The Global Burden of Foodborne Disease – a WHO Technical Perspective

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Overview

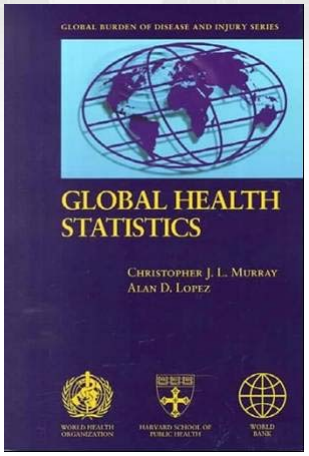
1. GBD principles and objectives; brief history
2. GBD 2010 study and WHO Global Health Estimates
3. CRA principles and methods
4. Methodological and data issues in FERG work
5. Conclusions

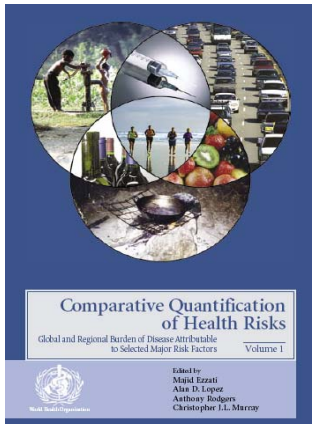
Global Burden of Disease (GBD)

A standardized framework for integrating all available information on mortality, causes of death, individual health status, and condition-specific epidemiology to provide an overview of the levels of population health and the causes of loss of health

- Consistent, comprehensive descriptive epidemiology
- Common metric or summary measure

Abbreviated GBD history (1)



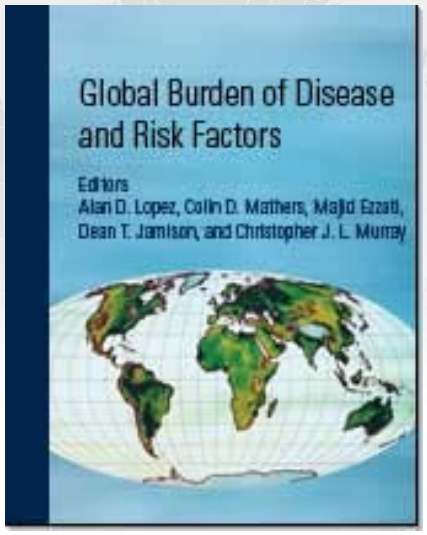


1991-96 Global Burden of Disease 1990 Study

- World Bank 1993; Murray & Lopez 1996

1999-04 WHO updates for years 2000-2002

- Mortality and COD – country level
- YLD – 17 regions
- Comparative Risk Assessment - 26 RFs
- WHO-CHOICE: generalized CEA
- Healthy LE (HALE) – 192 Member States



Abbreviated GBD history (2)

2004-06 Disease Control Priorities Project

- Lopez, Mathers et al 2006

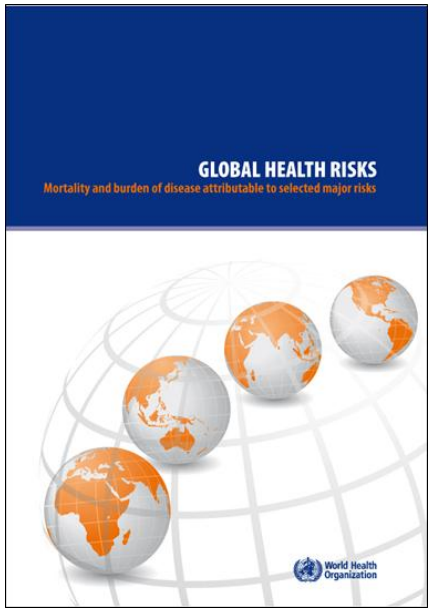
2005-09 WHO updates

- Projections to 2030
- GBD: 2004 update (pub. 2008)
- Global health risks (pub. 2009)

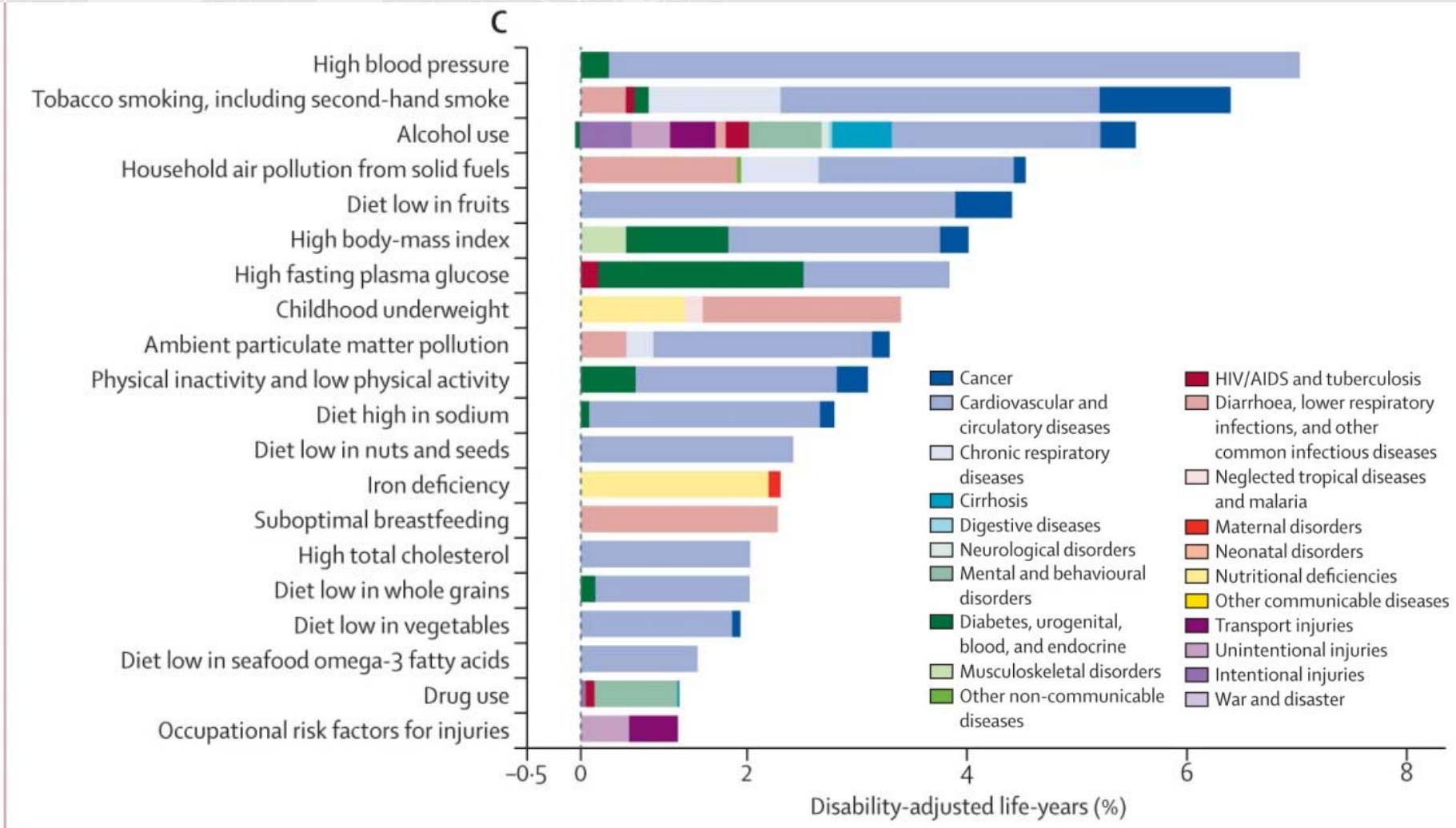
2007-12 GBD 2010 study (IHME)

- Published Dec 14 2012 in the Lancet
- Funded by Gates Foundation

2015 GBD 2013 published in Lancet



Burden of Disease attributable to 20 risk factors in 2010



Simplified calculation of DALYs

Time is used as the common metric for mortality and health states

$$DALY_i = YLL_i + YLD_i$$

$$YLL_i = \text{No. deaths (cause } i\text{)} \times \text{years lost per death}$$

$$YLD_i = Incidence_i \times \text{av. duration}_i \times \text{disability weight}_i$$

$$YLD_i = Prevalence_i \times \text{disability weight}_i$$

WHO DALY methods and parameters

- YLL calculated using a normative loss function derived from the frontier life expectancies by age projected for 2050 (Japan and Korea females)
- YLD durations are the actual estimated durations of health states/sequelae in the population
- No age weights or discounting
- Prevalence-based YLD calculation – as in GBD 2010

  yld = Prevalence * Disability weight

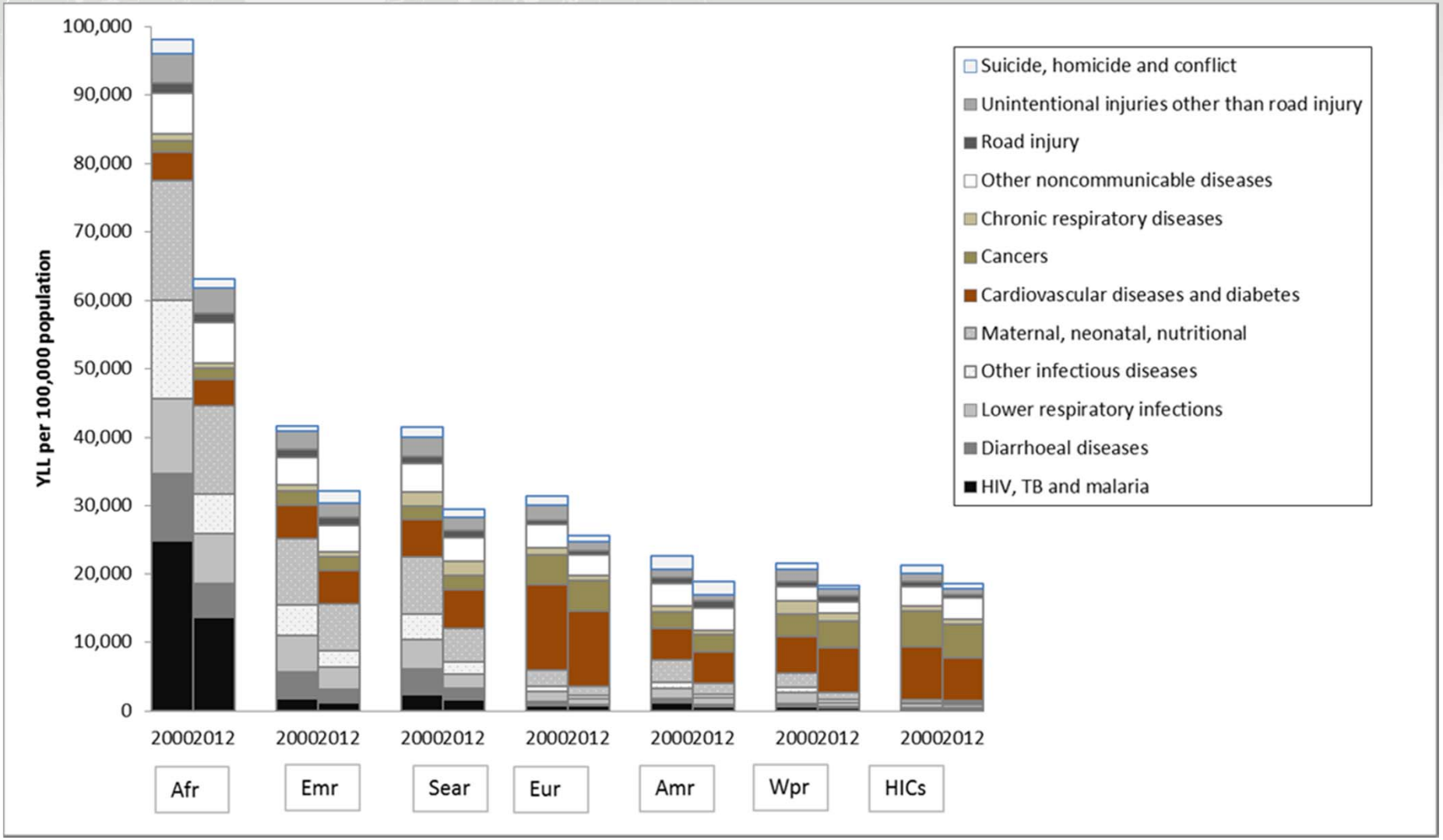
- Disability weights from the GBD 2010 disability weights study with revisions for vision and hearing loss, intellectual disability, alcohol and drug dependence, infertility, back and neck pain and skin problems

WHO Global Health Estimates

(www.who.int/evidence/bod)

1. Global/Regional/Country estimates for deaths by detailed cause list for years 2000 to 2012 – released in May 2014
2. UN interagency envelopes (child mortality, all cause mortality)
3. WHO program estimates for specific causes (child causes, HIV, TB, malaria, maternal, cancers, road injury, suicide, homicide etc)
4. WHO estimates for other causes for countries with useable death registration data
5. Use of IHME analyses for other causes for non-VR countries – as well as WHO analyses for selected causes
6. IHME analyses for YLD – with some revisions

YLL per 100,000 by cause and region, 2012



Comparative risk assessment: Concepts

Quantification of disease burden at population level caused by various risk factors in a **comparative** and **internally consistent** way

Comparative:

- same definitions and framework
- similar method for combining exposure and risk information
- same method for expressing results (mortality and DALYs)

Consistent:

- Linkage of disease burden by disease and by risk factor

Estimation of attributable and avoidable risk

- attributable: current burden from past/present exposure
- avoidable: future burden if current or future exposure was reduced

WHO Comparative Risk Assessment

- Quantification of disease burden at population level caused by various risk exposures in a comparative and internally consistent way
- Burden assessed using common currency across disease and injury outcomes (deaths and DALYs)
- Attributable burden = burden attributable to current and past exposure via comparison with a counterfactual exposure scenario
- Linkage of exposure to outcomes usually through assessment of relative risks rather than absolute risks
- Assessment of relative risks for causal relationships after correction for confounding and bias
- Theoretical or plausible minimum risk distribution (not necessarily zero exposure)
- Consistent use of WHO estimates for disease and injury burden

Population attributable fraction

= Proportion of incident disease/deaths in the population that can be attributed to the risk

Calculated by comparing current incidence/mortality with that which would occur under a counterfactual exposure distribution (chosen in CRA to be the theoretically achievable exposure distribution associated with minimum risk

For a dichotomous exposure (with relative risk RR for exposed/non-exposed)

PAF = (Total prevalence - $Prev_{CF}$)/ Total prevalence

= (prev * RR- prev) / (prev * RR +1 -prev)

For continuous exposure distribution P(x) with counterfactual distribution P'(x):

$$PAF = \frac{\int_{x=0}^{m} RR(x)P(x)\,dx - \int_{x=0}^{m} RR(x)P'(x)\,dx}{\int_{x=0}^{m} RR(x)P(x)\,dx}$$

Choice of Theoretical Minimum

Theoretically achievable minimum risk

Constant across the world ?

Will sometimes be zero exposure, or a recommended maximum acceptable exposure

Will sometimes be a counterfactual distribution

Behavioral risk factors: increasing or J-shaped dose-response

Environmental risk factors: increasing dose-response, lowest possible achievable

WHO standards for global health estimates:

1. An accurate listing of raw data used in the analysis
2. Correction of known biases in raw data
3. Use of WHO/UN standards and population estimates
4. CRA: causality criteria, assessment of hazards addressing bias and confounding, exposure estimation
5. Consistency with other WHO global health estimates
6. Clear explanation of the modeling approach, peer-reviewed (journal or WHO expert group)
7. Country consultation, if country estimates are produced
8. Statistical clearance for WHO publications involving official estimates of population-level health statistics

Clearance issues for FERG estimates (1)

General

- Documentation of exposure data and modelling of population estimates
- Documentation of evidence for causality in some cases
- Assessment of risks and appropriate calculation of attributable fractions for multicausal disease outcomes
- Consistency with WHO estimates for disease burden and other risks

Enteric diseases – bacterial, viral, protozoal:

- Extension of prior work on aetiological distribution of diarrheal diseases carried out in collaboration with the CHERG expert group
- Consistent with WHO/CHERG estimates for total diarrheal disease burden

Parasitic diseases:

- Consistency of epilepsy estimates for echinococcosis and neurocysticercosis with WHO estimates of overall prevalence of epilepsy (primary and secondary)

Clearance issues for FERG estimates (2)

Chemicals

- Peanut allergy – some concern about the initial use of a fairly severe weight for all cases of peanut allergy (mild to severe)
- Major inconsistencies of initial calculations for liver cancer with overall WHO “envelope” – related to use of an additive risk model rather than multiplicative model
- Lead and MeHg - need for consistency with WHO estimates of distribution and burden of intellectual disability, as well as with the distributional shift methods already used to estimate ID-attributable burden of lead
- Cadmium: chronic kidney disease – need for consistency with GBD estimates for CKD and for appropriate assessment of RRs and PAFs
- Arsenic – Concerns about estimating population exposure distributions, attributable fractions and increased risks for cancer and heart disease (causality?)

Aflatoxin issues

Initial calculations used JECFA cancer potency equations (JECFA 1998) for aflatoxin exposure a:

Excess HCC cases = 0.01*a per 100,000 in HBV-

Excess HCC cases = 0.3 *a per 100,000 in HBV+

Use of these equations gives aflatoxin attributed HCC > WHO estimates of total HCC in some countries and regions.

Risks for HBV and aflatoxin are multiplicative (JECFA, Liu et al 2012)

- Simpler PAF calculation based on average aflatoxin exposure by country
- Consistency with total HCC envelope and with other HCC burden estimates for alcohol, HBV and HCV

Relative risk of HCC for aflatoxin exposure level a is

$$RR_a = 1 + 0.01*a/ i_S$$

where i_S is the background HCC incidence rate in the HBV- study population

Conclusions: *Key components of WHO comparative risk assessment for foodborne diseases*

- Characterising exposure (categorical, continuous)
- Choice of counterfactual
- Identifying disease outcomes of exposure - causality, confounding
- Adequate data for estimation of population-level exposure
- Adequate data for quantifying exposure-disease relationships:
  - Population studies that control for confounders and bias
  - Nature of risk relationships: multiplicative, additive (relative/abs)
  - Generalizability of hazard estimates (multiple studies)
- Consistency with total burden estimates for disease outcomes
- Consistency with calculation methods for disease burden and other risks