

1 **Supporting Information file 2. – Disease burden of *Salmonella* spp. and *Campylobacter***  
 2 **spp. in the Netherlands using the pathogen- and incidence-based DALY approach**

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4 **I. Model input summary**

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6 In the following tables and figures we have summarized the model input parameters for  
 7 estimating the disease burden due to *Salmonella* spp. and associated sequelae, and due to  
 8 *Campylobacter* spp. and associated sequelae in the Netherlands (average 2005-2007).

9 Full details are available on request from the first author.

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11 **Table S2.1 - Reported laboratory-confirmed cases for *Campylobacter* spp. and**  
 12 ***Salmonella* spp. in the Netherlands (average of the years 2005-2007)**

Pathogen	Reported laboratory-confirmed cases	
	Male	Female
<i>Salmonella</i> spp.	698.7 <sup>a,b</sup>	728.7 <sup>a,b</sup>
<i>Campylobacter</i> spp.	1,855.7 <sup>a,b</sup>	1,670.7 <sup>a,b</sup>
Source:	Laboratory surveillance [1] (personal communication by Wilfrid van Pelt; National Institute of Public Health and the Environment; June 2011)	

13 a) The laboratory surveillance network is composed of public laboratories that do cover in the case of  
 14 *Salmonella* spp. about 64% of the Dutch population, and for *Campylobacter* spp. coverage is 52%.

15 Correction is included in the multiplication factors.

16 b) Cases are stratified by age, into the age-classes: 0; 1-4; 5-9; 10-14; 15-19; 20-24; 25-29; 30-34;  
 17 35-39; 40-44; 45-49; 50-54; 55-59; 60-64; 65-69; 70-74; 75-80; 80-84 and ≥ 85 years.

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19 **Table S2.2 -Pathogen-specific multiplication factors for the Netherlands**

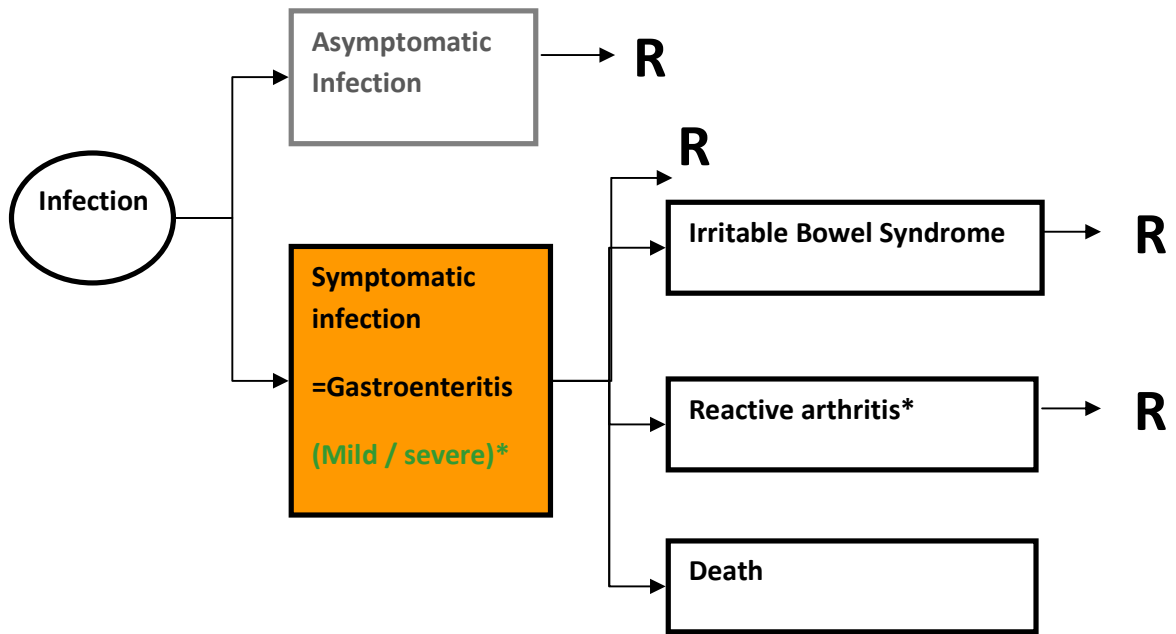
Pathogen	Multiplication factors (MF) <sup>a, b</sup>	Source
	<i>Most likely (range)</i>	
<i>Salmonella</i> spp.	19.8 (4.4 - 64.8)	[2]
<i>Campylobacter</i> spp.	18.85 (7.4 – 47.4)	[2]

20 a) MFs correct for underestimation (under-ascertainment and under-estimation). Additionally, the  
 21 current MFs also take into account that the coverage of the lab-confirmed cases is less than 100%  
 22 (see Table S2.1).

23 b) MFs should by definition be pathogen-, country-, age- and eventually also gender-specific (see  
 24 Supporting Information file 1). But published MFs in the literature fitting Dutch laboratory-  
 25 confirmed *Campylobacter* and *Salmonella* infections were only pathogen- and country-specific  
 26 (for details see Gibbons et al. [3]). In the current illustration, we therefore applied for each  
 27 pathogen separately the same MF to all age- and sex-classes.

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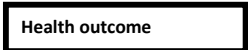
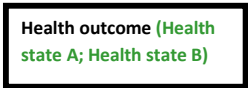

29 **Figure S2.1 Outcome tree for *Salmonella* spp.**



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31 \*Given the systematic uncertainty, we assumed that only “severe” Salmonella gastroenteritis (GE) cases  
 32 are at risk to develop Reactive arthritis (ReA). This assumption was modified in a scenario analysis where  
 33 we assumed that all Salmonella GE cases are at risk to develop ReA.

**Legend used in the outcome tree:**

	= Event: Infection with pathogen
	= Health outcome <b>without</b> morbidity/mortality (i.e. asymptomatic infection)
	= Health outcome resulting in morbidity/mortality
	= Health outcome resulting in morbidity/mortality; <b>in green and between brackets the different health states of the health outcome</b>
	= <b>Orange filled box indicates where the model/simulation starts, using estimated annual incidences (e.g. notified cases x multiplication factor)</b>
R	= Recovery from health outcome

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36 **Table S2.3 Percentages used in the *Salmonella* spp. outcome tree<sup>a</sup>**

Health outcome	Distribution of health states in health outcome <i>Most likely (range)</i>	Risk to develop that health outcome <i>Most likely (range)</i>	Sources/ Assumption
Gastroenteritis (GE)	6.24% (5.35% -7.61%) are severe GE cases	-	Laboratory-confirmed cases are a proxy for severe cases. Calculated from simulated incident cases and laboratory-confirmed salmonellosis cases in the Netherlands.
Death		0.1% (0.05%-0.3%) <sup>b</sup>	[4-6]
Irritable Bowel Syndrome (IBS)		8.8% (7.2% - 10.4%)	[7]
Reactive arthritis (ReA)		8% (2.3% - 15.0%) <sup>c</sup>	[5, 8]

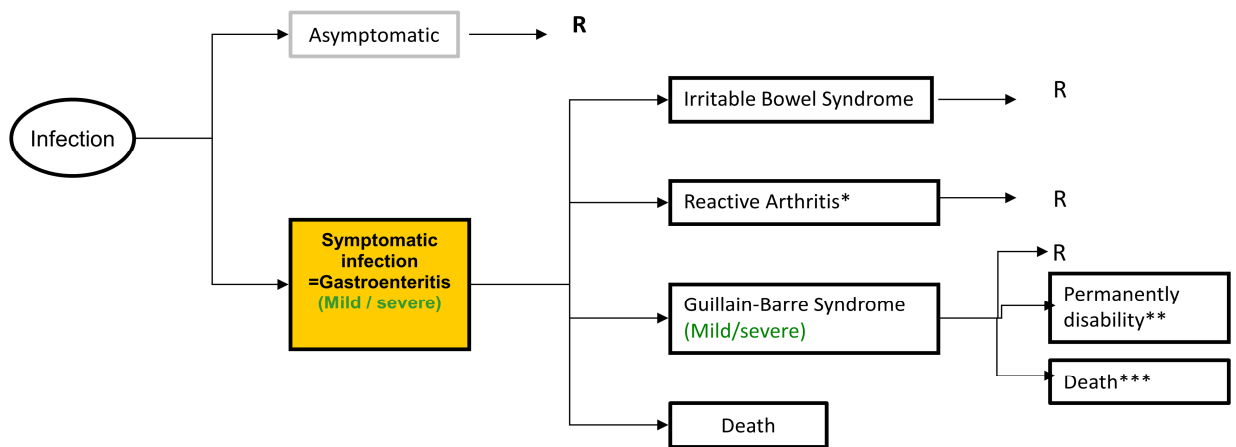
37 a) See Figure S2.1 for the *Salmonella* spp. outcome tree.

38 b) See Figure S2.3 for the distribution over age-classes

39 c) Only severe GE cases are at risk to develop ReA.

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41 **Figure S2.2 Outcome tree for *Campylobacter* spp.**




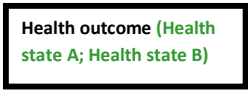



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43 \* Only severe gastroenteritis (GE) cases are at risk to develop reactive arthritis (ReA). This assumption was  
 44 modified in a scenario analysis where we assumed that all *Campylobacter* GE cases are at risk to develop  
 45 ReA. \*\* Non-fatal severe Guillain-Barré Syndrome (GBS) cases may develop permanent disability; \*\*\*  
 46 The majority of fatal GBS cases are severe GBS cases, for reasons of simplicity we therefore assumed that  
 47 only severe GBS cases may be fatal.

48

**Legend used in the outcome tree:**

 Infection	= Event: Infection with pathogen
 Health outcome	= Health outcome <b>without</b> morbidity/mortality (i.e. asymptomatic infection)
 Health outcome	= Health outcome resulting in morbidity/mortality
 Health outcome (Health state A; Health state B)	= Health outcome resulting in morbidity/mortality; <b>in green and between brackets the different health states of the health outcome</b>
 Health outcome	= <b>Orange filled box indicates where the model/simulation starts, using estimated annual incidences (e.g. notified cases x multiplication factor)</b>
R	= Recovery from health outcome

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51 **Table S2.4 Percentages used in the *Campylobacter* spp. outcome tree<sup>a</sup>**

Health outcome	Distribution of health states in health outcome <i>Most likely (range)</i>	Risk to develop that health outcome <i>Most likely (range)</i>	Sources/ Assumption
Gastroenteritis (GE)	9.6% (4.0% - 22.6%) are severe GE cases	-	Laboratory-confirmed cases are a proxy for severe cases. Calculated from simulated number of incident cases [9] and laboratory-confirmed campylobacterosis cases in the Netherlands.
Death		0.03% (0.001% - 0.05%) <sup>b</sup>	[4, 9]
Irritable Bowel Syndrome (IBS)		8.8% (7.2% - 10.4%)	[7]
Reactive arthritis (ReA)		7.9% (2.4% - 8.0%) <sup>c</sup>	[10-12]
Guillain-Barré Syndrome (GBS)	17% are mild GBS cases <sup>d</sup> ; 83% are severe GBS cases <sup>d</sup>	0.02%-0.09% <sup>d</sup>	[13-16]
GBS fatal		4.1% (2.4% - 6.0%) <sup>d,e</sup>	[15-18]
GBS permanent disability		100% of non-fatal severe GBS cases	[15, 16]

52 a) See Figure S2.2 for the *Campylobacter* spp. outcome tree.

53 b) See Figure S2.3 for the distribution over age-classes

54 c) Only severe GE cases are at risk to develop ReA.

55 d) See Figure S2.4 for the distribution over age-classes

56 e) In about 3.4 % (2% -5%) of all GBS cases is the disease fatal [15, 18]. The majority of fatal GBS cases are hereby severe GBS cases. For simplification  
57 reasons we therefore assumed that death due to GBS occurs only in severe cases, resulting in 4.1% (2.4% - 6.0%).

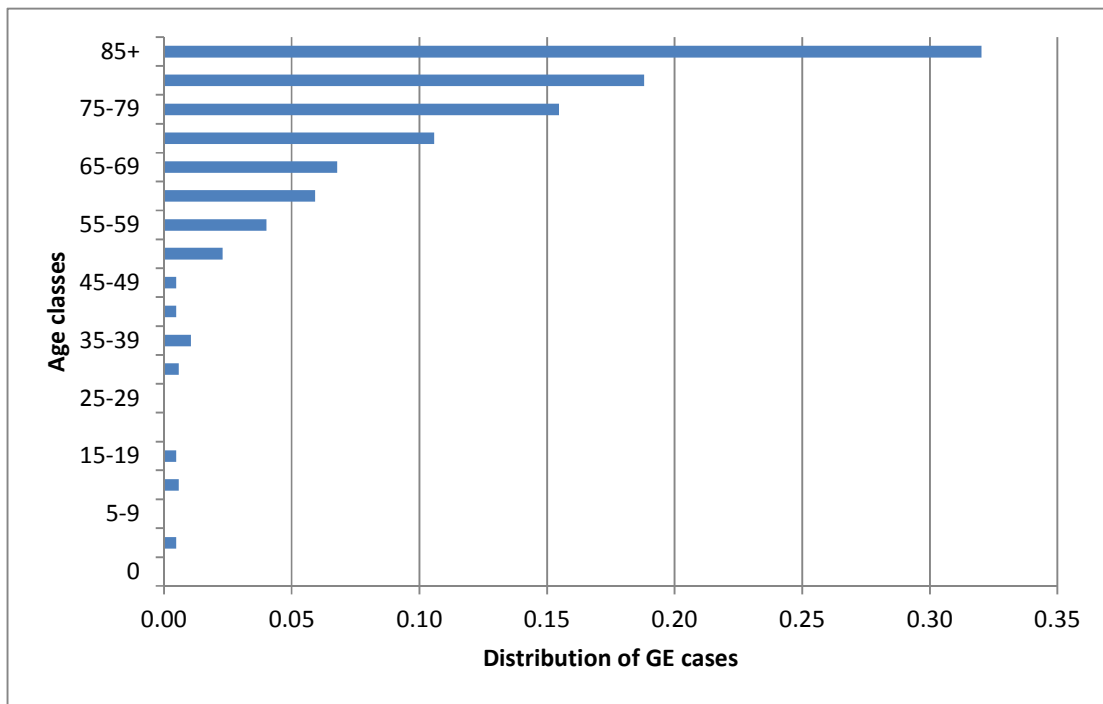
58 **Table S2.5 Disability weights and duration**

Health outcome (health state)	Disability weight (w)		Duration	
	w	Source	in years	Source
GE (health outcome)	0.105	[19]	0.017	[5]
IBS	0.042	[20]	5	[7]
ReA	0.059	Calculated based on Haagsma <i>et al.</i> [20] and Hannu <i>et al.</i> [10]	1 <sup>a</sup>	[20]
GBS (mild cases); clinical phase	0.090	[21]	1 <sup>a</sup>	[21]
GBS (severe cases); clinical phase	0.280	[21]	1 <sup>a</sup>	[21]
GBS (severe cases) permanent disability	0.160	[21]	Remaining Life Expectancy	[21]

59 a) Duration based on an annual profile disability weight

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61 **Figure S2.3 Assumed age-distribution of fatal GE cases (in percentage)**



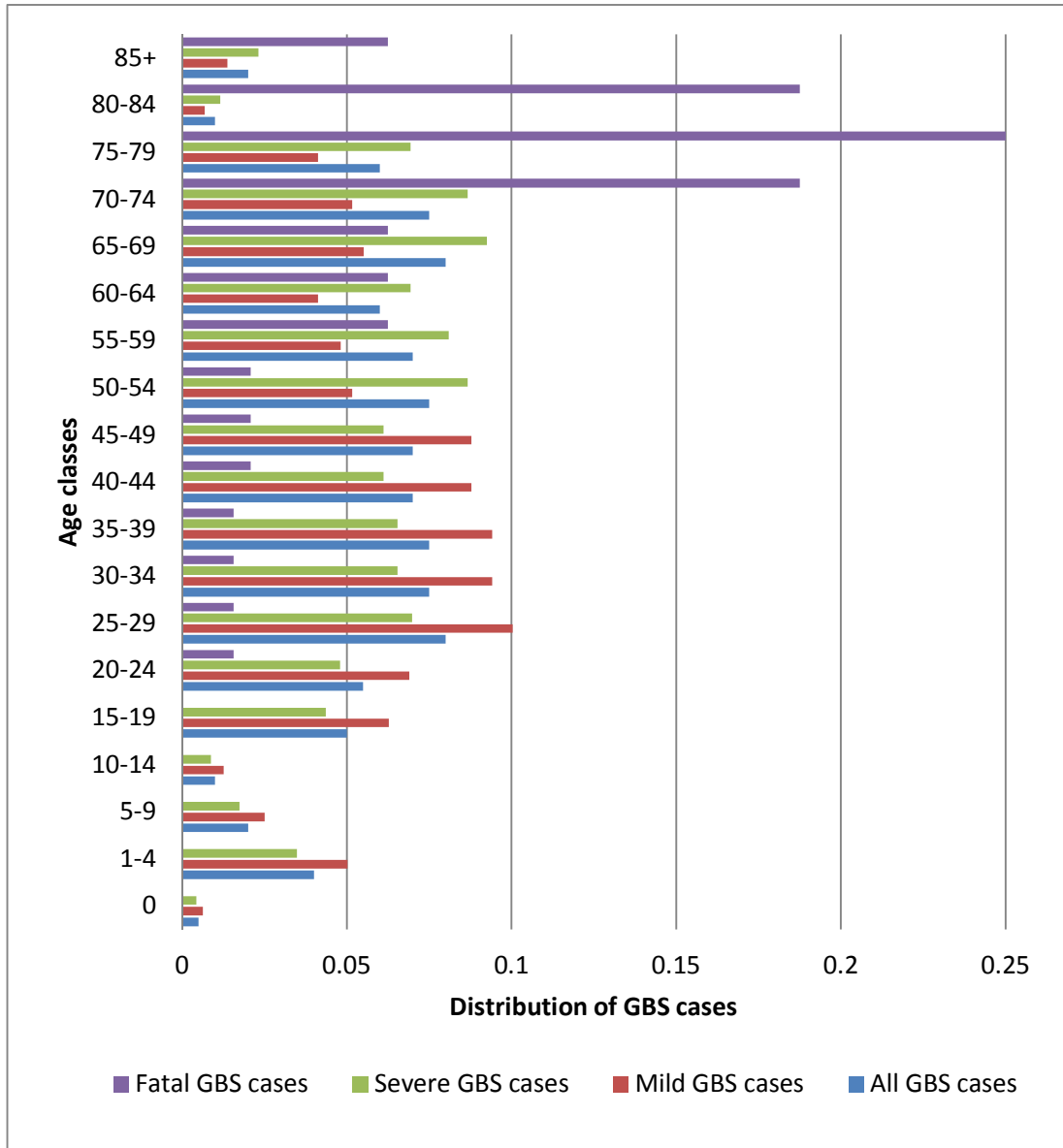
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63 Source: Based on all reported fatal Salmonellosis cases in Estonia, Germany and the Netherlands for the  
64 years 2005-2007

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66 **Figure S2.4 Assumed age-distribution of GBS cases (in percentage), as derived from**  
 67 **[15,16].**



68  
 69 Note: Fatal GBS cases are mostly severe GBS cases. For simplification reason we therefore assumed that  
 70 only severe GBS cases are fatal.

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 72  
 73

74 **II. Results**

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76 In the following tables and figures we have summarized some of the estimated results for  
77 *Salmonella* spp. and associated sequelae, and for *Campylobacter* spp and associated  
78 sequelae in the Netherlands (average 2005-2007). The results show undiscounted DALYs  
79 with uniform age-weights.

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81 **Table S2.6: The disease burden of *Salmonella* spp and associated sequelae in the Netherlands – Summary results, average and 95%**

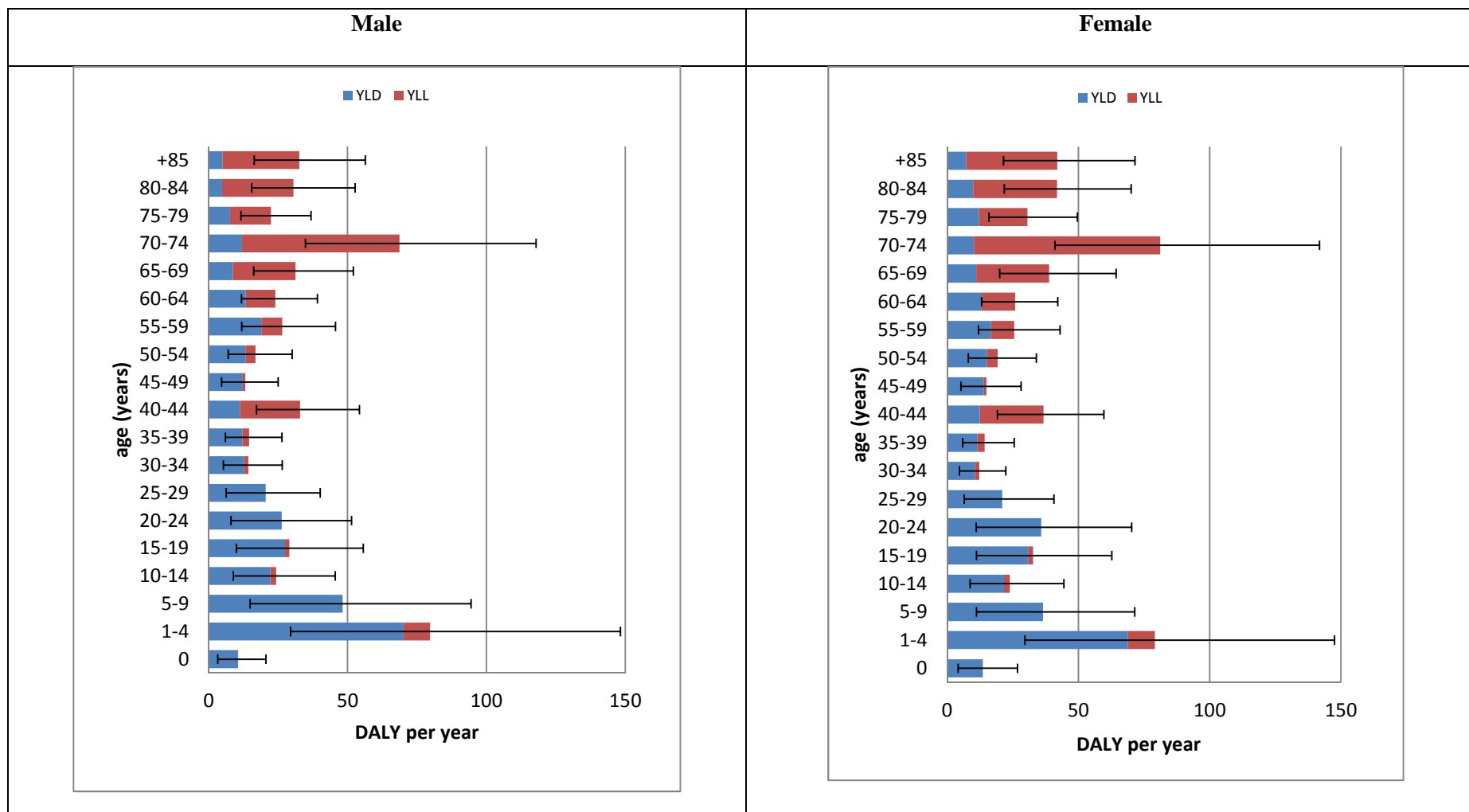
82 **CI in brackets and italic.**

Health outcome(s)	Cases	YLD per year	YLL per year	DALY per year	DALY per case <i>Symptomatic</i>	DALY per 100,000
<b>ACUTE ILLNESS</b>						
<b>GE (sum)</b>		<b>66</b>	<b>462</b>	<b>529</b>	<b>0.015</b>	<b>3.2</b>
		<i>(55-78)</i>	<i>(261-728)</i>	<i>(325-798)</i>	<i>(0.010-0.022)</i>	<i>(1.99-4.89)</i>
Cases	35,300	66		<b>66</b>		
	<i>(29,250-41,680)</i>	<i>(55-78)</i>		<i>(55-78)</i>		
Death	44		462	<b>462</b>		
	<i>(25-70)</i>		<i>(261-728)</i>	<i>(261-728)</i>		
<b>SEQUELAE</b>						
<b>IBS (sum)</b>		<b>652</b>	<b>0</b>	<b>652</b>	<b>0.018</b>	<b>4.0</b>
		<i>(529-790)</i>		<i>(529-790)</i>	<i>(0.017-0.020)</i>	<i>(3.2-4.8)</i>
Cases	3,110	652		<b>652</b>		
	<i>(2,520-3,760)</i>	<i>(529-790)</i>		<i>(529-790)</i>		
<b>ReA (sum)</b>		<b>11</b>	<b>0</b>	<b>11</b>	<b>0.0003</b>	<b>0.07</b>
		<i>(6-16)</i>		<i>(6-16)</i>	<i>(0.0002-0.0004)</i>	<i>(0.04-0.09)</i>
Cases	183	11		<b>11</b>		
	<i>(107-273)</i>	<i>(6-16)</i>		<i>(6-16)</i>		
<b>Sequelae (sum)</b>		<b>663</b>	<b>0</b>	<b>663</b>	<b>0.019</b>	<b>4.1</b>
		<i>(538-803)</i>		<i>(538-803)</i>	<i>(0.017-0.021)</i>	<i>(3.3-4.9)</i>
<b>ALL health outcomes</b>		<b>730</b>	<b>462</b>	<b>1,192</b>	<b>0.034</b>	<b>7.3</b>
		<i>(594-879)</i>	<i>(261-728)</i>	<i>(913-1,530)</i>	<i>(0.028-0.041)</i>	<i>(5.6-9.4)</i>

83 Note: Total infected cases are not reported as asymptomatic salmonella cases were not explicitly modelled. Reason for not considering asymptomatic infections was that  
84 they do not contribute to the disease burden.

85

86 **Figure S2.5 The average disease burden (DALY) of *Salmonella* spp. and associated sequelae in the Netherlands per age-group and**  
 87 **gender. The 95% uncertainty range is shown using error bars.**



89 **Table S2.7: The disease burden of *Campylobacter* spp. and associated sequelae in the Netherlands – Summary results, average and 95%**

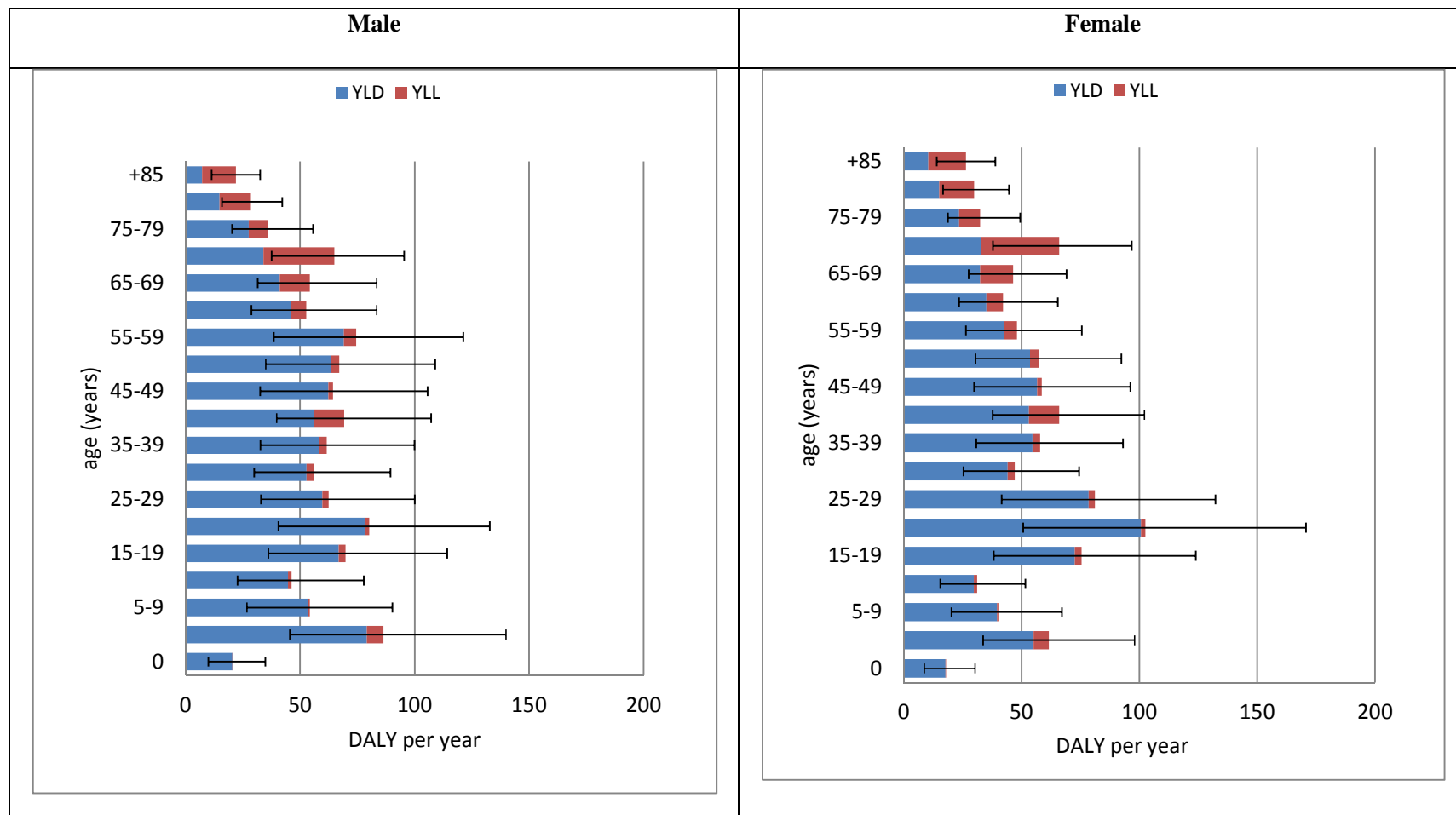
90 **CI in brackets and italic**

Health outcome(s)	Cases	YLD per year	YLL per year	DALY per year	DALY per case <i>Symptomatic</i>	DALY per 100,000
<b>ACUTE ILLNESS</b>						
<b>GE (sum)</b>		<b>144</b>	<b>227</b>	<b>371</b>	<b>0.005</b>	<b>2.3</b>
		<i>(127-160)</i>	<i>(122-328)</i>	<i>(262-479)</i>	<i>(0.003-0.006)</i>	<i>(1.6-2.9)</i>
Cases	76,500	144		<b>144</b>		
	<i>(67,800-85,550)</i>	<i>(127-160)</i>		<i>(127-160)</i>		
Death	22		227	<b>227</b>		
	<i>(12-31)</i>		<i>(122-328)</i>	<i>(122-328)</i>		
<b>SEQUELAE</b>						
<b>IBS (sum)</b>		<b>1,414</b>	<b>0</b>	<b>1,414</b>	<b>0.018</b>	<b>8,7</b>
		<i>(1,214-1,635)</i>		<i>(1,214-1,635)</i>	<i>(0.017-0.020)</i>	<i>(7.4-10.0)</i>
Cases	6,700	1,414		<b>1,414</b>		

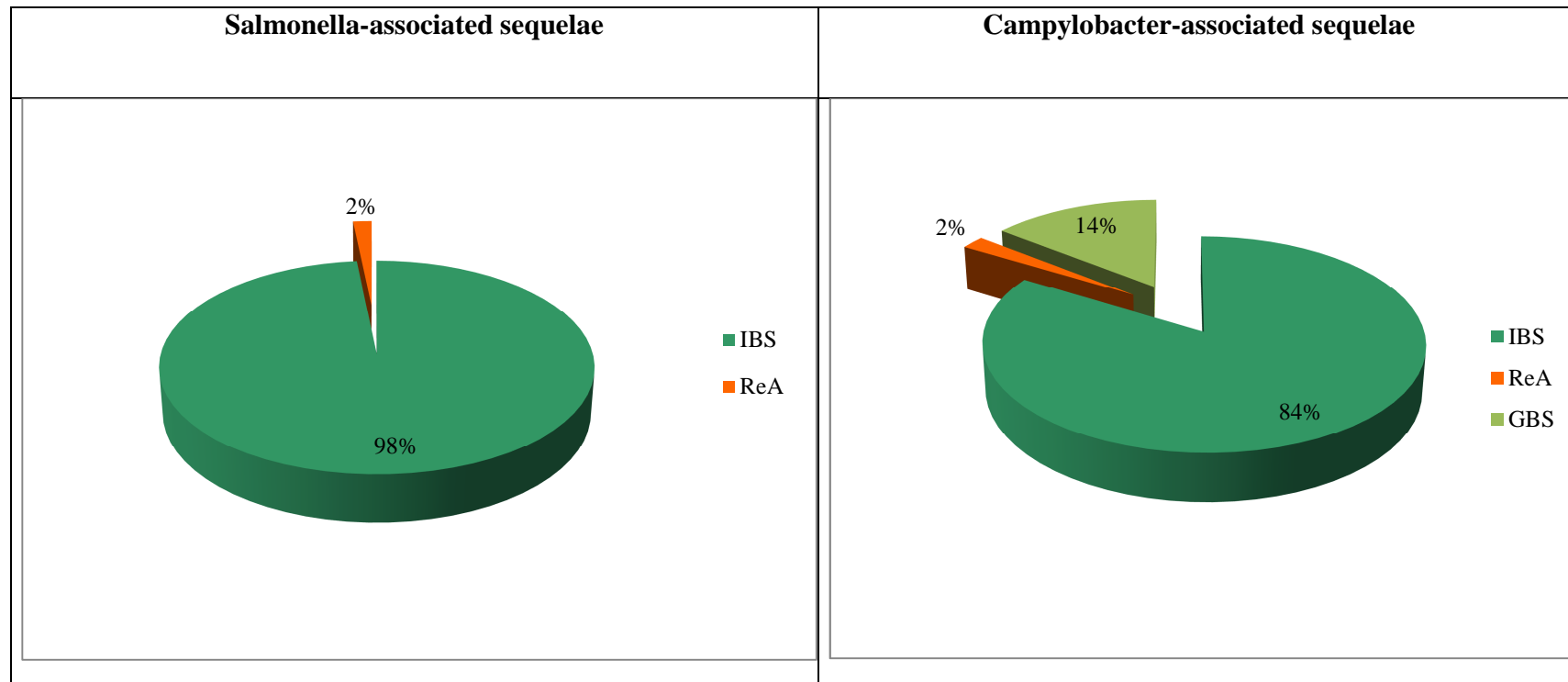
	(5,800-7,800)	(1,214-1,635)		(1,214-1,635)		
<b>ReA (sum)</b>		<b>34</b>	<b>0</b>	<b>34</b>	<b>0.0004</b>	<b>0.2</b>
		(20-52)		(20-52)	(0.0003-0.0007)	(0.1-0.3)
Cases	581	34		<b>34</b>		
	(335-889)	(20-52)		(20-52)		
<b>GBS (sum)</b>		<b>191</b>	<b>50</b>	<b>242</b>	<b>0.003</b>	<b>1.5</b>
		(76-314)	(18-91)	(94-398)	(0.001-0.005)	(0.6-2.4)
Cases	42	191		<b>191</b>		
	(18-67)	(76-314)		(76-314)		
Death	1.4		50	<b>50</b>		
	(0.5-2.6)		(18-91)	(18-91)		
<b>Sequelae (sum)</b>		<b>1,640</b>	<b>50</b>	<b>1,690</b>	<b>0.022</b>	<b>10.3</b>
		(1,379-1,920)	(18-91)	(1,406-1,994)	(0.019-0.025)	(8.6-12.2)
		<b>1,783</b>	<b>277</b>	<b>2,061</b>	<b>0.027</b>	<b>12.6</b>
<b>ALL Health Outcomes</b>		(1,512-2,075)	(165-387)	(1,737-2,406)	(0.024-0.030)	(10.6-14.7)

91 Note: Total infected cases are not reported as asymptomatic campylobacteria cases were not explicitly modelled. Reason for not considering asymptomatic infections was that  
92 they do not contribute to the disease burden.

93 **Figure S2.6 The average disease burden (DALY) of *Campylobacter* spp. in the Netherlands per age-group and gender. The**  
 94 **95% uncertainty range is shown using error bars.**



95 **Figure S2.7 - The distribution of undiscounted average burden of Salmonella-associated sequelae and Campylobacter-**  
96 **associated sequelae, respectively, over the associated sequelae.**





97 **References**

98

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