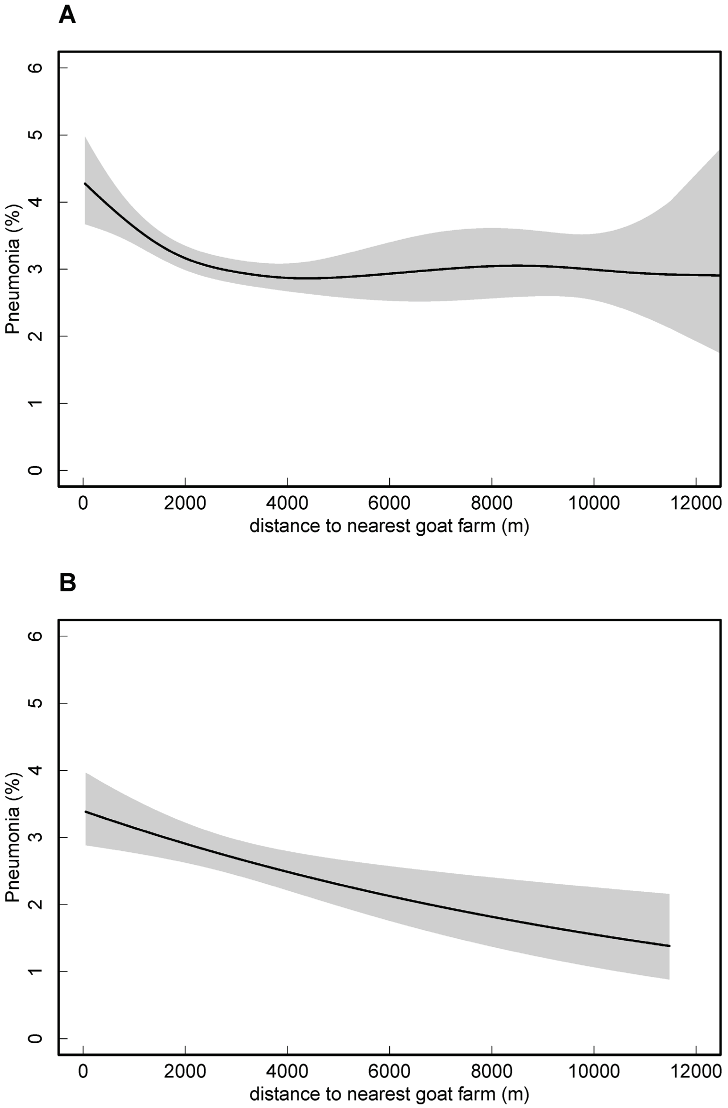


Figure 1. Spline plot for the association between cases of pneumonia and distance to nearest goat farm.

The spline is based on generalized additive modelling, with the gam-function (mgcv package R (Wood, 2018)). Panel A shows results for adults (n=73,510), and panel B shows results for children (n=16,673). The associations are adjusted for age (linear) and gender; the shaded area is the 95% confidence band. For adults, p (approximate probability that the slope equals 0) < 0.001, for children p = 0.002.

3.3 Multilevel analyses and meta-analyses

Accounting for potential differences between GP practices yielded a similar pattern regarding the associations with goat farms among adults in multilevel analyses (OR 500 m: 1.33, 95% CI 1.03-1.71; OR 2000 m: 1.07, 95% CI 0.98-1.18) and in meta-analyses (OR 500 m: 1.58, 95% CI 1.10-2.27; OR 2000 m: 1.07, 95% CI 0.97-1.18), although these analyses showed statistically significant ORs only for buffers of 500 meters (Table 1). Moreover, for this distance, a positive association was found in 6 out of the 7 GP practices (I^2 = 28.7%, Figure 2). For 1000 meters, a positive association was found for 11 out of 17 GP practices (I^2 = 44.2%), but for longer distances, less than half (1500 m; I^2 = 7.9%) or half (2000 m; I^2 = 1.1%) the practices had a positive association (Figure 2). For analyses regarding the proximity of poultry within 500 meters, all analyses, except those related to poultry other than chickens, showed results similar to those of single-level analyses. However, less consistent results were found for longer distances; significantly elevated ORs in single-level analyses were close to unity in multilevel and meta-analyses (Table 1), while I^2 ranged from 0 to 25.5%, indicating low heterogeneity.

3.4 Kernel model

Kernel analyses showed positive associations between pneumonia and proximity to goat farms for 2014, 2015 and 2016, with a risk increase ranging from 23.6% to 31.9%, a PAR ranging from 6.0 to 7.2% and a distance of 2000 meters providing the highest likelihood for each year (Table 2). Regarding the association between pneumonia and proximity to poultry farms, only for 2014, a (significant but small) risk increase was found. No significant risk increase was found for 2015 and 2016. This meant that in the multivariate kernel analyses, poultry farms were included in only 2014. Multivariate kernel analyses also included sheep farms for 2014 and 2015 and cattle farms for all years, since significant associations were found in univariate kernel analyses for these farm types (S4 Table).

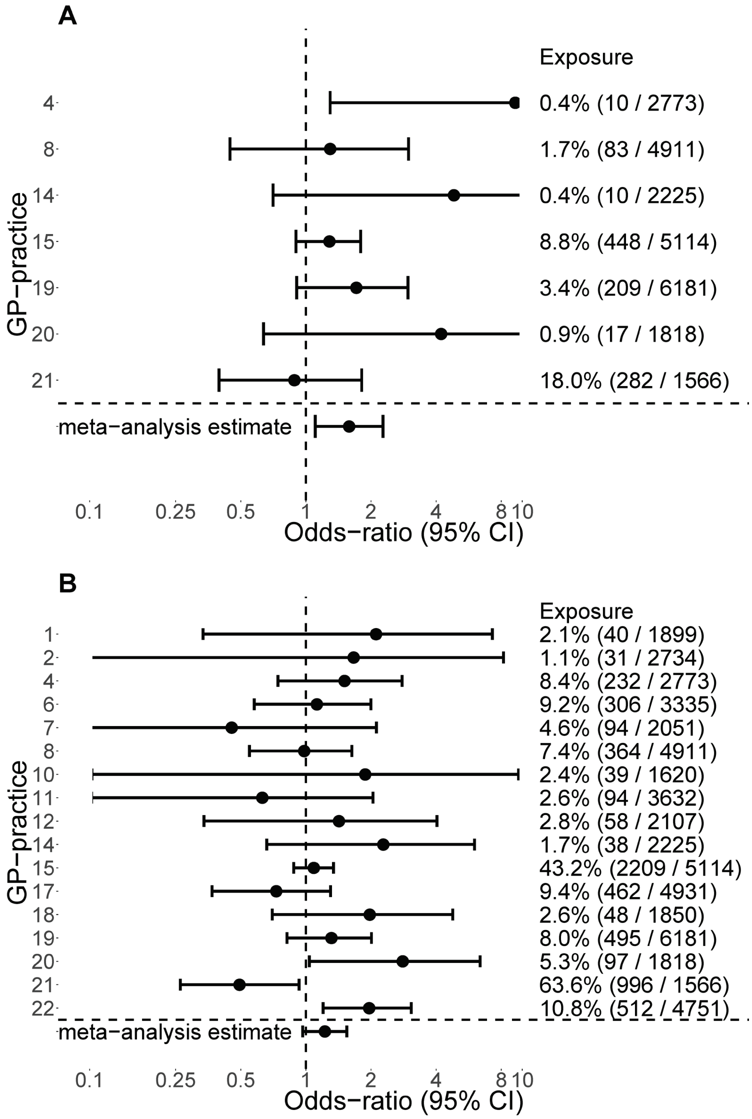
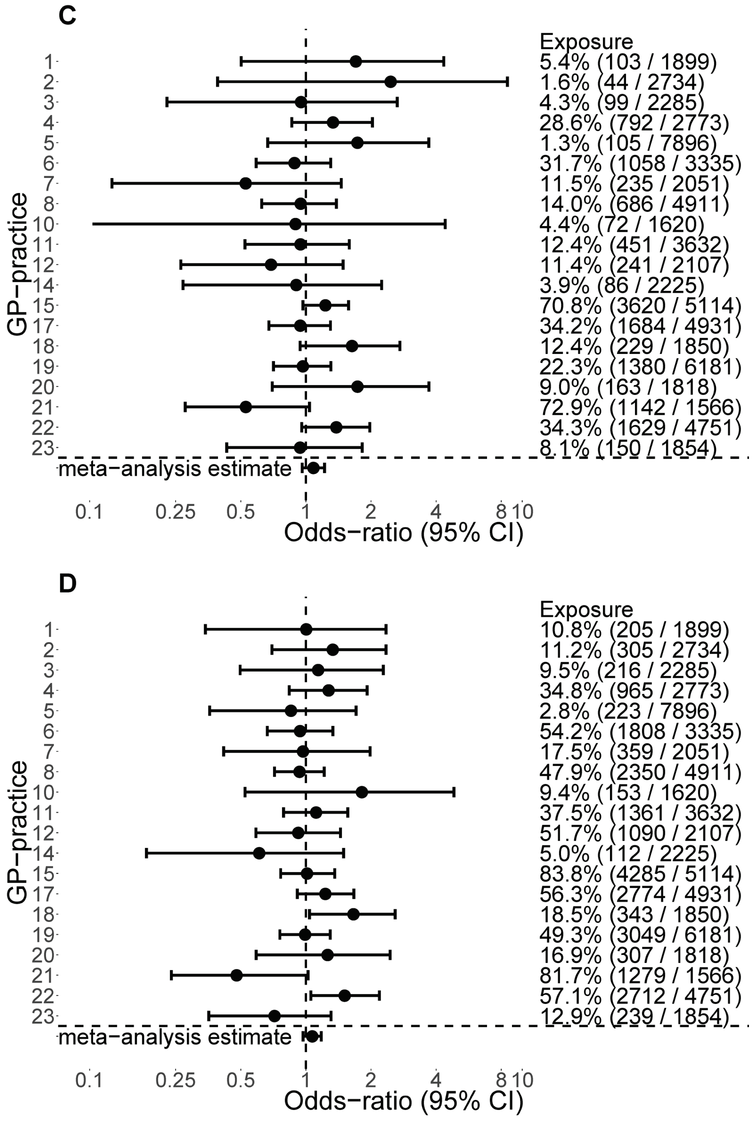


Figure 2. Forest plots for the association between GP-diagnosed pneumonia and the proximity of adults to goat farms.



Estimates for each GP practice and meta-analysis estimate are expressed as odds ratios for buffers of 500 meters (panel A), 1000 meters (panel B), 1500 meters (panel C) and 2000 meters (panel D), adjusted for age of the patients (linear) and gender. Estimates for GP practices with no individuals living within a buffer from a goat farm or with standard errors higher than 10 (indicating a low number of residents living within buffer) are not shown. **Logarithmic scale:** confidence bounds are cut off at 0.1 and 10. The meta-analysis estimates are also shown in Table 1.

Table 2. Results of multivariate kernel analyses.

Year	2014	2015	2016
Goat farms			
Distance (m)	2000	2000	2000
Risk increase (%)	31.9	23.6	25.4
PAR[1] (%)	7.8	6.0	7.2
Poultry farms			
Distance (m)	1000	Not applicable	Not applicable
Risk increase (%)	0.6	Not applicable	Not applicable
PAR[a] (%)	0.4	Not applicable	Not applicable

[a] Population attributable risk

Only the outcomes for poultry and goats are listed; for further details see S4 Table. 'Distance (m)' is the distance range for which the best fit in the individual farm-type analysis for the given year was found. The distances used in this multivariate model were the distances that gave the highest likelihood for that specific farm type in that year. 'Risk increase' denotes the average increase of the pneumonia risk for individuals living within the distance range of one farm of the given type and is calculated as described in Kalkowska et al. (2018).

3.5 Individual years

The association between pneumonia and residence near goat farms was consistent across 2014, 2015 and 2016 (Table 2, S5 Table). For pneumonia among adults living close to a poultry farm, an increased risk was found for 2014 in kernel analyses, but not in other years (Table 2). For 2014, pneumonia in adults was positively associated ($p<0.05$) with broiler farms as well, for several distances in single level analyses, and for adults living within 500 meters in multilevel and meta-analyses (S5 Table).

3.6 Results for children

ORs for the association between pneumonia among children and proximity to goat farms were similar to those for adults in single-level analyses and meta-analyses, but lower in multilevel analyses (Table 3). Pneumonia risk monotonically decreased with increasing distance (Figure 1B). For proximity to most types of poultry farms, the pattern among children with pneumonia was similar to that among adults; although, in general, associations were weaker than for adults, and negative, rather than positive, associations were found for proximity to broiler farms (Table 3).

3.7 Sensitivity analyses

In the first type of sensitivity analyses, change of assumptions regarding the selection of persons and model specification generally led to a change in ORs for proximity to goat and poultry farms of less than 10% (S6,S7 Table). Specification of a model with the number of animals in a buffer as an exposure variable, rather than presence or absence of a farm type, gave similar patterns for both goats and poultry (data not shown). In the second type of sensitivity analyses, in which single GP practices were excluded from the analyses, ORs related to proximity to goat farms could be affected by more than 25% in single-level analyses and meta-analyses, but were less affected in multilevel analyses (S8 Table); the direction of the association was not affected. In analyses in which the proximity to different types of animals were mutually adjusted for each other, the effect sizes were slightly affected, but results still showed clear positive associations for proximity to goat farms and no associations for proximity to poultry farms (S9 Table). In these and univariate analyses, significantly positive and negative associations between pneumonia and the proximity to farms other than goat or poultry farms were found (S3,S5,S9 Table). A positive association was shown with proximity to sheep farms, albeit less strong when compared to associations with proximity to goat farms. For cattle, pigs and mink, the positive and negative associations were generally less consistent over time between children and adults or between types of analyses, compared to associations with proximity to goat farms (S3,S5,S9 Table).

Table 3. Associations for children, between the occurrence of a registered pneumonia episode in 2014-2016 and the presence of goat and poultry farms within buffers from the home address (odds ratios, 95% confidence interval).

Buffer	500 meters	1000 meters	1500 meters	2000 meters
Goat farm				
n=16,673[a]	1.59%	9.73%	21.15%	34.80%
Single-level[b]	1.61 (0.85-2.78).	1.29 (0.97-1.67).	1.27 (1.03-1.55)*	1.15 (0.96-1.37).
Multilevel[c]	1.06 (0.58-1.95)	0.94 (0.69-1.29)	1.07 (0.84-1.37)	0.88 (0.70-1.10)
Meta-analysis[d]	1.56 (0.67-3.63)	1.19 (0.83-1.70)	1.27 (0.90-1.79)	0.94 (0.71-1.23)
Poultry farm				
n=16,673[a]	10.53%	47.86%	80.47%	93.55%
Single-level[b]	0.98 (0.72-1.29)	1.12 (0.94-1.33)	0.90 (0.73-1.11)	1.12 (0.79-1.67)
Multilevel[c]	0.92 (0.68-1.25)	0.98 (0.80-1.20)	0.78 (0.62-1.00)*	0.85 (0.57-1.28)
Meta-analysis[d]	1.10 (0.80-1.51)	0.93 (0.75-1.15)	0.69 (0.53-0.89)**	0.92 (0.86-0.98)**
Chicken farm				
n=16,673[a]	9.88%	43.63%	74.27%	92.07%
Single-level[b]	0.96 (0.71-1.28)	1.20 (1.00-1.42)*	1.00 (0.82-1.23)	1.19 (0.85-1.71)
Multilevel[c]	0.88 (0.65-1.21)	0.97 (0.80-1.19)	0.77 (0.61-0.96)*	0.83 (0.56-1.23)
Meta-analysis[d]	1.15 (0.82-1.61)	0.91 (0.73-1.13)	0.69 (0.54-0.87)**	0.92 (0.86-0.98)**
Farm with laying hens or parent stock				
n=16,673[a]	7.72%	37.47%	62.26%	85.14%
Single-level[b]	1.07 (0.77-1.46)	1.23 (1.03-1.47)*	1.18 (0.98-1.41).	1.26 (0.97-1.66).
Multilevel[c]	0.92 (0.65-1.29)	1.00 (0.81-1.23)	0.99 (0.80-1.22)	1.13 (0.83-1.52)
Meta-analysis[d]	1.34 (0.87-2.06)	0.96 (0.77-1.20)	0.93 (0.74-1.17)	0.83 (0.48-1.43)

Farm with broilers				
n=16,673[a]	2.64%	12.54%	34.35%	54.63%
Single-level[b]	0.60 (0.28-1.09).	0.92 (0.70-1.19)	0.85 (0.70-1.02).	1.01 (0.85-1.20)
Multilevel[c]	0.69 (0.35-1.36)	0.85 (0.64-1.12)	0.67 (0.54-0.82)***	0.77 (0.63-0.96)*
Meta-analysis[d]	1.65 (0.79-3.44)	0.96 (0.71-1.29)	0.67 (0.54-0.84)***	0.72 (0.57-0.90)**
Farm with other poultry				
n=16,673[a]	0.49%	5.28%	13.36%	22.77%
Single-level[b]	1.05 (0.26-2.84)	0.81 (0.52-1.21)	0.70 (0.52-0.92)*	0.59 (0.46-0.75)***
Multilevel[c]	1.41 (0.44-4.58)	1.25 (0.79-1.96)	1.07 (0.77-1.51)	0.85 (0.62-1.17)
Meta-analysis[d]	3.33 (0.92-12.02).	1.47 (0.89-2.45).	1.33 (0.79-2.25)	1.23 (0.65-2.32)

Each odds ratio indicates the outcome of a different regression model.

.p<0.15, *p<0.05, **p<0.01, ***p<0.001

[a] Percentages indicate the percentage of residents living within a buffer

[b] adjusted for age (linear) and gender

[c] adjusted for age (linear), gender and including GP practice as random intercept

[d] meta-analysis of logistic regression estimates (adjusted for age and gender) for individual GP practices

4 Discussion

In this study, we found a consistent association between proximity to goat farms and pneumonia, with an estimated PAR between 6.0 and 7.8% during 2014-2016. This estimate corresponded to about 1.2 to 1.3 pneumonia cases per 1000 residents in the study population that were attributable to living in the vicinity of goat farms, with the total incidence between 15.9 and 20.2 cases. Results thus confirm observations during 2009-2013 (Freidl et al., 2017; Kalkowska et al., 2018; Klous et al., 2018; Smit et al., 2012). Multilevel regression analyses and regression meta-analyses generally showed patterns similar to single-level regression analyses, but odds ratios were closer to unity (Table 1). This smaller effect size may be explained by the lower exposure contrast associated with the random-effect term in the multilevel analyses and with the stratification of the data by GP practice for the meta-analyses. The significantly positive association in the multilevel analyses and the association with several independent GP practices, which resulted in limited heterogeneity, strongly indicate that outcomes in single-level analyses were not driven by differences in registration practices between general practitioners. Furthermore, results were only slightly sensitive to adjustment for proximity to other types of animals and several alternative assumptions.

The indications for an association between pneumonia and proximity to poultry farms are weak, with no significant associations in most analyses. In previous studies in the Netherlands that found an association, the increased risk of pneumonia due to proximity to poultry farms was generally lower than that due to proximity to goat farms (Kalkowska et al., 2018; Smit et al., 2012). In the current study, the size of the association with poultry farms was even smaller, with only a small but significant association among all age groups in kernel analyses in 2014. Also in 2014, associations with broiler farms were significantly positive in regression analyses among adults, but not significant and in most analyses negative among children. The results may thus reflect disappearance of an effect, but they may also indicate a weak effect or a chance finding, as associations in two other studies in the Netherlands were not significant and positive in only some of the analyses (Freidl et al., 2017; van Dijk et al., 2017). Methodological differences are less likely to explain the variations in results, because previous kernel analyses differ from those in this study only in the use of older data on health outcomes and farm locations (Kalkowska et al., 2018). Nevertheless, a study in Pennsylvania, USA, where farming practices and rural conditions may differ from those in the Netherlands, found an association between poultry-farm proximity and community-acquired pneumonia (Poulsen et al., 2018).

Results for children generally showed similar patterns compared to those for adults. Yet, contrasting results were found for some analyses, particularly regarding broilers, which are difficult to explain. Moreover, ORs for children generally had wider CIs and limited statistical significance for shorter distances than those for adults, likely due to the smaller study population. Despite similar patterns, the spline plots suggest that the risk of pneumonia for children is increased for longer distances from goat farms than the risk for adults, but such a difference is not directly supported by results from analyses on distance intervals (S3 Table).

Single-level analyses, multilevel analyses and meta-analyses were used to account for the trade-off between bias related to potential differences in reporting between GPs and the limited exposure contrast among patients registered with the same GP. This trade-off cannot be resolved by any individual analysis for this study, but the combination of analyses indicate that results were not driven by differences in reporting between GPs or a limited exposure contrast. The resemblance of results for single-level and multilevel analyses regarding an association with goat farms was not observed in previous studies regarding 2007-2013. Over this period, in one study a multilevel model was used to analyze the association between pneumonia and the presence of a goat farm within 500 meters (van Dijk et al., 2017). Results of this study did not show the positive association found in single-level analyses for the same exposure variable (Freidl et al., 2017; Klous et al., 2018; Smit et al., 2012), yet the studies differed in several other aspects besides the multilevel structure.

Although this study suggests that residents living near goat farms may be at increased risk for pneumonia, the causes of this association remain unknown. Pneumonia is the main presentation of human Q fever. It is unlikely that Q fever is the cause of the currently found association because goats are vaccinated against *C. burnetii,* and, since 2013, the reported incidence of Q fever has been the same as before the epidemic of 2007-2010 (with fewer than 30 notified cases per year compared to several thousand during 2009, the peak year of the outbreak) (Hogerwerf et al., 2011). For associations with poultry farms, a relationship to particulate matter emissions from these farms has been hypothesized (Poulsen et al., 2018; Smit et al., 2017). However, this hypothesis is unlikely to explain the association with goat farms since these emissions from goat farms are generally much lower than those from poultry farms.

The use of EMR data for this study can be considered a strength because it provided a relatively large study population with an accurate epidemiological denominator but also has some limitations. One limitation of EMR is that such data do not provide information on possible confounders such as smoking and socio-economic status, so no adjustment was possible. Data on other diseases that may be a risk factor for pneumonia, like chronic obstructive pulmonary disorder (COPD), are available in EMR data, but these were not included because possible interactions with such health outcomes were out of the scope of this study; such health outcomes have been studied separately (Baliatsas et al., 2017; Baliatsas et al., submitted; van Dijk et al., 2017). Previous research on a smaller population that adjusted for these potential confounders and comorbidities found limited influence on the associations between pneumonia and proximity to goat farms (Freidl et al., 2017). Another potential confounding factor is occupational exposure, although we aimed to reduce that exposure as much as possible by excluding persons assumed to be living on livestock farms. Another factor is the season in which pneumonia was diagnosed, given that atypical microorganisms causing pneumonia may be detected more often outside the winter months (weeks 20-39), whereas during winter (weeks 40-19) typical pathogens are more common (Raeven et al., 2016). EMR data also do not provide information on a potential etiologic agent, since GPs generally base their diagnoses on clinical criteria only, and led it follow by presumptive treatment with antibiotics, which is in line with prevailing national and international professional guidelines, (Mandell et al., 2007; NHG, 2013). The lack of information on a potential etiologic agent, which is usually unavailable in self-reported data and in most of the hospital data, makes inferences about the nature of associations harder.

Another limitation of the study is the limited precision of exposure assessment, because it relies on a proxy of distances between homes and farms, with no information on duration and mode of exposure. This limited precision makes inference of potentially small associations harder. Rather than home location, the proximity of the workplace or school to farms could also indicate exposure, as persons generally spend a large part of their day at such locations. Unfortunately, no information on locations or occupation was available. Nevertheless, a previous study specifically studying mobility close to goat farms, found that such mobility only marginally contributed to pneumonia risk compared to the significantly elevated risk of living near goat farms, which suggests that residential proximity may be an appropriate measure for exposure (Klous et al., 2018). Apart from taking into account the location of persons during their day, exposure assessment could also be improved by considering factors like wind direction (de Rooij et al., 2019; de Rooij et al., 2018), which will be subject to future research. Finally, another weakness regarding exposure assessment is the precision of farm location data; although these data are used for environmental licensing, they may not be fully up to date or contain exact coordinates for all farm locations. Yet, distances to farm locations in this dataset have been used as suitable predictors for measured air pollutants (de Rooij et al., 2019; de Rooij et al., 2018), and potential imprecision should not lead to differential exposure misclassification.

In conclusion, the results of this study suggest that residents within proximity of goat farms have a higher risk for pneumonia of unknown etiology. Further research with molecular microbial techniques and more accurate diagnostic information would help in the understanding of the increased risk of pneumonia near goat farms and the determination of adequate preventive measures. Such research should primarily focus on local residents but because the exposure of goat farmers is generally higher than that of local residents, studies specifically targeting the farmers may provide more information regarding potential etiological agents as well. The present study is less conclusive about an association between pneumonia and the proximity to poultry farms.

Supporting information is available online.

S1 Table. Cut-off points for the minimum number of animals per farm as used for regression analyses, number of farms in the study area (postal codes starting with 52-60) and mean number of animals per farm
https://doi.org/10.1371/journal.pone.0223601.s001

S2 Table. Study population characteristics
https://doi.org/10.1371/journal.pone.0223601.s002

S3 Table. Donut analyses for adults: associations between having had a registered pneumonia-episode in 2014-2016 and the presence of farms within distance intervals (donuts) from an adult's home address (odds ratios, 95% confidence interval)
https://doi.org/10.1371/journal.pone.0223601.s003

S4 Table. Detailed results of kernel analyses. Results for individual and multivariate kernel analyses for community-acquired pneumonia around different farm types by year
https://doi.org/10.1371/journal.pone.0223601.s004

S5 Table. Buffer analyses per year for adults: associations between having had a registered pneumonia episode in 2014, 2015 and 2016 and the presence of farms within buffers from an adult's home address (odds ratios, 95% confidence interval)
https://doi.org/10.1371/journal.pone.0223601.s005

S6 Table. Sensitivity to assumptions among adults
https://doi.org/10.1371/journal.pone.0223601.s006

S7 Table. Sensitivity to assumptions among children
https://doi.org/10.1371/journal.pone.0223601.s007

S8 Table. Leave-one-out analyses for analyses of associations between pneumonia in 2014-2016 and living within 500 meters from a goat farm (odds ratios, 95% confidence interval)
https://doi.org/10.1371/journal.pone.0223601.s008

S9 Table. Mutual adjustment for 6 animal types among adults: associations between having had a registered pneumonia episode in 2014-2016 and the presence of farms within buffers from an adult's home address
https://doi.org/10.1371/journal.pone.0223601.s009

Acknowledgments

Wim van der Hoek (RIVM, The Netherlands) provided useful comments on the manuscript. Jan van de Kassteele and Maarten Schipper (RIVM, The Netherlands) helped to inspect the R-code and provided advice on the use of statistical methods. Eddie Bokkers and Imke de Boer (Wageningen University and Research, Wageningen, The Netherlands) provided useful feedback during the preparation of the analyses. We would like to thank the participating GPs for their cooperation, Elsbeth de Leeuw-Stravers, Eeke Steenaart and Rodrigo Davids for the communication with the GPs and/or their work on data management. We also thank Joke van der Giessen (RIVM, The Netherlands) and Hendrik-Jan Roest (Wageningen Bioveterinary Research, The Netherlands) for their help with funding acquisition. Finally, we thank Sally Ebeling for her help with editing the manuscript.

References

ANP, 2018. Ook Overijssel zet rem op geitenboerderijen [Overijssel puts a stop on goat farms as well]. Binnenlands Bestuur. Sijthoff Media Groep Amsterdam.

Baliatsas C., Borlée F., van Dijk C.E., van der Star B., Zock J.-P., Smit L.A., et al., 2017. 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. 220, 704-710. https://doi.org/10.1016/j.ijheh.2017.02.005.

Baliatsas C., Dückers M.L.A., Smit L.A.M., Heederik D., Yzermans C.J., submitted. Morbidity rates in an area with high livestock density: A registry-based study including different groups of respiratory patients

Bates D., Maechler M., Bolker B., Walker S., Christensen R.H.B., Singmann H., et al., 2017. Linear Mixed-Effects Models using 'Eigen' and S4. https://cran.r-project.org/web/packages/lme4/lme4.pdf (accessed 11/30 2017).

Borlée F., Yzermans C.J., Oostwegel F.S., Schellevis F., Heederik D., Smit L.A., et al., 2019. Attitude toward livestock farming does not influence the earlier observed association between proximity to goat farms and self-reported pneumonia. Environmental Epidemiology. 3, e041. https://doi.org/10.1097/EE9.0000000000000041.

Borlée F., Yzermans C.J., van Dijk C.E., Heederik D., Smit L.A.M., 2015. Increased respiratory symptoms in COPD patients living in the vicinity of livestock farms. Eur. Respir. J. 46, 1605-1614. https://doi.org/10.1183/13993003.00265-2015.

Casey J.A., Kim B.F., Larsen J., Price L.B., Nachman K.E., 2015. Industrial Food Animal Production and Community Health. Curr. Environ. Health Rep. 2, 259-271. https://doi.org/10.1007/s40572-015-0061-0.

de Rooij M.M., Hoek G., Schmitt H., Janse I., Swart A., Maassen C.B., et al., 2019. Insights into Livestock-Related Microbial Concentrations in Air at Residential Level in a Livestock Dense Area. J Environmental science technology. https://doi.org/10.1021/acs.est.8b07029.

de Rooij M.M.T., Heederik D.J.J., van Nunen E.J.H.M., van Schothorst I.J., Maassen C.B.M., Hoek G., et al., 2018. Spatial Variation of Endotoxin Concentrations Measured in Ambient PM(10) in a Livestock-Dense Area: Implementation of a Land-Use Regression Approach. Environmental health perspectives. 126, 017003-017003. https://doi.org/10.1289/EHP2252.

Douglas P., Robertson S., Gay R., Hansell A.L., Gant T.W., 2018. A systematic review of the public health risks of bioaerosols from intensive farming. International Journal of Hygiene and Environmental Health. 221, 134-173. https://doi.org/10.1016/j.ijheh.2017.10.019.

Freidl G.S., Spruijt I.T., Borlee F., Smit L.A., van Gageldonk-Lafeber A.B., Heederik D.J., et al., 2017. Livestock-associated risk factors for pneumonia in an area of intensive animal farming in the Netherlands. PLoS One. 12, e0174796. https://doi.org/10.1371/journal.pone.0174796.

Heederik D., Yzermans C., 2011. Mogelijke effecten van intensieve veehouderij op de gezondheid van omwonenden: onderzoek naar potentiële blootstelling en gezondheidsproblemen [Possible effects of intensive livestock on the health of local residents: a study to investigate potential exposure and health problems]. https://www.rijksoverheid.nl/documenten/rapporten/2011/06/21/mogelijke-effecten-intensieve-veehouderij-op-gezondheid-omwonenden (accessed 13/04 2017).

Hogerwerf L., Van Den Brom R., Roest H.I., Bouma A., Vellema P., Pieterse M., et al., 2011. Reduction of Coxiella burnetii prevalence by vaccination of goats and sheep, The

Netherlands. Emerging infectious diseases. 17, 379. https://doi.org/10.3201/eid1703.101157.

Kalkowska D.A., Boender G.J., Smit L.A.M., Baliatsas C., Yzermans J., Heederik D.J.J., et al., 2018. Associations between pneumonia and residential distance to livestock farms over a five-year period in a large population-based study. PLoS One. 13, e0200813. https://doi.org/10.1371/journal.pone.0200813.

Klous G., Smit L.A.M., Freidl G.S., Borlée F., van der Hoek W., Yzermans C.J., et al., 2018. Pneumonia risk of people living close to goat and poultry farms – Taking GPS derived mobility patterns into account. Environment International. 115, 150-160. https://doi.org/10.1016/j.envint.2018.03.020.

Lamberts H., Wood M., 1987. International classification of primary care: prepared for the World Organisation of national colleges, academies and academic associations of general practitioners/family physicians (WONCA) by the ICPC Working Party. Oxford University Press, Oxford.

Maassen K., Smit L., Wouters I., van Duijkeren E., Janse I., Hagenaars T., et al., 2016. Veehouderij en gezondheid omwonenden [livestock farming and the health of local residents]. RIVM (National Institute for Public Health and the Environment), Bilthoven.

Mandell L.A., Wunderink R.G., Anzueto A., Bartlett J.G., Campbell G.D., Dean N.C., et al., 2007. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. J Clinical infectious diseases. 44, S27-S72. https://doi.org/10.1086/511159.

Meijer A., Brandenburg A., de Vries J., Beentjes J., Roholl P., Dercksen D., 2004. Chlamydophila abortus infection in a pregnant woman associated with indirect contact with infected goats. Eur. J. Clin. Microbiol. Infect. Dis. 23, 487-490. https://doi.org/10.1007/s10096-004-1139-z.

NHG, 2013. NHG-standaard Acuut hoesten. https://www.nhg.org/standaarden/samenvatting/acuut-hoesten (accessed 02/05 2018).

Pebesma E., Bivand R., Cook I., Keitt T., Sumner M., Lovelace R., et al., 2018. Simple Features for R. https://cran.r-project.org/web/packages/sf/sf.pdf (accessed 01/03 2018).

Poulsen M.N., Pollak J., Sills D.L., Casey J.A., Nachman K.E., Cosgrove S.E., et al., 2018. High-density poultry operations and community-acquired pneumonia in Pennsylvania. Environmental Epidemiology. 2, e013. https://doi.org/10.1097/EE9.0000000000000013.

R Core Team, The R Stats Package. https://stat.ethz.ch/R-manual/R-devel/library/stats/html/00Index.html (accessed 05/02 2018).

Raeven V.M., Spoorenberg S.M.C., Boersma W.G., van de Garde E.M.W., Cannegieter S.C., Voorn G.P.P., et al., 2016. Atypical aetiology in patients hospitalised with community-acquired pneumonia is associated with age, gender and season; a data-analysis on four Dutch cohorts. BMC Infect. Dis. 16, 299. https://doi.org/10.1186/s12879-016-1641-9.

Roest H., Tilburg J., Van der Hoek W., Vellema P., Van Zijderveld F., Klaassen C., et al., 2011. The Q fever epidemic in The Netherlands: history, onset, response and reflection. Epidemiol. Infect. 139, 1-12. https://doi.org/10.1017/S0950268810002268.

Smit L.A.M., Boender G.J., De Steenhuijsen Piters W.A.A., Hagenaars T.J., Huijskens E.G.W., Rossen J.W.A., et al., 2017. Increased Risk Of Pneumonia In Residents Living Near Poultry Farms: Does The Upper Respiratory Tract Microbiota Play A Role? Pneumonia. 9, 1-9. https://doi.org/10.1186/s41479-017-0027-0.

Smit L.A.M., Heederik D., 2017. Impacts of Intensive Livestock Production on Human Health in Densely Populated Regions. GeoHealth. 1, 272-277. https://doi.org/10.1002/2017GH000103.

Smit L.A.M., Hooiveld M., van der Sman-de Beer F., Opstal-van Winden A.W.J., Beekhuizen J., Wouters I.M., et al., 2014. Air pollution from livestock farms, and asthma, allergic rhinitis and COPD among neighbouring residents. Occup Environ Med, 134-140. https://doi.org/10.1136/oemed-2013-101485.

Smit L.A.M., van der Sman-de Beer F., Opstal-van Winden A.W.J., Hooiveld M., Beekhuizen J., Wouters I.M., et al., 2012. Q Fever and Pneumonia in an Area with a High Livestock Density: A Large Population-Based Study. PLoS One. 7, e38843. https://doi.org/10.1371/journal.pone.0038843

van Dam M., Dijksma S.A.M., 2017. Reactie op diverse onderzoeken naar de relatie tussen veehouderij en gezondheid [Response to several studies on the relation between livestock production and human health]. https://www.rijksoverheid.nl/documenten/kamerstukken/2017/06/01/reactie-op-diverse-onderzoeken-naar-de-relatie-tussen-veehouderij-en-gezondheid (accessed 07/22 2019).

van Dijk C.E., Garcia-Aymerich J., Carsin A.-E., Smit L.A.M., Borlée F., Heederik D.J., et al., 2016. 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. 219, 278-287. https://doi.org/10.1016/j.ijheh.2016.01.002.

van Dijk C.E., Zock J.-P., Baliatsas C., Smit L.A.M., Borlée F., Spreeuwenberg P., et al., 2017. Health conditions in rural areas with high livestock density: Analysis of seven consecutive years. Environmental Pollution. 222, 374-382. https://doi.org/10.1016/j.envpol.2016.12.023.

Viechtbauer W., 2010. Conducting meta-analyses in R with the metafor package. Journal of Statistical Software. 36, 1-48. https://doi.org/10.18637/jss.v036.i03

Wood S., 2018. Package ‘mgcv’. https://cran.r-project.org/web/packages/mgcv/mgcv.pdf (accessed 05/02 2018).

Chapter 4

Proximity to livestock farms and exposure to livestock-related particulate matter are associated with lower probability of medication dispensing for obstructive airway diseases

Authors
Pim M. Post[ab], Danny Houthuijs[a], Hendrika A.M. Sterk[a], Marten Marra[a],
Jan van de Kassteele[a], Addo van Pul[a], Lidwien A.M. Smit[b], Wim van der Hoek[a],
Erik Lebret[ab], Lenny Hogerwerf[a]

[a]National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands;
[b]Institute of Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, the Netherlands

Published in *International Journal of Hygiene and Environmental Health* (231), 2021, 113651
DOI:10.1016/j.ijheh.2020.113651

ABSTRACT

Objectives: The aim of this study is to assess whether medication use for obstructive airway diseases is associated with environmental exposure to livestock farms. Previous studies in the Netherlands at a regional level suggested that asthma and chronic obstructive pulmonary disease (COPD) are less prevalent among persons living near livestock farms.

Methods: A nationwide population-based cross-sectional study was conducted among 7,735,491 persons, with data on the dispensing of drugs for obstructive airway diseases in the Netherlands in 2016. Exposure was based on distances between home addresses and farms and on modelled atmospheric particulate matter (PM_{10}) concentrations from livestock farms. Data were analysed for different regions by logistic regression analyses and adjusted for several individual-level variables, as well as modelled PM_{10} concentration of non-farm-related air pollution. Results for individual regions were subsequently pooled in meta-analyses.

Results: The probability of medication for asthma or COPD being dispensed to adults and children was lower with decreasing distance of their homes to livestock farms, particularly cattle and poultry farms. Increased concentrations of PM_{10} from cattle were associated with less dispensing of medications for asthma or COPD, as well (meta-analysis OR for 10th-90th percentile increase in concentration of PM_{10} from cattle farms, 95%CI: 0.92, 0.86-0.97 for adults). However, increased concentrations of PM_{10} from non-farm sources were positively associated (meta-analysis OR for 10th-90th percentile increase in PM_{10}-concentration, 95%CI: 1.29, 1.09-1.52 for adults).

Conclusions: The results show that the probability of dispensing medication for asthma or COPD is inversely associated with proximity to livestock farms and modelled exposure to livestock-related PM_{10} in multiple regions within the Netherlands. This finding implies a notable prevented risk: under the assumption of absence of livestock farms in the Netherlands, an estimated 2% to 5% more persons (an increase in tens of thousands) in rural areas would receive asthma or COPD medication.

1 Introduction

Previous research in the Netherlands suggests that persons living in the vicinity of livestock farms are less likely to have asthma or chronic obstructive pulmonary disease (COPD) (Borlée et al., 2015; de Rooij et al., 2019; Smit et al., 2014). The reduced asthma prevalence may be explained by more diverse microbial exposures in livestock-farming areas, leading to a reduced risk for development of allergic sensitization (von Mutius, 2016). This explanation is largely based on studies in children growing up on livestock farms, (Ege et al., 2011; Riedler et al., 2001) who tend to have a lower risk of atopic asthma and allergies. A lower atopy prevalence was also recently found among Dutch adults living in the vicinity of livestock farms (Borlée et al., 2018). In contrast, no biologically plausible explanation could be provided for the reduced prevalence of COPD in the vicinity of livestock farms (Smit et al., 2014). Furthermore, while prevalence was lower close to farms, the frequency of exacerbations among patients with COPD was higher and pulmonary function was lower, particularly with higher livestock-related air pollution levels (Borlée et al., 2017; Borlée et al., 2015; van Dijk et al., 2016a; van Kersen et al., 2020).

In countries other than the Netherlands, evidence is mixed regarding a protective effect of living in the vicinity of livestock farms (Casey et al., 2015; Douglas et al., 2018; Kauffmann et al., 2002; Schultz et al., 2019). Studies among farmers themselves are also inconclusive, as some have shown a protective effect with increased farming exposure, whereas others have indicated a higher risk of asthma with increasing farming exposures, particularly for non-atopic asthma (Wunschel and Poole, 2016). Studies among farmers generally have shown an increased prevalence of COPD compared to those in non-farmers, which is attributed to long-term dust exposure (Fontana et al., 2017; Guillien et al., 2019).

In previous research in the Netherlands on associations between asthma and COPD in relation to proximity to livestock farms, several measures of exposure were used, including nearest distances to several types of animal

---

Abbreviations
COPD, chronic obstructive pulmonary disease
GCN, large-scale concentration-maps the Netherlands [grootschalige concentratie-kaarten Nederland]
PAF, population-attributable fraction
PM, particulate matter
SES, socio-economic status

farms and particulate matter (PM) emissions from these farms (Smit et al., 2014). Recently, such exposure measures were extended with modelled concentrations of PM and endotoxins, which is a constituent of organic PM (de Rooij et al., 2019). Such modelled concentrations take into account the proximity to multiple farms and may better approximate the exposures behind the previously observed associations that are currently unknown.

The previous studies focused on a study population of 92,548 persons (22,406 children; 70,142 adults) living in a livestock-dense area in the southeast of Netherlands and a subset of that population (Borlée et al., 2015; de Rooij et al., 2019; Smit et al., 2014). This region may not be representative of other regions in the Netherlands, because it differs in the density of livestock farms and has relatively higher particulate matter concentrations2. This follows from the relatively larger contribution of the agricultural sector in this area besides for instance traffic sources and a relatively high contribution from abroad (with industry and traffic being the most important contributors).

Hence, previous research may be complemented by studies including the entire Netherlands, with a larger study population and modelled PM concentrations as an additional measure of exposure besides distance to the nearest livestock farm. The use of nationwide available data on medication dispensing for asthma and COPD allows full coverage of the Netherlands. Therefore, the aim of this study is to investigate the association between medication dispensing for asthma and COPD and environmental exposure related to livestock farms in the Netherlands.

---

[2] The yearly produced concentration maps (such as $PM_{2.5}$ and PM_{10}) can be viewed and/or downloaded via links on https://www.rivm.nl/gcn-gdn-kaarten/concentratiekaarten

2 Material and Methods

2.1 Study population

The basis of our study population was the Dutch population (16,670,000 individuals), with available data on anonymized address locations (key register for addresses and buildings: BAG), individual-level variables, and medication of all persons that were reimbursed by their statutory basic medical insurance[3]. Medication data covered the calendar year 2016. Persons were included if they were registered as living in the Netherlands on 01-01-2015 and had been living at the same home address for at least two years prior to that date. This and several other selection criteria are listed in Table S1, together with the excluded number of persons. Persons with data missing in either the address locations dataset or individual-level variables were excluded. Also, persons were excluded who lived in districts[4] that included houses within 2 km of the border with Belgium or Germany, as emissions of and distances to foreign livestock farms could not be accounted for in the analysis. Persons living in residential care homes were excluded, because of uncertainty whether their medication use is always registered through insurance. Two criteria were defined to exclude persons likely to be occupationally exposed to livestock: persons that lived at the same address as a farm registered in the farm location data and those that were registered as working in the livestock sector[5]. Lastly, persons living in urban agglomerations[6] were excluded.

2.2 Health outcome

The health outcome measure was the dispensing of drugs prescribed for obstructive airway diseases in 2016, indicated as a binary variable. Medication for obstructive airway diseases includes both inhalants and drugs for systemic use, which are indicated by an ATC-code (Anatomical Therapeutic Chemical

---

[3] “Risicovereveningsbestanden van het College voor Zorgverzekeringen”

[4] Dutch: “wijk”; no administrative unit but statistical unit used by Statistics Netherlands

[5] Economic activity data collected by Statistics Netherlands: SECSMBIBUS; company classification code (SBI-code): A 014

[6] The mapping of Statistics Netherlands is used, which defines urban agglomerations as connected areas with urban buildings where most human activities take place, where most jobs are present and where most public facilities are located.

classification: R03) in data collected by the administrative body responsible for Dutch health insurance (CVZ, Zorginstituut Nederland) for risk equalization among insurance companies. These data do not contain information about duration of use or dosage. The data include persons that are eligible to receive medication according to the standard health insurance policy, excluding medication dispensed during hospital admission and in nursing homes but including medication dispensed by outpatient pharmacies and in residential homes for the elderly. Children aged 0-5 years, those aged 6-17 and adults were distinguished, because diagnosis and treatment of asthma are generally different for children under 6 years of age compared to older children and adults, whereas older children will not be occupationally exposed and are less likely to smoke than adults.

2.3 Exposure indicators

Two proxies of environmental exposure related to livestock farms were used: one based on distances of homes to livestock farms in the Netherlands and one based on the modelled particulate matter concentration originating from livestock farms. Both proxies are conceptually related and provide different perspectives on possible exposure. Particulate matter concentration is not only an indicator of exposure to particulate matter but also to other farm-related emissions. Moreover, modelled concentrations, besides accounting for meteorological conditions, implicitly take into account the proximity of addresses to multiple farms of various sizes, whereas the distance-measure used only takes into account the proximity of the nearest farm. Both proxies should have expressed exposure in 2015, which would then indicate exposure of at least one year prior to medication use in 2016.

2.3.1 Distance to livestock farms

Exposure variables based on distances to farms were defined as the distance to the nearest livestock farm in meters, represented by fixed distance intervals (initially 0-500; 500-1000; 1000-1500; 1500-2000; and >2000 m). The distances between the residences and livestock farms, were calculated with ArcGIS (ESRI [Environmental Systems Research Institute], 2011), on the basis of locations of farms (landbouwtelling, Netherlands Enterprise Agency: RVO) and address locations (BAG) from 2015. Only farms with a minimum number of animals were taken into account, as in previous studies (Borlée et al., 2015; Smit et al., 2014) (Table S2), and a distinction was made between livestock farms of any type, as well as by type: cattle, pig, poultry, goat, sheep, and farms with any other animals.

2.3.2 Modelled particulate matter concentration

The exposure to livestock-related particulate matter up to 10 µm (PM_{10}) was calculated with the OPS (Operational Priority Substances) model (Sauter et al., 2018), which is an atmospheric transport and dispersion model for airborne pollutants. One of the applications of OPS, is the production of annual-averaged maps of concentration and deposition for the Netherlands at a 1 km by 1 km resolution for air quality monitoring purposes (e.g. (RIVM, 2016)) referred to as GCN and GDN maps (Largescale Concentration/Deposition maps of The Netherlands). The model uses Gaussian plumes to describe the relation between an individual source and an individual receptor. The contributions of the individual sources are summed to obtain the total concentration at a certain location or grid cell. It uses trajectories for long-range transport. The long-term version of the model is employed, which is statistical in the sense that calculations are performed for a number of typical meteorological situations (classes) occurring in, for example, a year. The sum of the values per class, weighted according to their relative frequency of occurrence, is the long-term value.

For this study, a resolution of 250 m by 250 m and meteorological conditions of 2015 were used. The PM_{10} emission strengths of point sources of the various farm locations throughout the Netherlands were requested from the Pollutant Release and Transfer Register[7] for the year 2015. These emissions are calculated by multiplying the number of animals per location with animal-specific and housing type-specific emission factors (Vonk et al., 2016). Emissions from abroad were not included for this model exercise. We distinguished between PM_{10} emissions from housing for goats, poultry, cattle, pigs, horses and ponies, donkeys, mink and rabbits; data for sheep were not available. The sum of the concentrations resulting from these emissions is referred to as “livestock-related PM_{10} exposure”. This sum does not include secondary inorganic aerosol, which can partly be attributed to ammonia emissions from livestock farms. However, it does not have a role in microbial

---

[7] www.emissieregistratie.nl. (Pollutant Release and Transfer Register). The Pollutant Release and Transfer Register is responsible for collecting, processing, managing, registering and reporting emission data, so that the Netherlands can meet (inter)national obligations in the field of emission reporting. Emission registration is a cooperative program between various parties; the management and control of emission registration is the responsibility of RIVM.

or other exposures that are of interest in this study. For analyses of specific animal categories, only goats, poultry, cattle, pigs and the combined concentrations from other animals were distinguished.

To improve the dispersion modelling on the local scale, animal category-specific particle size distributions were implemented. These distributions differ from those implemented by default that are used to obtain the large-scale picture of the air quality in the Netherlands. Specification of such distributions is important, as small and light particles are transported over longer distances than larger and heavier particles. The particle-size distributions were determined on the basis of measurement data of (Lai et al., 2014) and (Winkel et al., 2015) (see Supplementary Methods).

Exposure to PM_{10} from sources other than Dutch livestock farms as well as to secondary inorganic aerosols was determined by subtracting PM_{10} concentrations originating from livestock farms from the total PM_{10} concentration from all sources. These data were retrieved from the standard available annual GCN map for 2015, with meteorological conditions of 2015, emissions of 2014 and a grid, 1 km by 1 km, which includes emissions from all sectors within the Netherlands and abroad, including aggregated emissions from agriculture per country (RIVM, 2016). A comparison of these livestock-related PM_{10} concentrations from GCN maps and the calculations performed for this study showed only small differences, due to differences in resolution of both model grid and emission sources and year of emission data. Further, the subtraction assures that non-livestock PM_{10} concentrations exclude livestock-related emissions that do not originate from housing (e.g., supply of concentrates to farms). The nitrogen dioxide (NO_2) concentration, as another important source of air pollution was directly obtained from the standard available GCN maps.

2.4 Confounding variables

We included individual covariates relevant for studies on respiratory health because they are potential determinants and are available for analysis within a secure environment provided by Statistics Netherlands. Only age, sex, marital status, migration background and household income fulfilled these requirements. Data on sex, age, marital status and migration background originate from registry data (Basisregistratie Personen), and data on household income were compiled by Statistics Netherlands based on information from tax authorities and other sources. In addition, an indicator for neighbourhood socio-economic status (SES) in 2016, which is derived every 4 years by the Netherlands Institute for Social Research (Knol, 1998), was used. This indicator is constructed on the four-digit postal code level, with each postal code area comprising on average about 4,000 inhabitants. It is based on a principal-component analysis of the income level, unemployment rate and education level of the inhabitants of the postal-code area, which is rescaled to 5 categories, with 1 indicating highest and 5 indicating lowest SES.

2.5 Data privacy regime

Data were analysed within the secure environment provided by Statistics Netherlands, where researchers had access to information on the individual level but not to directly identifiable information such as address locations. No data used outside this secure environment contained information with which individuals could be identified. Exposure variables were calculated outside the secure environment and linked to a general address code (BAG), which was then re-coded by Statistics Netherlands and linked to the health outcome and associated demographic and socioeconomic variables under study.

2.6 Analyses

Logistic regression analyses were conducted separately for 14 regions with different agricultural characteristics as defined by Statistics Netherlands (Dutch: groepen van landbouwgebieden, Figure 1). Such separate analyses were performed because of computational limitations that hampered the joint analysis of 7.7 million individuals. Separate analyses were performed for each distance-exposure variable and PM_{10}-exposure variable, and results were combined across the 14 regions in meta-analyses. Analyses were conducted separately for children and adults with three different levels of adjustment: personal-level adjustment models included, in addition to the exposure variable, sex, age, marital status (not for children), migration background and household income; fully adjusted models included, in addition to these variables, SES of the postal code area and exposure to non-livestock PM_{10} and NO_2; mutually adjusted models included all animal categories simultaneously, as well as all other covariables. Distance-exposure and livestock-related PM_{10}-exposure variables were not adjusted for each other as this may lead to over-adjustment. Logistic regression analyses were performed with the glm function of the stats package in R (R Core Team). For PM_{10}-exposure analyses, random effects meta-analyses were performed with the metafor package in R (Viechtbauer, 2010). For distance-based exposure analyses, multivariate random effects meta-analyses were performed by including covariance matrices of the distance-categories in the mvmeta package in R (Gasparrini, 2018) to account for the covariance of distance categories. Heterogeneity between regions was assessed with the I^2-statistic.

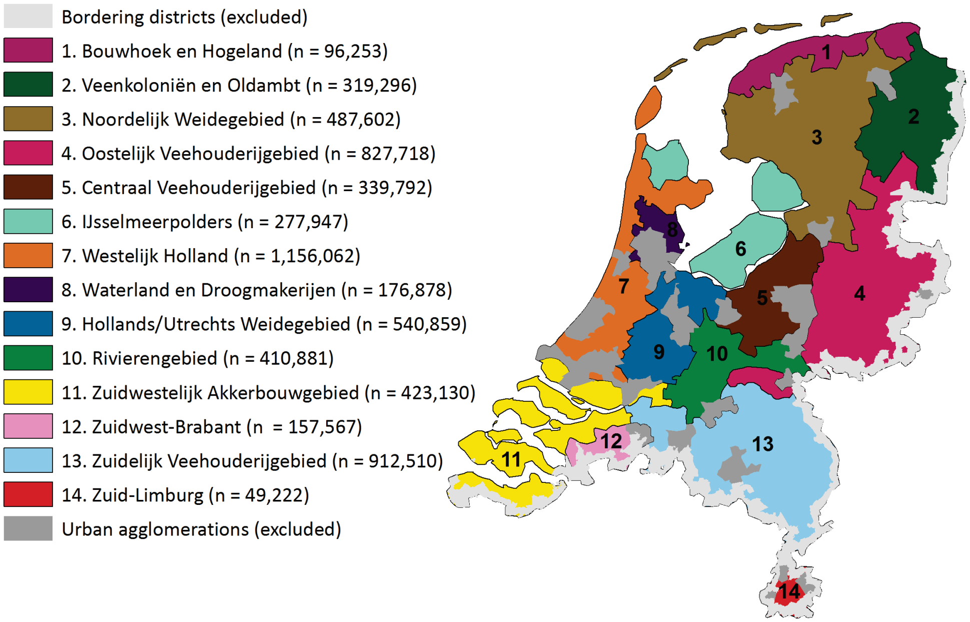


Figure 1. Specific regions in the Netherlands are shown. The numbers refer to those regions as noted in the manuscript, their Dutch names and number of adults living in the region within brackets. Dark grey indicates the urban agglomerations; light grey indicates the areas close to the border from which inhabitants were excluded.

Models based on distance-based exposure variables, included distance intervals of 500 m (0-500; 500-1000; 1000-1500; 1500-2000 and >2000 m). For the exposure variables “distance to nearest livestock farm” and “distance to nearest cattle farm”, the interval “1500-2000 m” was not included because of the low number of persons living further than 2000 m from cattle farms in some regions; hence, the largest distance category for these variables was “>1500 m”. For the mutually adjusted model based on distance variables, the distance intervals were refined by first making a model including distance intervals of

500 m. Because with this model most effects were observed within 1000 m, a new model was made including distance intervals of 250 m (0-250; 250-500; 500-750; 750-1000 and >1000 m). When high variance within a distance interval or little difference between adjacent distance intervals was observed, distance intervals were merged, keeping a minimum of three distance intervals per animal category.

2.7 Sensitivity analyses

Several types of sensitivity analyses concerning the analytical model, health outcome, exposure and selection of the study population were performed. Sensitivity analyses were compared to fully adjusted analyses. Sensitivity to the analytical model was studied by running multilevel analyses in which the district (Dutch: “wijk”[4]) was included as random effect as a proxy to adjust for potential differences in medication prescription practices between general practitioners and for differences between districts that could not be explained by the other covariables (van de Kassteele et al., 2017). The GLIMMIX procedure in SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) was used for these multilevel analyses

The health outcome in the main analyses concerns the prevalence of medication dispensing in 2016, thus assuming a consistent relation between exposure and health outcome over time. To distinguish new prescriptions from such a prevalence measure, incidence measures of medication dispensing were defined with a run-in time of either 2 or 5 years, thus excluding all persons who received medication in 2014 and 2015 or in 2011-2015. A further refinement in health outcome to help distinguishing asthma and COPD is an analysis of a subset of adults younger than 40 years who are unlikely to have COPD.

Sensitivity to the application of different exposure measures was performed by use of a different source of farm location data provided by the Pollutant Release and Transfer Register[7]. Sensitivity to different selection criteria was assessed by performing additional analyses in which persons that moved in the past two years, those that lived close to the border, those that were assumed to be living or working on a farm, or those that lived in urban agglomerations were added to the study population. For the last selection criterion, persons living in urban agglomerations were not included in analyses of the 14 regions, but logistic regression analyses were performed for the entire population in urban agglomerations, the results of which were included as a 15th region in meta-analyses.

2.8 Population attributable fractions

Where the odds ratios calculated from logistic regression analyses provided an indication of risk, the population attributable fractions (PAF) provided an indication of the *impact* of a risk factor on the total population; the PAFs took into account both the relative risk of an exposure and the number of persons exposed. Since the number of persons and effect sizes varied by region, the PAFs better reflected the overall impact than the odds ratios (ORs) from meta-analyses. PAFs were calculated using the following equation:

$$PAF = (C_p - C_0)/C_p \qquad (1)$$

Here C_p is the predicted number of cases of medication reception in the region under the original data (population), and C_0 is the number of predicted cases based on the model coefficients under the counterfactual situation that no livestock farms were present, i.e., no exposure to livestock-related particulate matter and all distances to the nearest livestock farm in the highest distance category.

Confidence intervals were obtained by simulating 1000 Monte Carlo estimates per region, with a different set of model coefficients for each simulation based on the variance-covariance matrix of the logistic regression model, with use of the mvrnorm function in R from the MASS package (Venables and Ripley, 2002). From these 1000 estimates, 1000 different numbers of predicted cases per region were calculated. The total number of predicted cases was determined by summing the predicted cases over the regions and over age groups. From these 1000 different numbers of predicted cases, PAFs were calculated by equation (1). The 95% confidence interval (CI) is assumed to be the range between the 2.5 and 97.5 percentiles of the 1000 PAFs.

We calculated PAFs for two different sets of models; one set included the distances to nearest farms in six animal categories, and the other set included exposure to animal-type specific particulate matter. Each of the two PAFs was based on summing the number of predicted cases from 42 models for three age groups and 14 regions.

3 Results

3.1 Characteristics of the study population

In total 7,735,491 persons (6,175,717 adults; 1,228,242 children between 6 and 17 years old; 331,532 children under 6) were included; 8,934,509 persons that did not fit the selection criteria were excluded (Table S1). In 2016, 608,173 adults (9.8%), 72,044 children between 6 and 17 (5.9%) and 25,727 children under age 6 (7.8%) received R03 medication (Table S3). In total, 29.2% of the included adults lived within 500 m from any livestock farm, with percentages ranging from 10% to 47% over the regions (Table 1). The median concentration of livestock-related PM_{10} for adults was 0.16 μg/m^3 (10th-90th percentile: 0.04-0.54 μg/m^3; Figure 2), similar to that for children. This particulate matter mostly originated from poultry farms (median: 0.13 μg/m^3; 10th-90th percentile: 0.03-0.41 μg/m^3). Concentrations of particulate matter from other types of farms were much lower, with a median for pig farms of 0.019 μg/m^3 (10th-90th percentile: 0.005-0.10 μg/m^3), for cattle 0.01 μg/m^3 (10th-90th percentile: 0.005-0.02) and concentrations for goats lower than 0.002 in 99% of cases. Personal characteristics of the study population can be found in Table S3.

3.2 Association with distance variables

Proximity to livestock farms was associated with lower R03 medication dispensing in 2016 for adults in personal-level adjusted and fully adjusted analyses, with a pooled odds ratio (OR) of 0.95 (95% confidence interval [CI]: 0.91-0.99) for living within 500 m of a livestock farm, compared to living further than 1500 m away (Table 1). Such an association was also found for children between ages 6 and 17 years, but no significant association was found for younger children (Table S4).

Also, proximity to the nearest cattle, poultry, pig, or goat farm or farm with other animals (except sheep) was significantly associated with lower R03 medication dispensing in meta-analyses among adults (Table 1). Yet, after mutually adjusting for different animal categories, associations remained significant only for cattle and poultry (Table 2). For both cattle and poultry farms, lower R03 medication dispensing with decreasing distance was apparent in multiple regions across the Netherlands (Figure 3; Figure S2). Such negative associations were also found in several regions for other animal categories, yet none of these associations remained statistically significant in the meta-analyses (Figure S3-6). Significantly positive associations were found for distances to the nearest sheep farm and nearest pig farm for some regions, but in other regions significantly negative associations were found (Figure S3,S5).

Table 1. Association between medication dispenses and distance to nearest livestock farms, expressed as odds-ratios (95% confidence interval) from meta-analyses over the 14 regions, for different levels of adjustment

Adults (>17, n = 6,175,717)	Exposure[a]	Personal-level adjusted[b]	Fully adjusted[c]
Distance to nearest livestock farm (m)			
0-500	29.2% (10-47%)	0.91 (0.87-0.96)***	0.95 (0.91-0.99)**
500-1000	37.6% (19-43%)	0.96 (0.93-0.99)*	0.98 (0.95-1.01)
1000-1500	20.2% (10-29%)	0.99 (0.97-1.00)	0.99 (0.98-1.01)
>1500	13.0% (1-44%)	1	1
Distance to nearest cattle farm (m)			
0-500	20.2% (4-37%)	0.90 (0.85-0.95)***	0.94 (0.90-0.97)***
500-1000	32.9% (10-42%)	0.95 (0.91-0.99)*	0.97 (0.95-1.00)
1000-1500	22.5% (12-30%)	0.98 (0.95-1.01)	0.99 (0.97-1.01)
>1500	24.4% (3-74%)	1	1
Distance to nearest pig farm (m)			
0-500	3.4% (0-11%)	0.93 (0.89-0.97)***	0.95 (0.92-0.98)**
500-1000	10.4% (0-30%)	0.96 (0.92-1.01)	0.99 (0.96-1.02)
1000-1500	13.3% (1-27%)	0.97 (0.92-1.02)	0.99 (0.98-1.01)
1500-2000	12.0% (1-20%)	0.98 (0.96-1.00)	0.99 (0.97-1.01)
>2000	61.1% (16-98%)	1	1
Distance to nearest poultry farm (m)[d]			
0-500	1.5% (0-6%)	0.91 (0.87-0.95)***	0.92 (0.89-0.95)***
500-1000	5.7% (0-21%)	0.94 (0.90-0.99)*	0.97 (0.94-1.00)*
1000-1500	8.7% (0-26%)	0.98 (0.93-1.02)	1.00 (0.97-1.03)
1500-2000	9.4% (0-21%)	0.99 (0.95-1.03)	1.00 (0.98-1.03)
>2000	74.6% (27-100%)	1	1
Distance to nearest goat farm (m)			
0-500	0.4% (0-1%)	0.88 (0.79-0.98)*	0.91 (0.85-0.99)*
500-1000	1.6% (0-4%)	0.93 (0.88-0.99)*	0.95 (0.90-1.00)*
1000-1500	3.4% (0-8%)	0.95 (0.90-1.00)	0.97 (0.92-1.02)
1500-2000	4.9% (1-15%)	0.94 (0.87-1.01)	0.97 (0.93-1.01)
>2000	89.8% (73-99%)	1	1

Distance to nearest sheep farm (m)			
0-500	8.0% (1-22%)	0.95 (0.89-1.01)	0.98 (0.92-1.04)
500-1000	15.8% (7-34%)	0.97 (0.93-1.02)	0.98 (0.93-1.03)
1000-1500	18.5% (10-28%)	0.97 (0.94-1.01)	0.98 (0.94-1.01)
1500-2000	17.3% (12-28%)	0.99 (0.97-1.01)	0.99 (0.97-1.01)
>2000	40.3% (9-64%)	1	1
Distance to nearest farm with other animals (m)			
0-500	8.1% (2-13%)	0.95 (0.92-0.97)***	0.96 (0.94-0.99)***
500-1000	21.5% (7-29%)	0.97 (0.94-0.99)*	0.98 (0.96-1.00)*
1000-1500	24.2% (12-29%)	0.99 (0.96-1.02)	0.99 (0.97-1.01)
1500-2000	20.2% (14-34%)	1.00 (0.97-1.02)	0.99 (0.97-1.01)
>2000	25.9% (4-66%)	1	1

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[a] Exposure: mean percentage of persons living in distance-interval, with lowest and highest exposure over the regions in brackets

[b] Personal-level adjusted: adjusted for age, sex, marital status, household income and migration background

[c] Fully adjusted: adjusted for the same variables as in the personal-level adjusted models as well as for SES-category, NO_2 exposure and exposure to non-livestock-related particulate matter

[d] Left out region 8 because of insufficient exposure

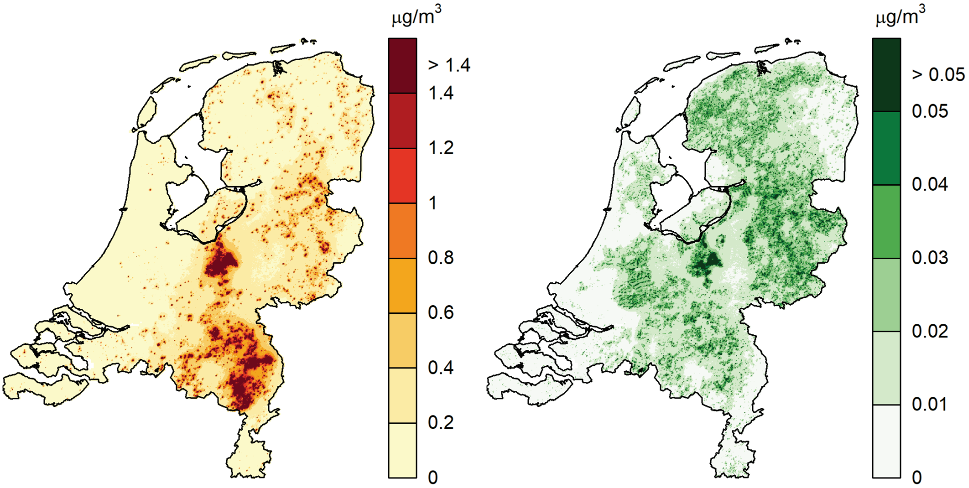


Figure 2. Modelled particulate matter concentration from all livestock farms (left) and cattle farms (right). The pattern of total livestock-related particulate matter concentrations is driven by emissions from poultry farms (Figure S1A). Figure S1 also shows modelled particulate matter concentrations from pig, goat, and other livestock farms

The value of I^2 for meta-analyses of mutually adjusted regression outcomes was 67% to 94% across animal categories, indicating considerable heterogeneity, which may be driven by the small confidence intervals for some regions. Importantly, regions with fewer than 20% of persons living within 500 m of a cattle farm (2,6,7,8,11,12) tend to have the lowest ORs for small distances (Figure 3).

In children, significantly negative associations with proximity to cattle farms were found in meta-analyses of mutually adjusted models, as well (Table S5). Meta-analyses for children also showed decreasing medication dispensing with decreasing distance in several other animal categories, but this was not consistently significant across age groups and analysis types (Table S4-5). Proximity of young children (0-5) to sheep appeared positively associated with medication dispensing, yet significant only when mutually adjusted for proximity to other animals (Table S4-5).

Table 2. Association between medication dispenses and distance to nearest livestock farms, expressed as odds-ratios (95% confidence interval) from a meta-analysis over the 14 regions of models in which exposures related to different animal categories were mutually adjusted for each other.

Adults (>17 years of age, n = 6,175,717)	Mutually adjusted[a]
Distance to nearest cattle farm (m)	
0-250	0.93 (0.91-0.95)***
250-500	0.96 (0.94-0.97)***
500-750	0.97 (0.96-0.99)**
750-1000	0.99 (0.97-1.01)
>1000	1
Distance to nearest pig farm (m)	
0-500	0.99 (0.96-1.02)
500-1000	1.03 (0.99-1.06)
>1000	1
Distance to nearest poultry farm (m)[b]	
0-250	0.89 (0.82-0.97)**
250-500	0.96 (0.92-0.99)*
500-750	0.96 (0.92-1.00)*
750-1000	0.98 (0.96-1.01)
>1000	1

Distance to nearest goat farm (m)	
0-500	0.95 (0.89-1.00)
500-1000	0.98 (0.95-1.01)
>1000	1
Distance to nearest sheep farm (m)	
0-500	1.01 (0.98-1.05)
500-1000	1.00 (0.98-1.03)
>1000	1
Distance to nearest farm with other animals (m)	
0-250	0.98 (0.96-1.01)
250-500	0.99 (0.97-1.00)
500-1000	0.99 (0.98-1.01)
>1000	1

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[a] Mutually adjusted: adjusted for age, sex, marital status, household income, migration background, SES-category, NO_2 exposure, exposure to non-livestock-related particulate matter and for exposure to particulate matter from other animals; all values in this table are the results of the same model

[b] Left out region 8 because of insufficient exposure

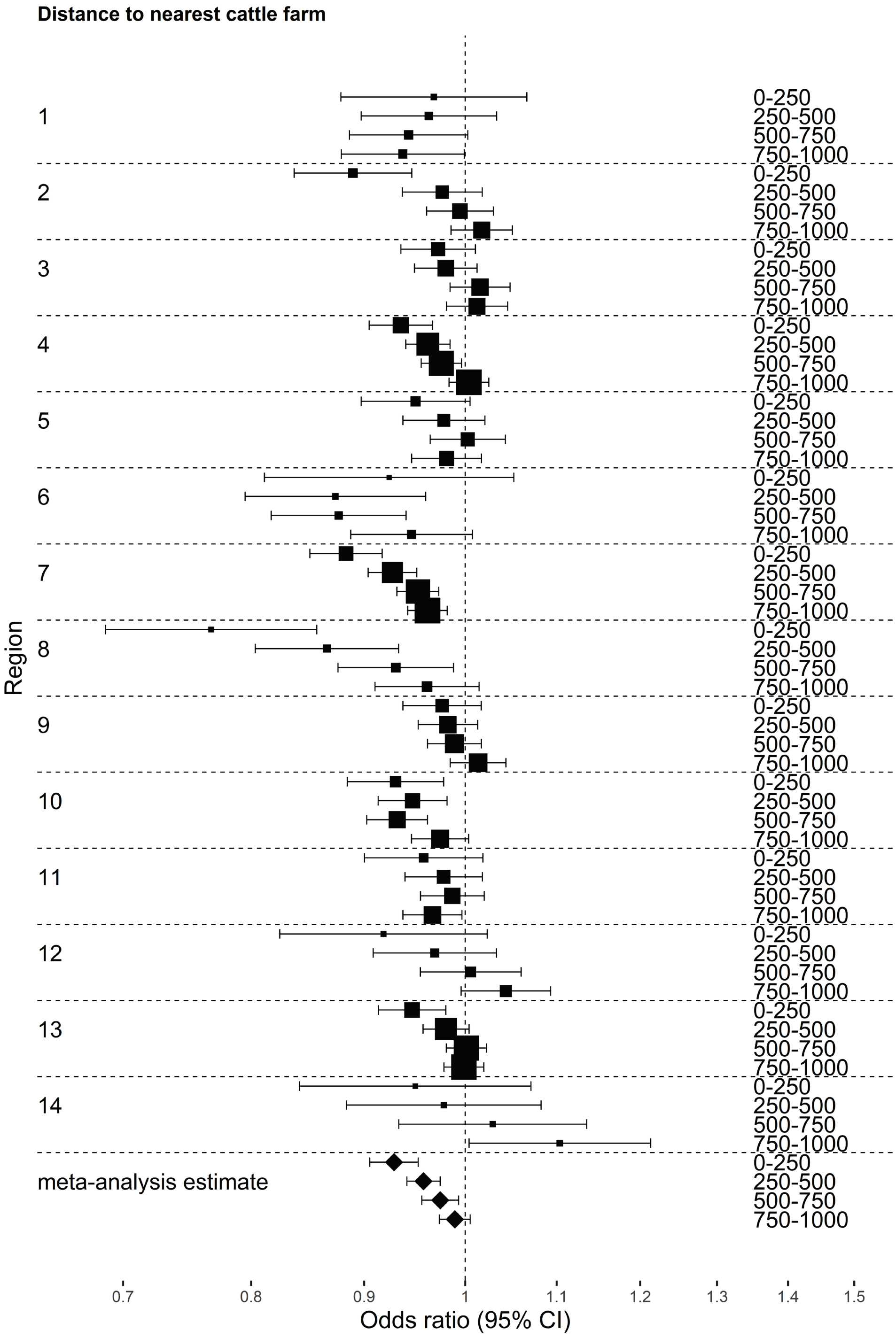

Distance to nearest cattle farm
Region
1
2
3
4
5
6
7
8
9
10
11
12
13
14
meta-analysis estimate
0-250
250-500
500-750
750-1000
0.7
0.8
0.9
1
1.1
1.2
1.3
1.4
1.5
Odds ratio (95% CI)

Figure 3. Forest plot for odds ratios of medication dispensing against distance to nearest cattle farm for mutually adjusted models for adults (adjusted for age, sex, marital status, household income, migration background, socio-economic status, exposure to nitrogen dioxide, distance to nearest poultry farm, distance to nearest pig farm, distance to nearest goat farm, distance to nearest sheep farm, distance to nearest farm with other animals, and exposure to non-livestock-related particulate matter). Regions refer to the regions in Figure 1, the reference category for all regions is >1000m. Meta-analysis summary results can also be found in Table 2.

Table 3. Association between medication dispenses and livestock-related PM_{10}-exposure, expressed as odds-ratios (95% confidence interval) from meta-analyses over the 14 regions, for different levels of adjustment

Adults (>17, n = 6,175,717)	Personal-level adjusted[a]	Fully adjusted[b]	Mutually adjusted[c]
Livestock-related PM_{10}[d]	0.98 (0.95-1.02)	0.97 (0.94-1.00)	n.a.
Non-livestock PM_{10}[de]	1.27 (1.08-1.49)**	1.27 (1.07-1.51)**	1.29 (1.09-1.52)**
Cattle-related PM_{10}[d]	0.92 (0.88-0.96)***	0.92 (0.87-0.97)**	0.92 (0.86-0.97)**
Pig-related PM_{10}[d]	1.40 (0.79-2.47)	1.00 (0.96-1.05)	1.06 (0.99-1.13)
Poultry-related PM_{10}[d]	0.99 (0.96-1.01)	0.98 (0.95-1.00)	0.99 (0.96-1.02)
Goat-related PM_{10}[d]	1.00 (0.99-1.01)	1.00 (0.99-1.00)	1.00 (1.00-1.01)
Other animal-related PM_{10}[d]	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.00 (0.99-1.00)

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[a] Personal-level adjusted: adjusted for age, sex, marital status, household income and migration background

[b] Fully adjusted: adjusted for the same variables as in the personal-level adjusted models as well as for SES-category, NO_2 exposure and exposure to non-livestock-related particulate matter

[c] Mutually adjusted: adjusted for the same variables as in the fully adjusted models as well as for exposure to particulate matter from other animals; all values in this column are the results of the same model

[d] per 10-90 percentile increase in exposure

[e] in fully-adjusted model, adjusted for livestock-related PM_{10}; in Mutually adjusted model adjusted for PM_{10} from animal categories. The estimates correspond to an OR of 1.06 (1.02-1.10) per 1 $\mu g/m^3$ increase.

3.3 Association with particulate matter exposure

A weak non-significant negative association was found between receipt of R03 medication in 2016 and exposure to PM_{10} from all livestock farms combined (Table 3). Exposure to PM_{10} from cattle farms was significantly negatively associated with receipt of R03 medication in multiple regions across the Netherlands and in a meta-analysis (OR from meta-analysis of mutually adjusted models: 0.92; 95% CI: 0.86-0.97; I^2 = 97%; Table 3; Figure 4). The I^2 value indicates considerable heterogeneity across regions, as seen in Figure 4. In regions with relatively low average cattle-PM_{10} concentrations (2,6,7,11,12,14), estimates were generally lower than in regions with higher concentrations (Figure 2,4). For poultry, in some regions significantly negative associations were found as well, but meta-analyses results were not significant (Figure S6). For pigs and goats, both significantly negative and positive associations were found in individual regions (Figure S8,9), with positive but not significant associations from meta-analyses for both children and adults (Table 3, Table S6). PM_{10} from sources other than livestock farms was positively associated with receipt of R03 medication in several regions and in a meta-analysis, but only for adults (Table 3, Table S6, Figure S10). Calculated heterogeneity across regions was considerable, ranging from 52% to 97% across animal categories.

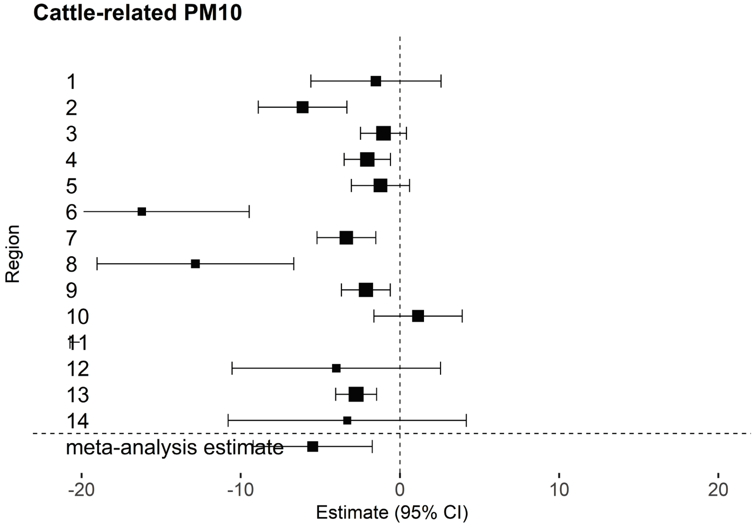


Figure 4. Forest plot for mutually-adjusted models for the association between medication dispenses and cattle-related PM_{10} exposure among adults (adjusted for age, sex, marital status, household income, migration background, socio-economic status, exposure to nitrogen dioxide, exposure to poultry-related, pig-related, goat-related and other animal-related particulate matter, and exposure to non-livestock-related particulate matter). Regions refer to the regions in Figure 1. Meta-analysis results can also be found in Table 3.

3.4 Sensitivity analyses

3.4.1 Sensitivity to model formulation

Inclusion of district as a random effect in multilevel models gave similar results as the single-level model, although coefficients varied between the models (Table S7,8).

3.4.2 Sensitivity to health outcome

Results of inclusion of a run-in time of either two or five years were similar to results of no inclusion of a run-in time. However, somewhat larger effect sizes were found for the distance to the nearest pig farm, whereas the association with pig-related particulate matter turned significantly negative (Table S9,11). The number of cases included for a run-in time of two years was 116,449 (21 per 1000) and for five years 83,952 (16 per 1000). Only inclusion of adults less than 40 years of age or older persons had a limited effect on the estimates, yet for adults less than 40, the positive association between medication dispensing and particulate matter from non-livestock sources was not significant (Table S10,11).

3.4.3 Sensitivity to exposure variables and selection criteria

Results were hardly sensitive to the use of different farm location data or different selection criteria: not excluding persons that moved in 2014 or 2015 or those living close to the border, excluding persons living in a district within five km from the border, or including those that were expected to live on a farm (Table S12,13). Including urban agglomerations as a 15th region also had little effect on meta-analysis estimates, but the estimates with pig-related particulate matter turned from non-significantly positive to non-significantly negative when agglomerations were included. Furthermore, associations within urban agglomerations were significantly positive for distance to the nearest sheep farm and for goat-related particulate matter in mutually adjusted analyses (not shown).

3.5 Population attributable fractions

The predicted fraction of persons (adults and children) that receives R03 medication attributable to the presence of livestock farms was -0.016 (95% confidence Interval, CI: -0.013 to -0.019) for a model with distance-based measures and -0.052 (95% CI: -0.045 to -0.059) for a model based on PM_{10}-exposure measures. Hence, on the basis of these models, the number of persons in the study-population receiving R03 medication could increase from 1.6% to 5.2% when no livestock farms were present. Cattle-related exposure contributed most to both estimates, because of both the strength of the associations and the number of persons living close to cattle farms (Figure 7). The population attributable fraction was positive, assuming no exposure from proximity to sheep farms or from pig-related particulate matter.

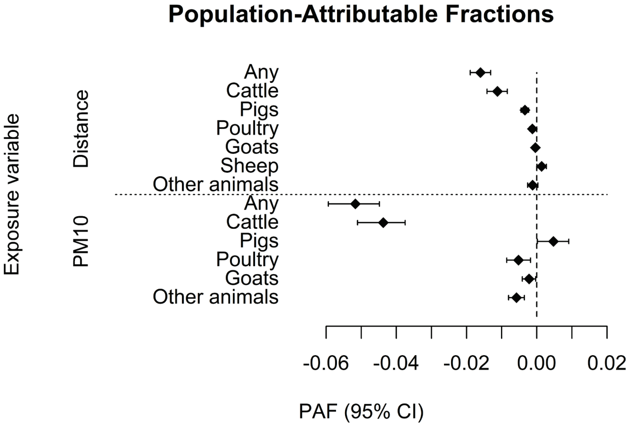


Figure 5. Population attributable fractions (PAFs) for models with distance to nearest livestock farm as exposure and those with livestock-related PM_{10} as exposure. The exposure variables refer to the counterfactuals in the two sets of 42 mutually adjusted models (14 regions, 3 age groups) from which the PAFs were estimated (mutually adjusted for exposure related to the animal categories, as well as for age, sex, marital status, household income, migration background, socio-economic status, exposure to nitrogen dioxide and exposure to non-livestock-related particulate matter).

4 Discussion

This study shows that environmental exposure to livestock farms is negatively associated with medication dispensing for chronic obstructive airway diseases; persons living close to livestock farms and those with higher modelled exposure to PM_{10} from livestock farms receive less medication than persons living further away and those with lower PM levels. A positive association between medication dispensing and exposure to non-livestock PM_{10} (including secondary inorganic aerosols) was found. The protective association seems most evident for environmental exposure related to cattle farms, for which associations with both distance and PM_{10} remained significant after mutually adjusting for exposure related to other animal categories; such protective association was found to a lesser extent for poultry farms, for which associations were most clear for the distance variables. Results differed per region, but for most regions negative associations were found for distance-based and particulate-matter-based exposure variables and for exposure related to cattle and poultry farms. Such consistency across regions shows that associations are not limited to a previously studied area in the southeast of the Netherlands. Results were only slightly sensitive for the model formulation or use of different selection criteria.

While effect sizes are relatively small, about two-thirds of the Dutch rural population lives within 1 km of a livestock farm (55% including urban agglomerates). Hence, with the assumption that the observed associations are causal, 2% to 5% more persons living in rural areas might receive medication for obstructive airway diseases if no livestock farms were present in the Netherlands, which equates to several tens of thousands of persons. The lower bound of this estimate is based on models including the distances to the nearest livestock farms of several types while the upper bound of the estimate is based on models including livestock-related particulate matter. The difference between these estimates may be explained by the inability of the distance to the nearest farm to take into account combined effects of proximity to multiple farms and characteristics such as farm size, which are implicitly accounted for in the modelled livestock-related particulate matter concentrations. The PAFs are in the same order of magnitude as what could be inferred from the odds ratios for asthma and COPD in relation to persons living within 500 m of a livestock farm from the study by (Smit et al., 2014). The PAFs that can be calculated from these odds ratios are about -0.053 for COPD and -0.016 for asthma (based on exposure of the entire Dutch population), with a factor 10 uncertainty around these estimates, depending on the assumptions (Post et al., 2020).

Some PAFs appeared to deviate from zero, even though the corresponding null-exposure variables did not show significant associations in meta-analyses. This difference can be explained by a difference in weights of regions between meta-analyses, in which weights are based on standard errors of the estimates, and PAF calculation, in which weights are based on the number of inhabitants of the region. The positive PAFs for pig-related particulate matter and distance to nearest sheep farm and the negative PAFs for distance to nearest pig farm, distance to nearest farm with other animals, and other animal-related particulate matter should thus be interpreted with caution. The inconsistent results between PAFs and meta-analysis results for these animals make such results less strong than results for cattle and poultry farms, for which results are more consistent.

In the present study, no distinction could be made between medication dispensing for asthma and that for COPD. Yet, COPD is generally not diagnosed among persons less than 40 years old, and in adults less than 40 the association between medication dispensing and environmental exposure related to livestock farms was similar to the association among all adults. Moreover, since the associations similar to those in adults were found in children, they likely apply to asthma. Persons 40 years or older receiving R03 medication can have either asthma or COPD, yet analysis in this group showed similar effect sizes compared to analysis in adults younger than 40.

Associations with both proxies used in this study support previous findings in the Netherlands regarding an inverse association between asthma and COPD and proximity to livestock farms that were based on self-reported and general practitioner diagnoses of asthma and COPD (Borlée et al., 2015; de Rooij et al., 2019; Smit et al., 2014). The findings therefore support the hypothesis that the inverse association between asthma and residence in the vicinity of livestock farms is caused by more diverse microbial exposure leading to reduced allergic sensitization (Ege et al., 2011; Ehrenstein et al., 2000; von Mutius, 2016). This hygiene hypothesis is not a plausible explanation for an inverse association with COPD, which is currently supported only by previous research in the Netherlands; most studies among farmers show an increased risk of COPD (Fontana et al., 2017; Guillien et al., 2019). The inverse association between medication dispensing for asthma and COPD and livestock-related exposure is not likely explained by a difference between urban and rural areas, because analyses were performed within regions and persons living in urban agglomerations were excluded.

An alternative explanation for fewer occurrences of medication dispensing close to livestock farms are individual differences in healthcare seeking behaviour. In previous research, such healthcare seeking behaviour appeared lower among persons living close to livestock farms but was not affected by distance to general practitioners (van Dijk et al., 2016b). Regional differences in healthcare seeking behaviour are not likely to have driven inverse associations, because these were observed for multiple regions and remained when adjusted for differences at district level in multilevel analyses. Another alternative explanation for the associations is that persons that have asthma or COPD or that are sensitive to such diseases or parents of asthmatic patients may be more inclined to move away from farms. However, this explanation appears in contradiction to sensitivity analyses in which a run-in time was implemented. These analyses suggest that not only prevalent but also new cases of asthma and COPD are inversely associated with livestock-related exposure, which is unlikely if moving is the result of being diagnosed with asthma or COPD.

In contrast to the association with livestock-related particulate matter, the association of medication dispensing for asthma and COPD with non-livestock-related particulate matter was positive. This finding appears to align well with existing evidence of increased or worsening asthma and COPD among persons exposed to air pollution (Salvi and Barnes, 2009; Viegi et al., 2001; World Health Organization, 2013), yet epidemiological evidence for association of incidence and prevalence of asthma and COPD in adults with air pollution exposure is less strong (Atkinson et al., 2015; EPA, 2019; Gowers et al., 2012; Hendryx et al., 2019; Liu et al., 2017; Schikowski et al., 2014). A positive association is biologically plausible, as several mechanisms have been identified by which particulate matter may induce asthma or COPD (Gowers et al., 2012; Schikowski et al., 2014).

Only associations with cattle farms remained significant for both distance and PM_{10}-related variables after mutually adjusting for other animal categories. Cattle farms are the most widely distributed type of farms in the Netherlands, with more than 20% of the study population living within 500 m from such farms. Hence, more persons live close to only a cattle farm and no other farms than live close to other farms but not to a cattle farm. This distribution may have hindered finding associations with other animal categories in mutually adjusted analyses, but makes it unlikely that associations with cattle-specific exposure are affected by correlated proximity to other farms. A significant inverse association between both COPD and asthma and the presence of a cattle farm within 500 m from a home address was also found in a previous study in the Netherlands (Smit et al., 2014), yet in that study the association did not remain significant when adjusted for proximity to other categories of animal farms. Significantly negative associations with proximity to pigs and goats, but not poultry, were also found by (Smit et al., 2014) and (Borlée et al., 2015), yet they were not consistently significant across studies and asthma and COPD health outcomes. Internationally, in studies on asthma among persons growing up on farms, traditional farms with cattle have been suggested to be an important factor in the protective effect (Illi et al., 2012).

The associations for cattle-related exposures are not likely explained by the amount of PM_{10} emitted from cattle farms, with the 10^{th}-90^{th} percentile interval for cattle-related PM_{10} concentration for adults more than 20 times lower than that of poultry farms and more than 270 times lower than that of the non-livestock PM_{10} concentration. These associations suggest that livestock-related PM_{10} is a proxy that best aligns with an air transmission route. Exposure to air containing molds, bacteria and endotoxins may indeed be a likely route causing a variety of positive and negative respiratory conditions (May et al., 2012; von Mutius and Vercelli, 2010). Besides air exposure, important exposure factors for a protective effect for asthma are consumption of unprocessed milk and contact with straw and animals (Brooks et al., 2013; Wlasiuk and Vercelli, 2012). A possible correlation of such exposure through farm visits with proximity to livestock farms cannot be ruled out, yet most of the persons living on farms should have been excluded from the analyses.

Although the models in this study were adjusted for several co-variables, some potentially important confounders were not included. Smoking, for example, is the primary risk factor for COPD (Kohansal et al., 2009; Viegi et al., 2001). We adjusted for several socio-economic factors known to correlate with such behaviour (van de Kassteele et al., 2017), yet we cannot be certain that some bias may be present in the results due to lack of adjustment for lifestyle factors. Small associations between lifestyle factors and general air pollution have previously been shown to influence risk estimates for mortality (Strak et al., 2017).

Other weaknesses of this study are the limited precision in both the health outcome and the exposure measures. The health outcome of medication dispensing for asthma and COPD can be regarded as a proxy for obstructive airway disease, but it may not be as accurate as information on prescriptions or use; it does not provide an indication about the severity of the disease because of lacking information on doses; and it does not provide sufficient information to distinguish between asthma and COPD. Lack of information on the severity of asthma and COPD hindered the investigation of exacerbations among persons with COPD, which were found to be increased among those living close to livestock farms (Borlée et al., 2015; van Dijk et al., 2016a).

Exposure misclassification may have occurred for various reasons. Such misclassification may be particularly large if exposures are not airborne, as airborne exposures aligns best with our exposure proxies. If airborne exposures have a role in the observed associations, misclassification of PM_{10} exposure may still have occurred. Such misclassification may arise, for example, because of exposure at the home address only, since most persons are not at their home address all day. In addition, exposure was determined only on a grid, 250 m by 250 m. Further, assumptions in dispersion modelling may have led to some misclassification. For example, plume rise due to either heat content or momentum was not included, as no general information on source characteristics required for this plume rise is available. Including plume rise has a diluting effect near the source, hence its exclusion may lead to an overestimation of source-specific concentrations, especially close to farms. Among other characteristics such as emission height, standard animal housing characteristics as used for the GCN maps were applied because no detailed database on this exists. The different forms of potential exposure misclassification make it difficult to give an overall estimate about their possible impact. Effects of exposure misclassification on reduction of statistical power is probably not an important issue, given the large number of persons under study.

In conclusion, the results of this study show that medication dispensing for asthma or COPD decreases with decreasing distance to livestock farms or increasing particulate matter exposure from cattle farms, in particular, in multiple regions within the Netherlands. As medication dispensing is likely indicative of prevalence of asthma or COPD, the results suggest an inverse association between asthma or COPD and livestock exposures. On the assumption that this association is causal, the number of persons with asthma or COPD in rural areas might be up to 5% higher with no livestock-related exposure. This number is considerable in view of the more than 700,000 cases we included in this study and hence is a motivation for additional research regarding potential underlying mechanisms. Such research could focus on ruling out alternative explanations such as healthcare seeking behaviour or finding more evidence of the role of microbial exposures in the associations and how such exposure relates to farming practices.

Supplementary Material is available online at
https://ars.els-cdn.com/content/image/1-s2.0-S1438463920305976-mmc1.pdf

Acknowledgements

We thank Arno Swart for his contribution to discussions about this study and comments on earlier versions of the manuscript. We also thank Ben Bom for his advice on exposure measures regarding farm location data and Wilco de Vries for providing information regarding the GCN data. Further, we thank the Pollutant Release and Transfer Register (Emissieregistratie) for providing the emission data required for the dispersion modelling. In addition, we than Sally Ebeling for her help with language-editing the manuscript.

References

Atkinson R.W., Carey I.M., Kent A.J., van Staa T.P., Anderson H.R., Cook D.G., 2015. Long-term exposure to outdoor air pollution and the incidence of chronic obstructive pulmonary disease in a national English cohort. Occupational and Environmental Medicine. 72, 42-48. https://doi.org/10.1136/oemed-2014-102266.

Borlée F., Yzermans C.J., Aalders B., Rooijackers J., Krop E., Maassen C.B., et al., 2017. Air pollution from livestock farms is associated with airway obstruction in neighboring residents. American journal of respiratory and critical care medicine. 196, 1152-1161. https://doi.org/10.1164/rccm.201701-0021OC.

Borlée F., Yzermans C.J., Krop E.J., Maassen C.B., Schellevis F.G., Heederik D.J., et al., 2018. Residential proximity to livestock farms is associated with a lower prevalence of atopy. Occup Environ Med. 75, 453-460. https://doi.org/10.1136/oemed-2017-104769.

Borlée F., Yzermans C.J., van Dijk C.E., Heederik D., Smit L.A.M., 2015. Increased respiratory symptoms in COPD patients living in the vicinity of livestock farms. Eur. Respir. J. 46, 1605-1614. https://doi.org/10.1183/13993003.00265-2015.

Brooks C., Pearce N., Douwes J., 2013. The hygiene hypothesis in allergy and asthma: an update. Curr. Opin. Allergy Clin. Immunol. 13, 70-77. https://doi.org/10.1097/ACI.0b013e32835ad0d2.

Casey J.A., Kim B.F., Larsen J., Price L.B., Nachman K.E., 2015. Industrial Food Animal Production and Community Health. Curr. Environ. Health Rep. 2, 259-271. https://doi.org/10.1007/s40572-015-0061-0.

de Rooij M.M.T., Smit L.A.M., Erbrink H.J., Hagenaars T.J., Hoek G., Ogink N.W.M., et al., 2019. Endotoxin and particulate matter emitted by livestock farms and respiratory health effects in neighboring residents. Environment International. 132, 105009. https://doi.org/10.1016/j.envint.2019.105009.

Douglas P., Robertson S., Gay R., Hansell A.L., Gant T.W., 2018. A systematic review of the public health risks of bioaerosols from intensive farming. International Journal of Hygiene and Environmental Health. 221, 134-173. https://doi.org/10.1016/j.ijheh.2017.10.019.

Ege M.J., Mayer M., Normand A.-C., Genuneit J., Cookson W.O., Braun-Fahrländer C., et al., 2011. Exposure to environmental microorganisms and childhood asthma. New England Journal of Medicine. 364, 701-709. https://doi.org/10.1056/NEJMoa1007302.

Ehrenstein V., Mutius V., Kries V., 2000. Reduced risk of hay fever and asthma among children of farmers. Clin. Exp. Allergy. 30, 187-193. https://doi.org/10.1046/j.1365-2222.2000.00801.x

EPA, 2019. Integrated Science Assessment for Particulate Matter. EPA (U.S. Environmental Protection Agency), Research Triangle Park, NC.

ESRI [Environmental Systems Research Institute], 2011. ArcGIS Desktop, Redlands, CA.

Fontana L., Lee S.-J., Capitanelli I., Re A., Maniscalco M., Mauriello M.C., et al., 2017. Chronic Obstructive Pulmonary Disease in Farmers: A Systematic Review. Journal of occupational and environmental medicine. 59, 775-788. https://doi.org/10.1097/JOM.0000000000001072.

Gasparrini A., 2018. Package 'mvmeta'. https://cran.r-project.org/web/packages/mvmeta/mvmeta.pdf (accessed 10/10 2019).

Gowers A.M., Cullinan P., Ayres J.G., Anderson H.R., Strachan D.P., Holgate S.T., et al., 2012. Does outdoor air pollution induce new cases of asthma? Biological plausibility and evidence; a review. Respirology. 17, 887-898. https://doi.org/10.1111/j.1440-1843.2012.02195.x.

Guillien A., Soumagne T., Dalphin J.-C., Degano B., 2019. COPD, airflow limitation and chronic bronchitis in farmers: a systematic review and meta-analysis. Occup Environ Med. 76, 58-68. https://doi.org/10.1136/oemed-2018-105310.

Hendryx M., Luo J., Chojenta C., Byles J.E., 2019. Air pollution exposures from multiple point sources and risk of incident chronic obstructive pulmonary disease (COPD) and asthma. Environmental Research. 179, 108783. https://doi.org/10.1016/j.envres.2019.108783.

Illi S., Depner M., Genuneit J., Horak E., Loss G., Strunz-Lehner C., et al., 2012. Protection from childhood asthma and allergy in Alpine farm environments-the GABRIEL Advanced Studies. Journal of Allergy and Clinical Immunology. 129, 1470-1477.e6. https://doi.org/10.1016/j.jaci.2012.03.013.

Kauffmann F., Oryszczyn M.P., Maccario J., 2002. The protective role of country living on skin prick tests, immunoglobulin E and asthma in adults from the Epidemiological study on the Genetics and Environment of Asthma, bronchial hyper-responsiveness and atopy. Clin. Exp. Allergy. 32, 379-386. https://doi.org/10.1046/j.1365-2222.2002.01325.x.

Knol F., 1998. Van hoog naar laag; van laag naar hoog [From high to low; from low to high]. Sociaal en Cultureel Planbureau, The Hague, The Netherlands.

Kohansal R., Martinez-Camblor P., Agustí A., Buist A.S., Mannino D.M., Soriano J.B., 2009. The Natural History of Chronic Airflow Obstruction Revisited. Am J Respir Crit Care Med. . 180, 3-10. https://doi.org/10.1164/rccm.200901-0047OC.

Lai H., Aarnink A., Cambra-López M., Huynh T., Parmentier H., Koerkamp P.G., 2014. Size distribution of airborne particles in animal houses. Agricultural Engineering International: CIGR Journal. 16, 28-42.

Liu S., Zhou Y., Liu S., Chen X., Zou W., Zhao D., et al., 2017. Association between exposure to ambient particulate matter and chronic obstructive pulmonary disease: results from a cross-sectional study in China. Thorax. 72, 788-795. https://doi.org/10.1136/thoraxjnl-2016-208910.

May S., Romberger D.J., Poole J.A., 2012. Respiratory health effects of large animal farming environments. Journal of Toxicology and Environmental Health, Part B. 15, 524-541. https://doi.org/10.1080/10937404.2012.744288.

Post P.M., Hogerwerf L., Bokkers E.A.M., Baumann B., Fischer P., Rutledge-Jonker S., et al., 2020. Effects of Dutch livestock production on human health and the environment. Science of The Total Environment, 139702. https://doi.org/10.1016/j.scitotenv.2020.139702.

R Core Team, The R Stats Package. https://stat.ethz.ch/R-manual/R-devel/library/stats/html/00Index.html (accessed 05/02 2018).

Riedler J., Braun-Fahrländer C., Eder W., Schreuer M., Waser M., Maisch S., et al., 2001. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. The Lancet. 358, 1129-1133. https://doi.org/10.1016/S0140-6736(01)06252-3

RIVM, 2016. Grootschalige concentratie- en depositiekaarten Nederland [Large-scale concentration- and depostionmaps the Netherlands]. RIVM (National Institute for Public Health and the Environment), Bilthoven.

Salvi S.S., Barnes P.J., 2009. Chronic obstructive pulmonary disease in non-smokers. The Lancet. 374, 733-743. https://doi.org/10.1016/S0140-6736(09)61303-9.

Sauter F., Van Zanten M., Van der Swaluw E., Aben J., De Leeuw F., Van Jaarsveld H., 2018. The OPS-model. Description of OPS 4.5. 2. RIVM (National Institute for Public Health and the Environment), Bilthoven.

Schikowski T., Mills I.C., Anderson H.R., Cohen A., Hansell A., Kauffmann F., et al., 2014. Ambient air pollution: a cause of COPD? Eur. Respir. J. 43, 250-263. https://doi.org/10.1183/09031936.00100112.

Schultz A.A., Peppard P., Gangnon R.E., Malecki K.M.C., 2019. Residential proximity to concentrated animal feeding operations and allergic and respiratory disease. Environment International. 130, 104911. https://doi.org/https://doi.org/10.1016/j.envint.2019.104911.

Smit L.A.M., Hooiveld M., van der Sman-de Beer F., Opstal-van Winden A.W.J., Beekhuizen J., Wouters I.M., et al., 2014. Air pollution from livestock farms, and asthma, allergic rhinitis and COPD among neighbouring residents. Occup Environ Med, 134-140. https://doi.org/10.1136/oemed-2013-101485.

Strak M., Janssen N., Beelen R., Schmitz O., Karssenberg D., Houthuijs D., et al., 2017. Associations between lifestyle and air pollution exposure: Potential for confounding in large administrative data cohorts. Environmental Research. 156, 364-373. https://doi.org/10.1016/j.envres.2017.03.050.

van de Kassteele J., Zwakhals L., Breugelmans O., Ameling C., van den Brink C., 2017. Estimating the prevalence of 26 health-related indicators at neighbourhood level in the Netherlands using structured additive regression. International Journal of Health Geographics. 16, 23. https://doi.org/10.1186/s12942-017-0097-5.

van Dijk C.E., Garcia-Aymerich J., Carsin A.-E., Smit L.A.M., Borlée F., Heederik D.J., et al., 2016a. 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. 219, 278-287. https://doi.org/10.1016/j.ijheh.2016.01.002.

van Dijk C.E., Smit L.A.M., Hooiveld M., Zock J.-P., Wouters I.M., Heederik D.J.J., et al., 2016b. Associations between proximity to livestock farms, primary health care visits and self-reported symptoms. BMC Fam. Pract. 17, 22. https://doi.org/10.1186/s12875-016-0421-3.

van Kersen W., Oldenwening M., Aalders B., Bloemsma L.D., Borlée F., Heederik D., et al., 2020. Acute respiratory effects of livestock related air pollution on a panel of COPD patients. Environment International. 136. https://doi.org/10.1016/j.envint.2019.105426.

Venables W., Ripley B., 2002. Modern Applied Statistics with S. Springer, New York.

Viechtbauer W., 2010. Conducting meta-analyses in R with the metafor package. Journal of Statistical Software. 36, 1-48. https://doi.org/10.18637/jss.v036.i03

Viegi G., Scognamiglio A., Baldacci S., Pistelli F., Carrozzi L., 2001. Epidemiology of Chronic Obstructive Pulmonary Disease (COPD). Respiration. 68, 4-19. https://doi.org/10.1159/000050456.

von Mutius E., 2016. The microbial environment and its influence on asthma prevention in early life. J. Allergy Clin. Immunol. 137, 680-689. https://doi.org/10.1016/j.jaci.2015.12.1301

von Mutius E., Vercelli D., 2010. Farm living: effects on childhood asthma and allergy. Nature Reviews Immunology. 10, 861. https://doi.org/10.1038/nri2871.

Vonk J., Bannink A., van Bruggen C., Groenestein C., Huijsmans J., van der Kolk J., et al., 2016. Methodology for estimating emissions from agriculture in the Netherlands. Statutory Research Tasks Unit for Nature & the Environment, Wageningen.

Winkel A., Mosquera J., Groot Koerkamp P.W.G., Ogink N.W.M., Aarnink A.J.A., 2015. Emissions of particulate matter from animal houses in the Netherlands. Atmospheric Environment. 111, 202-212. https://doi.org/10.1016/j.atmosenv.2015.03.047.

Wlasiuk G., Vercelli D., 2012. The farm effect, or: when, what and how a farming environment protects from asthma and allergic disease. Curr. Opin. Allergy Clin. Immunol. 12, 461-466. https://doi.org/10.1097/ACI.0b013e328357a3bc.

World Health Organization, 2013. Review of evidence on health aspects of air pollution–REVIHAAP Project. World Health Organization, Copenhagen, Denmark.

Wunschel J., Poole J.A., 2016. Occupational agriculture organic dust exposure and its relationship to asthma and airway inflammation in adults. J. Asthma. 53, 471-477. https://doi.org/10.3109/02770903.2015.1116089.

Chapter 5

Effects of a transition towards circular livestock farming practices on human health and environment

Pim M. Post[a,b], Lenny Hogerwerf[a], Erik Lebret[b]

[a] *National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands*
[b] *Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, the Netherlands*

Submitted for publication

ABSTRACT

Plans to sustainably develop agriculture are likely to lead to many changes in livestock farming, which in turn may lead to a shift in human health and environmental impacts. For timely anticipation of such shifts in impacts, this foresight study used expert consultation to assess how changes in livestock farming are expected to affect human health and environmental impacts positively and negatively. Experts were asked to score the effect of a transition towards circular livestock farming at three levels: considering the transition as a whole, considering specific changes in livestock farming practices on four example farms, and considering broader developments in livestock farming. Of 97 invited experts, 26 participated in this study, with backgrounds in various disciplines related to biodiversity, the global footprint, or public health. Experts provided scores for one or more of these three themes and 15 more specific indicators commensurate with their expertise. Most changes in livestock farming described in this study were judged to have only limited positive and negative effects (less than 50% change in effect) on human health and the environment. Several synergies and trade-offs were elicited. An example is a trade-off between feed conversion efficiency and zoonotic infectious diseases. Changes in livestock practices have also received contrasting expert scores on the same indicator. This could be traced back to different interpretations of changes, indicators or system boundaries. Moreover, expected changes in livestock farming practices with similar numbers of animals, were considered insufficient to achieve environmental and public health targets. Furthermore, some trade-offs lead to dilemmas in policy development and decision making. Resolving such dilemmas and different expert interpretations may require a continued dialogue on the transition towards circular and more sustainable livestock production.

1 Introduction

Livestock production affects human health and ecosystems through the emissions of bioaerosols, greenhouse gasses, ammonia, and several other compounds, through the spread of infectious diseases, through high global land use, and through several other impacts (Herrero et al., 2015; Post et al., 2020; Smit and Heederik, 2017; Steinfeld et al., 2006). In the Netherlands, which has a large livestock sector relative to the country's size, the current form of livestock production is recognized to be no longer sustainable. The Dutch Minister of Agriculture, Nature and Food Quality has recently launched a vision based on a circular food system. Transitioning towards a circular system should lead to efficient resource use in the agricultural sector and also provide the opportunity to address several other sustainability targets (Ministry of Agriculture, 2018; Ministry of Agriculture, 2019). Targets mentioned are climate change, the relation between farmers and citizens, animal welfare, market position, regional economy, and nature conservation. Such targets are not limited to the Netherlands. They reflect several sustainable development goals and many of the objectives in a European Commission proposal for reform of the European common agricultural policy (European Commission, 2018; United Nations, 2015).

Human health receives little attention in the Dutch vision, while changes in health impacts are likely to occur when shifting to a circular food system, particularly for the livestock sector. Living in livestock farms' vicinity is associated with several types of adverse and beneficial human health effects (Casey et al., 2015; Post et al., 2020; Smit and Heederik, 2017). Moreover, historical and recent examples of changes in animal production systems have shown unintended adverse impacts. For example, a ban on battery cages for laying hens led to increased particulate matter and endotoxin emissions (Takai et al., 1998; Winkel et al., 2016). Significant increases in dairy goat farming in the Netherlands likely contributed to a sizable Q-fever outbreak in 2007-2010 (Roest et al., 2011). Furthermore, circular feeding practices have led to the spread or emergence of infectious diseases such as Bovine Spongiform Encephalopathy and African Swine Fever in the past (Brown et al., 2001; Guinat et al., 2016; Smith and Bradley, 2003).

Although there are examples of potentially adverse effects in a transition towards a circular livestock system, information about such effects and the factors causing them is fragmented. We previously brought together such fragmented information for 17 different human health and environmental impacts, ranging from infectious disease impacts and odor annoyance to eutrophication and greenhouse gas emissions (Post et al., 2020). The data underlying that work originated from diverse sources, which are not always suitable to predict how impacts may change when changes in livestock practices occur. For example, antimicrobial use in animals is well monitored within the Netherlands and there is an increasing understanding of how antimicrobial use in animals and emerging antimicrobial resistance in humans may relate. Nevertheless, no model is available that can predict how a change in the housing system, animal breed, or feed source would affect resistance development. Such implicit knowledge and any crucial gaps in knowledge may be collected through expert consultation.

Here we explore an approach to *ex ante* address the following research question: "How will changes in livestock production in a transition towards a circular food system or more sustainable livestock sector affect human health and the environment, and what are potential trade-offs and synergies that may occur?"

The specifics of a circular food system or a more sustainable livestock sector are not well defined and seem to be intentionally left open in the ministerial vision (Ministry of Agriculture, 2018; Ministry of Agriculture, 2019). Different ideas exist about what role livestock production should play in a healthy and sustainable food system (van Zanten et al., 2018). These include meeting the increasing demand for animal products through sustainable intensification, mitigating several adverse effects by reducing consumption of animal products, and striving for optimal resource use by only keeping livestock to efficiently use feed-sources that are not suitable for human consumption (van Zanten et al., 2018).

We do not choose one of these ideas as being the preferred one. Instead, we are interested in what changes in livestock farming practices may occur in the context of the Dutch Ministers' vision, which we refer to as a transition towards circular livestock farming, and what the potential side-effects of these would be. Therefore, we build our approach around four different farms that apply some form of circular practices. These examples serve as a basis to identify possible changes in farming practices and related broader developments. Experts scored how such changes and developments may affect several human health and environmental indicators.

2 Methods

For answering the research question we used an approach based on expert consultation, in which experts were asked to judge changes that may occur in a transition towards circular livestock farming, according to their own expertise. Because live interaction between experts was difficult due to the COVID-19 pandemic, experts were consulted through a webform, and in several related interactions.

The webform consisted of three parts in which experts could provide scores (Figure 1), and some additional questions asking how experts experienced the consultation and scoring. The webform also contained some questions regarding the expertise of experts, which determined which questions were shown to them. In part one, experts were asked questions about the effect of livestock production in a transition towards circular livestock farming on one or more out of three broad themes, depending on their expertise. These broad themes included the environment or biodiversity in the Netherlands; the global footprint; and public health in the Netherlands.

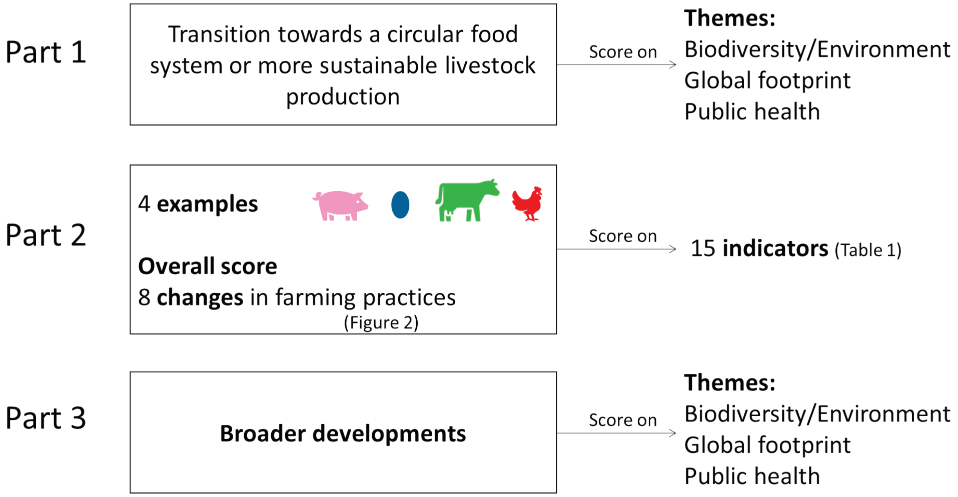


Figure 1. Overview of the webform.

In part two of the form, experts were asked questions about the effect of specific changes in farming practices that were described in the context of four *example* farms, on 15 human health and environmental *indicators*. The example farms represent major production sectors within the Netherlands (Cattle, Pigs, Broilers, Layers) and additionally reflect roughly two trends: a trend towards increasing efficiency and a trend towards maximum use of own resources. These trends fit the classification of Erisman and Verhoeven (2019), who additionally distinguish nature-based farms as a third type of farm that can be considered as applying circular practices. The example farms distinguished are:

- a highly efficient pig farm
- a highly efficient poultry farm
- a cattle farm with maximum use of own resources
- a poultry farm with maximum use of own resources

The descriptions of these examples are inspired by the vision document of the Dutch ministry of Agriculture, Nature and Food Quality, reports related to this vision, and a website with stories about farms that may serve as inspiration for the transition towards circular livestock farming (Erisman and Verhoeven, 2019; Ministry of Agriculture, 2018; Ministry of Agriculture, 2019; Platform Kringlooplandbouw [Platform circular agriculture], 2020; WUR E-depot, 2020). The descriptions and more information about how they are chosen are included in the supplementary material. For each of the example descriptions, a description of a reference farm was made as well, representing common agricultural practices of the corresponding animal sector. Differences in farming practices between the descriptions of example and reference farm were interpreted as changes in farming practices. These could be measures or interventions but also practices that change along with them. The changes were characterized according to eight different types of farming practices (Figure 2): “changes in housing systems”, “changes in animals”, “changes in herd management”, “changes in manure treatment and storage”, “changes in manure application and soil management”, “changes in feed”, “changes in water system” and “changes in side activities”.

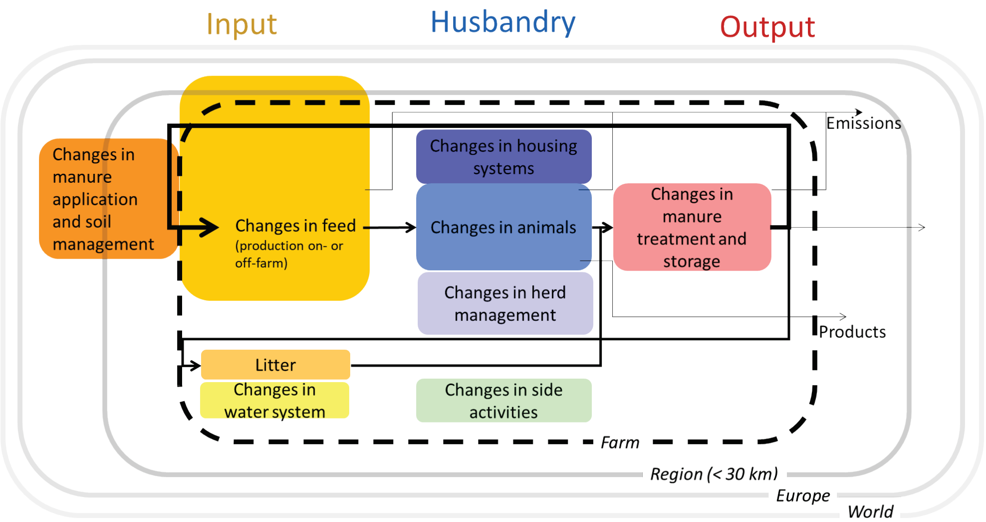


Figure 2. Scheme indicating changes on a farm or elsewhere in the production chain.

The selected indicators that were scored by experts in part two of the form, are presented in Table 1. The indicators reflect impact categories distinguished in Post et al. (2020), but are defined differently because the scores in part two of the webform focus on farm-level changes, whereas in Post et al. (2020) effects were assessed on a national level. The indicators should be unspecific enough to not require too much detail about expected changes for scoring by experts, specific enough for a meaningful assessment of selected themes and balanced between proximity to endpoints (e.g. human health, biodiversity loss, climate change) and farm level metrics (e.g. emissions, production quantity).

In part three of the webform, experts were asked questions about the effect of broader developments in the livestock sector on the environment or biodiversity in the Netherlands, on the global footprint or on public health in the Netherlands. These broader developments partly reflected the farm-level changes:

- a shift towards other (less productive) animal breeds
- continuous development of innovations in housing systems to limit emissions
- continuous innovations in manure treatment
- the demand for byproducts as source of animal feed in the Netherlands increases
- more farms produce a larger proportion of feed by themselves
- more farms will look for additional sources of income, such as a care farm

Broader developments suggested by experts are listed in the supplementary material.

Table 1. Selected indicators.

Indicator	Definition
Environment/Biodiversity in the Netherlands	
Organic matter balance arable land/feed crops	The total supply of organic matter from crop residues, organic fertilizers and green manure minus the degradation of organic matter and disposal per calendar year on the location of feed production (kg EOS per ha per year) *EOS = effective organic matter (not degraded within 1 year)*
Nitrogen-efficiency	$\frac{nitrogen\ disposal}{nitrogen\ supply}$, where: Nitrogen disposal: the amount of nitrogen (kg) in animals, plants, manure, etc., that leaves the farm Nitrogen supply: the amount of nitrogen (kg) that is supplied for feed production on or off the farm (manure, artificial fertilizers) and all other supply of nitrogen to the farm (in animals, litter)
Environmental indicator units (plant protection products)	Damage to organisms in soil, groundwater and surface water in the Netherlands because of use of plant protection products during feed production, determined based on dose, drift and toxicity and scaled to 1 ha feed production
Effects of use of biocides other than plant protection products on organisms in the environment[1]	Damage to organisms in soil, groundwater and surface water in the Netherlands because of use of biocides other than plant protection products (including deworming- and fly pesticides), during feed production, determined based on dose, drift and toxicity and scaled to total use on 1 farm
Global footprint	
Greenhouse gas emissions in production chain	Greenhouse gas emissions for the production of 1 kg animal protein in processes between harvest of crops for feed production and application of animal manure (CO_2-equivalents/kg protein)
Use of blue water in production chain	Use of blue water (surface- and ground-water) for the production of 1 kg animal protein in processes between harvest of crops for feed production and application of animal manure (m^3/kg protein)

Land use in production chain	Land use (within and outside the Netherlands) required for the feed production for 1 kg animal protein (ha/kg protein)
Public health effects in the Netherlands	
Primary particulate matter emissions	Primary particulate matter emissions from housing system (kg/year)
Endotoxin emissions	Endotoxin emissions from housing system (endotoxin units/year)
Ammonia emissions	Ammonia emissions on farm (kg/year)
Odor emissions	Odor emissions on farm (odor units/second, average per year)
Amount of traffic	Amount of traffic that visits the farm (number of trucks/week)
Number of human infections per year with known zoonotic diseases[2] originating from livestock	Number of human infections per year with known zoonotic diseases originating from a farm, which are being transmitted through direct contact with animals or through the environment. Consider not only possible exposure but also introduction of zoonotic pathogens on a farm and transmission between animals on a farm location.
Probability of development of antimicrobial resistance	Probability of development of antimicrobial resistance on the farm
Probability of development of emerging zoonotic disease[2]	Probability that a zoonotic disease emerges in a region, change in host or development of new characteristics

[1] Not included in rest of the text because no expert-scores were received for this indicator.

[2] A zoonotic disease is an infectious disease that can be transmitted from animals to humans

In each part of the webform, experts could provide a score and an explanation for their scores. Scores for part one and three, could be “a negative effect”, “no effect” or “a positive effect”. For part two, the following scores could be given: “a strong negative (adverse) effect of more than 50%”, “a negative (adverse) effect of between 10 and 50%”, “no effect (less than ± 10% effect)”, “a positive (beneficial) effect of between 10 and 50%”, “a strong positive (beneficial) effect of more than 50%”, or “I don’t know/effect unknown”. For some indicators indeed at least 50% change nationally may be required to reach policy targets for greenhouse gas emissions, particulate matter emissions or water quality.

Experts that were invited to fill out the webform, were selected based on their expertise regarding one or more indicators, or regarding the livestock sector. They were selected because their publications indicated their expertise, because they were known by the researchers, or because their name was suggested in interviews in the context of this study. Invited experts could suggest other experts as well.

In addition to the webform, authors had several additional interactions with some of the experts. To prepare the webform, 12 experts were interviewed to evaluate descriptions of *example farms* or to evaluate the selection and definition of *indicators*. Further, during analysis of the expert-scores from the webform, several experts were contacted and asked to clarify their scores. Finally, the results of the analyses were reported in a Dutch report and shared with the initially invited experts for feedback. An online meeting was set up to allow for expert interaction and further feedback, enrichment of interpretation of results and of conclusions.

3 Results

3.1 Response

A total of 97 experts were invited to fill out a webform, from the end of May to the beginning of August 2020. During this period the webform has been offline for three-and-half weeks due to external software problems, and experts were offered to fill out a paper replacement questionnaire. Of the 97 invited experts, twenty-one experts completely filled out the (web)form, and scores of an additional five out of fourteen experts that filled out part of the form could be used for the analyses. Twenty of these twenty-six experts worked at a university or research institute, three as advisor (in government or sector association), one as veterinarian/inspector, and two as policy officers (one of a societal organization and one of a feed company). The experts working as a researcher indicated that they did research on agriculture/livestock production (7), environment (7), sustainability (6), human health (6), infectious diseases (5), animal health (5), biodiversity (4), soil (3), behavioral economics (1), and “animal in the food system – holistic view” (1) . The main reason provided by experts to not participate was a lack of time. Five experts provided some form of feedback on the concept-report. Seven experts participated in the online meeting.

3.2 Few extreme scores

In all three parts of the webform, many neutral scores and few extreme scores were provided by experts. In part one, the majority of experts expected little or no effect of livestock farming on the global footprint (50% of the experts) and public health (68% of the experts), in a transition towards circular livestock farming, although more positive than negative scores were provided. Effects on biodiversity in the Netherlands were more often judged positively (57% of the experts), but according to several experts this depended on the specific definition of a circular agriculture and the scale on which nutrient cycles would be closed.

In part two of the webform, effects of specific changes in farming practices on the 15 indicators also received a neutral score in the majority of the cases and only few extreme scores, as can be seen in Figures 3 and 4. Figure 3 shows that the number of experts varied across indicators and that most experts judged that overall, example farms had either less than 10% effect or a positive effect of 10-50% on the indicators. Few extreme scores (more than 50% effect) were provided and also less negative scores than positive or neutral scores. Figure 4 shows that almost half (168/338) of the effects of a farming practice on an indicator were expected to be less than 10 percent (black dots). Few extreme scores were provided (Figure S1).

In part three of the webform, effects of broader developments in the livestock sector received neutral scores by the majority of experts, similar to the scores in part one, with also more positive scores than negative scores. Some arguments for these neutral scores were that the effect of animal breed would strongly depend on the number of animals that would be present in the Netherlands, and doubts about whether feed production in the Netherlands would be more efficient than elsewhere, if more farmers would produce their own feed.

3.3 Synergies

Despite many neutral scores, some synergies were identified as well, i.e. changes in farming practices that had a beneficial effect on several indicators and little or no negative effect on others (Figure 4). One change in farming practices that scored well on several indicators was a change in housing system in the example of the highly efficient pig farm, with the main change being a pig toilet to separate urine and solid manure. This change was judged to have positive effects on nitrogen-efficiency, greenhouse gas emissions, ammonia emissions and odor emissions. Also changes in management of manure and soil positively affected several indicators: effects on organic matter balance, nitrogen use efficiency, effects of pesticide application, and greenhouse gas emissions, although different experts scored differently regarding effects on land use and effects on ammonia emissions.

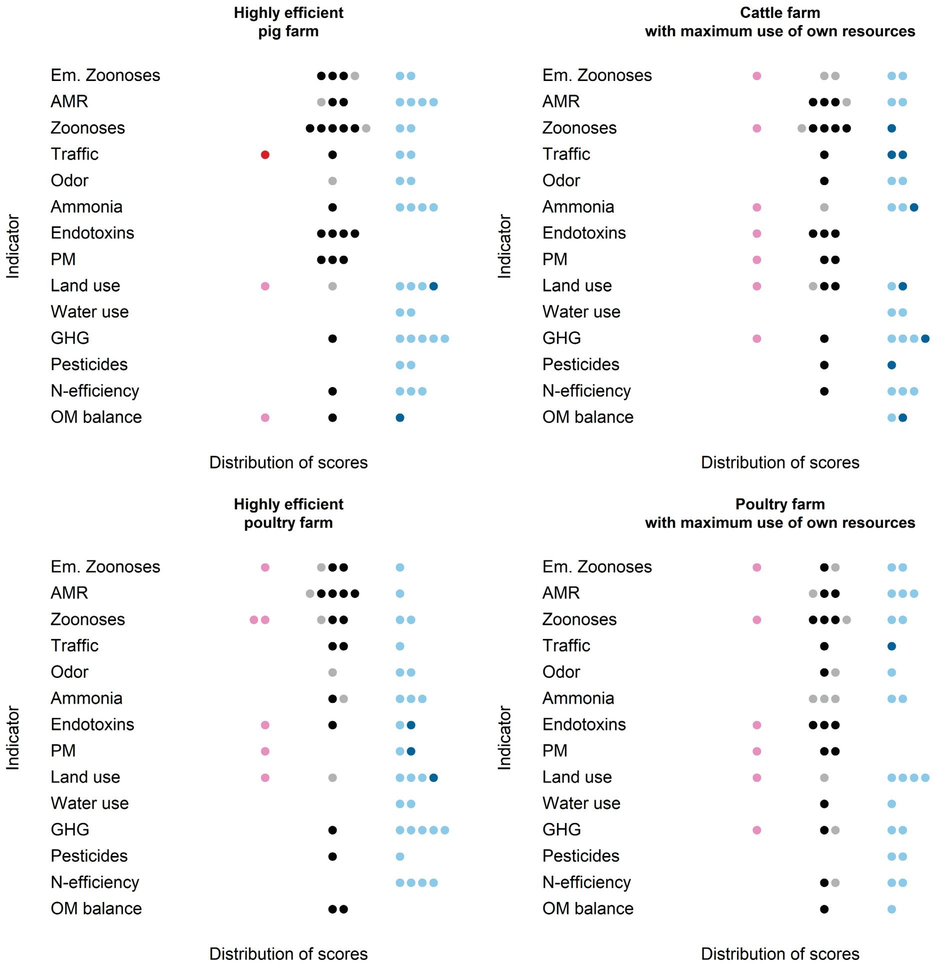


Figure 3. Expert scores regarding the overall effect of an example farm on the indicators of his or her expertise. Red dots represent a strong negative effect, pink dots represent a negative effect, black dots represent a neutral effect, light blue dots represent a positive effect, dark blue dots represent a strong positive effect, and grey dots represent “I don’t know/effect unknown”. More specific indicator definitions can be found in Table 1. Em. Zoonoses = emerging zoonoses; AMR = antimicrobial resistance; PM = particulate matter; GHG = greenhouse gasses; N-efficiency = nitrogen-efficiency; OM balance = organic matter balance.

3.4 Trade-offs

Several trade-offs related to changes in livestock farming practices were identified as well. One trade-off can be observed when examining the effects of changes towards dual-purpose cattle and slower growing poultry breeds, and changes in herd management in the cattle farm with maximum use of own resources (Figure 4). Such changes can be interpreted as a change towards less efficient resource use per unit of production, with related negative scores on land use and greenhouse gas emissions. In contrast to these detrimental effects, the changes were judged to be beneficial for zoonotic diseases and antimicrobial resistance, according to several experts.

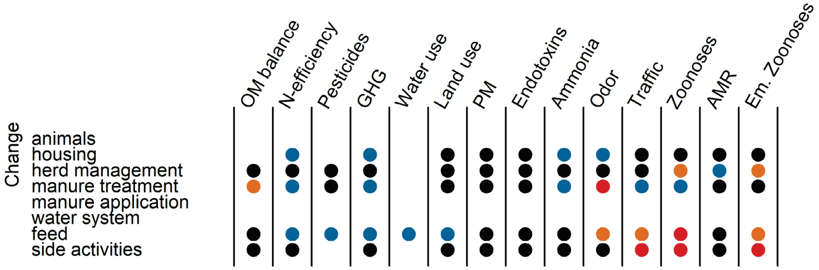
Another potential trade-off is related to the use of by-products as animal feed, as was part of three out of four examples (Figure 4). These feed sources were judged as having a positive effect on particularly land use, water use, greenhouse gas emissions, ammonia emissions and nitrogen use efficiency, yet potential risks for zoonotic diseases may occur if feed sources are insufficiently monitored and treated.

Manure treatment may have both positive and negative effects as well, but what these are depends on the farm type and type of treatment (Figure 4). For example, manure fermentation may have a negative effect on organic matter balance while manure from deep litter housing may have a positive effect. Furthermore, manure from deep litter housing may pose a risk for zoonotic pathogens, while manure fermentation may reduce such risk.

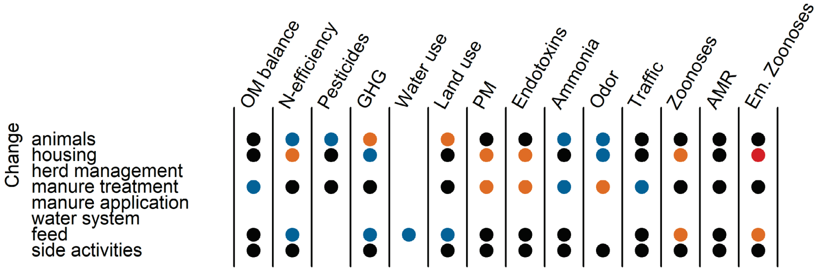
Some farming practices with potential risks do not have a clear beneficial effect that follows from this study (Figure 4). Examples are risks for the spread and emergence of zoonotic diseases due to farmers organizing side-activities such as farm visits, or due to the housing systems in the two examples of poultry farms. The latter were judged to have a potential risk for zoonotic disease spread or emergence, because the free range housing systems would pose a risk for introduction of new diseases.

A potential risk not apparent from the scores on changes in specific farming practices, is the accumulation of toxic compounds under circular agricultural practices. This concern was expressed by three experts in part one of the webform, in which experts were asked to judge the effects of a transition towards circular livestock farming.

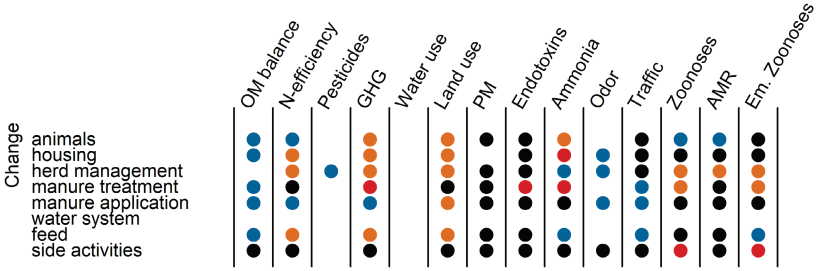
Highly efficient pig farm



Highly efficient poultry farm



Cattle farm with maximum use of own resources



Poultry farm with maximum use of own resources

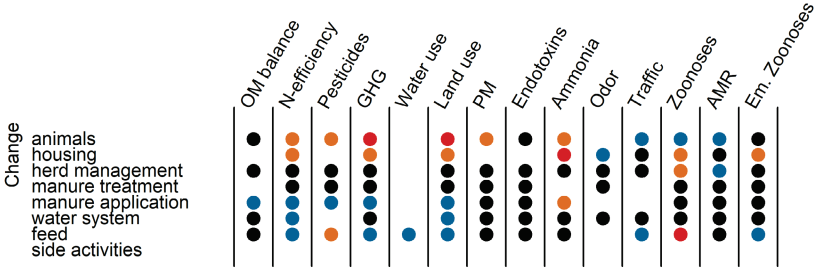


Figure 4. Effects of changes in farming practices on different indicators, that received a positive score from at least two experts and no negative score (blue), a negative score from at least two experts and no positive score (red), both positive and negative scores from different experts (orange), or a neutral score from at least two experts (black). More specific indicator definitions can be found in Table 1. Em. Zoonoses = emerging zoonoses; AMR = antimicrobial resistance; PM = particulate matter; GHG = greenhouse gasses; N-efficiency = nitrogen-efficiency; OM balance = organic matter balance.

3.5 Contrasting scores

Different experts did not always provide the same score for the same indicator. Several explanations for such differences have been identified (Table S1). In some cases a score may be context-dependent or requires more research to correctly estimate an effect. One example of this is the difference in scores regarding the effects of changes in manure treatment in the example of a highly efficient poultry farm. Whether the manure drying in this example leads to odor, endotoxin and fine dust emissions to the outside air, may depend on the functioning of the installed filters.

In other cases, experts may argue differently because they account differently for several smaller changes. For example, both positive and negative scores were given for the effects on greenhouse gas emissions of a change in housing system in the example of the cattle farm with maximum use of own resources. Several changes in the housing system were described in the example, including a change from a free stall to deep litter housing and the use of solar panels. These different changes may have contrasting effects on greenhouse gas emissions, and experts may have accounted for these differently.

Differences in argumentation may also result from different interpretations of indicator, change or system boundaries. A different interpretation of system boundaries was for example observed in the scores of a change in manure application in the example of a poultry farm with maximum use of own resources. That example of a farm with both broilers and crop production, was compared to a broiler farm with no own land to produce feed. In the example, manure was applied to the farmer's own arable land or that of neighbors, with hence on-farm ammonia emissions. Yet in the reference farm manure was brought to a biomass power plant, with hence fewer on-farm ammonia emissions but presumably more emissions for feed production elsewhere. Whether or not taking this chain-effect into account affects the score. Such chain-effect may be relevant and was part of some of the indicator definitions, such as that of nitrogen-efficiency (Table 1). The indicator for ammonia emissions did not include chain-effects because the primary reason for choosing that indicator was the local effects of ammonia emissions.

4 Discussion

This study used an expert consultation approach to *ex ante* assess the effects of expected changes in livestock farming practices, in a transition towards circular livestock farming. In line with the vision of the ministry of Agriculture, in this study, no explicit definitions for these concepts were provided (Ministry of Agriculture, 2018; Ministry of Agriculture, 2019). Most changes in livestock farming that have been described in this study were judged to have only limited (less than 50 % change) positive and negative effects on human health and the environment; and several synergies and trade-offs were identified. The study also indicates that expert scores may depend on interpretations of changes, system boundaries and indicators, which may be affected by differences in perspective of different experts.

4.1 Limited effect on human health and environment

Because most changes in livestock farming practices were judged to have a limited or no effect, these expected changes may not be sufficient to address societal concerns. The majority of changes in farming practices were judged to have less than 50% effect according to most experts and over half of the farming practices were even thought to have less than 10% effect (neutral score) on many of the environmental and human health indicators. This amount of neutral scores indicates that not all changes in farming practices affect all indicators, which is not surprising, as changes in farming practices may often be directed towards improvement in a limited set of indicators, thus ideally not affecting several other indicators. Developments in the livestock sector that are broader than changes on the farm-level, received a neutral score by the majority of experts as well.

These limited effects imply that expected changes in livestock farming practices are considered insufficient to reduce all human health and environmental impacts, given several formulated societal goals and policy targets. For example, the Dutch climate agreement requires a reduction of agricultural greenhouse gas emissions of almost 20% in 2030 compared to 2018 and in 2050 a reduction over all sectors of 95% compared to 1990 (Klimaatberaad, 2019; Ruyssenaars et al., 2020). Another ambition is a reduction of 50% particulate matter emissions from existing poultry housing and 70% reduction for new housing between 2017 and 2027 (van Dam and

Dijksma, 2017). Also strong ambitions for the reduction of nitrogen emissions have been formulated (Schouten, 2020).

The expectation that changes in livestock farming practices are hence not sufficient to address all human health and environmental concerns is in line with reports of the Netherlands Environmental Assessment Agency about the limited improvement of current agricultural policies regarding the environment in its biannual assessment on the state of the environment and environmental policy (Bouma et al., 2020). This does not mean that a transition towards circular livestock farming is not suitable for reaching human health and environmental ambitions. Reaching these may strongly depend on the specific definition of circular livestock farming and what it implies for import, export and the size of the livestock sector, as several experts have indicated.

4.2 Trade-offs

Several trade-offs of changes in farming practices have been identified. These were a trade-off between feed conversion efficiency and zoonotic diseases; a trade-off between the reduction of the environmental footprint and risk of zoonotic diseases when using by-products as feed; and several trade-offs in different forms of manure treatment. Some of these trade-offs may be addressed without fundamentally altering the context of the production system. For example, the risk of zoonotic diseases when using by-products as feed, may be of less concern when these by-products are properly treated and the quality is carefully monitored, as several experts have indicated.

However, not all trade-offs may be easily addressed. The trade-off between feed conversion efficiency and zoonotic diseases, for example, may indicate a limit as to how far efficiency can be pushed without compromising animal health, and indirectly human health, by affecting the spread of zoonotic diseases and development of antimicrobial resistance. This trade-off was observed because several experts indicated a beneficial effect on antimicrobial resistance and zoonotic diseases, in a system with slower growing broilers and in a farm on which cattle grew older. A higher efficiency than in these systems, without compromising health, may be possible under high levels of biosecurity, but the results of the expert elicitation do suggest that there is a limit to this efficiency. Such dilemmas were no surprise to experts who attended the online meeting following the consultation. In that meeting experts indicated that in some cases a fundamental redesign may be required to further increase sustainability, without unwanted side-effects. In other cases accepting a limited number of negative side-effects in favor of desired positive effects may be necessary.

4.3 On the same page

The many contrasting expert scores imply that scores are influenced by different expert perspectives. Contrasting expert scores partly resulted from differences in how experts interpreted a change in farming practice, an indicator or the production system. One reason for differences in interpretation was that some experts did take into account off-farm effects in their scores whereas others did not, even though the indicator definitions indicated whether such production chain effects should or should not be taken into account. Such production chain effects were included in indicator definitions for the greenhouse gas emissions, water use and land use indicators, whereas the focus for particulate matter, endotoxins, ammonia and odors was on on-farm emissions. The reason for these different choices is that some indicators are mainly relevant for a local concern (e.g. odor annoyance), whereas for others the local context is less relevant (e.g. greenhouse gas emissions). The differences in scores was also the reason why initially a live interaction between experts was planned, which became difficult due to the COVID-19 pandemic. Identifying and discussing differences in scores would indeed be valuable according to several experts, as this would help to learn from others with a different perspective. The implication of differences in interpretation, which may be driven by differences in background and interest, is that it may take long before experts, or stakeholders, gain mutual understanding, let alone agree on how trade-offs should be addressed.

4.4 Strengths and Limitations

The advantage of consulting experts is that it helps to elicit a variety of implicit expert knowledge. In several cases the approach elicited rather complex reasoning. For example, one expert reasoned that a change in management practices characterized by a reduction of antibiotics use would lead to less spread of zoonotic diseases, because the reduced antibiotics would imply that animals are healthier, rather than that they would have more diseases because they receive less antibiotics. For such reasoning, formal models may not always be equally suitable.

A drawback of depending on experts with different degrees of expertise is that it requires a considerable time-investment of experts, which is also a reason that several invited experts could not participate. Moreover, the pattern of expert scores strongly depends on the selection of experts, where one expert more or less could make a difference, even though for some scores there was considerable agreement among experts. On the other hand, one expert with a different opinion than others can already provide new insights. Checking the validity of such scores would be less difficult than inferring whether some relevant risks or trade-offs were not identified. To somewhat limit the range of expertise for each indicator, experts were asked to only score indicators that fitted their expertise.

Another key aspect of the approach used here are the four example farms that were described. Although these examples cover the most important animal sectors in the Netherlands, they cannot comprise the diversity of farming systems. The examples and related changes in farm characteristics were carefully chosen but nevertheless some features of the examples were judged unrealistic by some experts. This may be partly due to the wish to fit as much changes in farm characteristics as possible in the examples. Further, a comparison of examples is not directly warranted as the farms in the examples produce different types and amounts of products. Using different examples does help to make changes in a transition towards circular livestock farming more explicit, and to provide a wide set of possible changes in farm characteristics. Furthermore, apart from farm-specific lessons, the examples do provide some general lessons, for example regarding the use of by-products for animal feed, free range systems, and side-activities, which are described in multiple examples.

Another strength is that trade-offs and risks were identified that were reflected in several parts of the expert consultation. They were often observed in multiple parts of the webform or mentioned in interviews prior to and after the webform could be filled in. Most of the identified risks and trade-offs have also been described in the literature. For example, the potential risks of animal feed on human health have been described in Sapkota et al. (2007). The risk of introduction of pathogens in free range poultry farms have been described as well in the context of potential introductions of low-pathogenic avian influenza (Bouwstra et al., 2017; Elbers and Gonzales, 2020). Also, the presence of persistent animal medicines in the environment has been described before (Lahr et al., 2018; Lahr et al., 2017). This indicates that the approach used here is able to identify potential trade-offs and risks. On the other hand, no new risks were identified, which makes it unclear how suitable the approach would be for identifying such new risks; and how well experts are able to *ex ante* identify new risks.

This study also takes into account a wide range of human health and environmental impacts. Although broad enough to identify several trade-offs, the selective focus on human health and environmental impacts is of course not able to show trade-offs related to other domains such as animal welfare or economic aspects. Animal welfare, for example is a relevant aspect in free range poultry systems, which may pose risks for zoonotic diseases according to the judgements in this study.

Another limitation is that scores do not necessarily indicate how well a change in effect helps to address a societal concern. One reason for this is that scores show a relative effect rather than an absolute impact. For example, if a farm already has low particulate matter emissions, a change of 50% may be less relevant than if the farm would already have substantial emissions. A second reason is that scores on farm-level changes do not necessarily reflect what would happen if multiple farms would apply the same changes. For this reason, experts were not only asked to assess farm-level changes, but also to assess the effects of broader developments in the livestock sector. Despite these reasons, the many neutral scores provided by experts still imply an anticipated limited effect of farm-level or broader changes on several indicators.

4.5 Future steps

How to deal with trade-offs that are not easily addressed, was discussed in an online meeting with experts. In this meeting it was argued that in some cases a redesign of livestock farming is required. In other cases some of the adverse effects may need to be accepted in favor of beneficial effects, requiring a benefit-risk assessment. For example, on a care farm, more persons may be exposed to zoonotic diseases, but this may be accepted in the light of the societal function that the care farm provides. This requires weighing the several effects of livestock farming practices, which may take place on local, regional, national or international levels.

A continued dialogue in relation to the transition towards circular livestock farming may thus be required, which could benefit from additional research as well. An expansion in scope may be required to assess trade-offs not yet highlighted, for example by including other themes besides human health and environmental impacts, or by taking a regional or national level perspective instead of a farm-level perspective. Such national perspective, may foster further discussion about the scale on which nutrient-cycles should be closed and the related consequences for the size of the livestock sector in a country, which is something that several experts have drawn attention to.

Conversely, an expansion of the depth of analysis may be required as well. Further exploration of the reasons for differences in expert scores, or studying example farms or actual farms in more detail may elucidate under what conditions certain farming practices may or may not be desirable. Such more in-depth assessment may also help to explore the validity or size of perceived risks by addressing specific knowledge gaps, such as safety aspects of using by-products as animal feed, or the accumulation of persistent chemicals in the environment in the context of a circular agricultural practices. Furthermore, the importance of regular monitoring of the safety and quality of alternative feed sources has been stressed by several experts. Such regular monitoring may also help to identify potential risks of other changes in farming practices.

5 Conclusion

In conclusion, *ex ante* expert judgements show that anticipated changes in livestock farming practices, assuming a similar number of animals, have limited positive effects on human health and the environment. This effect appears too small to achieve environmental and public health targets set by government. Furthermore, there are several trade-offs, such as a trade-off between feed conversion efficiency and zoonotic diseases, and a trade-off between reducing environmental impacts but potentially increasing zoonotic disease risks when using by-products as feed. Not all of these may be easily addressed, requiring redesigning livestock farming or hard choices on prioritizing several beneficial or adverse effects. In addition, expert scores may depend on their different interpretations of changes, system boundaries and indicators. These identified trade-offs, and divergent perspectives provide a first impression of the effects of a transition towards circular livestock farming and may provide a basis for a continued dialogue on this topic.

Supplementary Material is available online at:
https://www.researchgate.net/publication/352933642_SupplementaryMaterial.pdf

Acknowledgements

We thank all experts providing input in any of the several parts of the expert consultation. We further thank Rob Maas, Mark Montforts and Leo Posthuma (National Institute for Public Health and the Environment, Bilthoven, the Netherlands) for their input on the design of the study.

References

Bouma J., Boot P., Bredenoord H., Dietz F., van Eerdt M., van Grinsven H., et al., 2020. Burger in zicht, overheid aan zet: Balans van de Leefomgeving 2020 [Citizens within sight, government's turn: Balance of the living environment 2020] PBL (Netherlands Environmental Assessment Agency), Den Haag.

Bouwstra R., Gonzales J., de Wit S., Stahl J., Fouchier R.A.M., Elbers A.R.W., 2017. Risk for Low Pathogenicity Avian Influenza Virus on Poultry Farms, the Netherlands, 2007–2013. Emerging Infectious Disease journal. 23, 1510. https://doi.org/10.3201/eid2309.170276.

Brown P., Will R.G., Bradley R., Asher D.M., Detwiler L., 2001. Bovine spongiform encephalopathy and variant Creutzfeldt-Jakob disease: background, evolution, and current concerns. Emerging Infectious Diseases. 7, 6-16. https://doi.org/10.3201/eid0701.010102.

Casey J.A., Kim B.F., Larsen J., Price L.B., Nachman K.E., 2015. Industrial Food Animal Production and Community Health. Curr. Environ. Health Rep. 2, 259-271. https://doi.org/10.1007/s40572-015-0061-0.

Elbers A.R.W., Gonzales J.L., 2020. Quantification of visits of wild fauna to a commercial free-range layer farm in the Netherlands located in an avian influenza hot-spot area assessed by video-camera monitoring. Transbound. Emerg. Dis. 67, 661-677. https://doi.org/10.1111/tbed.13382.

Erisman J.W., Verhoeven F., 2019. Kringlooplandbouw in de praktijk [Circular agriculture in practice]. Louis Bolk Instituut, Boerenverstand, Bunnik, Utrecht.

European Commission, 2018. Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL establishing rules on support for strategic plans to be drawn up by Member States under the Common agricultural policy (CAP Strategic Plans) and financed by the European Agricultural Guarantee Fund (EAGF) and by the European Agricultural Fund for Rural Development (EAFRD) and repealing Regulation (EU) No 1305/2013 of the European Parliament and of the Council and Regulation (EU) No 1307/2013 of the European Parliament and of the Council, Brussels.

Guinat C., Gogin A., Blome S., Keil G., Pollin R., Pfeiffer D.U., et al., 2016. Transmission routes of African swine fever virus to domestic pigs: current knowledge and future research directions. The Veterinary record. 178, 262-267. https://doi.org/10.1136/vr.103593.

Herrero M., Wirsenius S., Henderson B., Rigolot C., Thornton P., Havlík P., et al., 2015. Livestock and the environment: what have we learned in the past decade? Annu. Rev. Environ. Resour. 40, 177-202. https://doi.org/10.1146/annurev-environ-031113-093503.

Klimaatberaad, 2019. Klimaatakkoord [Climate agreement]. https://www.klimaatakkoord.nl/klimaatakkoord/documenten/publicaties/2019/06/28/klimaatakkoord (accessed 07/17 2019).

Lahr J., Derksen A., Wipfler L., van de Schans M., Berendsen B., Blokland M., et al., 2018. Diergeneesmiddelen & hormonen in het milieu door de toediening van drijfmest [Veterinary drugs & hormones in the environment because of application of liquid manure]. Wageningen Environmental Research, Wageningen.

Lahr J., Wipfler L., Bondt N., de Koeijer T., Berendsen B., Hoeksma P., et al., 2017. Aanzet tot milieuprioritering van diergeneesmiddelen uit dierlijke mest [Starting point for environmental prioritization of veterinary drugs from animal manure]. Water Matters: Kenniskatern voor Waterprofessionals-Dutch edition, 8-11.

Ministry of Agriculture, 2018. Landbouw, natuur en voedsel: waardevol en verbonden - Nederland als koploper in kringlooplandbouw [Agriculture, nature and food: valuable and connected - The Netherlands as a leader in circular agriculture]. Ministerie van Landbouw, Natuur en Voedselkwaliteit [Ministry of Agriculture, Nature and Food Quality], Den Haag.

Ministry of Agriculture, 2019. Realisatieplan Visie LNV: Op weg met nieuw perspectief [Realization plan Vision LNV: Under way with new perspective] Ministerie van Landbouw, Natuur en Voedselkwaliteit [Minstry of Agriculture, Nature and Food quality], Den Haag.

Platform Kringlooplandbouw [Platform circular agriculture], 2020. Initiatieven en inspiratie [Initiatives and inspiration]. https://www.platformkringlooplandbouw.nl/initiatieven-en-inspiratie (accessed 09/03 2020).

Post P.M., Hogerwerf L., Bokkers E.A.M., Baumann B., Fischer P., Rutledge-Jonker S., et al., 2020. Effects of Dutch livestock production on human health and the environment. Science of The Total Environment, 139702. https://doi.org/10.1016/j.scitotenv.2020.139702.

Roest H., Tilburg J., Van der Hoek W., Vellema P., Van Zijderveld F., Klaassen C., et al., 2011. The Q fever epidemic in The Netherlands: history, onset, response and reflection. Epidemiol. Infect. 139, 1-12. https://doi.org/10.1017/S0950268810002268.

Ruyssenaars P., Coenen P., Rienstra J., Zijlema P., Arets E., Baas K., et al., 2020. Greenhouse gas emissions in the Netherlands 1990-2018: National Inventory Report 2020. National Institute for Public Health and the Environment (RIVM).

Sapkota A.R., Lefferts L.Y., McKenzie S., Walker P., 2007. What do we feed to food-production animals? A review of animal feed ingredients and their potential impacts on human health. Environmental health perspectives. 115, 663-670. https://doi.org/10.1289/ehp.9760.

Schouten C., 2020. Voortgang stikstofproblematiek: structurele aanpak [Progress nitrogen problems: structural approach]. https://www.rijksoverheid.nl/documenten/kamerstukken/2020/04/24/voortgang-stikstofproblematiek-structurele-aanpak (accessed 02/18 2021).

Smit L.A.M., Heederik D., 2017. Impacts of Intensive Livestock Production on Human Health in Densely Populated Regions. GeoHealth. 1, 272-277. https://doi.org/10.1002/2017GH000103.

Smith P.G., Bradley R., 2003. Bovine spongiform encephalopathy (BSE) and its epidemiology. British Medical Bulletin. 66, 185-198. https://doi.org/10.1093/bmb/66.1.185.

Steinfeld H., Gerber P., Wassenaar T., Castel V., Rosales M., De Haan C., 2006. Livestock's long shadow. Food and Agriculture Organization of the United Nations (FAO), Rome.

Takai H., Pedersen S., Johnsen J.O., Metz J.H.M., Koerkamp P.W.G.G., Uenk G.H., et al., 1998. Concentrations and emissions of airborne dust in livestock buildings in Northern Europe. J. Agric. Eng. Res. 70, 59-77. https://doi.org/10.1006/jaer.1997.0280.

United Nations, 2015. Transforming our world: the 2030 agenda for sustainable development. https://sustainabledevelopment.un.org/content/documents/21252030%20Agenda%20for%20Sustainable%20Development%20web.pdf (accessed 08/24 2017).

van Dam M., Dijksma S.A.M., 2017. Reactie op diverse onderzoeken naar de relatie tussen veehouderij en gezondheid [Response to several studies on the relation between livestock production and human health]. https://www.rijksoverheid.nl/documenten/kamerstukken/2017/06/01/reactie-op-diverse-onderzoeken-naar-de-relatie-tussen-veehouderij-en-gezondheid (accessed 07/22 2019).

van Zanten H.H., Herrero M., van Hal O., Röös E., Muller A., Garnett T., et al., 2018. Defining a land boundary for sustainable livestock consumption. Global change biology. https://doi.org/10.1111/gcb.14321.

Winkel A., van Riel J.W., van Emous R.A., Aarnink A.J., Groot Koerkamp P.W., Ogink N.W., 2016. Abatement of particulate matter emission from experimental aviary housings for laying hens by spraying rapeseed oil. Poultry science. 95, 2836-2848. https://doi.org/10.3382/ps/pew261

WUR E-depot, 2020. Op weg naar een natuurinclusieve landbouw : factsheets [Towards a nature inclusive agriculture: factsheets]. https://library.wur.nl/WebQuery/edepot/472382 (accessed 09/03 2020).

Chapter 6

General discussion: Towards feeding a societal dialogue on the future of livestock farming

The aim of this thesis is to integrally assess the effects of Dutch livestock production on human health and the environment. Its outcomes may serve as input in the currently actual societal dialogue about the future of animal production in the Netherlands. As a point of departure, the effects of current Dutch livestock production on human health and environment were assessed in chapter 2. Chapter 3 and 4 were more specific and zoomed in on human respiratory health effects in the vicinity of livestock farms. In chapter 5 again a more integrated approach was used to *ex ante* assess the potential effects of future changes in livestock farming practices related to an envisioned transition towards circular livestock farming. The integrated assessments in this thesis focus on human health and environmental impacts related to livestock production in the Netherlands, including feed production and production of other inputs, but excluding consumption of animal products (Figure 1). The studied human health impacts thus include health effects related to environmental and for a small part occupational exposure. The main findings of the chapters are discussed below, as well as overarching findings about the different impacts of animal sectors, and more general lessons about uncertainties of the analyses, and about interdisciplinary research and knowledge integration. These findings are further synthesized at the end of the discussion, in the context of their potential contribution to a societal dialogue on the future of livestock farming.

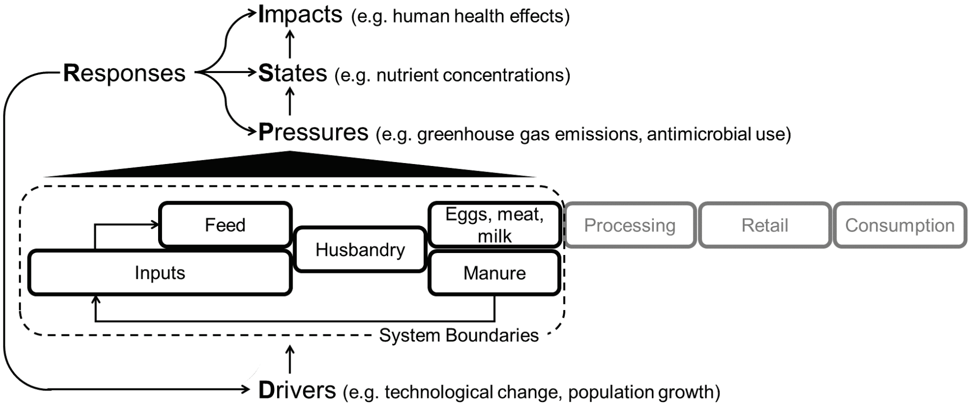


Figure 1. Schematic overview of livestock production chain, system boundaries, and related *Drivers, Pressures, States, Impacts* and *Responses*.

Chapter 2: Effects of Dutch livestock production on human health and the environment

Chapter 2 contains an assessment of the effects of current Dutch livestock production on 17 different human health and environmental impact categories. This resulted in the synthesis of a diverse palette of impacts that could be brought together under uniform system boundaries. Some impacts concern human health, some concern ecosystems, and some concern both. Some impacts occur locally (e.g. odor annoyance), some regionally (e.g. nitrogen deposition in terrestrial nature), and some globally (e.g. greenhouse gas emissions). Some of the human health impacts or their causes occur regularly, such as endemic zoonotic diseases or particulate matter emissions from livestock farms, which leads to either acute or chronic disease. Other impacts occur only with low probability, but can be high, such as outbreaks of emerging zoonotic diseases. Furthermore, some impacts are not regarded as a medically diagnosed disease in a classical sense, but nevertheless negatively affect human health and quality of life, as is the case for odor annoyance.

The impacts were expressed in 8 *Impacts* indicators, 6 *State* indicators and 8 *Pressure* indicators, in the sense of the *Drivers-Pressures-State-Impacts-Response* causal chain (EEA, 2005; Smeets and Weterings, 1999; Thomas, 1995). In this chain, *Impacts* expresses the actual impact, i.e. how human health or ecosystems are affected, while *States* (e.g. nutrient concentrations) or *Pressures* (e.g. greenhouse gas emissions) give a more indirect indication of impact (Figure 1). *Drivers* underlying the *Pressures,* and *Responses* to address the *Impacts* were not considered in the chapter. Where possible, quantitative estimates to the indicators were provided. These were expressed in absolute terms as well as relative to overall *Impacts*, such as the total health impact of particulate matter emissions related to any source.

The relative contribution of livestock production to impacts varied widely, ranging from a contribution of around 1% to the burden disease of pneumonia, and of around 2% to the total of Dutch fresh water use, to a contribution of 70% to Dutch agricultural land use, 75% to current critical nitrogen load exceedance in nature areas and 95% to the net transfer of phosphorus to soils. For impact categories for which such a relative contribution could not be determined, other comparison values were used. For example, the less than 2.5% of Dutch inhabitants severely annoyed by odors from livestock farms is comparable to the percentage severely annoyed by odor annoyance related to sewage systems. Or, another example, the livestock sector contributes about as much to the effects of pesticides on groundwater as the agricultural sector as a whole, but far less to effects of pesticides on surface waters.

In addition to comparing impacts in terms of relative impact, human health effects related to particulate matter emissions from livestock farms, zoonotic diseases, asthma, COPD (Chronic Obstructive Pulmonary Disease) and pneumonia, and occupational accidents could in principle be compared to each other in terms of burden of disease, as these were all expressed as Disability Adjusted Life Years (DALYs), yet with different underlying methods. The burden of disease was highest for particulate matter emissions and zoonotic diseases. In contrast, beneficial effects of living in proximity of livestock farms regarding asthma and COPD, when assumed causal, are in the same order of magnitude as the adverse effects of particulate matter, zoonotic diseases, accidents, pneumonia and exacerbations of COPD patients together. In addition to these health effects expressed as DALYs, the Dutch livestock sector causes human health impacts that do not fit this burden of disease framework, such as odor annoyance, which is often not defined as medically diagnosed disease in a classical sense, or emerging infectious disease risks, which by nature do occur irregularly.

The results of chapter 2 also give some indication of the location were livestock-related impacts occurs. For example, the percentage of persons experiencing severe odor annoyance is 8% in some municipalities, but about 2.5% nationally. Other impacts occur outside the Netherlands, with the total agricultural land use that is required for Dutch livestock production far exceeding all available agricultural land within the Netherlands. This is also reflected in greenhouse gas emissions and water use related to Dutch livestock production, which are higher outside than within the Netherlands. The integrated analysis of national livestock production, under the system boundaries shown in Figure 1, thus shows that actions in the livestock sector have effects on several spatial scales.

Bringing such variety of impact categories together on a national level adds to previous assessments that tended to focus on environmental impacts only or did not get to an assessment of the entire national production (Aequator Groen en Ruimte et al., 2008; Boone and Dolman, 2010; Bos et al., 2017; Hu et al., 2017; van Grinsven et al., 2011). Such national-level assessment not only forms a basis for prioritizing the management of impacts but also allows a comparison of impact to that of other sectors or countries, and it allows comparison of the impacts of cattle, poultry, pig, and small ruminant production at the sector level, rather than at the level of animal products. Such comparison between animal sectors and lessons for integration are discussed later on.

Chapters 3 and 4: Human health effects of living in the vicinity of livestock farms

Chapter 3 and 4 focused on effects shared under the impact category “Pneumonia, asthma, and COPD” introduced in chapter 2. This impact category refers to associations of proximity to livestock farms with pneumonia, asthma, and COPD that were observed in the last decade in the south-east of the Netherlands. These observations included an increased risk of pneumonia close to goat farms (Freidl et al., 2017; Kalkowska et al., 2018; Smit et al., 2012), a decreased prevalence of asthma, COPD and atopy close to livestock farms (Borlée et al., 2018; Borlée et al., 2015; Smit et al., 2014), as well as more severe COPD among COPD patients close to livestock farms (Borlée et al., 2017; Borlée et al., 2015; van Kersen et al., 2020). Causal mechanisms underlying these associations are poorly understood. The findings of these previous studies were expanded in chapter 3 and 4 through analysis of broader and different datasets with different methods, and corroborated earlier findings.

Chapter 3 built on earlier studies on the risk of pneumonia close to goat and poultry farms by using data from more recent years and comparing different methods that had been used earlier. Three complementary analyses types were used to deal with potential bias of spatial clustering of patients registered at the same GP-practice. A fourth type of analysis was used to also deal with the simultaneous proximity of multiple farms. All four analyses types indicated an increased risk of pneumonia among residents living close to goat farms, while an association with proximity to poultry farms was less evident.

Chapter 4 built on earlier studies that found a reduced prevalence of asthma and COPD in the proximity of livestock farms, by using data from a different source, covering the entire Netherlands, and looking at effects of livestock-related particulate matter emissions in addition to distances to nearest livestock farms. The health outcome data that were used consisted of nation-wide information on medication dispensing that are used for risk-equalization purposes for insurance companies. The additional exposure indicator based on livestock-related particulate matter emissions used in the study was used as a proxy for livestock-related exposure in line with hypothetical air transmission of agents causing a reduced asthma and/or COPD prevalence, and suitable to account for proximity to multiple farms simultaneously. The findings of chapter 4 show decreasing asthma and/or COPD medication dispensing with decreasing distance to livestock farms, particularly cattle farms, and with increasing cattle-related particulate matter concentrations, and thereby suggest corresponding associations with asthma and/or COPD.

Despite the increasing evidence for these positive and negative associations between respiratory health effects and proximity to livestock farms, underlying mechanisms are poorly understood. Exposure to some of the many different agents emitted from livestock farms likely plays a role here, with proximity to farms and concentrations of particulate matter emitted from these farms being proxies for such potential agents. Livestock farms emit particulate matter that consists of particles that may originate from manure, skin, feathers, feed or litter and may be a vector of microorganisms or components thereof (i.e. endotoxins) (Cambra-López et al., 2010; Cambra-López et al., 2011). In addition, various gasses are emitted from livestock farms, such as ammonia.

Such agents can affect respiratory disease in multiple, potentially interacting, ways. In some cases, zoonotic pathogens, prevalent in animals, can infect humans through transmission through air and cause respiratory disease. The most evident example of this in the Netherlands is Q-fever, as the bacterium that caused this disease was able to spread over long distances through air and showed an increase in the number of pneumonia cases within 5 km from goat farms during an outbreak in the Netherlands from 2007-2010 (Roest et al., 2011; Smit et al., 2012; van der Hoek et al., 2012). A different mechanism proposed is a disbalance in the upper respiratory tract microbiome caused by exposure to livestock farm emissions and leading to respiratory health effects caused by bacteria that are normally contained (Smit et al., 2017). Two other mechanisms potentially on the same causal path as the shifts in the upper respiratory tract microbiome are oxidative stress and innate immune responses. Oxidative stress in the respiratory tract, together with injury and inflammation is thought to lie at the basis of the causal chains of effects of particulate matter on both asthma development and asthma exacerbations, COPD exacerbations and respiratory infections (EPA, 2019; Gowers et al., 2012; Guarnieri and Balmes, 2014). Innate immune responses triggered by pattern recognition of microbial components play a role in the development or worsening of atopic asthma (Brooks et al., 2013; Holgate, 2012; Liu et al., 2019; von Mutius, 2016). A low susceptibility to asthma may result from exposure to a wide variety of microbial exposures, i.e. the hygiene hypothesis (Brooks et al., 2013; von Mutius, 2016). At the same time, innate pattern recognition mechanisms may play a role in the worsening of respiratory symptoms (Holgate, 2012; Liu et al., 2019).

Reproducing the previously found associations regarding respiratory health effects among neighboring residents of livestock farms, with data from other years, regions and sources provides more confidence in previously found associations. Yet, because mechanistic understanding remains poor, response possibilities remain limited. More targeted measures may require further research that aims to disentangle the several mechanisms that may underly observed health effects in the proximity of livestock farms.

Role of different animal sectors

Livestock production is far from uniform across animal categories, which thus contribute differently to the various impacts, as described in chapter 2, 3 and 4. Insight in the distinctive contribution to impacts of animal categories could be useful for tailoring mitigation measures to the different sectors. The cattle sector for example contributes more than half to greenhouse gas emissions and ammonia emissions. On the other hand, cattle contribute little to other impacts such as odor annoyance, and may even have a beneficial effect on the prevalence of asthma as indicated in chapter 4. The poultry and pig sectors contribute relatively more to impacts abroad because farms in these sectors generally do not produce their own feed. Poultry also has a relatively high contribution to primary particulate matter emissions and zoonotic diseases, while pig farms appear to contribute most to odor annoyance.

Also regarding respiratory diseases in residents living close to livestock farms, the work in this thesis indicated a distinctive role of different animal categories, with different contributions to studied associations and to modelled particulate matter concentrations. The associations of pneumonia with proximity to livestock farms described in chapter 3 were clearly most pronounced for goat farms, while previously reported associations with proximity to poultry farms were less evident, corresponding to recent evidence in other study areas in the Netherlands (Smit et al., 2019), but seemingly contrasting to a study in the United States (Poulsen et al., 2018). The associations of asthma/COPD medication dispenses with proximity to livestock farms described in chapter 4 was most pronounced for cattle farms, which was not entirely consistent with results of previous studies (Borlée et al., 2015; Smit et al., 2014). The modelled livestock-related particulate matter concentrations presented in chapter4 do indicate that animal sector contributions to particulate matter concentrations differ by an order of magnitude across animal categories. This suggests that not the absolute amount of particulate matter is important for observed associations but something else that also exponentially decreases with increasing distance, potentially the microbial composition in air emitted from livestock farms, which differs across animal farm types (Liu et al., 2019). Although it is clear that each animal category may play a different role in causing respiratory effects, what this role exactly is, is not established, partly due to the poor mechanistic understanding.

Insight in the contributions of different animal sectors is not only relevant for tailoring mitigation measures, but also gives insight in potential burden shifts across sectors. An example of such burden shift was described in chapter 2, with European regulations regarding the milk quotation system, and outbreaks of animal diseases, resulting in a steep growth in the number of goats in the Netherlands, which is thought to have contributed to the Q-fever epidemic in the Netherlands.

Chapter 5: Effects of a transition towards circular livestock farming practices on human health and the environment

While chapter 2, 3 and 4 dealt with current exposures and effects, chapter 5 is oriented towards the future. Guidance towards the future of the livestock sector is provided in a vision of the Dutch Ministry of Agriculture, Nature and Food Quality (Ministry of Agriculture, 2018; Ministry of Agriculture, 2019). This vision is based on a transition towards a circular agriculture, and simultaneously addresses several sustainability targets, such as climate change, the relation between farmers and citizens, animal welfare, market position, regional economy, and nature conservation, thus reflecting several sustainable development goals (United Nations, 2015) and many of the objectives in a European Commission proposal for reform of the European common agricultural policy (European Commission, 2018). To gain insight in possible side effects of these developments, the central question in chapter 5 was: How will changes in livestock production in a transition towards a circular food system or more sustainable livestock sector affect human health and the environment, and what are potential synergies and trade-offs that may occur?

To address this question, an *ex ante* expert elicitation approach was explored. The major part of this consultation was an online questionnaire in which experts were asked to provide scores according to indicators that fitted their expertise, built up in three parts: i) to assess the effects of a transition towards circular livestock farming as a whole, ii) to assess the effects on 15 indicators of specific changes in livestock farming practices in four example farms, and iii) to assess the effects of broader developments in livestock farming. These changes covered a broad set of farming practices of multiple animal sectors and of both farms that strived for high efficiency and farms that strived for the maximum use of their own resources.

The expert consultation suggested that anticipated changes in livestock farming practices, when animal numbers remain similar, are not sufficient to reach policy goals regarding climate, nitrogen and particulate matter for example. In addition, several synergies and trade-offs were identified. An example of a synergy, which was thought to bring multiple benefits for environmental and human health impacts, and no adverse effects, was a measure to separate solid and liquid manure on a pig farm, resulting in less emissions of ammonia, odors and greenhouse gasses. An example of a trade-off is the increased disease risk of the use of waste streams as feed, in favor of several environmental advantages because of the improved resource efficiency.

Such risk regarding the use of waste streams as feed may be addressed by implementing stricter control measures, but other trade-offs may be less easily addressed. In the case of a care farm, for example, a slightly increased risk on infections with zoonotic diseases may have to be accepted, in favor of the societal benefit of such a farm model. In other cases a redesign may be required to sufficiently address environmental and human health impacts.

These first insights into the potential effects of a transition towards circular livestock farming may inform and provide a basis for a regular dialogue on this topic. Not only on which specific trade-offs may be acceptable or may be easily mitigated with additional interventions, but also on more radical changes. Apart from some no-regret directions and risks that can be mitigated relatively easily, an answer on the preferred 'best' direction is not provided in chapter 5. Yet, several experts participating in the consultation of the chapter did indicate that a reduction in the size of the livestock sector may be a necessary consequence of the political ambition of a transition towards a circular agriculture. This is further discussed in the section *future directions*.

Uncertainty

Several types of uncertainties are present in the reported studies of this thesis. Characterizing these may help decision making (Funtowicz and Ravetz, 1990; Knol et al., 2009). In chapter 2, uncertainty is involved in impact estimates. These could not be uniformly characterized in a singular fashion, yet for most impact categories the identified sources of uncertainty were not expected to qualitatively affect the estimates. Much of this uncertainty was due to incomplete knowledge, i.e. epistemic uncertainty (Knol et al., 2009), which, although not for most, was considerable for some impact categories. For example, quantifying the relation between antimicrobial use in animals and the development of antimicrobial resistance in humans, and related health effects, remains challenging.

For some of the studied impact categories uncertainty was of a different nature, resulting from "natural or social variability in the system" (Knol et al., 2009). This form of ontic uncertainty for example applies to the risk of emerging zoonotic diseases or development of antimicrobial resistance, which typically have a low probability but potentially large impact. Especially the moment of occurrence of such risks may suffer from ontic uncertainty, and therefore require other forms of risk management such as resilience building (Renn, 2006).

An example in which the difference between epistemic and ontic uncertainty becomes blurred is the knowledge gap on the relation between proximity to goat farms and the risk on pneumonia, which chapter 3 aimed to reduce. Such effect is relatively small in terms of burden of disease, compared to other human health effects of Dutch livestock production described in chapter 2. This does not mean that the risk of pneumonia is not relevant or acceptable. The acceptability may be for a large part determined by whether the risk of pneumonia is seen as a constant risk, similar to the health effects caused by air pollution, or as an indication of a warning signal for a larger hazard, similar to the Q-fever epidemic in the Netherlands. During this epidemic effective measures were only taken after hundreds of persons were already infected (Roest et al., 2011) and this relatively recent experience may have led to increased precaution by policy-makers regarding the risk of pneumonia around goat farms, especially since the mechanism behind this association remains poorly understood. More research to improve mechanistic understanding may in this case decrease uncertainty. Yet interpreting the adverse health effects around livestock farms as a warning signal of a risk with low probability but potentially large impact, may also require a comparison to the probability and impact of other risks, similar to the approach used in the national security profile that was used in chapter 2 to characterize the risk of emerging infectious diseases (Analistennetwerk Nationale Veiligheid, 2016).

In addition to characterizing uncertainty according to the distinction between epistemic and ontic uncertainty, more characterizations apply to the uncertainty around the expert judgements in chapter 5 (Knol et al., 2009). The expert judgements for example involve methodological unreliability and at the same time value diversity across experts. Some sense of reliability could be obtained by analyzing to what extent experts agreed, but the number of participating experts for each indicator was limited. Reliability could be improved by further investigating the statements of experts, as chapter 5 at least provides a set of testable claims. Framing these findings as exploratory is hence one way to communicate uncertainty and thereby properly inform decision makers.

Next to uncertainty about estimates, chapter 5 involves uncertainty about the future. Anticipating future potential side-effects is useful according to consulted experts, but it cannot be judged to what extent the approach used in chapter 5 is suitable for timely identifying future risks. Moreover, the ontic uncertainties underlying several impacts may be an insuperable factor that hinders timely identification of risks as well. If timely identification is indeed not quite possible, appropriate monitoring of changes after implementation or, possibly in combination with, initially applying them in experimental settings, may help to identify potential side-effects in an early stage.

The rough characterization of uncertainties in this section shows that additional research to reduce epistemic uncertainties is more sensible for some impacts than for others. Often additional actions should be undertaken to manage uncertainty, such as building resilience or setting up monitoring programs. Further characterization of uncertainties may help improve decision making by improving the understanding of how the different types of uncertainties may affect the outcome of a decision.

Lessons learned for interdisciplinary research and integration

Apart from insights in the topic of livestock production, the work of this thesis does provide some more general lessons regarding interdisciplinary assessment. The work involved collaborations with, among others, veterinarians, environmental epidemiologists, animal scientists, environmental scientists, ecologists, infectious disease epidemiologists, meteorologists, health economists and statisticians. It hence involved integrating knowledge from these disciplines but also communicating with persons with different disciplinary perspectives. The lessons from such interdisciplinary research are discussed in this section.

Lessons for interdisciplinary cooperation

The main lessons regarding interdisciplinary cooperation relate to mutual understanding, as interdisciplinary research involves a process of dialogue and improving mutual understanding, hence learning to speak each other's language (Bromme, 2000). The importance of language for example becomes clear from concepts that are differently used across disciplines, such as the concept of "endpoint" which often means the (final) *Impact* in environmental science, but refers to the outcome of a disease in epidemiology. Another concept which can be interpreted differently is "the environment", in the context of environmental impacts, which in a narrow sense may refer to ecosystems or biodiversity but in a broader sense may include environmental pollution affecting human health as well. Even if the same concept or metric is used, different research traditions may lead to difficulties in reaching mutual understanding. An example is the DALY metric, which is calculated in different ways by different disciplines, and can thus not simply be interpreted as quantitatively describing the same phenomenon.

Mutual understanding may not only be hindered by language, but also because of a difference in perspective. For example, the atmospheric dispersion modelling in chapter 4 was used for epidemiological analyses, while such modelling is normally used for other purposes such as air quality monitoring and -regulatory practices. The modelling was performed by a researcher with a different background than the researchers that performed the epidemiological analyses. Yet since these analyses required output from the atmospheric dispersion model it required a mutual understanding of what dispersion model outputs were possible and what model outputs were useful as input for the epidemiological analysis. As epidemiological analyses are not the standard use of output of atmospheric dispersion modelling, mutual understanding of each other's needs was not self-evident.

The importance of mutual understanding also follows from chapter 5. In the expert consultation described in that chapter one reason for contrasting scores between experts was their different interpretation of indicators, of system boundaries or of changes in farming practices. Whether or not such differences in interpretation result from the different focus of different disciplines, clearly defining definitions or objectives (while interacting) helps to improve dialogue.

Lessons for knowledge integration

Several lessons regarding knowledge integration have been drawn throughout this thesis. Of great help for integration were the definition of system boundaries and the use of the DPSIR (*Drivers-Pressures-States-Impacts-Responses*) framework. Another lesson relating to integrated assessment is that trade-offs and synergies can be more easily identified when looking at changes in impacts and less easily when looking at one point in time. These lessons are further detailed below.

An important help in the integration in chapter 2 was the formulation of uniform system boundaries, to which all assessed impacts should relate (Figure 1). A similar form of integration was applied in chapter 5, in which different indicators were related to the same changes in farming practices. Although not strictly adhered to in all cases, the definition of system boundaries guided choices for the quantification of indicators, and helps to compare impacts to each other.

Another important help for integration was the relational DPSIR framework (also depicted in Figure 1). This framework helps to structure and communicate about the different impacts, but is certainly no panacea for integration. One challenge regarding the DPSIR framework was that operational integration across the DPSIR chain proved difficult for many indicators in this thesis, touching on the limits of knowledge or on inherent uncertainty. Each of the indicators used should give a direct or indirect indication of impact, but this relation could not be made explicit in all cases. For example, greenhouse gas emissions are known to contribute to climate change, but in this thesis – and in many other studies – the relation between such emissions to the actual climate system and potentially resulting risks of extreme weather events have not been made explicit. In that sense the DPSIR framework has been used as a relational framework and not as an operational model (Knol et al., 2010).

A second challenge was that categorization of all impact categories following each element of the DPSIR chain was not considered helpful. A reason is that not for all impact categories the distinction between *Drivers*, *Pressures*, *States* and *Impacts* is straightforward. For example, for the impact category zoonotic diseases, the corresponding human health impact may be considered the *Impact* of the DPSIR chain. Yet, for preceding shackles, it is not straightforward which should be *Drivers*, *Pressures* and *States*. One option is to consider the prevalence of a zoonotic disease in animals as a *Driver*, which causes a *Pressure* through transmission of the disease, a subsequent (possibly short) period in the environment being the *State*, and then infection of an exposed person and causing disease. Under a different interpretation, however, the *State* is the prevalence of a disease in animals, which is preceded by a *Pressure* causing this disease in animals, such as bad hygiene on a farm, and a *Driver* being the socio-economic factors causing the bad hygiene.

A third challenge regarding the use of DPSIR is that not all elements in the DPSIR-chain can be directly linked to livestock production. For example, greenhouse gas emissions (*Pressure*) can be linked to a specific sector, but this is already a bit more difficult for the concentration of greenhouse gasses in the atmosphere (*State*), and even more difficult for the effects of climate change (*Impact*).

The integrated assessment exercises in chapter 2 and 5 of this thesis also made clear that trade-offs and synergies can be more easily identified when looking at changes in impacts and less easily when looking at one point in time. Changes in impact resulting from changes in livestock farming practices were assessed in chapter 5. Assessing the effects of such changes on multiple indicators indicates which indicators increase and which decrease. Such increase or decrease directly provides an indication of whether there is improvement, as it is generally agreed that e.g. more particulate matter emissions is not desirable but a higher organic matter content in agricultural soils is desirable. Such assessment of improvement allows to see which indicators improve simultaneously because of a change in farming practices; or to see which indicators move in opposite direction. In chapter 2 no such changes were assessed, but the size of impact at one point in time, which limits studying trade-offs and synergies.

So, several lessons have been learned regarding integration. Useful tools were the definition of system boundaries and the DPSIR framework, although the latter is no panacea. Another lesson is that assessing a change rather than something static helps to find trade-offs and synergies. Further integration could be achieved by using approaches in which the impact categories are weighted relative to each other, such as multiple criteria decision analysis. In the case of chapter 2 such approaches would help to rank the impact categories and prioritize them for optional management, while when they are used in the context of the changes in farming practices in chapter 5, they can stimulate discussion on what changes in farming practices are desirable. Such weighting and comparing of impact categories involves value judgements of what is better or worse. This surpasses the scientific judgement of scientists and requires engagement of various stakeholders. Such transdisciplinary interactions will further compound issues related to semantics and understanding of system boundaries.

Future directions

The chapters of this thesis provide several observations regarding the size and diversity of the human health and environmental impacts of the Dutch livestock sector and their diversity. They describe knowledge gaps, impact patterns for the different animal sectors, and lessons regarding uncertainty and integration. These findings provide several starting points for further research, which may focus on filling knowledge gaps, such as those related to living in the proximity of livestock farms, on better characterizing uncertainties or on improving methods for integration. Filling knowledge gaps is likely to take considerable time. Yet, besides interesting research questions, this thesis also provides input for a dialogue on the future of the livestock sector. Such dialogue is ongoing and further characterized below. In addition, observations of this thesis that may feed this dialogue are discussed, as well as the future research that is stimulated by the dialogue.

A societal dialogue on the future of livestock farming

In the period dedicated to the studies in this thesis (2016-2021), many reports have been published, societal debates have taken place and political ambitions have been formulated, that are relevant to the future of livestock production in the Netherlands. Several years before the start of the project that resulted in this thesis, 15 ambitions for a sustainable livestock sector had been formulated by an initiative of multiple governmental, non-governmental and sectoral actors, which later fueled a proposal on how to monitor progress towards the ambitions (Bos et al., 2017; UDV, 2013). Right at the beginning of the thesis-project, a research report came out with results from a large regional project on the effects of livestock production on the health of local residents (Maassen et al., 2016). This fueled new research but also contributed to formulate ambitions to considerably reduce particulate matter emissions from poultry farms and to provincial decisions to limit the building of goat farms (ANP, 2018; van Dam and Dijksma, 2017). In the midst of this, the State Secretary for Economic Affairs (who was responsible for agricultural affairs, in the absence of a Ministry of Agriculture), asked for and received advice from the Dutch Social and Economic Council on increasing the pace for making the livestock sector more sustainable (SER, 2016). Meanwhile, the effort of reducing the use of antibiotics on livestock farms resulted in a considerable reduction in most sectors between 2007 and 2016 (SDa, 2020). In a new 2017-cabinet, a minister of agriculture was appointed again, who presented a vision for the future of agriculture in the Netherlands, based around circular resource use (Ministry of Agriculture, 2018; Ministry of Agriculture, 2019). More recently, the Council of State judged that Dutch programs to limit nitrogen deposition in nature areas were not compliant with European directives, resulting in advices for drastic changes in the livestock sector by an advisory board (Remkes et al., 2019), and subsequent national protests of farmers. Also internationally, a demand for change is reflected in the intended reform of the European common agricultural policy and the Farm to Fork Strategy under the European Green deal (European Commission, 2018; European Commission, 2020).

These developments indicate that the topic of this thesis is timely. It even appears to be ahead of a desire expressed in the recent design of a national environmental policy framework (Ministry of Infrastructure and Water Management, 2020). In this framework, four building blocks are formulated for improvement of environmental policy: more focus on prevention, managing risks on burden shifts, improvement of environmental quality given current environmental problems, and interaction and cooperation. As part of the focus on prevention, the desire is expressed to ask the National Institute for Public

Health and Environment (RIVM) to assess the health effects of the current societal transitions, including the transition to circular agriculture. Elements of such an assessment are provided in chapters 2 and 5 of this thesis.

In addition to policy ambitions and reports on the future of livestock production, the importance of stakeholder involvement has been recognized for decades and is increasingly implemented although not without critique (Glucker et al., 2013; Luyet et al., 2012; Turnhout et al., 2020). The involvement of stakeholders can come in to discuss normative considerations to which science can provide no answer, such as whether the identified risk of pneumonia among those living close to goat farms is acceptable. Moreover, involving stakeholders in setting out the direction of future development of the livestock sector is critical for the success of changes in that direction. One reason is that many of these changes require action by some of the stakeholders, most notably farmers. Farmers may be much more inclined to change their farming practices if they see the benefit of it and can profit from the benefits. Another reason that success depends on stakeholders, follows when success is defined as the mitigation of societal concerns, i.e. strategies and policies for the future of livestock production may be only successful if they sufficiently address stakeholder concerns.

Involvement of a broad range of stakeholders may also be helpful for signaling potential adverse side-effects in a transition of the livestock sector. Predicting such side-effects may be difficult, but when all relevant parties are involved in monitoring the transition, potential side-effects may be signaled in an early stage. In that sense, perspectives of stakeholders as well as those of policy-makers, complement science in assessing future developments in the livestock sector (Funtowicz and Ravetz, 1993; Metze and Turnhout, 2014; Scholz and Steiner, 2015).

A societal dialogue with involvement of stakeholders and continuous monitoring is in line with existing and forthcoming policies. For example, monitoring and evaluation of policy goals and regular stakeholder involvement are considered essential aspects in the establishment of environmental visions by municipalities, provinces and the national government for the new Dutch Environment and Planning Act (Government of the Netherlands, 2020; Ministry of the Interior and Kingdom Relations, 2018). Also in the context of agriculture, the vision of the Dutch Ministry of Agriculture, Nature and Food Quality leaves ample room for society to fill in the blanks as the vision is explicitly not a blueprint for how the envisioned agricultural transition should look like (Ministry of Agriculture, 2018; Ministry of Agriculture, 2019). These existing and forthcoming policies indicate that a societal dialogue on the future of livestock production is ongoing, and the involvement of stakeholders, combined with regular evaluation of policy goals and novel concerns as part of this dialogue, is increasingly stimulated.

Input for a societal dialogue

This section aims to summarize how a societal dialogue on the future of the Dutch livestock sector can benefit from the observations in this thesis. A prominent observation is the diversity of human health and environmental impacts of livestock production. The challenges of bringing together these impacts with different characteristics that are studied by a variety of disciplines, indicate that investing in mutual understanding across disciplines and backgrounds may be vital for a fruitful dialogue.

This thesis also provides insights in the relative size of impacts which may lead to reprioritization. For example, chapter 2 indicates that the relative contribution of the Dutch livestock sector to several environmental impacts is (percentagewise) higher than many of the human health impacts involved. This aligns with the views of several Dutch scientific experts with knowledge on livestock farming, that environmental unsustainability and biodiversity loss are of more concern than health effects among residents living close to livestock farms (Eijrond et al., 2019). However, a difference in relative contribution does not say anything about the relevance, value, or public acceptability of these impacts. For example, even if livestock production contributes only little to particulate matter emissions but particulate matter emissions are seen as an important problem, the livestock sector's contribution may still be relevant and undesirable.

Another observation is the potentially beneficial effect on prevalence of obstructive airway diseases associated with living in the proximity of livestock farms, which is considerable compared to adverse human health effects of livestock farming. Although much remains to be understood regarding this association, it highlights that under some conditions livestock production may have important beneficial effects.

Furthermore, this thesis provides insight in some specific trade-offs and synergies on the level of farming practices, yet from chapter 5 also becomes clear that the expected changes in livestock farming practices are considered insufficient to reach policy goals regarding climate, nitrogen and particulate matter for example. In order to take adequate steps in addressing human health and environmental concerns, it may be inevitable to also address more fundamental issues in the societal dialogue, addressing the drivers of change. A reduction in the number of livestock is one such issue, which is subject to fierce societal debate, but seems inevitable to reach greenhouse gas reduction targets

(Gil et al., 2019; Lesschen et al., 2020). A reduction in the number of livestock was also considered a necessary consequence of a circular food system by several experts participating in the expert consultation of chapter 5. In that context, a reduction in the size of the livestock sector should not be seen as an instrument to address societal concerns, but rather as a consequence of an alternative food system, in which livestock are not just raised to produce animal products (van Zanten et al., 2018; van Zanten et al., 2016).

Future research

As indicated before, future research could focus on filling knowledge gaps, on better characterizing uncertainties or on improving methods for integration. Yet, although methods of integration and characterization of uncertainties are not yet fully developed, whether such effort is useful for decision-making regarding the future of the livestock sector depends on the information needs of decision-makers and stakeholders. This requires interaction between researchers, decision-makers and stakeholders, which can be a part of the societal dialogue on the future of the livestock sector. This interaction may help further integration by giving input to the weighting of impacts and thereby further prioritization or trade-off identification. Moreover, for identifying the trade-offs and synergies, i.e. the choices and dilemmas to be discussed in the societal dialogue, this thesis indicates that an assessment of changes in the livestock sector is required. For such assessment of changes, solution-focused approaches have been proposed, which take alternative potential solutions as a starting point of the analysis, and thereby better align with decision-maker's needs (National Research Council, 2009; Zijp et al., 2016). It is such a solution-focused approach that may form the basis for further research in collaboration with stakeholders. Such solution-focused approach could be adopted at several levels, as illustrated below.

On the farm-level, research could further the study of example farms, as was done in chapter 5. An expansion of such examples may provide valuable input for learning about which practices would and which would not fit in the future of livestock production in the Netherlands. Not only setting such examples by developing new farming practices, in the form of alternative housing systems, alternative cropping systems, different feed sources, or other innovations, could benefit from research, but also evaluating the positive or negative human health, environmental or other impacts of these examples. This means evaluating real-world examples on a regular basis in a similar fashion as in chapter 5, while further developing indicators such as those used in chapter

5, making the assessment process more practical, and allowing for sufficient interaction among farmers, researchers and other stakeholders.

In addition to farm-level examples, the societal dialogue could benefit from insights in the effects of regional or national changes in livestock production. Taking analyses to the national or regional level could reveal effects that are not visible at the farm level, such as effects of changes in spatial configuration of livestock farms, affecting the health of local residents as well as the biodiversity in nature areas. A national perspective is for example provided in the scenario-studies of Lesschen et al. (2020) and Spijker et al. (2020). These studies address a number of different impact categories, such as greenhouse gas emissions, (health effects of) ammonia emissions, water quality, biodiversity, animal welfare and economic indicators, but do, for example, not address effects on infectious diseases, antimicrobial resistance, or primary particulate matter emissions. Hence, there are ample opportunities to build on existing *ex ante* assessments, including those in this thesis, by addressing a larger variety of concerns, and steering more in-depth analysis in interaction with relevant stakeholders.

In conclusion

In this thesis, information on a broad set of human health and environmental impacts has been brought together, which allows comparison of impacts of Dutch livestock production with impacts from other sectors and a comparison of impacts across animal sectors. In addition, specific human health impacts in the vicinity of livestock farms were studied; corroborating and expanding earlier findings on a risk of pneumonia in the vicinity to goat farms and a lower prevalence of asthma and COPD in the proximity of livestock farms. Effects of changes towards circular livestock farming have been explored as well, indicating that anticipated changes are considered insufficient to address all related effects in human health and the environment, when assuming an unchanged number of animals.

Methodologically, lessons have been drawn regarding uncertainties, interdisciplinary cooperation and knowledge integration. One conclusion is that several uncertainties pertain to the findings of this thesis, yet characterizing this uncertainty may in itself provide input for decision making. Regarding interdisciplinary cooperation, the work in this thesis has indicated several instances in which mutual understanding could be improved, sometimes by just being aware that researchers from other fields may hold different interpretations for the same terms. Furthermore, of key help for integration were the definition of system boundaries, and the DPSIR framework, although the latter is certainly no panacea for integration.

Future research could focus on filling knowledge gaps, on better characterizing uncertainties or on improving methods for integration. Yet a line of research that may particularly contribute to the societal dialogue on the future of livestock farming, is a solution-focused approach in which continuous interaction with stakeholders and policy-makers is embedded.

References

Aequator Groen en Ruimte, Ecorys Nederland B. V., Witteveen+Bos, 2008. Maatschappelijke effecten van de intensieve veehouderij: een vergelijking van productiesystemen [Societal effects of intensive livestock farming: a comparison of productionsystems]. https://www.rijksoverheid.nl/documenten/rapporten/2008/05/22/maatschappelijke-effecten-van-de-intensieve-veehouderij (accessed Web Page 2016).

Analistennetwerk Nationale Veiligheid, 2016. Nationaal veiligheidsprofiel 2016 [National security profile 2016]. RIVM (National Institute of Public Health and the Environment), Bilthoven.

ANP, 2018. Ook Overijssel zet rem op geitenboerderijen [Overijssel puts a stop on goat farms as well]. Binnenlands Bestuur. Sijthoff Media Groep Amsterdam.

Boone J.A., Dolman M.A., 2010. Duurzame Landbouw in Beeld 2010; resultaten van de Nederlandse land-en tuinbouw op het gebied van People, Planet en Profit [Sustainable Agriculture 2010; Performance of Dutch agriculture and horticulture in terms of People, Planet and Profit]. 105. Wettelijke Onderzoekstaken Natuur & Milieu [Wageningen, Statutory Research Tasks Unit for Nature and the Environment], Wageningen.

Borlée F., Yzermans C.J., Aalders B., Rooijackers J., Krop E., Maassen C.B., et al., 2017. Air pollution from livestock farms is associated with airway obstruction in neighboring residents. American journal of respiratory and critical care medicine. 196, 1152-1161. https://doi.org/10.1164/rccm.201701-0021OC.

Borlée F., Yzermans C.J., Krop E.J., Maassen C.B., Schellevis F.G., Heederik D.J., et al., 2018. Residential proximity to livestock farms is associated with a lower prevalence of atopy. Occup Environ Med. 75, 453-460. https://doi.org/10.1136/oemed-2017-104769.

Borlée F., Yzermans C.J., van Dijk C.E., Heederik D., Smit L.A.M., 2015. Increased respiratory symptoms in COPD patients living in the vicinity of livestock farms. Eur. Respir. J. 46, 1605-1614. https://doi.org/10.1183/13993003.00265-2015.

Bos A., Puente-Rodríguez D., Reijs J.W., van der Peet G., Koerkamp P.W.G., 2017. Monitoring verduurzaming veehouderij 1.0: een eerste proeve van een Monitorings-systematiek voor de 15 ambities van de Uitvoeringsagenda Duurzame Veehouderij, met initiële resultaten voor drie diersectoren en een aantal keteninitiatieven [Monitoring sustainable development of livestock 1.0]. Wageningen Livestock Research.

Bromme R., 2000. Beyond one's own perspective: The psychology of cognitive interdisciplinarity, in: Stehr P.W.a.N., (Ed.), Practicing interdisciplinarity. University of Toronto press, Toronto, Buffalo, London, pp. 115-133.

Brooks C., Pearce N., Douwes J., 2013. The hygiene hypothesis in allergy and asthma: an update. Curr. Opin. Allergy Clin. Immunol. 13, 70-77. https://doi.org/10.1097/ACI.0b013e32835ad0d2.

Cambra-López M., Aarnink A.J.A., Zhao Y., Calvet S., Torres A.G., 2010. Airborne particulate matter from livestock production systems: A review of an air pollution problem. Environmental Pollution. 158, 1-17. https://doi.org/https://doi.org/10.1016/j.envpol.2009.07.011.

Cambra-López M., Hermosilla T., Lai H.T., Aarnink A.J., Ogink N., 2011. Particulate matter emitted from poultry and pig houses: source identification and quantification. Transactions of the ASABA. 54, 629-642. https://doi.org/10.13031/2013.36466.

EEA, 2005. The European environment: state and outlook 2005. Office for Official Publications of the European Communities, Copenhagen.

EPA, 2019. Integrated Science Assessment for Particulate Matter. EPA (U.S. Environmental Protection Agency), Research Triangle Park, NC.

European Commission, 2018. Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL establishing rules on support for strategic plans to be drawn up by Member States under the Common agricultural policy (CAP Strategic Plans) and financed by the European Agricultural Guarantee Fund (EAGF) and by the European Agricultural Fund for Rural Development (EAFRD) and repealing Regulation (EU) No 1305/2013 of the European Parliament and of the Council and Regulation (EU) No 1307/2013 of the European Parliament and of the Council, Brussels.

European Commission, 2020. Farm to Fork Strategy. https://ec.europa.eu/food/farm2fork_en (accessed 02/22 2021).

Freidl G.S., Spruijt I.T., Borlee F., Smit L.A., van Gageldonk-Lafeber A.B., Heederik D.J., et al., 2017. Livestock-associated risk factors for pneumonia in an area of intensive animal farming in the Netherlands. PLoS One. 12, e0174796. https://doi.org/10.1371/journal.pone.0174796.

Funtowicz S.O., Ravetz J.R., 1990. Uncertainty and quality in science for policy, Vol 15. Springer Science & Business Media.

Funtowicz S.O., Ravetz J.R., 1993. Science for the post-normal age. Futures. 25, 17. https://doi.org/10.1016/0016-3287(93)90022-L.

Glucker A.N., Driessen P.P.J., Kolhoff A., Runhaar H.A.C., 2013. Public participation in environmental impact assessment: why, who and how? Environ. Impact Assess. Rev. 43, 104-111. https://doi.org/10.1016/j.eiar.2013.06.003.

Government of the Netherlands, 2020. Nationale omgevingsvisie: Duurzaam perspectief voor onze leefomgeving [National environmental vision: Sustainable perspective for our living environment]. Ministerie van Binnenlandse zaken [Ministry of the Interior and Kingdom Relations], Den Haag.

Gowers A.M., Cullinan P., Ayres J.G., Anderson H.R., Strachan D.P., Holgate S.T., et al., 2012. Does outdoor air pollution induce new cases of asthma? Biological plausibility and evidence; a review. Respirology. 17, 887-898. https://doi.org/10.1111/j.1440-1843.2012.02195.x.

Guarnieri M., Balmes J.R., 2014. Outdoor air pollution and asthma. The Lancet. 383, 1581-1592. https://doi.org/https://doi.org/10.1016/S0140-6736(14)60617-6.

Holgate S.T., 2012. Innate and adaptive immune responses in asthma. Nat. Med. 18, 673-683. https://doi.org/10.1038/nm.2731.

Hu Y., Cheng H., Tao S., 2017. Environmental and human health challenges of industrial livestock and poultry farming in China and their mitigation. Environment international. 107, 111-130. https://doi.org/10.1016/j.envint.2017.07.003.

Kalkowska D.A., Boender G.J., Smit L.A.M., Baliatsas C., Yzermans J., Heederik D.J.J., et al., 2018. Associations between pneumonia and residential distance to livestock farms over a five-year period in a large population-based study. PLoS One. 13, e0200813. https://doi.org/10.1371/journal.pone.0200813.

Knol A.B., Briggs D.J., Lebret E., 2010. Assessment of complex environmental health problems: Framing the structures and structuring the frameworks. Science of the Total Environment. 408, 2785-2794. https://doi.org/10.1016/j.scitotenv.2010.03.021.

Knol A.B., Petersen A.C., van der Sluijs J.P., Lebret E., 2009. Dealing with uncertainties in environmental burden of disease assessment. Environ. Health. 8, 21. https://doi.org/10.1186/1476-069X-8-21.

Liu D., Mariman R., Gerlofs-Nijland M.E., Boere J.F., Folkerts G., Cassee F.R., et al., 2019. Microbiome composition of airborne particulate matter from livestock farms and their effect on innate immune receptors and cells. Science of The Total Environment. 688, 1298-1307. https://doi.org/10.1016/j.scitotenv.2019.06.217.

Luyet V., Schlaepfer R., Parlange M.B., Buttler A., 2012. A framework to implement Stakeholder participation in environmental projects. Journal of environmental management. 111, 213-219. https://doi.org/http://dx.doi.org/10.1016/j.jenvman.2012.06.026.

Maassen K., Smit L., Wouters I., van Duijkeren E., Janse I., Hagenaars T., et al., 2016. Veehouderij en gezondheid omwonenden [livestock farming and the health of local residents]. RIVM (National Institute for Public Health and the Environment), Bilthoven.

Metze T., Turnhout E., 2014. Politiek, participatie en experts in de besluitvorming over super wicked problems. Bestuurskunde. 23, 3-12. https://doi.org/10.5553/bk/092733872014023002001.

Ministry of Agriculture, 2018. Landbouw, natuur en voedsel: waardevol en verbonden - Nederland als koploper in kringlooplandbouw [Agriculture, nature and food: valuable and connected - The Netherlands as a leader in circular agriculture]. Ministerie van Landbouw, Natuur en Voedselkwaliteit [Ministry of Agriculture, Nature and Food Quality], Den Haag.

Ministry of Agriculture, 2019. Realisatieplan Visie LNV: Op weg met nieuw perspectief [Realization plan Vision LNV: Under way with new perspective] Ministerie van Landbouw, Natuur en Voedselkwaliteit [Minstry of Agriculture, Nature and Food quality], Den Haag.

Ministry of Infrastructure and Water Management, 2020. Een schone taak: bouwstenen voor een veilig, gezond en schoon leefmilieu [A clean task: building blocks for a safe, healthy and clean living environment]. Ministerie van Infrastructuur en Waterstaat [Ministry of Infrastructure and Water Management], Den Haag.

Ministry of the Interior and Kingdom Relations, 2018. Besluit van 3 juli 2018, houdende procedurele regels en regels over algemene onderwerpen over het beschermen en benutten van de fysieke leefomgeving (Omgevingsbesluit) [Decree of 3 July 2019, containing procedural rules and rules on general subjects regarding protecting and using of the physical living environment (Evironmental decree)].

National Research Council, 2009. Science and decisions: advancing risk assessment. The National Academies Press, Washington, D.C.

Poulsen M.N., Pollak J., Sills D.L., Casey J.A., Nachman K.E., Cosgrove S.E., et al., 2018. High-density poultry operations and community-acquired pneumonia in Pennsylvania. Environmental Epidemiology. 2, e013. https://doi.org/10.1097/EE9.0000000000000013.

Remkes J.W., Dijkgraaf E., Freriks A., Gerbrandy G.J., Maij W.H., Nijhof A.G., et al., 2019. Niet alles kan [Not everything is posisble]. Adviescollege Stikstofproblematiek [Advisory board nitrogen problems], Amersfoort.

Renn O., 2006. White Paper on Risk Governance: Towards and Integrative Approach. International Risk Governance Council (IRGC), Geneva.

Roest H., Tilburg J., Van der Hoek W., Vellema P., Van Zijderveld F., Klaassen C., et al., 2011. The Q fever epidemic in The Netherlands: history, onset, response and reflection. Epidemiol. Infect. 139, 1-12. https://doi.org/10.1017/S0950268810002268.

Scholz R.W., Steiner G., 2015. The real type and ideal type of transdisciplinary processes: part I—theoretical foundations. Sustainability Science. 10, 527-544. https://doi.org/10.1007/s11625-015-0326-4.

SDa, 2020. Het gebruik van antibiotica bij landbouwhuisdieren in 2019 SDa (Autoriteit Diergeneesmiddelen), Utrecht.

SER, 2016. Versnelling Duurzame Veehouderij [Acceleration Sustainable Livestock]. 2016. SER (Social and Economic Council), Den Haag.

Smeets E., Weterings R., 1999. Environmental indicators: Typology and overview. European Environment Agency Copenhagen.

Smit L., Huss A., Jacobs J., Baliatsas C., Dückers M., Boender G.J., et al., 2019. Veehouderij en Gezondheid Omwonenden III: Longontsteking in de nabijheid van geitenhouderijen in Gelderland, Overijssel en Utrecht. Institute for Risk Assessment Sciences (IRAS), Universiteit Utrecht.

Smit L.A.M., Boender G.J., De Steenhuijsen Piters W.A.A., Hagenaars T.J., Huijskens E.G.W., Rossen J.W.A., et al., 2017. Increased Risk Of Pneumonia In Residents Living Near Poultry Farms: Does The Upper Respiratory Tract Microbiota Play A Role? Pneumonia. 9, 1-9. https://doi.org/10.1186/s41479-017-0027-0.

Smit L.A.M., Hooiveld M., van der Sman-de Beer F., Opstal-van Winden A.W.J., Beekhuizen J., Wouters I.M., et al., 2014. Air pollution from livestock farms, and asthma, allergic rhinitis and COPD among neighbouring residents. Occup Environ Med, 134-140. https://doi.org/10.1136/oemed-2013-101485.

Smit L.A.M., van der Sman-de Beer F., Opstal-van Winden A.W.J., Hooiveld M., Beekhuizen J., Wouters I.M., et al., 2012. Q Fever and Pneumonia in an Area with a High Livestock Density: A Large Population-Based Study. PLoS One. 7, e38843. https://doi.org/10.1371/journal.pone.0038843

Spijker E., Anger-Kraavi A., Pollitt H., van de Ven D.-J., 2020. Evaluating integrated impacts of low-emission transitions in the livestock sector. Environmental Innovation and Societal Transitions. 35, 482-492. https://doi.org/https://doi.org/10.1016/j.eist.2019.11.003.

Thomas R., 1995. A general strategy for integrated environmental assessment at the European Environment Agency. RIVM (National Institute for Public Health and the Envrionment), Bilthoven.

Turnhout E., Metze T., Wyborn C., Klenk N., Louder E., 2020. The politics of co-production: participation, power, and transformation. Curr. Opin. Environ. Sustainability. 42, 15-21. https://doi.org/10.1016/j.cosust.2019.11.009.

UDV, 2013. Uitvoeringsagenda Duurzame Veehouderij 2023: 4e Voortgangsrapportage [implementation agenda sustainable livestock 2023: 4th progress report]. http://www.uitvoeringsagendaduurzameveehouderij.nl/files/1013/8268/5066/UDV-voortgangsrapportage-2013.pdf (accessed 11/06 2017).

United Nations, 2015. Transforming our world: the 2030 agenda for sustainable development. https://sustainabledevelopment.un.org/content/documents/21252030%20Agenda%20for%20Sustainable%20Development%20web.pdf (accessed 08/24 2017).

van Dam M., Dijksma S.A.M., 2017. Reactie op diverse onderzoeken naar de relatie tussen veehouderij en gezondheid [Response to several studies on the relation between livestock production and human health]. https://www.rijksoverheid.nl/documenten/kamerstukken/2017/06/01/reactie-op-diverse-onderzoeken-naar-de-relatie-tussen-veehouderij-en-gezondheid (accessed 07/22 2019).

van der Hoek W., Schneeberger P., Oomen T., Wegdam-Blans M., Dijkstra F., Notermans D., et al., 2012. Shifting priorities in the aftermath of a Q fever epidemic in 2007 to 2009 in The Netherlands: from acute to chronic infection. Eurosurveillance. 17. https://doi.org/10.2807/ese.17.03.20059-en.

van Grinsven H., Willems J., Dam J.v., van Zeijts H., Westhoek H., van der Sluis S., 2011. Welke veestapel past in Nederland? Inbreng voor de maatschappelijke discussie over begrenzing en sturing van de omvang van de veestapel [How many farm animals fit in the Netherlands? Contribution to a societal discussion on limiting and steering the number of farm animals. Planbureau voor de Leefomgeving (Netherlands Environmental Assessment Agency), Den Haag.

van Kersen W., Oldenwening M., Aalders B., Bloemsma L.D., Borlée F., Heederik D., et al., 2020. Acute respiratory effects of livestock related air pollution on a panel of COPD patients. Environment International. 136. https://doi.org/10.1016/j.envint.2019.105426.

von Mutius E., 2016. The microbial environment and its influence on asthma prevention in early life. J. Allergy Clin. Immunol. 137, 680-689. https://doi.org/10.1016/j.jaci.2015.12.1301

Zijp M.C., Posthuma L., Wintersen A., Devilee J., Swartjes F.A., 2016. Definition and use of Solution-focused Sustainability Assessment: a novel approach to generate, explore and decide on sustainable solutions for wicked problems. Environment international. 91, 319-331. https://doi.org/10.1016/j.envint.2016.03.006.

Samenvatting

Het karakteriseren van de effecten van de veehouderij op volksgezondheid en milieu

De productiviteit en omvang van de Nederlandse veehouderij zijn enorm toegenomen in de afgelopen halve eeuw. Zuivel, vlees en eieren zijn belangrijke export producten die bijdragen aan de status van Nederland als de op één na grootste landbouwexporteur ter wereld als het gaat om economische waarde. De keerzijde daarvan is merkbaar aan de toenemende zorgen rond volksgezondheid en milieu. Zo heeft de Nederlandse veehouderij wereldwijd effect op de uitstoot van broeikasgassen; de uitputting van eindige bronnen, zoals land, water en fosfor; de ontwikkeling van antimicrobiële resistentie; en de dreiging van opkomende infectieziekten die van dier op mens kunnen worden overgedragen (zoönosen). Continentaal draagt de veehouderij via ammoniak emissies bij aan verspreiding van secundair fijnstof. Lokaal draagt zij bij aan nutriëntenoverschotten die de water- en bodemkwaliteit beïnvloeden; milieueffecten van bestrijdingsmiddelen; geurhinder; en beïnvloedt zij de volksgezondheid met de uitstoot van fijnstof, endotoxinen en pathogenen.

Dergelijke zorgen kunnen niet allemaal los van elkaar aangepakt worden. Zo heeft de omschakeling van de legbatterij naar scharrel huisvesting voor leghennen in het verleden gezorgd voor een toename van de fijnstof-uitstoot ten gunste van verbeteringen op het gebied van dierwelzijn. Om bestaande zorgen aan te pakken en tegelijk afwenteling en neveneffecten te voorkomen is dus een integrale aanpak nodig. Daarom is het doel van dit proefschrift om de effecten van de Nederlandse veehouderij op volksgezondheid en milieu integraal te beoordelen. De uitkomsten kunnen als input dienen in de maatschappelijke dialoog over de toekomst van de veehouderij.

Hoofdstuk 2: Effecten van de Nederlandse veehouderij op gezondheid en milieu

In hoofdstuk 2 worden de effecten van de huidige Nederlandse veehouderij productie op volksgezondheid en milieu beoordeeld. Dat is gedaan door het bepalen van, voornamelijk kwantitatieve, effecten van de hele Nederlandse veehouderijproductie op 17 verschillende impact categorieën. Die zeggen iets over volksgezondheid of milieu, uiteenlopend van impacts van fijnstof, opduikende zoönosen en geurhinder, tot stikstofdepositie en broeikasgasemissies. Schattingen van de effecten zijn geschaald naar productie van de gehele Nederlandse veehouderij, inclusief de effecten gerelateerd aan het produceren van voer en verwerken van mest. Slacht, retail en consumptie zijn buiten beschouwing gelaten.

De effecten zijn uitgedrukt aan de hand van 22 verschillende indicatoren. Idealiter zeggen die indicatoren direct iets over de aard en de mate waarin de gezondheid of milieukwaliteit aangetast wordt. Dergelijke Impacts kunnen gezien worden als het einde van een causale keten van *Drivers, Pressures, States* en Impacts met maatregelen (*Responses*) die op elk van de schakels van die keten kunnen ingrijpen. Indicatoren uitdrukken als Impact was niet altijd mogelijk. Zo zeggen broeikasgasemissies wel iets over de bijdrage aan klimaatverandering, maar niets over de effecten die die klimaatverandering uiteindelijk in de samenleving teweeg brengt. Van de 22 gebruikte indicatoren zijn in totaal 8 indicatoren gebruikt die een Impact uitdrukken, en 14 meer indirecte indicatoren, die bijvoorbeeld de concentratie van stikstof in oppervlaktewater (*State*) uitdrukken of de uitstoot van broeikasgassen (*Pressure*).

Uit de resultaten van hoofdstuk 2 blijkt dat de veehouderijproductie voor 4% bijdraagt aan de totale Nederlandse ziektelast (uitgedrukt in DALYs - disability-adjusted life years) gerelateerd aan fijnstof, zoönosen, en arbeidsongevallen. Omgekeerd is geschat dat naast een nadelig gezondheidseffect, een vergelijkbaar grote ziektelast van astma en COPD juist voorkomen wordt. Deze aandoeningen lijken namelijk in de nabijheid van veehouderijen minder vaak voor te komen, al is causaliteit en het mechanisme daarachter nog onduidelijk. Er zijn ook gezondheidseffecten die minder goed in ziektelast zijn uit te drukken, zoals voor opduikende zoönosen die een grote impact kunnen hebben maar een kleine kans hebben om op te duiken en daardoor niet elk jaar ziektelast veroorzaken.

De resultaten laten ook zien dat de bijdrage van de veehouderij aan milieu-impact uiteenloopt van 2% van het watergebruik en 9% van de broeikasgasemissies in Nederland tot 70% van het landgebruik in Nederland en 95% voor de overdracht van fosfor naar bodems. Bovendien is de milieu-impact niet beperkt tot de Nederlandse grenzen, bijvoorbeeld omdat een aanzienlijk deel van het veevoer buiten Nederland geproduceerd wordt en omdat de uitgestoten ammoniak niet stopt bij de grens.

De beschreven effecten zijn niet uitgedrukt in één effect-maat, al is een deel van de gezondheidseffecten wel uitgedrukt in dezelfde maat voor ziektelast: de DALY. In principe is het definiëren van één maat waarin alle effecten worden uitgedrukt mogelijk, maar daarvoor moet bijvoorbeeld wel bepaald worden hoe je het aantasten van ecosystemen moet vergelijken met het aantasten van gezondheid, en hoe je geurhinder vergelijkt met andere gezondheidseffecten. Dat is niet objectief te bepalen, maar vraagt bijvoorbeeld de betrokkenheid van belanghebbenden om de verschillende impacts tegen elkaar af te wegen. Alhoewel niet alles is teruggebracht tot één maat, helpt het bij elkaar brengen van de verschillende effecten van de Nederlandse veehouderij wel om inzichtelijk te maken hoe de verschillende diersectoren daaraan bijdragen.

Uit hoofdstuk 2 blijkt dat rundvee, varkens, pluimvee en kleine herkauwers verschillend bijdragen aan de impacts. Rundvee levert bijvoorbeeld de grootste bijdrage aan broeikasgasemissies, vermesting, stikstofdepositie, secundair fijnstof en landgebruik in Nederland, terwijl varkens en pluimvee meer bijdragen aan landgebruik in het buitenland. Pluimvee draagt het meest bij aan de ziektelast van primair fijnstof en zoönosen.

Hoofdstuk 3 en 4: Effecten op de volksgezondheid in de nabijheid van veehouderijen

In hoofdstuk 3 en 4 is specifiek gekeken naar effecten van de Nederlandse veehouderij op luchtwegaandoeningen bij omwonenden van veehouderijen. In hoofdstuk 3 is onderzocht of er in de periode 2014-2016 een verhoogd risico op longontsteking was onder omwonenden van geitenbedrijven en pluimveebedrijven, zoals uit eerdere studies bleek die mogelijk beïnvloed konden zijn door de nasleep van de Q-koorts epidemie uit 2007-2009. Het risico op longontsteking is onderzocht door gegevens te analyseren over 90.183 huisartspatiënten uit het Zuidoosten van Nederland. In de analyses is op verschillende manieren rekening houden met omstandigheden die de analyse bemoeilijken. De analyse wordt namelijk ingewikkelder als een huisartspatiënt dicht bij een andere patiënt woont met dezelfde huisarts. Beide personen wonen dan waarschijnlijk in de buurt van hetzelfde veehouderij bedrijf, maar als zij een verhoogde kans op longontsteking hebben is het lastig om te bepalen of dat komt door de nabijheid van het bedrijf of door de manier waarop hun huisarts de diagnose stelt. Ook wonen nabij meer dan één veehouderij vergt een aangepaste analyse. Om met deze omstandigheden rekening te houden zijn vier verschillende analysetechnieken gebruikt. Met alle analysetechnieken bleek onder volwassenen het risico op longontsteking significant verhoogd bij het wonen binnen 500 meter van één of meerdere geitenbedrijven. De nabijheid van een pluimveebedrijf had minder duidelijk een verhoogd risico op longontsteking. De specifieke oorzaak voor de gevonden associatie blijft vooralsnog onduidelijk.

In hoofdstuk 4 is onderzocht of wonen nabij veehouderijen of in verhoogde concentraties fijnstof uit veehouderij, samenhangt met de uitgifte van medicatie voor astma of COPD. Informatie over het wel of niet krijgen van dergelijke medicatie was beschikbaar voor de gehele Nederlandse bevolking. Gegevens over 7.735.491 personen die niet in grootstedelijke agglomeraties woonden en voldeden aan verschillende andere selectiecriteria zijn gebruikt. Met de adresgegevens van deze personen is de afstand tot verschillende typen veehouderij vastgesteld. Ook is de jaargemiddelde concentratie van fijnstof uit de veehouderij op het woonadres berekend.

Nabijheid en veehouderij-gerelateerde fijnstof blootstelling bleek inderdaad samen te hangen met medicatie uitgiftes: in de buurt van, met name rundveebedrijven, werd minder medicatie verstrekt dan verder weg en dat was ook het geval bij hogere concentraties rundvee-gerelateerd fijnstof in vergelijking met lagere concentraties. Dit komt overeen met bevindingen uit eerder onderzoek. Het is bovendien in overeenstemming met de hygiëne hypothese, die stelt dat blootstelling aan een meer diverse set aan pathogenen de eerste levensfase zorgt voor een verlaagde kans op het ontwikkelen van astma en allergieën. Deze hygiëne hypothese verklaart een samenhang met COPD minder goed. Een alternatieve verklaring voor de verlaging van het aantal uitgiftes van medicatie is (culturele) verschillen in medische consumptie tussen mensen die dichterbij of verder van veehouderijen wonen. Een hogere concentratie van fijnstof van andere bronnen dan de veehouderij (zoals verkeer) liet juist een verhoogde hoeveelheid medicatie uitgiftes zien, dat is ook in lijn met wat in eerder onderzoek is gevonden over de invloed van dergelijke fijnstof bronnen op astma en COPD.

Hoofstuk 5: Effecten van veranderende bedrijfspraktijken in de veehouderij op volksgezondheid en milieu

Hoofdstuk 5 is een verkenning van veranderingen in de veehouderij die optreden bij een transitie naar kringlooplandbouw en meer duurzame veehouderij, zoals beschreven in de visie van het ministerie van Landbouw, Natuur en Voedselkwaliteit uit 2018. Om te verduurzamen verwerken veehouderijen in de toekomst bijvoorbeeld mest op een andere manier of wordt ander diervoer gebruikt. Andere manieren om te verduurzamen zijn het aanpassen van stallen en houden van andere dierrassen, zoals trager groeiende vleeskuikens en zogenaamde dubbeldoelkoeien. De effecten van deze veranderingen op gezondheid en milieu zijn beoordeeld door 26 deskundigen uit de onderzoekswereld, van de overheid, uit de sector of van maatschappelijke organisaties. De experts hadden expertise op het gebied van biodiversiteit, de ecologische voetafdruk of volksgezondheid. Ze hebben een webformulier ingevuld waarin gevraagd werd om aan de hand van indicatoren die pasten bij hun expertise, effecten te beoordelen op drie onderdelen: de transitie naar kringlooplandbouw en meer duurzame veehouderij als geheel; veranderingen van bedrijfspraktijken op vier specifieke voorbeeldbedrijven; en bedrijfsoverstijgende ontwikkelingen.

De scores van experts lieten zien dat de veranderingen in bedrijfspraktijken bij een gelijkblijvend aantal dieren een beperkt effect hebben op gezondheid en milieu. Dat lijkt onvoldoende om beleidsdoelen voor bijvoorbeeld klimaat, stikstof en fijnstof te halen. Ook zijn voor veel van de beschreven veranderingen zowel voordelen als nadelen gesignaleerd. Zo zijn trager-groeiende vleeskuikens volgens experts wel gezonder maar ook minder efficiënt en daarmee minder gunstig voor verschillende milieueffecten. Daarnaast gaven niet alle experts dezelfde scores. Om beter te leren waar die verschillen vandaan komen is meer interactie gewenst dan mogelijk was in dit onderzoek.

Overkoepelende lessen en toekomstige richtingen

In de algemene discussie in hoofdstuk 6 zijn de bevindingen uit de overige hoofdstukken samengevat en zijn overkoepelende lessen beschreven. Zo zeggen verschillende hoofdstukken iets over de rol van verschillende diersectoren, die voor elk type impact weer anders is. Ook komen verschillende vormen van onzekerheid terug in de hoofdstukken. Onzekerheid over een risico op opduikende zoönosen bijvoorbeeld, maar ook onzekerheden in kennis over de oorzaken van een toe- of afname van longontstekingen, astma en COPD in de buurt van veehouderijen. Die verschillende typen onzekerheden bepalen ook of de nadruk moet liggen op meer onderzoek, zorgen voor weerbaarheid en veerkracht, het opzetten van monitoringsprogramma's, of andere manieren om onzekerheid te beheersen. Daarnaast zijn lessen getrokken voor interdisciplinair onderzoek en het integreren van kennis van verschillende thema's. De benaderingen die gebruikt werden om te integreren waren nuttig, maar omdat impacts gerelateerd aan de veehouderij zo verschillend zijn was het wel een uitdaging om ze samen te brengen, wat aangeeft dat dit integreren maatwerk vergt en tijd nodig heeft. Een andere les uit dit interdisciplinaire onderzoek heeft betrekking op de samenwerking tussen onderzoekers. Voor die samenwerking is het belangrijk om te realiseren dat onderzoekers uit andere vakgebieden ergens een heel ander perspectief op kunnen hebben. Dat kan soms al zitten in een verschil in interpretatie van een woord als "milieu".

Ook zijn in hoofdstuk 6 toekomstige richtingen bediscussieerd, waarbij met name beschreven is hoe dit proefschrift een maatschappelijke dialoog over de toekomst van de veehouderij kan voeden en wat voor aanknopingspunten dat biedt voor toekomstig onderzoek. De toekomst van de veehouderij is namelijk in de eerste plaats een maatschappelijk vraagstuk, waarbij verschillende belanghebbenden een waardevolle en soms noodzakelijke inbreng kunnen hebben. Bovendien sluit een aanpak waarin het monitoren van nieuwe ontwikkelingen en betrekken van belanghebbenden centraal staat aan bij huidig en toekomstig beleid. In een dialoog over de toekomst van de veehouderij kunnen bijvoorbeeld verschillende gezondheids- en milieueffecten afgewogen worden, maar ook controversiële kwesties worden besproken zoals een inkrimping van de veestapel. Zo'n dialoog geeft aanleiding om in onderzoek voorbeelden van veehouderijbedrijven verder uit te diepen om zo beter te leren waar de knelpunten zitten. Ook kan een dialoog geholpen worden met meer integraal onderzoek naar veranderingen op nationaal niveau, ook wat betreft andere thema's dan volksgezondheid en milieu.

Tot slot

Het doel van dit proefschrift was om de effecten van de Nederlandse veehouderij op volksgezondheid en milieu integraal te beoordelen. Daartoe is eerst informatie van 17 verschillende impact categorieën bij elkaar gebracht. Deze variëren van een bijdrage van 2% van het watergebruik in Nederland tot 95% van de stroom van fosfor naar bodems, maar gaan bijvoorbeeld ook over geurhinder en een risico op opduikende zoönosen. Luchtwegaandoeningen onder omwonenden van veehouderijen zijn in meer detail bestudeerd. Rond geitenbedrijven is, net als in eerdere studies, een verhoogde kans op longontsteking te zien. Medicatiegebruik voor astma en COPD was juist lager in de buurt van veehouderijen, met name in de buurt van rundveebedrijven. Over de specifieke oorzaak van deze gezondheidseffecten zijn nog veel vragen. Wel is duidelijk dat rundvee, varkens, pluimvee en kleine herkauwers allemaal een eigen rol spelen in de gezondheids- en milieueffecten.

Om de integrale beoordeling nog een stap verder te brengen met het oog op de toekomst van de veehouderij, zijn ook veranderingen in de veehouderij bij een transitie naar kringlooplandbouw verkend. Zulke veranderingen hebben volgens experts een beperkt positief effect op volksgezondheid en milieu. Dat lijkt onvoldoende op beleidsdoelen voor bijvoorbeeld klimaat, stikstof en fijnstof te halen. Daarbij zijn er ook risico’s gesignaleerd en hebben sommige veranderingen zowel positieve als negatieve kanten.

De bevindingen in dit proefschrift geven aanknopingspunten voor een maatschappelijke dialoog over de toekomst van de veehouderij. Zo’n dialoog kan ondersteund worden met toekomstig onderzoek waarin regelmatige interactie met belanghebbenden en beleidsmakers is voorzien. Om relevant te zijn voor die laatste groepen zou dat onderzoek niet zozeer georiënteerd moeten zijn op het beschrijven van de problemen, maar zouden mogelijke oplossingen voor de uitdagingen in de veehouderij het uitgangspunt moeten zijn.

Summary

Characterizing effects of livestock farming on human health and the environment

The productivity and size of the Dutch livestock sector have vastly increased in the past half century. Dairy, meat and eggs are important export products that contribute to the status of the Netherlands as being the world's second largest exporter of agricultural products in terms of economic value. The downside of this becomes clear from the increasing concerns regarding public health and environment. For example, the Dutch livestock sector affects global greenhouse gas emissions; depletion of finite resources such as land, water and phosphorus; development of antimicrobial resistance and the risk of emerging infectious diseases that can be transmitted from animals to humans (zoonoses). Continent-wide, livestock contributes to ammonia emissions and spread of secondary particulate matter. Locally, the sector contributes to an excess of nutrients that affect water- and soil quality; environmental effects of pesticides; odor annoyance; and it affects the public health with emissions of particulate matter, endotoxins and pathogens.

Such concerns cannot all be addressed separately. For example, the ban of battery cages for housing laying hens has in the past led to increasing particulate matter emissions, to the advantage of improvements in animal welfare. Hence, to address existing concerns and prevent unwanted side-effects, an integrated approach is required. Therefore, the aim of this thesis is to integrally assess the effects of Dutch livestock on human health and environment. The outcomes of this may serve as input in the societal dialogue about the future of animal production in the Netherlands.

Chapter 2: Effects of Dutch livestock production on human health and environment

In chapter 2, the effects of the current Dutch livestock production on human health and environment are assessed. That assessment consisted of a largely quantitative estimation of effects of the entire Dutch livestock production on 17 different human health or environmental impact categories, ranging from impacts of particulate matter, emerging zoonoses and odor annoyance, to nitrogen deposition and greenhouse gas emissions. Effect estimates are scaled to the production of the entire Dutch livestock sector, including effects related to production and treatment of manure. Slaughter, retail and consumption were not taken into account.

The effects are expressed according to 22 different indicators. Ideally, these indicators directly express the nature and extent to which human health and environmental quality are affected. Such impacts can be regarded as the end of a causal chain of *Drivers, Pressures, States* and *Impacts* with measures (*Responses)* that can be targeted at each of the shackles in the chain. Expressing indicators as Impact was not always possible. For example, greenhouse gas emissions indicate the contribution to climate change but not the effects that such climate change has on society. Of 22 used indicators, 8 gave an indication of Impact, and 14 gave a more indirect indication, for example expressing the concentration of nitrogen in surface water (*State)* or emission of greenhouse gas emissions (*Pressure*).

The results of chapter 2 show that livestock production contributes 4% to the total Dutch burden of diseases (expressed in DALYs – disability-adjusted life years) related to particulate matter, zoonoses, and accidents. Conversely, apart from an adverse human health effect, about an equally large burden of diseases of asthma and COPD is estimated to be prevented. These conditions appear to occur less often in the vicinity of livestock farms, although causality and the underlying mechanism are still unclear. In addition, for some human health impacts, burden of disease is less suitable to express the health effect, such as for emerging zoonoses that may have a large impact but a small probability of occurrence and therefore do not cause a disease burden each year.

The results also show that the contribution of livestock production to environmental impact ranges from 2% of the water use and 9% of Dutch greenhouse gas emissions to 70% of the Dutch land use and 95% of the transfer of phosphorus to soils. Moreover, the environmental impact is not limited to the Dutch borders, for example because a considerable part of livestock feed is produced outside the Netherlands and because emitted ammonia does not stop at the border.

The described effects are not expressed in one metric, although part of the human health effects are expressed in the same metric for burden of disease: DALY. Defining one metric in which all impacts are expressed, is possible in principle, but requires a suitable way to compare e.g. ecosystem integrity to human health, or to compare odor annoyance to other health effects. Such comparisons cannot be made objectively, but for example require the involvement of stakeholders to weigh different impacts. Despite not expressing all impacts in a uniform metric, synthesizing the various effects of Dutch livestock production helps to provide insight in the contribution of different animal sectors.

The estimates in chapter 2 show that cattle, pigs, poultry and small ruminants contributes differently to the various impacts. Cattle, for example, has the largest contribution to greenhouse gas emissions, eutrophication, nitrogen deposition, secondary particulate matter and land use in the Netherlands, while pigs and poultry contribute more to land use abroad. Poultry contributes most to the burden of disease related to primary particulate matter and zoonoses.

Chapter 3 and 4: Effects on public health in the vicinity of livestock farms

The studies in chapter 3 and 4 focused on the effects of Dutch livestock farming on respiratory diseases among local residents. The risk of pneumonia among persons living close to goat farms and poultry farms was the focus of chapter 3, in which the aim was to assess such whether such risk was present in 2014-2016, as indicated in studies analyzing earlier years that may have been influenced by the Q-fever epidemic of 2007-2009. The risk of pneumonia was investigated by analyzing data on 90,183 General Practitioner (GP)-patients living in the Southeast of the Netherlands. The analyses took into account several complicating factors, such as dealing with GP-patients that live close to different patients with the same GP. In such cases, both persons probably live close to the same livestock farm, but when they both have an increased risk of pneumonia, it is hard to determine whether that is caused by the proximity of that farm or by the diagnosing practices of their GP. Another complicating factor is when one person lives close to multiple livestock farms. To take these complicating factors into account, four analysis techniques were used. All types of analyses showed a significantly increased risk of pneumonia among adults living within 500 meters from one or more goat farms. Whether the proximity of a poultry farm caused an increased risk as well was less clear. The specific cause of the found association remains unclear.

The aim of the study in chapter 4 was to assess whether living close to livestock farms or in increased concentrations of particulate matter from livestock farms, is associated with medication dispensing for asthma and COPD. Information about receiving such medication was available for the entire Dutch population. Data on 7,735,491 persons that did not live in urban agglomerates and fulfilled several other selection criteria were used. Information on the addresses of these persons was used to determine the distances to several types of livestock farms. The annual average concentration of livestock-related particulate matter was modelled as well.

Proximity and livestock-related particulate matter were indeed associated with medication dispensing: in the proximity of, namely cattle farms, less medication was dispensed than further away, and this was also the case in higher concentrations of cattle-related particulate matter compared to lower concentrations. This is in line with findings from earlier research. Moreover, it is in line with the hygiene hypothesis, which states that exposure to a more diverse set of pathogens in early life lowers the risk of developing asthma and allergies. This hygiene hypothesis explains the association with COPD less well. An alternative explanation for the lower medication dispensing is (cultural) differences in medicine consumption between persons that live close or further away from livestock farms. A higher concentration of particulate matter from other sources than livestock farming (such as traffic) showed a contrastingly higher amount of medication dispensing, which is in line with what has been found in earlier research on the effects of such sources of particulate matter on asthma and COPD.

Chapter 5: Effects of changing livestock farming practices on public health and environment

Chapter 5 is an exploration of changes in livestock farming that may occur in a transition towards circular agriculture and more sustainable livestock farming, as described in the vision of the ministry of Agriculture, Nature and Food

Quality of 2018. To become more sustainable, future livestock farms will for example treat manure differently or use different types of feed. Other ways to become more sustainable is to redesign housing systems and raising different animal breeds, such as slower growing broilers or so-called dual-purpose cows. The effects of these changes on public health and environment were assessed by 26 experts from the field of research, from government, from the sector or from societal organizations. The experts had expertise on biodiversity, the ecological footprint, or public health. They filed out a webform in which they were asked to use indicators that fitted their expertise to assess effects on three parts: the transition towards circular agriculture and more sustainable livestock farming as a whole; changes in farming practices on four different example farms; and broader developments.

The scores of experts showed that changes in farming practices had a limited effect on human health and environment with unchanged number of animals. That appears insufficient to reach policy goals regarding climate change, nitrogen and particulate matter. Furthermore, many of the described changes were thought to have both advantages and disadvantages. For example, slower growing broilers are healthier according to experts but also less efficient and therefore less favorable for several environmental impacts. In addition, not all experts provided the same scores. To better learn what causes these differences, more interaction is required than was possible in this study.

Overarching lessons and future directions

In the general discussion in chapter 6, the findings of the previous chapters are summarized and overarching lessons are drawn. For example, several chapters give an impression of the role of different animal sectors, which is different for each type of impact. The chapters also indicate different types of uncertainties. For example, uncertainty about the risk of emerging zoonoses, but also uncertainties regarding the knowledge on causes of an increase or decrease of pneumonia, asthma and COPD in the vicinity of livestock farms. Those different types of uncertainties determine whether they can best be managed by more research, building resilience, or by setting-up monitoring programs for example. In addition, lessons have been drawn for interdisciplinary research and integrating knowledge of different themes. The approaches that have been used for integration were useful but it has been challenging to synthesize the livestock-related impacts because they are so diverse, which indicates that integration requires custom approaches and time. A different lesson from this interdisciplinary research relates to the cooperation between researchers. For such cooperation it may be important to realize that researchers from different disciplines may have different perspectives. This can sometimes be as little as a differences in interpretation of a word like “environment”.

In chapter 6, future directions have been discussed as well, mainly describing how this thesis can feed a societal dialogue on the future of livestock farming and what starting points it provides for future research. A societal dialogue is referred to because the future of livestock farming is in the first place a societal problem, about which different stakeholders may have a valuable and in some cases necessary input. Moreover, an approach in which monitoring new developments and involving stakeholders is key, is in line with current and future policies. In a dialogue on the future of livestock farming several human health and environmental effects may be weighed, but also controversial topics may be discussed, such as a decrease in the number of livestock animals. Such a dialogue stimulates research in which examples of livestock farms are further investigated to learn more on potential trade-offs. A dialogue may also benefit from more integrated research on changes on a national level, also regarding other themes besides public health and environment.

In conclusion

The aim of this thesis was to integrally assess the effects of the Dutch livestock sector on public health and environment. For that aim, information on 17 different impact categories have been synthesized. These range from a contribution of 2% of the water use in the Netherlands to 95% of the transfer of phosphorus to soils, but for example also concern odor annoyance and the risk of emerging zoonoses. Respiratory diseases among residents living close to livestock farms were studied in more detail. Close to goat farms, an increased risk of pneumonia was observed, corresponding with earlier observations. In contrast, medication dispensing for asthma and COPD was lower close to livestock farms, especially in the vicinity of cattle farms. The specific causes of these health effects remain largely unknown. What is clear, is that cattle, pigs, poultry, and small ruminants, each have their own role in causing human health and environmental effects.

To bring the integrated assessment a step further in light of the future of livestock farming, experts were consulted to explore het effects of changes in livestock farming in a transition towards circular agriculture. Such changes are expected to have a limited positive effect on public health and environment. These effects appear insufficient to reach policy goals regarding climate change, nitrogen and particulate matter for example. In addition, risks have been identified as well and some changes have both beneficial add adverse effects.

The findings in this thesis provide starting points for a societal dialogue on the future of livestock farming. Such a dialogue may benefit from future research in which frequent interactions with stakeholders and policy makers is an integral part. To make such research relevant for the latter groups, it should not focus on describing the problems, but take potential solutions for the challenges in livestock farming as a starting point.

Dankwoord

Allereerst dank ik natuurlijk Lenny, zonder jou was dit proefschrift er niet geweest. Jij nam het initiatief voor dit project met een super breed kader, dat ook de nodige dwarsverbanden binnen het RIVM heeft opgeleverd. Jij gaf mij veel ruimte om er mijn eigen draai aan te geven, maar hield ook de nodige controle. Jouw kritische houding op zowel inhoud als proces was niet altijd makkelijk maar heeft mij veel gebracht. Bovendien heb ik jouw enthousiasme en bron van ideeën erg gewaardeerd de afgelopen jaren. Dat zorgde er soms voor dat ik dacht “hoe moet ik dit nu allemaal weer gaan doen”, maar dat ging dan ook gepaard met een lading nieuwe energie om aan de slag te gaan.

Erik, jouw rol als promotor was er soms, zeker in het begin, eentje op afstand, maar op momenten en zeker in het laatste jaar eentje met grote betrokkenheid. Meer of minder intensief, het was altijd waardevol om te kunnen putten uit jouw ruime ervaring. Op de inhoud, maar zeker ook op het proces, waar je altijd een goede vraagbaak was voor advies.

Eddie en Imke, het contact met jullie in de eerste paar jaar van mijn onderzoek heb ik als erg waardevol ervaren. Imke, al had ik niet heel frequent contact met jou, je hebt tussen alle drukte door toch telkens tijd gevonden om goed mee te denken. Soms betekende dat een vrij radicale koerswijziging, maar dat is mijns inziens ten goede gekomen aan het resultaat.

Eddie, jouw nuchtere en ervaren blik in combinatie met je goede toegankelijkheid en bereikbaarheid is erg waardevol geweest in de eerste paar jaar. Qua inhoud stond je soms wat verder van de onderwerpen van de studies af maar met jou spreken hielp me eigenlijk altijd wel weer verder.

Leo, jouw rol als promotor kwam pas helemaal op het eind maar wel op een moment dat jouw blik op het geheel nog ten goede kon komen aan het eindresultaat. Jouw betrokkenheid bij mijn onderzoek was er al eerder. Toen al was jouw blik doorgaans heel verfrissend en prikkelend. Ik ben dankbaar om met jou te hebben mogen werken.

Ook de leden van de beoordelingscommissie wil ik graag bedanken: prof. dr. Arjan Stegeman, prof. dr. Jan Willem Erisman, prof. dr. Roel Coutinho, dr. Bram Bos, en prof. dr. Peter Driessen. Dank voor het kritisch beoordelen van dit proefschrift.

Er zijn in totaal 37 verschillende medeauteurs die meegewerkt hebben aan de verschillende hoofdstukken in mijn proefschrift. Naast Lenny, Erik, Eddie, Imke en Leo die ik genoemd heb zijn dat Addo, Alex, Anja, Anne, Anke, Bert, Christos, Danny, Dick, Gert Jan, Heike, Henk, Henk Jan, Jan, Jim, Joris, Lapo, Lidwien, Marie-Josée, Marina, Marten, Martine, Michiel, Paul, Ric, Rob, Ronald, Roy, Susanna, Thomas, Wilco en Wim. Jullie wil ik allemaal bedanken. For the two of these co-authors who do not speak Dutch, I also want to thank you for your input.

Er zijn een aantal medeauteurs die ik in het bijzonder wil bedanken. Ik begin met Michiel. Jouw rol bij het tot stand komen van het tweede hoofdstuk van mijn proefschrift ("het V-OH paper") was een belangrijke. Door jouw bijdrage aan de, vaak moeizame, coördinatie van het geheel maar ook op inhoudelijk vlak. Dat bestond vaak uit herhaalde gesprekken en discussies, waarin ik (soms te) koppig kon zijn, maar waarin we uiteindelijk denk ik wel een stap verder zijn gekomen.

Danny, jij bent vooral betrokken geweest bij het vierde hoofdstuk van mijn proefschrift ("het SALFAS project"), maar dat was wel een grote betrokkenheid. Ik kon met jou lekker de diepte in gaan over de milieu-epidemiologische analyses en daarbij putten uit jouw ruime ervaring. Soms vonden er ook gesprekken plaats op de fiets naar huis en toen het fietsen naar huis niet meer gebeurde omdat we met zijn allen thuiszaten, heb ik je thuis nog mogen bezoeken. Daarbij was er naast de inhoud ook ruimte om het te hebben over dingen die niets met het project te maken hadden.

Marina, jij hebt een bijdrage geleverd aan twee van de hoofdstukken van dit proefschrift. Met name binnen SALFAS was jouw bijdrage aan de modelering van fijnstof belangrijk. Het was soms zoeken naar wat we daarin van elkaar nodig hadden, maar met een mooi resultaat waarover we ook een keer samen hebben mogen presenteren.

Marie-Josée, jouw bijdrage aan het tweede hoofdstuk ("het V-OH paper") is misschien niet heel zichtbaar maar wel heel waardevol geweest. Met de ziektelast-berekeningen van zoönosen uit de veehouderij gaf je een enorm solide basis, die ook de andere ziektelast berekeningen gesterkt heeft. Daarover kon ik met jou sparren en dat heb ik erg gewaardeerd.

Lidwien, jij bent ook betrokken geweest bij twee hoofdstukken in mijn proefschrift. Bij de één wat meer dan bij de ander. Ik ben blij dat ik gebruik heb mogen maken van jouw kritische blik en jouw ruime kennis over de gezondheidseffecten onder omwonenden van veehouderijen.

Anke, jij had een hele afgebakende rol binnen het derde hoofdstuk van mijn proefschrift. Wij konden samen de diepte in voor het berekenen van afstanden tot veehouderijen, waarbij je me goede adviezen kon geven die ook bij latere analyses goed van pas kwamen. Daarnaast had je altijd oog voor hoe het met mij ging en of mijn onderzoek nog goed op de rails zat.

Naast medeauteurs zijn er nog verschillende anderen die inhoudelijk hebben bijgedragen aan de hoofdstukken in het proefschrift, door bijvoorbeeld het aanleveren van data, of door mee te denken. Zij staan genoemd na elk hoofdstuk, maar hier wil ik er nog een aantal uitlichten. In het bijzonder wil ik Ben bedanken. GIS-analyses en kaartjes waren toch wel een belangrijk onderdeel van mijn promotieonderzoek. Jouw advies heeft me daar erg bij geholpen en het was fijn om als je er op woensdag was, altijd bij je binnen te kunnen lopen.

Ook de experts die betrokken zijn geweest bij de expert consultatie die beschreven is in hoofdstuk 5 wil ik hier bedanken. In totaal hebben 26 experts de moeite genomen om een uitgebreide online vragenlijst in te vullen, maar ook daarvoor en daarna heb ik met verschillende onderzoekers, beleidsmedewerkers en boeren gesproken. Dank voor jullie tijd en bereidheid om mee te werken.

Nu wil ook Wim noemen. Naast medeauteur op één van de hoofdstukken was jij ook mijn afdelingshoofd gedurende ruim vier jaar. Dat heeft er voor gezorgd dat je inhoudelijk goed hebt kunnen bijdragen maar ook altijd goed kon adviseren over proces en communicatie. Ik kon altijd bij je binnenlopen met mijn vragen om jouw ervaren en nuchtere blik daar op te laten schijnen.

Niet alleen voor de inhoudelijke bijdragen aan dit proefschrift ook voor de fijne tijd in de afgelopen jaren wil ik verschillende collega's bedanken. Natuurlijk mijn kamergenoten bij EPI: Maarten, Bernice, Irene, Emma, Abigail, Tizza, Janneke. Dank voor jullie gezelligheid, en het kunnen sparren over code, e-mails en figuren. We konden samen leuke dingen doen (bijvoorbeeld Lindy Hop) maar ook elkaar steunen op moeilijkere momenten. Ook de andere collega's van "de derde verdieping" en ook de tweede hebben bijgedragen aan de goede tijd met bijvoorbeeld een vast lunch groepje, en marktbezoek op vrijdag.

Dan de collega's van de RES-afdeling. Soms had ik het gevoel wel wat verder af te staan van waar de rest mee bezig was, maar door onderdeel te zijn van de RES-afdeling is mijn blikveld wel weer verruimd, en bijvoorbeeld voor legionella konden er toch wat mooie dingen ontstaan. Bovendien was het altijd leuk om met jullie te kunnen borrelen, koken, op kraamvisite te gaan of foto's van pinguïns te kijken.

Dan is er nog de rest van EPI die ik wil bedanken voor de fijne tijd. Voor de borrels en uitjes maar ook voor bijvoorbeeld de lunchwandelingen. En met name het secretariaat voor alle praktische hulp die in de afgelopen jaren nodig was.

De afgelopen jaren heb ik niet alleen bij EPI gewerkt. Ook in Wageningen, bij APS was ik regelmatig te vinden. Ik heb me daar altijd welkom gevoeld, en de gesprekken die ik daar voerde waren regelmatig verfrissend. De borrels, promoties die ik heb mogen meevieren waren altijd gezellig. En ook samen met een aantal van jullie naar een EAAP congres gaan was leuk. Dank voor jullie gastvrijheid.

Ook op het IRAS heb ik regelmatig gewerkt. Bij de analyses voor het derde hoofdstuk van dit proefschrift was dat voor een aantal maanden mijn voornaamste werkplek en ook daarna kwam ik er nog regelmatig. Het was fijn om er een vaste kamer te hebben om te werken maar ook het “buddy-systeem” van afgelopen jaar heeft er goed voor gezorgd dat het contact met een aantal van jullie goed in stand bleef. Dank voor de leuke contacten die ik gehad heb. And for the non-Dutch speaking persons: thanks for the nice contacts I had at IRAS.

Vrienden, familie en schoonfamilie hielpen mij de afgelopen jaren om mijn onderzoek in begrijpelijke taal te kunnen uitleggen; mijn moeder in het bijzonder door mee te lezen met de samenvatting. Daarnaast zorgden zij voor afleiding en ook voor steun op moeilijke momenten, die er ook waren de afgelopen jaren. Bovendien is het fijn om af en toe over een ander onderwerp te praten, bijvoorbeeld over promotieonderzoek in een totaal ander vakgebied. En Floris, mijn dank voor jouw kritische blik op de proefdruk wil ik in deze allerlaatste versie ook niet onbenoemd laten.

Els, jouw steun de afgelopen jaren was van onschatbare waarde, al is het maar omdat je mij graag het beste gunt. Jij was een belangrijke sparringpartner voor zo’n beetje alle onderdelen van mijn onderzoek. Of het nou ging om tegen je aan ratelen om mijn gedachten te ordenen, het laten zien van een plaatje, of om een moeilijke situatie te bespreken. Daarbij konden we elkaars steun ook op andere vlakken gebruiken de afgelopen jaren en natuurlijk ook samen leuke dingen doen. Ik hoop dat we elkaar nog lang mogen versterken.

About the author

Pim Post was born on the 10th of January 1991 in Amsterdam, The Netherlands. After having graduated from grammar school at Pieter Nieuwland College in Amsterdam in 2009, he enrolled in the Bèta-Gamma bachelor-program of the University of Amsterdam. The first year of this interdisciplinary program consisted of courses involving various disciplines from the natural and social sciences. After the first year, Pim majored in Biology, but kept feeding his broad interest with additional courses in philosophy, mathematics and psychology. This interdisciplinary interest determined Pim's choices when following the Master's program in Biological Sciences, with research projects on the evolution of cooperation at IBED, University of Amsterdam, and on the assessment of ecosystem services in the Life Cycle Assessment framework, at VU, Amsterdam.

His interdisciplinary background was very useful when starting his PhD-research in 2016 at the National Institute for Public Health and the Environment (RIVM) on the effects of Dutch livestock production on human health and environment, described in this thesis. During his research at RIVM, Pim collaborated with various researchers from several departments within RIVM, but also from Wageningen University and Research, Utrecht University (IRAS), and the Netherlands Institute for Health Services Research (NIVEL).

List of publications

Othoniel B., Rugani B., Heijungs R., Beyer M., Machwitz M., **Post P.**, 2019. An improved life cycle impact assessment principle for assessing the impact of land use on ecosystem services. Science of The Total Environment. 693, 133374. https://doi.org/10.1016/j.scitotenv.2019.07.180.

Post P.M., Hogerwerf L., Huss A., Petie R., Boender G.J., Baliatsas C., et al., 2019. Risk of pneumonia among residents living near goat and poultry farms during 2014-2016. PLoS One. 14, e0223601. https://doi.org/10.1371/journal.pone.0223601.
Presented at International One Health Congress 2018, Saskatoon

Post P.M., Hogerwerf L., Bokkers E.A.M., Baumann B., Fischer P., Rutledge-Jonker S., et al., 2020. Effects of Dutch livestock production on human health and the environment. Science of The Total Environment. 737, 139702. https://doi.org/10.1016/j.scitotenv.2020.139702.
Presented as poster at IECID 2017, Trieste; oral at EAAP 2019, Gent

Post P.M., Houthuijs D., Sterk H.A.M., Marra M., van de Kassteele J., van Pul A., et al., 2021. Proximity to livestock farms and exposure to livestock-related particulate matter are associated with lower probability of medication dispensing for obstructive airway diseases. International Journal of Hygiene and Environmental Health. 231, 113651. https://doi.org/10.1016/j.ijheh.2020.113651.
Presented as poster at ISEE 2019, Utrecht