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标题: Determinants of price negotiations for new drugs. The experience of the Italian Medicines Agency

简介: Objectives

The aim of this paper is to investigate the determinants of the difference between the price proposal submitted by the industry and the final negotiated price. We used Italy as a case-study.

Methods

Data were gathered through the information system used by Italian Medicines Agency. The time-frame for this analysis is 2013–2017. Factors influencing the delta price were analyzed through a regression analysis.

Results

44 orphan drugs and 89 new other molecular entities obtained reimbursement in the last five years. Following the negotiation process, prices were lowered by 25.1% and 28.6% on average for orphan drugs and other molecules respectively. The price reduction was higher for innovative drugs (-32.2%). Statistically significant determinants associated to higher price reduction were: i) the implementation of a product specific monitoring registry, ii) the negotiation of a financial-based Managed Entry Agreement, iii) a target population larger than 20,000 patients, iv) an expected National Health Service expenditure larger than €200 million.

Discussion

The impact of some variables on the delta price was predictable (e.g. for drugs with an expected higher budget impact and a larger population target), others were more surprising (e.g. a significant price reduction for “innovative” drugs). The implementation of financial-based agreements, which often rely on confidential arrangements, was one of the determinants with higher impact on price reduction.

全文链接: http://pan.ckcest.cn/rcservice//doc?doc_id=43741

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标题: National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis

简介: Background

Reducing neonatal mortality is an essential part of the third Sustainable Development Goal (SDG), to end preventable child deaths. To achieve this aim will require an understanding of the levels of and trends in neonatal mortality. We therefore aimed to estimate the levels of and trends in neonatal mortality by use of a statistical model that can be used to assess progress in the SDG era. With these estimates of neonatal mortality between 1990 and 2017, we then aimed to assess how different targets for neonatal mortality could affect the burden of neonatal mortality from 2018 to 2030.

Methods

In this systematic analysis, we used nationally-representative empirical data related to

neonatal mortality, including data from vital registration systems, sample registration systems, and household surveys, to estimate country-specific neonatal mortality rates (NMR; the probability of dying during the first 28 days of life) for all countries between 1990 (or the earliest year of available data) and 2017. For our analysis, we used all publicly available data on neonatal mortality from databases compiled annually by the UN Inter-agency Group for Child Mortality Estimation, which were extracted on or before July 31, 2018, for data relating to the period between 1950 and 2017. All nationally representative data were assessed. We used a Bayesian hierarchical penalised B-splines regression model, which allowed for data from different sources to be weighted differently, to account for variable biases and for the uncertainty in NMR to be assessed. The model simultaneously estimated a global association between NMR and under-5 mortality rate and country-specific and time-specific effects, which enabled us to identify countries with an NMR that was higher or lower than expected. Scenario-based projections were made at the county level by use of current levels of and trends in neonatal mortality and historic or annual rates of reduction that would be required to achieve national targets. The main outcome that we assessed was the levels of and trends in neonatal mortality and the global and regional NMRs from 1990 to 2017.

Findings

Between 1990 and 2017, the global NMR decreased by 51% (90% uncertainty interval [UI] 46–54), from 36.6 deaths per 1000 livebirths (35.5–37.8) in 1990, to 18.0 deaths per 1000 livebirths (17.0–19.9) in 2017. The estimated number of neonatal deaths during the same period decreased from 5.0 million (4.9 million–5.2 million) to 2.5 million (2.4 million–2.8 million). Annual NMRs vary widely across the world, but west and central Africa and south Asia had the highest NMRs in 2017. All regions have reported reductions in NMRs since 1990, and most regions accelerated progress in reducing neonatal mortality in 2000–17 versus 1990–2000. Between 2018 and 2030, we project that 27.8 million children will die in their first month of life if each country maintains its current rate of reduction in NMR. If each country achieves the SDG neonatal mortality target of 12 deaths per 1000 livebirths or fewer by 2030, we project 22.7 million cumulative neonatal deaths by 2030. More than 60 countries need to accelerate their progress to reach the neonatal mortality SDG target by 2030.

Interpretation

Although substantial progress has been made in reducing neonatal mortality since 1990, increased efforts to improve progress are still needed to achieve the SDG target by 2030. Accelerated improvements are most needed in the regions and countries with high NMR, particularly in sub-Saharan Africa and south Asia.

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标题: National, regional, and state-level all-cause and cause-specific under-5 mortality in India in 2000–15: a systematic analysis with implications for the Sustainable Development Goals

简介: Background

India had the largest number of under-5 deaths of all countries in 2015, with substantial

subnational disparities. We estimated national and subnational all-cause and cause-specific mortality among children younger than 5 years annually in 2000–15 in India to understand progress made and to consider implications for achieving the Sustainable Development Goal (SDG) child survival targets.

Methods

We used a multicausal model to estimate cause-specific mortality proportions in neonates and children aged 1–59 months at the state level, with causes of death grouped into pneumonia, diarrhoea, meningitis, injury, measles, congenital abnormalities, preterm birth complications, intrapartum-related events, and other causes. AIDS and malaria were estimated separately. The model was based on verbal autopsy studies representing more than 100 000 neonatal deaths globally and 16 962 deaths among children aged 1–59 months at the subnational level in India. By applying these proportions to all-cause deaths by state, we estimated cause-specific numbers of deaths and mortality rates at the state, regional, and national levels.

Findings

In 2015, there were 25·121 million livebirths in India and 1·201 million under-5 deaths (under-5 mortality rate 47·81 per 1000 livebirths). 0·696 million (57·9%) of these deaths occurred in neonates. There were disparities in child mortality across states (from 9·7 deaths [Goa] to 73·1 deaths [Assam] per 1000 livebirths) and regions (from 29·7 deaths [the south] to 63·8 deaths [the northeast] per 1000 livebirths). Overall, the leading causes of under-5 deaths were preterm birth complications (0·330 million [95% uncertainty range 0·279–0·367]; 27·5% of under-5 deaths), pneumonia (0·191 million [0·168–0·219]; 15·9%), and intrapartum-related events (0·139 million [0·116–0·165]; 11·6%), with cause-of-death distributions varying across states and regions. In states with very high under-5 mortality, infectious-disease-related causes (pneumonia and diarrhoea) were among the three leading causes, whereas the three leading causes were all non-communicable in states with very low mortality. Most states had a slower decline in neonatal mortality than in mortality among children aged 1–59 months. Ten major states must accelerate progress to achieve the SDG under-5 mortality target, while 17 are not on track to meet the neonatal mortality target.

Interpretation

Efforts to reduce vaccine-preventable deaths and to reduce geographical disparities should continue to maintain progress achieved in 2000–15. Enhanced policies and programmes are needed to accelerate mortality reduction in high-burden states and among neonates to achieve the SDG child survival targets in India by 2030.

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标题: National, regional, and state-level burden of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b disease in children in India: modelled estimates for 2000–15

简介: Background

India accounts for a disproportionate burden of global childhood illnesses. To inform

policies and measure progress towards achieving child health targets, we estimated the annual national and state-specific childhood mortality and morbidity attributable to *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) between 2000 and 2015.

Methods

In this modelling study, we used vaccine clinical trial data to estimate the proportion of pneumonia deaths attributable to pneumococcus and Hib. The proportion of meningitis deaths attributable to each pathogen was derived from pathogen-specific meningitis case fatality and bacterial meningitis case data from surveillance studies. We applied these proportions to modelled state-specific pneumonia and meningitis deaths from 2000 to 2015 prepared by the WHO Maternal and Child Epidemiology Estimation collaboration (WHO/MCEE) on the basis of verbal autopsy studies from India. The burden of clinical and severe pneumonia cases attributable to pneumococcus and Hib was ascertained with vaccine clinical trial data and state-specific all-cause pneumonia case estimates prepared by WHO/MCEE by use of risk factor prevalence data from India. Pathogen-specific meningitis cases were derived from state-level modelled pathogen-specific meningitis deaths and state-level meningitis case fatality estimates. Pneumococcal and Hib morbidity due to non-pneumonia, non-meningitis (NPNM) invasive syndromes were derived by applying the ratio of pathogen-specific NPNM cases to pathogen-specific meningitis cases to the state-level pathogen-specific meningitis cases. Mortality due to pathogen-specific NPNM was calculated with the ratio of pneumococcal and Hib meningitis case fatality to pneumococcal and Hib meningitis NPNM case fatality. Census data from India provided the population at risk.

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标题: Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study

简介: Background

Socioeconomic status is associated with differences in risk factors for cardiovascular disease incidence and outcomes, including mortality. However, it is unclear whether the associations between cardiovascular disease and common measures of socioeconomic status—wealth and education—differ among high-income, middle-income, and low-income countries, and, if so, why these differences exist. We explored the association between education and household wealth and cardiovascular disease and mortality to assess which marker is the stronger predictor of outcomes, and examined whether any differences in cardiovascular disease by socioeconomic status parallel differences in risk factor levels or differences in management.

Methods

In this large-scale prospective cohort study, we recruited adults aged between 35 years and 70 years from 367 urban and 302 rural communities in 20 countries. We collected data on families and households in two questionnaires, and data on cardiovascular risk factors in a third questionnaire, which was supplemented with physical examination. We

assessed socioeconomic status using education and a household wealth index. Education was categorised as no or primary school education only, secondary school education, or higher education, defined as completion of trade school, college, or university. Household wealth, calculated at the household level and with household data, was defined by an index on the basis of ownership of assets and housing characteristics. Primary outcomes were major cardiovascular disease (a composite of cardiovascular deaths, strokes, myocardial infarction, and heart failure), cardiovascular mortality, and all-cause mortality. Information on specific events was obtained from participants or their family.

Findings

Recruitment to the study began on Jan 12, 2001, with most participants enrolled between Jan 6, 2005, and Dec 4, 2014. 160 299 (87·9%) of 182 375 participants with baseline data had available follow-up event data and were eligible for inclusion. After exclusion of 6130 (3·8%) participants without complete baseline or follow-up data, 154 169 individuals remained for analysis, from five low-income, 11 middle-income, and four high-income countries. Participants were followed-up for a mean of 7·5 years. Major cardiovascular events were more common among those with low levels of education in all types of country studied, but much more so in low-income countries. After adjustment for wealth and other factors, the HR (low level of education vs high level of education) was 1·23 (95% CI 0·96–1·58) for high-income countries, 1·59 (1·42–1·78) in middle-income countries, and 2·23 (1·79–2·77) in low-income countries (pinteraction<0·0001). We observed similar results for all-cause mortality, with HRs of 1·50 (1·14–1·98) for high-income countries, 1·80 (1·58–2·06) in middle-income countries, and 2·76 (2·29–3·31) in low-income countries (pinteraction<0·0001). By contrast, we found no or weak associations between wealth and these two outcomes. Differences in outcomes between educational groups were not explained by differences in risk factors, which decreased as the level of education increased in high-income countries, but increased as the level of education increased in low-income countries (pinteraction<0·0001). Medical care (eg, management of hypertension, diabetes, and secondary prevention) seemed to play an important part in adverse cardiovascular disease outcomes because such care is likely to be poorer in people with the lowest levels of education compared to those with higher levels of education in low-income countries; however, we observed less marked differences in care based on level of education in middle-income countries and no or minor differences in high-income countries.

Interpretation

Although people with a lower level of education in low-income and middle-income countries have higher incidence of and mortality from cardiovascular disease, they have better overall risk factor profiles. However, these individuals have markedly poorer health care. Policies to reduce health inequities globally must include strategies to overcome barriers to care, especially for those with lower levels of education.

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