



What is the relation between doses and illness in different risk groups?

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DOSE-RESPONSE (DR) MODEL

Response

How many *Listeria monocytogenes* do I need to ingest before I get ill?

?

Dose

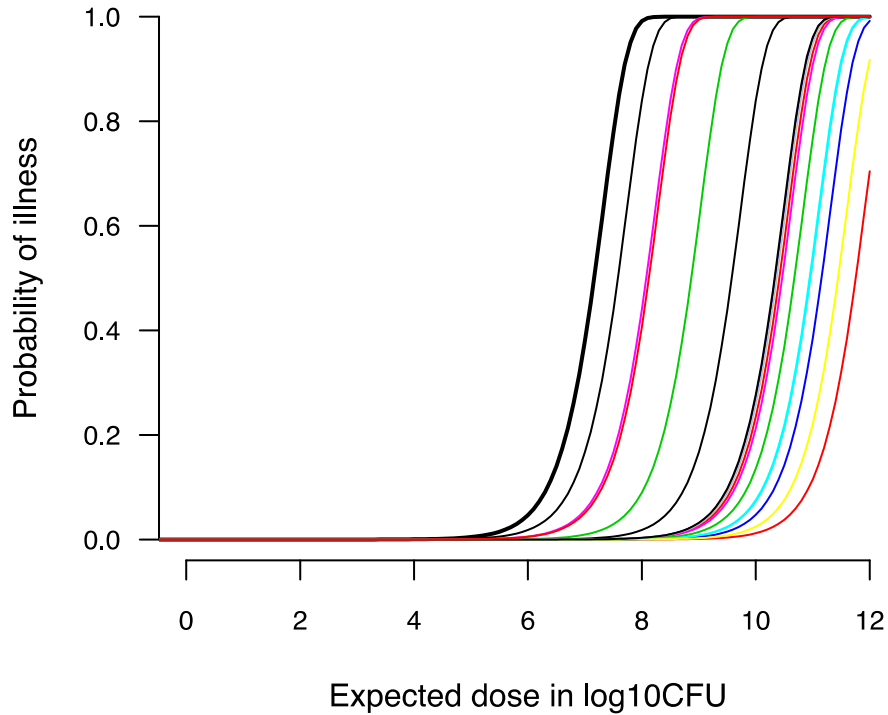
THE CONCEPTUAL PROCESS

- Four biologically plausible steps:
 1. **Ingestion** of D organisms by a host individual
 2. ingested organisms **passing** through the various barriers and **surviving** until they reach the **target site**
 3. surviving organism(s) resulting in **infection**
 4. infection resulting in **illness**

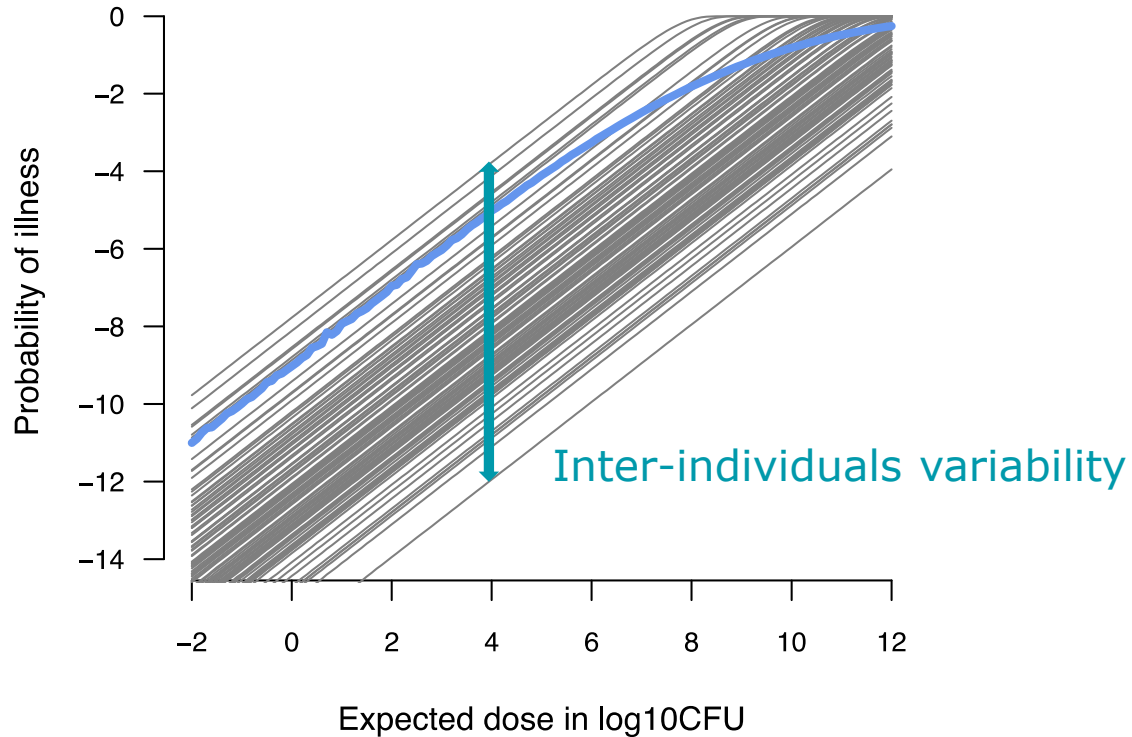
EXPONENTIAL MODEL

- $P_{ill}(\lambda, r) = 1 - \exp(-\lambda r)$
- Actual ingested dose is uncertain but can be described by a Poisson distribution with a mean equal to λ
- *Minimal infective dose* = 1 cell with a probability of illness (r)
- r is considered variable:
 - Log-Normal distribution
 - Total Variation = between individual variation + between strain variation
 - Stratification: risk groups

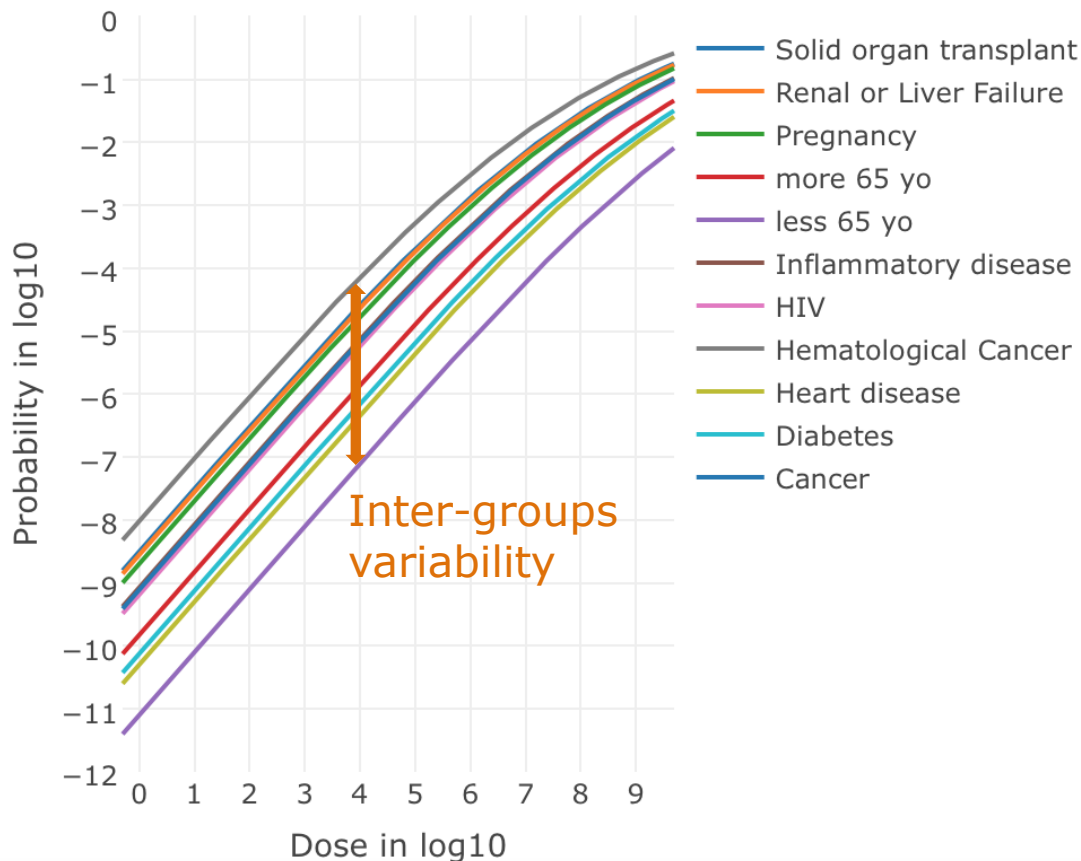
CONDITIONAL DR MODEL



CONDITIONAL VS MARGINAL DR MODEL



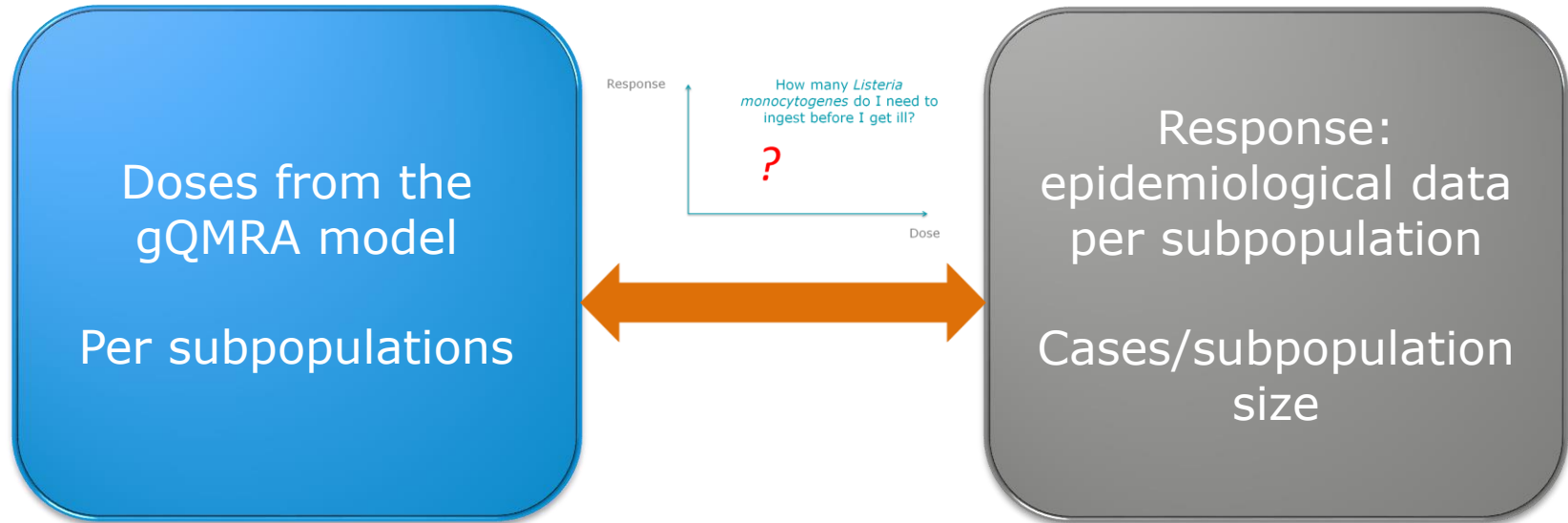
DR MODELS IN POUILLOT ET AL. (2015)



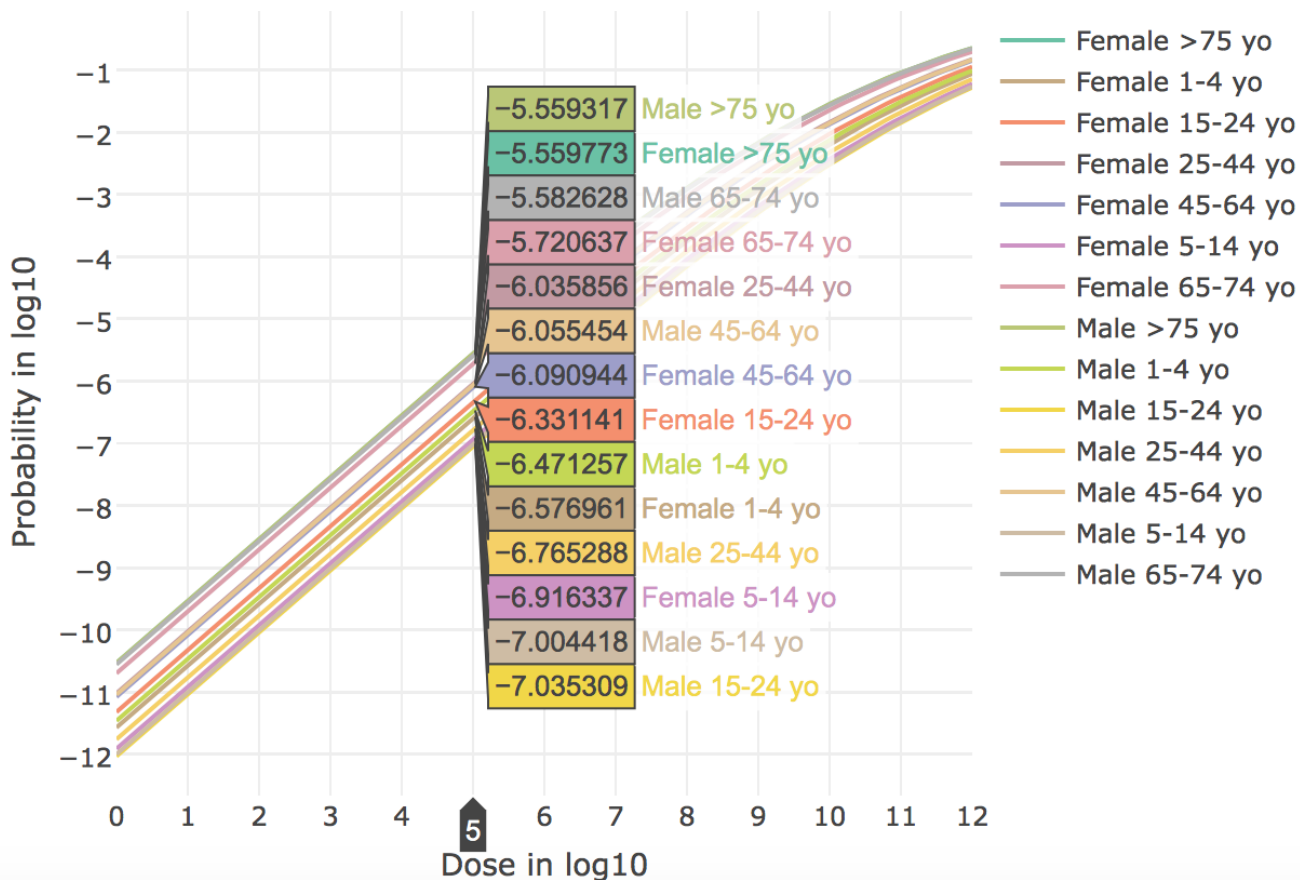
INVASIVE HUMAN LISTERIOSIS CASES, EU/EEA, 2008–2015

Subpopulations	Population	Listeriosis cases	Relative risk
Female 1–4 yo	9,981,292	49	0.17
Male 1–4 yo	10,507,387	62	0.20
Female 5–14 yo	24,769,674	52	0.07
Male 5–14 yo	26,071,451	51	0.07
Female 15–24 yo	27,917,371	209	0.26
Male 15–24 yo	29,107,545	72	0.08
Female 25–44 yo	67,013,021	1,067	0.54
Male 25–44 yo	68,019,328	351	0.18
Female 45–64 yo	65,803,889	1,219	0.63
Male 45–64 yo	63,791,535	2,001	1.07
Female 65–74 yo	24,249,576	1,328	1.87
Male 65–74 yo	20,921,720	2,142	3.50
Female ≥ 75 yo	25,539,929	2,537	3.40
Male ≥ 75 yo	15,476,863	2,862	6.33
Total population	479,170,581	14,002	1

DATA USED TO ESTIMATE DR MODELS



DR MODELS IN EFSA (2017)



CONCLUSIONS

- The probability of a single CFU to cause illness in a specific host population is reflected in the parameter r
- This r parameter includes both the virulence of different *L. monocytogenes* isolates and the susceptibility of different human subpopulations
- r values range from 10^{-15} for < 65 yo without underlying conditions, to 10^{-12} for the most susceptible subpopulations, and can, when estimated for specific outbreaks with highly susceptible populations, be as high as 10^{-7}
- Pouillot et al. (2015) model, incorporating the virulence and susceptibility variability for 11 population groups, suggests that most human listeriosis cases are linked to the ingestion of food contaminated with medium to high ($3.5 - 7.5 \log_{10}$ CFU/serving) concentrations of *L. monocytogenes*
- Pouillot et al. (2015) model approach was used to assess an EU specific DR model