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

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FERG Computational Task Force

Established in 2012

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

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 conduct of foodborne disease burden studies and policy situation analysis and equipping Countries with the skills to monitor 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)

FERG ad hoc Resource Advisers
External experts who join the FERG to supplement the group’s skills

FERG methodological framework
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 \times D \times DW
- YLL = Years of Life Lost = M \times 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

FERG methodological framework
Computational Task Force Workflow
Computational Task Force Workflow

FERG methodological framework
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
Categorical attribution; Attributional model

**Mycobacterium bovis**
Disease Model

- **INC** tuberculosis
- **PROB**—local attributable proportion *M. bovis*

- **INC** tuberculosis deaths
- **PROB**—local attributable proportion *M. bovis*
Categorical attribution; Transitional model

**Echinococcus granulosus**

Disease Model

INC
CE cases seeking treatment

PROB—global
pulmonary CE

PROB—global
hepatic CE

PROB—global
CNS CE

PROB—global
death

INC
CE cases not seeking treatment

PROB—global
pulmonary CE

PROB—global
hepatic CE

PROB—global
CNS CE

PROB—global
death
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 $\rightarrow$ hazard attribution
Counterfactual analysis; Attributional model

Aflatoxin Disease Model

- **INC** HCC
  - **PROB**—local PAR aflatoxin

- **MRT** HCC
  - **PROB**—local PAR aflatoxin

- **YLD** HCC
  - **PROB**—local PAR aflatoxin

- **YLL** HCC
  - **PROB**—local 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

FERG methodological framework
Computational Task Force Workflow
Need for imputation

Number of data gaps

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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

\[
\log(\theta_{ij}) \sim Normal(\mu_i, \sigma^2_w) \\
\mu_i \sim Normal(\mu_0, \sigma^2_b)
\]

- \(\theta_{ij}\) = incidence in country \(j\) belonging to region \(i\)
- \(\mu_i\) = regional mean; \(\mu_0\) = global mean
- \(\sigma^2_w\) = within-region variance; \(\sigma^2_b\) = between-region variance
Imputation model

- Provide reasonable value + uncertainty range
- Bayesian random effects log-Normal regression model
  - **green** countries: no imputation
  - **orange** countries: $LN(\mu_i, \sigma^2_w)$
    - “random” country within concerned subregion
    - UI describes variability within subregions
  - **red** countries: $LN(\mu_0, \sigma^2_b + \sigma^2_w)$
    - “random” country within a “random” subregion
    - UI describes variability between and within subregions
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

FERG methodological framework
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

![Graph showing foodborne disability-adjusted life years for different pathogens, with median, 50% UI, 90% UI, and 95% UI indicated.]
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

- Disease Model
- CTF Database Raw
- Imputation

- Disease Epidemiology
- Disease
- Incident Cases
- YLDs
- DALYs
- Deaths
- YLLs

- Probabilistic Burden Assessment
- Projected frontier life expectancy 2050
- UN WPP 2012
- 2010 population data

- Disability Weight Activity

- Source Attribution
- Foodborne Attribution

- Foodborne - by sequela, age, sex, country

FERG methodological framework
Foodborne attribution

- 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
  - See next presentation
  - FB disease burden
    - = overall disease burden × proportion FB
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