quality characteristic with values with the less desirable attributes. This approach assumes that the relation between different study attributes is constant across age, sex, and region. In some cases, when such a relation does not exist, we estimated the crosswalks separately by age and sex using data collected with multiple definitions, such as for different decibel thresholds for hearing loss. The idea of using results of studies done with different definitions or diagnostic approaches in the final systematic analysis has substantially expanded the empirical basis available for assessing prevalence across age, sex, and regions. It does, however, draw attention to the importance of investigators publishing or making available data from existing studies using alternative case definitions or diagnostic approaches.

Another limitation of the study is that long-term follow-up data for injuries were available only from high-income countries. Long-term follow-up in developing countries could be different. Because of higher case-fatality rates in such countries, the average severity in surviving cases might be better than it is in high-income countries, if medical and surgical intervention extends the lifespan of those with more severe disabilities. Alternatively, the probability of long-term disability could be higher because of care that lowers mortality but does not restore function as effectively as does care in developed countries.

For the first time, we have adjusted GBD results for YLDs for comorbidity. The analysis of comorbidity, however, has several major limitations. Very few data are available that have been collected with a sufficiently large sample size and covering enough sequelae to estimate the correlation matrix for sequelae prevalence by age. National health information systems that capture detailed ICD-coded encounter data could provide a source of data for this type of analysis in the future. In general, if substantial dependent comorbidity (ie, one disease predisposes a person to be more or less likely to have another disease) exists, our estimates of YLDs might be slightly overestimated.[83] The effect, however, is unlikely to be large because of the validation results seen in the 171 354 respondents in MEPS.[77] In the microsimulation step for each country, age, sex, and year, we used 20 000 simulated individuals, then repeated the microsimulation 1000 times to capture uncertainty in the prevalences of all sequelae and disability weights. The effect of the microsimulation, especially for rare disorders, is to increase the estimated uncertainty in YLDs. For most disorders, this increase in uncertainty is small, but it can be quite substantial for rare disorders. The comorbidity process will tend to overestimate uncertainty in uncommon disorders. There are many potential uses of the comorbidity results of the GBD other than correction to YLD calculations. For instance, estimations of the expected number of individuals with multiple disorders might be useful for health planning purposes. We expect that comorbidity will be an important area for future burden research.

Consideration of comorbidity has put more emphasis on understanding the distribution of severity of disease. We directly model combinations of disorders and their effect on individual disability weights; to avoid double-counting, severity distributions for each disorder need to be estimated either controlling for comorbidity or in individuals without comorbidities, although the latter might be intractably affected by selection bias. In either case, the available data are limited. Datasets like the MEPS[77] that collect repeated observations over time on functional health status and collect ICD-coded information on multiple conditions can be extremely useful for future assessments of severity. Other data collection strategies are possible but future burden of disease research needs to foster new data collection that provides direct assessments of severity distributions. Studies of severity need also to take into account that individuals might be asymptomatic for some time, and to quantify this as part of the protocol. In datasets in which clinical diagnoses can be verified, more routine collection of information using a standard self-reported functional health status instrument will enhance their utility.

In view of the fact that there is almost no relation between the prevalence of a sequela and the severity of the sequela as captured in the disability weights, recognition that our results depend on the validity of the disability weights themselves is crucial. Some disability weights have changed substantially compared with GBD 1990 weights, such as for blindness or profound hearing loss. Elsewhere, Salomon and colleagues[30] describe the methods used to measure the GBD 2010 disability weights in multiple populations around the world. The shift to the use of samples of the general population, rather than small panels of health-care professionals as used for the GBD 1990 disability weights, we believe strengthens the findings presented here. Nevertheless, the crucial mechanism by which the general public can assess the level of health for different health states is through brief descriptions in lay language. Salomon and colleagues[30] lay out a future research agenda to better understand how alternative lay descriptions of health states might affect the resulting disability weight.

One important function for health information systems should be to provide national decision makers with timely information about the burden of non-fatal health outcomes. The GBD 2010 analysis of YLDs provides important insights into which types of data can be informative for assessing non-fatal health outcomes. Not surprisingly, there is an important role for household surveys that involve interviews and the collection of blood and other functional tests (eg, hearing, vision, and lung function). Making sure a household survey collects data with a general functional health status instrument and collects information on a broad array of sequelae can make such data collection opportunities even more valuable. Building on the analysis of YLDs and YLLs as well, construction of a household interview and examination

survey instrument that can capture the main sources of disease burden would be useful. The detail in the GBD 2010 now makes this approach feasible. Beyond household surveys, however, we have seen that ICD-coded hospital discharge and ambulatory care data, when individual records are available and other sociodemographic data have been collected, can be very valuable, especially if these datasets can be linked. Disease registries for cancer, renal disease, and congenital anomalies have also been an important resource, drawing attention to the importance of tracking individuals with chronic disorders over time who come into contact with health services.

Health priorities have, for much of the past 100 years or more, been largely driven by the imperative of improving the survival of populations, particularly child survival. This was justified, in view of the availability of technologies to treat and prevent childhood illness. However, societies also spend substantial resources on keeping people healthy, not only on keeping them alive into old age, so the availability of strategies to monitor their effectiveness in doing so is important. In this Article, we have shown that quantification of health loss in populations is possible, using comparable metrics that identify the leading causes of non-fatal illness in different regions, at different ages, and at different points in time. The principal findings, namely that mental health, musculoskeletal health, and the rising importance of diabetes need urgent policy responses, are well established. Monitoring progress in reducing the effect of these, and other major contributors to health loss, is as important for improving population health as monitoring progress against the leading causes of death. YLDs provide a convenient framework and metric to do so; ensuring the routine availability of data collection suitable for computation of these measures of health loss should be a key focus of national health information system strategies.

Contributors

CJLM, ADL, and TV prepared the first draft. TV, AF, MN, RL, CM, ME, KS, JS, ADL, and CJLM finalised the draft on the basis of comments from all other authors and reviewer feedback. CJLM and ADL had the idea for the study and provided overall guidance. All other authors developed cause-specific models, reviewed results, provided guidance on the selection of key covariates, and reviewed the paper.

Conflicts of interest

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A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010

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For interactive versions of figures 3, 4, and 6 see http://healthmetricsandevaluation.org/gbd/visualizations/regional

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Summary

Background Quantification of the disease burden caused by different risks informs prevention by providing an account of health loss different to that provided by a disease-by-disease analysis. No complete revision of global disease burden caused by risk factors has been done since a comparative risk assessment in 2000, and no previous analysis has assessed changes in burden attributable to risk factors over time.

Methods We estimated deaths and disability-adjusted life years (DALYs; sum of years lived with disability [YLD] and years of life lost [YLL]) attributable to the independent effects of 67 risk factors and clusters of risk factors for 21 regions in 1990 and 2010. We estimated exposure distributions for each year, region, sex, and age group, and relative risks per unit of exposure by systematically reviewing and synthesising published and unpublished data. We used these estimates, together with estimates of cause-specific deaths and DALYs from the Global Burden of Disease Study 2010, to calculate the burden attributable to each risk factor exposure compared with the theoretical-minimum-risk exposure. We incorporated uncertainty in disease burden, relative risks, and exposures into our estimates of attributable burden.

Findings In 2010, the three leading risk factors for global disease burden were high blood pressure (7·0% [95% uncertainty interval 6·2–7·7] of global DALYs), tobacco smoking including second-hand smoke (6·3% [5·5–7·0]), and alcohol use (5·5% [5·0–5·9]). In 1990, the leading risks were childhood underweight (7·9% [6·8–9·4]), household air pollution from solid fuels (HAP; 7·0% [5·6–8·3]), and tobacco smoking including second-hand smoke (6·1% [5·4–6·8]). Dietary risk factors and physical inactivity collectively accounted for 10·0% (95% UI 9·2–10·8) of global DALYs in 2010, with the most prominent dietary risks being diets low in fruits and those high in sodium. Several risks that primarily affect childhood communicable diseases, including unimproved water and sanitation and childhood micronutrient deficiencies, fell in rank between 1990 and 2010, with unimproved water

and sanitation accounting for 0·9% (0·4–1·6) of global DALYs in 2010. However, in most of sub-Saharan Africa childhood underweight, HAP, and non-exclusive and discontinued breastfeeding were the leading risks in 2010, while HAP was the leading risk in south Asia. The leading risk factor in Eastern Europe, most of Latin America, and southern sub-Saharan Africa in 2010 was alcohol use; in most of Asia, North Africa and Middle East, and central Europe it was high blood pressure. Despite declines, tobacco smoking including second-hand smoke remained the leading risk in high-income north America and western Europe. High body-mass index has increased globally and it is the leading risk in Australasia and southern Latin America, and also ranks high in other high-income regions, North Africa and Middle East, and Oceania.

Interpretation Worldwide, the contribution of different risk factors to disease burden has changed substantially, with a shift away from risks for communicable diseases in children towards those for non-communicable diseases in adults. These changes are related to the ageing population, decreased mortality among children younger than 5 years, changes in cause-of-death composition, and changes in risk factor exposures. New evidence has led to changes in the magnitude of key risks including unimproved water and sanitation, vitamin A and zinc deficiencies, and ambient particulate matter pollution. The extent to which the epidemiological shift has occurred and what the leading risks currently are varies greatly across regions. In much of sub-Saharan Africa, the leading risks are still those associated with poverty and those that affect children.

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Introduction

Measurement of the burden of diseases and injuries is a crucial input into health policy. Equally as important, is a comparative assessment of the contribution of potentially modifiable risk factors for these diseases and injuries. The attribution of disease burden to various risk factors provides a different account compared with disease-by-disease analysis of the key drivers of patterns and trends in health. It is essential for informing prevention of disease and injury.

Understanding the contribution of risk factors to disease burden has motivated several comparative studies in the past few decades. The seminal work of Doll and Peto[1] provided a comparative assessment of the importance of different exposures, particularly tobacco smoking, in causing cancer. Peto and colleagues[2] subsequently estimated the effects of tobacco smoking on mortality in developed countries since 1950. Although these risk factor-specific or cause-specific analyses are useful for policy, a more comprehensive global assessment of burden of disease attributable to risk factors can strengthen the basis for action to reduce disease burden and promote health. The Global Burden of Disease Study (GBD) 1990 provided the first global and regional comparative assessment of mortality and disability-adjusted life-years (DALYs) attributable to ten major risk factors.[3] However, different epidemiological traditions for different risks limited the comparability of the results. Subsequently, Murray and Lopez[4] proposed a framework for global comparative risk assessment, which laid the basis for assessment of 26 risks in 2000.[5–7] Since this work, WHO has provided estimates for some risks by the same methods but with updated exposures and some updates of the effect sizes for each risk.[8] Analyses have also been done for specific clusters of diseases, like cancers,[9] or clusters of risk factors, like maternal and child under-nutrition.[10] National comparative risk assessments (including in Australia, Iran, Japan, Mexico, South Africa, Thailand, USA, and Vietnam) have also been undertaken with similar approaches.[11–16]

GBD 2010 provides an opportunity to re-assess the evidence for exposure and effect sizes of risks for a broad set of risk factors by use of a common framework and methods. Particularly, since this work was done in parallel with a complete re-assessment of the burden of diseases and injuries in 1990 and 2010, for the first time changes in burden of disease attributable to different risk factors can be analysed over time with comparable methods. Since uncertainty has been estimated for each disease or injury outcome,[17,18] the comparative risk assessment for GBD 2010 has also enabled us to incorporate uncertainty into the final estimates. We describe the general approach and high-level findings for comparison of the importance of 67 risk factors and clusters of risk factors, globally and for 21 regions of the world, over the past two decades.

Methods

Overview

The basic approach for the GBD 2010 comparative risk assessment is to calculate the proportion of deaths or disease burden caused by specific risk factors—eg, ischaemic heart disease caused by increased blood pressure—holding other independent factors unchanged. These calculations were done for 20 age groups, both sexes, and 187 countries and for 1990, 2005 (results for 2005 not shown, available from authors on request), and 2010. We present aggregated results for 21 regions.

Table 1 shows the included risk factors and their organisation into a hierarchy with three levels. Level 1 risks are clusters of risk factors that are related by mechanism, biology, or potential policy intervention. Most risks are presented at level 2. For occupational carcinogens, a third level is included to provide additional detail about specific carcinogens. For suboptimal breastfeeding we

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also include a third level to distinguish between non-exclusive breastfeeding during the first 6 months and discontinued breastfeeding from 6 to 23 months.

We calculated burden attributable to all (67) risk factors and clusters of risk factors except for physiological risks and air pollution. These two clusters present analytical challenges for computation of the aggregate burden. For example, the effects of high body-mass index are partly mediated through high blood pressure, high total cholesterol, and high fasting plasma glucose, and household air pollution from solid fuels (wood, crop, residues, animal dung, charcoal, and coal) contributes to ambient particulate matter pollution.

We ranked results for 43 risk factors and clusters of risk factors, grouping together occupational carcinogens, non-exclusive and discontinued breastfeeding, and tobacco smoking with second-hand smoke on the basis of common exposure sources.

Our estimation of disease burden attributable to a risk factor had five steps: 1) selection of risk–outcome pairs to be included in the analysis based on criteria about causal associations; 2) estimation of distributions of exposure to each risk factor in the population; 3) estimation of etiological effect sizes, often relative risk per unit of exposure for each risk–outcome pair; 4) choice of an alternative (counterfactual) exposure distribution to which the current exposure distribution is compared. We selected an optimum exposure distribution, termed the theoretical-minimum-risk exposure distribution for this purpose; and 5) computation of burden attributable to each risk factor, including uncertainty from all sources. Further details about the data and methods used for specific risk factors are available on request.

Selection of risk–outcome pairs

The inclusion criteria for each risk–outcome pair that we applied were: 1) the likely importance of a risk factor to disease burden or policy based on previous work; 2) availability of sufficient data and methods to enable estimation of exposure distributions by country for at least one of the study periods (1990 and 2010); 3) sufficient evidence for causal effects based on high-quality epidemiological studies in which the findings were unlikely to be caused by bias or chance, analogous to the criteria used for assessment of carcinogens with convincing or probable evidence (panel). Sufficient data to estimate outcome-specific etiological effect sizes per unit of exposure were also needed; and 4) evidence to support generalisability of effect sizes to populations other than those included in the available epidemiological studies or satisfactory models for extrapolating them. Table 1 shows the risk–outcome pairs that were included in the final analysis, on the basis of these criteria.

Distribution of exposure to each risk factor

For most risk factors, a systematic search was done to identify published and, when possible, unpublished data sources to estimate risk factor exposure distributions in 1990 and 2010. Strategies to identify data sources included searching survey databases such as the WHO Global Database on Child Growth and Malnutrition, searching general citation databases such as Google Scholar and PubMed, manual searching of reference lists of articles and conference abstracts, and contacting experts in the relevant fields. Data sources included censuses, health examination and nutrition surveys, and community-based epidemiological studies.

Because data for risk factor exposure are often incomplete or missing for many populations, models were used to generate a complete set of current exposure distributions for risk factors for each country and for both years, including uncertainty. Table 1 shows for each risk factor the main sources of data and the modelling approach used for estimation of present risk factor exposure distributions. Briefly, risk factor models were designed to use available data and information for exposures in countries, for several years, and for different age groups to generate estimates for all countries, for both years, and for all relevant age groups. Estimation of exposure was done with statistical models that used predictors such as time, geography, and other variables that were relevant to the exposure of interest—eg, income per person.

For each risk factor, we tested a wide array of covariates for prediction of exposure distributions, drawing from covariates included in databases created or collated at the Institute for Health Metrics and Evaluation for GBD 2010. If relevant, the model also included age. Finally, each analysis accounted for important study characteristics such as national versus subnational representativeness, and the measures and instruments used for measuring exposure.

In addition to this general approach, specific methods were used for some risk factors. For tobacco including second-hand smoke, much scientific literature exists about alternative methods to estimate cumulative exposure, based on the premise that present prevalence and consumption data do not take into account likely variations in duration and intensity of smoking. In this case, we used the method of Peto and Lopez,[2] which uses lung cancer mortality as a marker (ie, smoking impact ratio) of cumulative population exposure to smoking for cancers and chronic respiratory disease. We used epidemiological data to estimate lung cancer mortality in non-smokers separately for China, other countries in the high-income Asia Pacific region, and all remaining countries.[119,120] For all other outcomes, we used 10-year lagged tobacco smoking prevalence. We also applied an approach analogous to the smoking impact ratio for occupational exposure to asbestos, for which we used mesothelioma mortality, separately estimated, as a marker of asbestos exposure.

For ambient particulate matter pollution, two complete, high resolution estimates exist of the concentration of particulate matter smaller than 2·5 μm in aerodynamic

	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
1. Unimproved water and sanitation							
1.1. Unimproved water source	Proportion of households using an unimproved water source (unprotected wells or springs, vendor-provided water, tanker trucks, surface water, and other unspecified sources)	Intestinal infectious diseases	All ages	Population surveys and censuses	Spatiotemporal Gaussian process regression[19-21]	All households use an improved water source (household connection, a public tap or standpipe, a tubewell or borehole, a protected well or spring, or rainwater collection)	New meta-analysis
1.2. Unimproved sanitation	Proportion of households using unimproved sanitation (traditional latrines, open latrines without squatting slabs, bucket latrines, hanging latrines, open defecation or no facilities, and other unspecified facilities)	Intestinal infectious diseases	All ages	Population surveys and censuses	Spatiotemporal Gaussian process regression[19-21]	All households use improved sanitation (public sewers, septic systems, flush or pour-flush facilities, ventilated improved latrines, simple pit latrines with squatting slabs, and composting toilets)	New meta-analysis
2. Air pollution							
2.1. Ambient particulate matter pollution	Ambient concentration of particles with an aerodynamic diameter smaller than 2·5 μm, measured in μg/m³	Lower respiratory infections; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease; COPD	Age <5 years for lower respiratory tract infection; ≥25 years for all others	Surface monitor measurements, aerosol optical depth from satellites, and TM5 global atmospheric chemistry transport model[22-26]	Average of satellite and chemistry transport estimates, calibrated to surface monitor measurements	5·8–8·8 μg/m³	Integrated exposure–response curve
2.2. Household air pollution from solid fuels	Proportion of households using solid fuels for cooking (coal, wood, charcoal, dung, and agricultural residues)	Lower respiratory infections; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease; COPD; cataracts	Age <5 years for lower respiratory tract infection; ≥25 years for all others	Population surveys and censuses	Mixed effect regression	All households using clean fuels for cooking (vented gas, electricity)	Integrated exposure–response curve for lower respiratory tract infection, IHD, and stroke; new meta-analysis for cataracts, COPD, and lung cancer
2.3. Ambient ozone pollution	Ambient concentrations of ozone in air, measured in parts per billion	COPD	Age ≥25 years	TM5 global atmospheric chemistry transport model[22-24]	TM5 global atmospheric chemistry transport model[22-24]	33·3–41·9 parts per billion	Jerrett and colleagues[27]
3. Other environmental risks							
3.1. Residential radon	Residential radon, measured in Bq/m³	Trachea, bronchus, and lung cancers	All ages	Direct household measurements from surveys	Mixed effect regression	10 Bq/m³	Darby and colleagues[28]
3.2. Lead exposure	Blood lead (measured in μg/dL) and bone lead (measured in μg/g)	Intellectual disability; systolic blood pressure, which has effects on: RHD; IHD; ischaemic stroke; haemorrhagic and other non-ischaemic stroke; HHD; aortic aneurysm; the aggregate of cardiomyopathy and myocarditis and endocarditis; the aggregate of atrial fibrillation and flutter, PVD, other CVD; CKD	<15 years for intellectual disability; ≥25 years for all others	Examination surveys and epidemiological studies	DisMod 3	Bone lead level expected from age-specific cumulative exposure to blood lead of 0·09652 μmol/L[29]	Lanphear and colleagues,[30] Navas-Acien and colleagues[31]

(Continues on next page)

	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
(Continued from previous page)							
4. Child and maternal undernutrition							
4.1. Suboptimal breastfeeding							
4.1.1. Non-exclusive breastfeeding	Proportion of children younger than 6 months with predominant, partial, or no breastfeeding	Intestinal infectious diseases; the aggregate of lower respiratory infections, upper respiratory infections, and otitis media	Age 0–5 months	Population surveys	Spatiotemporal Gaussian process regression[19–21]	All children exclusively breastfed for first 6 months	Lamberti and colleagues,[32] Black and colleagues[10]
4.1.2. Discontinued breastfeeding	Proportion of children aged 6–23 months with discontinued breastfeeding	Intestinal infectious diseases	Age 6–23 months	Population surveys	Spatiotemporal Gaussian process regression[19–21]	Continued breastfeeding until 2 years	Lamberti and colleagues,[32] Black and colleagues[10]
4.2. Childhood underweight	Proportion of children less than −3 SDs, −3 to −2 SDs, and −2 to −1 SDs of the WHO 2006 standard weight-for-age curve	Intestinal infectious diseases; measles; malaria; the aggregate of lower respiratory infections, upper respiratory infections, and otitis media; protein–energy malnutrition	Age <5 years	Examination surveys and epidemiological studies	Spatiotemporal Gaussian process regression[19–21]	Proportion of the WHO 2006 reference population in each SD range	Black and colleagues[10]
4.3. Iron deficiency	Haemoglobin, measure in g/L	The aggregate of maternal haemorrhage and maternal sepsis; iron-deficiency anaemia	All ages	Examination surveys and epidemiological studies	Mixed effect regression	Country-specific	Stoltzfus and colleagues[33]
4.4. Vitamin A deficiency	Proportion of children with serum retinol concentration <70 μmol/L	Intestinal infectious diseases; measles; vitamin A deficiency	Age 6 months to 5 years	Examination surveys and epidemiological studies	DisMod 3	No childhood vitamin A deficiency	Imdad and colleagues,[34,35] adjusted for background prevalence
4.5. Zinc deficiency	Proportion of the population with inadequate zinc intake based on estimated mean daily amount of absorbable zinc per head in the food supply compared with mean physiological requirements	Intestinal infectious diseases; lower respiratory infections	Age 1–4 years	Food and Agricultural Organization food balance sheets	Mixed effect regression	No inadequate zinc intake	Yakoob and colleagues,[36] adjusted for background prevalence
5. Tobacco smoking, including second-hand smoke							
5.1. Tobacco smoking	Smoking impact ratio for cancers and chronic respiratory disease, 10-year lagged tobacco smoking prevalence for all other causes including cardiovascular diseases	Tuberculosis; oesophageal cancer; nasopharynx cancer; pancreatic cancer; kidney and other urinary organ cancers; bladder cancer; stomach cancer; leukaemia; liver cancer; trachea, bronchus, and lung cancers; cervical cancer; colon and rectal cancer; mouth cancer; diabetes mellitus; IHD; cerebrovascular disease; the aggregate of HHD, atrial fibrillation and flutter, aortic aneurysm, PVD, and other CVD; COPD; the aggregate of pneumoconiosis, asthma, other interstitial lung disease, and other chronic respiratory diseases	Age ≥25 years	Mortality data including vital registration, verbal autopsy, and population surveys for smoking prevalence	CoDEM[37]	No tobacco smoking	Re-analysis of the Cancer Prevention Study 2[38–40]
5.2. Second-hand smoke	Proportion of children and non-smoking adults reporting exposure to second-hand smoke	The aggregate of lower respiratory infections, upper respiratory infections, and otitis media; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease	Age <5 years for the aggregate of lower respiratory infections, upper respiratory infections, and otitis media, age ≥25 years for all others	Population surveys	Spatiotemporal Gaussian process regression[19–21]	No second-hand smoke exposure	US Department of Health and Human Services,[41] Oono and colleagues,[42] Jones and colleagues[43,44]

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