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

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## 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 fskx-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:

$P_{inf} = 1 - {}_1F_1(a, a + b, -D)$ (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.

$P_{ill|inf} = 1 - (1 + D/\eta)^{-r}$ (Equ. 3)

Like $a$ and $b$, the parameters $r$ and $\eta$ 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 $\eta$. 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 $\eta$ (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 $a$, $b$, $r$, $\eta$ 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.

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 *Campylobacter jejuni* |
| 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^rnorm(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^rnorm(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 |

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 $\log_{10}(D) \sim N(-1,1.5)$. 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

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).

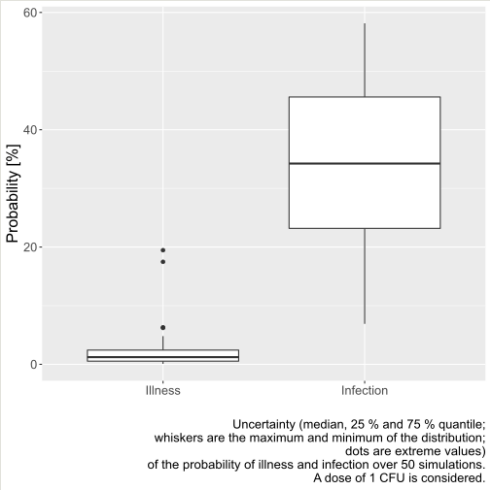


Figure 1. doi

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).

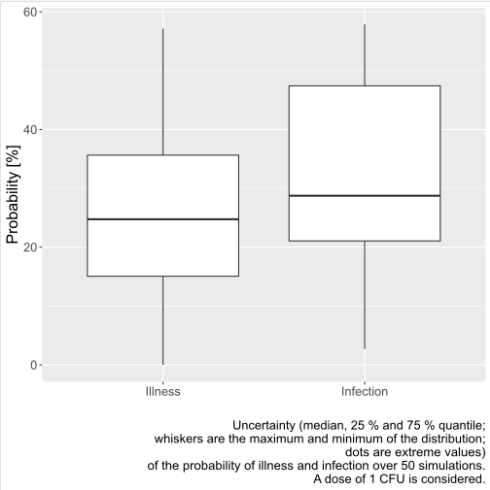


Figure 2. doi

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).

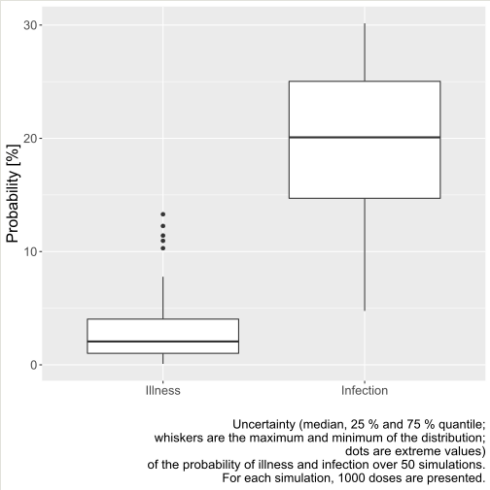


Figure 3. doi

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).

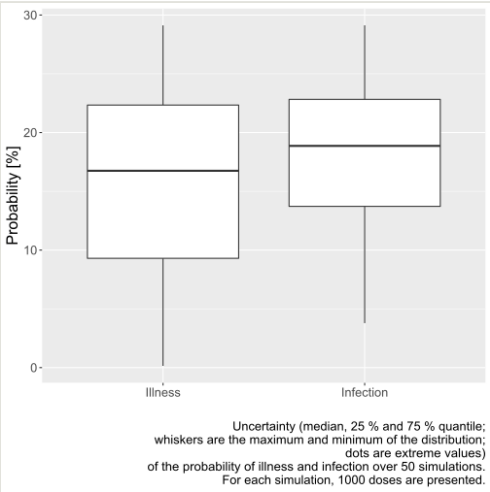


Figure 4. doi

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).

### 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 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.

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## Author contributions

Esther M. Sundermann: Conceptualisation, Software (creation of the fskx-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

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## Supplementary material

**Suppl. material 1: CampylobacterDRM.fskx** doi

**Authors:** Esther M. Sundermann
**Data type:** fskx-model
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