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Burden of disease estimates of seven pathogens commonly transmitted through foods in Denmark, 2017

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21 **Abstract**

22 Burden of disease metrics are increasingly established to prioritize food safety interventions. We estimated
23 the burden of disease caused by seven foodborne pathogens in Denmark in 2017: *Campylobacter*,
24 *Salmonella*, shiga-toxin producing *Escherichia coli*, norovirus, *Yersinia enterocolitica*, *Listeria*
25 *monocytogenes*, and *Toxoplasma gondii*. We used public health surveillance data and scientific literature to
26 estimate incidence, mortality and total DALY of each, and linked results with estimates of the proportion of
27 disease burden that is attributable to foods. Our estimates showed that *Campylobacter* caused the highest
28 burden of disease, leading to a total burden of 1,709 DALY (95% Uncertainty Interval 1,665-1,755), over
29 three-fold higher than the second highest ranked pathogen (*Salmonella*: 492 DALY (95% UI 481-504)).
30 *Campylobacter* still led the ranking when excluding DALY attributable to non-foodborne routes of exposure.
31 The total estimated incidence was highest for norovirus, but this agent ranked sixth when focusing on
32 foodborne burden. *Salmonella* ranked second in terms of foodborne burden of disease, followed by *Listeria*
33 and *Yersinia*. Foodborne congenital toxoplasmosis was estimated to cause the loss of around 100 years of
34 healthy life, a burden that was born by a low number of cases in the population. The ranking of foodborne
35 pathogens varied substantially when based on reported cases, estimated incidence and burden of disease
36 estimates. Our results reinforce the need to continue food safety efforts throughout the food chain in
37 Denmark, with a particular focus on reducing the incidence of *Campylobacter* infections.

38

39 **1. Introduction**

40 Foodborne diseases (FBD) have been recognized as an important health concern in Denmark for decades.
41 High incidence of human cases and/or large-impact outbreaks at different points in time have motivated
42 the implementation of comprehensive pathogen-specific control plans, for example focused on *Salmonella*
43 *spp.* (Wegener et al., 2003), *Listeria spp.* (EC, 2005) and *Campylobacter spp.* (Fødevarestyrelsen, 2018;
44 Rosenquist et al., 2009). These action plans have had varied degrees of success. For example, while

45 *Salmonella* control programmes have resulted in a substantial decrease in the reported incidence of
46 salmonellosis, *Campylobacter* Action Plans have had limited effect (Wegener, 2010).

47 Notifications of cases to public health surveillance suggest changes in the relative importance of diseases
48 and effectiveness of intervention strategies over time, but the overall impact of FBD in Denmark is largely
49 unknown. It is widely recognized that reported cases represent only the “tip of the iceberg”, and that for
50 many pathogens the true incidence of disease in the population is unknown (Kirk et al., 2014; Majowicz et
51 al., 2010; Mead, 1999; Scallan et al., 2011). Only a fraction of all cases caused by contaminated foods are
52 captured by public health surveillance systems. For a case to be identified, the ill person must seek medical
53 care; the doctor must request a faecal sample; the causative pathogen must be identified at a laboratory;
54 and the results must be reported to public health officials. Any drop-outs in this process lead to
55 underdiagnosis and underreporting, which varies between causative agents depending on the severity of
56 symptoms and the awareness about the pathogen (Haagsma et al., 2012). In addition, FBD have a wide
57 variety of manifestations with different severity, duration and sequelae, and comparisons based solely on
58 incidence do not provide a complete picture of their relative public health impact (Havelaar et al., 2012).

59 Health metrics that incorporate these parameters such as the disability-adjusted life year (DALY) are
60 increasingly accepted as a way to translate and compare the health impact of foodborne diseases and
61 facilitate evidence-based risk ranking (Cassini et al., 2016; Havelaar et al., 2015).

62 The objective of this study was to estimate the incidence and foodborne burden of disease (in DALY) of
63 seven pathogens in Denmark, a country with a free public healthcare system and nationwide data on
64 notifiable FBDs available.

65 **2. Methods**

66 We estimated the burden of disease caused by five enteric pathogens (four bacteria: *Salmonella*,
67 *Campylobacter*, *Yersinia enterocolitica*, shiga-toxin producing *Escherichia coli* (STEC); one virus: norovirus),

68 and two invasive pathogens, the bacteria *Listeria monocytogenes* and the parasite *Toxoplasma gondii*.
69 Pathogens were selected on the basis of their public health relevance, reflected either by reported
70 incidence, number of outbreaks or severity of symptoms. Among these seven agents, only the enteric
71 bacterial infections were notifiable in Denmark.

72 The enteric bacteria and norovirus cause mild-to-severe gastroenteritis, and may lead to severe sequelae or
73 death. *Toxoplasma gondii* infections can be pre-natal (leading to congenital toxoplasmosis (CT)) or post-
74 natal (referred to as *acquired toxoplasmosis*). Due to lack of data on the latter, we only included the
75 congenital form. CT may lead to fetal death, neonatal death or neurological life-long symptoms in young
76 children. Infection with *L. monocytogenes* can cause mild disease in otherwise healthy people, manifesting
77 with usually mild and self-limiting gastroenteritis. However, in high-risk groups such as the elderly,
78 immunocompromised or foetus and neonates (in-utero infection), infection can be invasive and lead to
79 severe clinical disease, manifesting as sepsis, meningitis or encephalitis, spontaneous abortion and death
80 (Jensen et al., 2016). We included only the invasive form of listeriosis.

81 To estimate the foodborne disease burden for all pathogens in 2017, we i) estimated the incidence and
82 mortality of each; ii) estimated the disease burden of all health outcomes of each pathogen in terms of
83 DALY; and iii) linked these estimates with estimates on the proportion of the total burden that is
84 attributable to foods. Detailed methodology of each step is presented below and in Appendices 1 to 4.

85 **2.1. Incidence and mortality of disease**

86 We applied different approaches to each pathogen to estimate the total incidence and mortality of disease,
87 dependent on available data.

88 **2.1.1. Enteric bacterial infections**

89 In Denmark, human *Salmonella*, *Campylobacter*, STEC and pathogenic *Yersinia enterocolitica* infections are
90 notifiable through the laboratory surveillance system. Physicians send specimens from suspected cases to
91 one of the clinical microbiology laboratories, the laboratories report positive results to the National Public

92 Health Institute (*Statens Serum Institut*, SSI) within one week, and results are recorded in the Register of
93 Enteric Infections maintained by SSI (www.ssi.dk). Only first-positive cases are reported (episodes), *i.e.* each
94 patient-infectious agent combination is only recorded once in any six-month period. If available,
95 information on the subtype of the pathogen (e.g. serotype, serogroup, sequence) is registered.

96 To adjust for underdiagnosis and underreporting of enteric bacterial infections, we re-constructed the
97 surveillance pyramid as described by Haagsma et al. (2012). The model consists of a set of non-pathogen
98 specific and pathogen-specific parameters defined by probability distributions (Appendices 1A and 1B).
99 These parameters were informed by data collected through a population-based telephone survey
100 conducted in 2009 (Müller et al., 2012), by evidence from National Health Registries, or by literature
101 review. Estimated multipliers were applied to surveillance data from 2017 (available at www.ssi.dk/data).
102 Reported *Yersinia enterocolitica* cases did not include cases caused by biotype 1A, which are considered
103 non-pathogenic (EFSA, 2007). We did not differentiate between pathogens' subtypes. Data were
104 segregated in six age categories and by gender to account for differences in the incidence of disease in
105 different age and gender groups.

106 **2.1.2. Norovirus infection**

107 There is no reporting system for norovirus infections or for gastroenteritis outbreaks in Denmark, except
108 for suspected foodborne outbreaks. Because reported outbreak-related cases only represent a small
109 fraction of total cases, these data were insufficient to describe the epidemiology and public health impact
110 of the disease. To estimate the total incidence of norovirus infections in Denmark, we adapted a previously
111 described approach (Pires et al., 2015). In brief, we collected the total national diarrhoea incidence and
112 mortality envelopes as published by the Global Burden of Disease Study (available at
113 <http://ghdx.healthdata.org/gbd-results-tool>). Then we estimated the proportion of diarrhoea cases/deaths
114 attributable to norovirus based on data extracted from a systematic review (Ahmed et al., 2014), before
115 estimating the number of norovirus-specific cases and deaths by multiplying the incidence and mortality

116 envelopes with the attributable proportions. To account for asymptomatic carriage, we defined a norovirus
117 attributable factor based on prevalence studies with healthy controls (Ahmed et al., 2014). Finally, to
118 account for norovirus illnesses not associated with diarrhoea, but which were vomiting-only, we defined a
119 vomiting inflation factor based on prevalence data from the same study. More details on the methods are
120 available in Appendix 2.

121 **2.1.3. Congenital toxoplasmosis**

122 The incidence of CT was estimated on the basis of a cohort study. The Danish National Neonatal Screening
123 Programme for Congenital Toxoplasmosis (DNNSP) was conducted from January 1, 1999 to July 31, 2007
124 (Schmidt, 2005; Schmidt et al., 2006), and included >98% of all newborns in Denmark. We assumed that the
125 incidence of CT in newborns observed during the DNNSP was applicable to 2017. The screening method
126 applied in the cohort was expected to identify 70%–80% of newborns with CT. We combined the observed
127 average annual incidence of CT per 10,000 live-born children with the number of live-born children in
128 Denmark in 2017 (Statistics Denmark, available at <https://www.dst.dk/en>) to estimate the annual incidence
129 in 2017. Model parameters and data sources are described in detail in Appendix 3.

130 **2.1.4. Invasive listeriosis**

131 Because invasive listeriosis is a severe illness, all cases in the population were assumed diagnosed and
132 notified to the public health surveillance system. Age and gender-specific incidence of listeriosis in 2017
133 was collected from the National Listeria Surveillance database (available at <http://www.ssi.dk/data>). Under
134 Danish surveillance, pregnancy associated infections are notified as a single case (the woman), fetal loss or
135 still-born babies are thus not recorded.

136 **2.2. Health outcomes and mortality**

137 All included infections can lead to more than one symptom and/or sequelae. The possible health outcomes
138 of each infection were identified through literature review, and were described in an outcome tree. All
139 outcome trees and probabilities of exhibiting each outcome following infection are presented in Appendix

140 4. All enteric infections cause diarrhoea and/or vomiting, which define the incident case; in other words, all
141 cases caused by each enteric pathogen will manifest this outcome. The sequelae varied between pathogens
142 with only some similarity. Specifically, salmonellosis, campylobacteriosis and yersiniosis may all lead to the
143 sequelae reactive arthritis (ReA) and irritable bowel syndrome (IBS). Guillian Barré Syndrome (GBS) is a
144 potential sequelae of campylobacteriosis, and STEC infections can lead to haemolytic uremic syndrome
145 (HUS) and end-stage renal disease (ESRD). No possible sequelae were considered for norovirus infections.
146 All enteric infections may cause death.

147 The invasive infections CT and listeriosis have different manifestations. CT comprises a variety of health
148 outcomes, and children may be symptomatic at birth, later in life or remain apparently asymptomatic.
149 Health outcomes of CT were defined as by Havelaar et al., 2007: foetal loss, sequelae manifesting in the
150 first year of life (chorioretinitis, intracranial calcification, hydrocephalus, CNS abnormalities, and neonatal
151 death), and sequelae appearing after the first year of life (chorioretinitis). Non-specific symptoms following
152 CT (e.g., anaemia, jaundice, pneumonitis, and diarrhoea) were not included. CT was only considered
153 possible for infants of previously seronegative mothers that became infected during pregnancy; the
154 possibility of peri-conceptional transmission or vertical transmission in mothers deemed seropositive prior
155 to conception was excluded. Detailed information on the classifications have been published previously
156 (Nissen et al., 2017).

157 For listeriosis, we followed the model defined by the European Centre for Disease Control and Prevention
158 (ECDC, 2015), which accounted for the probability that acquired invasive symptomatic cases present with
159 meningitis and for the probability of death following infections. For perinatal cases, the disease burden for
160 health outcomes of early- and late-onset listeriosis are combined into one category.

161

162 **2.3. Disability-adjusted life years**

163 DALY are the sum of years lived with disability (YLD), and the years of life lost due to premature death
164 caused by a disease (YLL) (Devleesschauwer et al., 2014). For each disease, we combined the estimated
165 incidence of each health outcome with disability weights (DW) previously collected (Salomon et al., 2015)
166 with duration of disease and life expectancy statistics as published by Denmark Statistics (available at
167 <http://www.statbank.dk/HISB8>) to estimate YLD. To estimate YLL, we combined the estimated mortality
168 with Standard Expected Years of Life Lost (WHO, 2018). Table 1 presents all input parameters for DALY
169 calculations. To estimate the associated uncertainty, we applied a stochastic model using the DALY
170 Calculator interface developed in R (<http://daly.cbra.be/>).

171 **2.4. Proportion foodborne**

172 To estimate the burden of disease that was due to consumption of contaminated foods, we applied the the
173 attributable foodborne proportions to the total disease burden, previously estimated Hald et al. (2016).
174 This study conducted a global expert elicitation, with expert panels representing different world regions
175 and groups of hazards, to estimate attribution proportions for foodborne, environmental, direct contact or
176 person-to-person transmission. Because estimates were not produced at a national level, we applied
177 estimates for the sub-region that includes Denmark (WHO sub-region EUR-A), which corresponds to
178 European countries with very low child and adult mortality
179 (https://www.who.int/choice/demography/mortality_strata/en/). For simplification purposes, we
180 multiplied point estimates without accounting for uncertainty range of neither of the parameters.

181 **3. Results**

182 **3.1. Incidence of disease**

183 In 2017, 4,231 cases of campylobacteriosis, 1,065 cases of salmonellosis, 354 cases of yersiniosis, 338 cases
184 of STEC infections and 58 cases of listeriosis were reported to the Danish public health surveillance system.

185 No cases of congenital toxoplasmosis were notified, and 298 outbreak-associated norovirus infections were
186 registered. When correcting for underreporting and underdiagnosis, we estimated that 185,060 cases of
187 norovirus (95% Uncertainty Interval (UI) 156,506-212,627), 58,141 cases of campylobacteriosis (95% (UI)
188 49,617– 71,781), 10,386 cases of salmonellosis (95% UI 8,792- 12,153), 5,019 cases of yersiniosis (95% UI
189 4,312- 5,839), 10,565 cases of STEC (95% UI 7,209-14,562) and 10 cases of CT (95% UI 8-12) occurred in
190 Denmark in 2017 (Table 2). The incidence of norovirus infection was significantly higher in children <5 years
191 of age (21,657 cases per 100,000 population) than in older age groups (between 1,500 and 3,200 in age
192 groups between 5 and 69, and 5,200 in >70 years of age) (see detailed results in Appendix 2.B). Among
193 bacterial infections, age and gender differences were larger for *Campylobacter*, with higher incidences in
194 middle aged men, and STEC, with children <5 more affected (results not shown). The total estimated
195 multiplier to correct for underreporting was lower for *Salmonella spp.* (7.7, 95% UI 3.7-18.1), and highest
196 for STEC (19.7; 95% CI 6.0-105.2), while for *Campylobacter* and *Y. enterocolitica* the estimations were
197 similar (11.0 (95% CI 6.0-23.8 and 10.9 (95% CI 6.0-23.3), respectively).

198 **3.2. Disability-adjusted life years**

199 *Campylobacter* caused the highest burden of disease (1,709 DALY), followed by *Salmonella* (492 DALY) and
200 norovirus (485 DALY) (Table 2). Listeriosis caused 196 DALY, the majority (95%) caused by years of life lost
201 due to mortality (186 YLL). Despite the low number of cases, congenital toxoplasmosis was responsible for
202 the loss of 165 years of healthy life.

203 The contribution of health outcomes to the total disease burden varied between pathogens. Diarrhoea was
204 responsible for between 30 and 52% of total DALY attributed to cases of infection by diarrhoeal agents; this
205 contribution was lowest for *Campylobacter* and highest for STEC (Figure 1). IBS was responsible for 26, 19
206 and 32% of total DALY for *Campylobacter*, *Salmonella* and *Yersinia*, respectively. Mortality (YLL) was
207 responsible for 30-40% of DALY for enteric pathogens, but explained a much higher proportion of the total
208 disease burden of invasive infections: 70% of CT and 92% of listeriosis.

209 Figure 2 plots the burden of disease at population level (total DALY) against the burden at individual level
210 (DALY per case, a measure for disease severity) for each pathogen. CT and listeriosis caused a high
211 individual-level burden. Norovirus has a low individual-level burden, and a moderate population-level
212 burden when compared to remaining hazards. *Campylobacter* caused the highest population burden, and a
213 moderate individual-level disease burden. None of the seven infections caused both high individual and
214 population-level burdens.

215 **3.3. Foodborne DALY**

216 When multiplying total mean DALY with the estimated foodborne attribution proportions for each, we
217 found that *Campylobacter* caused the highest foodborne burden (1,299 DALY), followed by *Salmonella* (374
218 DALY) and *Listeria* (196 DALY) (Table 2). Two pathogens (*Listeria* and *Yersinia*) were assumed to be 100%
219 foodborne. In contrast, with a foodborne attribution proportion of 18%, the foodborne burden of norovirus
220 infections was 86 DALY, which represented a marked decrease in the ranking of diseases (from third to
221 sixth).

222 **4. Discussion**

223 We ranked seven pathogens commonly transmitted through foods in Denmark on the basis of their public
224 health impact. Our estimates show that *Campylobacter* caused the highest foodborne disease burden,
225 leading to a total burden of 1,709 DALY, over three-fold higher than the second highest ranked pathogen
226 (*Salmonella*). With an estimated 76% of all cases attributed to consumption of contaminated foods,
227 *Campylobacter* still led the ranking when excluding DALY that are due to other routes of exposure, such as
228 environmental or person-to-person transmission. Focusing on the foodborne disease burden, *Salmonella*
229 ranked second, followed by *Listeria* and *Yersinia*. Foodborne CT was estimated to lead to the loss of around
230 100 years of healthy life, a burden that was born by a low number of cases in the population.

231 *Campylobacter* and *Salmonella* lead the ranking in both burden of disease and estimated incidence. All
232 cases of campylobacteriosis and salmonellosis had diarrhoea (the health outcome that defined an *incident*
233 *case*), but because diarrhoea is mostly mild and of short duration, it only explained approximately 35% of
234 the total burden for these infections. Sequelae such as IBS and reactive arthritis lead to a substantial
235 fraction of healthy life years lost, because they are long-lasting severe conditions. Even though norovirus
236 had the highest estimated incidence, the disease burden that can be attributed to contaminated foods was
237 low because severity and duration of disease are low, and because a small fraction of cases are caused by
238 ingestion of contaminated foods (human-to-human transmission playing a major role; (Hald et al., 2016)).
239 Some diseases with low incidence in the population, specifically listeriosis and congenital toxoplasmosis,
240 caused a substantial disease burden because health outcomes are very severe and/or mortality is high. Still,
241 the interpretation of such burden estimates differs: the larger contribution of the DALY of *Listeria* infections
242 is due to the years of life lost, though most deaths occur in older age groups. In contrast, while 70% of the
243 DALY of CT is due to mortality, deaths occur in newborns or unborn babies (i.e. neonatal or fetal losses);
244 this means that one single case will lead to a high number of years of life loss (equivalent to the life
245 expectancy). In addition, the remaining 30% of the burden is explained by few cases living with a disease
246 that leads to a marked reduction in quality of life and during the individual's whole life (e.g. compromised
247 vision or neurological disease).

248 Our estimates demonstrate a large and variable degree of underreporting of the different pathogens.
249 Notably, the pathogen with the largest degree of underreporting and underdiagnosis (i.e. with the largest
250 difference between reported and estimated total cases) was STEC, for which a multiplier of around 19 was
251 estimated (compared with 7 for *Salmonella*, 11 for *Campylobacter* and 11 for *Yersinia*). The larger degree of
252 underreporting is linked with the likelihood of samples being tested for these pathogens. Even though the
253 symptoms of mild, uncomplicated disease by all these three pathogens may be similar, physicians and
254 laboratories are more likely to request testing for *Salmonella* and *Campylobacter*, while other infections
255 often go undiagnosed in the population. For STEC, the likelihood of it being included in the panel of agents

for laboratory analysis has been increasing in Denmark in recent years (Espenhain, 2013), which should be reflected in a corresponding decrease in underreporting. Because the data available to estimate underreporting of foodborne pathogens was somewhat dated (Müller et al., 2012), our underreporting factor for STEC is likely to be an overestimate.

The data used to correct the reported incidence for under ascertainment, underreporting and underdiagnosis were collected in a survey of a representative sample of the population that evaluated incidence and care seeking behaviour of cases of gastroenteritis in Denmark (Müller et al., 2012). Other studies conducted in different countries estimated multipliers to correct for underreporting and underdiagnosis of FBDs using different methodologies (Haagsma et al., 2012; Kubota et al., 2011; Scallan et al., 2011; Tam et al., 2012). Estimates vary substantially, which may reflect differences in health seeking practices, public healthcare and surveillance systems, in data availability and study methodologies. Using EU-wide data and data on disease risk in Swedish travellers, Havelaar et al. estimated lower underreporting correction factors for *Campylobacter* and *Salmonella* infections in Denmark (4.1 and 4.4, respectively) (Havelaar et al., 2013). Our estimates were derived from a country-specific cross-sectional study designed to estimate national incidence of disease, and thus are more robust. Nevertheless, our surveillance-pyramid model has a number of limitations, mostly linked to model assumptions and uncertainties in underlying data. We made a number of assumptions, including that the degree of underreporting was the same for all age groups; participants of the population survey that reported duration of symptoms above 2 days had bacterial infections and thus their care-seeking behaviour data could be used to estimate underreporting of the enteric pathogens included in this study; the likelihood of having a stool sample submitted for laboratory analysis was higher for hospitalized patients; the probability of a positive laboratory test being reported to national public health surveillance was the same for all cases, regardless of severity. All these may have led to under- or overestimation of underreporting of enteric pathogens. Other limitations of the approach have been discussed by (Haagsma et al., 2012).

280 We identified health outcomes and sequelae of the seven pathogens through literature reviews. Other
281 burden of disease studies have included health outcomes that we have chosen not to include, e.g. Irritable
282 Bowel Disease (IBD) as a sequelae of *Salmonella* and *Campylobacter* infections (Havelaar et al., 2012).
283 Contesting previous evidence, Jess et al. (2011) showed that the estimated increased risk of IBD after
284 infection with *Salmonella* or *Campylobacter* may be due to detection bias related to repeated stool testing
285 in patients with unclear gastrointestinal symptoms rather than aetiology, suggesting that risk estimates
286 derived for this and other health outcomes may be overestimated (Jess et al., 2011). Other recent studies
287 have also excluded IBD from their health-outcome trees (Van Lier et al., 2016; de Noordhout et al., 2017)

288 As a composite health measure, DALY provides a comprehensive overview of the impact of diseases as it
289 encompasses the relative disabilities and mortality, sustained both during the acute phase and related to
290 the short and long-term complications of diseases (Cassini et al., 2016). The recent World Health
291 Organization's Global Burden of Foodborne Disease Project (FERG) estimated DALY for FBDs at global and
292 regional level (WHO, 2015). This initiative was crucial for raising awareness on the importance of foodborne
293 diseases globally and showed substantial variation in the overall burden and most important diseases in
294 different regions (Havelaar et al., 2015). It also showed that global and regional studies face substantial
295 methodological and data challenges, particularly because they need to secure data harmonization, which
296 often leads to a simplification of approaches and data. National burden of disease studies are crucial to
297 address these limitations and inform disease-prevention strategies at country level (Lake et al., 2015).

298 Norovirus was responsible for the highest disease incidence. Even if only one in every five cases is
299 estimated to be due to foodborne transmission, norovirus is recognized as one of the most important
300 causes of foodborne disease worldwide.

301 Reducing the burden of FBD depends upon informed risk management decisions and effective intervention
302 strategies that are focused on the most important food safety problems. By ranking FBDs at a national level
303 by accounting for underreporting of cases, total incidence, mortality and severity of diseases in the

304 population, we provide evidence on the priority causative agents. To be able to define and prioritize
305 interventions, the next step is to identify the most important sources and transmission routes (Pires et al.,
306 2009). Foodborne hazards are transmitted through a variety of foods and exposure pathways. While
307 naturally all hazards classified as *foodborne* can be transmitted through consumption of foods, many can
308 also be transmitted through other transmission routes (e.g. contaminated environment, such as water, or
309 direct contact with animals (Hald et al., 2016)). An integrated food safety approach to reduce the burden of
310 foodborne diseases requires identifying the most important causative agents, and the most important
311 causative sources of each disease (Havelaar et al., 2007a). Source attribution estimates have been used to
312 guide interventions to control salmonellosis in several countries, including Denmark (Wegener, 2010).
313 Ongoing and future efforts focusing on other pathogens are likely to lead to similar effects.

314 Burden of disease is a valid and robust method to compare the relative health impacts of diseases.
315 Combining with economic analysis allows for identification of the FBD with highest health and economic
316 impact in society (Christensen and Dejgård, 2017). We showed that *Campylobacter* caused the highest
317 public health impact among all FBDs in Denmark, even though it was surpassed by norovirus in terms of
318 total estimated cases. *Campylobacter* has been the most reported FBD in Denmark in the last decades
319 (Anonymous, 2018), and it is also the most reported FBD in Europe and globally. It has also been estimated
320 to cause the highest economic impact among FBD in Denmark when accounting for the cost of illness (i.e.
321 considering direct and indirect health care costs, and costs due to absence of work (Christensen and
322 Dejgård, 2017). These indicate that *Campylobacter* should be prioritized in mitigation efforts to reduce the
323 foodborne disease burden. However, such a prioritization should not be at the expense of extensive and
324 effective control programmes already in place for *Salmonella* and *Listeria monocytogenes*, which are
325 paramount to maintain low prevalence in the food chain. Broiler chickens have been recognized as the
326 most important source of *Campylobacter* infections in Denmark, and a number of initiatives to reduce
327 *Campylobacter* prevalence in broilers have been attempted (Boysen et al., 2013; Rosenquist et al., 2009).
328 However, these interventions have not had the desired effect in terms of reduction of the public health

329 burden of campylobacteriosis in the population. The lack of public health effect may be related to other
330 factors counterbalancing the effect of the implemented interventions, particularly with the role of other
331 sources of exposure. This highlights the need for identifying the relative contribution of all potential
332 sources of a pathogen in order to prioritize food safety intervention strategies. The calculations of benefits
333 and setting priorities in control and prevention of human disease are complicated by the cross-sectoral
334 nature of foodborne zoonosis management, with consequences appearing in public health but investments
335 needed in prevention in the food producing sector (Wilson, 2013). As an example, controlling *Salmonella* in
336 the pig sector includes high biosecurity in pig herds and sensible animal movement patterns between
337 farms. These interventions will not only reduce the risk of foodborne salmonellosis, but will have other
338 benefits for the pig sector, the animal health sector, food safety and food security, and may eventually be
339 more economically-beneficial for the food industry than e.g. controlling *Campylobacter* at poultry slaughter
340 houses, if non-direct benefits are included.

341 Since return for public money is not only measured in rational scientific and economic criteria, but includes
342 more intangible and unmeasurable benefits, our analysis may not provide the full answer in prioritization
343 prevention of foodborne diseases (Brookes, 2015). However, our study has provided clear scientific
344 evidence that *Campylobacter* results in the biggest foodborne disease burden in Denmark today, and that
345 efforts to prevent exposure to other pathogens through foods should be maintained or reinforced. Our
346 burden of disease estimates can be updated periodically and provide a steppingstone from which policy
347 analysis can be made to support decision-making.

348 **List of appendices**

349 Appendix 1. Parameters, calculations and data sources to estimate incidence of *Salmonella*, *Campylobacter*,
350 STEC and *Yersinia enterocolitica* infections.

351 Appendix 2. Methods to estimate incidence and mortality of norovirus.

352 Appendix 3. Parameters, calculations and data sources to estimate incidence of congenital toxoplasmosis
353 and health outcomes.

354 Appendix 4. Health outcome trees for *Campylobacter*, *Salmonella*, shiga-toxin producing *Escherichia coli*,
355 norovirus, *Yersinia enterocolitica*, *Listeria monocytogenes*, and *Toxoplasma gondii*.

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453 Table 1. Input parameters for the calculation of disability-adjusted life years of seven foodborne pathogens.

Health outcome	Duration (days)	Disability Weight				References
Diarrhoea Salmonella, Campylobacter and Yersinia	PERT(1.0, 3.0, 7.0)	Mild: 0.074 (0.049-0.104)	Moderate: 0.188 (0.125-0.264)	Severe: 0.247 (0.164-0.348)	Overall: PERT(0.0817, 0.05, 0.123)	Salomon et al. (2015)
Diarrhoea STEC	PERT(5.0, 7.0, 10.0)	Mild: 0.061 (0.036-0.093)	Moderate: 0.202 (0.133-0.299)	Severe: 0.281 (0.184-0.399)	Overall: PERT(0.0817, 0.05, 0.123)	Majowicz et al. (2014); Salomon et al. (2015)
Diarrhoea gastroenteritis	PERT(1.0, 3.0, 7.0)	0.072				Kirk et al., 2015
Reactive arthritis	222	Not visiting General practitioner (GP): 0.127	Visiting GP: 0.21	Hospitalized: 0.37	Mesle et al. (1998); Salomon et al. (2015)	
Irritable bowel syndrome (IBS)	1825	0.042				Haagsma et al. (2010)
Gulliaine Barré Syndrom (GBS) (Campylobacter)	Life-long	Mild: 0.090	Severe: 0.280	Residual symptoms: 0.160	Havelaar et al. (2000)	
Hemolytic uremic syndrome (HUS) (STEC)	PERT(14.0, 28.0, 42.0)	0.21				Kirk et al. (2015)

End-stage renal disease (STEC)	Life-long	PERT(0.397,0.573,0.749)	Havelaar et al. (2004)
Chorioretinitis (CT)	Life-long	PERT(0.019,0.031,0.049)	Salomon et al. (2015)
Intracranial calcification (CT)	Life-long	0.01	Havelaar et al. (2007)
Hydrocephalus (CT)	Life-long	PERT(0.16,0.36,0.56)	Havelaar et al. (2007)
Central nervous system abnormalities (CT)	Life-long	0.36	Havelaar et al. (2007)
Neonatal death (CT)	Life-long	1	Havelaar et al. (2007)

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463 Table 2. Reported and estimated total cases and deaths, years of life lived with disability (YLD), years of life
 464 lost (YLL) and disability-adjusted life years (DALY) caused by seven pathogens in Denmark, 2017.

Rank	Pathogen	Reported cases	Estimated cases	Estimated deaths	Years of life lived with disability (YLD)	Years of life lost (YLL)	Disability-adjusted life years (DALY)	DALY/100,000	Proportion foodborne (%)	Foodborne DALY
1	Cam pylo bact er	4,231	58,141 [49,617– 71,781]	56	1013 [969– 1,060]	696	1709 [1,665– 1,755]	29.7 [29.0 – 30.5]	76	1,299
2	Salm onell a	1,065	10,386 [8,792– 12,153]	28	210 [199– 222]	282	492 [481– 504]	8.6 [8.4 – 8.8]	76	374
3	Noro virus	-	185,060 [156,506– 212,627]	25.9 [20.4– 31.7]	128.6 (106.3– 153.4)	356.3 (280.4– 435.8)	485 [398–573.1]	8.6 [7.0– 10.1]	18	86
4	Liste riosis	58	58	12	14.2 [11.4–16.9]	186.4	196 [193.5– 198.5]	3.4 [3.4– 3.5]	100	196
5	Cong enita l toxoplas mosis	-	10 [8–12]	1 [1–2]	53 [32–77]	112 [81– 153]	165 [126–222]	-	61	100
6	Yersinia enterocol	354	5,019 [4,312– 5,839]	5	96 [89 – 110]	64	160 [152 – 174]	2.8 [2.7 – 3.0]	100	160

	ítica									
7	STEC	338	10,565 [7,209- 14,562]	1	30 [22 - 41]	33	63 [51 - 77]	1.1 [0.9 – 1.3]	60	38

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471 Figure 1. (A) Contribution of years lived with disability (YLD) and years of life lost (YLL) for the total disability
 472 adjusted life years (DALY), and (B) Contribution of health outcomes for YLD of seven foodborne pathogens
 473 in Denmark, 2017 (%).

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476 Figure 2. Plot of the burden of disease at the population level (total disability-adjusted life years, DALYs)
 477 and the burden of disease at individual level (DALY per case) for seven infectious pathogens commonly
 478 transmitted through foods in 2017, Denmark.

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482 Figure 2. Plot of the burden of disease at the population level (total disability-adjusted life years, DALYs)
483 and the burden of disease at individual level (DALY per case) for seven infectious pathogens commonly
484 transmitted through foods in 2017, Denmark.

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Appendix 1. Methods to estimate incidence of campylobacteriosis, salmonellosis, Shiga-toxin producing *Escherichia coli* infections and yersiniosis in Denmark

Appendix 1A. Non-pathogen specific parameters used to estimate the true incidence of Campylobacteriosis, salmonellosis, STEC infections and yersiniosis in Denmark.

Notation	Description	Distribution	Reference
Probability of seeking medical care			
PCSnb	Non-bloody diarrhea	$\sim \text{Beta}(14;26)^*$	Müller et al., (2012)
PCSb	Bloody diarrhea	$\sim \text{Beta}(4;3)^{**}$	Müller et al., (2012)
Probability of submitting a stool sample for analysis			
PSSnb	Non-bloody diarrhea	$\sim \text{Beta}(7;16)$	Müller et al., (2012)
PSSb	Bloody diarrhea	$\sim \text{Beta}(2;3)$	Müller et al., (2012)
PSSh	Hospitalized patients	$\sim \text{Pert}(0.3;0.7;0.9)$	Pires (2014)
Probability of reporting a positive laboratory result			
PRR	All cases	$\sim \text{Beta}(9;1)$	MiBa

*Data from cases that reported having diarrhea for 3 or more days.

** Data from patients that reported having bloody diarrhea, regardless of duration.

Appendix 1B. Pathogen-specific parameters used to estimate the true incidence of Campylobacteriosis, salmonellosis, STEC infections and yersiniosis in Denmark.

Notation	Description	Distribution	Reference
Campylobacter			
PTP	Probability of testing for Campylobacter in sample	$\sim \text{Beta}(9.9;0.1)$	S. Ethelberg, PC*
Sen	Sensitivity of laboratory analysis	$\sim \text{Triang}(0.7;0.76;0.82)$	(Haagsma et al., 2012)

Pbd	Proportion of bloody diarrhea in cases	$\sim \text{Beta}(4.74;21.3)$	(Haagsma et al., 2012)
Ph	Proportion of hospitalized cases	$\sim \text{Beta}(2,221;15,771)$	(Espenhain, 2013)
Salmonella			
PTP	Probability of testing for Salmonella in sample	$\sim \text{Beta}(9.9;0.1)$	S. Ethelberg, PC ^o
Sen	Sensitivity of laboratory analysis	$\sim \text{Triang}(0.85;0.88;0.91)$	Haagsma et al., (2012)
Pbd	Proportion of bloody diarrhea in cases	$\sim \text{Beta}(2.34;3.81)$	Haagsma et al., (2012)
Ph	Proportion of hospitalized cases	$\sim \text{Beta}(5,811;22,085)$	(Espenhain, 2013)
STEC			
PTP	Probability of testing for STEC in sample	$\sim \text{Beta}(4;6)$	S. Ethelberg, PC*
Sen	Sensitivity of laboratory analysis	$\sim \text{Beta}(7;3)$	Haagsma et al., (2012)
Pbd	Proportion of bloody diarrhea in cases	$\sim \text{Beta}(2.79;0.73)$	Haagsma et al., (2012)
Ph	Proportion of hospitalized cases	$\sim \text{Beta}(165;424)$	(Espenhain, 2013)
Yersinia e.			
PTP	Probability of testing for Yersinia in sample	$\sim \text{Beta}(9.9;0.1)$	S. Ethelberg, PC*
Sen	Sensitivity of laboratory analysis	$\sim \text{Triang}(0.7;0.76;0.88)$	E. Moller Nielsen PC*
Pbd	Proportion of bloody diarrhea in cases	$\sim \text{Beta}(18;75)$	(Schiellerup, Krogfelt, & Locht, 2008)
Ph	Proportion of hospitalized cases	$\sim \text{Beta}(369;3,555)$	(Helms, Simonsen, & Molbak, 2006)

PA1	Proportion of biotype 1A	S. Ethelberg PC*
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*PC: Personal communication

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Appendix 2.A. Methodology to estimate incidence and mortality of norovirus infections

Incidence

To estimate the total annual incidence of norovirus infections in Denmark, we adapted the method described by (Pires et al., 2015). First, we collected the estimated total annual cases of gastroenteritis episodes in Denmark, along with its 95% Uncertainty Interval (UI) from the Global Burden of Disease Data Tool (available at <http://ghdx.healthdata.org/gbd-results-tool>). We then estimated the **proportion of diarrheal cases due to norovirus** by extracting the etiological proportions of diarrheal cases for the pathogen from a systematic review of studies reporting stool sample isolation and detection from outpatients and community studies of patients with diarrhea (Ahmed et al., 2014). Assuming that the proportion of diarrhea patients that were positive for norovirus in studies conducted in European Union (EU) countries represent the norovirus etiology-proportion in Denmark, we restricted our analyses to studies conducted within the EU. To take into account differences in the relative importance of this agent for different **age groups**, we estimated two etiology proportions: one for children under five years of age, and one for the population aged five or more. Adjustment of these proportions to account for the fraction of norovirus carriers that do not manifest disease was based on data from case-control studies (Ahmed et al., 2014). To estimate this adjustment factor (AF), the number of norovirus positives and negatives samples among those with acute GE (AGE), as well as the number of norovirus positives and negatives among controls were abstracted, and a random effects model was used to estimate the pooled odds ratio translating the odds of AGE in a norovirus-positive case being caused by norovirus; using these estimates, the fraction of norovirus-positive samples that reflected norovirus illness (attributable fraction) was calculated. The AF was estimated based on data from case-control studies conducted in countries classified as developed. We then applied the adjusted norovirus etiology proportion to the total cases of diarrhea to estimate the annual number of norovirus diarrhea episodes in the country. In a last step, we applied a fraction of norovirus disease that manifests without diarrhea (i.e. a 'vomiting inflation factor', VIF) estimated based on data from the same literature review and supplemental information from volunteer challenge studies in order to include non-diarrheal norovirus (Ahmed et al., 2014). The VIF was estimated based on a subset of the systematic review by (Ahmed et al., 2014), supplemented with challenge studies. Table A2.1. describes all input parameters and data sources of the model.

Mortality

We applied the same approach to estimate the annual number of deaths caused by norovirus infections. In the absence of national diarrhea-mortality estimates, the total number of diarrhea deaths was retrieved from the WHO's Cause of Death Projections 2030 and 2015 for High Income Countries (as defined by the World Bank Regions) (<http://apps.who.int/gho/data/view.main.PROJRATEWBDCPHIINCOMEV?lang=en>; accessed 25th May 2016). Under the assumption that patients with severe norovirus infections that have been hospitalized serve as a proxy for norovirus-associated mortality, we estimated the proportion of diarrheal deaths attributable to norovirus by extracting the etiological proportions of diarrheal cases for the pathogen from a systematic review of studies reporting stool sample isolation and detection from **inpatient studies** of patients with diarrhea (Ahmed et al., 2014), using the same age groups as described above. We adjusted this etiology proportion to account for overestimation of norovirus disease due to asymptomatic carrying of the pathogen (AF), and estimated vomiting-only related deaths using the same method as described above.

Table A2.1. Input parameters and data sources for the estimation of total and foodborne incidence and mortality of norovirus in Denmark.

Input parameter	Description	Data source
Etiology proportion (Ep)	Proportion of diarrhea cases and deaths envelopes that is attributable to norovirus (%)	(Ahmed et al., 2014)
Total incidence of diarrhea	Estimated incidence of diarrhea in Denmark (cases per 100,000 inhabitants)	(Müller, Korsgaard, & Ethelberg, 2012)
Total mortality of diarrhea	Estimated mortality of diarrhea in high income countries (deaths per 100,000 inhabitants)	WHO, 2016
Adjustment factor (AF)	Fraction of AGE episodes with positive sample for norovirus that are caused by norovirus (%)	(Ahmed et al., 2014)
Vomiting inflating factor (VIF)	Fraction of norovirus disease that manifests with vomit but without diarrhea (%)	(Ahmed et al., 2014)

Appendix 2.B. Estimated burden of disease of norovirus infections

Table A2.2. Estimated total norovirus cases, deaths and disability adjusted life years (DALYs) in age groups in Denmark, 2017.

	Cases			Deaths			DALYs		
	Diarrhea	Vomiting	Total	Diarrhea	Vomiting	Total	Diarrhea	Vomiting	Total
0-4	55 146 (47 641-62 098)	9 474 (3 747-16 018)	64 620 (54 290-75 082)	0 (0-0)	0 (0-0)	0 (0-0)	61.4 (47.1-80.6)	3.4 (1.2-6.9)	64.9 (49.9-84.6)
5-14	17 212 (14 115-20 176)	4 007 (2 394-5 938)	21 218 (17 174-25 341)	0 (0-0)	0 (0-0)	0 (0-0)	9.8 (8-11.5)	1.5 (0.7-2.6)	11.2 (9.1-13.5)
15-49	32 120 (26 361-37 599)	7 478 (4 490-11 068)	39 598 (32 085-47 251)	0 (0-0)	0 (0-0)	0 (0-0)	18.3 (15-21.4)	2.7 (1.3-4.9)	21 (16.9-25.1)
50-69	18 853 (15 438-22 083)	4 389 (2 620-6 488)	23 242 (18 777-27 779)	1.8 (1.5-2.1)	0.3 (0.1-0.6)	2.1 (1.7-2.6)	61.6 (50.9-71.4)	9.9 (3.5-17.5)	71.4 (57.9-85.5)
70+	29 512 (24 216-34 637)	6 870 (4 088-10 134)	36 382 (29 462-43 331)	20.5 (16.6-24.1)	3.3 (0.8-6.4)	23.8 (18.7-29.1)	272.4 (222.2-318.6)	44.1 (12.9-82)	316.5 (251.6-383.4)
ALL	152 842 (130 907-173 247)	32 219 (21 123-45 238)	185 060 (156 506-212 627)	22.3 (18-26.2)	3.6 (0.9-7)	25.9 (20.4-31.7)	423.4 (354.9-488.2)	61.6 (23.3-107.7)	485 (398-573.1)

Table A2.3. Estimated foodborne norovirus cases, deaths and disability adjusted life years (DALYs) in age groups in Denmark, 2017.

	Cases			Deaths			DALYs		
	Diarrhea	Vomiting	Total	Diarrhea	Vomiting	Total	Diarrhea	Vomiting	Total
0-4	9 848 (8 391-11 310)	1 691 (667.1-2 879)	11 540 (9 592-13 582)	0 (0-0)	0 (0-0)	0 (0-0)	11 (8.3-14.5)	0.6 (0.2-1.2)	11.6 (8.8-15.2)
5-14	3 074 (2 489-3 655)	715.6 (426.9-1 065)	3 789 (3 033-4 585)	0 (0-0)	0 (0-0)	0 (0-0)	1.7 (1.4-2.1)	0.3 (0.1-0.5)	2 (1.6-2.4)
15-49	5 736 (4 637-6 798)	1 336 (793.8-1 991)	7 072 (5 636-8 530)	0 (0-0)	0 (0-0)	0 (0-0)	3.3 (2.6-3.9)	0.5 (0.2-0.9)	3.7 (3-4.5)
50-69	3 367 (2 723-4 002)	783.9 (466.7-1 170)	4 151 (3 319-5 023)	0.3 (0.3-0.4)	0.1 (0-0.1)	0.4 (0.3-0.5)	11 (9-12.9)	1.8 (0.6-3.1)	12.8 (10.2-15.4)
70+	5 270 (4 274-6 263)	1 227 (726.8-1 825)	6 497 (5 172-7 853)	3.7 (2.9-4.4)	0.6 (0.1-1.1)	4.2 (3.3-5.2)	48.6 (39.3-57.6)	7.9 (2.3-14.8)	56.5 (44.5-69.2)

ALL	27 295 (22 996-31 512)	5 754 (3 768-8 102)	33 049 (27 578-38 704)	4 (3.2-4.7)	0.6 (0.2-1.2)	4.6 (3.6-5.7)	75.6 (62.5-88.5)	11 (4.1-19.3)	86.6 (70.5-103.3)
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Table A2.4. Estimated foodborne years of life lost due to disability YLDs), years of life lost (YLL) and disability adjusted life years (DALYs) in age groups in Denmark, 2017.

	YLDs			YLLs			DALYs		
Age	Diarrhea	Vomiting	Total	Diarrhea	Vomiting	Total	Diarrhea	Vomiting	Total
0-4	11 (8.3-14.5)	0.6 (0.2-1.2)	11.6 (8.8-15.2)	0 (0-0)	0 (0-0)	0 (0-0)	11 (8.3-14.5)	0.6 (0.2-1.2)	11.6 (8.8-15.2)
5-14	1.7 (1.4-2.1)	0.3 (0.1-0.5)	2 (1.6-2.4)	0 (0-0)	0 (0-0)	0 (0-0)	1.7 (1.4-2.1)	0.3 (0.1-0.5)	2 (1.6-2.4)
15-49	3.3 (2.6-3.9)	0.5 (0.2-0.9)	3.7 (3-4.5)	0 (0-0)	0 (0-0)	0 (0-0)	3.3 (2.6-3.9)	0.5 (0.2-0.9)	3.7 (3-4.5)
50-69	1.9 (1.5-2.3)	0.3 (0.1-0.5)	2.2 (1.8-2.7)	9.1 (7.3-10.8)	1.5 (0.4-2.8)	10.6 (8.2-13)	11 (9-12.9)	1.8 (0.6-3.1)	12.8 (10.2-15.4)
70+	3 (2.4-3.6)	0.4 (0.2-0.8)	3.4 (2.7-4.2)	45.6 (36.5-54.3)	7.4 (1.9-14.3)	53.1 (41.3-65.5)	48.6 (39.3-57.6)	7.9 (2.3-14.8)	56.5 (44.5-69.2)
ALL	20.9 (17-25.2)	2.1 (1-3.6)	23 (18.7-27.8)	54.7 (43.8-65.1)	8.9 (2.2-17.2)	63.6 (49.5-78.6)	75.6 (62.5-88.5)	11 (4.1-19.3)	86.6 (70.5-103.3)

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Appendix 3. Model parameters and data sources to estimate incidence of congenital toxoplasmosis and health outcomes.

Notation	Description	Value/Distribution/Estimation	Reference
Lb	Number of live births in 2017	61397	Statistics Denmark, accessed on 18 April, 2016
Sb	Stillbirths after gestational week 22 in 2017	246	Statistics Denmark, accessed on 18 April, 2016
Sa	Number of reported spontaneous abortions occurring up to 22 weeks of gestation	10163	(Anonymous, 2016)
Tp	Total number of pregnancies in 2017	$Lb + Sb + Sa = 71805$	-
PSeroConv	Probability of seroconversion during pregnancy	Beta(140, 89735)	(Lebech et al., 1999)
SeroConv	Number of seroconverting pregnant women	$Tp * PSeroConv$	-
PToxoAb	Probability of fetal loss in seroconverting mothers	Beta(48, 2630)	(Derouin, Bultel, & Roze, n.d.)
FoetalLoss	Number of foetal losses due to CT >22 weeks of gestation	$Seroconv * PToxoAb * ((40 - 22)/40)$	-
IncCT	Annual incidence of CT diagnosed in the first year of life (cases per 10,000)	1.9	-
Sens	Sensitivity of the diagnostic approach	Uniform(0.7, 0.8)	(Lebech et al., 1999)
CasesCT	Total cases of postnatal CT	$DiagnCT / Sens$	-
ProbCS1	Probability of developing sequelae in the first year of life	Beta(13, 36)	(Röser, Nielsen, Petersen, Saugmann-Jensen, & Nørgaard-Pedersen, 2010; D R Schmidt et al., 2006; Dorte Remmer Schmidt,

			2005)
ProbCh1	Probability of developing chorioretinitis	Beta(8, 6)	(Röser et al., 2010; D R Schmidt et al., 2006; Dorte Remmer Schmidt, 2005)
ProbIC	Probability of developing intracranial calcifications	Beta(11, 3)	(Röser et al., 2010; D R Schmidt et al., 2006; Dorte Remmer Schmidt, 2005)
ProbHC	Probability of developing hydrocephalus	Beta(2, 12)	(Röser et al., 2010; D R Schmidt et al., 2006; Dorte Remmer Schmidt, 2005)
ProbCNS	Probability of developing CNS abnormalities	Beta(2, 12)	(Röser et al., 2010; D R Schmidt et al., 2006; Dorte Remmer Schmidt, 2005)
ProbND	Probability of neonatal death	Beta(1, 13)	(Havelaar, Kemmeren, & Kortbeek, 2007; Röser et al., 2010; D R Schmidt et al., 2006; Dorte Remmer Schmidt, 2005)
ProbCS2	Probability of being asymptomatic in the first year of life	1 - ProbCS1	-
ProbCh2	Probability of developing chorioretinitis later in life (1 to 12 years of age)	Beta(7, 18)	(Röser et al., 2010; D R Schmidt et al., 2006; Dorte Remmer Schmidt, 2005)

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Appendix 4. Health outcome and transition probabilities of seven foodborne pathogens

Figure A4.1. Health outcomes of *Campylobacter* infection

Figure A4.2. Health outcomes of *Salmonella* infection

Figure A4.3. Health outcomes of norovirus infection

Figure A4.4. Health outcomes of shiga-producing *Escherichia coli* (STEC) infection

Figure A4.5. Health outcomes of *Yersinia enterocolitica* infection

Figure A4.7. Health outcomes of *Listeria monocytogenes* infection (ECDC BCoDE toolkit, 2019)

Table A4.1. Health outcomes, transition probabilities and data sources of enteric pathogens.

Health-outcome	Campylobacter	Salmonella	Yersinia	STEC	Norovirus	Reference
Reactive arthritis (ReA)				NA	NA	(Havelaar et al., 2012; Schiellerup et al., 2008)
Probability of developing ReA	Beta(46;565)	Pert(0.023;0.08;0.	Beta(22;71)	NA	NA	

for patients with GE visiting a general practitioner		15)				
Probability of seeking care for a patient with ReA	Beta(10;37)			NA	NA	
Probability of hospitalization for ReA patients	Beta(2;45)			NA	NA	
Irritable Bowel Syndrome (IBS)	Pert (7.2; 8.8; 10.4)			NA	NA	(Haagsma et al., 2010)
Guillain-Barre syndrome (GBS)	Beta (60; 29,942)	NA	NA	NA	NA	(Havelaar et al., 2000)
Hemolytic uremic syndrome (HUS)	NA	NA	NA	Data	NA	Surveillance (SSI)
End-stage renal disease (ESRD)	NA	NA	NA	~Beta (24; 710)	NA	(Havelaar et al., 2004)
Mortality	Diarrhoea-associated mortality estimated as excess mortality risk based on odds ratios for Campylobacter (1.86), Salmonella (2.85) and Yersinia (2.1)			Beta (4; 2176)	See 2.1.	(Helms et al., 2003)
	GBS-associated: Pert(0.01; 0.02; 0.05);					(Havelaar et al., 2000)

Table A4.2. Health outcomes and transition probabilities of *Listeria monocytogenes* (from ECDC's BCoDe)

Health outcome	Transition probability	Source
Acquired listeriosis		
Symptomatic infection		(CDC, 2014)
(Uncomplicated)	Pert(0.12, 0.149, 0.182)	
(Complicated)	Pert(0.579, 0.655, 0.727)	
Fatal cases	Age-specific case fatality applied to severe cases (range 0-0.23)	TESSy 2009–2013
Permanent disability following meningitis	Uniform(0.011, 0.421)	(Aouaj et al., 2002; CDC, 2014)
Perinatal listeriosis		
Fatal cases	0.187	TESSy 2009–2013
Permanent disability due to meningitis	Uniform(0.011, 0.421)	(Aouaj et al., 2002)

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