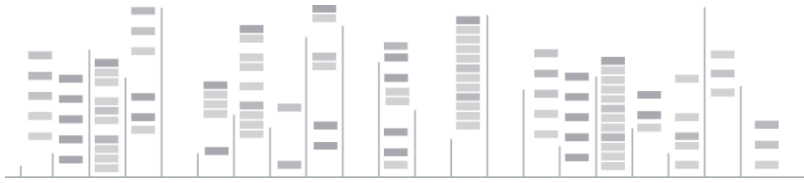


# Bayesian modelling of *Clostridium perfringens* dose response

S. Jaloustre and M.L. Delignette-Muller

Financé par

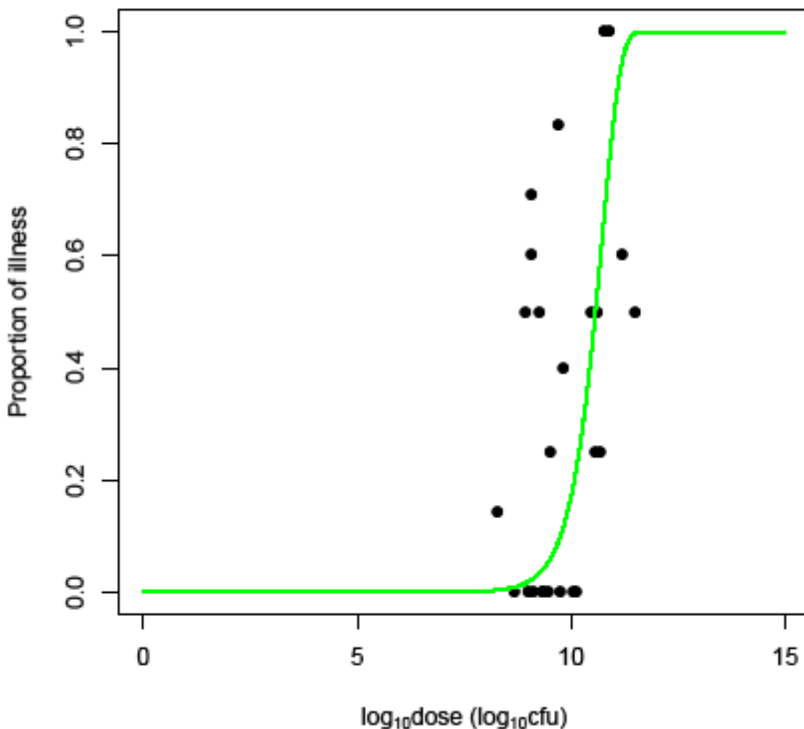




# Aim of this study

Estimate the parameters of a *Clostridium perfringens* dose response model using different sources of data in order to predict the risk of food borne diarrhea due to *Clostridium perfringens* vegetative cells both taking into account sources of

- Variability
- Uncertainty





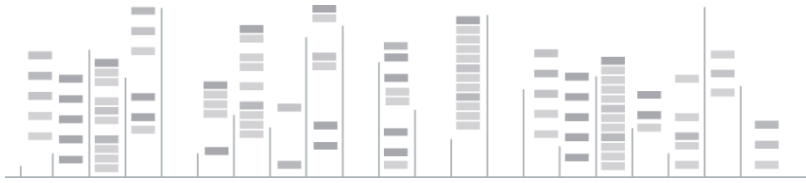
# Human volunteer feeding study data

## Published data

- 25 attack rates from 4 papers published from 1954 to 1971
- Healthy volunteers, laboratory strains

## Information on ingested dose directly available

- A mean dose and a dose range
  - dispersion of *C. perfringens* concentration in food described by a Relative Standard Deviation (RSD)
- A mean dose
  - dispersion of *C. perfringens* concentration in food simulated using the RSD



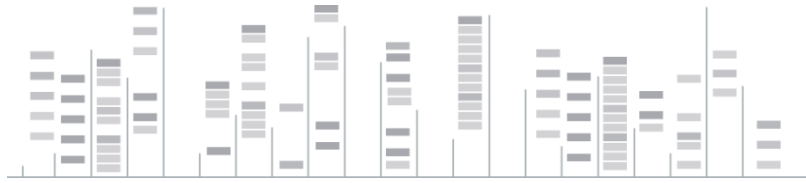
# Outbreak data

## Published and personal data

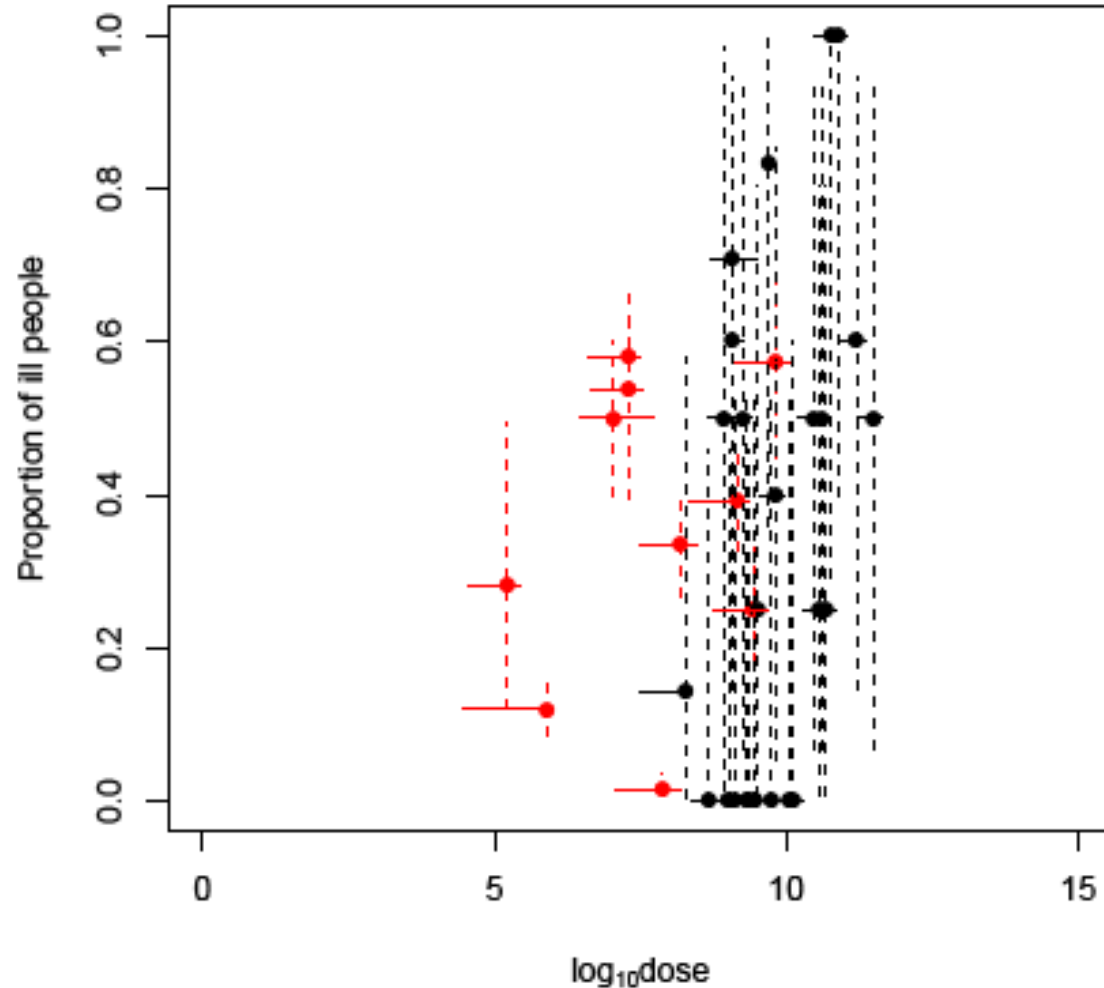
- 6 attack rates from 2 papers published in 1953 and 1968
- 4 attack rates collected in Central Laboratory for Veterinary Services
- Susceptible people, wild strains

## Information on ingested dose

- C. perfringens* concentration in food
  - dispersion of *C. perfringens* concentration in food simulated using the RSD
- Serving size
  - Data of a study on French dietary habits
  - Variability on serving size



# Whole dataset

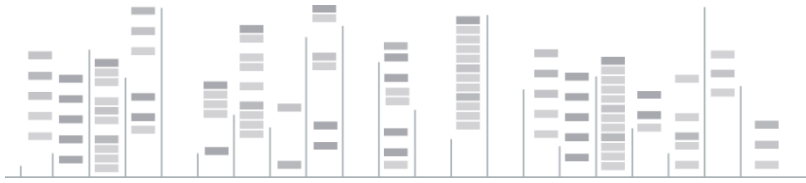


Human volunteer  
feeding studies

Outbreaks

! uncertainty on  
response

— uncertainty on  
actual ingested  
dose



# Dose response model

➤ 'Single hit' model on actual doses :

$$P_{ill}(d, r) = 1 - (1 - r)^d$$

With  $d$  the actual ingested dose

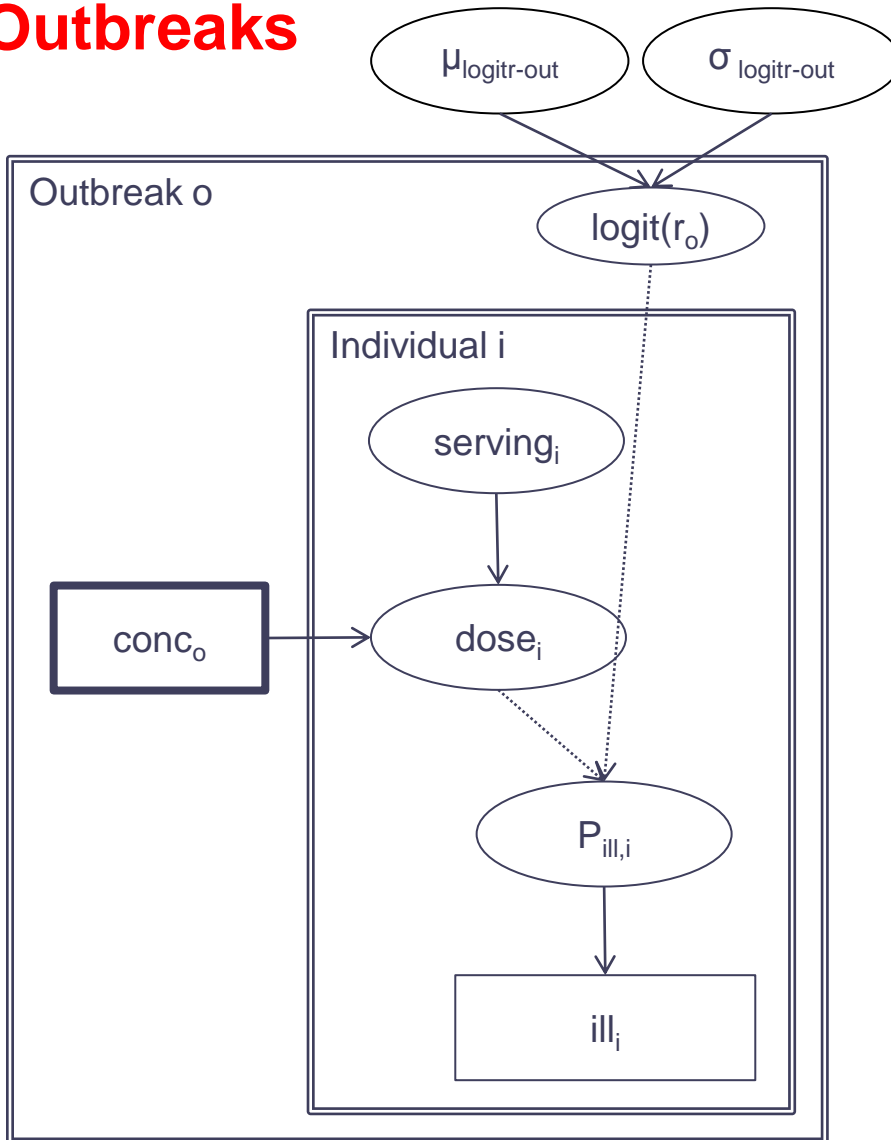
➤ Parameter :

- |  $r$  probability for a cell to resist barriers and provoke illness
- | Assumed variable : description of a between-exposure variability on

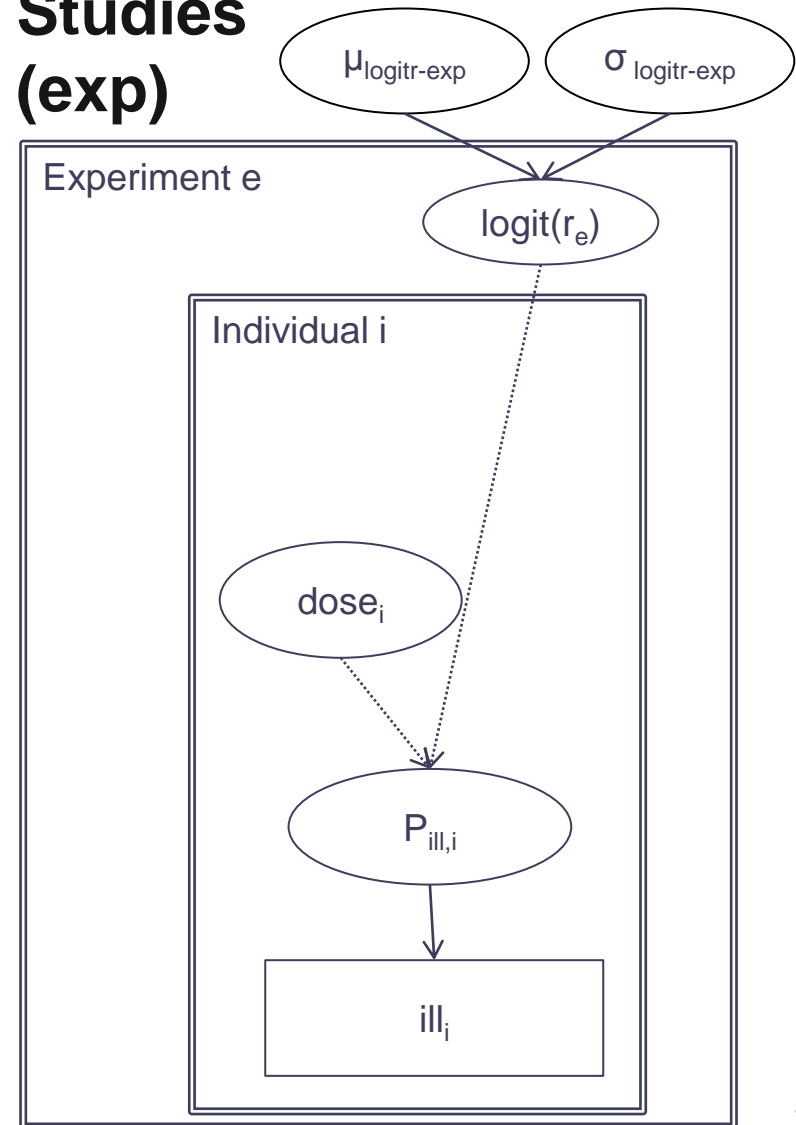
$$\text{logit}(r) = \ln\left(\frac{1}{1-r}\right)$$

# Bayesian hierarchical model : directed acyclic graph

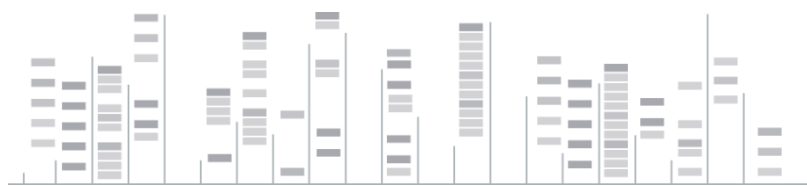
## Outbreaks



## Studies (exp)

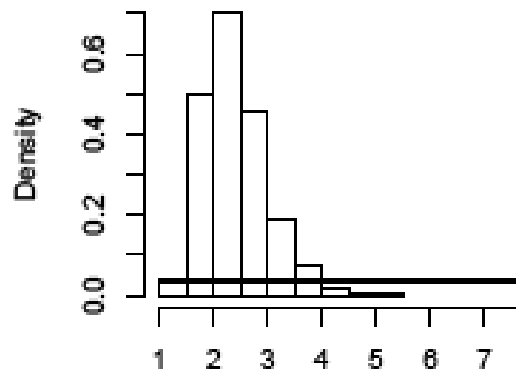
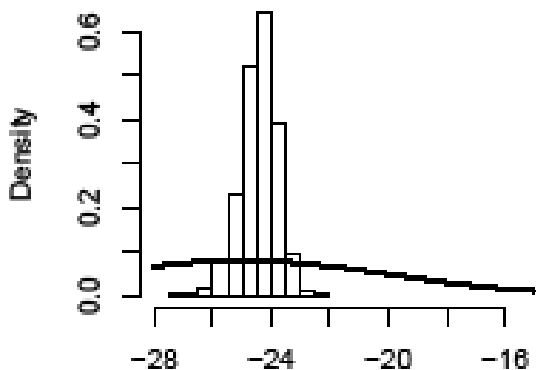


# Parameters distributions



$\mu_{\text{logitr-exp}}$

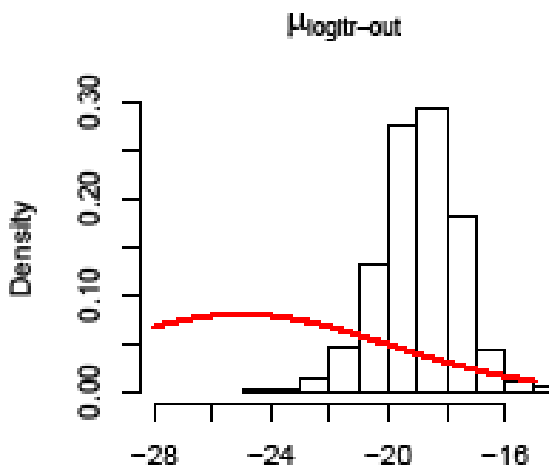
$\sigma_{\text{logitr-exp}}$



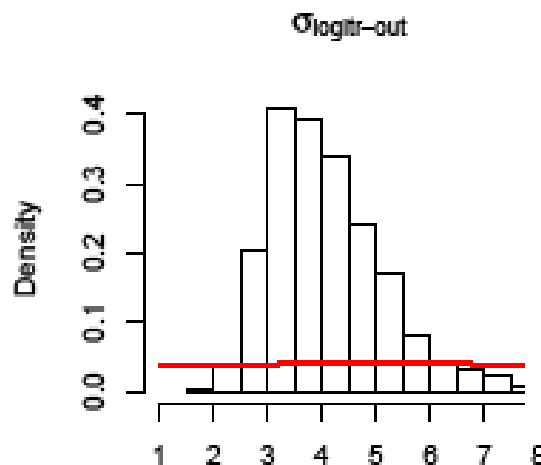
## Prior dist. (lines)

- $\mu_{\text{logitr-exp}}$  and  $\mu_{\text{logitr-out}}$  : Golden *et al.* (2009)
- $\sigma_{\text{logitr-exp}}$  and  $\sigma_{\text{logitr-out}}$  : non informative priors

## Posterior dist. (histograms)



$\mu_{\text{logitr-out}}$

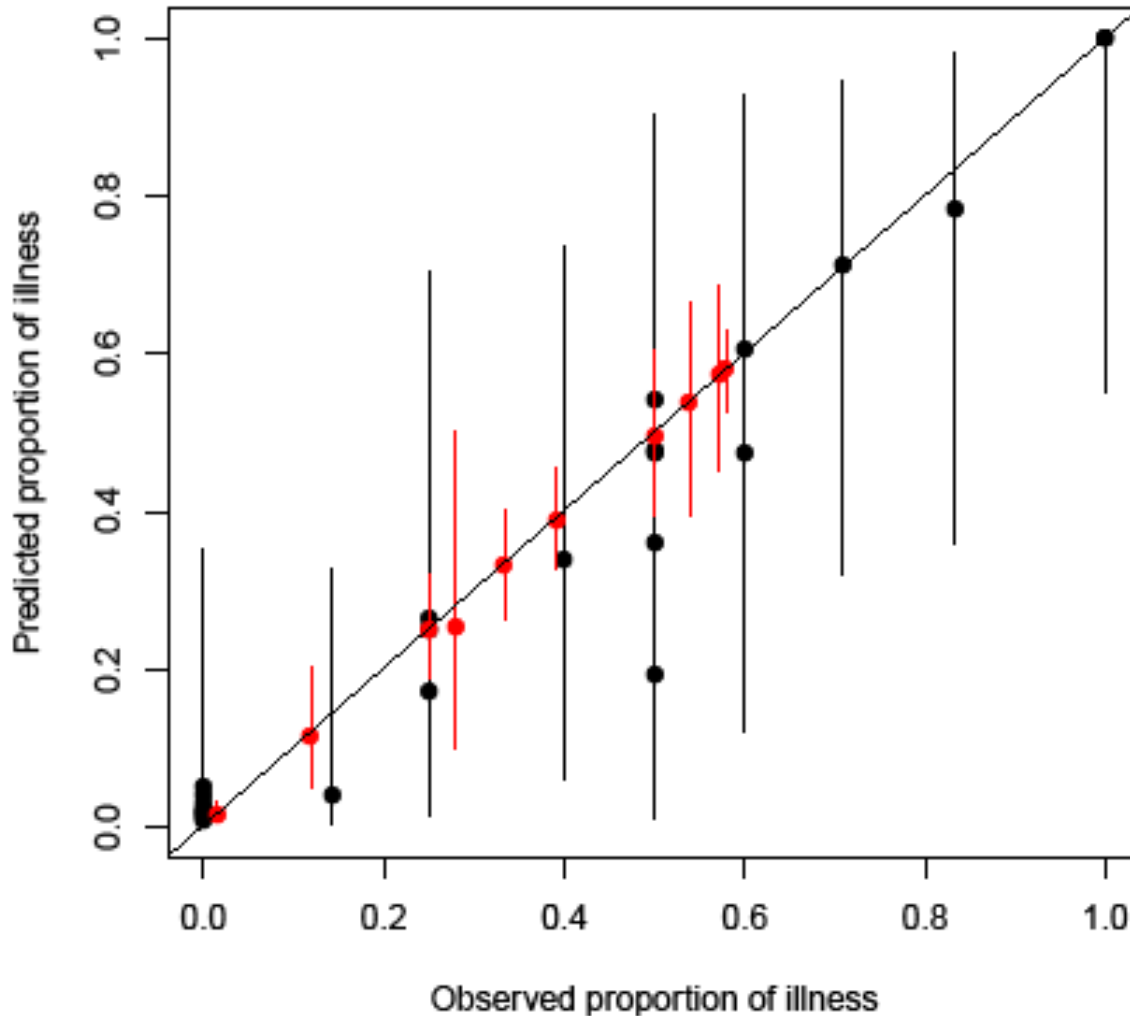


$\sigma_{\text{logitr-out}}$

- Non over lapping  $\mu_{\text{logitr-exp}}$  and  $\mu_{\text{logitr-out}}$  95% confidence intervals



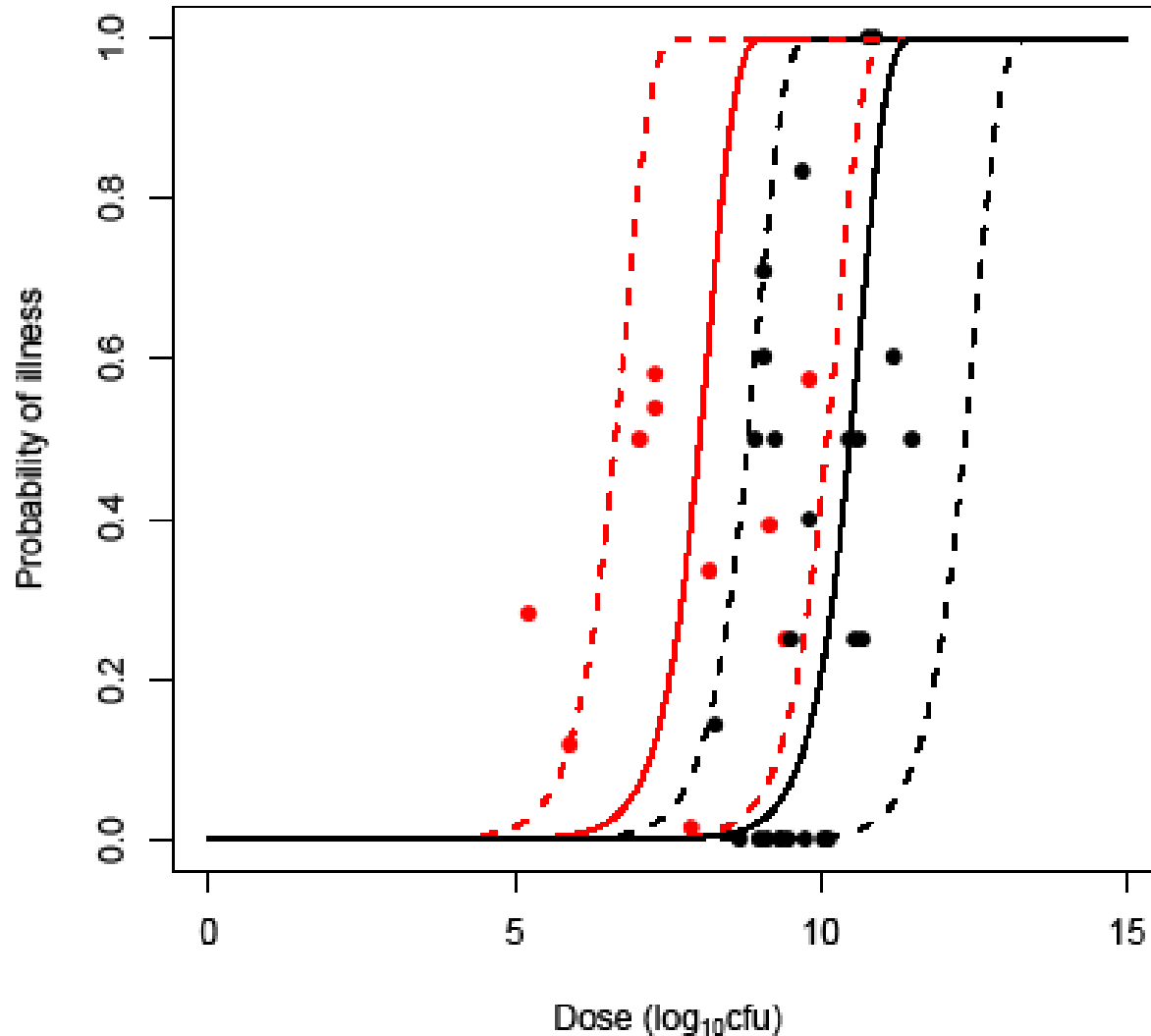
# Ability of the models to describe all the observed data



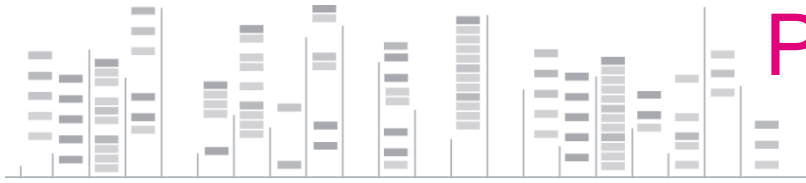
Human volunteer  
feeding studies

Outbreaks

# Description of the observed data



Human volunteer  
feeding studies  
Outbreaks



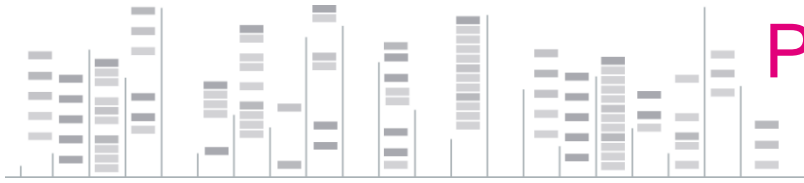
# Prediction of the probability of illness

- Using fixed doses ranging from 5 to 9  $\log_{10}$ cfu
  - Three models : outbreak and experiment models (variability and uncertainty) and the model published by Golden *et al.* (2009) (only variability)
  - Taking into account uncertainty on estimated parameters (outbreak and experiment models) and variability on  $r$  (2D Monte Carlo simulations)
- Mean probability of illness with its 95% confidence interval (outbreak and experiment models)



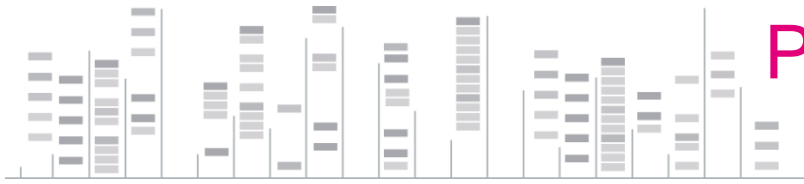
# Predicted probabilities of illness

Dose (log <sub>10</sub> cfu)	Prediction by the model		
	'Outbreak model'	'Experiment model'	Published by Golden <i>et al.</i> (2009)
5	$5.2 \cdot 10^{-2}$ [ $7.8 \cdot 10^{-3}$ , $1.9 \cdot 10^{-1}$ ]	$3.7 \cdot 10^{-5}$ [ $6.8 \cdot 10^{-6}$ , $1.5 \cdot 10^{-3}$ ]	$2.0 \cdot 10^{-5}$
7	$2.9 \cdot 10^{-1}$ [ $1.5 \cdot 10^{-1}$ , $5.1 \cdot 10^{-1}$ ]	$3.3 \cdot 10^{-3}$ [ $6.8 \cdot 10^{-4}$ , $2.8 \cdot 10^{-2}$ ]	$2.4 \cdot 10^{-3}$
9	$7.3 \cdot 10^{-1}$ [ $4.8 \cdot 10^{-1}$ , $8.8 \cdot 10^{-1}$ ]	$1.2 \cdot 10^{-1}$ [ $5.2 \cdot 10^{-2}$ , $2.5 \cdot 10^{-1}$ ]	$9.6 \cdot 10^{-2}$



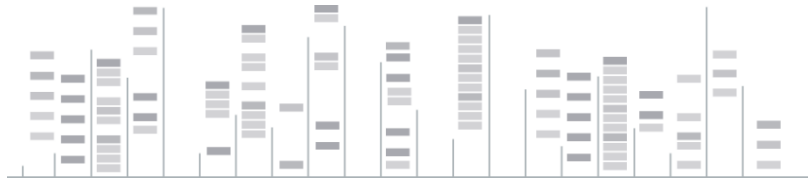
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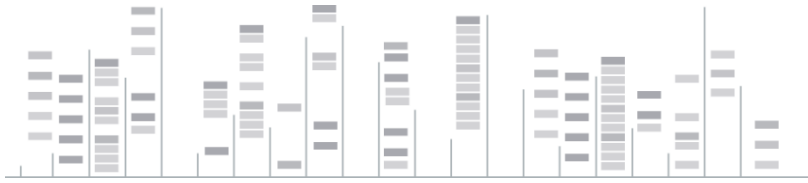
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# Discussion

- ↪ Exploration of between host, strain or food matrix variability on  $r$  not possible due to the lack of data
- ↪ Uncertainty on actual doses described using published data
  - | Dispersion of *C. perfringens* concentration in food
  - | Variability on serving size
- ↪ Uncertainty on the number of exposed and ill people in outbreak data



# Conclusions

- Source of data impacts risk prediction
- Avoid to use human volunteer feeding study data to fit a dose response model
- Strong uncertainty on risk prediction
- Necessary to enhance outbreak detection and better report them