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Published in:
Food Control

Link to article, DOI:
10.1016/j.foodcont.2023.110199

Publication date:
2023

Document Version
Peer reviewed version

Citation (APA):

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SMP designed the study, developed methods and analyzed data, interpreted results, wrote the manuscript. JP, HGR, STT and JSK developed methods and analyzed data, interpreted results, and contributed to writing the manuscript.
Risk ranking of foodborne diseases in Denmark: reflections on a national burden of disease study

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Declarations of interest: none

Key words

Burden of disease; prioritization; DALY; food safety; pathogens; chemicals
Abstract

National burden of foodborne disease (FBD) studies are useful for risk ranking and identifying priorities for food safety resource allocation. FBD are caused by microbiological and chemical hazards, which have different incidence and mortality, and lead to health-outcomes varying in severity and duration. Due to their different origins and characteristics, distinct prevention strategies can be implemented.

We present the Danish initiative to estimate the burden of FBD caused by pathogens and chemicals. We describe the methodological approaches and data used, present an overview of results for the reference year 2019, and discuss lessons learned throughout more than seven years of the project.

Our estimates show that the leading causes of FBD in Denmark include both pathogens and chemicals, suggesting that food safety strategies should be diversified to tackle different issues. The experiences with this national study are useful for other countries planning to implement a burden of FBD study.
1. Introduction

The complexity of the food system makes tackling food safety a challenge. Food safety hazards include a wide range of pathogens and chemicals, which can lead to diverse health outcomes, and are present in different foods and at different levels of contamination. To identify and implement interventions that effectively reduce the burden of foodborne diseases in the population and to make the best use of the available resources, countries need information that can support them in setting priorities. The National Food Institute launched a national initiative to rank foodborne diseases in Denmark in 2015. The Danish burden of foodborne disease study aims to i) estimate the national burden of foodborne diseases by microbiological and chemical hazards in the Danish population, ii) estimate the relative contribution of foods to this burden, and iii) rank foodborne diseases based on their public health impact.

A key methodological choice made at the beginning of the project was to use the disability-adjusted life year (DALY) to measure health impact. The DALY is a population health metric that integrates morbidity and mortality of potential health outcomes of a disease and allows for comparison of disease burden across diseases and countries (Murray, 1994). The DALY is the key metric of the Global Burden of Disease study (GBD) (Abbafati et al., 2020) and has been widely used to measure the burden of foodborne diseases at national (A. Havelaar et al., 2012; Scallan et al., 2015) and international levels, including by the World Health Organization (WHO) (A. H. Havelaar et al., 2015; WHO, 2015). The WHO published estimates of the global burden of foodborne diseases in 2015 and encourages the implementation of national burden of foodborne disease studies (Pires et al., 2021; WHO, 2015).

While the methodology to estimate the burden of disease by foodborne pathogens was generally well-established and useful for inspiration and adaptation for the Danish study, estimating the burden of foodborne chemicals had proven challenging and required further research (Gibb et al., 2015). Thus, we invested substantial resources to develop methods to estimate the burden of
chemical hazards through dietary exposure. Other challenges that needed addressing included the
collection and integration of burden of disease estimates derived through different
methodological approaches; the development of strategies for selection of health outcomes; and
the communication of burden of disease estimates to different audiences and stakeholders.

We believe that the lessons learned over the course of more than seven years of the Danish
initiative to estimate the burden of foodborne diseases can be useful for informing ours as well as
other national burden of foodborne disease projects, especially those that are in their planning
stages. Thus, the aim of this paper is to present the Danish initiative to estimate the burden of
foodborne diseases. We describe the methodological approaches taken and evaluate the results
obtained for the reference year 2019, focusing on the challenges of integrating burden estimates
from foodborne pathogens and chemical hazards for risk ranking and prioritization.

2. Materials and methods

2.1. Danish burden of foodborne disease study

For the estimation of the national burden of foodborne diseases, microbial and chemical hazards are
selected based on their public health relevance. Public health relevance is evaluated differently for
the two types of hazards. Foodborne pathogens are selected based on reported incidence of
disease; existence and frequency of disease outbreaks in the population; severity of symptoms; and
available epidemiological evidence or risk assessments. Chemical hazards are selected based on
available data and on the presumed public health impact of specific chemical contaminants in the
population. When resources allow or hazards are prioritized, new hazards are added to the running
list and contribute to the expansion of the Danish national burden of disease study. In the Danish
burden of foodborne disease study, the above criteria have so far led us to include the following 14
hazards: *Salmonella* spp. (non-typhoidal), *Campylobacter* spp., norovirus, *Toxoplasma gondii*, *Listeria
monocytogenes*, *Yersinia enterocolitica*, Shigatoxin-producing *Escherichia coli* (STEC), Hepatitis A
Virus, Methylmercury (MeHg), Lead (Pb), Cadmium (Cd), Inorganic arsenic (i-As), Acrylamide, and
peanut allergy. Aligned with the WHO estimates of the global burden of foodborne diseases (Gibb et al., 2015; A. H. Havelaar et al., 2015), we included peanut allergy under chemicals and toxins.

The first step in estimating the burden of disease of any given hazard is to calculate the attributable incidence of disease in the population. There are two overall approaches to calculate the attributable incidence: the top-down and the bottom-up approach (Devleesschauwer et al., 2015).

The top-down approach takes its starting point in the total number of reported or estimated cases of disease in the population, which is either corrected for underdiagnosis and underreporting, or attributed to the causal agent of disease, by combining it with an etiology proportion or a population attributable fraction (PAF) (Devleesschauwer et al., 2015). The bottom-up approach takes its starting point in the exposure to the given hazard from foods and combines this with exposure-response data to estimate the attributable incidence of disease. The bottom-up approach is also sometimes referred to as a risk assessment approach, as it builds on the methods used for traditional risk assessment of chemicals and quantitative microbial risk assessment (Devleesschauwer et al., 2015).

Based on the attributable incidence, the burden of disease due to a given foodborne hazard can be estimated in terms of DALYs. The so-called incidence and hazard-based approach is the gold standard for estimating the burden of foodborne hazards, for both pathogens and chemicals (Devleesschauwer et al., 2014; Schroeder, 2012). Taking this approach, the burden of a specific foodborne hazard is defined as that resulting from all health states that are causally related to the hazard concerned, whatever the time scale or severity, and the future burden associated with health effects that start in the reference year but may have longer durations is assigned to this year. These health states may include acute symptoms, chronic stages, sequelae, and death.

2.1.1. Burden of disease of foodborne pathogens

To estimate the disease burden of foodborne pathogens, we take a top-down approach and use public health surveillance data and (1) estimate the incidence and mortality of each pathogen; (2)
estimate the disease burden of all health outcomes of each pathogen in terms of DALYs; and (3) link these estimates with estimates on the proportion of the total burden that is attributable to foods. Because infections by most foodborne pathogens are largely underreported, we estimate the incidence of disease for most pathogens by correcting the reported cases to the Danish National Infectious Disease Institute (SSI) for underdiagnosis and underreporting of these infections based on the data from a survey on care seeking behavior in the population (Müller et al., 2012). If pathogens are not notifiable and public health surveillance data are sparse, we estimate the incidence of that etiology by partitioning the total incidence of diarrhea to that pathogen. If we can assume that all infections are captured by the surveillance system, for example because the symptoms of the infection are severe and all patients are expected to visit a physician and be diagnosed (e.g., infections with *Listeria monocytogenes*), we assume no underreporting. The approaches taken for estimating incidence are described in detail in (Pires et al., 2019). Then, we identify all potential health outcomes of each infection through literature reviews and build disease models (also called “health outcome trees”) based on the available epidemiological evidence on the probability of developing each health outcome, as described in (Nissen et al., 2017; Pires et al., 2019). Last, we estimate the incidence of each health outcome in the population and estimate DALYs. DALYs are calculated by adding the number of years of life lost due to premature mortality (YLL) and the number of years lived with disability (YLD), adjusted for severity (DALY=YLL+YLD). YLL is the product of the number of deaths (*M*) and the average remaining life expectancy (*RLE*) at the time of death (*YLL=M* *RLE*). YLD is the product of the number of incident cases of each health outcome (*I*), the average duration until remission or death (*D*), and the disability weight (*DW*), which reflects the reduction in health-related quality of life on a scale from 0 (no impact on full health) to 1 (death) (*YLD=I* *D* *DW*).

2.1.2. Burden of disease of foodborne chemicals For most chemical hazards, estimation of the burden of foodborne chemicals takes a risk assessment approach, i.e., takes a starting point in an assessment of exposure to the chemical hazards through
the consumption of foods. The risk assessment approach relies on the same data and methods as traditional toxicological risk assessment of chemicals and has two methodological steps: i) estimate foodborne exposure to the hazard in the population, and ii) estimate the probability of occurrence of the selected health outcomes following exposure to the hazard based on exposure-response models to derive the attributable incidence. While it is the preferred methodology for environmental chemicals, there are only a few examples of burden of disease estimates for foodborne chemicals that are based on a top-down approach. These include the disease burden of cyanogenic glycosides from cassava, which was estimated by means of a categorical attribution model (Gibb et al., 2015) and aflatoxin B1 disease burden, for which a PAF was derived to estimate the fraction of hepatocellular carcinoma burden attributed to aflatoxin exposure from maize and peanuts via the counterfactual analysis (WHO, 2015). Data to derive mortality, used as input to estimate YLL, may be collected from the scientific literature, from health registries (i.e., case-fatality ratios or survival rates), or from multiplying PAFs with mortality or DALY “envelopes” (i.e., total number of deaths or estimated DALYs attributed to a disease). The steps to estimate DALYs are the same as for pathogens. All models have been described in detail in (Jakobsen et al., 2016; Jakobsen, Fabricius, et al., 2020; Jakobsen, Pilegaard, et al., 2020; Thomsen et al., 2022).

2.1.3. Source attribution

To estimate the burden of disease of foodborne pathogens that is attributed to the consumption of contaminated foods, we apply attributable foodborne proportions estimated by the WHO to the total disease burden (Hald et al., 2016). Because estimates were not produced at a national level, we applied estimates for the subregion that includes Denmark (WHO subregion EUR-A), which corresponds to European countries with very low child and adult mortality (WHO, 2015, 2017). Although we have national estimates of attribution to specific foods for some pathogens, namely Salmonella (Munck NSM, Njage P, Litrup E, 2018) and Campylobacter (Pires & Christensen, 2017), these are not available neither for all years nor all pathogens and thus were not included in this risk ranking exercise. When taking a risk assessment approach relying on an exposure assessment...
derived from food intake and contamination data, the source attribution step is already included in
the burden methodology. This is often the case for foodborne chemicals and toxins. However, this
approach does not allow for the estimation of the relative burden of disease to other main exposure
routes (such as environmental or occupational transmission). In some instances, the dose metric in
exposure-response functions is in the form of biomarkers (e.g., blood lead levels or methyl mercury
in hair). In those cases, we convert dietary exposure levels to corresponding biomarker levels, thus
still integrating attribution to food sources directly in the risk assessment approach. Thus, the
burden of disease estimations for all chemical hazards in our study are only for dietary exposure,
and thus attribution to foods is 100%. With approaches in which the exposure assessment builds on
data on biomarkers of chemical exposure, source attribution may be used for estimating burden of
disease of chemicals attributable to food consumption. So far, we have not applied that approach in
our study.

2.2. Data and data sources

The data used to estimate the burden of disease due to foodborne pathogens and chemicals in
Denmark are presented in Table 1. Some of these vary depending on the hazard, either due to the
characteristics of the hazard itself or due to data availability limitations.

2.3. Quantification of uncertainty and variability

We propagated uncertainty around the input parameters throughout the calculations using Monte
Carlo simulations in all models (1,000 iterations), except for acrylamide, for which we applied a
deterministic approach. In the models to estimate the burden of disease of foodborne pathogens,
we quantified uncertainty in the estimation of underreporting of human cases and in the estimation
of incidence. For all hazards, we accounted for uncertainty in the probability of occurrence of health
outcomes, and in disability weights. In the models to estimate burden of disease of chemicals, when
information on the variability of input parameters was available, this was included in the model but
separated from uncertainty by applying two-dimensional Monte Carlo simulation (100,000 iterations for variability). All calculations were conducted in R version 4.0.3 (R Core Team 2018).

3. Results

3.1. Incidence, deaths and DALYs

We present the results of the burden of disease of 14 foodborne hazards in the reference year 2019. Together, these 14 hazards caused 133,388 cases, 90 deaths and 5,928 DALYs. In Table 2, hazards are ranked by highest to lowest total DALYs within each main group (“pathogens” and “chemicals”). While we also present the total disease burden estimated for foodborne pathogens (i.e., including non-foodborne transmission), we focus on the foodborne burden for the purposes of ranking.

Results show that the pathogens causing the highest foodborne disease burden were Campylobacter (1,285 DALYs), Salmonella (416 DALYs), and Yersinia enterocolitica (220 DALYs). Norovirus was estimated to cause a very high number of cases, but few DALYs (23 DALYs). In contrast, Toxoplasma gondii led to few cases (11) and a high number of DALYs (144 DALYs). Even if to a lower extent, we observed the same patterns for Listeria monocytogenes (60 cases born 185 DALYS).

Among chemicals, lead (1,261 DALYs, upper bound), peanut allergy (906 DALYs), and methylmercury (592 DALYs) caused the highest disease burden. Even if substantially lower (5 DALYs), the burden of inorganic arsenic was born by few cases, which reflects a high severity of disease.

3.2. Overall ranking

When ranking all foodborne hazards (Fig. 1), we observed that Campylobacter was the leading cause of foodborne disease burden in Denmark, followed by peanut allergy, lead, and methylmercury. The following five places in the ranking were occupied by foodborne pathogens: Salmonella, Y. enterocolitica, L. monocytogenes, STEC and congenital toxoplasmosis. The hazards causing the lowest burden were hepatitis A virus (4 DALYs) and cadmium (0.04 DALYs (UI 0.035; 0.044)). The uncertainty bounds around the DALY estimates overlap for some of the hazards, ultimately affecting
the risk ranking. While the estimated uncertainty around the estimates for foodborne pathogens is quite small, uncertainty for some of the chemicals (lead, Peanut, MeHg) may affect the ranking of the top five hazards.

Figure 2 plots the estimated DALYs for each hazard against the estimated DALY per case caused by each hazard. The DALY per case metric represents the average burden suffered across all cases in the population by that hazard. Results show that Campylobacter has the highest estimated total DALYs but a low DALY per case, while acrylamide has a low total estimated DALY but a high DALY per case. The diseases and hazards plotted closer to the upper right corner of the graph (congenital toxoplasmosis and L. monocytogenes) cause a considerable burden at population and individual levels, compared to the other included hazards.

4. Discussion

4.1. Overall findings

Ranking of foodborne diseases is essential to inform evidence-based food safety priorities and monitor the effect of interventions. In Denmark, food safety activities have been built around a One Health framework for several decades, with integration of data from robust public health, animal, food, and environmental surveillance programs for generating scientific evidence for risk assessment and risk ranking.

The Danish burden of foodborne disease study builds on research and evidence-based policy efforts that have been well established for decades. This is the first study in Denmark that analyses data and ranks food safety risks including microbiological and chemical hazards. Campylobacter caused the highest burden of disease in 2019 (1,285 DALYs), a finding consistent in all previous iterations of the study (Pires, 2014; Pires et al., 2019, 2022). Number two in our ranking was lead, leading to the loss
of 1,261 years of healthy life in one year, followed by peanut allergy, methylmercury, and Salmonella. Had we taken the lower bound estimate for lead, this hazard would have ranked third. For most of the pathogens that led to a high burden measured in DALYs, the burden was driven by a high estimated incidence. A large proportion of these cases experience mild symptoms, which is translated into a low average DALY/case. Although a similar pattern was observed for some of the chemicals, including methylmercury and lead, for acrylamide and inorganic arsenic the opposite was observed. For T. gondii, a relatively low number of cases of disease but a high DALY/case were also estimated, illustrating the high severity of disease caused by this hazard. The high disability experienced by fewer people stresses the importance of looking for several metrics when establishing food safety priorities.

The top-ranking hazards have varied characteristics and lead to a diverse range of diseases. Campylobacter and Salmonella are pathogens originating from various animal reservoirs and can contaminate several foods. They are susceptible to temperature: they grow at optimal temperatures (which leads to higher contamination of foods) and die at temperatures >70°C, which means that these pathogens can be eliminated from foods through heat-treatment during cooking (Doyle & Mazzotta, 2000; International Commission of Microbiological Specifications for, 1996). There are other cooking and hygiene practices that influence the risk of infection for individuals. In contrast, peanut allergy is rare when compared to infection with Campylobacter and Salmonella. However, it is a life-long condition that causes disability every day of an allergic person’s life, including anxiety related to accidental exposure and psychosocial aspects of peanut allergy (Lieberman et al., 2021). Likewise, lead and methylmercury cause intellectual disability, which was assumed irreversible and thus also lifelong. While most pathogens included in our study have characteristics similar to Campylobacter and Salmonella, chemical hazards vary substantially in terms of food sources, vulnerable groups, as well as the duration and severity of associated health outcomes.
Linked to these differences, the intervention strategies that can be defined based on this evidence are also very distinct. Food safety interventions to control pathogens in foods and prevent foodborne diseases include pre-harvest control, i.e. ensuring that the animal reservoirs (broilers, layer chicken, pigs, cattle) are pathogen-free by implementing monitoring and surveillance programmes at farm level, applying good biosecurity practices, and implementing strict measures in positive flocks and herds; post-harvest measures, which include interventions at slaughter and during food processing; monitoring of foods at retail; investigation of outbreaks and actions to prevent further cases; and raising awareness on food safety concerns and food handling practices (da Costa et al., 2021; Pessoa et al., 2021; Wegener, 2010; Wegener et al., 2003). Historically, several intervention programs were implemented at specific points in time to address food safety priorities (Wegener, 2010). All these interventions have been based on the collection, management, integration, analysis, and communication of food safety information.

The implementation of food safety programs is the shared responsibility of governmental institutions and industry. Interventions to prevent exposure to chemical hazards will mostly involve control measures to limit contamination of foods and maximum levels used to keep highly contaminated foods off the market but may also include communication regarding the avoidance of particularly contaminated foods. In contrast to the food safety interventions to control pathogens, which, if successful, have a shorter time from intervention to effect (i.e., decreased incidence and burden of disease), the effects of food safety interventions needed to control exposures to chemical hazards will usually not be measurable before several years have passed due to the long time from exposure to the onset of a health effect. These differences in time perspectives from intervention to effect are important to bear in mind when using the ranking of microbial and chemical hazards for food policy purposes.

In a recent study, we estimated the economic impact of the burden of disease of pathogens in 2019 building on the estimates of the incidence and mortality of foodborne pathogens (Pires et al., 2022).
Those estimates have not yet been done for chemical hazards. We included direct costs in the health sector, indirect costs of lost productivity, and estimates of the value of unpaid time lost to morbidity and premature deaths. That study showed that the pathogens leading to the highest total health costs were norovirus (185 million €), Campylobacter (124 million €), STEC (46 million €) and \textit{L. monocytogenes} (43 million €). STEC led to the highest direct health costs, which is explained by the larger number of complicated hospitalizations associated with STEC infections when compared to other pathogens. These results demonstrate that the rankings of disease burden and cost of illness are not necessarily the same, and that hazards that have a high incidence of disease, even if less severe, have a high economic impact. These results are also important to inform policies.

4.2. Reflections on ranking pathogens and chemicals

The structure and methodology of the Danish burden of foodborne disease study were largely informed by the World Health Organization’s initiative to estimate the Global Burden of Foodborne Diseases (WHO, 2015). The WHO encourages national foodborne disease studies, i.e., efforts at country level that deliver burden of disease estimates for hazards prioritized locally and at a frequency that is also defined locally (Pires et al., 2021; World Health Organization, 2021). Our study leveraged on access to national surveillance and monitoring data, and expertise, methodological flexibility to make use of these data, and stepwise selection and inclusion of hazards to address national priorities. The burden of disease estimates for these hazards were published in other, separate peer-reviewed articles (Jakobsen et al., 2016; Jakobsen, Fabricius, et al., 2020; Jakobsen, Pilegaard, et al., 2020; Nissen et al., 2017; Pires et al., 2019, 2022; Thomsen et al., 2022), but this is the first time they are presented collectively and compared across microbial and chemical hazards.

While our study supports the case for having pathogens and chemicals intermixed in the overall risk ranking based on DALYs, a common health metric that is useful precisely for such comparisons, the interpretation of results is not linear. First, the severity of disease by the two types of hazards is dramatically different, and communication of relatively similar estimates of burden of disease (for
example for inorganic arsenic and norovirus) that are caused by such different number of cases is challenging. Second, the traditions in the metrics used to inform food safety interventions in the microbiological and toxicological domain have been diverse, and the leaps from those to use and interpret composite metrics are also different in magnitude. For example, microbiological risk assessments and risk rankings have often used metrics such as incidence and mortality of foodborne infections in the population (Pires et al., 2021; World Health Organization, 2021). Thus, interpreting the DALY for risk ranking in this domain is facilitated and may be understood as an advancement or integration of the two (along with severity). In contrast, toxicological risk assessments of chemicals traditionally focus on assessing the risk of populations being exposed to doses of a chemical that are beyond levels that can be considered safe (WHO/FAO, 2009). Thus, such findings are not equivalent to actual public health impact on the population due to current exposure levels and cannot be directly translated into current levels of disease in the population. The interpretation of these metrics is different from the DALY, and it is possible that efforts to communicate risk ranking results based on DALY estimates need to be tailored to stakeholders interested in risk ranking but not familiar with the differences between risk assessment and burden of disease metrics.

There are various methods that can be used to conduct food safety risk rankings (van der Fels-Klerx et al., 2018). Among quantitative methods, the DALY and other summary measures of population health are often preferred because they incorporate morbidity, mortality, and severity. For example, a mild disease (i.e., with a low DALY/case) caused by a highly prevalent risk may have a lower total DALY than a severe disease (i.e., with a high DALY/case) that is caused by a hazard that is rare (FAO, 2020). Within our list of hazards, these differences are illustrated for example by norovirus and the carcinogen inorganic arsenic. While this approach for risk ranking can be applied by utilizing existing DALY estimates, such as those derived by WHO-FERG (WHO, 2015), country-specific estimates, derived by applying national data, are more precise and representative of food safety priorities at national level.
Lastly, it is relevant to highlight that a national burden of foodborne disease study such as this Danish study is a reflection of the food safety interventions implemented in that country or region. Therefore, if hazards are ranked low, this may simply indicate that the current food safety measures are effective, and not that resources should be allocated elsewhere. Therefore, the interpretation of the results should be done along with an assessment of the current strategies in place.

4.3. Lessons learned

It is useful to update burden of disease estimates when new data become available and new hazards are introduced

For some of the pathogens, we performed disease burden calculations for several reference years (Anonymous, 2022). Changes in estimated burden from these earlier iterations to the 2019 estimates reflect only changes in reported incidence data, because the model for estimation of total incidence and DALYs are the same. For chemical hazards, changes over time reflect solely changes in population structure and disease incidence and mortality, as exposure data used are the same as in the earlier published estimates. Still, and even if only capturing some changes, we believe that regular updates of risk ranking results are useful to inform and adjust food safety policy at national level, particularly for pathogens. For chemicals, updates are mainly relevant when new food consumption and contamination data become available or if new research becomes available, e.g., with respect to new health outcomes associated with exposure to a chemical or updated dose-response data. Furthermore, updates of the full risk-ranking exercise are important every time we can add new hazards to the study.

It is useful to start small and expand the burden of disease study when resources and data allow

The motivations, advantages, and support structures for national burden of foodborne disease studies have been discussed at length elsewhere (Pires et al., 2021). We would highlight the usefulness of starting small and adding hazards along the way. This step-by-step approach allows for building research and methodological capacity, for gradual discovery of the data sources and access
connections, and for making the best of available resources. Gradually and as resources allow, the project can move from individual studies to a standardized and routine approach. Along the way, the best approach for presenting, communicating, and making use of the generated evidence can be established.

Communication of burden of disease estimates should be targeted to different stakeholders

The DALY is a well-established metric to quantify and compare the importance of diseases, risk factors and injuries, but its use to rank foodborne diseases is relatively recent. Communication of estimates should be accompanied by a transparent presentation of the methods and data used, as well as the interpretation of burden of disease estimates. The strategies and materials of communication may be different for a scientific audience, stakeholders, or the general population.

4.4. Way forward

The lessons learned with the design, implementation, and growth of our burden of foodborne disease study present an opportunity to define the way forward to continuous improvement and impact of our study. Our plans focus on expanding our study with more hazards in coming years, and on developing digital platforms for visualization and interaction with burden of disease estimates and thus improve knowledge translation. Once developed, this platform should allow for transparent sharing of the data sources, as well as an interactive visualization of burden of disease estimates with different types of stratification, as selected by the end-user. We will also focus on sharing models with other research groups and thus reduce the time and resources required for national burden of disease studies and contribute to the harmonization of approaches across countries. To overcome this, we will in the future store our validated models, data files, and metadata in repositories. All models will be adapted to or developed in FSKX format (Food Safety Knowledge Exchange) (Filter et al., 2022), which is an open-source information exchange format for script-based models from the food safety domain. This will be done in collaboration with the “Risk Assessment Modelling and Knowledge Integration Platforms” (RAKIP), which was established by
three European institutions specialized in food safety risk assessment (ANSES, BfR and DTU National Food Institute) as a joint project to establish new community resources and facilitating the efficient knowledge integration and exchange.

5. Conclusions

The Danish burden of disease study has been growing over its life span and has been useful to identify food safety priorities in the country for pathogens but awaits implementation in decision making for chemicals. Results show that food safety interventions need to be established to prevent exposure to pathogens and chemicals in our foods, which demonstrates the need for different types of interventions in food systems. While the stakeholders in charge of such interventions may differ, it is useful to provide comparable and integrated evidence on the public health impact of different types of hazards at national level. Lessons learned throughout the development of the Danish burden of disease study can be useful for other national studies. With these in mind, we have the following six recommendations: 1) establish a multi-disciplinary team for the burden of disease study that has knowledge in microbiological risk assessment, toxicological risk assessment, and modelling; 2) establish connections with experts and stakeholders within the fields of microbiological and chemical food safety, public health surveillance, food monitoring, and food consumption data that can guide and contribute to the study at different points, which will ensure that the relevant expertise is included in the study, and that the study’s metrics and results are interpreted by those experts and stakeholders during implementation and upon presentation of results; 3) start small, tackling few hazards, apply existing model frameworks, and grow as resources, experience and capacity develop, thus ensuring methodological finetuning and understanding of needs in a progressive way; 4) present intermediate results and considerations to relevant stakeholders regularly to achieve a better understanding of the study’s results and how these can be translated into policy; 5) connect with international researchers and institutions with similar interests, and contribute to joint scientific developments, methodological alignment, and comparisons of results across countries; and 6) continuously strive to improve communication of results.
Acknowledgements
We would like to acknowledge all authors of the individual studies that are part of the project, and Dr. Morten Poulsen for the feedback provided in the last version of the manuscript.

Funding
This work was partly supported by the Metrix-project (financed by the Danish Ministry for Environment and Food).

References


List of Figures

Figure 1. Ranking of foodborne hazards in Denmark based on estimated disability adjusted life years (DALYs) attributed to food, 2019.

Figure 2. Total estimated disability adjusted life years (DALY) and DALY per case for 14 foodborne hazards in Denmark, 2019.
### Table 1. Overview of data required to estimate the burden of foodborne pathogens and chemicals in Denmark.

<table>
<thead>
<tr>
<th>Input parameter</th>
<th>Source</th>
<th>Salmonella spp. (non-typhoidal)</th>
<th>Campylobacter spp.</th>
<th>Norovirus</th>
<th>Toxoplasma gondii</th>
<th>Listeria monocytogenes</th>
<th>Yersinia enterocolitica</th>
<th>Shigatoxin-producing Escherichia coli (STEC)</th>
<th>Hepatitis A Virus</th>
<th>Methylmercury</th>
<th>Lead</th>
<th>Cadmium</th>
<th>Inorganic arsenic</th>
<th>Acrylamide</th>
<th>Peanut allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported cases</td>
<td>Register of Enteric Infections (<a href="http://www.ssi.dk">www.ssi.dk</a>) (Voldstedlund et al., 2014)</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Underreporting factors</td>
<td>Population survey of diarrhea episodes and care seeking behaviour (Müller et al., 2012)</td>
<td>x</td>
<td>x</td>
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<td>x</td>
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<td>Incidence of syndrome</td>
<td>Institute of Health Metrics and Evaluation (Global Health Data)</td>
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<tr>
<td>Prevalence of disease</td>
<td>Literature (Eller et al., 2009; Kjaer et al., 2008; Mortz et al., 2005; Osterballe et al., 2009)</td>
<td>x</td>
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<td>Global Health Estimates, WHO (WHO, n.d.)</td>
<td>x</td>
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<tr>
<td>Seroprevalence</td>
<td>Literature (Lebech et al., 1999)</td>
<td>X</td>
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<td>Food consumption data</td>
<td>Danish Food Consumption Survey (Pedersen et al., 2015)</td>
<td>x x x x x x</td>
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<td>Food monitoring (Petersen et al., 2015)</td>
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<td>Exposure-response function</td>
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<td>Probability of health outcome or sequelae</td>
<td>Various sources, literature review</td>
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<td>Disability weights</td>
<td>Global Burden of Disease study (Salomon et al., 2015)</td>
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<td>Duration of disease</td>
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<td>Population data</td>
<td>National statistics (Statistics Denmark, 2020)</td>
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<tr>
<td>Number of births</td>
<td>National statistics (Statistics Denmark, 2020)</td>
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<td>Life expectancy table*</td>
<td>WHO life expectancy and national life expectancy (Statistics Denmark, 2020)</td>
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</table>
*We use the World Health Organization life expectancy table to estimate years of life lost (YLL) and national life expectancy to estimate years of life lived with disability (YLD)*
Table 2. The estimated annual burden of disease for 14 foodborne hazards as described by different indicators, Denmark 2019

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Registered Cases</th>
<th>Estimated Cases</th>
<th>Estimated* or Registered** Deaths</th>
<th>Total costs (million Euro)</th>
<th>Total DALY</th>
<th>DALY/100,000</th>
<th>Foodborne attribution (%)</th>
<th>Foodborne burden (DALY)</th>
</tr>
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<tbody>
<tr>
<td><strong>Pathogens</strong></td>
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<td></td>
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</tr>
<tr>
<td>Campylobacter</td>
<td>5389</td>
<td>58983</td>
<td>41*</td>
<td>124</td>
<td>1691</td>
<td>29</td>
<td>76%</td>
<td>1285</td>
</tr>
<tr>
<td>Salmonella</td>
<td>1122</td>
<td>8657</td>
<td>10*</td>
<td>30</td>
<td>548</td>
<td>9.4</td>
<td>76%</td>
<td>416</td>
</tr>
<tr>
<td>STEC</td>
<td>619</td>
<td>12136</td>
<td>10**</td>
<td>46</td>
<td>255</td>
<td>4.4</td>
<td>60%</td>
<td>153</td>
</tr>
<tr>
<td>Y. enterocolitica</td>
<td>4861</td>
<td>5273</td>
<td>4*</td>
<td>5</td>
<td>220</td>
<td>3.8</td>
<td>100%</td>
<td>220</td>
</tr>
<tr>
<td>L. monocytogenes</td>
<td>60</td>
<td>60</td>
<td>17***</td>
<td>43</td>
<td>185</td>
<td>3.2</td>
<td>100%</td>
<td>185</td>
</tr>
<tr>
<td>Norovirus</td>
<td>-</td>
<td>48142</td>
<td>7*</td>
<td>185</td>
<td>87</td>
<td>1.5</td>
<td>26%</td>
<td>23</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>34</td>
<td>126</td>
<td>1*</td>
<td>1</td>
<td>9</td>
<td>0.2</td>
<td>42%</td>
<td>4</td>
</tr>
<tr>
<td>Toxoplasma gondii</td>
<td>-</td>
<td>11</td>
<td>1**</td>
<td>-</td>
<td>144</td>
<td>2.5</td>
<td>61%</td>
<td>88</td>
</tr>
<tr>
<td><strong>Chemicals</strong></td>
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<tr>
<td>Methylmercury</td>
<td>NA</td>
<td>417</td>
<td>0*</td>
<td>-</td>
<td>592</td>
<td>10.2</td>
<td>100%</td>
<td>592</td>
</tr>
<tr>
<td>Lead²</td>
<td>NA</td>
<td>996</td>
<td>0*</td>
<td>-</td>
<td>1261</td>
<td>21.6</td>
<td>100%</td>
<td>1261</td>
</tr>
<tr>
<td>Cadmium</td>
<td>NA</td>
<td>0</td>
<td>9*</td>
<td>-</td>
<td>0.04</td>
<td>0.00</td>
<td>100%</td>
<td>0.04</td>
</tr>
<tr>
<td>Inorganic arsenic</td>
<td>NA</td>
<td>1</td>
<td>1*</td>
<td>-</td>
<td>5</td>
<td>0.1</td>
<td>100%</td>
<td>5</td>
</tr>
<tr>
<td>Acrylamide³</td>
<td>NA</td>
<td>3</td>
<td>0*</td>
<td>-</td>
<td>30</td>
<td>0.5</td>
<td>100%</td>
<td>30</td>
</tr>
<tr>
<td>Peanut allergy</td>
<td>NA</td>
<td>252</td>
<td>0**</td>
<td>-</td>
<td>858</td>
<td>15.0</td>
<td>100%</td>
<td>858</td>
</tr>
</tbody>
</table>

¹Registered cases include Y. enterocolitica subtype 1A. ²For lead, we reflected uncertainty in the conversion from blood lead levels to corresponding dietary exposure by applying two scenarios: an "upper bound scenario" (UB), and a "lower bound scenario" (LB). For the purpose of risk ranking, we selected to use the UB estimate, i.e. the highest estimate of investigated scenarios (Thomsen et al., 2022). ³For acrylamide, we estimated DALY using two different exposure response functions. For the purpose of
the risk ranking, we selected to use the most conservative estimate, i.e. the highest estimate of investigated scenarios (Jakobsen et al., 2016). *Estimated; ** registered.

For chemical hazards, we only estimated the burden of disease due to dietary exposure, and thus the foodborne proportion is by default 100%.
Highlights

- The Danish burden of foodborne disease study ranks pathogens and chemicals based on estimated DALY
- Top foodborne hazards were Campylobacter, lead, peanut allergy, methylmercury, and *Salmonella*
- Experiences from our national foodborne burden are useful for other country studies
- We recommend forming multidisciplinary team, connecting with stakeholders, growing organically
Declaration of interests

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Hernan Gomez Redondo reports financial support was provided by Danish Ministry for Environment and Food. Sara Monteiro Pires reports financial support was provided by Danish Ministry for Environment and Food. Lea S. Jakobsen reports financial support was provided by Danish Ministry for Environment and Food. Sofie T. Thomsen reports financial support was provided by Danish Ministry for Environment and Food.