

A ready-to-use dose-response model of *Campylobacter jejuni* implemented in the FSKX-standard

Esther M. Sundermann[‡], Maarten Nauta[§], Arno Swart[‡]

[‡] German Federal Institute for Risk Assessment, Berlin, Germany

[§] Technical University of Denmark, National Food Institute (DTU Food), Kemitorget, Denmark

| National Institute for Public Health and the Environment, Bilthoven, Netherlands

Corresponding author: Esther M. Sundermann (esther-maria.sundermann@bfr.bund.de), Maarten Nauta (mjna@ssi.dk), Arno Swart (arno.swart@rivm.nl)

Academic editor: Matthias Filter

Abstract

Dose-response models are an important part of quantitative microbiological risk assessments. In this paper, we present a transparent and ready-to-use version of a published dose-response model that estimates the probability of infection and illness after the consumption of a meal that is contaminated with the pathogen *Campylobacter jejuni*. To this end, model and metadata are implemented in the fsqx-standard. The model parameter values are based on data from a set of different studies on the infectivity and pathogenicity of *Campylobacter jejuni*. Both, challenge studies and outbreaks are considered, users can decide which of these is most suitable for their purpose. We present examples of results for typical ingested doses and demonstrate the utility of our ready-to-use model re-implementation by supplying an executable model embedded in this manuscript.

Keywords

exchange format, mathematical modelling, infection probability, illness probability, campylobacteriosis, food safety, executable document

Introduction

Thermotolerant *Campylobacter* is the most commonly reported zoonotic disease in the EU (European Food Safety Authority and European Centre for Disease Prevention Control 2019) and a leading cause of zoonotic enteric infections worldwide (World Health Organization 2013). To support the control of *Campylobacter*, quantitative microbiological

risk assessments (QMRAs) have been performed in various countries as well as in an international context (World Health Organization and Food Agriculture Organization of the United Nations 2009, Nauta et al. 2009, EFSA Panel on Biological Hazards 2011, Chapman et al. 2016, EFSA Panel on Biological Hazards et al. 2020). Several foods are indicated as potential sources of *Campylobacter* (Silva et al. 2011), but QMRAs have predominantly focused on what is generally considered the main route of transmission: the broiler meat production chain and human exposure associated with the consumption of broiler meat. Published models vary extensively in the way the exposure assessment is performed (Nauta et al. 2009, Chapman et al. 2016), but, until recently, the vast majority of QMRAs have applied a dose-response model (DRM) based on the challenge study performed by Black et al. (1988) (Teunis and Havelaar 2000, Teunis et al. 2005). This challenge study involved only a small group of healthy male volunteers who were exposed to a specific *Campylobacter* strain. However, it has for a long time been considered the best basis for *Campylobacter* dose-response modelling in QMRA. It has been referred to as the "classic" DRM (EFSA Panel on Biological Hazards 2011).

After an earlier reconsideration of the "classic" DRM (Teunis et al. 2005), Teunis et al. (2018) published an analysis including newly published dose-response data, including various challenge studies on humans and primates as well as four studies based on outbreaks associated with the consumption of raw milk. The DRM applied to these data suggested a different dose-response curve and higher infectivity of *Campylobacter*. This led to the statement of Teunis et al. (2018) that the "classic" DRM has been "an unfortunate choice" as the default DRM used for *Campylobacter*. Teunis et al. (2018) have described their analyses in detail and provide the software code for their model. However, application of their model in a QMRA of *Campylobacter* remains challenging, as a ready-to-use model is not provided and developing one requires considerable expertise in modelling and programming.

In this paper, we provide the DRM developed by Teunis et al. (2018) in the Food Safety Knowledge Exchange (FSKX) Format, which is a standardised exchange format for mathematical models and simulation results. This open format contains model script, visualisation script, and simulation settings (de Alba Aparicio et al. 2018) as well as a harmonised way to annotate the model by providing a metadata schema that uses, whenever possible, controlled vocabularies (Haberbeck et al. 2018). Thus, it facilitates re-usability, the application of the model in a QMRA, and an efficient knowledge exchange. The research project "Risk Assessment Modelling and Knowledge Integration Platforms (RAKIP)" initiated the development of the FSKX format and included the metadata schema to annotate knowledge. The RAKIP community, with partners from the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), the Technical University of Denmark, National Food Institute (DTU Food), and the German Federal Institute for Risk Assessment (BfR), continues to improve and extend the community-driven metadata schema (Haberbeck et al. 2018, German Federal Institute for Risk Assessment 2019). We illustrate how the user can explore the performance of the *Campylobacter* DRM published by Teunis et al. (2018) and apply them to user-defined inputs.

Model metadata

The model metadata are a schema to annotate the model in a harmonised way. It is part of the FSKX-file (see Suppl. material 1 for the FSKX-file). For details about the metadata schema and the used definitions, see Haberbeck et al. (2018) and <https://foodrisklabs.bfr.bund.de/rakip-harmonization-resources/> (the used metadata schema version is 1.04).

General metadata

Source: PUBLISHED SCIENTIFIC STUDIES

Identifier: CampylobacterDRTeunis2018

Rights: Creative Commons Attribution 4.0 (CC BY 4.0)

Availability: Open access

Language: English

Software: FSK-Lab

Language Written In: R

Objective: The objective of the model is to estimate the probability of infection and illness after ingestion of a dose of *Campylobacter jejuni*.

Product/matrix

Name: Any product

Description: Any product

Hazard

Hazard type: Microorganisms

Hazard name: *Campylobacter jejuni*

Hazard unit: Colony forming unit (CFU)

Adverse Effect: Asymptomatic or symptomatic infection with *Campylobacter jejuni* (campylobacteriosis)

Population

Name: General population or outbreaks

Target Population: Two target populations are defined: the general population and groups involved in a food-borne outbreak.

Scope

The dose-response model provides the probability of infection and illness as a function of the exposure, i.e., the ingested dose of *Campylobacter jejuni*. Model parameters are based on datasets from human and primate challenge studies and outbreaks.

Data background

Study Title: Acute illness from *Campylobacter jejuni* may require high doses while infection occurs at low doses.

Study Description: Data from a set of different studies on the infectivity and pathogenicity of *Campylobacter jejuni* were analysed with a multilevel model. This allowed us to include effects of host species (non-human primates and humans), different strains of the pathogen, and differentiation between outbreak and non-outbreak settings. To this end, three groups of studies were included: (1) four controlled human infection studies (challenge studies) involving three distinct strains (81-176, CG8421, and A3249), (2) four studies on outbreaks of unknown strains and, in one case, strain 81-176, and (3) five challenge studies in three species of non-human primates of strains 81-176, 78-37, and V212X. All studies recorded both asymptomatic infection and illness as endpoints. The data are used to parameterise the dose-response model; see Section "Material and methods" and Teunis et al. (2018) for details.

Materials and methods

Model description

Dose-response models for infection are usually based on a limited number of biologically motivated axioms (World Health Organization and Food and Agriculture Organization of the United Nations 2003). The basic starting point is that each organism has a (usually low) single-hit probability r of initiating infection. Secondly, each organism acts independently of the others (no synergism). Putting these axioms together yields a simple non-probabilistic model for the probability of infection (P_{inf}) given exposure to n organisms:

$$P_{inf} = 1 - (1 - r)^n$$

(Equ. 1)

With this expression as a basis, several extensions can be made by assuming variability distributions for r (heterogeneity in infectivity or susceptibility) or n (heterogeneity in the doses received). In Teunis et al. (2018), the dose n is assumed to be Poisson distributed with parameter D , the mean number of organisms per dose, and the single-hit probability r varies between exposures following a

Beta(a, b) distribution,

yielding:

(Equ. 2),

where ${}_1F_1$ is the Kummer confluent hypergeometric function. The model to describe the probability for illness among infected subjects ($P_{ill|inf}$, Equ. 3) is based on other principles. It is no longer a matter of a single organism initiating infection, but rather the resulting growth of the population of organisms that should "outrun" the defensive measures of the immune system.

$$P_{ill|inf} = 1 -$$

(Equ. 3)

Like a and b , the parameters r and n are parameters that were estimated from data (see Subsection "Parameter estimation" for details). To determine the probability of illness or illness given infection, the corresponding equations are used and parameterised with the uncertainty distributions for a , b , r , and n . The user may supply the Poisson-mean dose D . The unconditional probability of illness is calculated by multiplying the conditional probability for illness ($P_{ill|inf}$, Equ. 3) and the probability of infection (P_{inf} , Equ. 2):

$$P_{ill} = P_{ill|inf} P_{inf}$$

(Equ. 4)

Note that the probability of illness is for the exposed population only. The fraction of the population that is exposed should be derived from an exposure assessment. This assessment is part of a full QMRA.

Parameter estimation

The parameters a and b (used to describe P_{inf} , Equ. 2) as well as the parameters r and

η (used to calculate $P_{ill|inf}$, Equ. 3) were estimated from the data from the challenge studies and outbreak studies as performed in Teunis et al. (2018). In the same paper, it

was described how parameters

a, b, r, η

are transformed. Subsequently, in Appendix B of the same paper, it was explained how the means and standard deviations of these transformed parameters can be used with a bivariate normal distribution to characterise uncertainty (see Teunis et al. (2018) for details and Table 2 for the model parameter values). Together with the Poisson-mean dose D , this allows us to calculate the probability of infection and illness.

In the next section, we describe how to implement the model and run model simulations using FSKX-format.

Simulations

All model parameters and their descriptions are presented in Table 1. The default simulation represents values derived from challenge studies; the values are summarised in Table 2. Another simulation setting, which considers values derived from outbreaks, is also available (see Table 2). This simulation differs from the default simulation only by the parameter "challenge". This parameter is "true" and "false" for the default and the outbreak simulation, respectively. In these two scenarios considered, a dose of one CFU is set, hence outcomes represent the single hit probabilities of illness and infection. These scenarios are interesting since they are lower bounds of infection or illness risk, and secondly since they allow us to compare the results to single hit infection probabilities of other pathogens. Two more scenarios are presented Table 2, again for both the challenge and outbreak situation, but, instead of a constant dose, we set the dose to

$$\log_{10}(D) \sim N$$

. This distribution models the concentration distribution in poultry meat, based on data presented in Swart and Havelaar (2012). In the following section, the model can be executed with default or customised parameters. It is also possible to work with the model on the local computer, for example, using the KNIME extension FSK-Lab (see <https://foodrisklabs.bfr.bund.de/fsk-lab/> and de Alba Aparicio et al. 2018).

Executable model

To be able to execute a model, you need to have an account registered with <https://data.d4science.org/>.

Read more [here](#).

In order to execute the model, please register at the [virtual research environment](#).

Execute with default simulation parameters: [execute](#)

The default simulation runs for 1 minute 4 seconds on the [virtual research environment](#).

Execute another simulation scenario or create a personalised simulation scenario: [execute](#)

Results

Results are visualised as boxplots that show the probability of illness and infection for the human population that consumes *Campylobacter jejuni*-contaminated food. The dose-response model is applied using the challenge studies dataset and the outbreak studies dataset separately (Teunis et al. 2018). All figures (Figs 1, 2, 3, 4) provide detailed information about the uncertainty of the probability of infection and illness; the white box represents the 25 % and 75 % quantile with the median indicated as the black bar inside of the box. The whiskers correspond to the maximum and minimum of the distribution, when not more than ± 1.5 times the inter-quartile range. The dots represent extreme values. The high values found for the probability of infection and the probability of illness for outbreak strains, are in agreement with the results obtained by Teunis et al. (2018).

The effect of a mean dose of 1 CFU of *Campylobacter* on human health

Figs 1, 2 are generated by the visualisation script of the attached FSKX-model (Suppl. material 1) with parameters from Table 1 and the values presented in Table 2. As to be expected, the median probability of illness is always lower than the probability of infection. Although the trend is the same, the probability of illness differs drastically between the results based on the challenge studies and the outbreaks dataset, with a higher probability of illness if the outbreak studies data are applied.

The effect of various mean doses of *Campylobacter* on human health

Figs 3, 4 show results that are created by the visualisation script of the attached FSKX-model (Suppl. material 1). The used parameter values are equal to those used in Figs 1, 2 except for the mean dose which is set to 1000 randomly generated values sampled from a normal distribution of concentrations with mean $-1 \log \text{CFU}$ and standard deviation of 1.5 (based on Swart and Havelaar (2012); see Table 2 for parametrisation). Again, the trends of (1) a lower median probability of illness compared to the probability of infection and (2) the probability of illness differs drastically between the results based on the challenge and the outbreak dataset are the same in both figures. Compared to Figs 1, 2, Figs 3, 4 show an overall lower chance to become infected and ill. Note that Figs 1, 2 show y-axes that represent values up to 60 %, while the ones in Figs 3, 4 represent up to about 30 %. Note that, in these analyses, the distribution of mean doses is assumed to represent uncertainty, not variability between ingested doses. The result is uncertainty in probability of infection or illness.

Conclusion

Dose-response models, as part of the hazard characterisation, are an indispensable ingredient of any QMRA model (Codex Alimentarius Commission 1999). Each microbial pathogen requires its own dose-response model, since infectivities of different species may differ substantially. In addition, pathogenicity may differ between bacterial strains of a taxonomical unit and even susceptibilities between individuals vary, due to individual host characteristics or acquired immunity (Havelaar and Swart 2014). However, scarcity of data to characterise the variability between bacterial strains and hosts precludes dose-response models specified at this level of detail.

In the current study, we focus on a recently published dose-response model for *Campylobacter jejuni* (Teunis et al. 2018). This model is based on a variety of dose-response studies and offers an alternative to the "classic" dose-response model of Teunis and Havelaar (2000). The "classic" model has been most frequently used in *Campylobacter* risk assessments so far (Nauta et al. 2009) and is based on the study of Black et al. (1988). As shown by Teunis et al. (2018), the recent model suggests that *Campylobacter* is more virulent than previously assumed.

We present the recent model of Teunis et al. (2018) annotated with all metadata and implemented in the ready-to-use FSKX-format. This allows easy model integration and simulation result interpretation in future QMRA studies. On the one hand, the model in the FSKX-file is available as an R programming language code that can be integrated into a fully fledged QMRA model. On the other hand, for a swift assessment of infection and illness probabilities at given mean doses, the current "executable paper" provides a convenient resource. Moreover, by using software like FSK-Lab, the user is able to join the model with an exposure assessment and perform a complete QMRA. In conclusion, we

provide an annotated, ready-to-use implementation of the *Campylobacter jejuni* dose-response model.

Acknowledgements

We wish to acknowledge the original work of Peter F.M. Teunis, Axel Bonačić Marinović, David R. Tribble, Chad K. Porter, and Stylianos Georgiadis.

Funding program

EMS is funded by the European Union's Horizon 2020 research and innovation programme under grant agreement No 731001 and the JIP MATRIX within the One Health EJP. One Health EJP has received funding from the European Union Horizon 2020 research and innovation programme under grant agreement No 773830.

Author contributions

Esther M. Sundermann: Conceptualisation, Software (creation of the fsx-model), Project administration, Visualisation, Data Curation, Writing - Original Draft, Writing - Review & Editing, Maarten Nauta: Writing - Original Draft, Writing - Review & Editing, Arno Swart: Methodology, Software (development of the model), Writing - Original Draft, Writing - Review & Editing

References

- Black RE, Levine MM, Clements ML, Hughes TP, Blaser MJ (1988) Experimental *Campylobacter jejuni* infection in humans. *Journal of Infectious diseases* 157 (3): 472-479. <https://doi.org/10.1093/infdis/157.3.472>
- Chapman B, Otten A, Fazil A, Ernst N, Smith BA (2016) A review of quantitative microbial risk assessment and consumer process models for *Campylobacter* in broiler chickens. *Microbial Risk Analysis* 2-3: 3-15. <https://doi.org/10.1016/j.mran.2016.07.001>
- Codex Alimentarius Commission (1999) Principles and guidelines for the conduct of microbiological risk assessment. In: Food and Agriculture Organization of the United Nations, World Health Organization (Eds) *International Food Standards*. CAC/GL-30. Rome, Italy.
- de Alba Aparicio M, Buschhardt T, Swaid A, Valentin L, Mesa-Varona O, Günther T, Plaza-Rodriguez C, Filter M (2018) FSK-Lab – An open source food safety model integration tool. *Microbial Risk Analysis* 10: 13-19. <https://doi.org/10.1016/j.mran.2018.09.001>
- EFSA Panel on Biological Hazards (2011) Scientific opinion on *Campylobacter* in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain. *EFSA Journal* 9 (4): 2105. <https://doi.org/10.2903/j.efsa.2011.2105>

- EFSA Panel on Biological Hazards, Koutsoumanis K, Allende A, Alvarez-Ordóñez A, Bolton D, Bover-Cid S, Davies R, De Cesare A, Herman L, Hilbert F (2020) Update and review of control options for *Campylobacter* in broilers at primary production. EFSA Journal 18 (4): 6090.
- European Food Safety Authority, European Centre for Disease Prevention Control (2019) The European Union one health 2018 zoonoses report. EFSA Journal 17 (12). URL: <https://www.efsa.europa.eu/en/efsajournal/pub/5926>
- German Federal Institute for Risk Assessment (2019) <https://www.bfr.bund.de/cm/350/feed-and-food-safety-in-times-of-global-production-and-trade.pdf>
- Haberbeck LU, Plaza-Rodriguez C, Desvignes V, Dalgaard P, Sanaa M, Guillier L, Nauta M, Filter M (2018) Harmonized terms, concepts and metadata for microbiological risk assessment models: The basis for knowledge integration and exchange. Microbial Risk Analysis 10: 3-12. <https://doi.org/10.1016/j.mran.2018.06.001>
- Havelaar AH, Swart AN (2014) Impact of acquired immunity and dose-dependent probability of illness on quantitative microbial risk assessment. Risk Analysis 34 (10): 1807-19. <https://doi.org/10.1111/risa.12214>
- Nauta M, Hill A, Rosenquist H, Brynestad S, Fetsch A, van der Logt P, Fazil A, Christensen B, Katsma E, Borck B (2009) A comparison of risk assessments on *Campylobacter* in broiler meat. International Journal of Food Microbiology 129 (2): 107-123. <https://doi.org/10.1016/j.ijfoodmicro.2008.12.001>
- Silva J, Leite D, Fernandes M, Mena C, Gibbs P, Teixeira P (2011) *Campylobacter* spp. as a foodborne pathogen: A review. Frontiers in Microbiology 2 (200). <https://doi.org/10.3389/fmicb.2011.00200>
- Swart A, Havelaar A (2012) Analyse monitoring data 'convenant *Campylobacter* aanpak pluimveevlees in Nederland'. Rijksinstituut voor Volksgezondheid en Milieu RIVM. URL: <http://hdl.handle.net/10029/261559>
- Teunis PFM, Havelaar AH (2000) The beta Poisson dose-response model is not a single-hit model. Risk Analysis 20 (4): 513-20. <https://doi.org/10.1111/0272-4332.204048>
- Teunis PFM, Van den Brandhof W, Nauta M, Wagenaar J, Van den Kerkhof H, Van Pelt W (2005) A reconsideration of the *Campylobacter* dose–response relation. Epidemiology & Infection 133 (4): 583-592. <https://doi.org/10.1017/s0950268805003912>
- Teunis PFM, Bonacic Marinovic A, Tribble DR, Porter CK, Swart A (2018) Acute illness from *Campylobacter jejuni* may require high doses while infection occurs at low doses. Epidemics 24: 1-20. <https://doi.org/10.1016/j.epidem.2018.02.001>
- World Health Organization, Food and Agriculture Organization of the United Nations (2003) Hazard characterization for pathogens in food and water: guidelines. Microbiological Risk Assessment Series 3 URL: <http://www.fao.org/3/y4666e/y4666e00.htm>
- World Health Organization, Food Agriculture Organization of the United Nations (2009) Risk assessment of *Campylobacter* spp. in broiler chickens: interpretative summary. Microbiological Risk Assessment Series No 11, Geneva, Switzerland. URL: https://www.who.int/foodsafety/publications/micro/MRA11_En.pdf
- World Health Organization (2013) The global view of campylobacteriosis: report of an expert consultation. Utrecht, Netherlands, 9-11 July 2012 URL: <https://apps.who.int/iris/bitstream/handle/>

[10665/80751/9789241564601_eng.pdf;jsessionid=4C4696E0E17C189DA6C361F20B78EBFA?sequence=1](#)

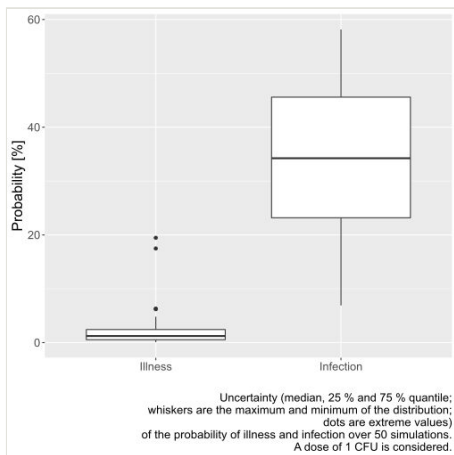


Figure 1.

The probability of illness and infection for the human population after consumption of a mean dose of 1 CFU of *Campylobacter jejuni* contaminated food. The probabilities are calculated based on the challenge studies dataset (the so-called default simulation).

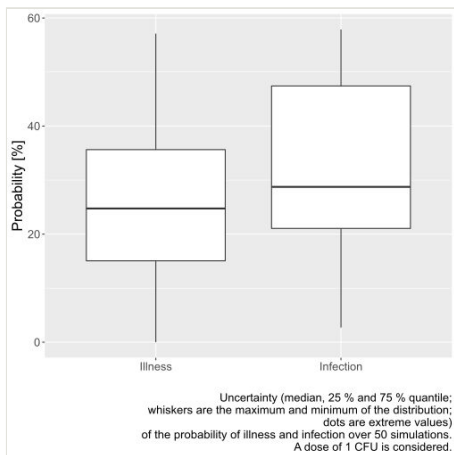


Figure 2.

The probability of illness and infection for the human population after consumption of a mean dose of 1 CFU of *Campylobacter jejuni*-contaminated food. The probabilities are calculated based on the outbreak dataset (the so-called outbreak simulation).

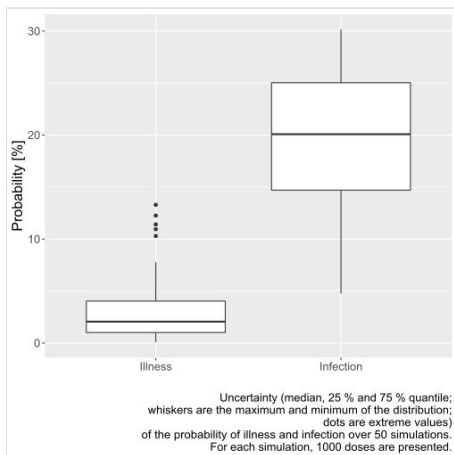


Figure 3.

The probability of illness and infection for the human population after consumption of *Campylobacter jejuni*-contaminated food. The probabilities are calculated based on the challenge studies dataset with 1000 various mean doses (the so-called ChallengeVarMeanDoses simulation).

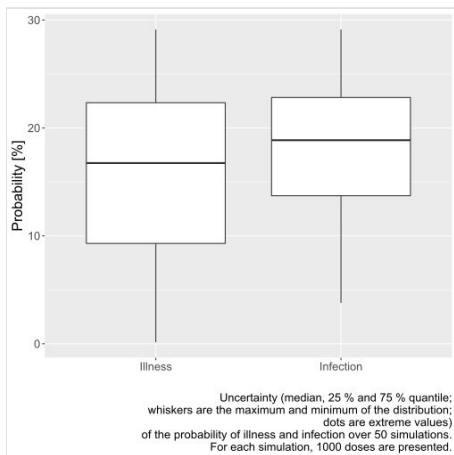


Figure 4.

The probability of illness and infection for the human population after consumption of *Campylobacter jejuni*-contaminated food. The probabilities are calculated based on the outbreak dataset with 1000 various mean doses (the so-called OutbreakVarMeanDoses simulation).

Table 1.

Description of the model parameters of the dose-response model of *Campylobacter jejuni*.

Id	dose
Classification	INPUT
Name	Doses
Description	A range (vector) of mean doses of <i>Campylobacter jejuni</i>
Unit	CFU
Data Type	DOUBLE
Source	Article
Value	rep(1,10000)
Min Value	0
Id	n_sim
Classification	INPUT
Name	Number of parameter simulations
Description	Number of simulations
Unit	[]
Data Type	INTEGER
Source	Article
Value	50
Min Value	1
Id	Pexp
Classification	INPUT
Name	Probability of exposure
Description	In exposure models, the Pexp is often called the prevalence.
Unit	[Probability]
Data Type	DOUBLE
Source	User supplied
Value	1
Min Value	0

Max Value	1
Id	challenge
Classification	INPUT
Name	Analysis done on the basis of challenge study data or outbreak data
Description	TRUE if challenge, FALSE if outbreak
Unit	[]
Data Type	BOOLEAN
Source	Data
Value	TRUE
Id	mean_w_inf_ch
Classification	INPUT
Name	Mean of w1
Description	w1 is a measure of infectivity (location). Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	-0.177
Id	mean_z_inf_ch
Classification	INPUT
Name	Mean of z1
Description	z1 is a measure of variation in infectivity (spread). Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	0.054
Id	var_w_inf_ch
Classification	INPUT

Name	Variance of w1
Description	w1 is a measure of infectivity (location). Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	1.303
Id	var_z_inf_ch
Classification	INPUT
Name	Variance of z1
Description	z1 is a measure of variation in infectivity (spread). Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	1.07
Id	cov_wz_inf_ch
Classification	INPUT
Name	Covariance of (w1,z1)
Description	w1 is a measure of infectivity (location) and z1 is a measure of variation in infectivity (spread). Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	-0.041
Id	mean_w_ill_ch
Classification	INPUT
Name	Mean of w2
Description	w2 is a location parameter. Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE

Source	Article
Value	-2.744
Id	mean_z_ill_ch
Classification	INPUT
Name	Mean of z2
Description	z2 is a spread parameter. Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	-0.00489
Id	var_w_ill_ch
Classification	INPUT
Name	Variance of w2
Description	w2 is a location parameter. Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	1.337
Id	var_z_ill_ch
Classification	INPUT
Name	Variance of z2
Description	z2 is a spread parameter. Value of the challenge-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	0.993
Id	cov_wz_ill_ch

Classification	INPUT
Name	Covariance of (w2,z2)
Description	w2 is a location parameter and z2 is a spread parameter. Value of the challenge-scenario.
Unit	∅
Data Type	DOUBLE
Source	Article
Value	0.01
Id	mean_w_inf_ob
Classification	INPUT
Name	Mean of w1
Description	w1 is a measure of infectivity (location). Value of the outbreak- scenario.
Unit	∅
Data Type	DOUBLE
Source	Article
Value	-0.226
Id	mean_z_inf_ob
Classification	INPUT
Name	Mean of z1
Description	z1 is a measure of variation in infectivity (spread). Value of the outbreak-scenario.
Unit	∅
Data Type	DOUBLE
Source	Article
Value	0.017
Id	var_w_inf_ob
Classification	INPUT
Name	Variance of w1
Description	w1 is a measure of infectivity (location). Value of the outbreak-scenario.
Unit	∅

Data Type	DOUBLE
Source	Article
Value	1.404
Id	var_z_inf_ob
Classification	INPUT
Name	Variance of z1
Description	z1 is a measure of variation in infectivity (spread). Value of the outbreak-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	1.003
Id	cov_wz_inf_ob
Classification	INPUT
Name	Covariance of (w1,z1)
Description	w1 is a measure of infectivity (location) and z1 is a measure of variation in infectivity (spread). Value of the outbreak-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	-0.053
Id	mean_w_ill_ob
Classification	INPUT
Name	Mean of w2
Description	w2 is a location parameter. Value of the outbreak-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	6.241

Id	mean_z_ill_ob
Classification	INPUT
Name	Mean of z2
Description	z2 is a spread parameter. Value of the outbreak-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	-0.0086
Id	var_w_ill_ob
Classification	INPUT
Name	Variance of w2
Description	w2 is a location parameter. Value of the outbreak-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	40.99
Id	var_z_ill_ob
Classification	INPUT
Name	Variance of z2
Description	z2 is a spread parameter. Value of the outbreak-scenario.
Unit	[]
Data Type	DOUBLE
Source	Article
Value	0.995
Id	cov_wz_ill_ob
Classification	INPUT
Name	Covariance of (w2,z2)
Description	w2 is a location parameter and z2 is a spread parameter. Value of the outbreak-scenario.

Unit	[]
Data Type	DOUBLE
Source	Article
Value	0.184
Id	Qillmean
Classification	OUTPUT
Name	Mean probability of illness for each simulation over all doses
Description	
Unit	[Probability]
Data Type	VECTOROFNUMBERS
Min Value	0
Max Value	1
Id	Qinfmean
Classification	OUTPUT
Name	Mean probability of infection for each simulation over all doses
Description	
Unit	[Probability]
Data Type	VECTOROFNUMBERS
Min Value	0
Max Value	1

Table 2.

The simulation settings for the dose-response model. The settings specify the parameter names and the values (see Table 1 for details about the parameters).

defaultSimulation	
dose	rep(1,10000)
n_sim	50
Pexp	1
challenge	TRUE
mean_w_inf_ch	-0.177
mean_z_inf_ch	0.054
var_w_inf_ch	1.303
var_z_inf_ch	1.07
cov_wz_inf_ch	-0.041
mean_w_ill_ch	-2.744
mean_z_ill_ch	-0.00489
var_w_ill_ch	1.337
var_z_ill_ch	0.993
cov_wz_ill_ch	0.01
mean_w_inf_ob	-0.226
mean_z_inf_ob	0.017
var_w_inf_ob	1.404
var_z_inf_ob	1.003
cov_wz_inf_ob	-0.053
mean_w_ill_ob	6.241
mean_z_ill_ob	-0.0086
var_w_ill_ob	40.99
var_z_ill_ob	0.995
cov_wz_ill_ob	0.184
Outbreak	
dose	rep(1,10000)
n_sim	50

Pexp	1
challenge	FALSE
mean_w_inf_ch	-0.177
mean_z_inf_ch	0.054
var_w_inf_ch	1.303
var_z_inf_ch	1.07
cov_wz_inf_ch	-0.041
mean_w_ill_ch	-2.744
mean_z_ill_ch	-0.00489
var_w_ill_ch	1.337
var_z_ill_ch	0.993
cov_wz_ill_ch	0.01
mean_w_inf_ob	-0.226
mean_z_inf_ob	0.017
var_w_inf_ob	1.404
var_z_inf_ob	1.003
cov_wz_inf_ob	-0.053
mean_w_ill_ob	6.241
mean_z_ill_ob	-0.0086
var_w_ill_ob	40.99
var_z_ill_ob	0.995
cov_wz_ill_ob	0.184
ChallengeVarMeanDoses	
dose	$10^{\text{norm}(1000, -1, 1.5)}$
n_sim	50
Pexp	1
challenge	TRUE
mean_w_inf_ch	-0.177
mean_z_inf_ch	0.054
var_w_inf_ch	1.303
var_z_inf_ch	1.07

cov_wz_inf_ch	-0.041
mean_w_ill_ch	-2.744
mean_z_ill_ch	-0.00489
var_w_ill_ch	1.337
var_z_ill_ch	0.993
cov_wz_ill_ch	0.01
mean_w_inf_ob	-0.226
mean_z_inf_ob	0.017
var_w_inf_ob	1.404
var_z_inf_ob	1.003
cov_wz_inf_ob	-0.053
mean_w_ill_ob	6.241
mean_z_ill_ob	-0.0086
var_w_ill_ob	40.99
var_z_ill_ob	0.995
cov_wz_ill_ob	0.184
OutbreakVarMeanDoses	
dose	10*norm(1000, -1, 1.5)
n_sim	50
Pexp	1
challenge	FALSE
mean_w_inf_ch	-0.177
mean_z_inf_ch	0.054
var_w_inf_ch	1.303
var_z_inf_ch	1.07
cov_wz_inf_ch	-0.041
mean_w_ill_ch	-2.744
mean_z_ill_ch	-0.00489
var_w_ill_ch	1.337
var_z_ill_ch	0.993
cov_wz_ill_ch	0.01

mean_w_inf_ob	-0.226
mean_z_inf_ob	0.017
var_w_inf_ob	1.404
var_z_inf_ob	1.003
cov_wz_inf_ob	-0.053
mean_w_ill_ob	6.241
mean_z_ill_ob	-0.0086
var_w_ill_ob	40.99
var_z_ill_ob	0.995
cov_wz_ill_ob	0.184

Supplementary material

Suppl. material 1: CampylobacterDRM.fskx

Authors: Esther M. Sundermann

Data type: fskx-model

[Download file](#) (1.15 MB)