

Global burden of disease study : Past, present, and future

Christopher J.L. Murray

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Outline

- 1) **Study goals**
- 2) GBD study overview
- 3) Key results from GBD 2013
- 4) Some debates
- 5) GBD 2015 main innovations
- 6) New analytical directions

Global Burden of Disease Study Goals

1. Provide valid, reliable, timely and local assessments of the state of health and trends of all populations in the world at national or subnational level.
2. Communicate effectively these results to the scientific community, health decision-makers, the media, and the public.

Global Burden of Disease Study Goals

To achieve these goals, we need to

1. Identify, access and analyze the world's data on health
2. Use the best methods and where needed innovate the methods used to synthesize and analyze health data
3. Create a vibrant global collaboration to tap into expertise relevant to the GBD around the world.

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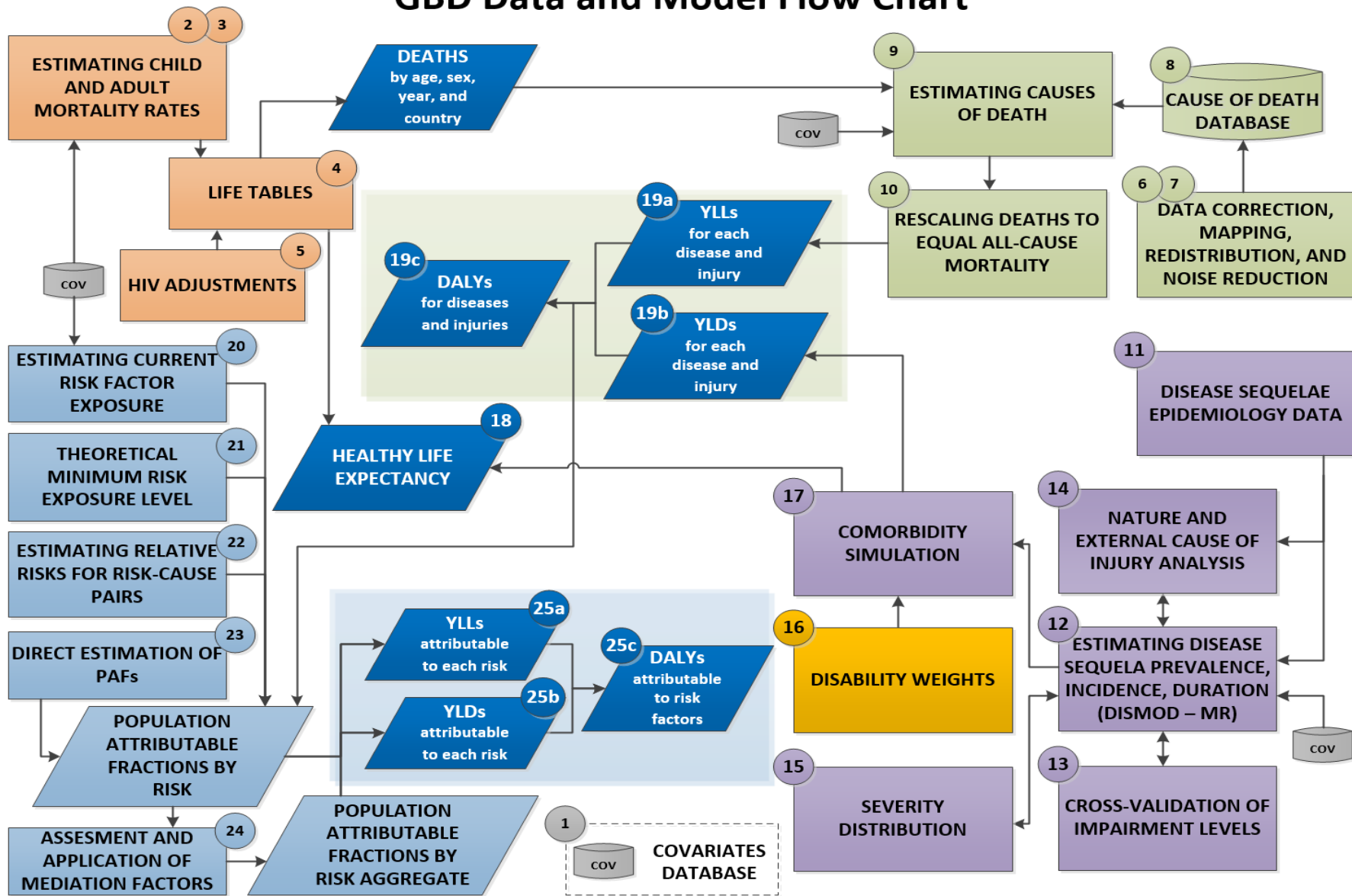
Global Burden of Disease

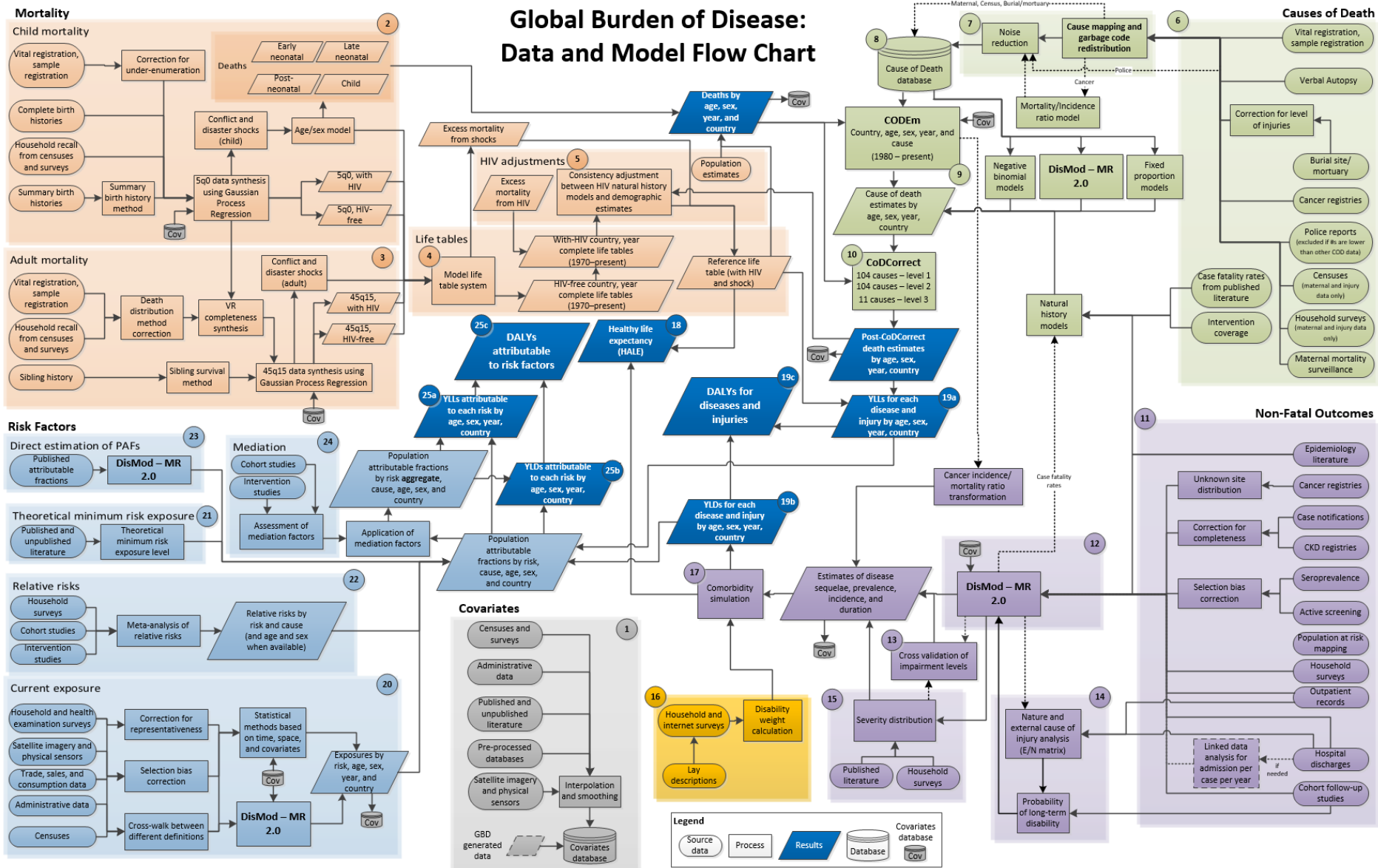
1. A **systematic, scientific** effort to quantify the **comparative** magnitude of **health loss** from all major diseases, injuries, and risk factors by age, sex, and population and over time.
2. 195 countries and territories from 1990 to present. Sub-national assessments for some countries (e.g. **China, Mexico, UK, US, Brazil, Japan, India, Saudi Arabia, Kenya, South Africa**)
3. 306 diseases and injuries, 2,337 sequelae, 79 risk factors or clusters of risk factors.
4. Updated annually; release planned for September each year.
5. Findings published in major medical journals (*Science, The Lancet, JAMA, New England Journal of Medicine, PLOS Medicine*), policy reports, and online data visualizations.

A global study with a global network of investigators: 1,656 investigators, 119 countries



GBD Data and Model Flow Chart





Multiple metrics for health

1. **Traditional metrics:** Disease and injury prevalence and incidence, death numbers and rates.
2. **Years of life lost** due to premature mortality (YLLs) – count the number of years lost at each age compared to a reference life expectancy of 86 at birth.
3. **Years lived with disability** (YLDs) for a cause in an age-sex group equals the prevalence of the condition times the disability weight for that condition.
4. **Disability-adjusted life years (DALYs)** are the sum of YLLs and YLDs and are an overall metric of the burden of disease.
5. **Healthy life expectancy (HALE)** is a positive summary measure counting the expected years of life in full health.

Some core GBD methods

1. Cause of death garbage code analysis – redistribution of causes that cannot be underlying cause of death.
2. Cause of death ensemble modeling (CODEm)
3. Bayesian meta-regression of available incidence, prevalence, cause-specific mortality data using DisMod-MR 2.0.
4. Comorbidity microsimulation to estimate co-occurrence of multiple sequelae.
5. Joint risk factor analysis

Highet et al. Population Health Metrics 2015, 15:1
http://www.pophealthmetrics.com/content/15/1/1



RESEARCH Open Access

Algorithms for enhancing public health utility of national causes-of-death data

Morleen Highet¹, Susanna Molladi, Kyle Foreman, Sarah O'Brien, Farshad Pourmalek and Rafael Lozano

Abstract

Background: Coverage and quality of cause-of-death (COD) data varies across countries and time. Valid, reliable, and timely assessment of trends in cause of death from the last century are limited by three problems: (1) changes in the International Classification of Diseases and Related Health Problems (ICD) over time; (2) the use of placeholder codes where subintended causes of death are lost; and (3) many deaths assigned to causes that cannot be considered underlying causes of death, often called garbage codes (GCs). The Global Burden of Disease (GBD) team at the Institute of Health Metrics and Evaluation (IHME) has developed various methods to enhance comparability of COD data across countries and time.

Methods: We present two methods to enhance the utility of national cause-of-death data. First, we developed a method to redistribute garbage codes to underlying causes of death based on the proportion of deaths assigned to each garbage code. Second, we developed a method to redistribute garbage codes to underlying causes of death based on the proportion of deaths assigned to each garbage code. We applied these methods to national cause-of-death data from 1980 to 2010, and compared the results to the original data. We found that the redistribution of garbage codes improved the comparability of COD data across countries and time.

Conclusions: Our methods for redistributing garbage codes to underlying causes of death improved the comparability of COD data across countries and time. These methods should be applied to national cause-of-death data to enhance the utility of COD data for public health research and policy-making.

Keywords: Cause of death, ensemble models, predictive validity, spatial-temporal models, maternal mortality, Global Burden of Disease

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RESEARCH Open Access

Modeling causes of death: an integrated approach using CODEm

Kyle J. Foreman¹, Rafael Lozano², Alan D. Lopez³ and Christopher J. Murray⁴

Abstract

Background: Data on causes of death by age and sex are a critical input into health decision-making. Priority setting in public health should be informed not only by the current magnitude of health problems but by trends in them. However, cause of death data are often not available or are subject to substantial problems of comparability. We propose five general principles for cause of death model development, validation, and reporting.

Methods: We detail a specific implementation of these principles that is embedded in an analytic tool – the Cause of Death Ensemble model (CODEm) – which requires a large variety of possible models to estimate trends in causes of death. Possible models are identified using a covariate selection algorithm that yields many plausible combinations of covariates, which are then run through four model classes. The model classes include mixed effects linear models and spatial-temporal Gaussian Process Regression models for cause fractions and death rates. All models for each cause of death are then assessed using out-of-sample predictive validity and combined into an ensemble with optimal out-of-sample predictive performance.

Results: Ensemble models for cause of death estimation outperform any single component model in tests of out-of-sample predictive validity, frequency of predicting correct temporal trends, and achieving 95% coverage of the prediction interval. We present detailed results for CODEm applied to maternal mortality and summary results for several other causes of death, including cardiovascular disease and several cancers.

Conclusions: CODEm produces better estimates of cause of death trends than previous methods and is less susceptible to bias in model specification. We demonstrate the utility of CODEm for the estimation of several major causes of death.

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Risk hierarchy

Behavioral

Child and maternal malnutrition

Suboptimal breastfeeding
Childhood undernutrition
Iron deficiency
Vitamin A deficiency
Zinc deficiency

Tobacco smoke

Smoking
Second-hand smoke

Alcohol and drug use

Alcohol use
Drug use

Dietary risks

Diet low in fruits
Diet low in vegetables
Diet low in whole grains
Diet low in nuts and seeds
Diet low in milk
Diet high in red meat
Diet high in processed meat
Diet high in sugar-sweetened beverages
Diet low in fiber
Diet suboptimal in calcium
Diet low in seafood omega-3 fatty acids
Diet low in polyunsaturated fatty acids
Diet high in trans fatty acids
Diet high in sodium

Low physical activity

Sexual abuse and violence

Childhood sexual abuse
Intimate partner violence

Unsafe sex

Environmental/Occupational

Unsafe water, sanitation and handwashing

Unsafe water source
Unsafe sanitation
No handwashing with soap

Air pollution

Ambient particulate matter pollution
Household air pollution from solid fuels
Ambient ozone pollution

Other environmental risks

Residential radon
Lead exposure

Occupational risks


Occupational carcinogens
Occupational asthmagens
Occupational particulate matter, gases, and fumes
Occupational noise
Occupational injuries
Occupational ergonomic factors

Metabolic

High fasting plasma glucose
High total cholesterol
High blood pressure
High body-mass index
Low bone mineral density
Low glomerular filtration rate

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Some GBD 2013 publications

Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

Global Burden of Disease Study 2013 Collaborators*

Summary Background with disability in 188 countries

Methods Es with some i additions to reviews, use severity spli cause and in

Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

GBD 2013 Risk Factors Collaborators*

Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

GBD 2013 Mortality and Causes of Death Collaborators*

Summary Background Up-to-date i essential for the formati 2013 (GBD 2013) we esti whether there is epidem

Methods We estimated ag accuracy applied to an u death as in the GBD 2010 an updated verbal autopsy Turkey, and Russia. We strategies across the 240 i sufficient information. 1 prevalence studies. For p approach. We computed i all pairs of countries (Gin

Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition

GBD 2013 DALYs and HALE Collaborators*

Summary Background The Global Burden of Disease Study 2013 (GBD 2013) aims to bring together all available epidemiological data using a coherent measurement framework, standardised estimation methods, and transparent data sources to enable comparisons of health loss over time and across causes, age–sex groups, and countries. The GBD can be used to generate summary measures such as disability-adjusted life-years (DALYs) and healthy life expectancy (HALE) that make possible comparative assessments of broad epidemiological patterns across countries and time. These summary measures can also be used to quantify the component of variation in epidemiology that is related to sociodemographic development.

Methods We used the published GBD 2013 data for age-specific mortality, years of life lost due to premature mortality (YLLs), and years lived with disability (YLDs) to calculate DALYs and HALE for 1990, 1995, 2000, 2005, 2010, and 2013 for 188 countries. We calculated HALE using the Sullivan method; 95% uncertainty intervals (UIs) represent uncertainty in age-specific death rates and YLDs per person for each country, age, sex, and year. We estimated DALYs for 306 causes for each country as the sum of YLLs and YLDs; 95% UIs represent uncertainty in YLL and YLD rates. We quantified patterns of the epidemiological transition with a composite indicator of sociodemographic status, which we constructed from income per person, average years of schooling after age 15 years, and the total fertility rate and mean age of the population. We applied hierarchical regression to DALY rates by cause across countries to decompose variance related to the sociodemographic status variable, country, and time.

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[http://dx.doi.org/10.](http://dx.doi.org/10.1016/j.lancet.2015.08.028)

Article

- 1) Based on demand from Jeremy Hunt, Secretary of State for Health, GBD 2010 used to benchmark the UK with western Europe.

2) Public Health England – GBD collaboration to study sub-national BoD. Findings released September 2015.

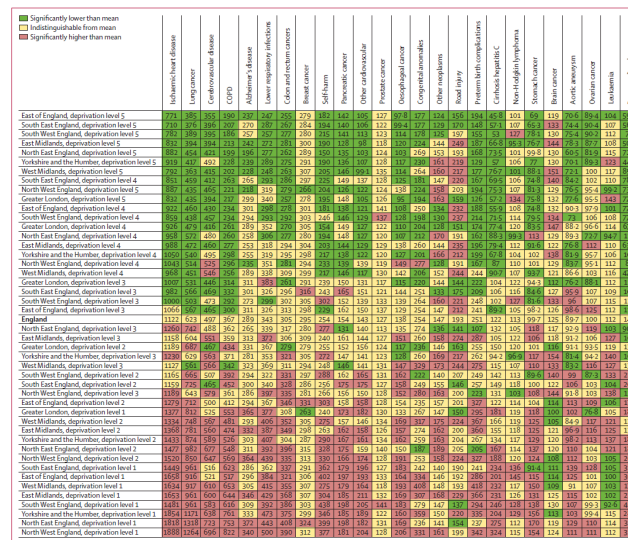


Figure 3: Age-standardised rates of years of life lost (YLLs) for England relative to the deprivation levels in the nine English regions for both sexes combined in 2013

UK health performance: findings of the Global Burden of Disease Study 2010

Articles

Changes in health in England, with analysis by English regions and areas of deprivation, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

John A Wainwright, Adam D M Briggs, Christopher J I Murray, David Dixon, Eric J Tawman, Haidong Wang, Mahesh Nagbadi, Mahamed M Houssein, Karam Usman Chah, Ayar M Kadi, Thawee Jirjany, Chhannay, Jeyaraj S, Subash, Anshu Prakash,

David F. Day, Russell Cook, Cherie Caster, Martin Pfohl, Vicky Kutter, Barbara Neubauer*, Joseph Alt*, H. Kent Anderson*, David K. Banerjee*,
Dorick A. Bennett*, Eduardo Bermejo*, Kenneth S. Blevins*, Stanley M. Boynton*, Rupert P. Brown*, Carol T. G. Brown*, Nigel G. Cunniff*,
J. Jukka A. Chytrý*,
evs*, Ulrich K. Grosse*,
Joachim F.,
* Wilhelm F. Wundt*,
des F. Wundt*,
* Adrien C. G. G.

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Pre	Other	Protest	Occasion	Conspire	Other	Road	Prefer	Carth	Non-	Stom	Brain	Aurist	Over	Look	Don't	
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140	106	122	99	87	129	170	148	57	107	65	133	74	90	107	56	7
141	113	124	114	128	135	197	155	51	127	78	130	75	94	102	112	72
128	98	118	120	124	144	240	187	66	98	76	144	75	87	108	50	10
135	103	124	103	269	353	193	168	73	101	99	130	80	81	115	72	4

146	109	138	117	230	219	129	5	106	77	130	101	89.3	123	44.5
146	99.1	135	114	264	160	127	17	76.7	101	88.1	53.1	72.1	101	87.5
149	137	128	128	181	147	220	167	69.6	106	74.8	140	84.2	102	78.1
146	122	124	138	234	358	201	194	75.3	107	81.3	129	76.5	95.4	98.2
148	105	126	95	184	363	359	126	57.2	134	75.4	131	77.6	95.5	143
138	121	141	108	250	334	238	188	55.9	108	74.8	132	90.3	97.9	101
146	119	137	128	198	130	237	214	71.5	114	79.5	134	73	106	108

143	127	122	110	204	151	174	77.4	120	83.5	147	88.2	92.6	114	67.1	
143	127	120	107	212	170	191	162	88.1	99.3	113	129	89.1	76.7	94.7	111
144	127	120	138	260	144	235	196	79.4	112	91.6	122	77.6	112	110	61.6
133	122	120	127	201	166	212	199	67.8	104	102	138	81.9	95.7	106	108
139	139	119	149	277	128	191	167	87	110	101	129	83.3	95.1	112	87.8
140	117	130	142	206	152	244	244	90.9	107	93.7	121	85.6	103	116	47.8
150	131	127	115	220	144	244	222	104	122	94.3	112	76.2	88.4	112	115
156	151	121	144	251	139	175	206	106	116	94.6	112	80.0	102	100	104

152	139	133	139	264	360	221	248	102	127	31.6	333	96	107	115	127	near 100% in males
153	139	133	139	264	360	221	248	102	127	31.6	333	96	107	115	127	not between matches
154	150	137	139	254	347	232	241	89.2	105	98.2	126	98.6	125	112	118	are most matches
155	143	127	138	254	347	231	251	122	113	99.7	125	126	100	112	140	are most therefore
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131	164	127	151	260	356	174	274	287	105	122	106	115	91.2	106	127	king disorders, an
152	156	124	117	236	346	166	255	150	120	101	111	91.1	93.5	119	134	
147	141	123	135	260	369	217	262	94.2	95.2	127	154	81.4	94.2	140	101	

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163	165	131	162	122	140	207	249	142	113	99.5	140	95	87	133	114
175	175	127	158	249	355	146	257	149	118	100	122	106	103	104	204
156	150	128	152	280	263	200	223	131	103	108	144	91.8	103	138	121
158	158	128	154	235	457	201	327	122	114	104	114	113	109	106	174
173	182	130	133	267	147	150	295	181	119	118	100	102	76.8	105	180
157	146	134	159	327	175	224	367	166	119	125	105	84.9	117	121	129

167	158	126	157	274	7	200	360	155	118	125	121	96-9	116	125	139
167	161	134	162	259	263	204	267	134	127	129	120	98-2	113	137	184
175	159	140	150	187	189	205	205	167	134	137	120	110	104	121	281
166	154	128	191	253	158	224	327	188	120	124	108	112	103	105	202
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179	164	118	193	408	148	193	416	232	126	130	105-3	94	107	103	272

198	215	112	209	302	286	229	306	231	126	131	125	115	102	102	230
198	205	141	183	279	347	137	294	246	128	138	130	107	99.3	92.6	407
185	189	122	160	359	150	220	335	204	129	156	113	103	99.4	115	280
198	182	131	169	236	141	184	237	275	112	170	119	129	110	114	315
181	204	128	206	331	261	199	342	324	115	154	124	111	111	112	314

programmes for more than six decades. have been undertaken. Health expenditure has been compared to other countries. We used data from O 2010) to examine the patterns of health systems, and how UK outcomes compare to 1990 and 2010.

centially in absolute terms in the UK from 2000 to 2010. However, the UK

raies, age-standardized YLL rates, and life expectancy in most age groups, there have been no major changes. Production of 1–2% is notable for men and women aged 20–54 (137%, 16–277), childbirth (57%, –35 to 307), 0 to 2010. In 2010, compared with EU15, diabetes, liver cancer, and chronic kidney disease, obstructive pulmonary disease, lower

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Journal of Internal Medicine 258: 103–110

Dr B. H. Meltzer, *Psychiatrist, Institute of Psychiatry, London, UK*

programme. Since 1990, the UK Government has introduced public health measures for tobacco

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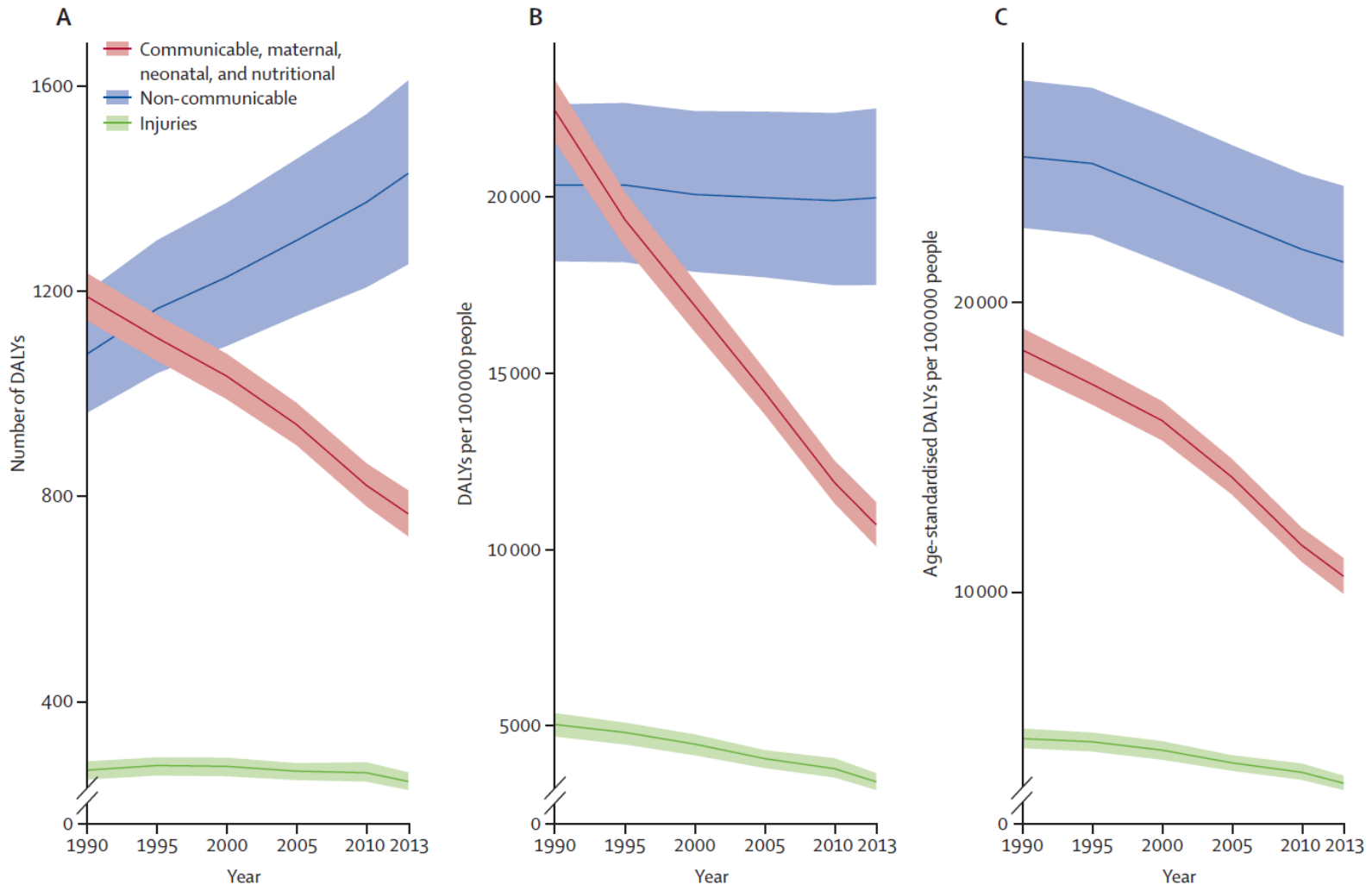
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Outline

- 1) Study goals
- 2) GBD study overview
- 3) **Key results from GBD 2013**
- 4) Some debates
- 5) GBD 2015 main innovations
- 6) New analytical directions

Total DALYs, crude DALY rates, and age-standardised DALY rates from 1990 to 2013



Data viz

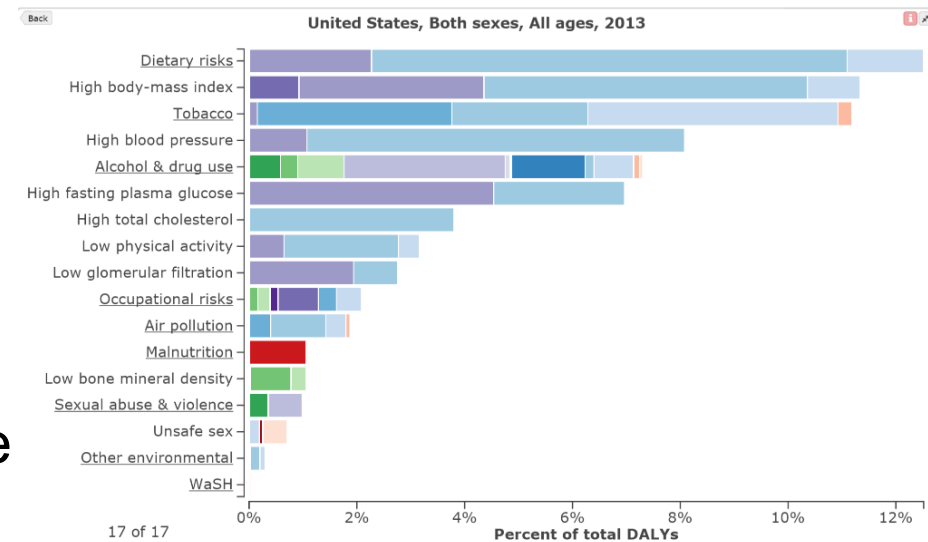
www.healthdata.org

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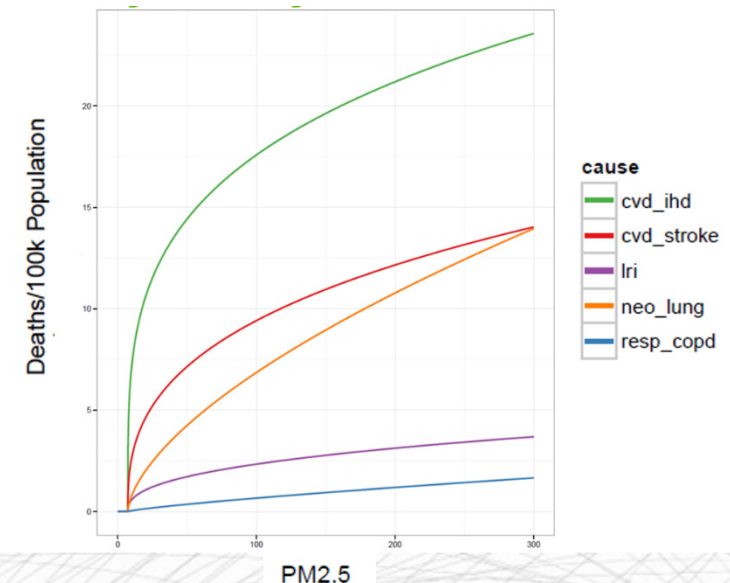
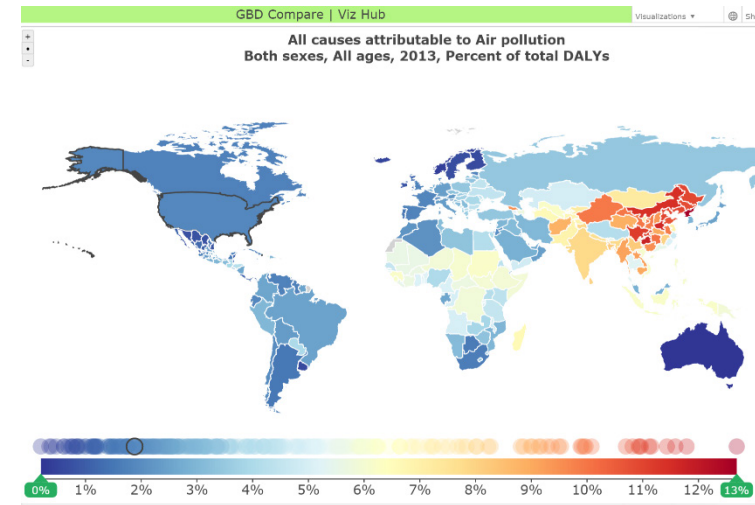
Are diet effects over-estimated?

- 1) Diet components and joint effects based on meta-analyses of cohort studies and randomized trials (mortality and intermediate outcomes).
- 2) Huge potential health gains through diet modification but substantial controversy about magnitude of the effects in the clinical community.
- 3) More systematic capture of all cohort studies and internal validation of combined diet effects on mortality should be undertaken



Integrated exposure response curve (IER)

- 1) Relative risk curve as a function of PM_{2.5} constructed from pooling data from ambient air pollution, indoor air pollution, second-hand smoke and tobacco studies for CVD and chronic respiratory outcomes.
- 2) Ambient air pollution studies show excess risk at low levels PM_{2.5} leading to a concave risk curve.
- 3) Policy implication is that health gains from reducing high levels of PM_{2.5} to moderate is quite small but gains from moderate to low are large.

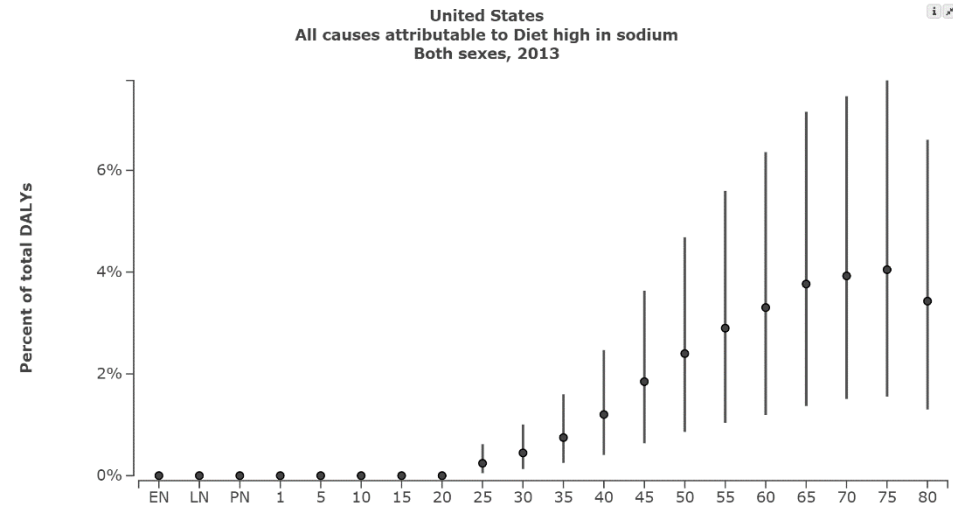


Systolic blood pressure

- 1) GBD 2013 relative risks based on meta-analysis of pooled cohort and trial data show excess risk for SBP>110-115 mm Hg.
- 2) JNC8 argued that benefits unclear below SBP 150.
- 3) SPRINT results confirm magnitude of SBP results quantified in the GBD.
- 4) HOPE-3 questions benefits in those without disease and SBP below 130

Salt and mortality: implications of PURE

- 1) GBD 2013 considerable debate within collaboration on the theoretical minimum risk level (TMREL) for salt – level below which there is no further benefit.
- 2) IOM review and then PURE findings led to widening uncertainty interval for TMREL from 1gm Na/day to 5gm Na/day.



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GBD 2015

1. **New subnational analyses:** India, South Africa, United States, Sweden, Saudi Arabia, Brazil, Japan, Kenya.
2. Added selected territories with high quality data: American Samoa, Puerto Rico, Marshall Islands, Bermuda, Greenland
3. **Enhanced analysis of epidemiological transition:** major emphasis in the analysis of estimating the average pattern of age, sex, and cause-specific burden as a function of socio-demographic status.
4. HIV estimation and all-cause mortality estimation linked at the draw level – ensemble model to estimate HIV using both demographic data sources and EPP-Spectrum natural history model

GBD 2015

- 5) New causes including Ebola, division of leukemias into ALL, CLL, AML, CML, motor neuron disease
- 6) GATHER guidelines compliance
- 7) DisMod-MR 2.1 added estimation for subnational units in analytical cascade
- 8) Explicit risk-outcome evidence matrix
- 9) Summary exposure estimation – risk weighted prevalence for each risk factor on a 0 to 1 scale
- 10) Improvements to GBD Compare

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Major extensions to the GBD

- 1) Next annual update to 2016 to be released in September 2017.
- 2) Mapping the burden of disease at the pixel level – beginning with malaria, HIV, tuberculosis, diarrhea and lower respiratory infections will estimate burden at the 5 X 5 km square level.
- 3) Forecasting platform – creating a burden of disease forecasting platform to create short, medium and long-range forecasts for the GBD. Platform will also allow for exploration of alternative scenarios.
- 4) Extending risk factors to social determinants and intervention coverage

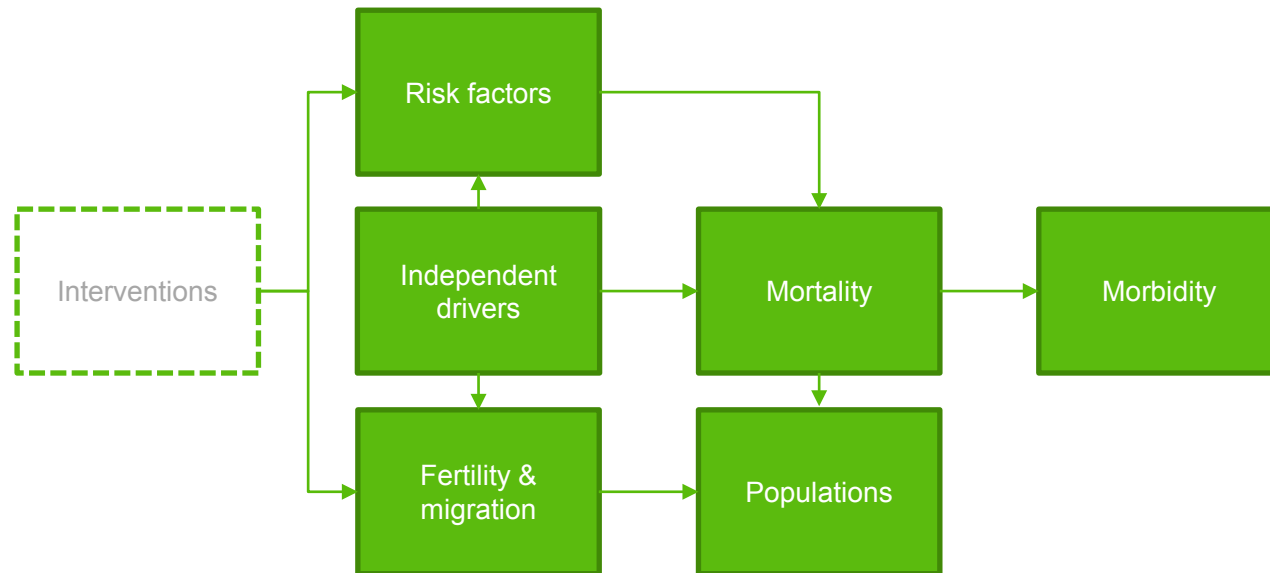
nature International weekly journal of science



Two distinct goals for health futures platform

- 1) Generate and regularly update past trends and relationships scenario (PTRS) for mortality, morbidity and population from now to 25 years in the future by age, sex, cause and GBD geographies (over 500 now)
- 2) Create a comprehensive framework to assess alternative scenarios of interest to relevant stakeholders with different trajectories for independent drivers

Scenarios framework



Distal risks and interventions

- 1) Expansion of GBD Comparative Risk Assessment to encompass distal risks such as income per capita, poverty, education, electrification....
- 2) Expansion to include the absence of certain well characterized interventions e.g. rotavirus vaccine.