Dose response for *Listeria monocytogenes*

IAFP Webinar

Organized by:

Microbial Modeling and Risk Analysis PDG

All opinions and statements are those of the individual making the presentation and not necessarily the opinion or view of IAFP

Moderator

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- Wageningen University
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- Audio is via your computer speakers
- Questions should be submitted via the Text Chat section at the bottom of the screen (can be done during the presentations, handled at the end).

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Contact information for presenters

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Dr. Régis Pouillot

Former visiting scientist US Food and Drug Administration Division of Risk and Decision Analysis

Dr. Régis Pouillot worked as a visiting scientist for the US Food and Drug Administration Division of Risk and Decision Analysis until January 2017.

His personal research interests include the development of innovative models and data analyses for quantitative risk assessments of microbial and chemical hazards. He published numerous peer reviewed articles and contributed to major reports in this field.

He holds a Doctorate in Veterinary medicine, a Master of Public Health and PhD in Biostatistics from the University of Paris.

He was recently awarded as the 2016 “Outstanding Practitioner” of the Society for Risk Analysis in recognition for his exceptional contributions to the field of Risk Analysis.

Dose response for *Listeria monocytogenes*

What did we learn from recent outbreaks?

Régis Pouillot, DVM, PhD

IAFP MMRA PDG Webinar, June 1st 2017

Listeria monocytogenes

- Few complete outbreak data are available to derive a dose-response
  - Hispanic cheese outbreak in Los Angeles county, 1985
  - *Listeria monocytogenes* infection from butter in Finland for transplant patients, 1998-1999
  - …

Lyytikäinen *et al.*, J Infect Dis, 2000, Linnan *et al.*, N Engl J Med, 1988, FDA/FSIS 2003, FAO/WHO 2004

Specific issues with listeriosis

- Dose …
  - Long incubation period → Difficulties to find leftovers
  - Bacterial growth → Correspondence between the number of bacteria found in the sample and the actual quantity of ingested *L. monocytogenes*
  - Heterogeneity in the level of contamination → Did the cases ingested the most contaminated products?
- … Response
  - Heterogeneity in the response → the underlying conditions of the consumers might be more important than the dose

Recent Data Collection in US

- Focus on data collection
  - Celery Outbreak, TX, 2010
  - Cantaloupe Outbreak, Multistate, 2011
  - Caramel Apple, Multistate, 2015
  - Ice Cream, Multistate, 2015
  - …

The case of Celery

- Celery Outbreak, TX, 2010
  - 10 cases in inpatients of an hospital
    - Data on underlying health issues
  - Growth studies
  - Transfer studies
  - Limited prevalence and contamination level data

Knudson Gaul, L *et al.*, Clin Infect Dis, 2013, Sahu *et al.*, Food Control, 2017; Kaminski *et al.*, JFP, 2014

The case of Cantaloupe

- 2011 - Jensen farms cantaloupe outbreak
- 147 cases, 30 deaths across 28 States

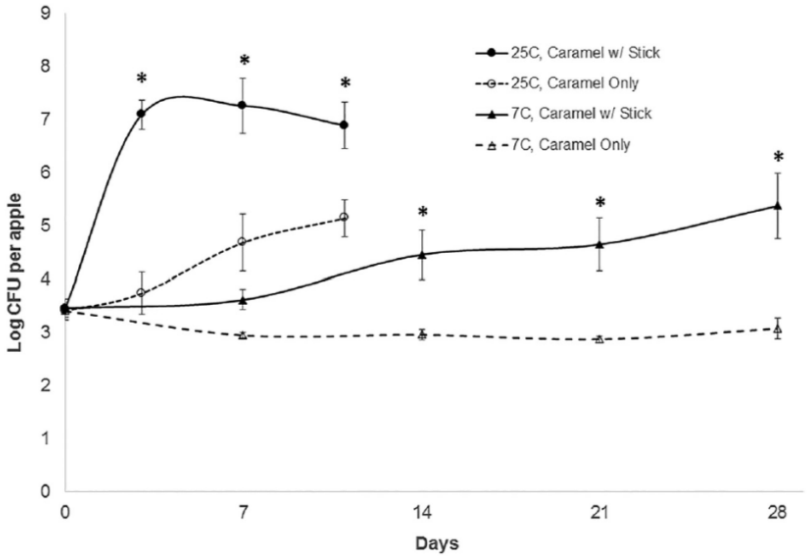
- No enumeration data

USDA photo by Scott Bauer. Image Number K7355-11.
http://www.ars.usda.gov/is/graphics/photos/k7388-11.htm

The case of the Caramel Apples

- 35 illness including
  - 11 associated with a pregnancy
  - 3 meningitis among otherwise healthy children aged 5-15
- Apple does not support growth (pH 3.2)
- Caramel does not support growth (low a_w)
- Caramel coated apple *with a stick* supports growth
  - Up to 7 $\log_{10}$ in few days at ambient temperature
- Actual level at time of consumption?

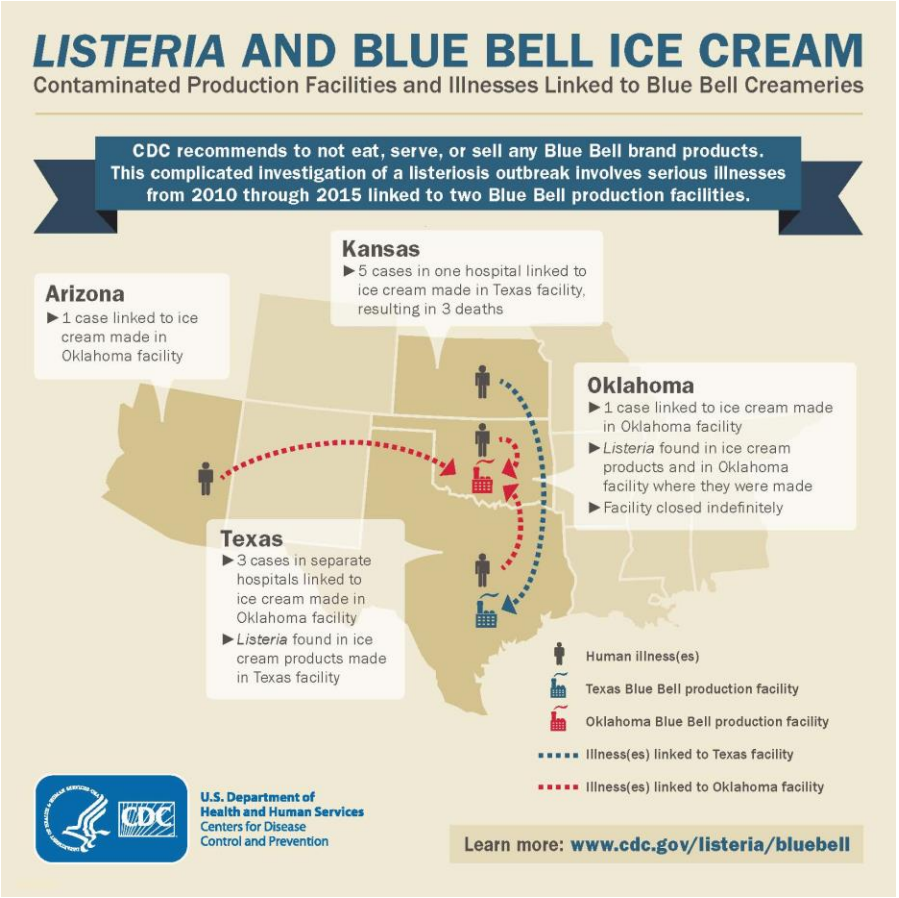
Photo: http://www.cdc.gov/listeria/outbreaks/caramel-apples-12-14/images/caramel-apple2-450px.jpg



CDC website, K. A. Glass *et al.*, *mBio* **6**, e01232-15 (2015).

The case of Ice-Cream

- 4 cases, linked to one product of factory A , observed in inpatients of a single hospital
  - one additional case in the hospital, but the strain was not recovered from ice cream
- 5 cases linked to a second factory (factory B)
- … over 5 years!



CDC website

The case of Ice-Cream

- FDA collected more than 10 ½ pallets of samples from the company's Factory A
  - FDA optimized enumeration methods for the contamination in these products using both MPN and direct plating methods
    - The MPN method used a 3 × 10 g, 5 × 1.0 g, 8 × 0.1 g and 8 × 0.01 g dilution scheme (3-5-8-8)
- FDA collected sales data
  - With address → Categorization → Hospitals, Schools, …

Chen *et al.*, JFP, 79(11) 2016; Chen *et al.*, IJFM, 241, 2017

Timeline

Jan 2010: First case linked to the brand

Sale log starting date: **Nov 7th, 2013**

Jan 2014: First case linked to the factory A: Patient #1

Mar 2014: Second case linked to the factory A: Patient #2

Product B available, tested positive: **May 21st, 2014**

Oct 2014: Third case linked to the factory A: Patient #3

Product A available, tested positive: **Nov 6th, 2014**

Product C available, tested positive: **Dec 8th, 2014**

Jan 2015: Fourth case linked to the factory A: Patient #4

Cleaning and overhauling of the production line: **Jan 2015**

Mar 13th, 2015: Products removed from the market

Pouillot *et al.*, EID 22(12) 2016

The 4 cases

- Onset ranges from January 2014 through January 2015 (over one year)
- All 4 were >67 and < 84 years of age
- All 4 had underlying conditions that contributed to compromised immune function before exposure
- Ate the product *via* milk shakes
  - Two patients had two milkshakes
  - One patient had three milkshakes
  - (unrecorded data for the fourth one)

Pouillot *et al.*, EID 22(12) 2016

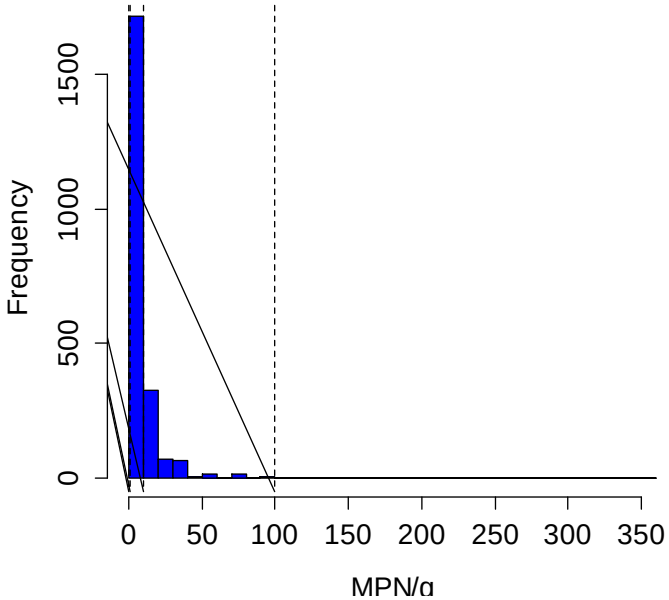
Enumeration data

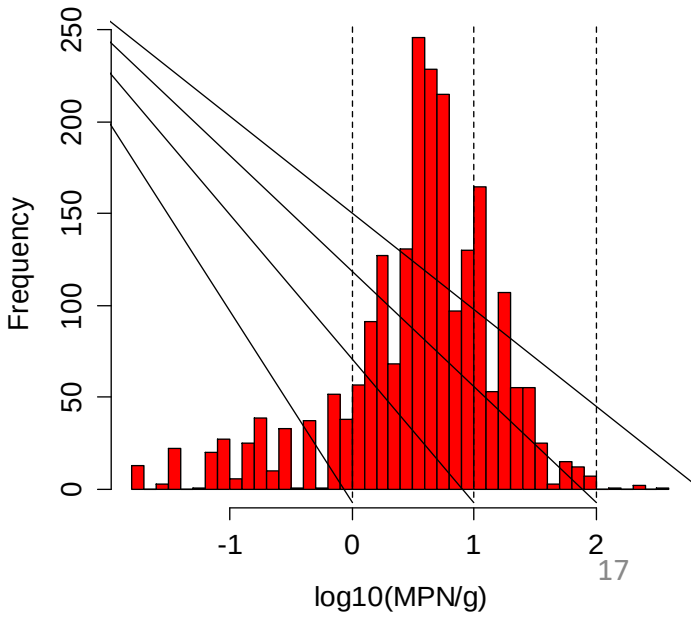
- "Product A", from factory A
  - 2,290 samples of Product A tested

    all but 13 samples were positive
    (99.4% positive)

  - Highly consistent low contamination levels
    - 58% below 5 MPN/g
    - 77% below 10 MPN/g
    - 92% below 20 MPN/g
    - 98% below 50 MPN/g
    - 99.8% below 100 MPN/g

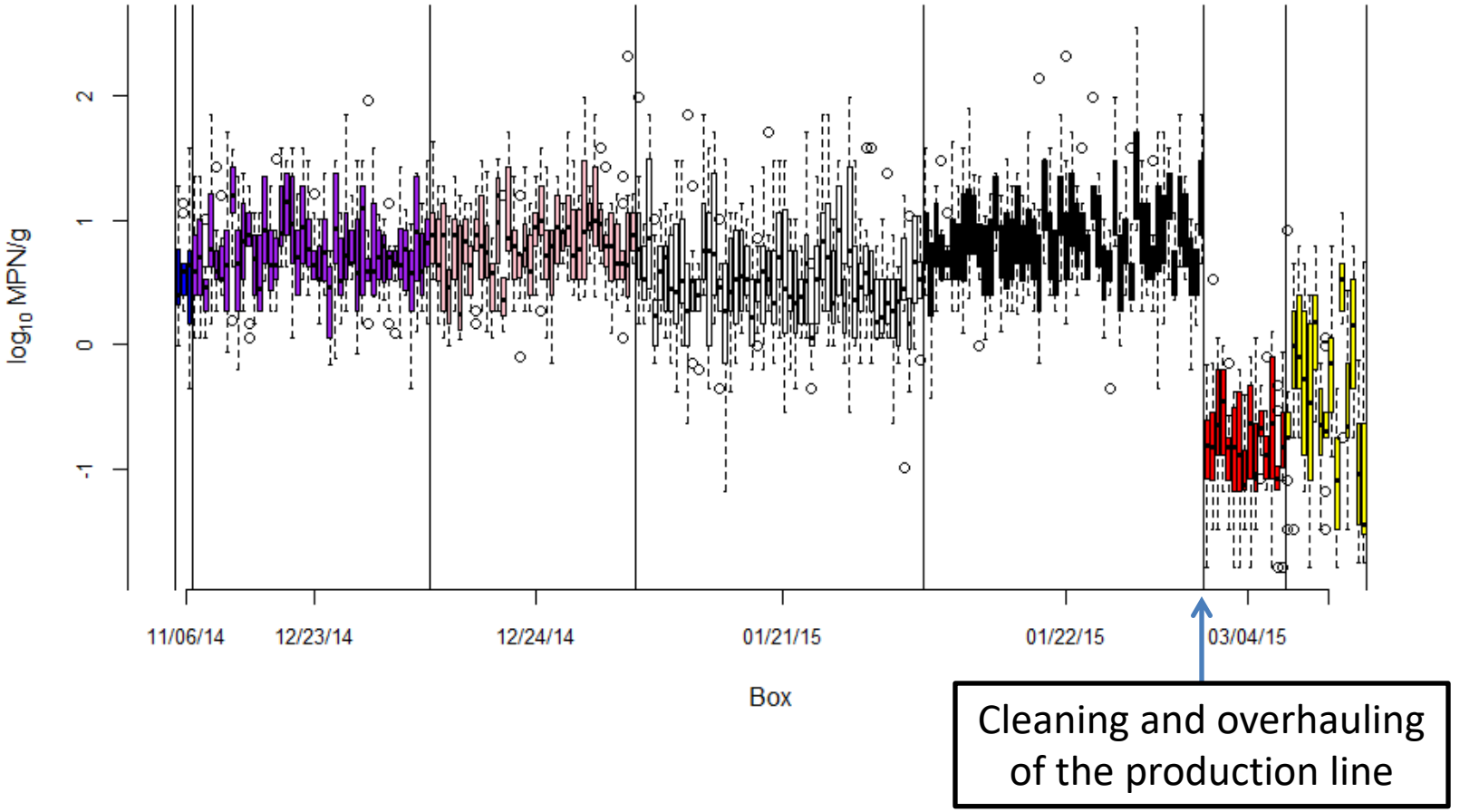
  - 4 samples > 100 MPN/g*
    - one >208 MPN/g (direct plating: 357 cfu/g),
    - two = 208 MPN/g (direct plating: 142 cfu/g and Non Available),
    - one 139 MPN/g (direct plating: 177cfu/g)



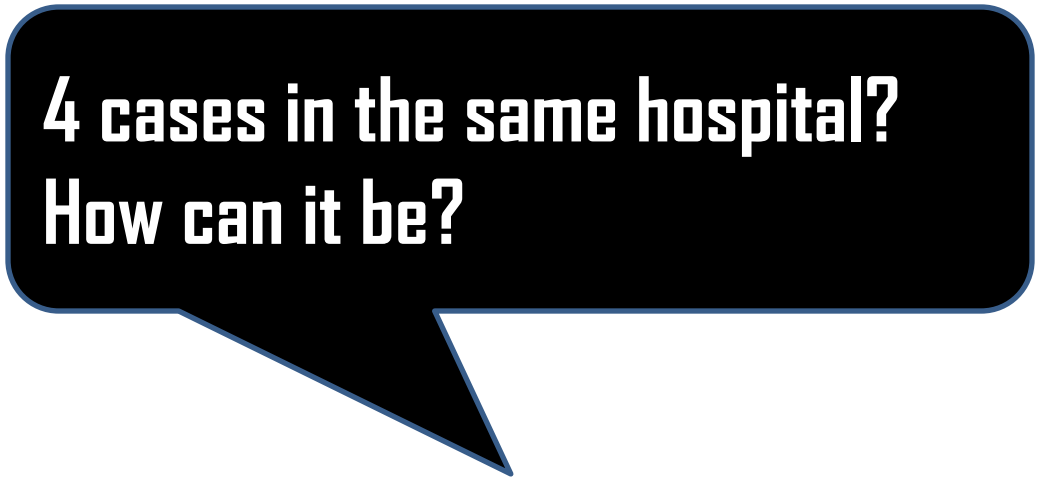


Chen *et al.*, J Food Prot 79: 1828:45

Enumeration of *L. monocytogenes* in Different Lots of "Product A"



Chen *et al.*, J Food Prot 79: 1828:45

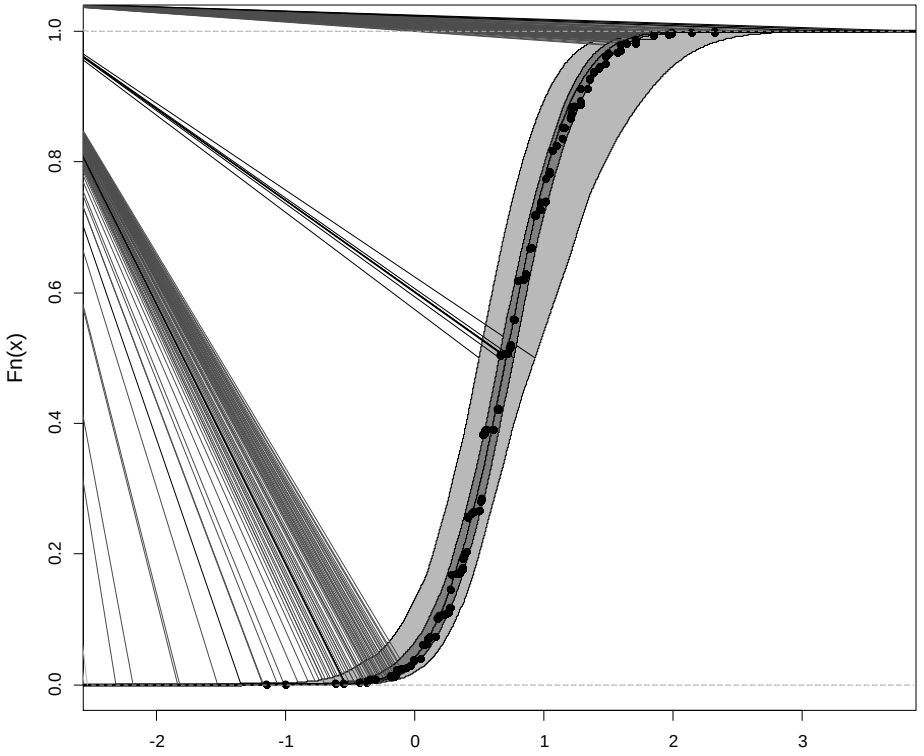


- Raises the concern of a systematic problem within the hospital **BUT**
- It appears that this hospital bought 55% of "Product A" sold to hospitals
  - The probability to have the 4 cases in this particular hospital was not that low (9%, actually)

Pouillot *et al.*, EID 22(12) 2016

- Under the assumption of no growth, the probability to have a high level of contamination of the product A was low…
  - But not null
- Product A → Milk Shake
  - Growth in milk shake: limited (Chen *et al.*, 2016)
  - Contamination of the milk shake machine: possible (the machine was "inoculated" multiple times, every days, during a long period of time), but not detected
- Answer: probably yes… but impossible to say.

Did the cases eat a low number of bacteria ?



Pouillot *et al.*, EID 22(12) 2016

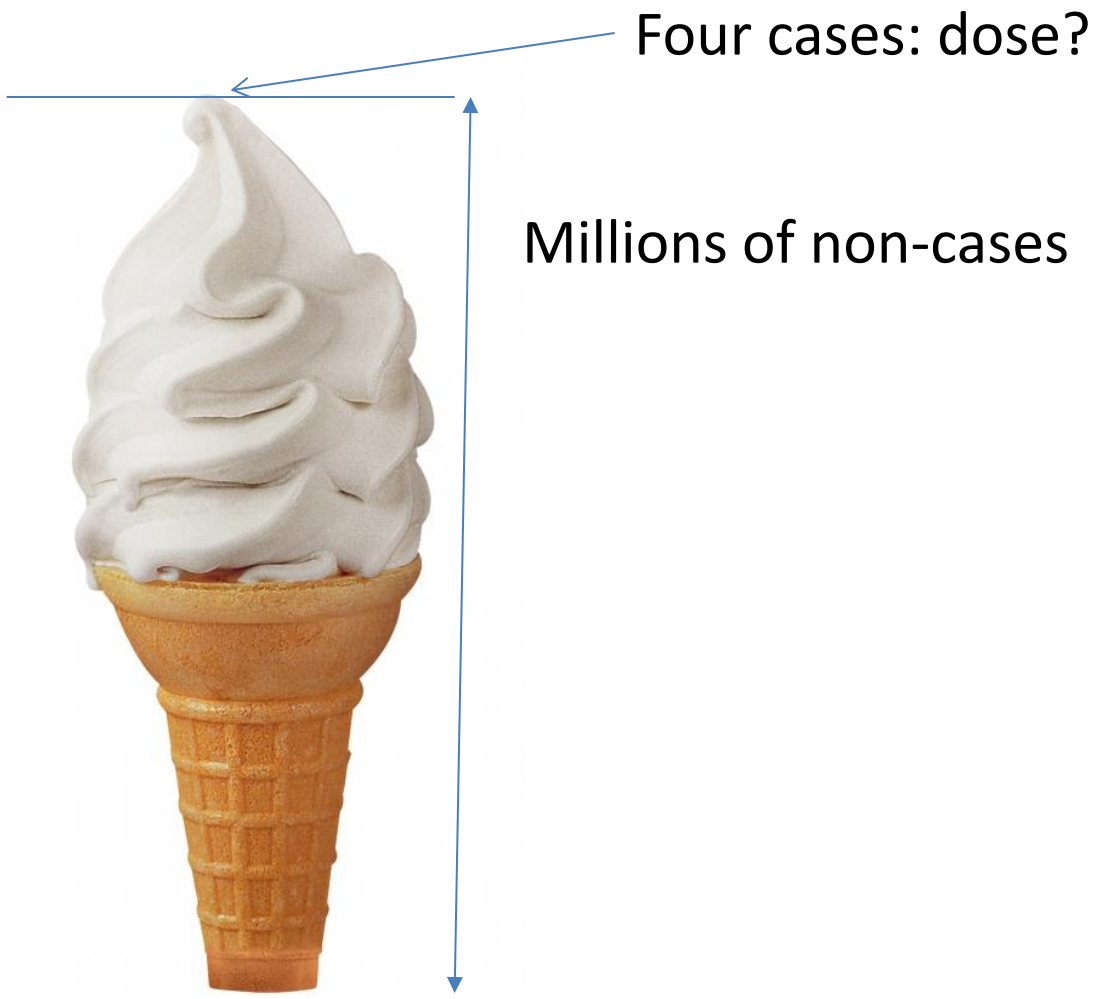
Did some individuals and susceptible individuals eat contaminated products and did not get sick?

- Best selling ice cream brand in the US in 2014*,
- 100% contaminated products during months / years
- Our estimates
  - **Millions** of *contaminated* servings sold to the population
  - **Tens of thousands** *contaminated* servings sold to pregnant women: no case identified
  - **Thousands** *contaminated* servings sold to highly susceptible population $\rightarrow$ 4 identified cases

- Answer: Yes, a lot!

* source: wikipedia

The tip of the ice cream



Back to the dose response

- What is actually needed to derive a dose-response from outbreak data

  Ingested Dose $\rightarrow$ Outcome (sick, not sick) ?

  Do we need the actual dose for each consumer? **No**

- Exponential dose response

  Prob(infection|dose) = 1 – exp(- r × dose)

$$r_{\text{subpopulation}} = \frac{\text{nb of cases in the subpopulation}}{\text{nb of } \textit{L. monocytogenes} \text{ ingested by the subpopulation}}$$

See supplemental material, Pouillot *et al.*, EID, 22(12) 2113:9

- Number of cases in the population
  - 4 in the highly susceptible population, observed

- Number of *L. monocytogenes* ingested by the population

  = number of servings in the population × average number of *L. monocytogenes* per serving
  - number of servings: function of the starting date of the contamination: at least one year, maybe 5 or more?
  - Average number of *L. monocytogenes* per serving
    - Robust estimation from the thousands of tested samples (if we assume that the least months are representative of the whole episode)
    - … if no growth

Results

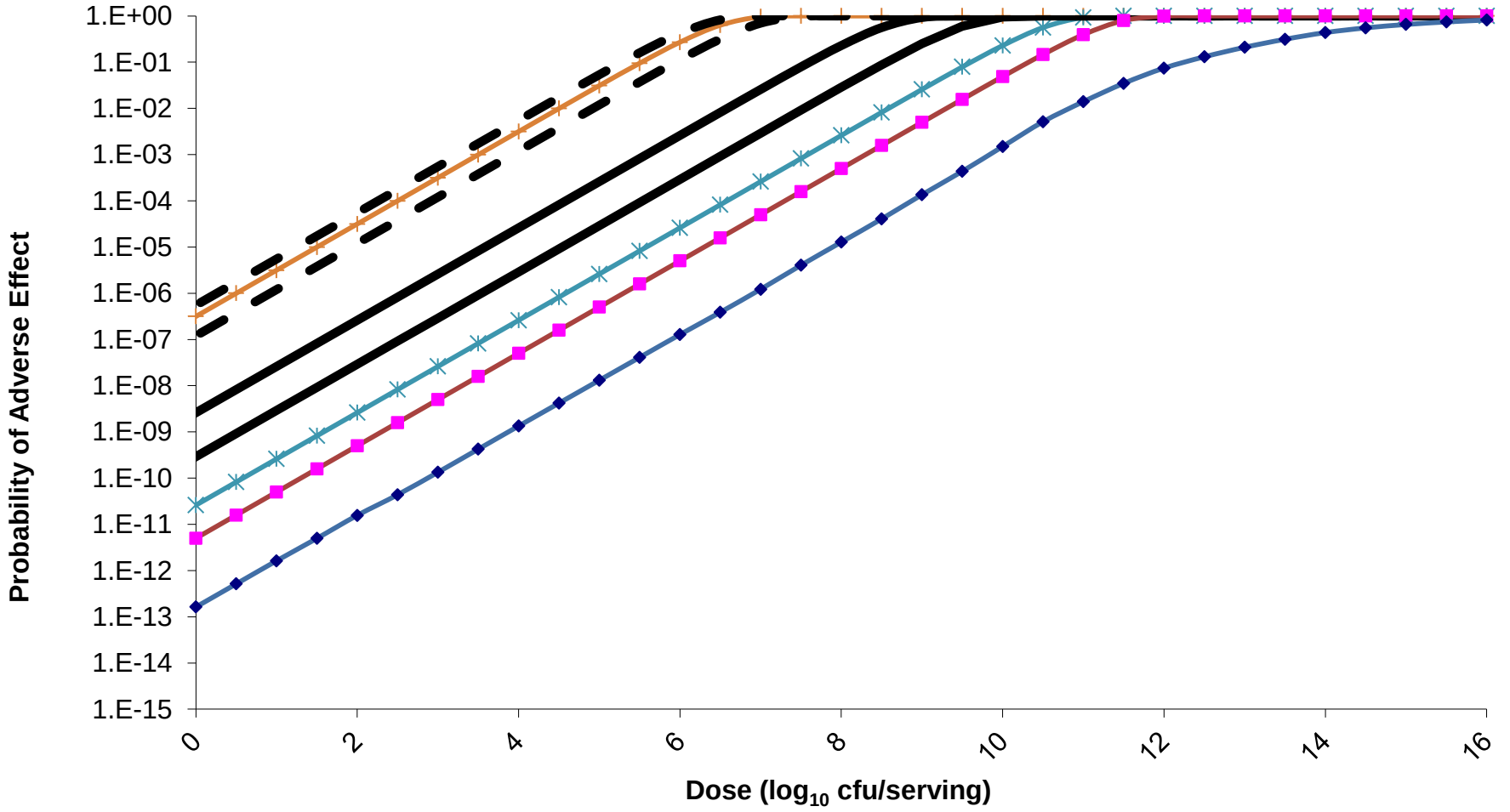
Scenario model		Whole population (4 cases)	Highly susceptible (4 cases)	Pregnant (0 case)	Age > 75 y (4 cases)
Lower	Nb of ingested cells	1.5×10^{9}	7.7×10^{6}	2.2×10^{7}	1.2×10^{8}
	***r* parameter**	**2.6×10^{-9}**	**5.5×10^{-7}**	**$<2.3 \times 10^{-8}$**	**1.7×10^{-8}**
Upper		1.4×10^{10}	3.3×10^{7}	2.0×10^{8}	$<1.0 \times 10^{9}$
	***r* parameter**	**2.9×10^{-10}**	**1.2×10^{-7}**	**$<2.6 \times 10^{-9}$**	**1.9×10^{-9}**

Compare to FAO/WHO : $r = 3.2 \times 10^{-7}$ from the Finnish butter outbreak

$r = 2.6 \times 10^{-11}$ from the Hispanic cheese outbreak

$r = 5.0 \times 10^{-12}$ from epidemiological data

Pouillot *et al.*, EID, 22(12) 2113:9


1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
1.E-08
1.E-09
1.E-10
1.E-11
1.E-12
1.E-13
1.E-14
1.E-15
Probability of Adverse Effect
0
2
4
6
8
10
12
14
16
Dose (log10 cfu/serving)
Butter
Hispanic-style Cheese
Ice cream, All populations, lower estimate
Ice cream, All populations, higher estimate
Ice cream, Highly Susceptible population, lower estimate
Ice cream, Highly Susceptible population, higher estimate
FAO/WHO
HHS/USDA

Conclusions

- We'll probably **never** get better data
  - Impossible to know for sure what was the ingested dose of specific individuals
  - Not needed to derive a dose response model!
- **Paradox**: more information on the non-cases than on the cases.
- Corresponding dose-response model **comparable to previous dose-response models developed from outbreaks**
  - Other outbreaks: limited diffusion of products contaminated at relatively high level
  - Here: large distribution of products contaminated at low level
- Probability of infection following the ingestion of a given dose **higher than for models derived from epidemiological data**
  - Bias when working on outbreaks: what about large diffusion of contaminated products that never lead to a recorded outbreak?

Keys for the Risk managers

- A no-growth product, with a very low average level of contamination (8 cfu/g) **did** cause an "outbreak"
  - Directly **OR** indirectly
    - It is likely that most patients were exposed to ice cream with < 100 cfu/g
    - A high dose can't be excluded
      - "inoculation" of the shaker at each serving. Biofilm? Growth?
- The large distribution of a no-growth product, with a low average level of contamination **didn't** cause a massive outbreak
- The underlying health of the patient, cell-mediated immune status, medications and repeated exposure (?) may be more important than the dose
- Sufficient for risk management?
    - Few products that support growth (e.g. cheese) $\rightarrow$ Outbreak
    - Very large distribution of a contaminated product that does not support growth (e.g. ice-cream) $\rightarrow$ Outbreak (directly or not)

Thank you

Co-authors of the manuscripts and everyone involved in the data collection for these outbreaks

Prevalence and Level of *Listeria monocytogenes* in Ice Cream Linked to a Listeriosis Outbreak in the United States

YI CHEN,[1]*† LAUREL S. BURALL,[2]† DUMITRU MACARISIN,[1]† RÉGIS POUILLOT,[3] ERROL STRAIN,[3] ANTONIO J. DE JESUS,[1] ANNA LAASRI,[1] HUA WANG,[1] LAILA ALI,[1] APARNA TATAVARTHY,[1] GUODONG ZHANG,[1] LIJUN HU,[1] JAMES DAY,[1] JIHUN KANG,[2] SURASRI SAHU,[2] DEVAYANI SRINIVASAN,[2] KARL KLONTZ,[3] MICKEY PARISH,[4] PETER S. EVANS,[1] ERIC W. BROWN,[1] THOMAS S. HAMMACK,[1] DONALD L. ZINK,[4] AND ATIN R. DATTA[2]*

Comparative evaluation of direct plating and most probable number for enumeration of low levels of *Listeria monocytogenes* in naturally contaminated ice cream products

Yi Chen [a,*,1], Régis Pouillot [b,1], Laurel S. Burall [c], Errol A. Strain [b], Jane M. Van Doren [b], Antonio J. De Jesus [a], Anna Laasri [a], Hua Wang [a], Laila Ali [a], Aparna Tatavarthy [a], Guodong Zhang [a], Lijun Hu [a], James Day [a], Ishani Sheth [a], Jihun Kang [c], Surasri Sahu [c], Devayani Srinivasan [c], Eric W. Brown [a], Mickey Parish [d], Donald L. Zink [d], Atin R. Datta [c], Thomas S. Hammack [a], Dumitru Macarisin [a]

Infectious Dose of *Listeria monocytogenes* in Outbreak Linked to Ice Cream, United States, 2015

Régis Pouillot, Karl C. Klontz, Yi Chen, Laurel S. Burall, Dumitru Macarisin, Matthew Doyle, Kären M. Bally, Errol Strain, Atin R. Datta, Thomas S. Hammack, Jane M. Van Doren

Among other papers…

Prof. Fernando Perez Rodriguez, University of Córdoba (Spain).

Prof. Fernando Perez Rodriguez undertook his degrees in Biological Science and in Food Science and Technology from the University of Córdoba in 1999 and 2002, respectively. He completed his PhD from the University of Córdoba (2007).

He has published over 70 peer-reviewed papers, book chapters, and books concerning predictive microbiology, quantitative risk assessment, and nutrition in foods. Fernando is the leading manager and designer of the on-line risk assessment supporting tool “MicroHibro” and has actively participated in the development of the tool “Baselineapp”.

Due to his expertise, he has participated as a scientific advisor in several expert panels at a national and international level, in the Spanish Food Safety Agency and as a Risk Assessment Expert of the European Food Safety Authority (EFSA) and Food and Agriculture Organization (FAO) providing scientific advice and reports.

He is a member of the International Association for Food Protection and the Spanish Society of Microbiology. He is a professor for Food Microbiology and Hygiene at the University of Córdoba (Spain).

Selection of a *Listeria monocytogenes* dose-response model for risk assessment in ready-to-eat products

Dr. Prof. Fernando Perez Rodriguez
Department of Food Science and Technology
University of Córdoba (Spain)

Outline

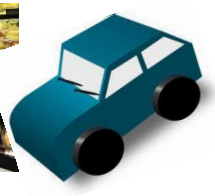
1. Risk assessment scheme
2. D-R models: types and approaches
3. Review of *Listeria* D-R models
4. Selection of *Listeria* D-R models for QMRA
5. D-R model integration into QMRA

Quantitative Microbial risk assessment

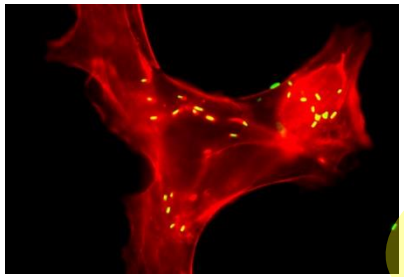
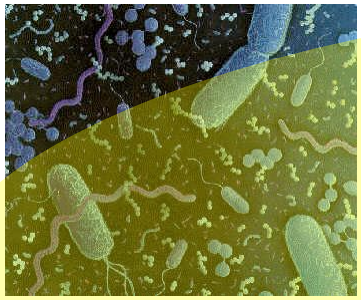
EXPOSURE ASSESSMENT



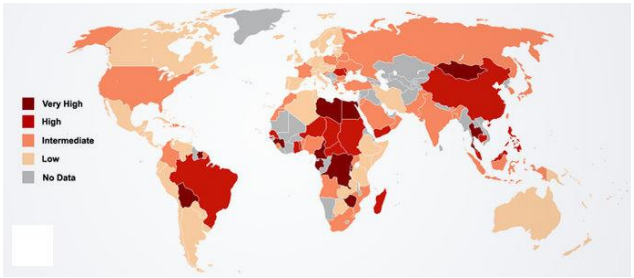


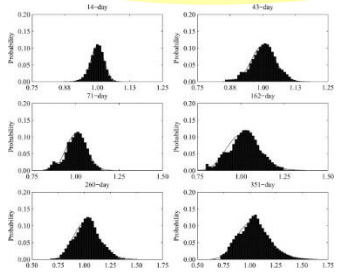



HAZARD CHARACTERIZATION

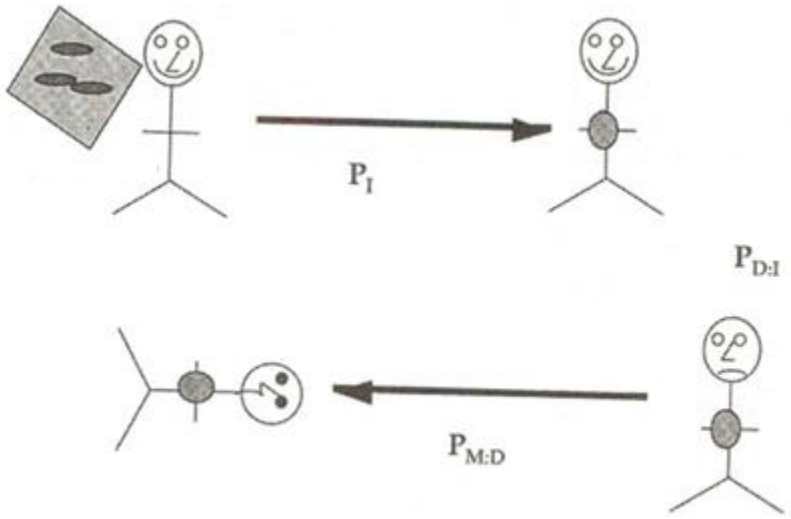

RISK CHARACTERIZATION





Dose-response (D-R) model

- Mathematical function that may be used to describe the relationship between dose and the magnitude of a response on a continuous scale in an individual.



Adapted from Haas et al. 1999

Approaches for D-R modelling

- "Black box" models:

$$f(\text{P x C x Freq x Serv}) = \text{Surveillance}$$

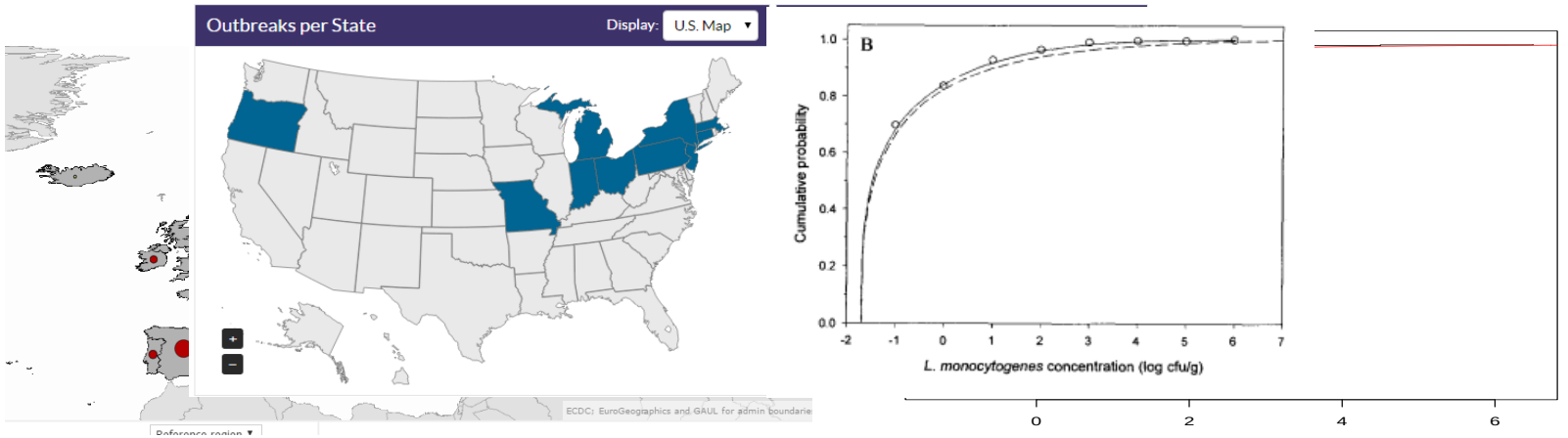
- knowledge-based model: the extent and severity of the disease as a result of the ingestion of cells by an individual or a population is known.

- Mixture model: in some cases, a mixture of the previous two models is created, e.g. a surrogate animal model "calibrated" with the actual incidence of the disease in a human population.

D-R modelling

Black box" models:

- Empirical models are extensively applied in risk assessment, assuming a distribution of population tolerance: **Limited in case of extrapolation**



Surveillance = f(P, C, Freq, Serv)

D-R models

- Mechanistic models are potentially **more flexible**: on a set of biologically plausible, mechanistic assumptions.
- They should account for the host-pathogen-food interaction (Hoelzer et al., 2013)
- Mechanistic models are based on the Independence of Action of microorganisms:
- No-theshold mechanistic models are the most frequent models

Next-generation microbial D-R models

- Key-event dose-response models (Buchanan et al. 2009)

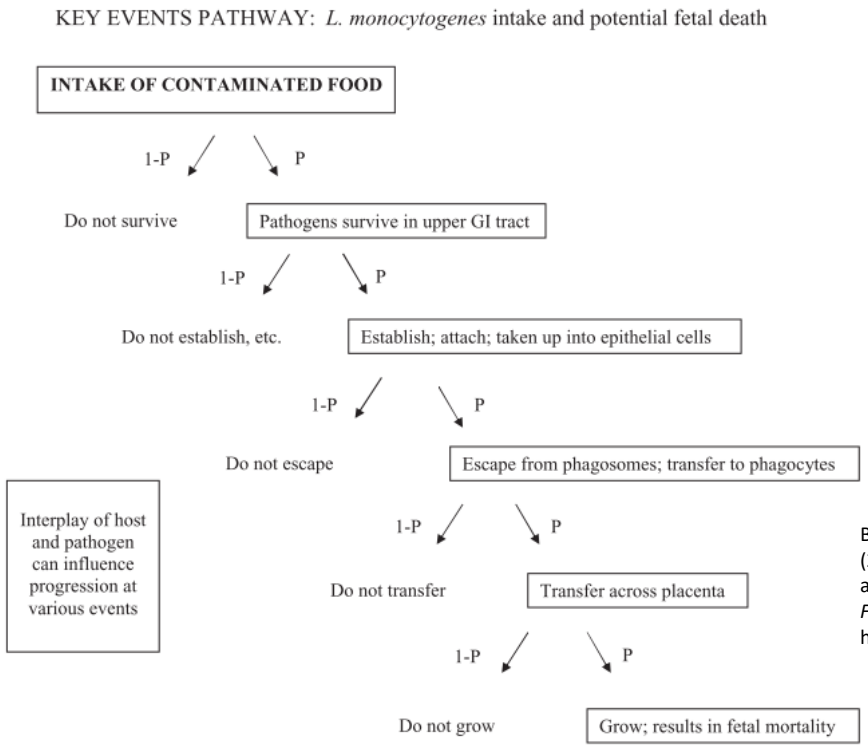


Figure 1 Key biological events occurring between intake of pathogen and the specific effect of concern (fetal listeriosis). At each event, both host and pathogen factors can be examined with regard to: i) how they may influence probability of progression toward the effect of concern (i.e., how they affect the number of organisms exiting a given event, given the number of organisms entering the event), and ii) how they influence inter- and intra- host response variability.

Buchanan, R. L., Havelaar, A. H., Smith, M. A., Whiting, R. C., & Julien, E. (2009). The Key Events Dose-Response Framework: its potential for application to foodborne pathogenic microorganisms. *Critical Reviews in Food Science and Nutrition*, *49*(8), 718–28. https://doi.org/10.1080/10408390903116764

Listeriosis

L. monocytogenes is a psychrotropic microorganism able to produce a foodborne diseases

Listeriosis is mostly related to relatively high doses and

Elderly population (>64) is most affected group, particularly >84 year (ECDC/EFSA, 2016)

In 2014: “EU case fatality was 17.7% among the 1,524 confirmed cases with known outcome”

D-R models for *L. monocytogenes*

Pathogen	Host	Food Matrix
• Virulence of strains with/without PMSC in *inlA*.	• Outbreak data, species differences in pathophysiology, guinea pigs and rhesus monkey dose-response data	• Prevalence and concentration of strains with/without PMSC in *inlA*
• Determinants of virulence variability among strains: fixed genetic determinant, transient determinant (e.g. stress response) Differential gene expression as a function of the environment (e.g. food)	• Improved outbreak data • New animal models • Better understanding of determinant of susceptibility • Alternative models	• Food implicated in outbreaks; characterization of contamination patterns, representativeness and accuracy of count data
• D-R data for strains with varying virulence • Association of strains with clinical manifestation (e.g. meningitis) • Growth and concentration *of L. monocytogenes* in the intestinal lumen. • Impact of *L. monocytogenes* gene expression at each step of infection	• Better understanding of *L. monocytogenes* pathophysiology (role microbiota) • Better understanding of host susceptibility	• Food characteristics modulating *L. monocytogenes* gene expression • Food characteristics related to listeriosis and listeria growth • Identifying infective dose and concentration in outbreaks.

based on the Dose-Response Workshop outcomes (adapted from Hoelzer et al. (2013)).

Available | Data need | Long-term

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Review of D-R models for *L. monocytogenes*

- Differences in the population groups
  - Low-risk group vs. High risk group
  - Age-based groups: Intermediate-age*, Elderly (over 60-65) and Pregnant
  - Elderly, pregnant and immunocompromised population
- Different r-values (point-estimates)
- Mostly USA-originated D-R models
- Endpoint: 80% illness, infection (animals) and death

Review of D-R models for *L. monocytogenes*

- Different mechanistic models in literature:
  - Exponential dose-response model (77 %)
  - Weibull-gamma model (12%)
- Specific dose-response model developed by internationally recognized institutions:
  - FDA/FSIS (2003)
  - WHO (2004)
- FDA/FSIS (2003) has been employed in 21 % risk assessments for *L. monocytogenes*
- WHO (2004) has been included in 32 % of studies.

D-R models for *L. monocytogenes*

The exponential form of the DR model relationship is mostly preferred due to

- Mechanistic, it does not present threshold,
- it is a one-parameter model,
- and it has been widely used by different organizations including FAO/WHO and FDA/FSIS

Exponential dose-response model

$$P(\text{ill};\ d,\ r) = 1\text{-}\exp(\text{-}rd)$$

where “ill” stands for “illness”, “d” refers to “dose”, and r is the probability of developing listeriosis from the ingestion of one bacteria cell in a given specific serving.

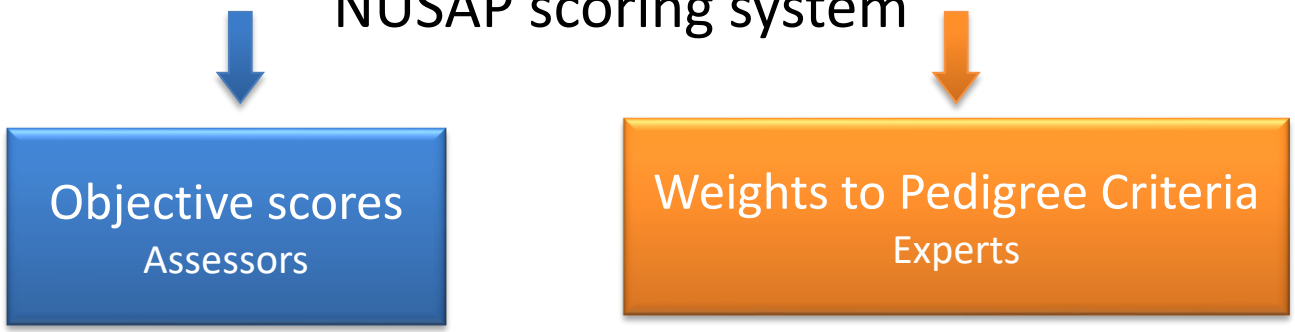
Selection of D-R models for risk assessment

Tool to evaluate the quality of the Exponential dose-response models currently available:

Application of Numeral Unit Spread Assessment Pedigree (NUSAP) system

The NUSAP system (Boone et al., 2009) is intended to assess data quality resulting from uncertainties that are hard to quantify such as methodological and epistemological uncertainties, and that are not systematically taken into account in scientific studies.

NUSAP scoring system



Selection of D-R models for risk assessment

Pedigree criteria

Proxy:

- Year of publication of the dose-response model.
- Geographical origin of primary data. Not applicable for animal models.

Empirical basis:

- Primary source of data.
- Number of independent sources for the primary source of data.
- Number of subpopulation groups from which data were analysed.

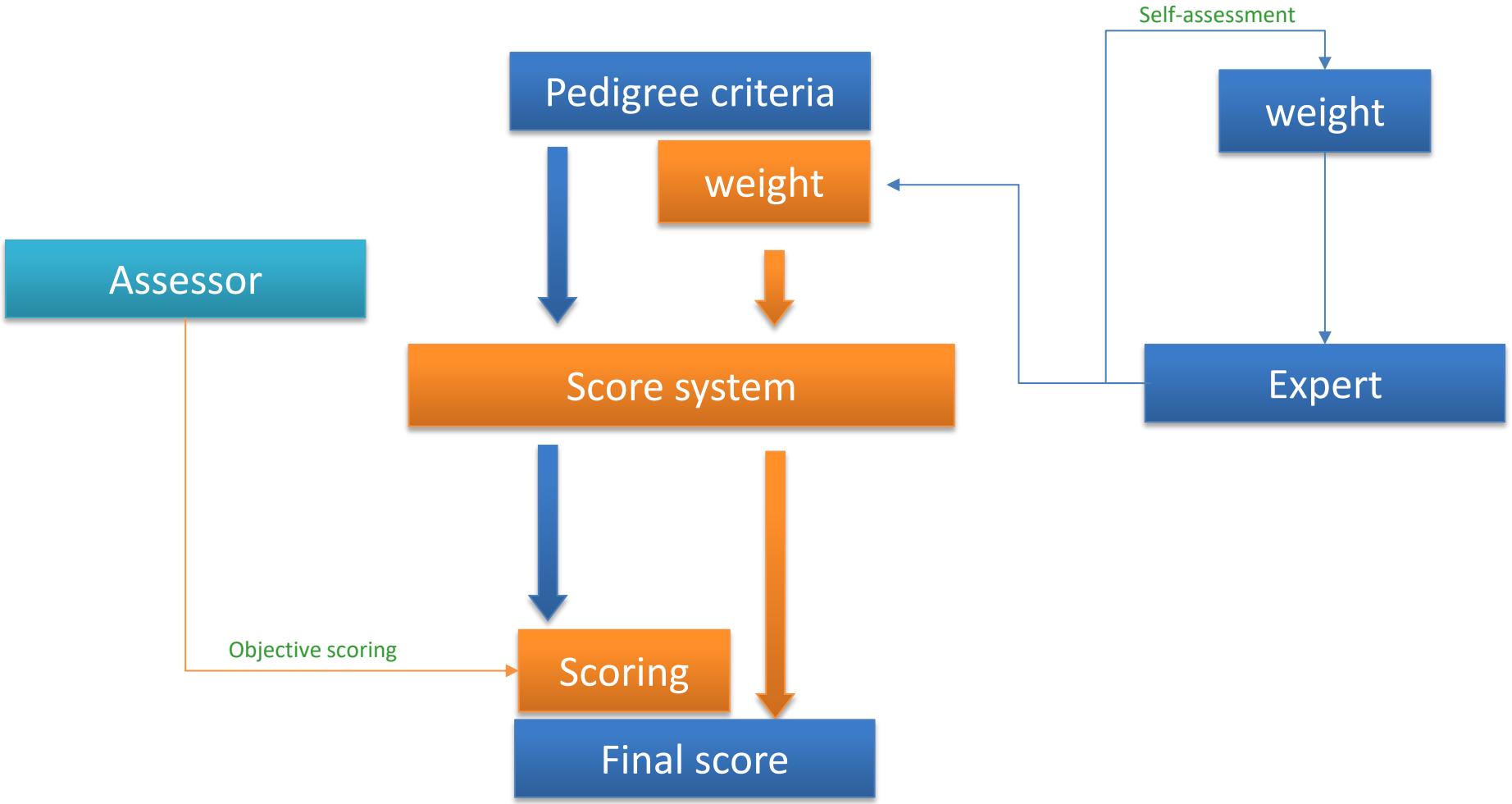
Methodological rigor

- Inclusion of variability and uncertainty.
- Statistical analysis. Not applicable for Buchanan et al. (1997) approach.
- Number and descriptions of endpoints.
- Publication source.

Validation:

- Validation of the dose-response model with other datasets.

Selection of D-R models for risk assessment



Selection of D-R models for risk assessment

Example with "proxy":

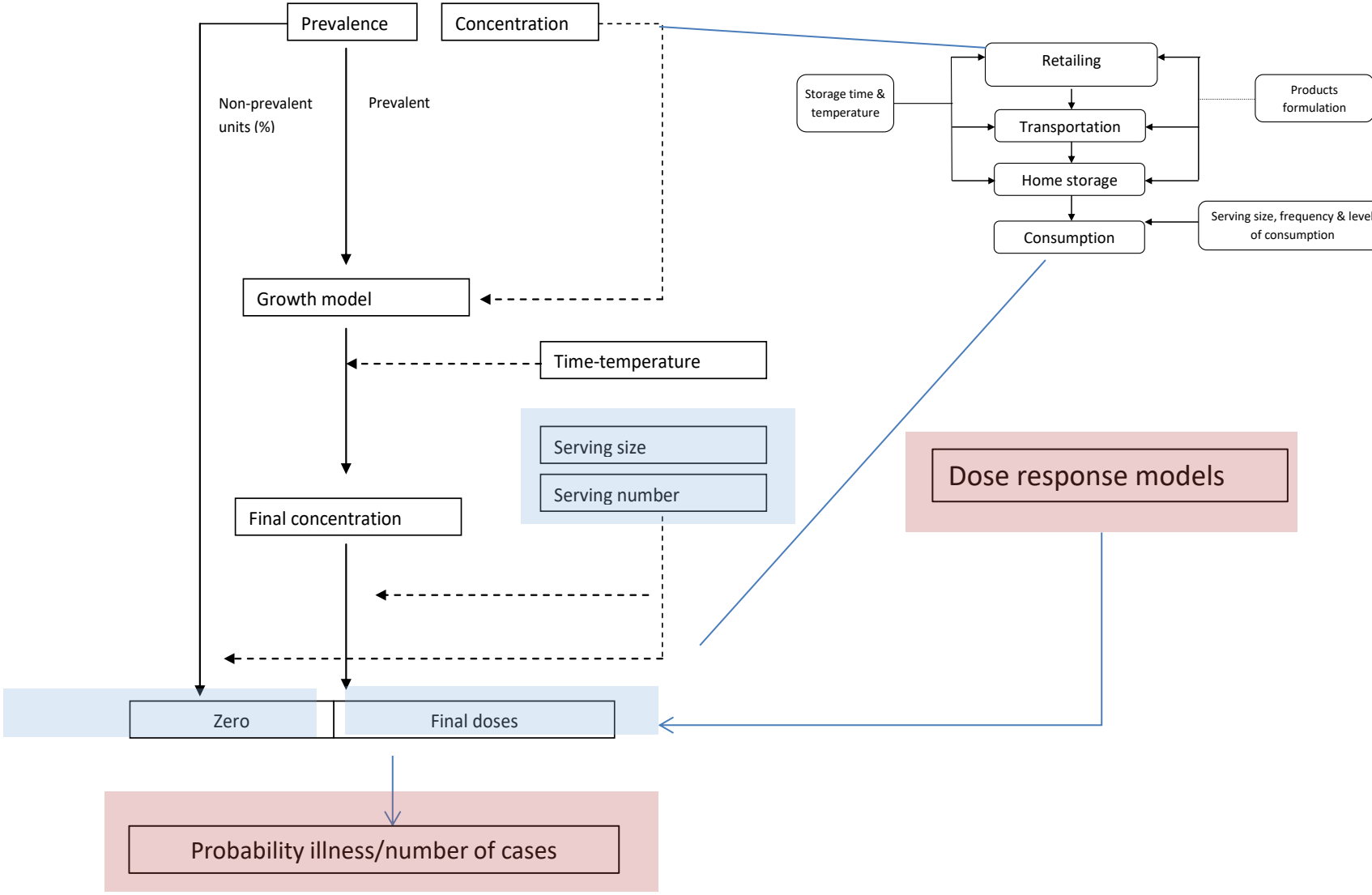
PEDIGREE CRITERIA SCORES	Proxy	
	Time	Space
Score: 4	Exact measure of the desired quantity (e.g., measurements from the same geographically representative area as that being investigated)	
	Data from the last 5 years (measured, if not available publication date).	Data from more than 1 European country.
Score: 3	Good fit or measure (e.g., measurements used from another geographical area but representative)	
	Data from the last 10 years (measured, if not available publication date).	Data from 1 European country.
Score: 2	Well correlated but not measuring the same thing (e.g., large geographical differences, less representative)	
	More than 10 years old study.	Data from US, Canada or NZ.
Score: 1	Weak correlation (e.g., very large geographical differences, low representativeness)	
	More than 20 years old.	Data from other countries.

Selection of D-R models for risk assessment

Outcome:

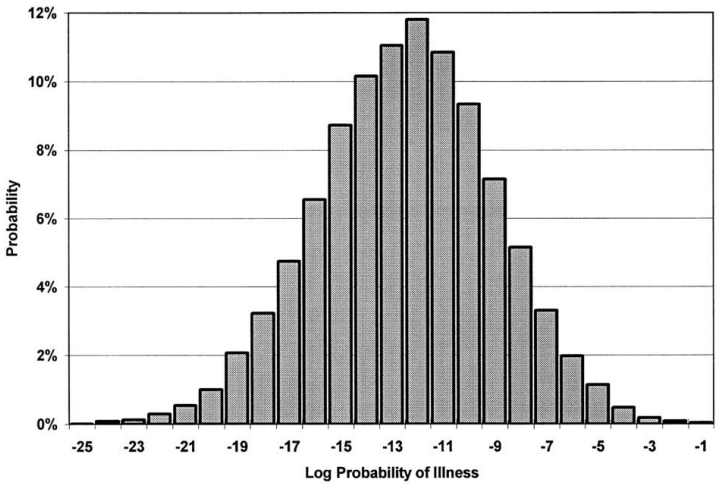
- Arithmetic *versus* geometric sequence (arithmetic sequence, i.e. 1, 2, 3 and 4).
- General agreement in the difficulty of FDA/FSIS model to be implemented; the model is neither readily reproduced nor readily defined
- the use of two dose-response models: Pouillot et al. (2015), representing a novel approach to describe *L. monocytogenes* dose-response relationship; and FAO/WHO (2004), an institutional approach internationally recognized and easy to reproduce.

D-R models into risk assessment



D-R models into risk assessment

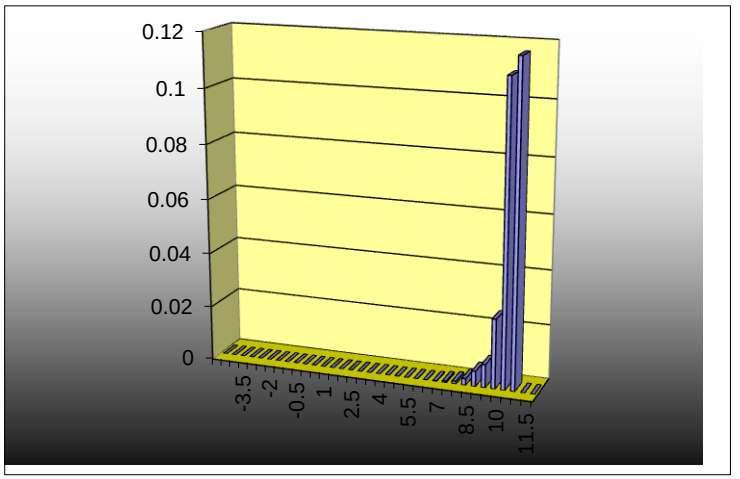
Individual risk:



Probability distribution for probability of illness from a single hamburger meal predicted by the *E. coli* O157:H7 Process Risk (Adapted from Cassin et al. 1998)

$Pill_i$ = $Prevalence_i$ x $Dose_i$ x r-value

Population risk:

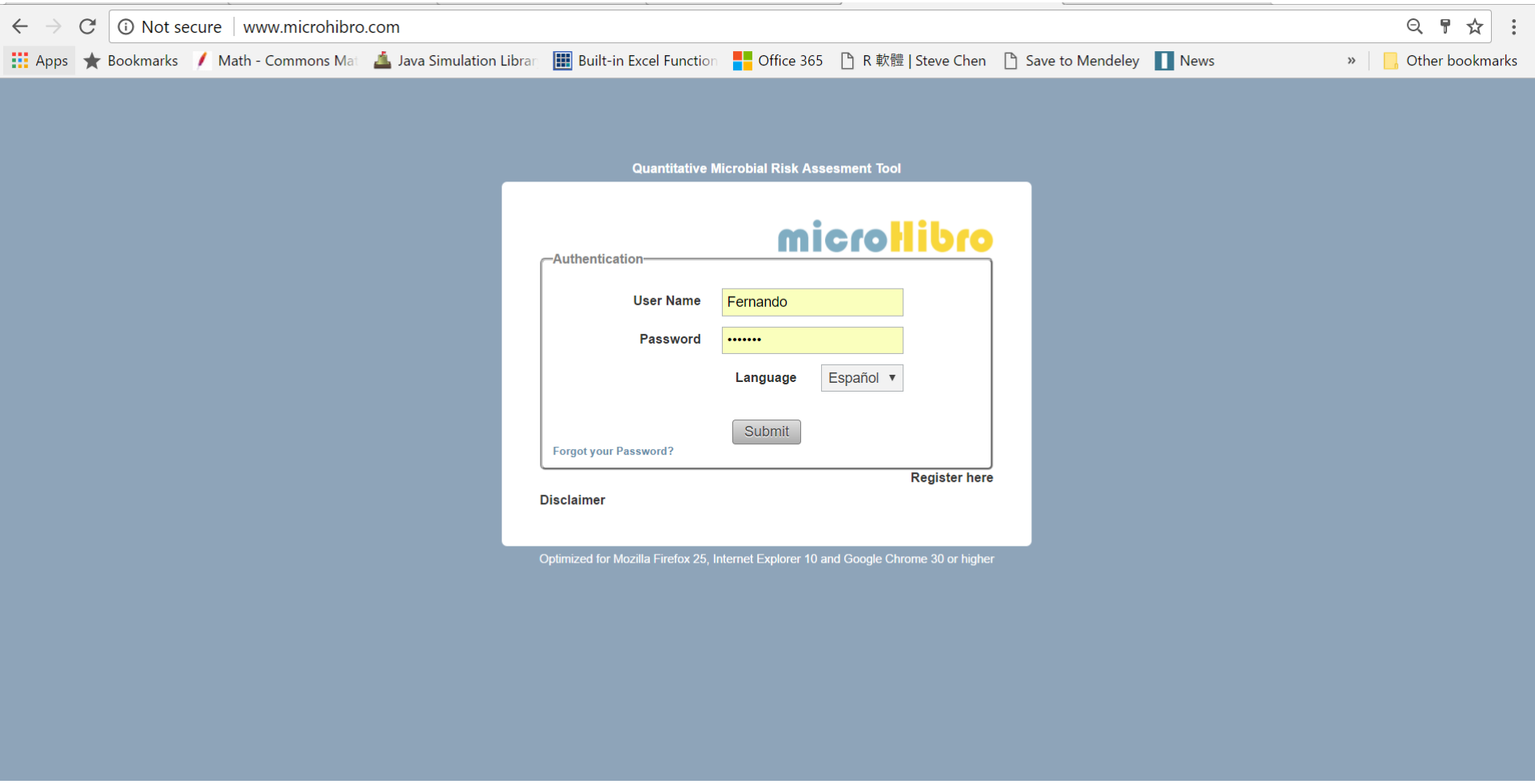


Integration of probability distribution for the probability of illness for the whole population (total number of exposures)

$$cases = \sum_{n=1}^{23} \pi_n \cdot P \cdot N \cdot f_n = \sum_{n=1}^{23} D_n \cdot r \cdot P_{ill_i} \cdot N \cdot f_n = P \cdot N \cdot r \sum_{n=1}^{23} D_n \cdot$$

$$\sum_{i=1}^{m} P_{ill_i}$$

D-R models into risk assessment



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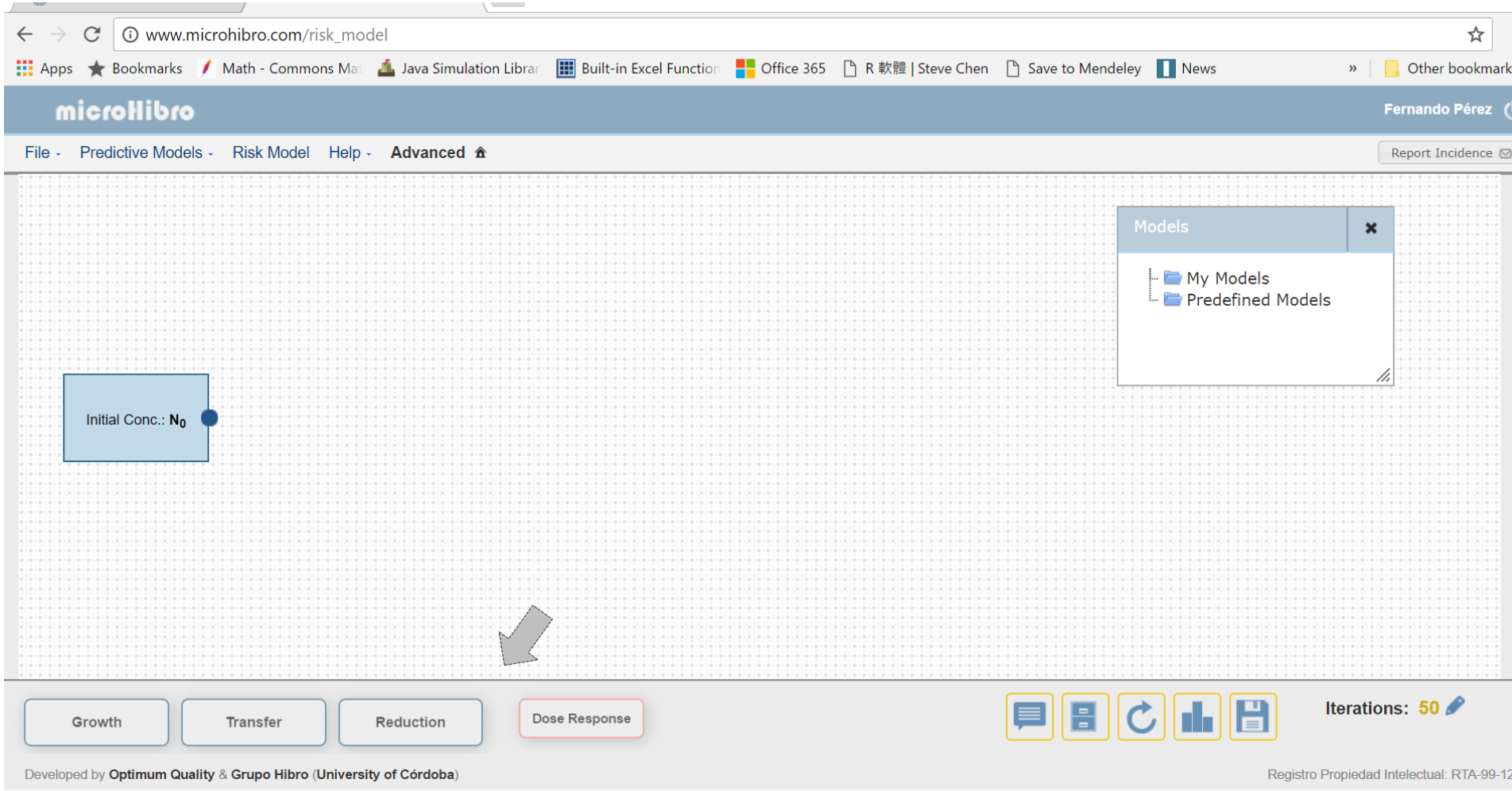
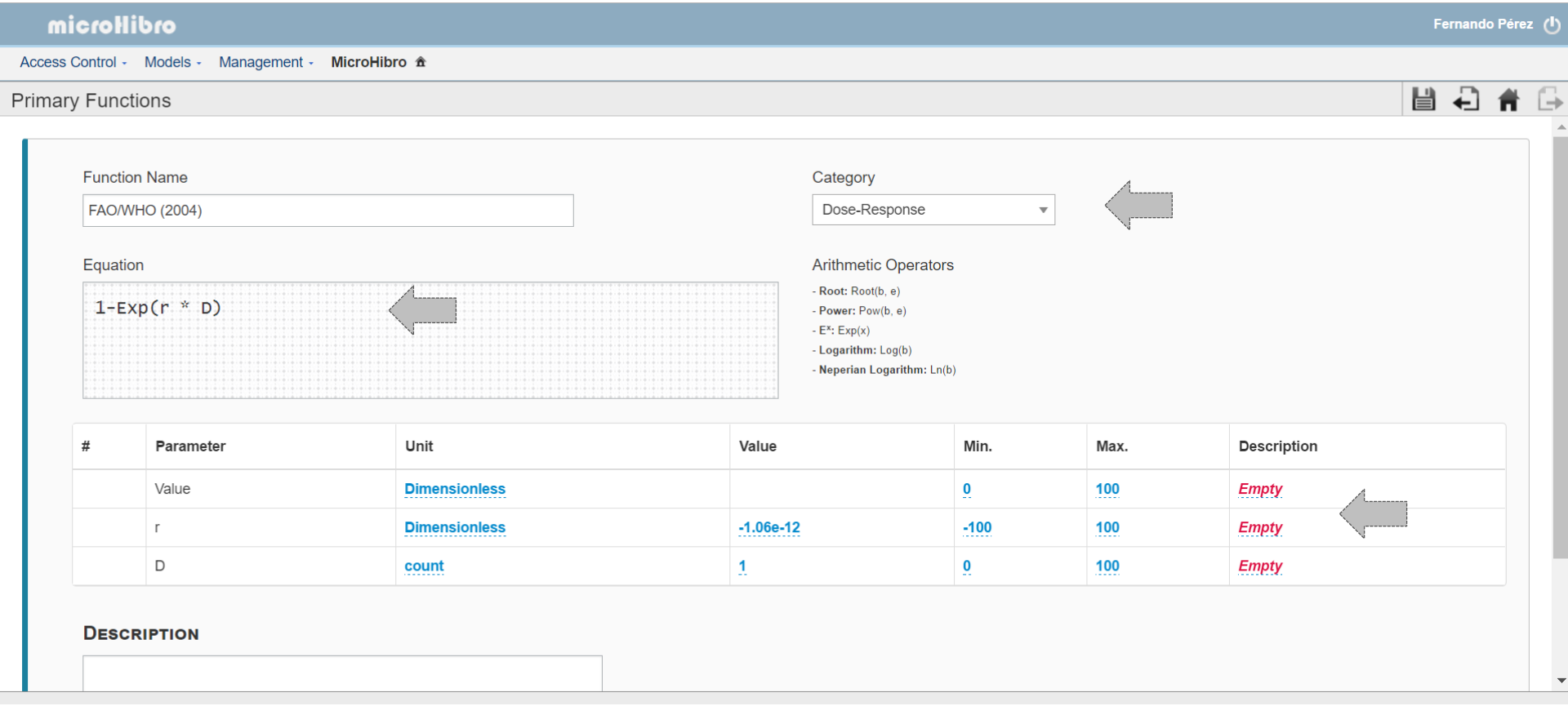
D-R models into risk assessment

-Risk model for listeriosis in EU Elderly from Cooked meat-



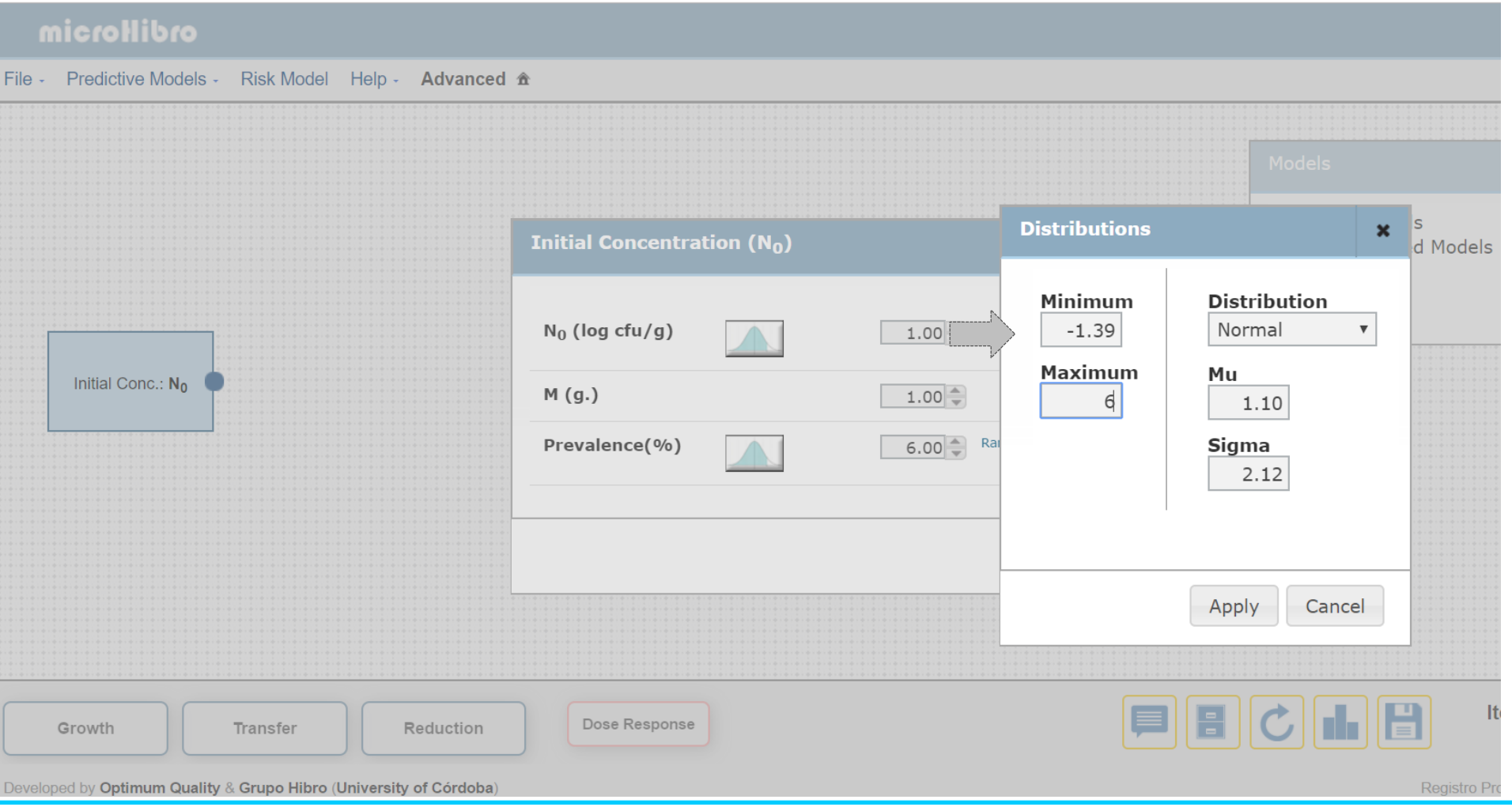
D-R models into risk assessment

-Introducing D-R model parameters from FAO/WHO (2004)-



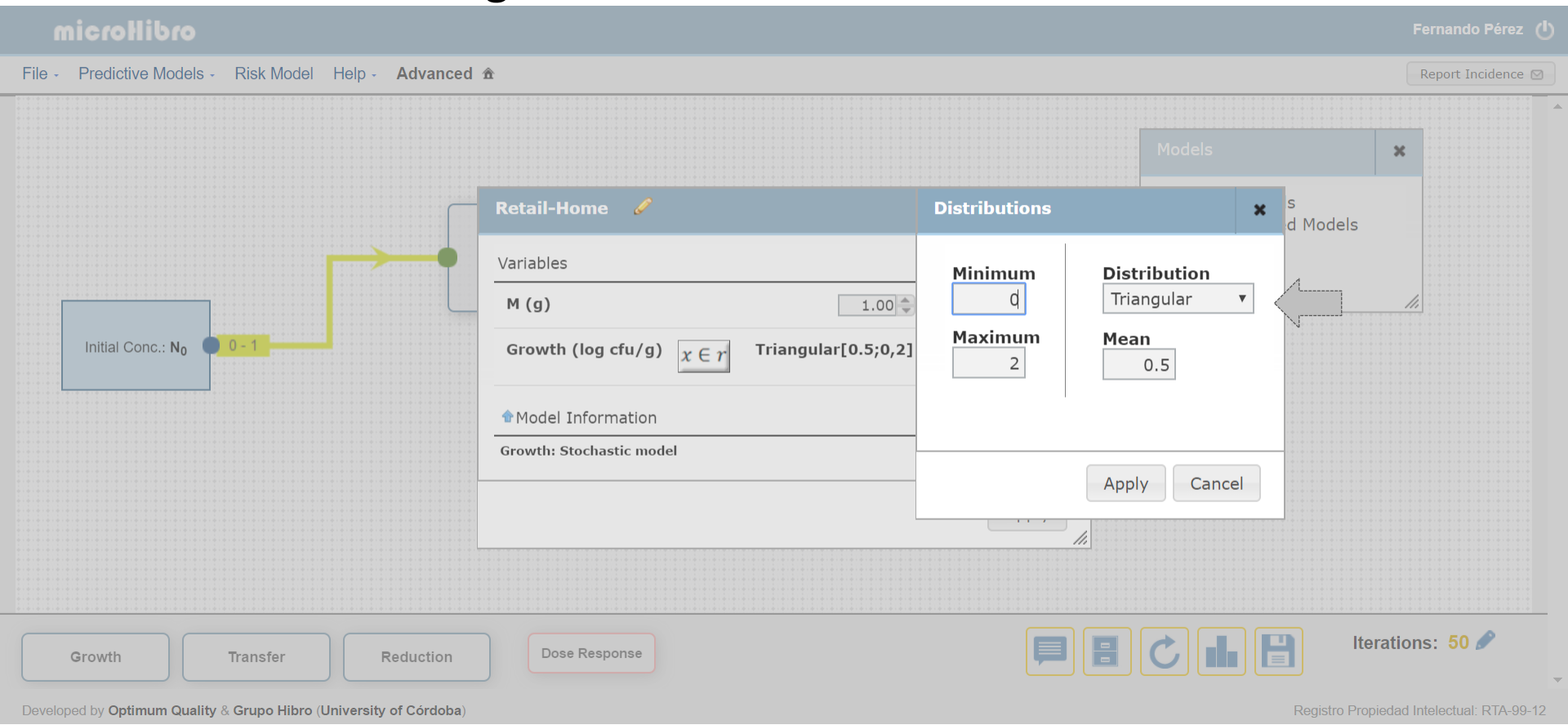
D-R models into risk assessment

-Initial concentration at retail-



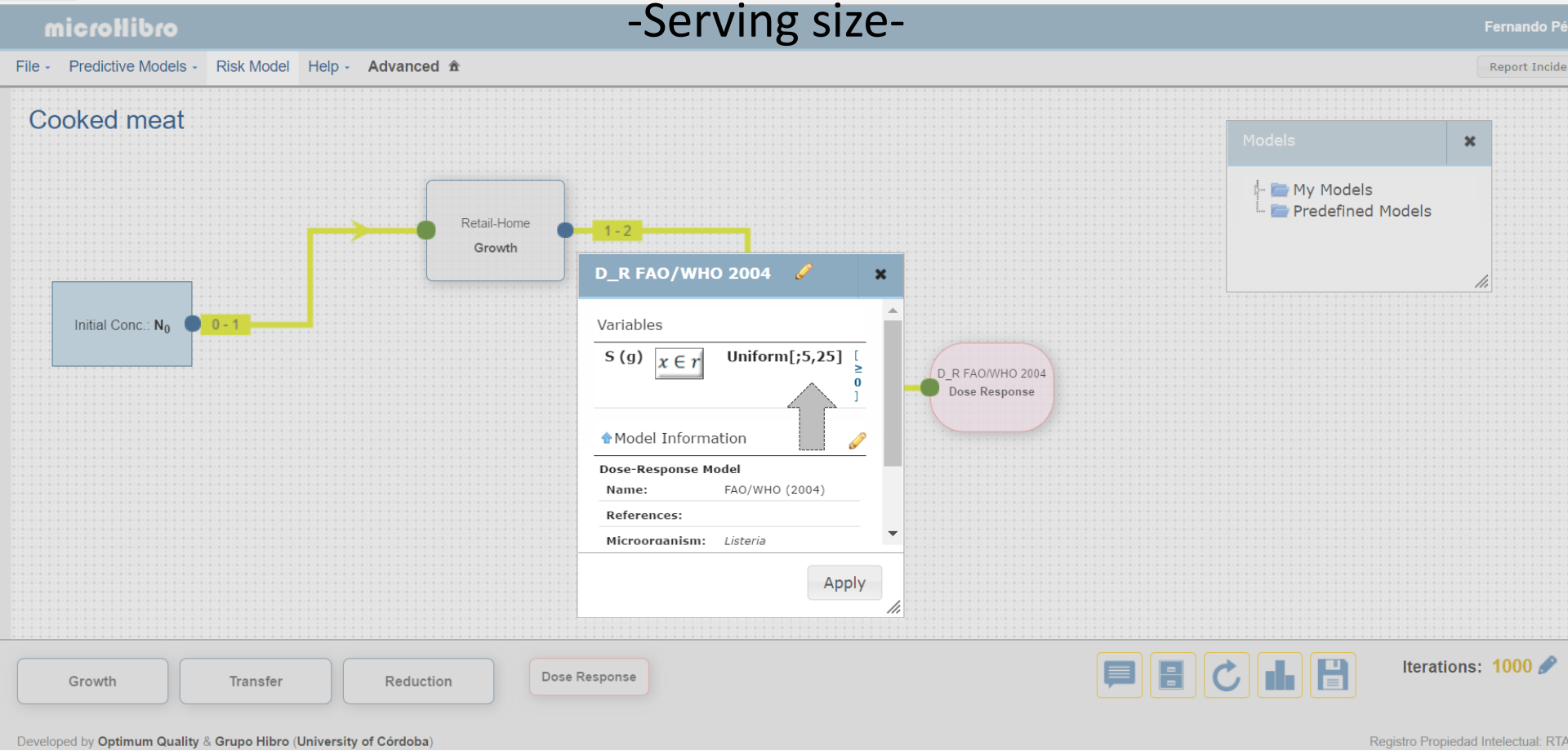
D-R models into risk assessment

-log increase from retail to home-



D-R models into risk assessment

-Serving size-



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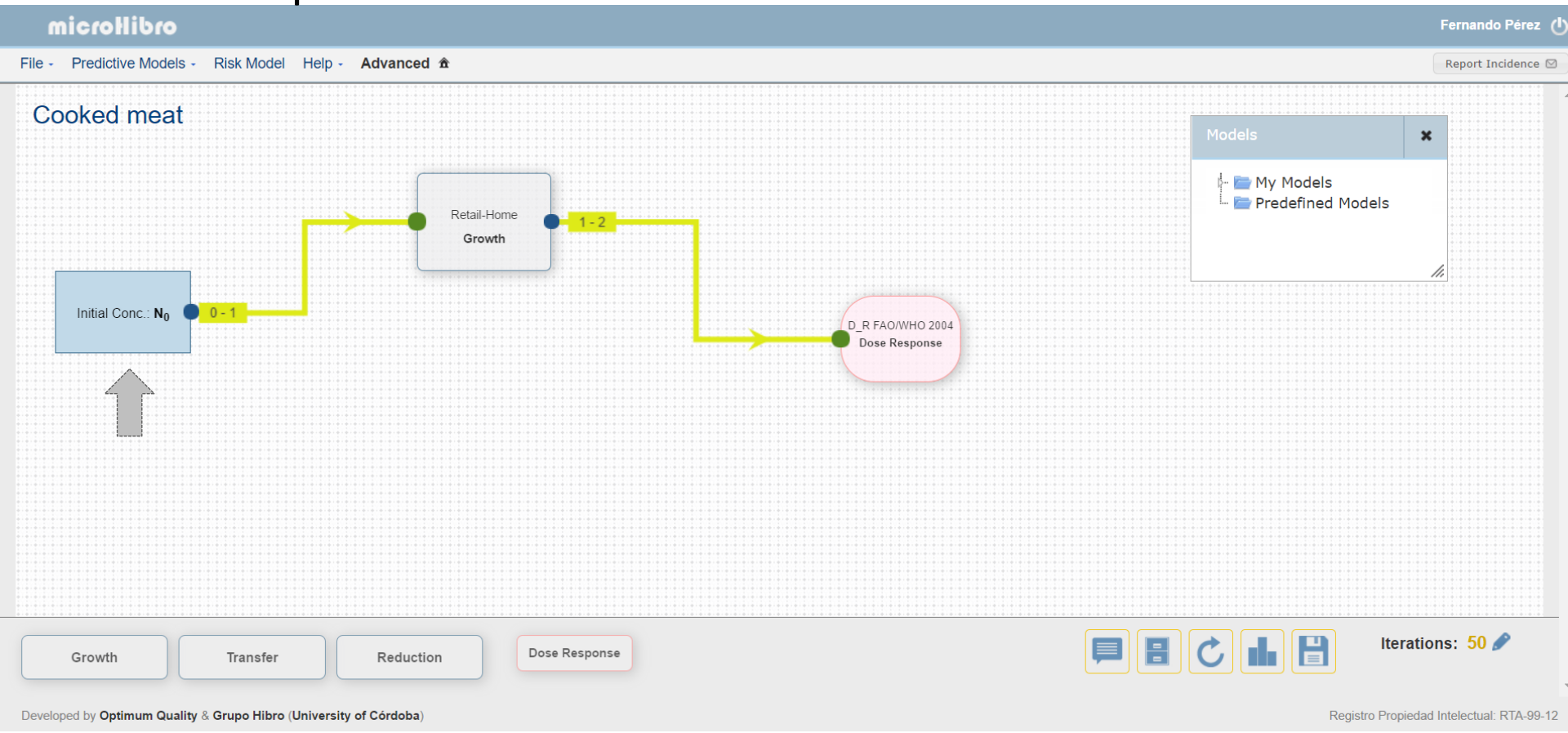
D-R models into risk assessment

-Exposure Assessment- Hazard Characterization-



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D-R models into risk assessment

MicroHibro 1.7.7 ® - Google Chrome

www.microhibro.com/risks/results

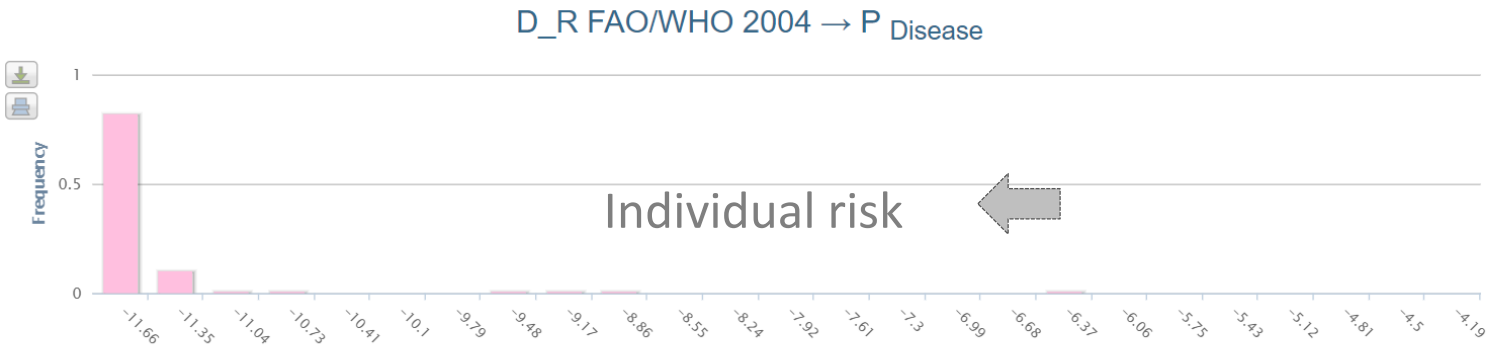
-Simulation output-

Inputs

- N_0
- Retail-Home
  - Growth (log cfu/g)
- D_R FAO/WHO 2004

Outputs

- Retail-Home
  - N_f 1
- D_R FAO/WHO 2004
  - P Disease



Median	Mean	Mode	Maximum	Minimum	Standar deviation
1.0715e-12	2.4322e-12	1.0715e-12	0.000064565	1.0715e-12	0.89

P_5	P_{10}	P_{20}	P_{30}	P_{40}	P_{50}	P_{60}	P_{70}	P_{80}	P_{90}	P_{99}
1.0715e-12	1.0715e-12	1.0715e-12	1.0715e-12	1.0715e-12	1.0715e-12	2.1380e-12	2.1380e-12	2.1380e-12	3.1623e-12	1.5740e-7

3.53E09 servings in EU →

$N_{Servings}$	#Illness cases
3.56E+0	388.77

Calculate

Elderly population risk

Take-home message

- Different approaches for modelling Dose-response (D-R):
  Single hit without threshold as a “pseudo-mechanistic model”
- The Exponential model mostly used for describing Listeriosis D-R relationship
- NUSAP scoring system as tool to guide D-R model selection in risk assessment
- NUSAP High scores for FAO/WHO (2004) and Pouillot et al. (2015)
- The D-R integration into QMRA can be intended to estimate individual and population risk
- Easy-to-use software can be employed to implement D-R models in an stochastic environment

Questions

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- Keep your browsers open to complete the survey !!