Methodological framework for WHO estimates of the global burden of foodborne disease
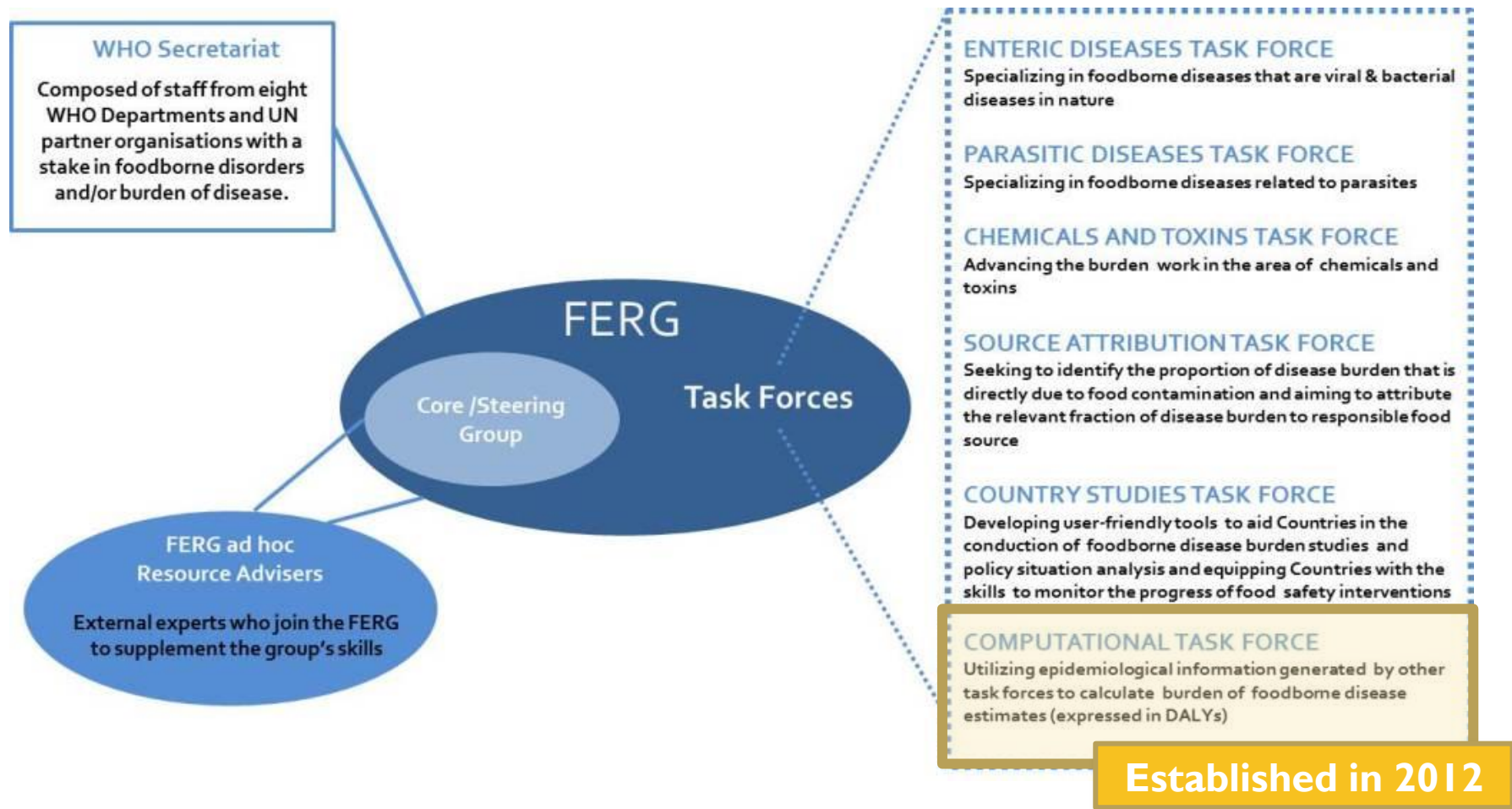
Brecht Devleesschauwer

FERG Computational Task Force

WHO Secretariat

Composed of staff from eight WHO Departments and UN partner organisations with a stake in foodborne disorders and/or burden of disease.

FERG

Core /Steering Group

Task Forces

FERG ad hoc Resource Advisers

External experts who join the FERG to supplement the group's skills

ENTERIC DISEASES TASK FORCE
Specializing in foodborne diseases that are viral & bacterial diseases in nature

PARASITIC DISEASES TASK FORCE
Specializing in foodborne diseases related to parasites

CHEMICALS AND TOXINS TASK FORCE
Advancing the burden work in the area of chemicals and toxins

SOURCE ATTRIBUTION TASK FORCE
Seeking to identify the proportion of disease burden that is directly due to food contamination and aiming to attribute the relevant fraction of disease burden to responsible food source

COUNTRY STUDIES TASK FORCE
Developing user-friendly tools to aid Countries in the conduction of foodborne disease burden studies and policy situation analysis and equipping Countries with the skills to monitor the progress of food safety interventions

COMPUTATIONAL TASK FORCE
Utilizing epidemiological information generated by other task forces to calculate burden of foodborne disease estimates (expressed in DALYs)

Established in 2012

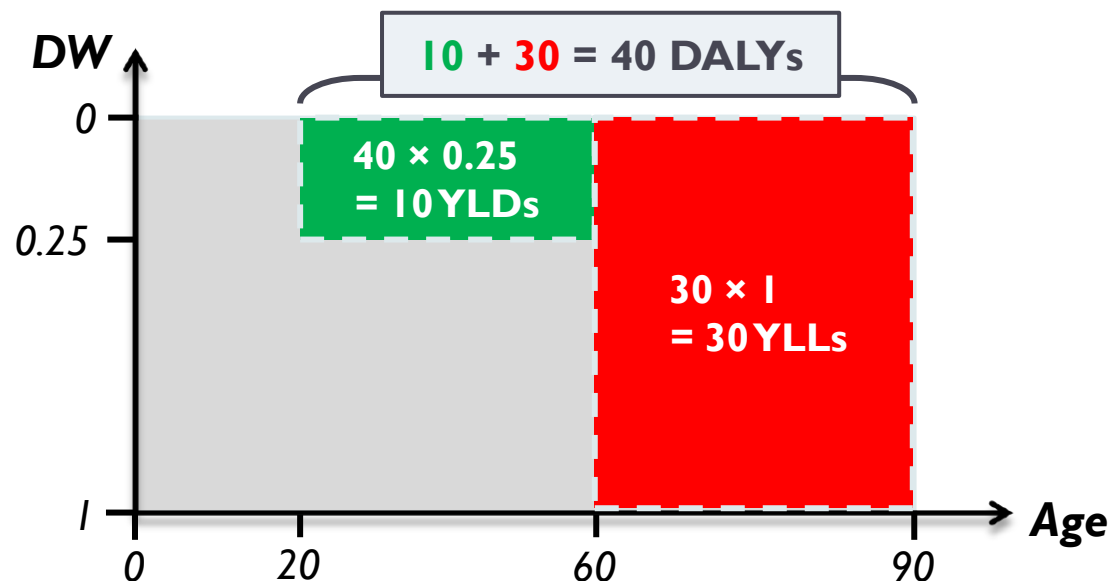# Methodological choices

Burden of foodborne disease

▸ Illnesses, deaths

▸ Disability-Adjusted Life Years (DALYs)

   ▸ **1 DALY = 1 healthy life year lost**

   ▸ Summary measure of population health

      ▸ Morbidity + mortality

      ▸ Disease occurrence + disease severity

   ▸ DALY = YLD + YLL

      ▸ YLD = Years Lived with Disability

           = Number of incident cases × Duration × Disability Weight

      ▸ YLL = Years of Life Lost

           = Number of deaths × Residual Life Expectancy

Disability-Adjusted Life Years

DALY = YLD + YLL

▸ YLD = Years Lived with Disability = N × D × DW

▸ YLL = Years of Life Lost = M × RLE

Methodological choices

Burden of foodborne disease

▸ Illnesses, deaths

▸ Disability-Adjusted Life Years (DALYs)

▸ Hazard-based

  ▸ Burden of hazard = burden of causally related **health states**

    ▸ Acute illness, chronic sequelae, death

    ▸ Different severity levels

  ▸ Represented by **disease model, outcome tree**

  ▸ FERG: 31+6 hazards; 75 health states

Methodological choices

Burden of foodborne disease

▸ Illnesses, deaths

▸ Disability-Adjusted Life Years (DALYs)

▸ Hazard-based

▸ Incidence-based

  ▸ Future burden resulting from current exposure

    ▸ more sensitive to current epidemiological trends

    ▸ more consistent with the estimation of YLLs

▸ Reference year 2010

  ▸ Number of **incident** illnesses, deaths, DALYs **in 2010**

▸ Calculated at country level

  ▸ Presented at subregion level (14)

14 subregions
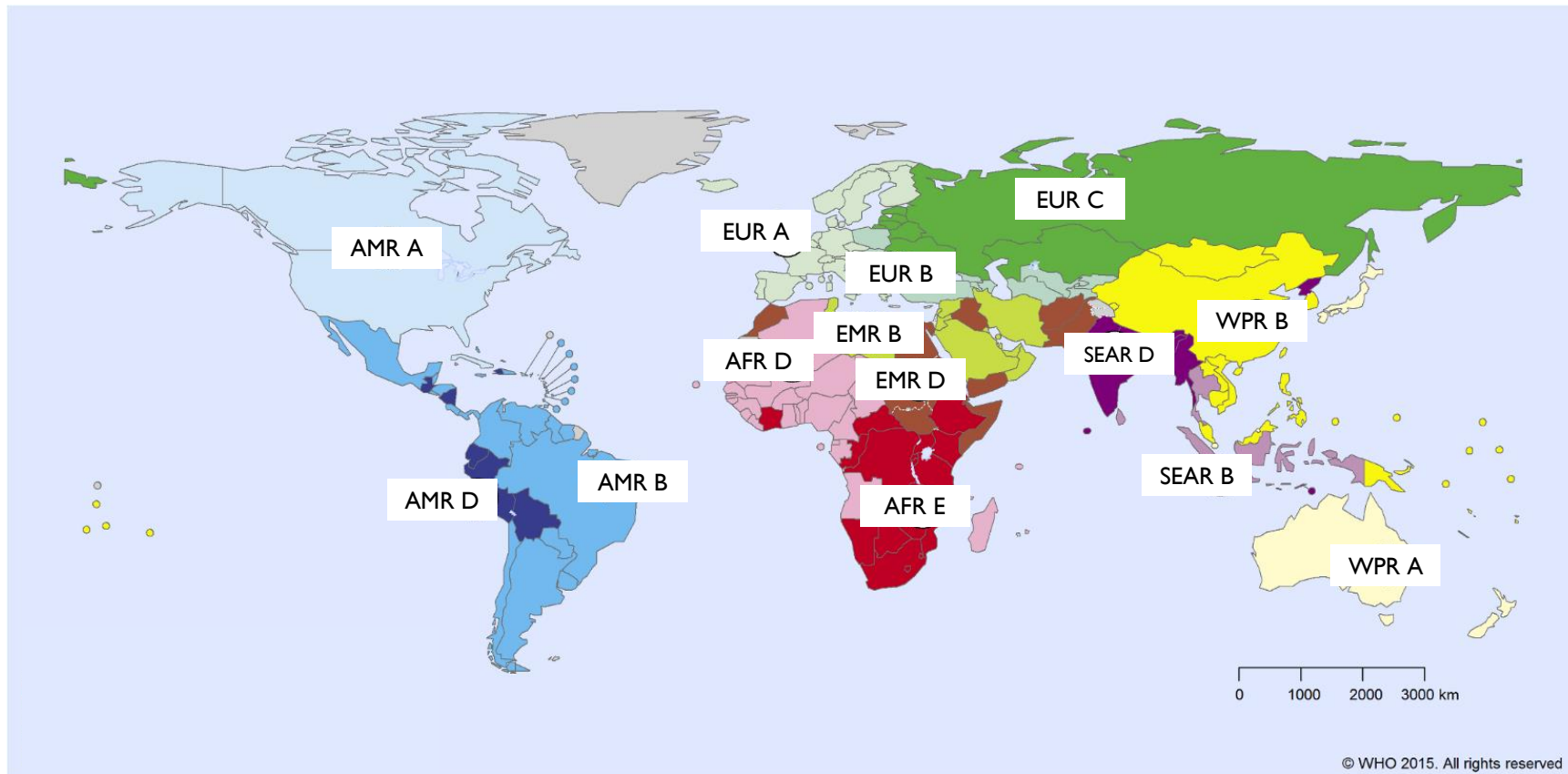
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
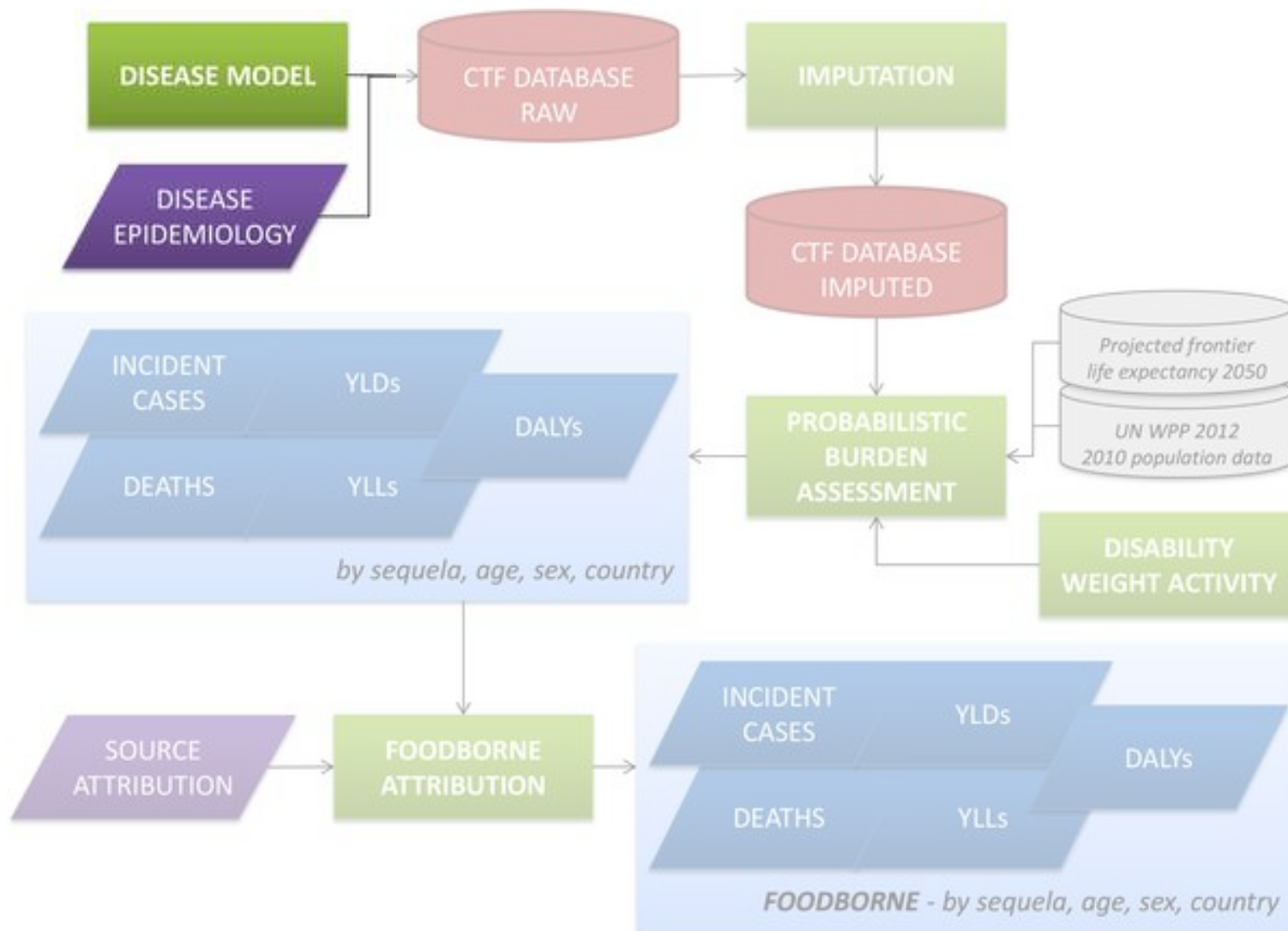
Data Source: World Health Organization
Map Production: Foodborne Disease Burden Epidemiology Reference Group (FERG), World Health Organization

Computational Task Force Workflow
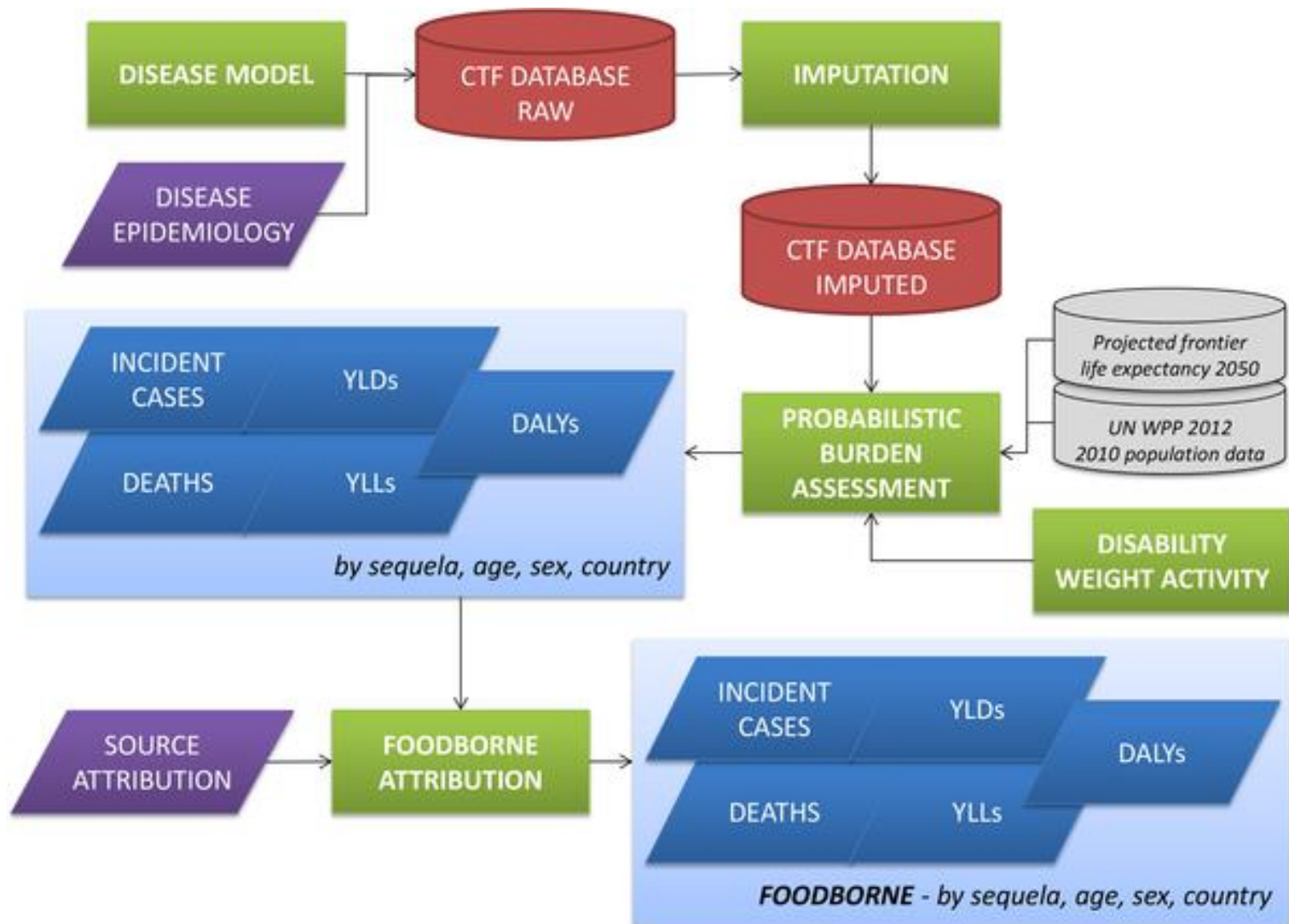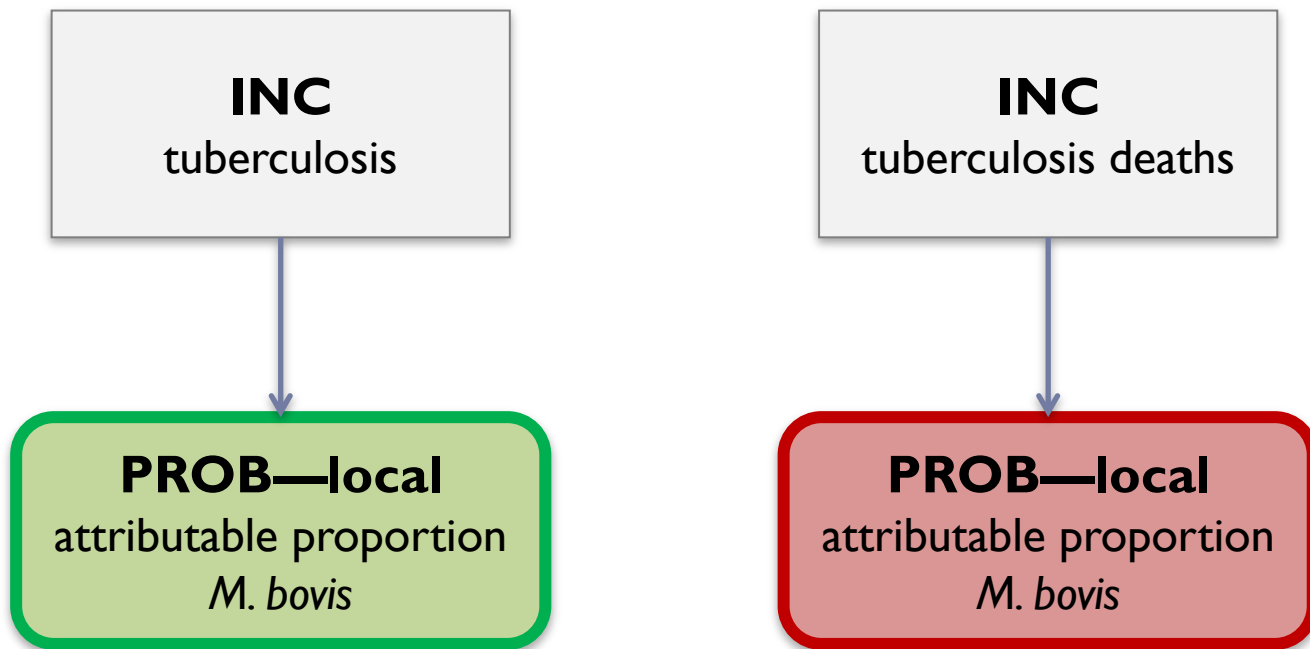
Computational Task Force Workflow

Disease models and epidemiological data

▸ Hazard-based task forces: systematic reviews

▸ **Computational** disease model

 ▸ Disease biology + Data availability

 ▸ Directed acyclic graphs (nodes and arrows)

▸ Quantifying hazard disease burden

 ▸ Categorical attribution
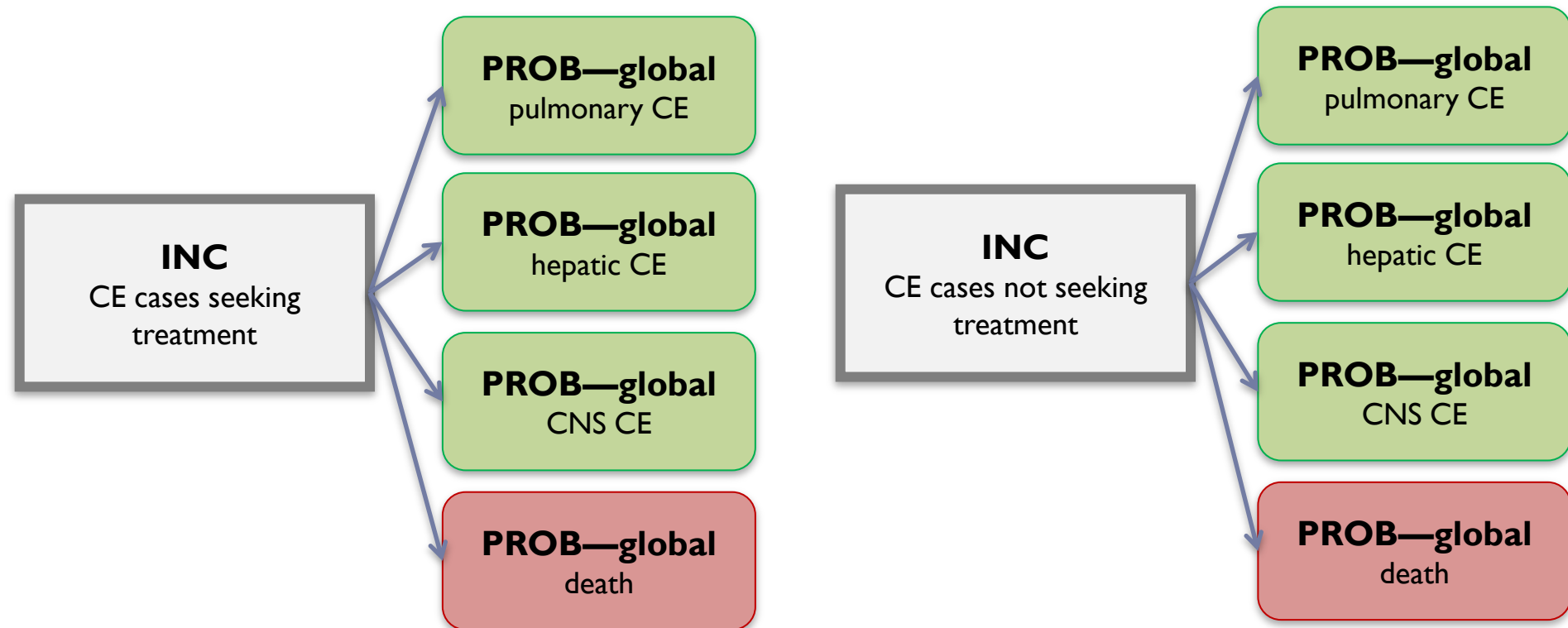
 ▸ Counterfactual analysis

 ▸ Risk assessment

Disease models and epidemiological data

▸ Hazard-based task forces: systematic reviews

▸ Computational disease model

▸ **Quantifying hazard disease burden**

  ▸ **Categorical attribution**

    ▸ Outcome identifiable as caused by hazard in individual cases

    ▸ All viral, bacterial and parasitic hazards; cyanide in cassava, peanut allergen

    ▸ Attributional model: *symptom* → *hazard attribution*

    ▸ Transitional model: *infection/exposure* → *symptom*

Mycobacterium bovis
Disease Model

INC	INC
tuberculosis	tuberculosis deaths

PROB—local
attributable proportion
M. bovis

PROB—local
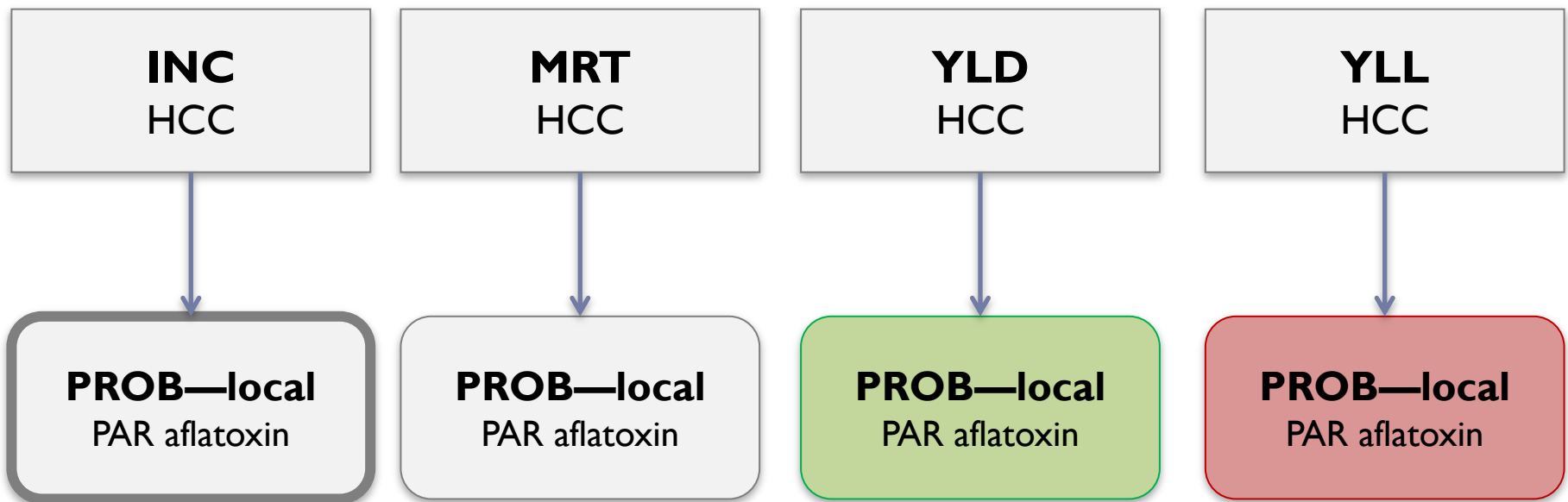attributable proportion
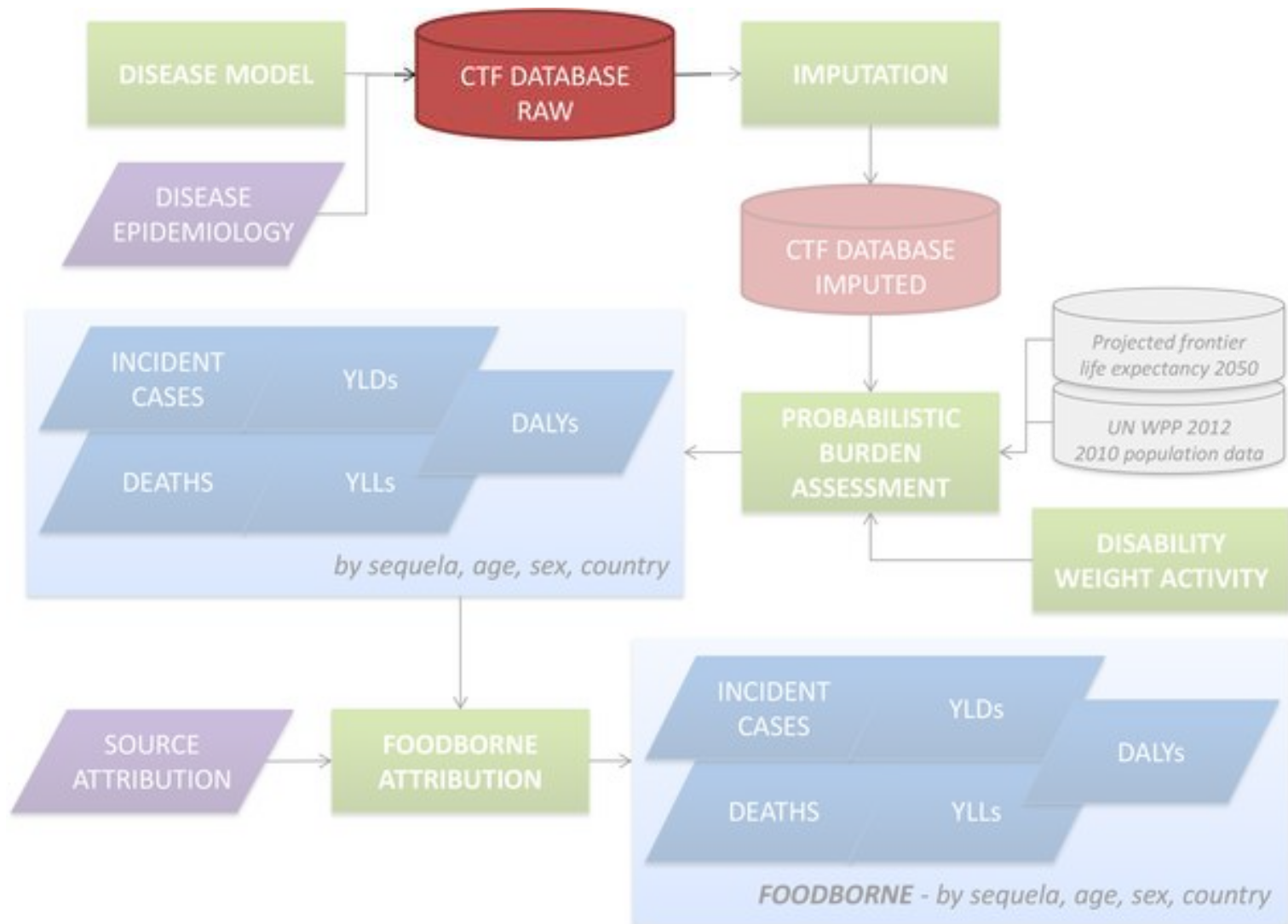*M. bovis*

Echinococcus granulosus
Disease Model

Disease models and epidemiological data

▸ Hazard-based task forces: systematic reviews

▸ Computational disease model

▸ **Quantifying hazard disease burden**

  ▸ Categorical attribution

  ▸ **Counterfactual analysis**

    ▸ Causal attribution cannot be made on an individual basis

    ▸ Aflatoxin and hepatocellular carcinoma

    ▸ Statistical association: Population Attributable Risk (PAR)

    ▸ Attributional model: *symptom* → *hazard attribution*

Counterfactual analysis; Attributional model

Aflatoxin
Disease Model

INC	**MRT**	**YLD**	**YLL**
HCC	HCC	HCC	HCC

PROB—local	**PROB—local**	**PROB—local**	**PROB—local**
PAR aflatoxin	PAR aflatoxin	PAR aflatoxin	PAR aflatoxin

Disease models and epidemiological data

▸ Hazard-based task forces: systematic reviews

▸ Computational disease model

▸ **Quantifying hazard disease burden**

  ▸ Categorical attribution

  ▸ Counterfactual analysis

  ▸ **Risk assessment**

    ▸ Combining exposure and dose-response data

    ▸ Not necessarily consistent with existing health statistics
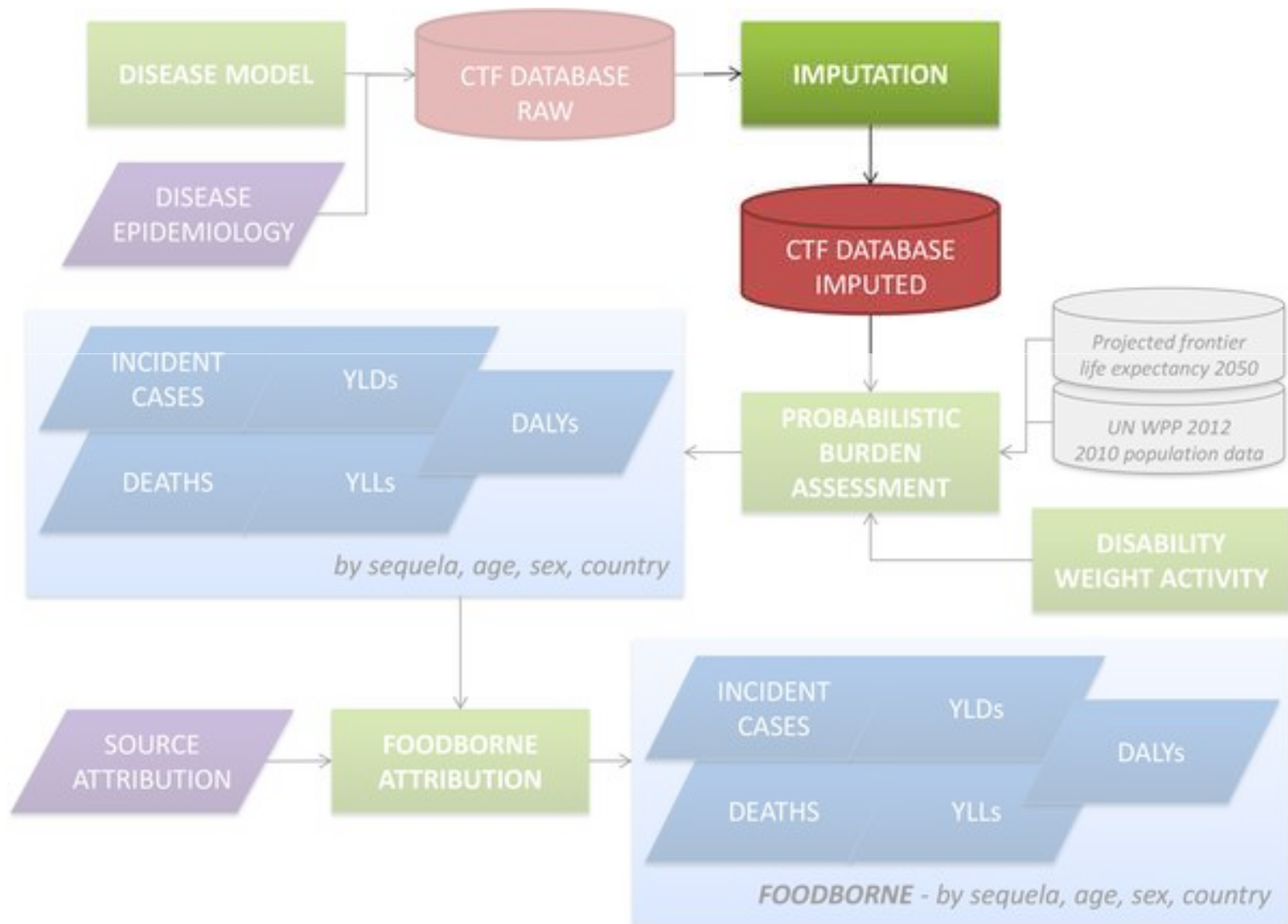
    ▸ Dioxin and impaired fertility, hypothyroidy

Note: underreporting

▶ Not explicitly addressed in CTF framework

▶ Captured by framework

  ▶ Attributional models: corrected envelopes

  ▶ Use of survey instead of surveillance data
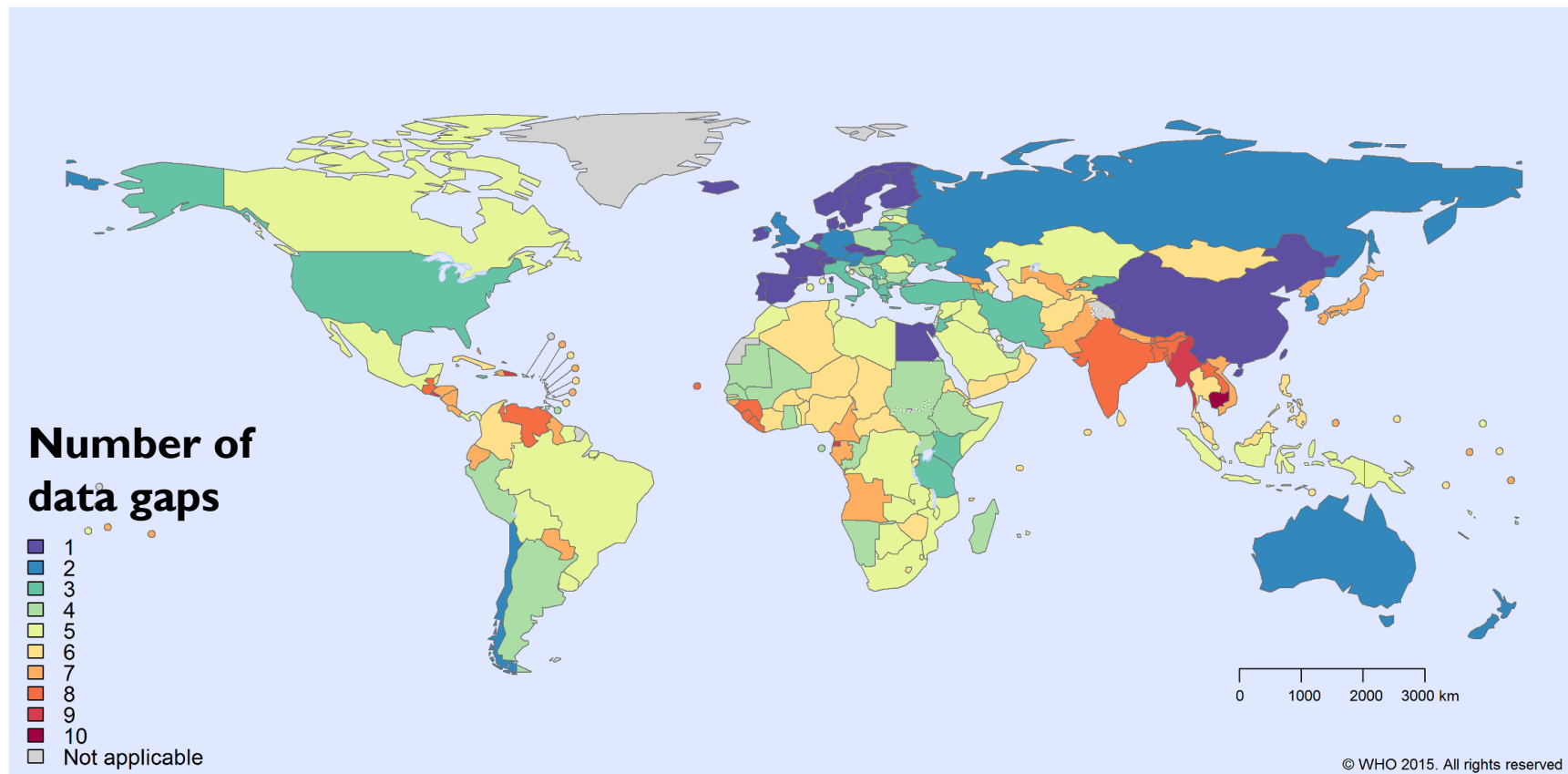
  ▶ Underreporting factor included in disease model

Computational Task Force Workflow

Computational Task Force Workflow

Need for imputation

Number of data gaps

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- Not applicable

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Data Source: World Health Organization
Map Production: Foodborne Disease Burden Epidemiology Reference Group (FERG), World Health Organization

Imputation model

▸ Provide reasonable value + uncertainty range

▸ Bayesian random effects log-Normal regression model

$$\log(\theta_{ij}) \sim Normal(\mu_i, \sigma_w^2)$$
$$\mu_i \sim Normal(\mu_0, \sigma_b^2)$$

θ_{ij} = incidence in country j belonging to region i

μ_i = regional mean; μ_0 = global mean

σ_w^2 = within-region variance; σ_b^2 = between-region variance

Imputation model

▸ Provide reasonable value + uncertainty range

▸ Bayesian random effects log-Normal regression model

  ▸ **green** countries: no imputation

  ▸ **orange** countries: $LN(\mu_i, \sigma_w^2)$

    ▸ "random" country within concerned subregion

    ▸ UI describes variability within subregions

  ▸ **red** countries: $LN(\mu_0, \sigma_b^2 + \sigma_w^2)$

    ▸ "random" country within a "random" subregion

    ▸ UI describes variability between and within subregions
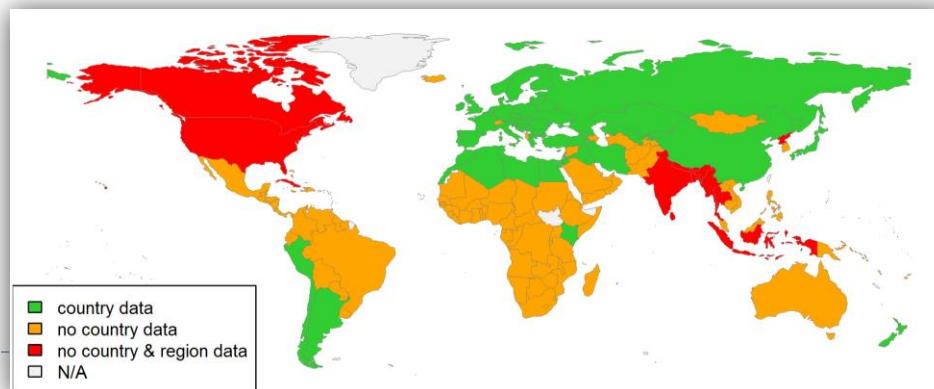
■ country data
■ no country data
■ no country & region data
□ N/A

Imputation model

‣ Provide reasonable value + uncertainty range

‣ Bayesian random effects log-Normal regression model

‣ **Only when data from different subregions available**

  ‣ If not: no imputation, no global estimates

  ‣ *Bacillus cereus, Clostridium perfringens, Clostridium botulinum, Staphylococcus aureus*, and peanut allergens

Computational Task Force Workflow

Disability weights

▸ Severity of health states, relative reduction in health

    ▸ 0 = perfect health

    ▸ 1 = death

▸ Adopted from WHO Global Health Estimates

    ▸ Based on GBD 2010, except:

        ▸ Primary infertility: alternative value

        ▸ Hypothyroidy: GBD 2013

    ▸ Direct mapping or proxy health state(s)

▸ Severity levels (mild, moderate, severe)

    ▸ Included in disease model as distinct health states

    ▸ Weighted average, based on epidemiological data

Computational Task Force Workflow
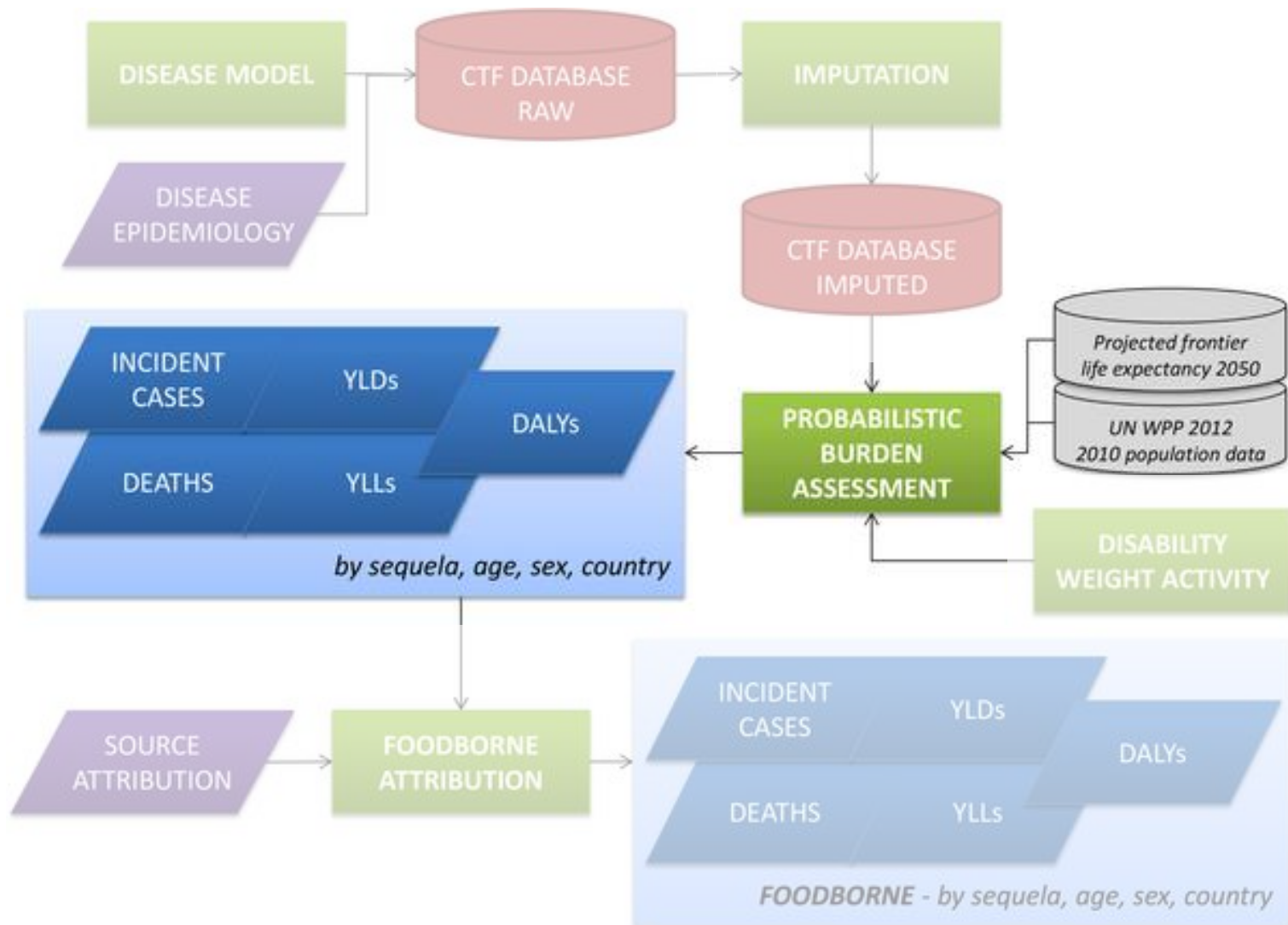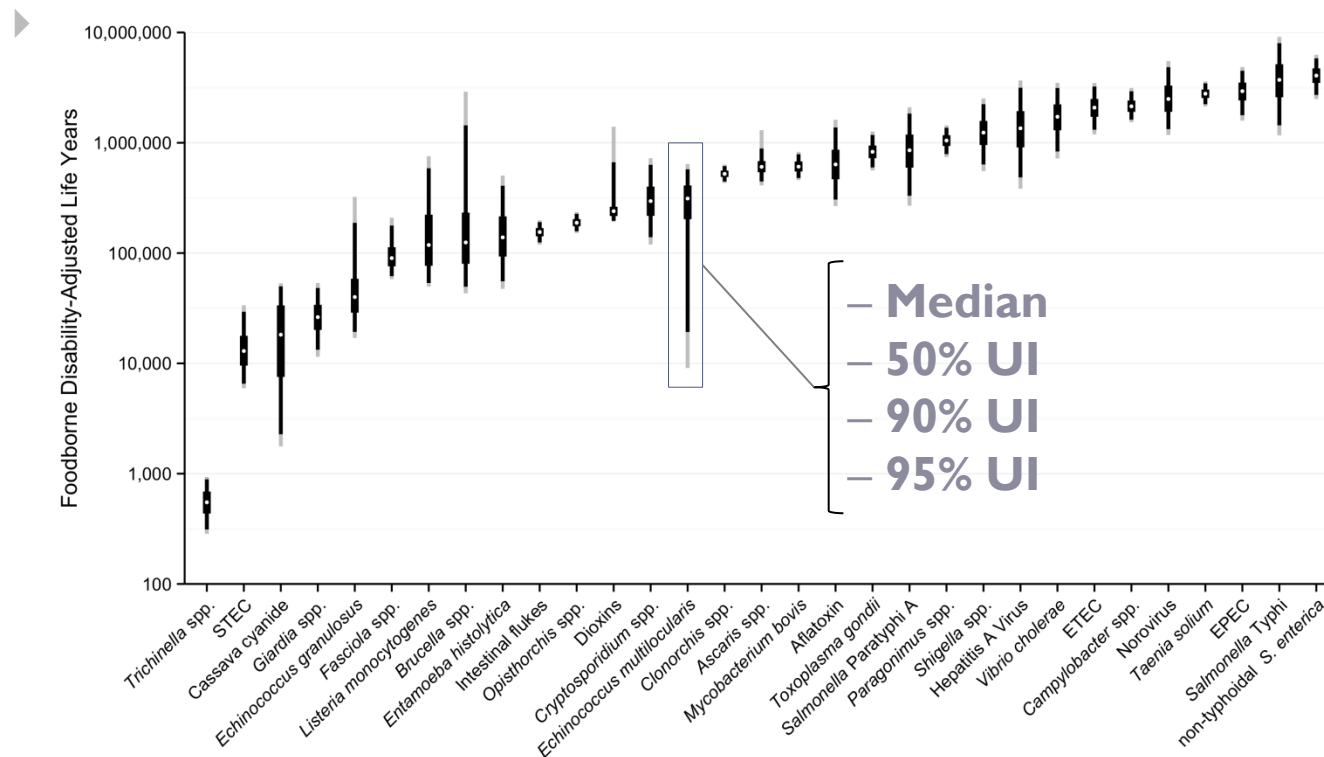
Probabilistic burden assessment

▸ Incidence, mortality, YLD, YLL, DALY rate
  ▸ Per hazard, outcome, country, age, sex
▸ Absolute numbers: 2010 population sizes
▸ Standard life expectancy for YLLs
  ▸ highest projected LE for 2050
  ▸ LE at birth of 92, males and females
▸ No age weighting, no time discounting
▸ No correction for comorbidity, except
  ▸ HIV infected invasive salmonellosis cases and deaths
  ▸ HIV infected *M. bovis* deaths

Probabilistic burden assessment

▸ *Probabilistic*: parameter + imputation uncertainty

  ▸ 10,000 Monte Carlo simulations

  ▸ Uncertainty distribution instead of single estimate

    ▸ Median, 95% uncertainty interval

    ▸

Probabilistic burden assessment

- *Probabilistic*: parameter uncertainty
  - 10,000 Monte Carlo simulations
  - Uncertainty distribution instead of single estimate
    - Median, 95% uncertainty interval
- Implemented in R and JAGS
  - All code available as 'FERG' package
  - https://github.com/brechtdv/FERG

Computational Task Force Workflow

Foodborne attribution

▸ **FB disease burden**

= overall disease burden × proportion FB

▸ **Some hazards considered 100% foodborne**

▸ *L. monocytogenes*, *M. bovis*, foodborne trematodes, *T. solium*, *Trichinella* spp., aflatoxin, cyanide in cassava, dioxin, peanut allergens

▸ **Remaining hazards: structured expert elicitation**

▸ Cooke's classical method

▸ Measuring expert performance → *performance weights*

▸ **calibration**: are the expert's probability statements statistically *accurate?*

▸ **informativeness**: is the probability mass concentrated in a small region – *precision?*

Major pathways included for the Biological hazards

Hazard	Food	Animal Contact	Human-to-human	Water	Soil	Air	Other
Diarrheal Disease							
Campylobacter spp.	x	x	x	x	x		x
Cryptosporidium spp.	x	x	x	x			x
Entamoeba histolytica	x		x	x			x
Enteropathogenic *E. coli*	x	x	x	x			x
Enterotoxigenic *E. coli*	x	x	x	x			x
Giardia spp.	x	x	x	x			x
Norovirus	x		x	x			x
Non-typhoid *Salmonella* spp.	x	x	x	x	x		x
Shigella spp.	x		x	x	x		x
Shiga toxin-producing *E. coli*	x	x	x	x	x		x
Vibrio cholerae	x		x	x			x
Brucella spp.	x	x		x	x		x
Hepatitis A	x		x	x			x
Typhoid *Salmonella* spp.	x		x	x			x
Parasitic Disease							
Toxoplasma gondii	x	x		x	x		x
Echinococcus granulosus	x	x		x	x	x	x
Echinococcus multilocularis	x	x		x	x	x	x
Ascaris spp.	x	x	x	x	x		x

Number of experts enrolled and finally included in the elicitation

Hazard groups		Experts enrolled	Experts interviewed	Returned answers
Diarrheal disease				
Bacterial (incl. *S.* Typhi) pathogens and Norovirus	Sub regional	49	37	37
Intestinal protozoa	Global	12	9	9
Other infectious disease				
Brucella spp.	Global	10	8	7
Hepatitis A virus	Global	9	7	7
Toxoplasma gondii	Global	11	10	9
Ascaris spp.	Global	8	6	7
Echinococcus spp.	Global	7	6	6
Chemicals				
Lead	Global	10	9	6
Total		100	78	72

Due to the structure of the sub regional panels, the number of experts varied between 10 and 15 depending on the hazard and subregion.
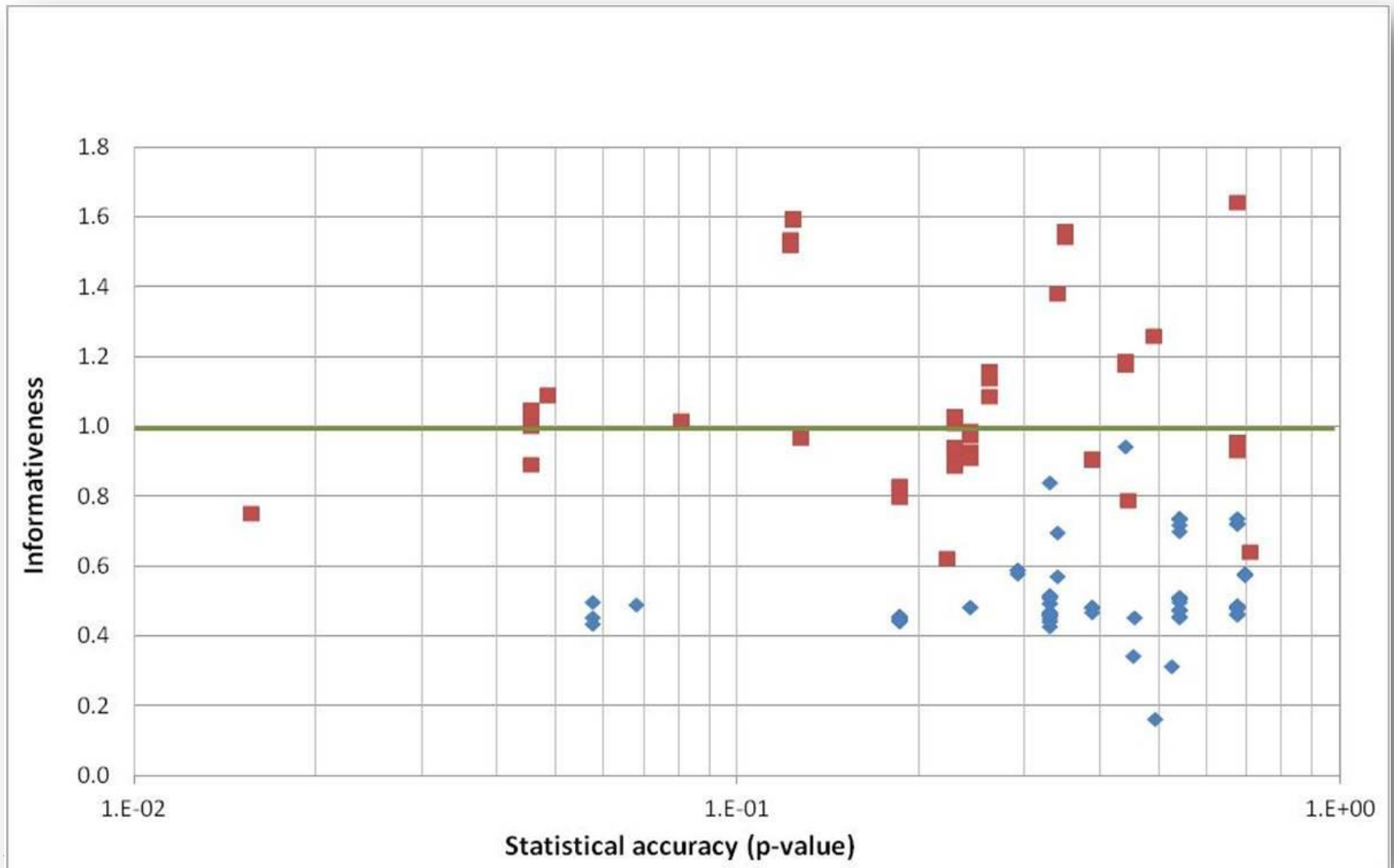*Some experts served on more panels.*

▶

Distribution of experts according to working experience (>3 years) per subregion
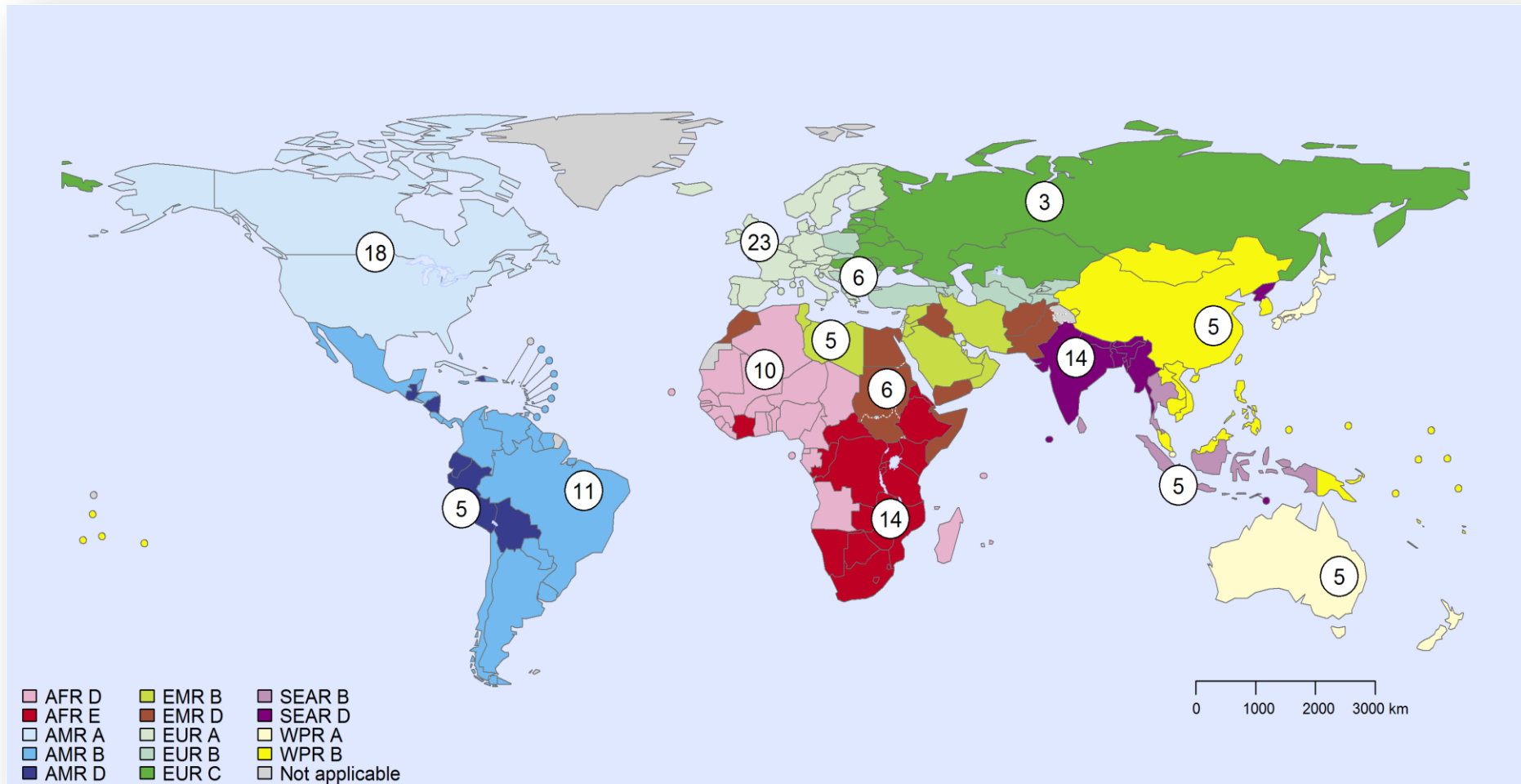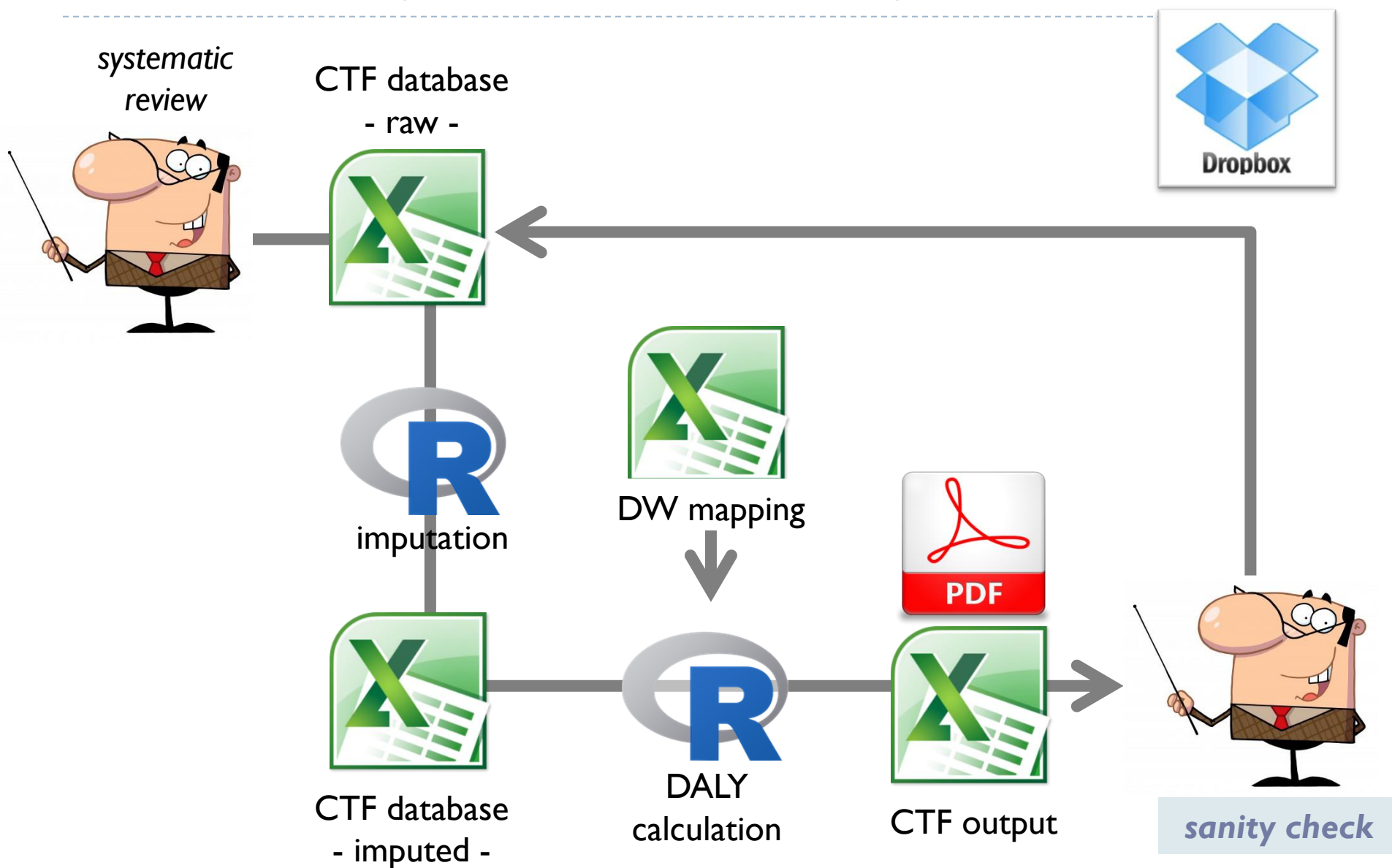

The sub regions are defined on the on the basis of child and adult mortality. Stratum A: very low child and adult mortality, Stratum B: low child mortality and very low adult mortality, Stratum C: low child mortality and high adult mortality, Stratum D: high child and adult mortality, and Stratum E: high child mortality and very high adult mortality (Ezzati et al., 2002).

Statistical accuracy versus informativeness of the included experts when using **equal weight** or **performance weight** combinations

Traceability & transparency

systematic review

CTF database
- raw -

imputation

DW mapping

CTF database
- imputed -

DALY calculation

CTF output

sanity check

FERG Computational Task Force