



BCoDE – Burden of Communicable Diseases in Europe

A consistent and quantitative approach to risk-benefit assessment and risk ranking: the role of burden of disease estimates

Alessandro Cassini, Expert for Burden of Disease and Forecasting

EFSA Challenging boundaries in risk assessment – sharing experiences

Parma, 7 November 2012

Overview

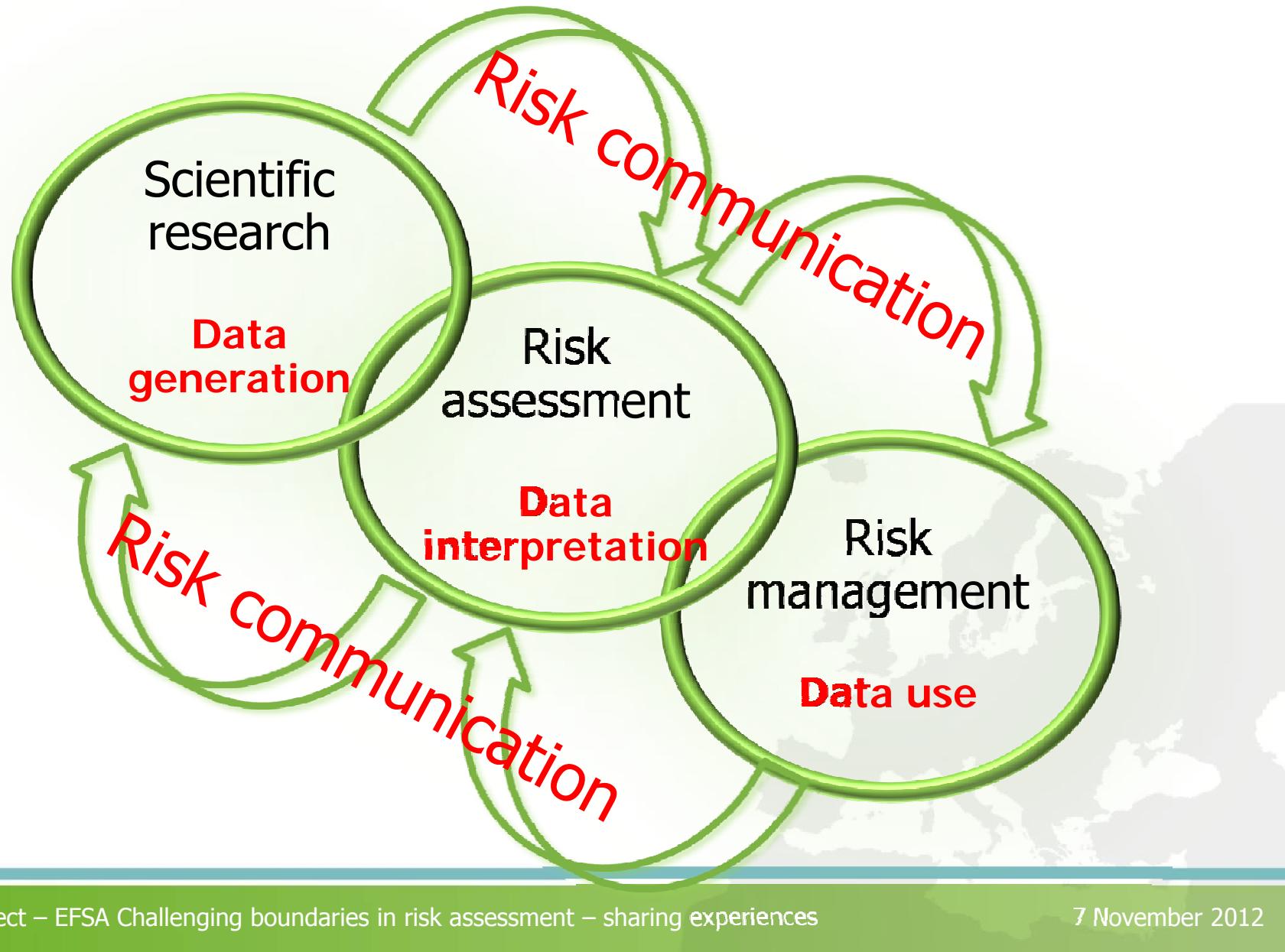
1. Risk ranking and risk-benefit assessment
2. The BCoDE project
3. Risk assessment using composite health measures: some examples
4. The BCoDE toolkit implementation within EU Member States



1. Risk ranking and risk-benefit assessment



Risk analysis



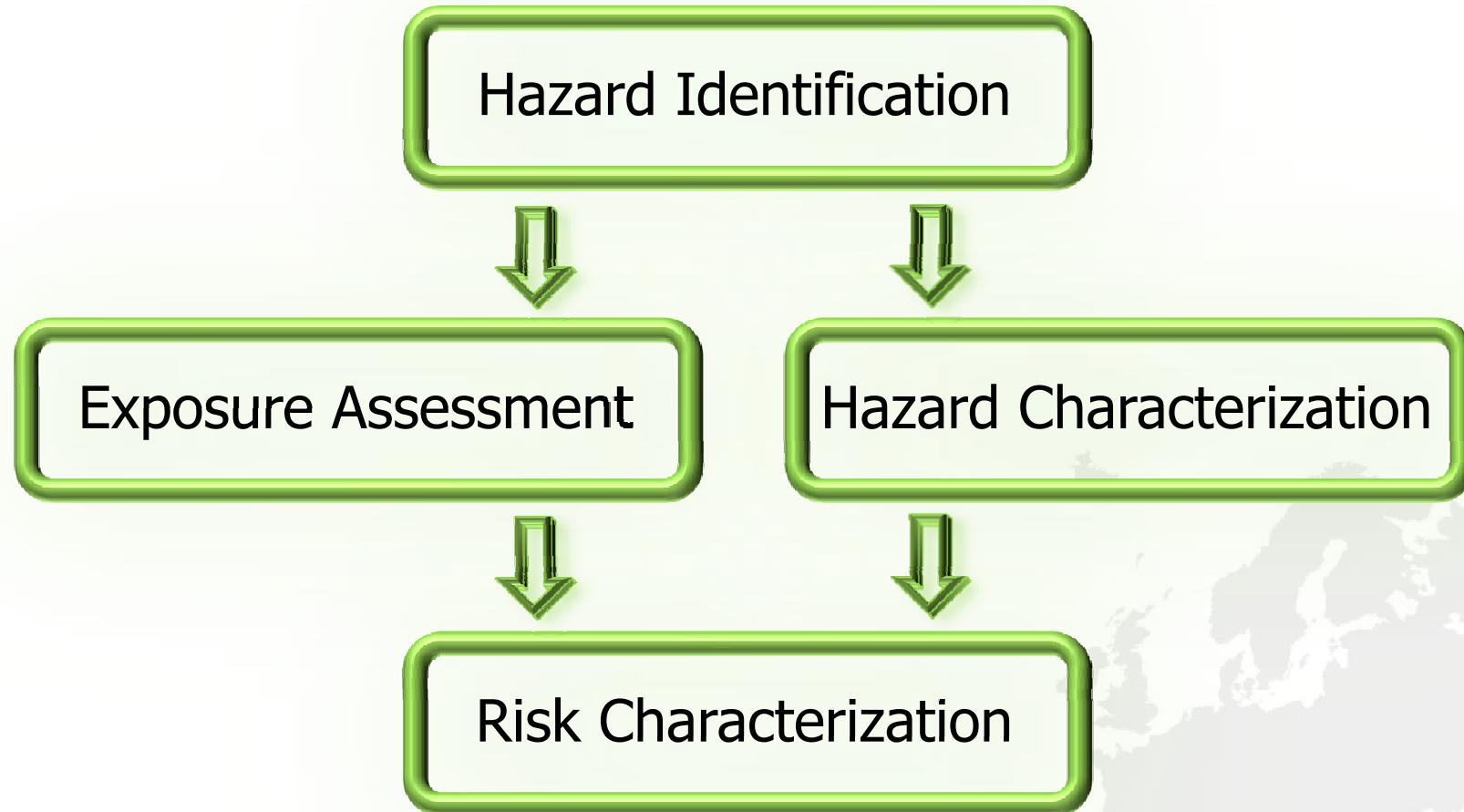
Risk assessment: using Health Technology Assessment tools

Use of information technology deriving from multidisciplinary fields with the purpose of assessing risks in a systematic and evidence-based approach

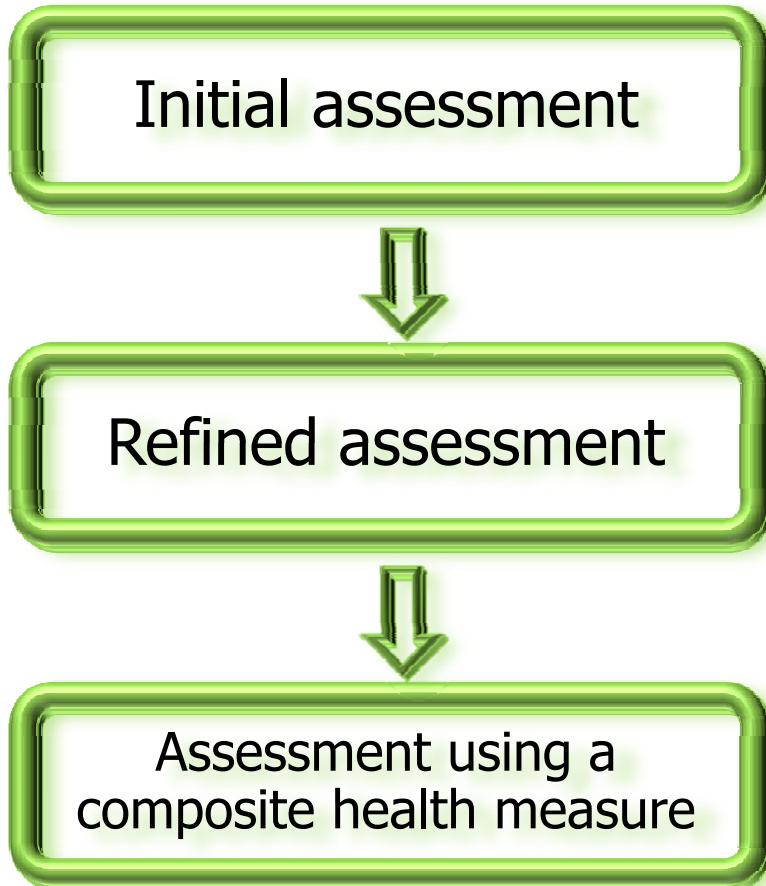
Its goal is to produce input to decision making in policy and practice



Risk-benefit assessment paradigm



Stepwise approach to risk-benefit assessment



Risk assessment modelling options

- Opinion based
- Qualitative
- Semi-quantitative
- **Quantitative**

A CHM is useful to:

1. Aggregate
2. Express
3. Compare benefits and risks

Expression of a
Single Net Health Impact Value

Guidance on human health risk-benefit assessment of foods. EFSA Journal 2010;8(7):1673

2. The BCoDE project



Global Burden of Disease: estimating the relative impact of all diseases

Comparing incidences or mortality data of very different diseases cannot provide the full picture

There is a need to summarize epidemiological data in a single health metric in order to compare these different diseases

In 1993 WHO and WB initiated the project called Global Burden of Disease (GBD)

The purpose is to estimate the relative impact of all diseases in the world



World Health Organization

Burden of Communicable Diseases in Europe (BCoDE)

- In 2009 ECDC initiated the BCoDE study in order to assess the comparative impact of infectious diseases in Europe
- Calculations are based on natural history of disease and related disabilities: models use a pathogen-based and incidence-based approach
- Estimates will allow comparison across infectious diseases: more epidemiological information and a tool for health policy prioritization and evaluation of interventions
- Other outputs of the project concern overview of surveillance data quality and availability
- A user-friendly and ready-to-use tool for communicable disease burden estimation was created for burden estimation



Apples and pears

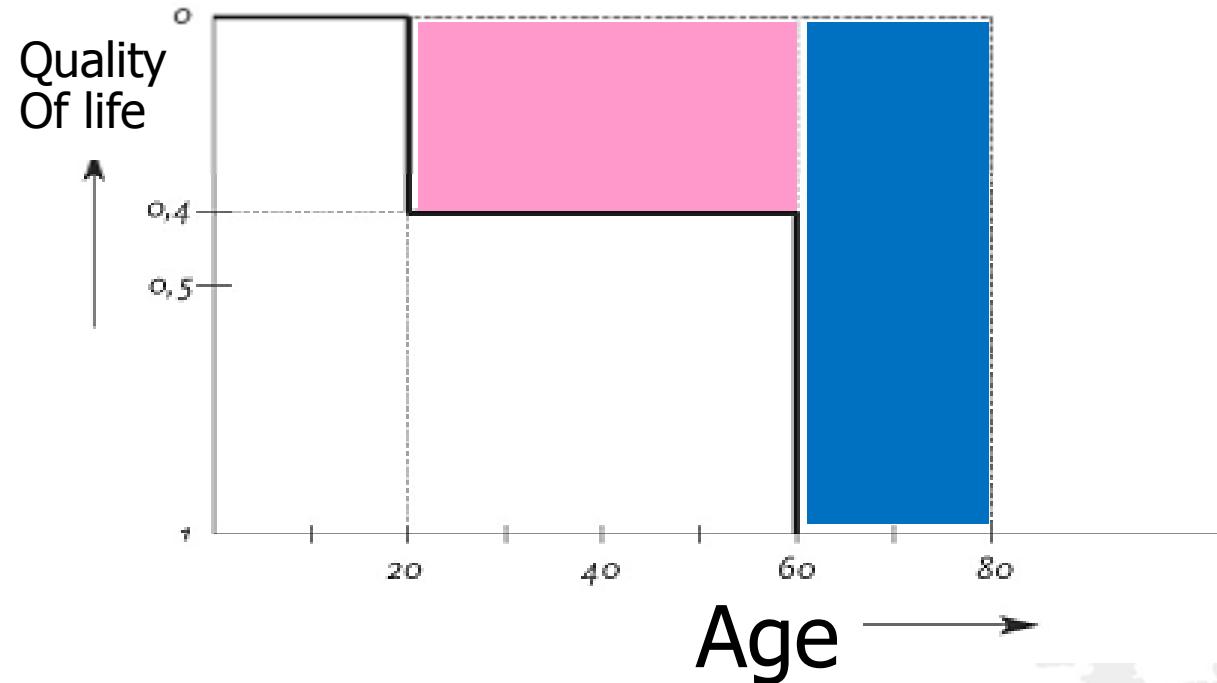
The primary scope of the BCoDE project is to quantify the magnitude of communicable diseases in Europe in a comprehensive manner in order to assess the relative burden of each communicable disease.



Choice on a common currency in order to compare impact of diseases, risks and benefits

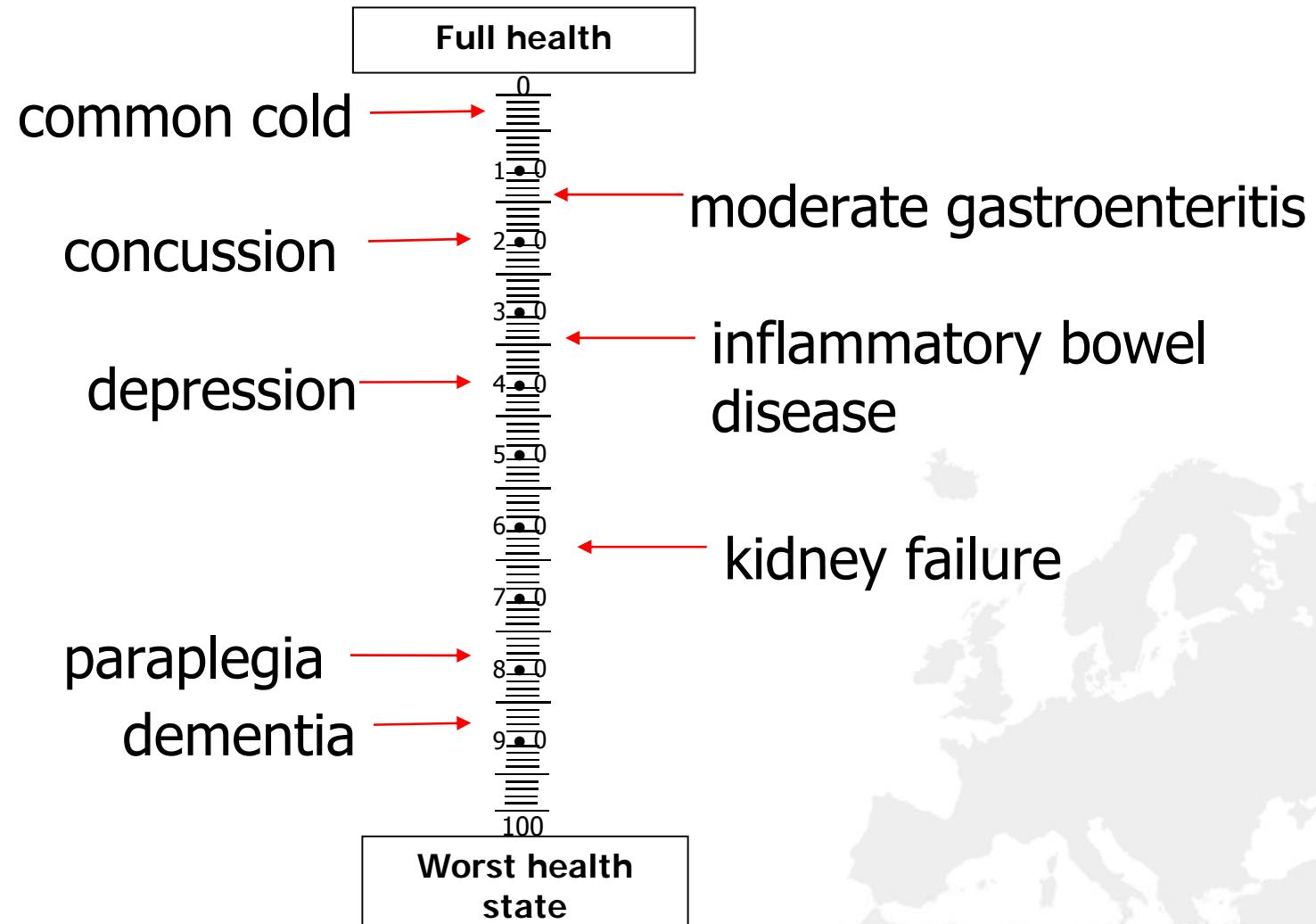


Disability Adjusted Life Year

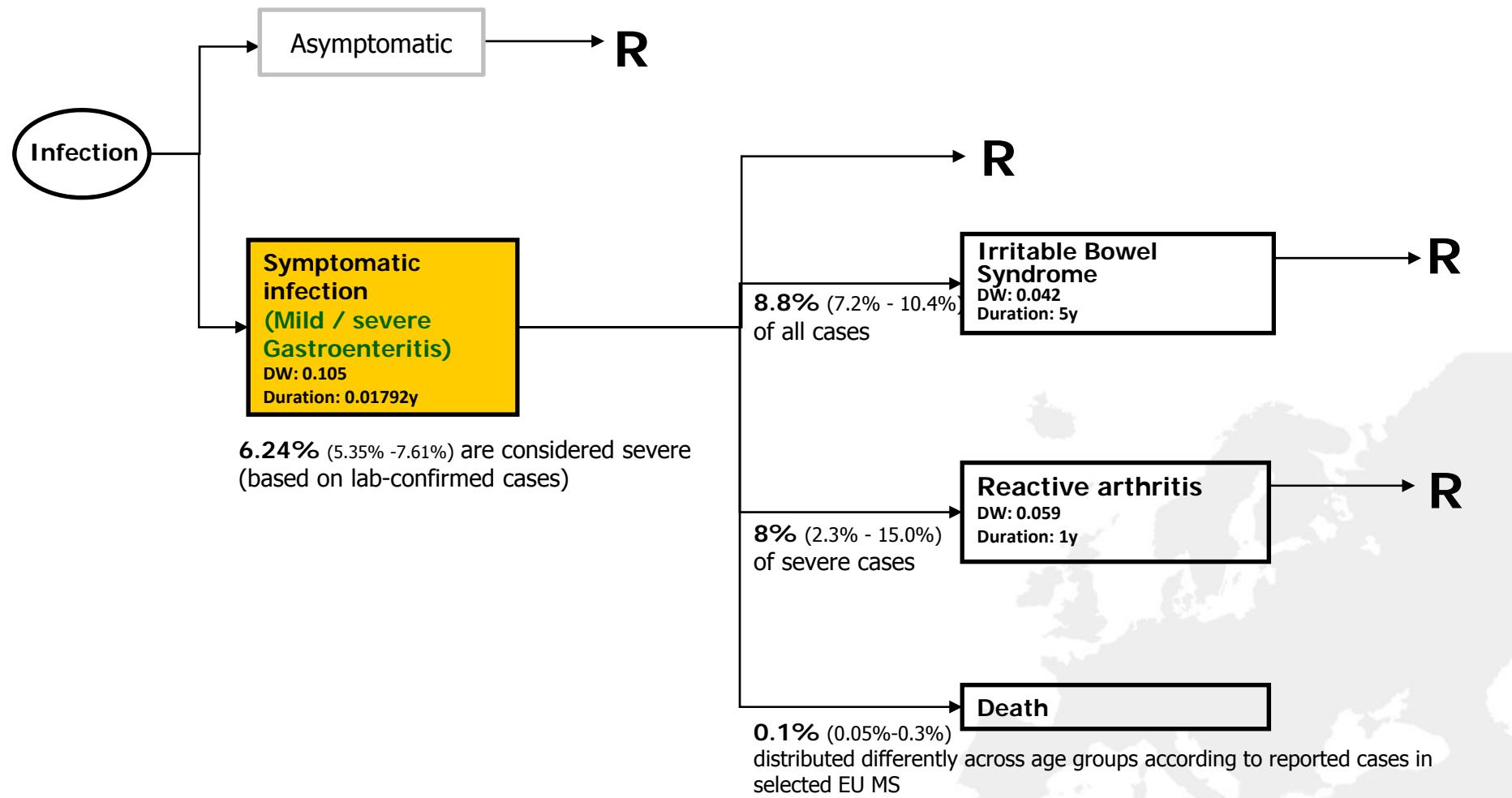


DALY = years of life lost (YLL) + years lived with disability (YLD)
 $= 20 \text{ years} + 16 \text{ years} = 36 \text{ years}$

What are disability weights?



Each disease is represented by an outcome tree: salmonellosis example



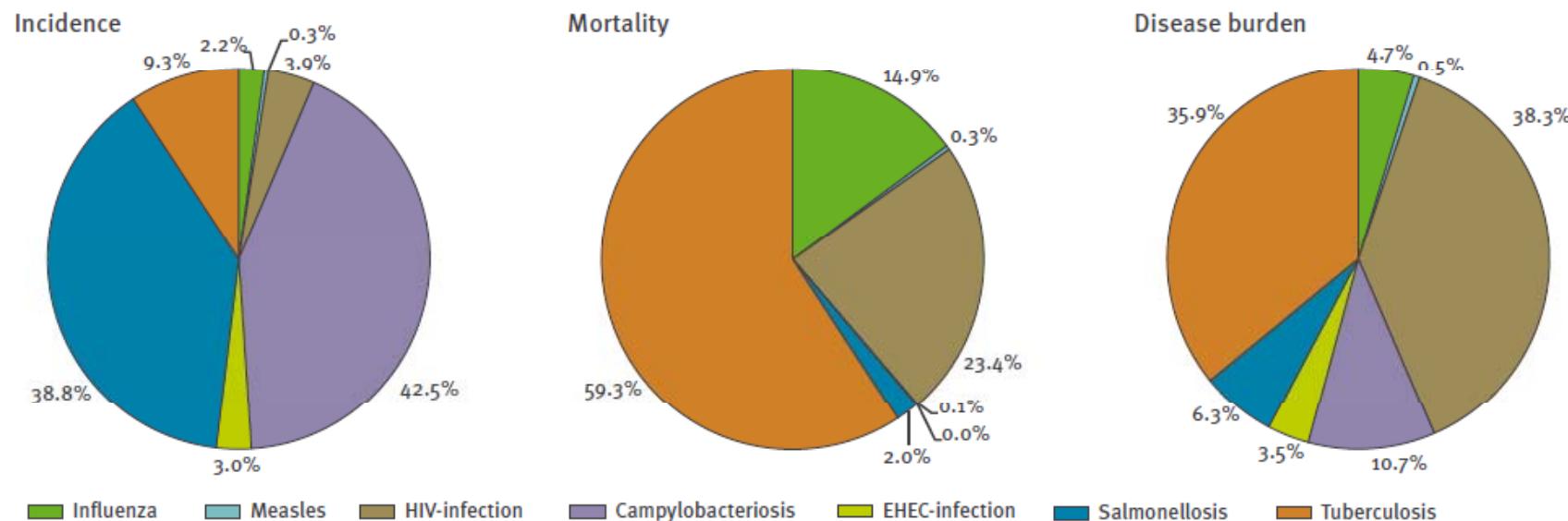
3. Risk assessment using composite health measures: some examples



BCoDE pilot study: disease pie changes according to the measure

Figure: Relative burden of the seven selected diseases based on different indicators:

- incidence (mean number of reported new cases per year in the period 2003-2005)
- mortality (mean number of reported deaths per year in the period 2003-2004)
- disease burden (DALYs per year based on above-mentioned incidence and mortality), RIVM Study 2007



Based on data for twelve countries (data available for all seven diseases): Austria, Czech Republic, Germany, Ireland, Latvia, Lithuania, the Netherlands, Poland, Slovenia, Sweden, United Kingdom, Norway

van Lier EA, Havelaar AH, Nanda A. The burden of infectious diseases in Europe: a pilot study. Euro Surveill. 2007;12(12):pii=751

Changing the ranking

CHMs combine information on mortality and non-fatal health outcomes to represent the health of a particular population in a single numerical index (Field and Gold, 1998)

Mortality

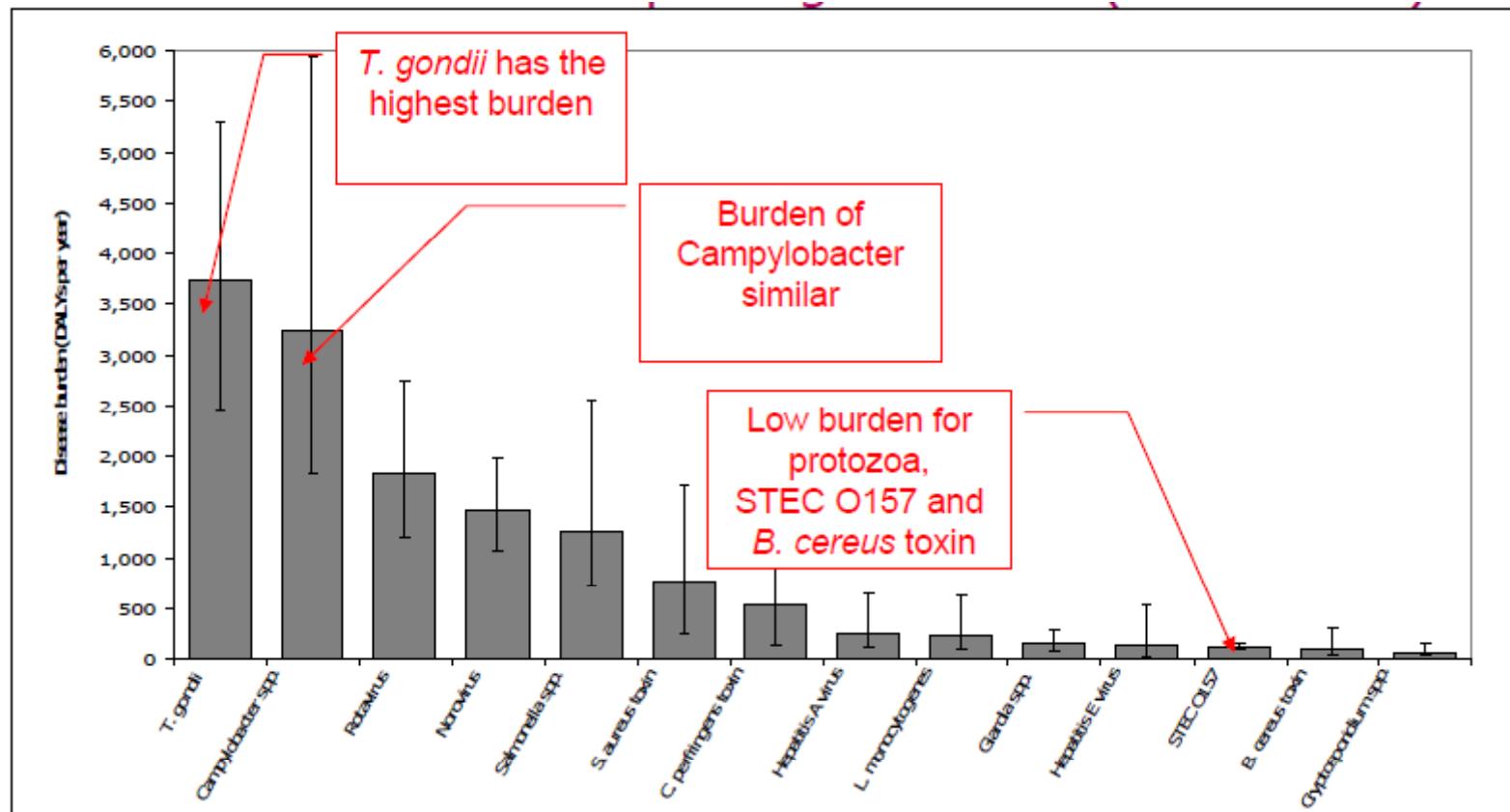
		%
1.	Ischaemic heart disease	12.2
2.	Cerebrovascular disease	9.7
3.	Lower respiratory infections	7.1
4.	COPD	5.1
5.	Diarrhoeal diseases	3.7
6.	HIV/AIDS	3.5
7.	Tuberculosis	2.5
8.	Trachea, bronchus, lung cancers	2.3
9.	Road traffic accidents	2.2
10.	Prematurity, low birth weight	2.0

DALYs

		%
1.	Lower respiratory infections	6.2
2.	Diarrhoeal diseases	4.8
3.	Depression	4.3
4.	Ischaemic heart disease	4.1
5.	HIV/AIDS	3.8
6.	Cerebrovascular disease	3.1
7.	Prematurity, low birth weight	2.9
8.	Birth asphyxia, birth trauma	2.7
9.	Road traffic accidents	2.7
10.	Neonatal infections and other	2.7

Leading Causes of Mortality and Burden of Disease, Global Burden of Disease Study 2004,
Health Statistics and Informatics Department, WHO 2004

Ranking of diseases according to burden



Havelaar et al., Int J Food Microbiol 2012; 156:231 2012; 231-238

Burden attribution to transmission pathways and food groups

Attribution of the incidence, fatalities and disease burden to the major transmission pathways in the Netherlands, 2009.

Transmission pathway	Food	Environment	Human	Animal	Travel	Total ^a
Incidence ($\times 1000$)	681 ^b 314–1310 ^c	221 123–391	627 383–1010	87 44–165	149 81–267	1770 945–3140
Fatal cases	78 45–144	39 21–68	73 31–144	18 11–29	25 14–44	233 122–430
Disease burden (DALY per year, not discounted)	6020 3360–10,700	2820 1770–4460	2370 1560–3620	1060 630–1860	1270 770–2160	13,500 8110–22,800
Disease burden (DALY per year, discounted)	4970 2630–9260	2200 1350–3590	2100 1370–3260	910 530–1670	1090 640–1910	11,300 6500–19,700

Attribution of the incidence, fatalities and disease burden of foodborne disease to food groups in the Netherlands, 2009.

Food group	Beef/ mutton	Pork	Poultry	Eggs	Dairy	Fish/ shellfish	Fruit/ vegetables	Beverages	Cereal products	Other food	Human/ animal	Total
Incidence ($\times 1000$)	107 ^a 42–222 ^b	44 19–87	59 23–128	22 9–46	56 25–108	58 30–104	44 21–83	16 8–30	40 19–77	123 55–236	114 66–192	684 314–1310
Fatal cases	9.1 4.8–19	9.3 6.1–15	14 9.3–21	5.9 4.7–8.0	5.7 3.4–11	6.6 3.4–13	6.0 3.2–11	2.0 1.1–3.5	3.0 1.6–6.0	5.3 2.2–14	12 5.5–23	78 45–144
Disease burden (DALY per year, not discounted)	951 501–1730	1300 807–2020	1050 593–1940	243 131–489	435 233–803	384 221–668	377 221–644	96 51–185	170 81–345	450 189–956	573 342–954	6030 3370–10,740
Disease burden (DALY per year, discounted)	760 372–1460	924 551–1490	914 493–1760	216 108–455	373 189–717	328 182–590	310 174–551	88 45–173	158 72–329	419 167–912	489 281–839	4980 2630–9270

Havelaar et al., Int J Food Microbiol 2012; 156:231–238

4. The BCoDE toolkit implementation within EU Member States



The Toolkit for burden estimation: a service for EU member states



A user-friendly and ready-to-use toolkit for communicable disease burden estimation is going to be finalized by April 2012



EU member states and EEA/EFTA countries are encouraged to employ the toolkit and calculate their national burden of communicable diseases



First page



BCoDE

File Options

About Exit

Main page

Workflow

Create models

View country data

Edit disease data

Run models

View detailed results

View aggregated results

Current and future burden of communicable diseases in the European Union and EEA/EFTA countries: the BCoDE toolkit

www.ecdc.europa.eu

Information page

■ BCoDE

File Options

Workflow

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Workflow

General introduction

This BCoDE toolkit will enable nominated EU Member State experts (end users) to estimate the national burden of communicable diseases, expressed in Disability-Adjusted Life Years (DALYs), a composite health measure encompassing mortality and morbidity data.

Thus the objectives of using this toolkit are:

- to introduce new epidemiological concepts based on evidence-based tools for decision making as part of the health technology assessment (HTA) progress;
- to enable comparisons across different diseases for prioritization purposes (tools helping health policy processes);
- to evaluate quality and availability of data as part of the assessment of national surveillance systems;
- to identify specific gaps for guiding new research in communicable diseases;
- to increase awareness about the impact of infectious diseases in each Member State and allow for quantitative estimates and comparison across diseases.

Each disease is represented by an outcome tree which is a flowchart that illustrates the natural history of a disease by ordering relevant health outcomes following infection and by illustrating their conditional dependency.

Therefore, each disease burden is computed through complex models including the following variables:

- **Number of cases;**
- **Multiplication factors adjusting for underestimation (under-reporting and under-ascertainment);**
- Duration of disease (for each health outcome);
- Mortality;
- Disability weights (for each health outcome);
- Percentage of cases developing the health outcomes.

In the current version of the BCoDE toolkit only two parameters are to be entered by the user: number of cases and multiplication factors (in bold above). All the other parameters are locked and fixed (the latter have stemmed from literature reviews and expert opinions, and represent an average European setting).

Please refer to the BCoDE Methodology Protocol (http://ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DisForm.aspx?ID=688) and the disease reports for more information on the methodology and the data behind this version of the BCoDE toolkit.

How to use the toolkit

Computation of estimates is performed in a number of steps that are found in the menu on the left:

- **Create models** - choose your country and the disease(s) you want to estimate the burden for. Then click on "Create the Models".
- **View country data** - demographic data can be viewed, but not edited.
- **Edit disease data** - this is the most important interface of the toolkit where you can see the outcome trees, you can copy and paste (input) or manually enter disease data and where you can also adjust for underestimation.

To view the outcome trees of each disease previously selected in the "Create models" interface, please use the scroll down menu at the top of this interface. To view information about the natural history of each disease, please click on the outcomes or on the transition arrows. To input or manually enter disease data, please click on "Set model parameters" A new pop-up window will appear for inputting:

- case data age and gender specific;
- multiplication factors adjusting for under-ascertainment AND under-reporting OR adjusting for under-estimation in one step. Uncertainty will be illustrated according to the type of distribution chosen (constant, uniform or pert).

Two more tables are shown in this pop-up window: the country-specific age distribution and the yearly incidence per 100 000; the latter will change automatically according to the number of cases inputted or entered in the first table and the multiplication factor/s chosen. Once all relevant data are entered, click on "Apply changes" and close the window. Use the scroll down menu on top of the "Edit disease data" window to select other diseases to input and repeat the operations above.

- **Run models** - now the models can be run with a specified number of iterations for sampling the uncertainty intervals. Specify the desired number of iterations, let it calculate and when finished click on "Close window".
- **View detailed results** - results are given per disease by age, gender and by sequelae. To view the results of other diseases, choose the disease in the scroll down menu on top of this window.
- **View aggregated results** - results for different diseases are compared through two bubble charts and a table which lists the selected diseases from the one with the highest DALY per 100 000 to the lowest.

For details please consult the documentation or contact the BCoDE coordination centre (bcode@ecdc.europa.eu).

Selection of countries and diseases

BCoDE

File | Options

Select countries and diseases

SELECT COUNTRIES (1 SELECTED)



Country

- Austria
- Belgium
- Bulgaria
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Iceland
- Ireland
- Italy
- Latvia
- Liechtenstein
- Lithuania
- Luxembourg
- Malta
- ...

SELECT DISEASES (4 SELECTED)

- Disease
- Hepatitis B
- Influenza
- Measles
- Salmonellosis
- VTEC/STEC
- Campylobacteriosis
- Chlamydia
- Cryptosporidiosis
- Giardiasis
- Hepatitis A
- Shigellosis
- Tuberculosis
- Hepatitis C
- HIV
- Invasive Pneumococcal Disease
- Invasive Meningococcal Disease
- Invasive Haemophilus Influenzae
- Legionellosis
- Gonorrhoea
- Syphilis
- Mumps
- Pertussis
- Diphtheria
- Rabies
- Rubella
- Tetanus
- Listeriosis
- Q Fever
- Tick-Borne Encephalitis
- Poliomyelitis
- Toxoplasmosis
- vCJD

MODELS

4 models created

model 1: Italy - Salmonellosis
 model 2: Italy - Campylobacteriosis
 model 3: Italy - Hepatitis A
 model 4: Italy - Listeriosis

Create models

Delete all models

About | Exit

Main denominators

BCoDE

File Options

Select country **Italy** NOTE: Data cannot be modified

LIFE EXPECTANCY DATA

Age	Female	Male
0	82.43	79.94
1-4	80.28	77.77
5-9	75.47	72.89
10-14	70.51	67.91
15-19	65.55	62.93
20-24	60.63	57.95
25-29	55.72	52.99
30-34	50.83	48.04
35-39	45.96	43.10
40-44	41.13	38.20
45-49	36.35	33.38
50-54	31.68	28.66
55-59	27.10	24.07
60-64	22.64	19.65
65-69	18.32	15.54
70-74	14.24	11.87
75-79	10.59	8.81
80-84	7.56	6.34
85+	4.25	3.54
Total	30,669,543.00	28,949,747.00

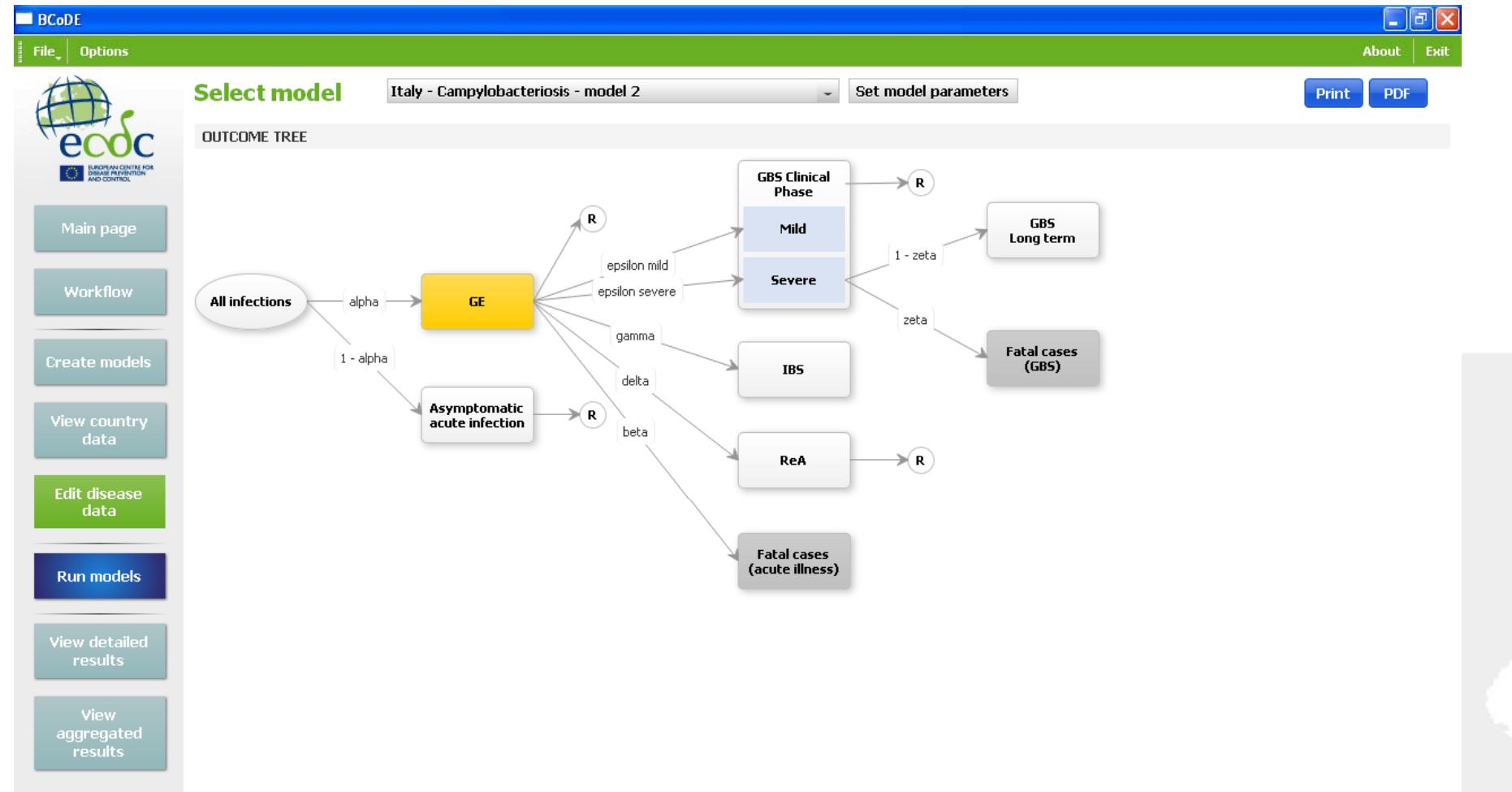
AGE DISTRIBUTION DATA

Age	Female	Male
0	271,156.00	287,468.00
1-4	1,092,219.00	1,156,783.00
5-9	1,350,328.00	1,427,907.00
10-14	1,350,853.00	1,430,329.00
15-19	1,447,484.00	1,535,010.00
20-24	1,518,274.00	1,579,522.00
25-29	1,789,761.00	1,825,851.00
30-34	2,209,320.00	2,252,120.00
35-39	2,390,342.00	2,430,143.00
40-44	2,450,106.00	2,465,168.00
45-49	2,185,216.00	2,157,048.00
50-54	1,969,855.00	1,910,744.00
55-59	1,928,031.00	1,838,712.00
60-64	1,770,421.00	1,653,133.00
65-69	1,751,643.00	1,558,842.00
70-74	1,588,755.00	1,306,953.00
75-79	1,441,619.00	1,035,404.00
80-84	1,154,195.00	676,185.00
85+	1,009,965.00	422,425.00

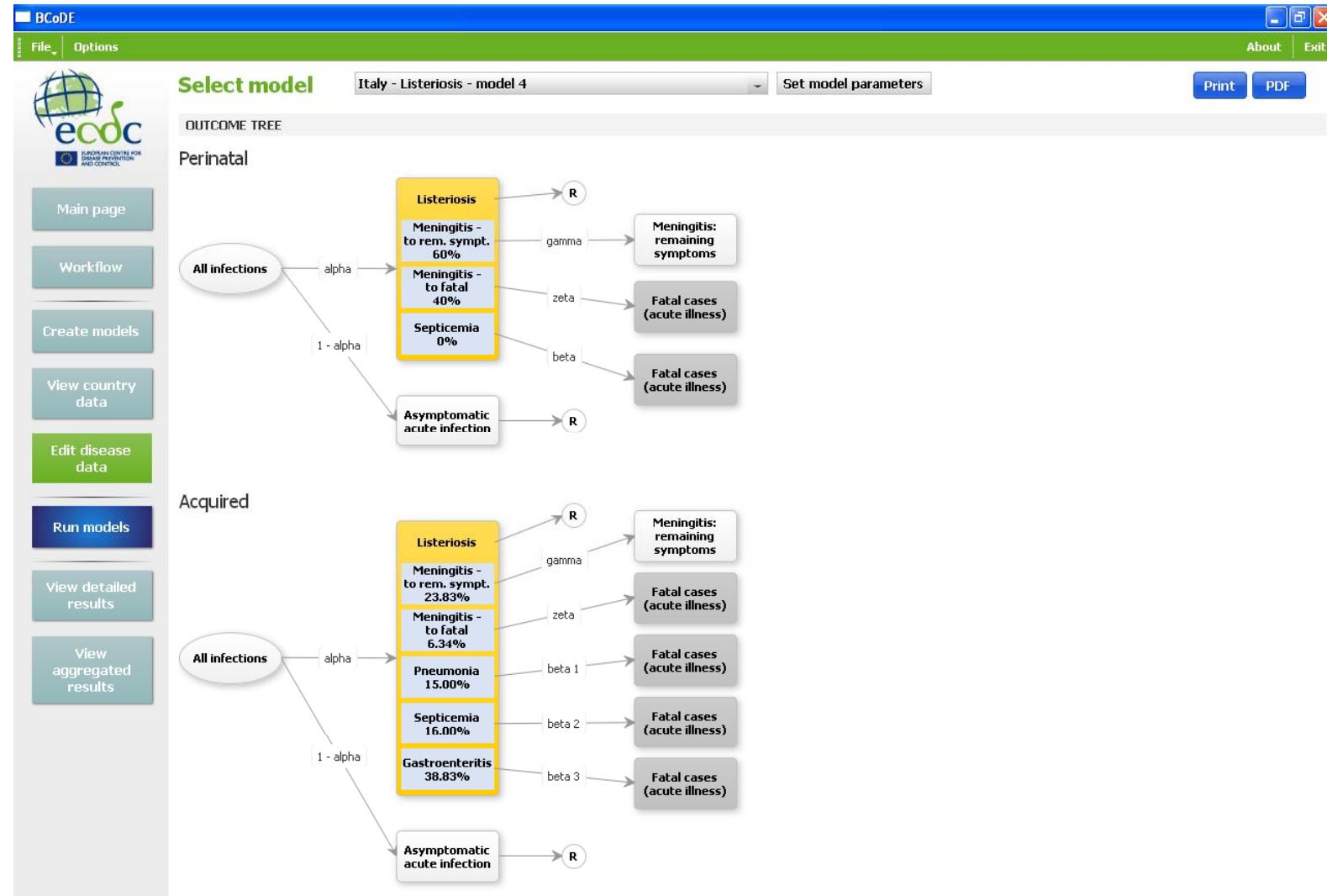
Source WHO 2008
Weblink <http://apps.who.int/ghodata/?vid=720>

Source EUROStat: Database by themes->Population->Pop.
Weblink <http://epp.eurostat.ec.europa.eu/>

Browsing outcome trees (information by navigation)



Browsing outcome trees 2



Inputting incidence data

BCoDE

File Options About Exit

Select model Italy - Hepatitis A - model 7 Set model parameters Print PDF

OUTCOME TREE R

Main Work Create View data Edit data Run View results View aggregated results

Set model parameters

Italy - Hepatitis A - model 7 Apply changes

INPUT - MULTIPLICATION FACTORS

Underestimation Underreporting and Underascertainment

Distribution type: Pert
Lower bound: 1
Most likely: 7.9
Upper bound: 100

Average: 22.10

Value values

INPUT - AVERAGE NUMBER OF CASES PER YEAR

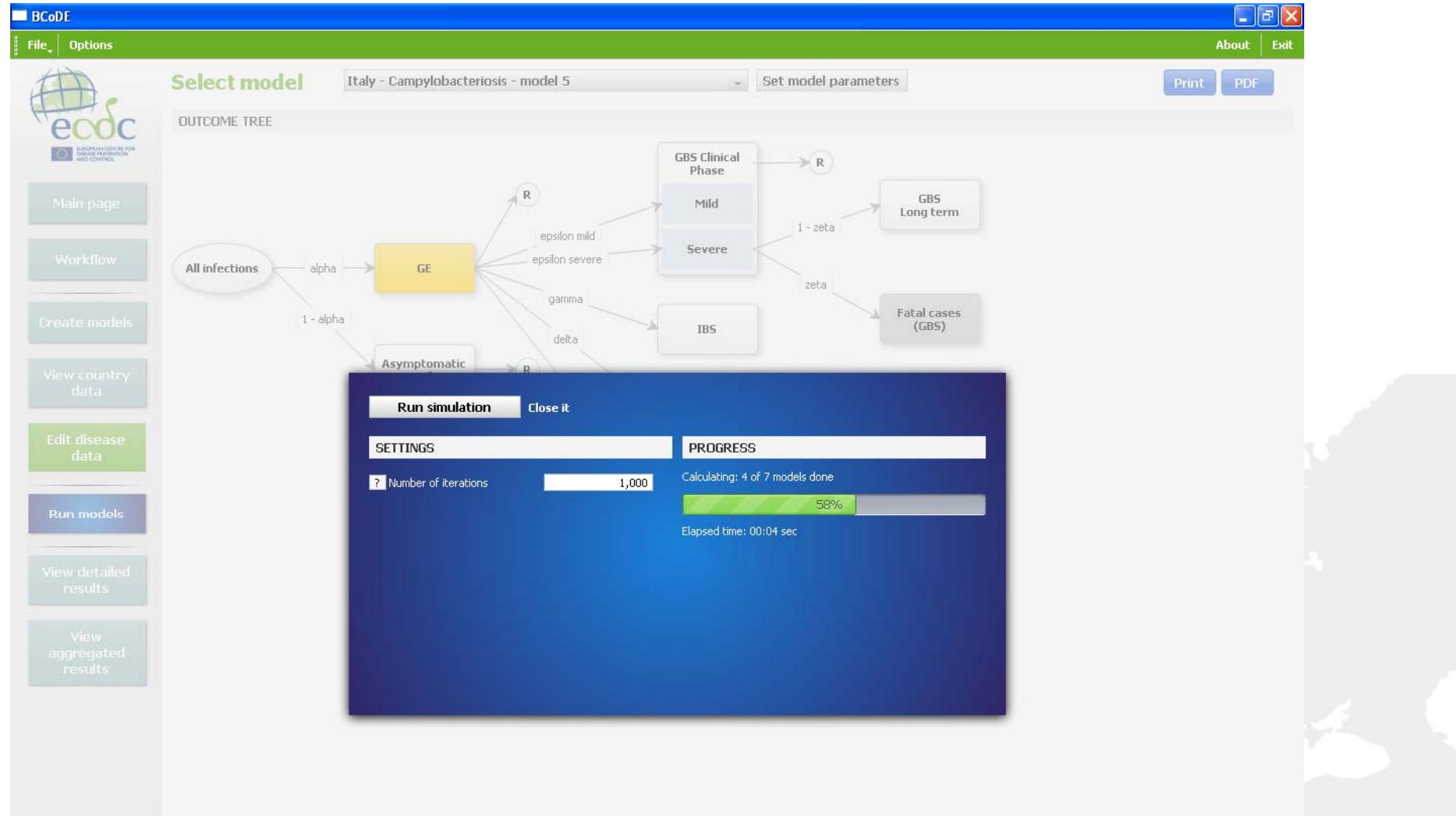
FIXED - AGE DISTRIBUTION

OUTPUT - YEARLY INCIDENCE PER 100,000

Age	Female	Male	Age	Female	Male	Age	Female	Male
0	1.00	3.00	0	271,156.00	287,468.00	0	8.15	23.06
1-4	18.00	21.00	1-4	1,092,219.00	1,156,783.00	1-4	36.42	40.12
5-9	41.00	50.00	5-9	1,350,326.00	1,427,907.00	5-9	67.10	77.39
10-14	27.00	44.00	10-14	1,350,853.00	1,430,329.00	10-14	44.17	67.98
15-19	28.00	48.00	15-19	1,447,484.00	1,535,010.00	15-19	42.75	69.11
20-24	32.00	80.00	20-24	1,518,274.00	1,579,522.00	20-24	46.58	111.93
25-29	31.00	102.00	25-29	1,789,761.00	1,825,851.00	25-29	38.28	123.46
30-34	35.00	127.00	30-34	2,209,320.00	2,252,120.00	30-34	35.01	124.62
35-39	31.00	118.00	35-39	2,390,342.00	2,430,143.00	35-39	28.66	107.31
40-44	25.00	89.00	40-44	2,450,106.00	2,465,168.00	40-44	22.55	79.79
45-49	14.00	57.00	45-49	2,185,216.00	2,157,048.00	45-49	14.16	58.40
50-54	12.00	34.00	50-54	1,969,855.00	1,910,744.00	50-54	13.46	39.32
55-59	7.00	18.00	55-59	1,928,031.00	1,838,712.00	55-59	8.02	21.63
60-64	6.00	10.00	60-64	1,770,421.00	1,653,133.00	60-64	7.49	13.37
65-69	4.00	7.00	65-69	1,751,643.00	1,558,842.00	65-69	5.05	9.92
70-74	2.00	3.00	70-74	1,588,755.00	1,306,953.00	70-74	2.78	5.07
75-79	2.00	2.00	75-79	1,441,619.00	1,035,404.00	75-79	3.07	4.27
80-84	2.00	2.00	80-84	1,154,195.00	676,185.00	80-84	3.83	6.54
85+	2.00	2.00	85+	1,009,965.00	422,425.00	85+	4.38	10.46
Total	320.00	817.00	Total	30,669,543....	28,949,747....	Total	431.91	993.77

Source: EUROStat: Database by themes->Popul...
Weblink: <http://epp.eurostat.ec.europa.eu/>

Running the simulation



Viewing detailed results per each disease

BCoDE

File Options

Select model: Italy - Campylobacteriosis - model 5

About Exit

Print PDF

Main page

Workflow

Create models

View country data

Edit disease data

Run models

View detailed results

View aggregated results

Results table

Illness	Cases	Incidence	YLD Per Year	YLL Per Year	DALY Per Year	DALY Per Case Symptomatic	DALY Per 100,000
Total Infected	1,144,900.00						
Acute							
GE			2,153.98	3,312.21	5,466.19	4.77e-3	9.17
cases	1,144,900.00	0.02	2,153.98		2,153.98		
death	320.38	5.37e-6		3,312.21	3,312.21		
Acute Total			2,153.98	3,312.21	5,466.19	4.77e-3	9.17
Sequelae							
GBS Clinical Phase			155.38	722.92	878.30	7.67e-4	1.47
cases	626.18	1.05e-5	155.38		155.38		
death	21.48	3.60e-7		722.92	722.92		
GBS Long term			2,691.35	0.00	2,691.35	2.35e-3	4.51
cases	499.69	8.38e-6	2,691.35		2,691.35		
death	0.00	0.00		0.00	0.00		
IBS			21,081.34	0.00	21,081.34	0.02	35.36
cases	100,805.18	1.69e-3	21,081.34		21,081.34		
death	0.00	0.00		0.00	0.00		
ReA			512.91	0.00	512.91	4.48e-4	0.86
cases	8,693.39	1.46e-4	512.91		512.91		
death	0.00	0.00		0.00	0.00		
Sequelae Total			24,440.98	722.92	25,163.90	0.02	42.21
All Health Outcomes Total			26,594.96	4,035.13	30,630.10	0.03	51.38

Viewing detailed results per each disease 2

BCoDE

File Options

Main page

Workflow

Create models

View country data

Edit disease data

Run models

View detailed results

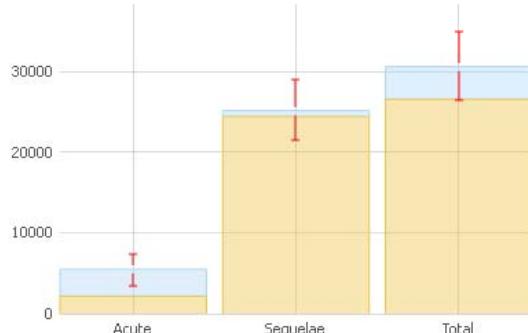
View aggregated results

IBS		21,081.34	0.00	21,081.34	0.02	35.36
cases	100,805.18	1.69e-3	21,081.34		21,081.34	
death	0.00	0.00		0.00	0.00	
ReA		512.91	0.00	512.91	4.48e-4	0.86
cases	8,693.39	1.46e-4	512.91		512.91	
death	0.00	0.00		0.00	0.00	
Sequelae Total		24,440.98	722.92	25,163.90	0.02	42.21
All Health Outcomes Total		26,594.96	4,035.13	30,630.10	0.03	51.38

Results charts

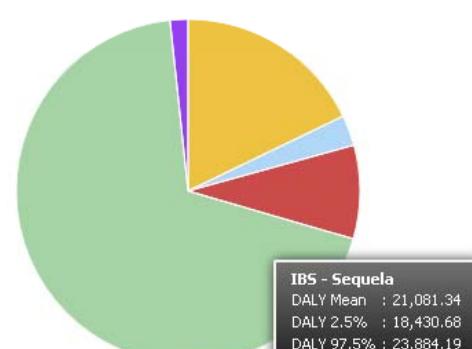
BURDEN OF DISEASE

YLD - Mean YLL - Mean DALY error

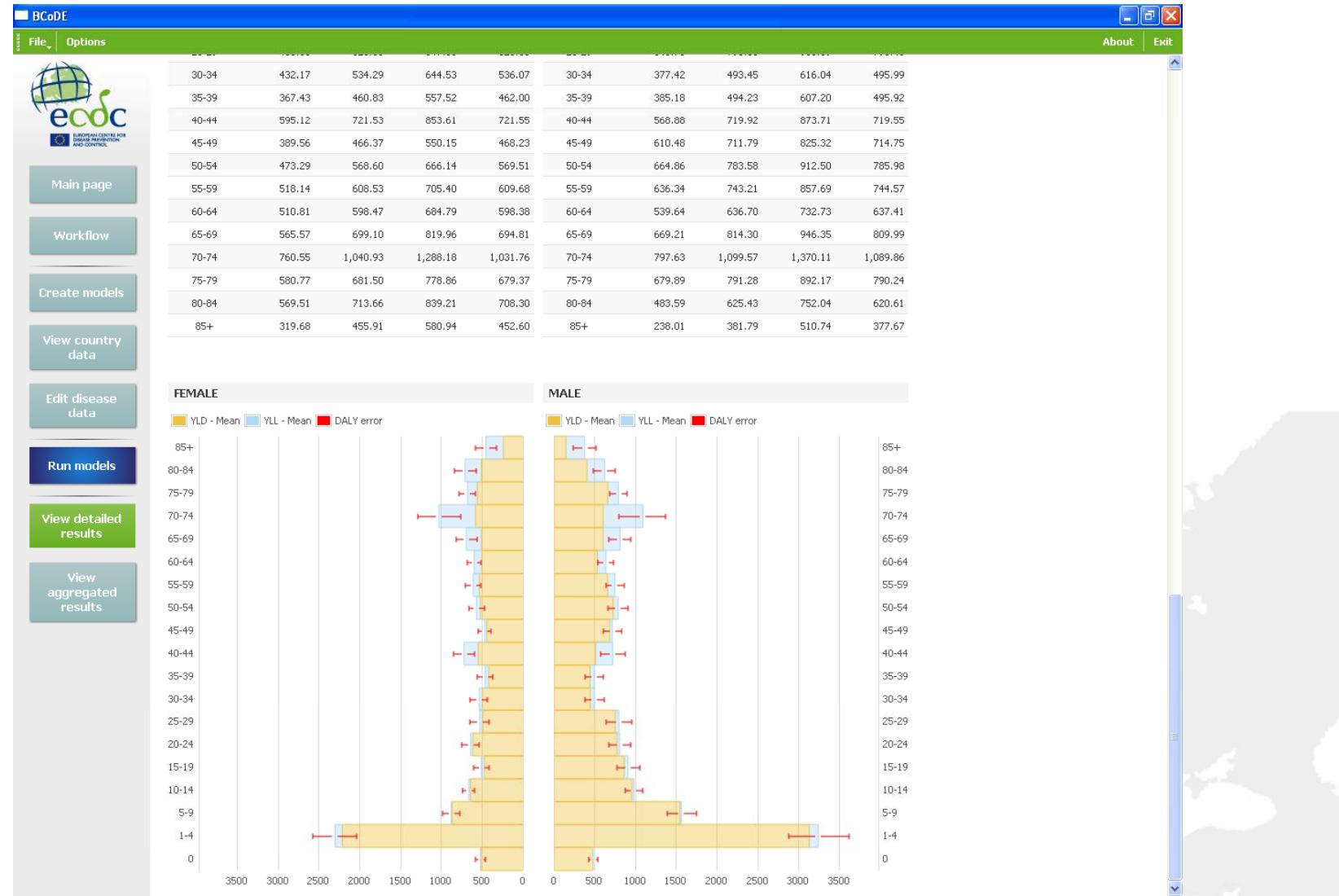


BURDEN OF DISEASE

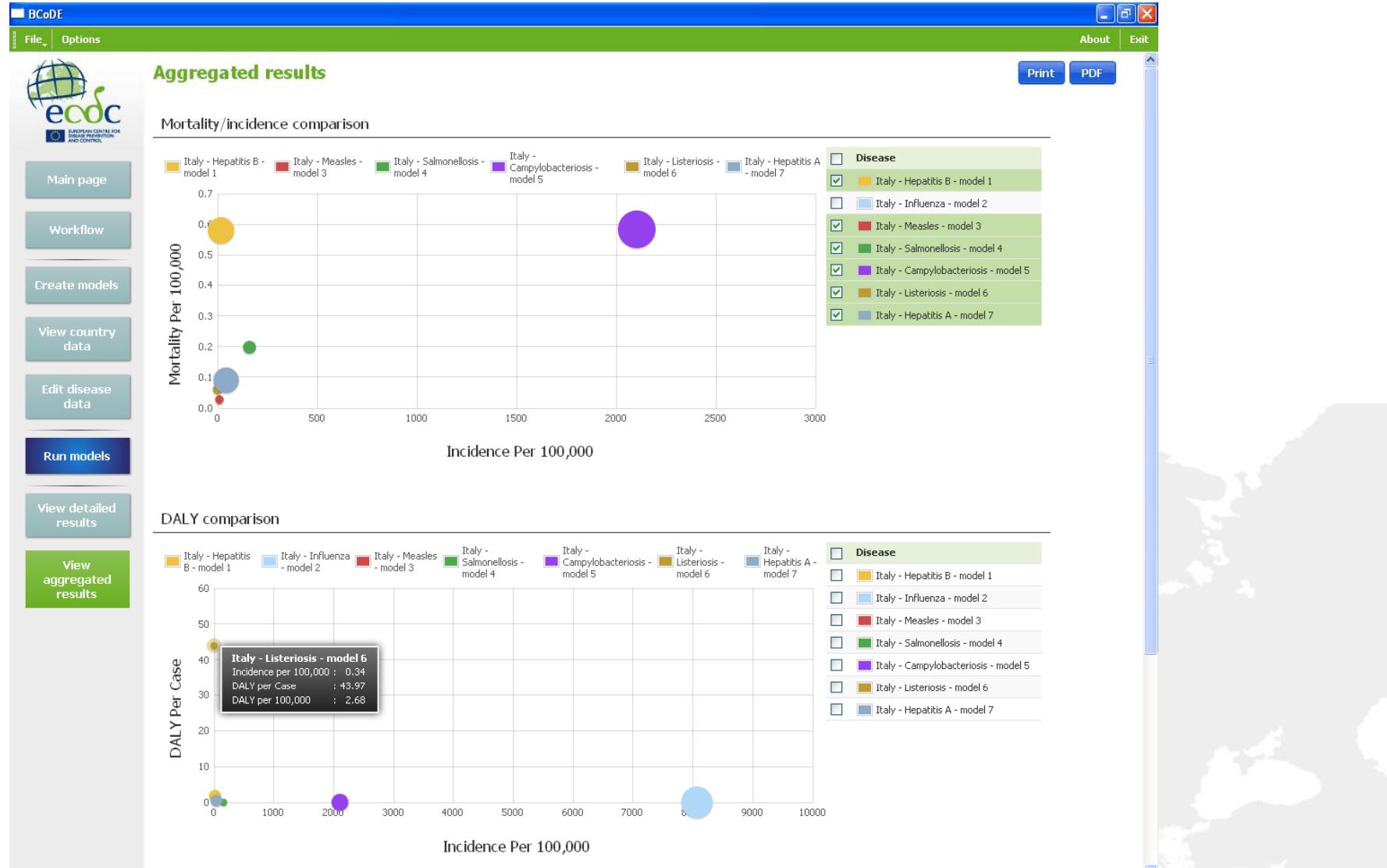
GE GBS Clinical Phase GBS Long term IBS ReA



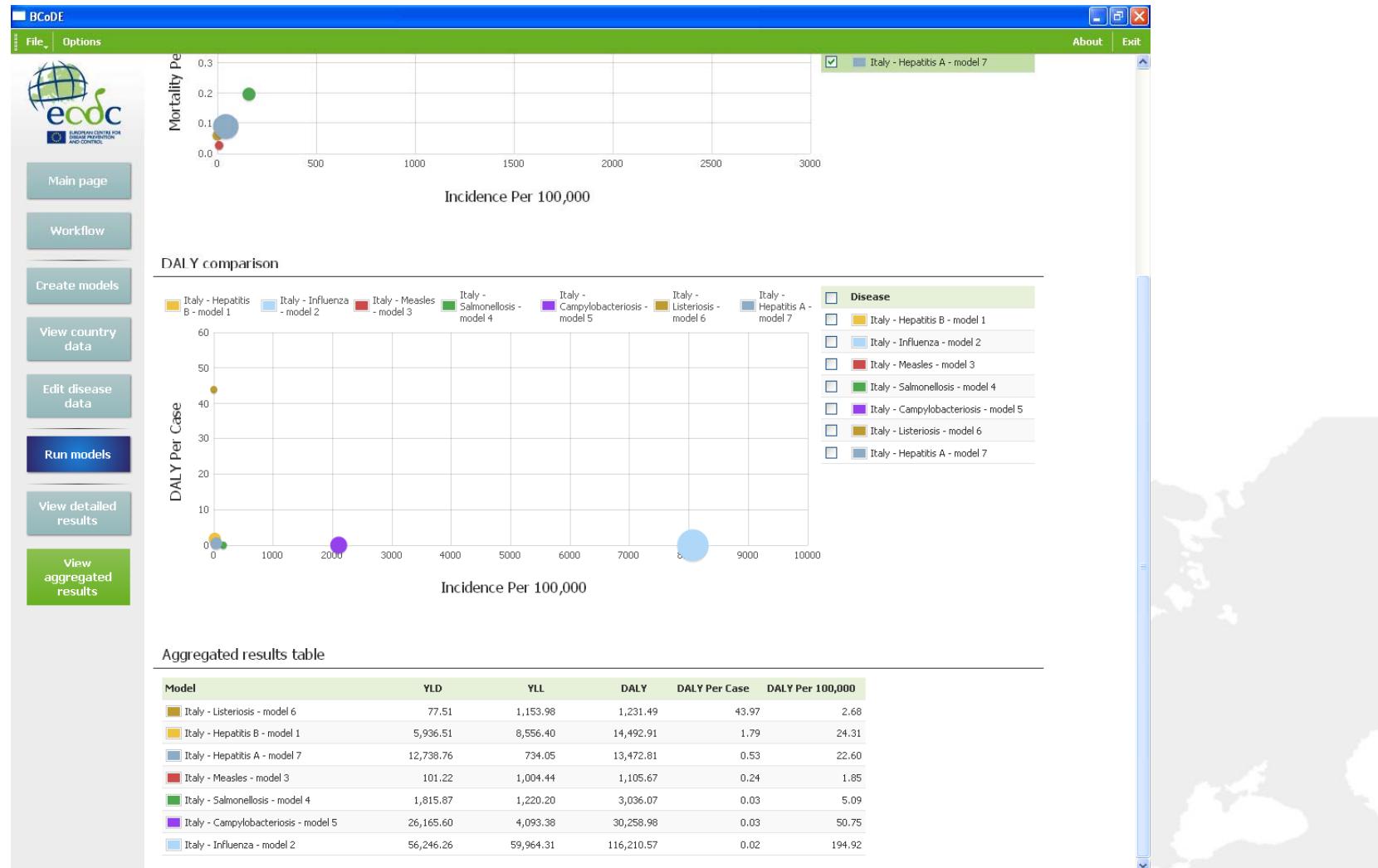
Viewing detailed results per each disease 3



Viewing aggregate results



Viewing aggregate results 2 (risk ranking)



Key messages from today

BCoDE project's objective is to improve evidence-based decision making in prioritisation of CDs in Europe

ECDC and the BCoDE European consortium have:

- Undergone extensive literature reviews;
- Outlined the methodology
- Tested the methodology in four European countries
- Created a software, user-friendly toolkit for burden estimation

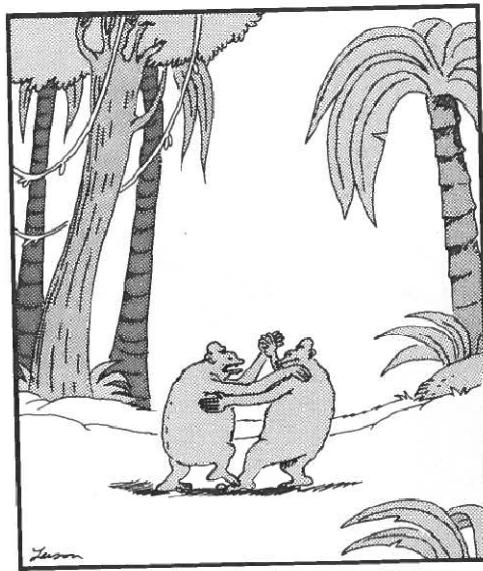
The national expert is now invited to estimate its national burden of communicable diseases



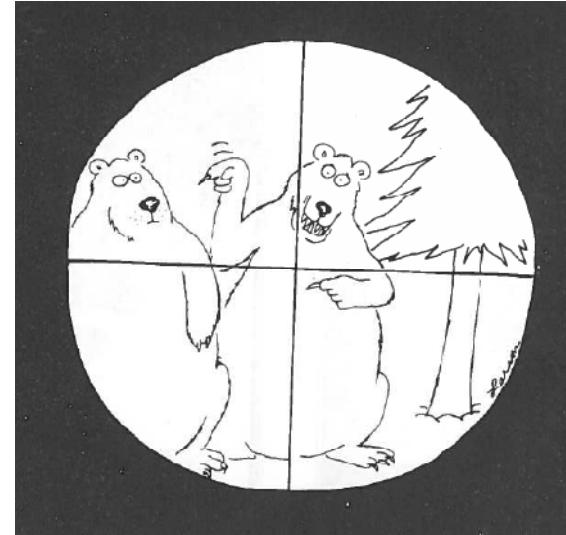
Key messages from today 2

Incidence data (cases and multiplication factor) is the most sensitive input

It's very important to target the correct users, i.e. country and disease experts



"I'm afraid you misunderstood... I said I'd like a mango."



Uncertainty and limitations must also be expressed

Never under-estimate the weight of communication

Questions and thank you

For suggestions, comments and questions please email:

BCoDE@ecdc.europa.eu

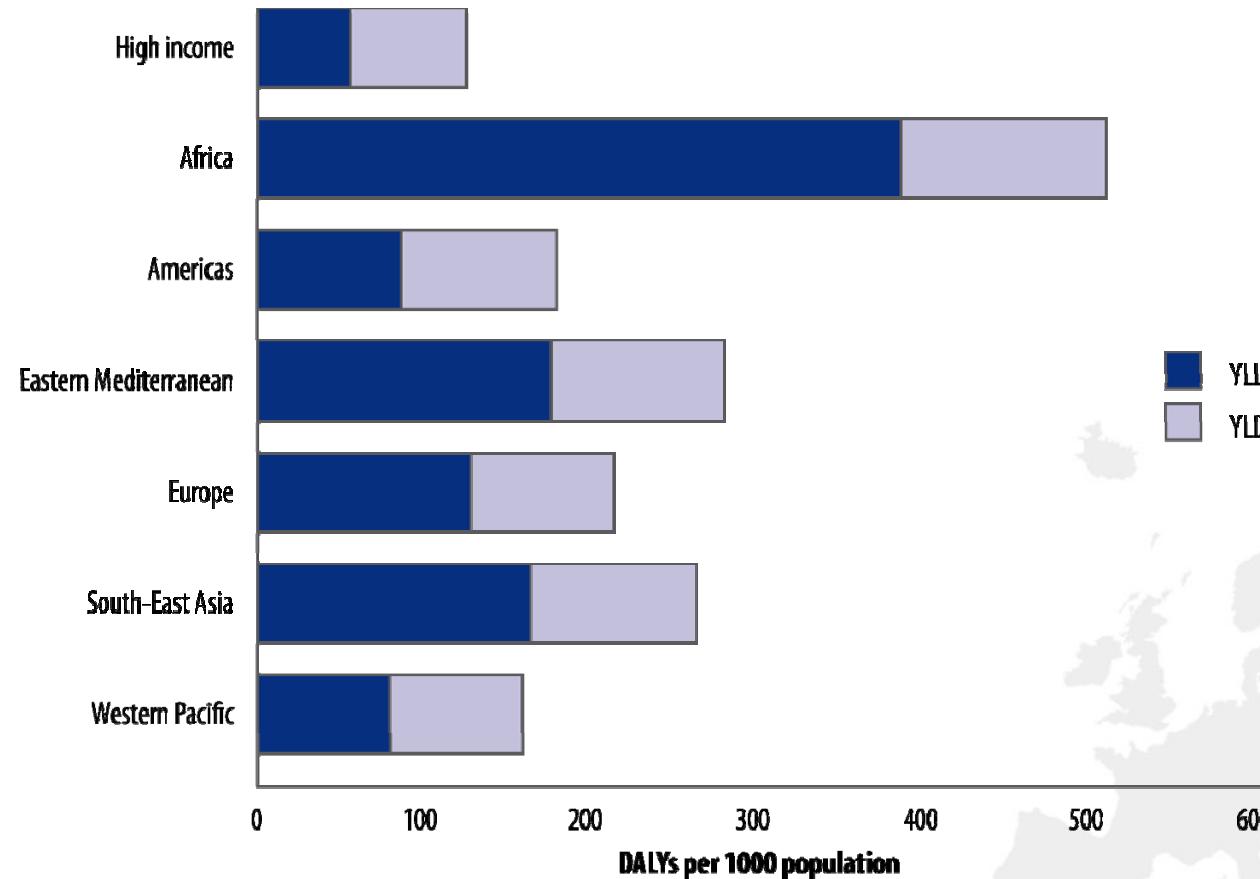
Alessandro.Cassini@ecdc.europa.eu



5. Backup slides: using burden of disease estimates

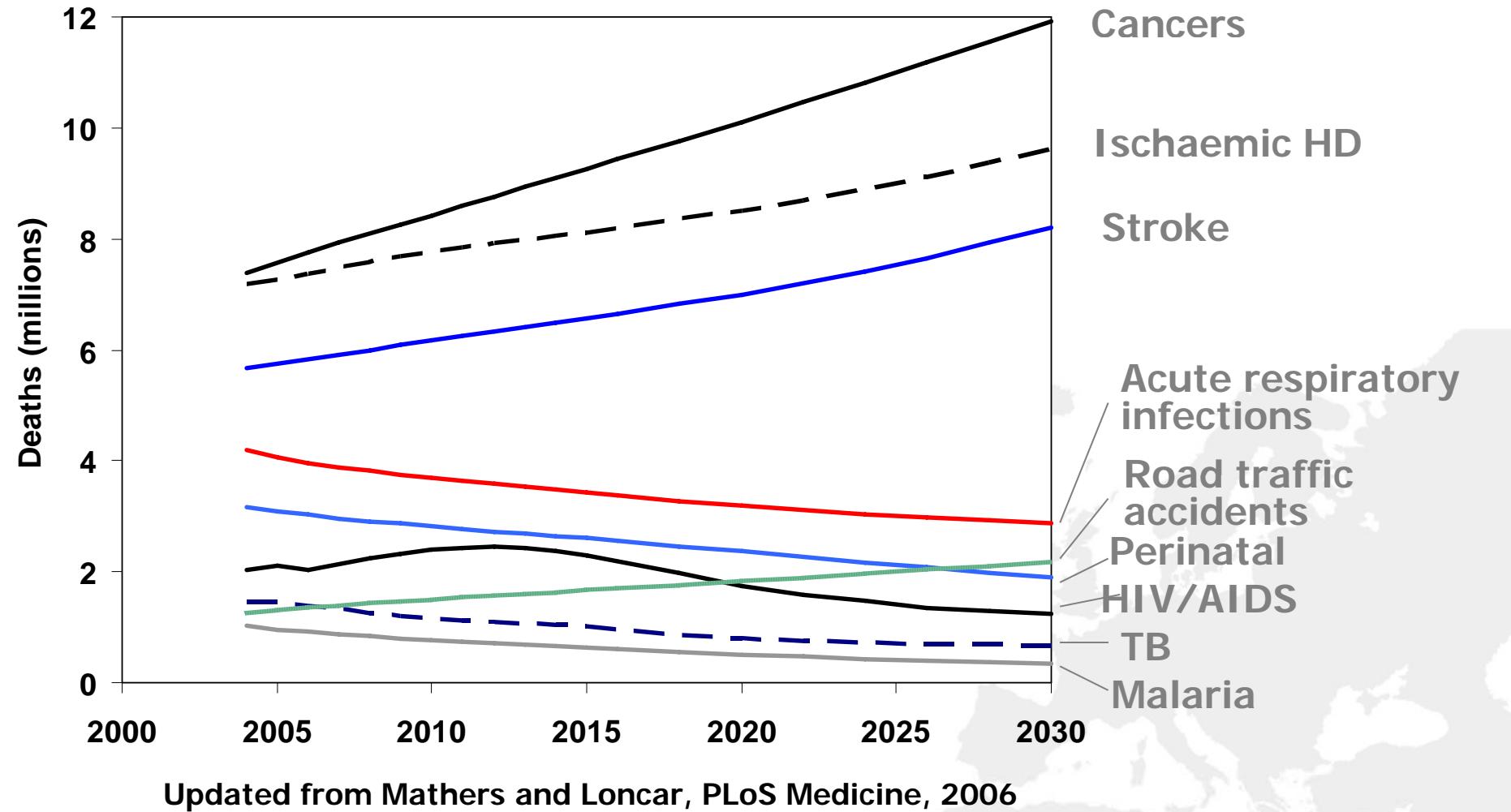


YLL, YLD and DALYs by region, 2004

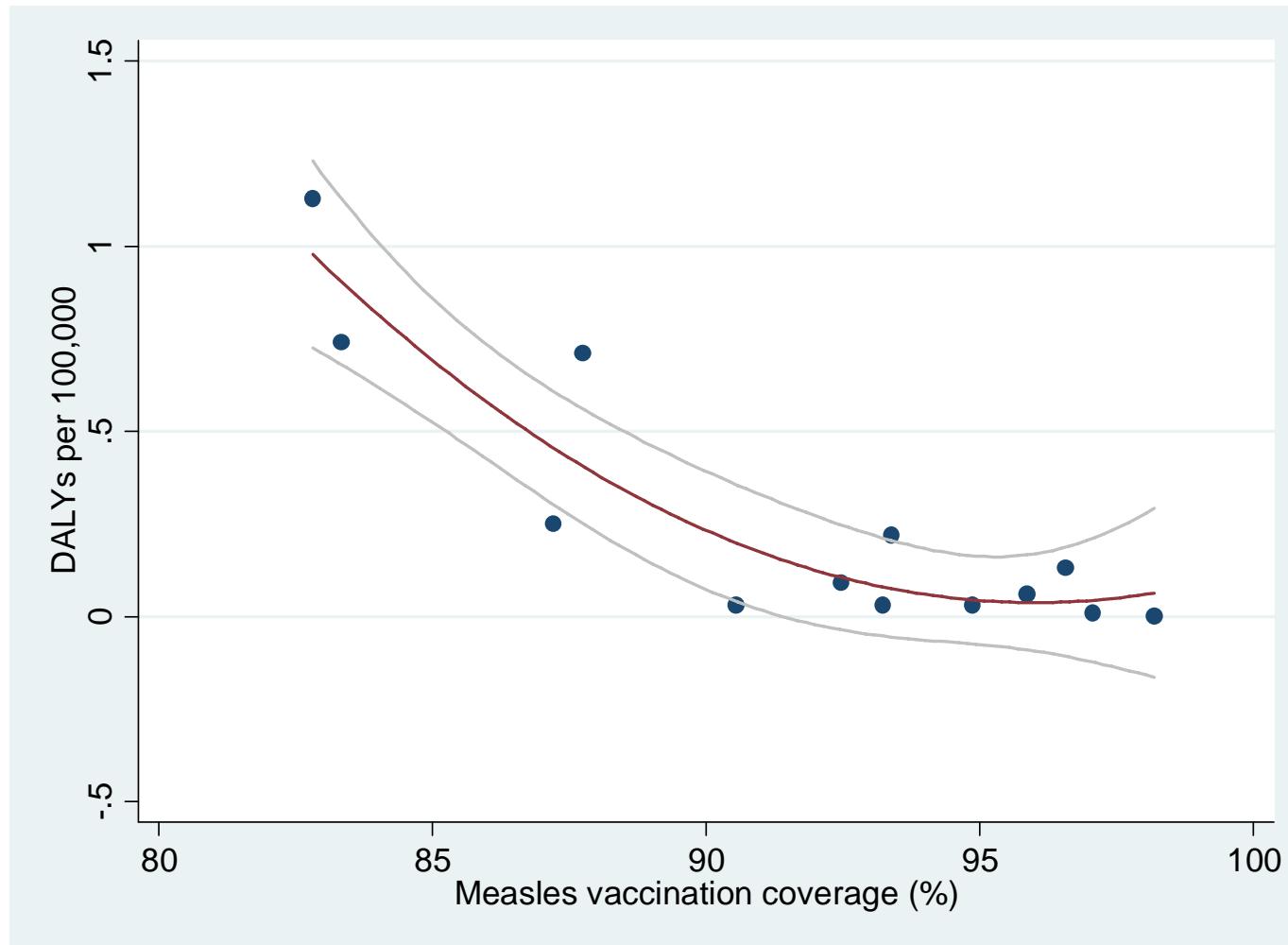


Health Statistics and Informatics Department, WHO 2004

Global projections for selected causes, 2004 to 2030

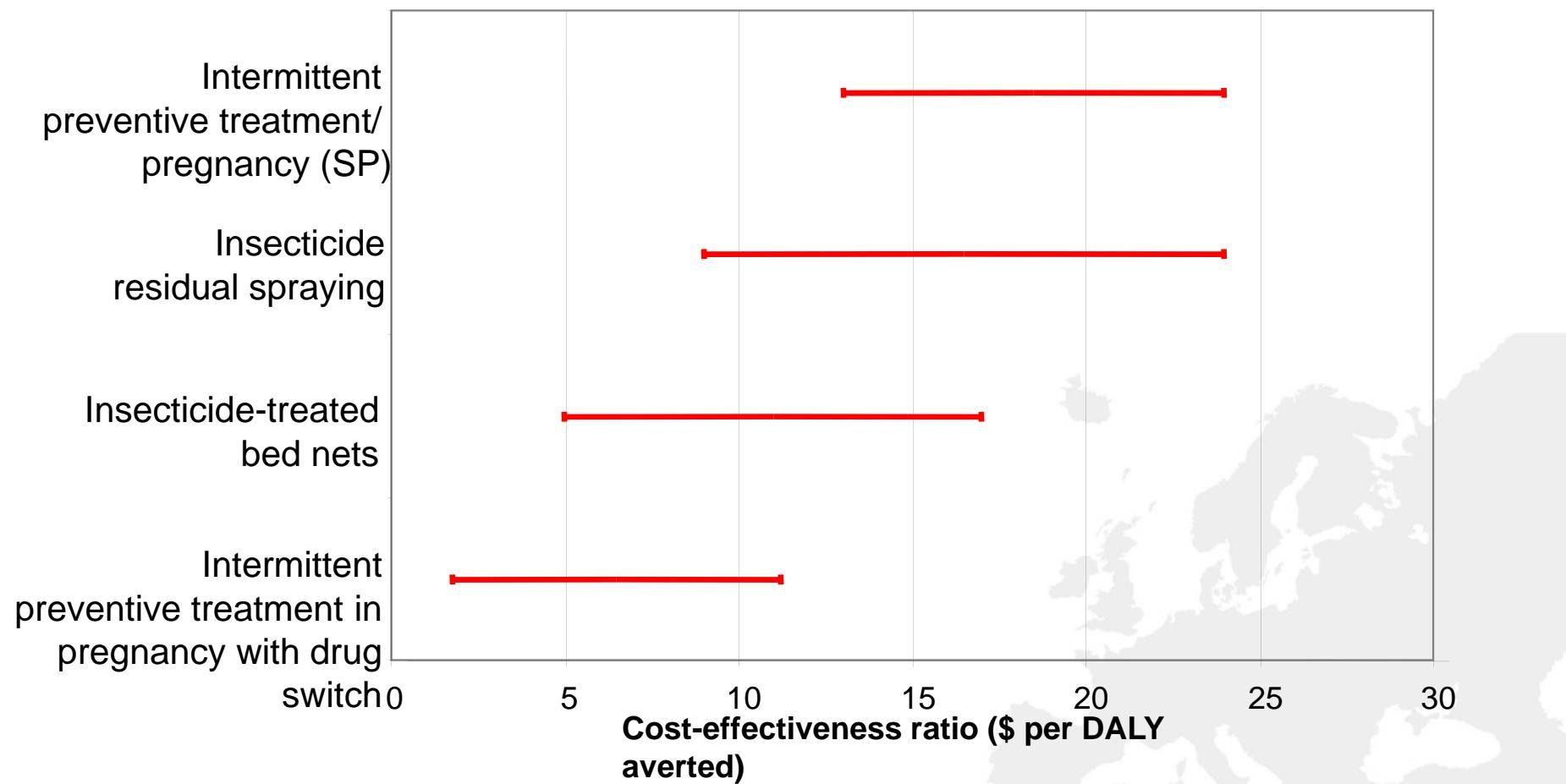


Quadratic correlation between vaccination coverage and burden of measles in different MS



R-squared=0.76; p<0.05

Cost-Effectiveness of Interventions Against Malaria in Sub-Saharan Africa



R. Laxminarayan et al (DCPP authors), 2006 in *Disease Control Priorities in Developing Countries*

Ranking of communicable diseases by DALYs



Disease Condition

HIV-AIDS

Neglected Tropical Diseases

Malaria

Tuberculosis

Disease Burden

84.5 million

56.6 million

46.5 million

34.7 million

Hotez PJ, Molyneux DH, Fenwick A, Ottesen E, Ehrlich Sachs S, Sachs JD
PLoS Medicine 2006; 3: e102

Disease Burden and Research and Development Funding

Condition	Global Disease Burden (million) DALYs*	R&D Funding (\$Millions)	R&D Funding per DALY*
Cardiovascular	148.190	9402	\$63.45
HIV/AIDS	84.458	2049	\$24.26
Malaria	46.486	288	\$6.20
Tuberculosis	34.736	378	\$10.88
Diabetes	16.194	1653	\$102.07
Dengue	0.616	58	\$94.16

Malaria and R&D Alliance: *Science*, 13 January 2006: *Disability-Adjusted Life Year.

DCPP estimates in millions are: cardiovascular = 208.8; HIV = 71.5; malaria = 40.0; tuberculosis = 36.1; Diabetes = 20.0; dengue = 0.5

Each disease is represented by an outcome tree: campylobacteriosis example

