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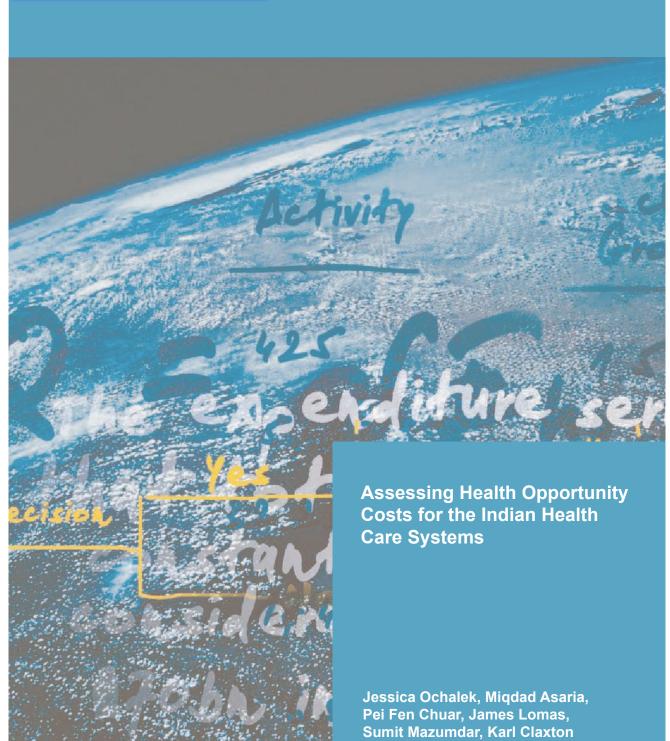
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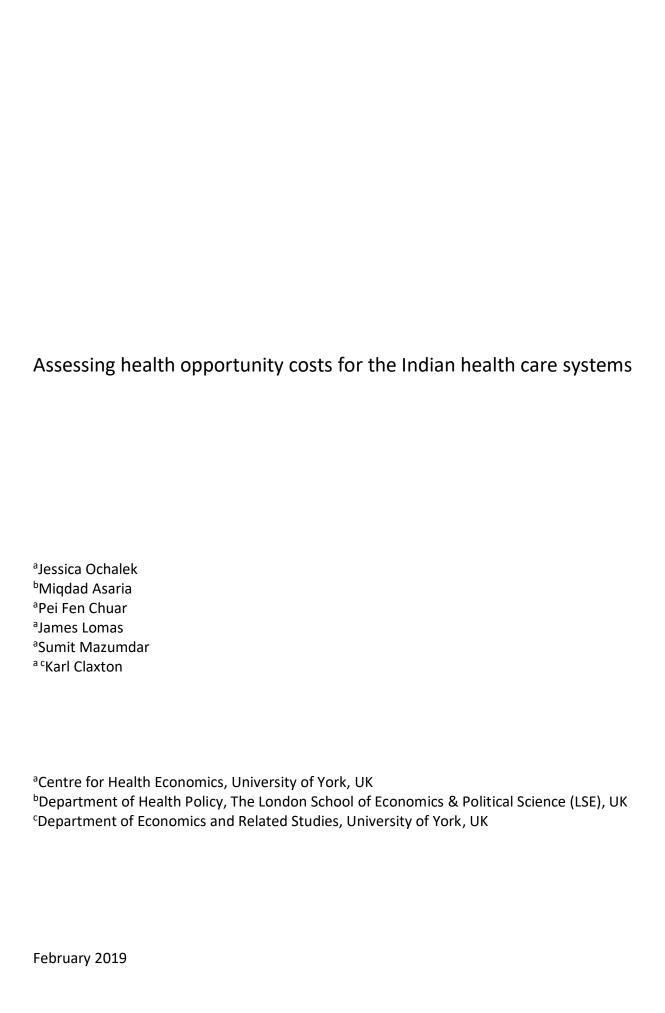






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Abstract

The economic evaluation of health care interventions including new health technologies such as branded pharmaceuticals requires an assessment of whether the improvement in health outcomes they offer exceeds the improvement in health that would have been possible if the additional resources required had, instead, been made available for other health care activities. Therefore, some assessment of these health opportunity costs is required if the best use is to be made of the resources available for health care. This report provides a brief review of the literature on the assessment of health opportunity costs, outlines how existing estimates of the effect of changes in health expenditure on mortality, as well as survival and morbidity, can be used to provide some initial assessment of the possible health opportunity costs associated with additional health care costs for the different states of India. The resulting estimated range for India is 14,116 to 22,275 2015 INR (223 to 351 2015 USD). Estimated ranges for the states range from 4,747 to 7,338 2015 INR (75 to 116 2015 USD) for Bihar to 27,370 to 42,701 2015 INR (432 to 673 2015 USD) for Himachal Pradesh and higher for Delhi. This wide range of possible estimates based on existing work are discussed and some suggestions are made of how further research could provide estimates that more closely reflect evidence of the health effects of health care expenditure in the Indian states.

Introduction

Evidence on the expected costs and health effects of making a new health technology available to specific populations in a particular setting and health care system (HCS) are often summarised as incremental cost-effectiveness ratios (ICERs). These ratios are often expressed as the cost per Quality Adjusted Life Year (QALY) gained or the cost per Disability Adjusted Life Year (DALY) averted (Salomon et al. 2012). These measures provide a useful summary of how much additional resource is required to achieve a measured improvement in health (the additional cost required to gain one QALY or to avert one DALY). Whether the cost per QALY gained or DALY averted offered by an intervention is regarded as worthwhile requires a comparison with a cost-effectiveness 'threshold'. An effective intervention will only improve health outcomes overall (i.e. produce a positive net health benefit) if the additional health benefits exceed the health opportunity costs associated with the additional health care costs that must be found from existing commitments or that use additional expenditure that could have been devoted to other health care activities. Such an assessment of health opportunity cost reflects the maximum a HCS can afford to pay for the health benefits that a new health technology offers, without reducing health outcomes overall. Therefore, an evidence based assessment of health opportunity costs is critical to the appropriate pricing of new branded pharmaceuticals while they are protected by patent (Claxton et al. 2008; Claxton et al. 2011).

To ensure that decisions improve rather than reduce health outcomes overall, judgements about cost-effectiveness ought to be founded on evidence of the likely health opportunity costs in the HCS where the use of a new technology is being considered. Most previous work concerning health opportunity costs has focused on national HCS, but many countries have decentralised HCS at a regional, state or state level. It is therefore important that health opportunity costs are informed by research at the level at which budgets are set and decisions are made (and opportunity costs are incurred).

A persistent problem has been that the cost-effectiveness 'thresholds' (e.g. cost per QALY or cost per DALY thresholds) recommended or cited by decision making and advisory bodies (both national and supra-national) reflect a lack of conceptual clarity about what they ought to represent and what type of evidence might inform their assessment (Revill et al. 2014; Culyer 2016). As a consequence these values are not evidence based and have simply become established norms or implied values, which describe the criteria used to judge cost-effectiveness (Claxton, Sculpher, et al. 2015). Other proposed thresholds reflect a view of what value ought to be placed on improvements in health. They imply what health care expenditure ought to be (the social demand for health) rather than an evidence-based assessment of health opportunity costs given actual levels of expenditure, i.e. a 'supply side' estimate of the amount of health that a HCS currently delivers with more or less resources.

The problem of estimating a cost-effectiveness 'threshold' that represents expected health opportunity costs is the same as estimating the relationship between changes in health care expenditure and health outcomes. Estimates of the marginal productivity of health expenditure in producing health (QALYs) are becoming available for some high income countries based on approaches to estimation which exploit within-country data (Martin et al. 2008; Vallejo-Torres et al. 2016; Edney et al. 2017; Claxton, Martin, et al. 2015). This evidence from national HCS contexts in high income countries can be used to give some indication of possible values in other contexts (Woods et al. 2016) based on estimates of the income elasticity of demand for health and assumptions about the relative underfunding of HCS (i.e. the shadow price for public expenditure on health). Another approach has taken estimates of the effect of health care expenditure on health outcomes based on country-level data (typically expressed as elasticities) and applied these to

country-level baseline health and demographic data to generate overall cost per DALY 'thresholds' for low- and middle-income countries (LMICs) (Ochalek et al. 2018).

India's Ministry of Health and Family Welfare is in the process of establishing a medical technology assessment board (MTAB) as part of a recent commitment to moving toward universal health coverage using health technology assessment (HTA) to inform reimbursement decisions for state budgets for health care (Downey et al. 2017). MTAB will be the central organization undertaking HTA in India, with key partners in India and internationally. Ensuring the agency's recommendations improve, rather than reduce, health outcomes overall requires quantifying the health that would have been possible if the money required to reimburse or fund one intervention was instead made available for other interventions (i.e. the health opportunity cost) (Prinja et al. 2015). However, like in many other jurisdictions, there is no explicit and empirically-informed 'threshold' that reflects the likely health opportunity costs so it is not possible to assess the likely net health effect of approving a new health technology or establish what price ought to be paid for new pharmaceuticals protected by patent. This report details the methodology that was used to generate state-level estimates of health opportunity costs (cost per DALY 'thresholds'). In broad terms, this involved tailoring the approach taken by Ochalek et al. (2018) to consider health opportunity costs that occur at the provincial level using state specific data on health expenditure, epidemiology and demographics.

Methods

The effect of different levels of health care expenditure on mortality outcomes has been investigated in a number of published studies using country-level data, many including high- as well as low- and medium-income countries (Gallet & Doucouliagos 2017). The challenge is to control for all the other reasons why mortality might differ between countries in order to isolate the causal effect of differences in health expenditure (Nakamura et al. 2016). This is a particular challenge even if available measures are complete, accurate and unbiased because health outcomes are likely to be influenced by expenditure (increases in expenditure improves outcomes), but outcomes are also likely to influence expenditure (poor outcomes prompt greater efforts and increased expenditure). This problem of endogeneity, as well as the inevitable aggregation bias, risks underestimating the health effects of changes in expenditure. Instrumental variables have been used in a number of studies to try and overcome this problem and estimate outcome elasticities for all-cause adult, maternal and child mortality (Bokhari et al. 2007 among others). The Bokhari et al (2007) model specification applies an instrumental variable approach to cross-sectional data from the year 2000 for 127 countries and models both public expenditure on health and a country's GDP as endogenous variables (both in per capita terms). Specifically, the identification strategy of Bokhari et al (2007) employs two instrumental variables: military expenditure per capita of neighbouring countries and a measure of institutional quality. These represent typical instrumental variables following in the tradition of earlier papers such as Filmer & Pritchett (1999). In addition, Bokhari et al (2007) perform a logarithmic transformation of their data so that coefficients can be interpreted as elasticities, and allow for the outcome elasticity with respect to expenditure of countries to vary by two variables: the level of infrastructure (proxied by 'paved roads per unit of area') and shock in donor funding (measured by absolute deviation in current donor funding from historical mean).

This approach to estimation using country-level data can provide country specific cost per DALY averted values by applying estimated elasticities, which take account of measures of a country's infrastructure and changes in donor funding, to country specific mortality rates, conditional life expectancies and population distribution (all by age and gender) as well as estimates of disability burden of disease and total health care expenditure. We re-estimate the effect of changes in expenditure using Bokhari et al (2007)'s dataset after expanding the dataset to include under-5 mortality from the World Bank in addition to adult male and adult female mortality, which enables greater coverage of the population, as well as: i) a measure of survival, years of life lost (YLLs); ii) a measure of morbidity, years of life disabled (YLDs); and iii) DALYs, a generic measure of overall ill health, from the Global Burden of Disease (GBD) database. Elasticities are estimated at the countrylevel and differ only with respect to the interaction of measures of infrastructure and donor funding. The estimated elasticities for India (see Table 2) are applied to state specific data on health expenditure, epidemiology and demographics, i.e. in the absence of elasticity estimates at state level the estimate for India are assumed to be common across the states. Nonetheless, the health effects of changes in health expenditure will differ across states due to differences in health expenditure, epidemiology and demographics.

There are four ways in which the estimated elasticities in Table 2 can be used to estimate the likely DALYs averted as a consequence of a 1% change in health expenditure in each state, *i*. Each of the four ways in which a cost per DALY can be estimated are summarised in Table 1 and are briefly described below, with details of the data used reported in Appendix A.

Table 1. Alternative approaches to calculating DALYs averted

		DALY 1	DALY 2	DALY 3	DALY 4
Survival effects (YLLs averted)		Based on indirectly estimating effects on survival from mortality (A)	Directly estimat	ed (D)	
	Direct effect	Uses indirectly estimated effects on survival from mortality as a surrogate for morbidity effects (B)	Uses directly estimated survival effects as a surrogate for morbidity effects (E)		Directly estimated (G)
Morbidity Effects (YLDs averted)	Indirect effect	Uses average overall population health as a surrogate for increase in YLD burden associated with increase in YLLs averted (C)		Directly estimated (F)	

DALY 1

The first estimate is based only on estimates of the mortality effects of changes in expenditure. As these are the most prevalent estimates available across the literature, this enables DALY 1 to be calculated using elasticities from various sources, such as the all-cause mortality elasticities that have been estimated in the UK as part of work on health opportunity costs (Claxton et al. 2017; Andrews et al. 2017).

The estimated elasticity for children under-5, \in mortality, can be applied to the number of deaths observed in this age group in each state (denoted by the i subscript) to provide an estimate of the number of deaths averted as a consequence of a 1% change in state health expenditure.

(1) directly estimated deaths averted
$$_{i}^{0-4}=1\%*\left|\epsilon_{India}^{mortality^{0-4}}\right|*deaths_{i}^{0-4}$$

Similarly, the estimated elasticities for male and female adults (ages 15-60) are applied to observed deaths by age and gender in each state, i.e. assuming that the proportionate effect on mortality applies equally across age groups within 15-60 age range.

(2) directly estimated deaths averted
$$i^{15-60} = 1\% * \left| \epsilon_{India}^{mortality^{15-60}} \right| * deaths_i^{15-19} + \cdots + 1\% * \left| \epsilon_{India}^{mortality^{15-60}} \right| * deaths_i^{55-60}$$

Once the likely deaths averted by a 1% change in health expenditure have been estimated in this way (see (1) and (2), the survival effects can be established by applying conditional life expectancy (CLE) at age of death to each death averted within each age group (see (3) and (4)). An estimate of survival gains of a change in health expenditure based on mortality effects (mortality based YLL averted) is simply the sum of these effects (5).

- (3) mortality based YLL averted_i⁰⁻⁴ = $CLE_i^{0-4} * deaths$ averted_i⁰⁻⁴
- (4) mortality based YLL averted $_i^{15-60} = CLE_i^{15-19} * deaths averted_i^{15-19} + CLE_i^{20-24} * deaths averted_i^{20-24} + \cdots + CLE_i^{55-59} * deaths averted_i^{55-59}$
- (5) mortality based YLL averted $_i^{0-4}$ & $_{15-60}$ = mortality based YLL averted $_i^{0-4}$ + mortality based YLL averted $_i^{15-60}$

However, this measure (5) excludes potential survival effects in ages 5-14 years and also those over the age of 60. To try to reflect the possible survival effects across all ages the estimate of the mortality based YLL averted in (5) can be adjusted using the YLL in these age group as a proportion of the YLL across all ages, σ_i (6).

(6) mortality based YLL averted_i^{all ages} =
$$\frac{mortality\ based\ YLL\ averted_i^{0-4\ \&\ 15-60}}{\sigma_i}$$

where,

(7)
$$\sigma_i = \frac{YLL_i^{0-4} + YLL_i^{15-60}}{YLL_i^{all\ ages}}$$

The YLL for each age group is simply the observed deaths in that age group multiplied by the conditional life expectancy for that age, i.e. it represents the survival burden of disease in each age and gender group. For example,

(8)
$$YLL_i^{0-4} = CLE_i^{0-4} * absolute deaths_i^{0-4}$$

(9)
$$YLL_i^{15-60} = CLE_i^{15-19} * absolute\ deaths_i^{15-19} + CLE_i^{20-24} * absolute\ deaths_i^{20-24} + \cdots + CLE_i^{55-59} * absolute\ deaths_i^{55-59}$$

The $YLL_i^{all\ ages}$ is calculated in a similar way to (8) and (9), as the sum of the product of absolute deaths and conditional life expectancy across all age groups in the population.

Therefore, the extrapolation of the survival effects from those age groups where mortality effects can be estimated (5) to all age groups in the population (6) assumes that the survival effects of changes expenditure are in proportion to the survival burden of disease at each age.

There are likely to be direct and indirect effects on morbidity of changes in expenditure. For example, changes in expenditure that affect mortality and survival are also likely to have an effect on morbidity through the prevention and treatment of disease (i.e. a direct effect decreasing YLD burden). However, an indirect effect may also be present as reductions in mortality and the resulting increased survival is likely to increase the number of years during which morbidity is experienced.

To calculate the possible direct effect we assume that the effect of changes in expenditure on morbidity is proportional to the effect on survival (B in Table 1), i.e. assuming that the estimated effects on morbidity can be used as a surrogate for likely effects on morbidity where these effects have not been directly estimated. The ratio of YLD to YLL in each state γ_i , is applied to estimates of the state specific survival effects from (6) (see the first term of (12) below).

(10)
$$\gamma_i = \frac{YLD_i^{all\ ages}}{YLL_i^{all\ ages}}$$

To account for the indirect effect of increasing the number of years during which morbidity is experienced due to the survival effects, we apply the per capita YLD burden for each state to the state specific survival effects (see the second term in (11) below and C in Table 1). Mortality based YLD averted are therefore calculated as:

(11)
$$\begin{array}{c} \textit{mortality} & \textit{all ages} \\ \textit{based YLD averted}_i & = \textit{mortality based YLL averted}_i^{\textit{all ages}} * \gamma_i - \\ \textit{mortality based YLL averted}_i^{\textit{all ages}} * \textit{per capita YLD burden}_i \\ \end{array}$$

where the first term reflects the possible direct effects of expenditure in reducing morbidity (B in Table 1) and the second term captures the indirect effect of increases in morbidity due to increases in survival (C in Table 1).

The total DALYs averted due to a 1% change in health expenditure in each state is the sum of the survival effects (the YLL averted in (6), A in Table 1) and the net morbidity effects (YLD averted in (11), B-C in Table 1). This illustrates how estimates of mortality effects of health expenditure, in the form of elasticities, can be used to provide an indication of the likely survival (YLL averted) and morbidity effects (YLD averted). Although the elasticities applied to data from the states are for India as a whole, the health effects of a 1% change in state health expenditure will differ by state due to differences in the number observed deaths by age and gender and differences in age and gender specific conditional life expectancies. The amount of expenditure required to avert one DALY will also differ by state due to differences in total health expenditure.

(12)
$$cost\ per\ DALY\ averted_i = \frac{1\%*government\ expenditure\ on\ health_i}{DALYs\ averted_i}$$

Nonetheless a number of assumptions have been required: i) that elasticities are similar across states; ii) that the estimates survival effects of changes in mortality are a good surrogate for morbidity effects; and iii) that the morbidity burden of disease is distributed across states in the same proportion as the survival burden of disease which can be calculated for each state.

DALY 2

The effect of changes in health expenditure on measures of survival burden of disease (YLL) can also be estimated directly from the cross-country data (See Table 2). The estimated elasticity for YLL, ϵ^{YLL} , is only available at a national rather than state level. However, assuming that elasticities are similar across states this elasticity can be applied to state specific $YLL_i^{all\ ages}$ which are calculated from observed mortality and conditional life expectancies by age and gender (e.g., see (8) and (9)) above). Therefore, YLLs averted due to a 1% change in health expenditure can be directly estimated (13) rather than applying conditional life expectancies to estimates of deaths averted by age and gender (as required in (1) to (7) above).

(13) directly estimated YLL averted =
$$1\% * |\epsilon_{India}^{YLL}| * YLL_i^{all\ ages}$$

The possible direct and indirect effects on morbidity of changes in health expenditure which effects survival can be calculated in the same way as previously; assuming that the estimated effects on survival can be used as a surrogate for likely effects on morbidity and with the indirect effect of increases in morbidity based on directly estimated survival effects. Therefore, the net morbidity effects are calculated in the same way as in (11) but with *directly estimated YLL_i averted* replacing mortality based YLL_i averted (E-C in Table 1).

DALY 3

As well as direct estimates of the effect on survival burden of disease, the effect of changes in health expenditure on measures of morbidity burden of disease (YLD) can also be estimated directly from the cross-country data (See Table 2). DALY 3 uses direct estimates of the effect on survival burden in the same way as DALY 2 but combines these with direct estimates of the effect on morbidity. The estimated elasticity for YLD is only available at a national rather than state level. However, assuming that elasticities are similar across states this elasticity can be applied to state specific estimates of morbidity burden available from the Institute for Health Metrics (IHME) (Indian Council of Medical Research et al. 2016). The directly estimated YLD averted for a 1% change in state health expenditure is simply the product of the estimated YLD for that state and the estimated YLD elasticity for India (14).

(14) directly estimated YLD averted =
$$1\% * |\epsilon_{India}^{YLD}| * YLD_i^{all\ ages}$$

The total DALYs averted due to a 1% change in health expenditure in each state is the sum of the directly estimated survival effects (YLL averted in (14), D in Table 1) and the directly estimated morbidity effects (YLD averted in (14), F in Table 1).

DALY 4

The combined effect of changes in expenditure on survival and morbidity burden of disease (DALYs can be estimated directly from the cross-country data using country-level estimates of DALY burden of disease (See Table 2). As for mortality, YLL and YLD the estimated elasticity for DALYs is only available at a national rather than state level but can be applied to state specific estimates of DALY burden assuming that the estimated elasticity is similar across states. State specific estimates of DALY burden ($DALY_i^{all\ ages}$) are calculated as the sum of $YLL_i^{all\ ages}$ and $YLD_i^{all\ ages}$ for each state i. Therefore, a direct estimate of DALYs averted for a 1% change in provincial health expenditure is simply the product of the estimated DALY burden for that state and the estimated elasticity for India (16).

(15) directly estimated DALY averted =
$$1\% * |\epsilon_{India}^{DALY}| * DALY_i^{all\ ages}$$

These four alternative ways to estimate health opportunity costs, as measured by the cost per DALY averted, make slightly different assumptions. One common one is that estimated elasticities, which are currently only available at a national level, can be applied equally across states. This might not be unreasonable since the differences in elasticities between countries are quite small based on Bokhari et al (2007), although this model only allows for two interaction terms which both have modest effects.

Nonetheless, the comparison of DALY 1 with DALY 4 does give some indication of whether it is reasonable to use estimates of the mortality effect of changes in health expenditure as a surrogate for likely survival and morbidity effects. This is particularly useful as other studies in high income countries have estimated elasticities for mortality outcomes using high quality within-country data which overcomes some of the difficulties and challenges of estimation based on aggregate country-level data.

Results

Estimated elasticities for India

The extended Bokhari et al. (2007) model generated country-specific elasticity results for all of the countries in the model (n=127), where the elasticities differed due to the specification of the relationship of expenditure with health, which includes interaction terms with level of infrastructure and shocks in donor funding. The elasticities for India for each of the six measures of health outcome are reported in Table 2 along with the average elasticities of all LMICs in the dataset.

Table 2. Estimated elasticities for India

	India	LMICs (average)			
Mortality (deaths per 1,000)					
Children under-5	-0.3483	-0.3273			
Adults females	-0.1937	-0.1744			
Adult males	-0.1967	-0.1788			
DALYs	-0.2034	-0.2108			
YLLs	-0.2900	-0.2980			
YLDs	-0.0270	-0.0306			

The elasticities generated for India are comparable to the mean of estimates generated for other LMICs. Estimated elasticities differ due to the presence of interaction terms combining spending and level of infrastructure (proxied by 'paved roads per unit of area') and the absolute deviation in donor funding from the historical mean. India has a relatively high value for the level of infrastructure compared to other LMICs (it has the 22nd highest value for this variable of all the 127 countries in the Bokhari dataset, including HICs) and also a lower than average deviation in donor funding (it has a low level of donor funding, more generally, compared to other LMICs). Between these two factors, the differences in the elasticities for India compared to other LMICs can be explained, where the direction and size of the difference depends upon the signs of the estimated coefficients on the interaction terms and relative magnitude of each of these.

Cost per DALY averted

The estimates of cost per DALY averted for India as a whole and for each state are reported in Table 3 and are also expressed as a % of GDP per capita.

The estimates of cost per DALY for India as a whole are not the average of the cost per DALY ratios across the states but the ratio of the sum of changes in expenditure to the sum of DALYs averted across the states. The cost per DALY for India as a whole using DALY 1 and DALY 4 falls between those using DALY 2 and 3, which does give some indication that it might be reasonable to use estimates of the mortality effect of changes in health expenditure as a surrogate for likely survival and morbidity effects. This is also reflected in the results by state where DALY 1 and DALY 4 tend to provide relatively similar estimates, with the exception of two states (Delhi and Himachal Pradesh).

DALY 1 and 2 consistently provide the lowest cost per DALY for India as a whole and across the states. This reflects the fact that the estimated elasticity for mortality and survival effects (YLL) are similar and both greater in magnitude than for morbidity effects (YLD) (see Table 2). This larger effect on survival (whether based on mortality or YLL averted) is then used as a surrogate for morbidity effects when estimating DALY 1 and 2. However, DALY 3 consistently provides the highest cost per DALY averted estimate for India and for each of the states with the exception of Andhra Pradesh. This reflects fewer DALYs averted due to the much lower magnitude of the estimated

elasticity for morbidity effects (YLD), i.e. the smaller effect on morbidity more than offsets the larger effect on survival compared to DALYs 1 and 2. Although these differences and the differences in the elasticities reported in Table 2 might indicate that both mortality effects and survival effects may overestimate morbidity effects, this should not be over-interpreted as the estimated elasticities are not based on Indian within-country data but country-level data with limited interactions for country-level effects. However, in general the comparison of DALY 1 and DALY 4 does suggest that using estimates of the mortality effect of changes in health expenditure as a surrogate for likely survival and morbidity effects may not be unreasonable albeit with additional uncertainty.

Table 3. Cost per DALY averted and as a percent of GDP per capita by state

Cost per DALY averted (2015 INR)						
	Rank (by average, highest to lowest)	DALY 1	DALY 2	DALY 3	DALY 4	
India	14	14,116	14,484	22,275	19,182	
		14%	14%	22%	19%	
Andhra Pradesh	21	8,238	6,447	8,620	8,704	
		13%	10%	14%	14%	
Assam	18	6,171	7,553	11,326	9,972	
		10%	12%	18%	16%	
Bihar	22	4,747	4,797	7,338	6,381	
		13%	13%	20%	18%	
Chhattisgarh	12	11,411	11,313	16,688	14,935	
		12%	12%	18%	16%	
Gujarat	7	13,541	13,515	20,860	17,881	
		9%	9%	14%	12%	
Haryana	11	11,103	11,718	18,107	15,469	
		6%	7%	11%	9%	
Himachal Pradesh	2	28,669	27,370	42,701	36,341	
		19%	18%	28%	24%	
Jammu and Kashmir	5	16,886	17,474	27,180	23,411	
		21%	22%	34%	29%	
Jharkhand	20	6,186	6,921	10,824	9,226	
		9%	11%	16%	14%	
Karnataka	8	13,798	13,040	21,032	17,298	
		9%	9%	14%	11%	
Kerala	3	22,454	17,841	31,794	23,783	
		14%	11%	20%	15%	
Madhya Pradesh	17	6,698	7,470	10,437	9,830	
		10%	11%	16%	15%	
Maharashtra	10	12,629	11,120	18,538	14,806	
		8%	7%	12%	9%	
Odisha	15	8,514	9,134	13,606	12,023	
		11%	12%	18%	16%	
Punjab	9	13,766	12,253	19,431	16,257	
		10%	9%	15%	12%	

Rajasthan	13	10,421	11,716	17,154	15,497
		12%	13%	19%	17%
Tamil Nadu	6	16,798	14,244	23,570	18,898
		11%	9%	16%	12%
Uttar Pradesh	19	6,600	7,281	10,432	9,615
		13%	14%	20%	19%
Uttarakhand	4	20,781	19,086	28,215	25,273
		13%	12%	18%	16%
West Bengal	16	8,040	7,554	12,859	10,060
		9%	9%	15%	11%
Delhi	1	26,166	29,478	59,057	39,761
		9%	10%	21%	14%

The four alternative ways to calculate cost per DALY averted each provide relatively similar estimates across most states. To some extent this might be expected as it is assumed that estimated elasticities, which are currently only available at a national level, can be applied equally across states. Insofar as states have similar health expenditure per capita and similar mortality rates, conditional life expectancies and population distribution, the cost per DALY averted will inevitably be very similar. This also explains why the cost per DALY averted differs for some states where per capital heath expenditure is higher and where the population, mortality rates and conditional life expectancies differ (e.g., Himachal Pradesh, Jammu and Kashmir, Kerala and Delhi).

Figure 1 illustrates the range of estimates for India and for each state by under-5 mortality rate. The average of the range of values for each state is not the average for the four cost per DALY ratios but the ratio of a 1% change in expenditure to the average DALYs averted across these four estimates. A pattern is evident between mortality rate and cost per DALY averted. While the low under-5 mortality in Delhi would, other things equal tend to increase the cost per DALY averted, it is higher in Delhi than in Tamil Nadu and Maharashtra, which have similar under-5 mortality rates primarily because Delhi has higher government expenditure on health.

40,000₹ ¬

Average estimates of cost per DALY averted by state and for India

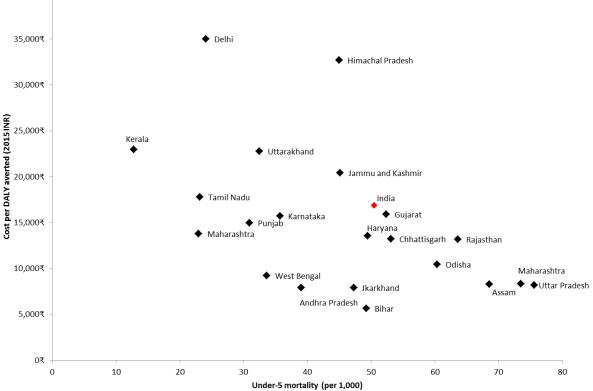


Figure 1. Cost per DALY averted by under-5 mortality rate

Figure 2 illustrates the same cost per DALY averted estimates but now by per capita government expenditure on health. It suggests that the cost per DALY averted increases with per capita health expenditure which is, in general, what might be expected, although this is to some extent inevitable given the methods used to generate these estimates. It also illustrates the similarity in the range of estimates for most states but also why others (Delhi and Jammu and Kashmir) differ. The apparent similarity in the range of cost per DALY averted between most states should not be over interpreted as estimates would also be expected to differ if states are able to generate health at different rates, which would be reflected in differing elasticities. This underscores the importance of further research to estimate these values at the provincial level in India using within-country and within-state data.

Average estimates of cost per DALY averted by state and for India

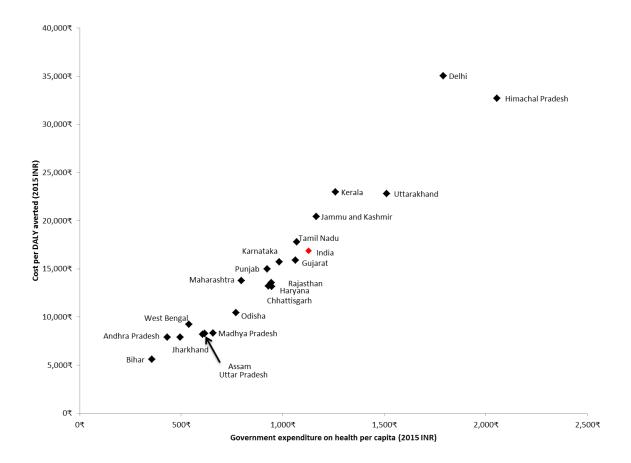


Figure 2. Cost per DALY averted by per capita government expenditure on health

Discussion

Estimates of the health opportunity costs of additional health care expenditure are critical for informing assessments of whether the improvement in health outcomes offered by investing additional resources in a new health technology exceeds the improvement in health that would have been possible if the additional resources required had, instead, been made available for other health care activities. Commonly established implied norms, such as 1-3x GDP per capita, are often inappropriately applied in practice to judge cost-effectiveness (Bertram et al. 2016). Such values generally reflect the social demand for health (i.e. a view of what value ought to be placed on improvements in health) rather than an evidence-based assessment of health opportunity costs given actual levels of expenditure. As such, they do not reflect the health that the HCS is currently able to deliver with the resources available, i.e. the 'supply side' of the HCS. Adopting 'thresholds' to judge cost effectiveness which are too high and do not reflect the 'supply side' will lead to decisions that reduce overall health because the health gained from adopting a new technology will be more than offset by the health opportunity costs elsewhere in the HCS. It will also mean that the HCS will pay too much for the benefits offered by new branded pharmaceuticals because the additional cost of patented innovations will do more harm than good for population health during the remaining patent period. As well as leading to net harms for population health it may also exacerbate health inequalities and unwarranted variations in access to other health care, depending on where the health opportunity costs of additional health care costs tend to fall.

The framework of analysis set out in this report illustrates how estimates of the relationship between mortality and variations in health care expenditure can be employed alongside state specific data on demography, epidemiologic profile and expenditure to inform estimates of health opportunity costs. While data is readily available for the latter, reliable estimates of the relationship between mortality and variations in health care expenditure present a challenge.

This report employed an estimate for India estimated using the model used by Bokhari et al (2007), which applies an instrumental variable method to cross-sectional data and models both public expenditure on health and a country's GDP as endogenous variables. While Bokhari et al. (2007) find a statistically and economically significant effect of public expenditure on health reducing mortality outcomes, there is no clear and consistent finding in the literature that evaluates the relationship between mortality and variations in health care expenditure using country-level data (Gallet & Doucouliagos 2017). This is often driven by the methodological approach adopted by each study, addressing the considerable challenges including the important country-level heterogeneity, much of which is unobserved and controlled for using existing data, even if it is assumed that systematically unbiased measurements are available. Estimates of mortality elasticities based on country-level data tend to be lower than those based on within-country data which are likely to reflect the greater dangers of aggregation bias using country-level data and the difficulty of fully accounting for unobserved heterogeneity and endogeneity using the instruments for health expenditure that are available across countries.

Unusually for a LMIC, a number of studies have analysed the relationship between certain types of mortality and public expenditure on health using somewhat historic data from across the states of India. Delalikar (2005) analyse a panel dataset comprising data from 1980-1999. While public expenditure on health was largely increasing for most states at the same time as infant mortality falling during this period, no statistically significant association is found after controlling for a linear time trend. The authors also investigate how the elasticity varies by state income, finding that the infant mortality elasticity declines as income increases. Bhalotra (2007) analyses data from a longer time period of 1970-1998 and is able to replicate this null-result of Delalikar (2005). However, by allowing for lagged effects of expenditure and constructing the infant mortality variable at an

individual level, they are also able to analyse heterogeneous effects and a strong effect of health expenditure in reducing infant mortality in rural areas. Their econometric analysis uses a probit model and so an elasticity is not directly estimated, but the authors calculate that the long-run infant mortality elasticity is roughly -0.24. Unfortunately, neither of these studies estimate any of the elasticities required to implement the Ochalek et al. (2018) framework. A third paper by Farahani et al. (2010) analyses cross-sectional data from 1998 and employs an IV approach (state fiscal deficit). They also estimate a probit model and so coefficients and marginal effects are not directly interpretable as elasticities, but the authors calculate an all-cause mortality elasticity estimate of -0.2. The authors estimate a range of effect-modifiers including gender, rurality, socioeconomic status and age of the individual. Again, unfortunately, none of the elasticities used in the Ochalek et al. (2018) framework are estimated by this study. Much like the literature using data from across countries, there is no consistent finding from analyses that consider data from across Indian states. However, the literature on health effects of public expenditure on health does emphasise the

importance of heterogeneity across states and therefore the value to estimating state-specific

elasticities as future research.

Importantly, the framework of analysis employed here can be adapted to use the results of any econometric study which is thought to identify plausible effects on mortality of changes or differences in health expenditure study as inputs (see interactive tool: Ochalek et al. 2017). In addition to the studies discussed above, a number of recent studies have used within-country data to estimate elasticities. However, these tend to be limited to high-income countries (Martin et al. 2008; Claxton, Martin, et al. 2015; Vallejo-Torres et al. 2016; Edney et al. 2017). The implied allcause mortality elasticity estimate, -1.0278, found by Claxton et al (2017) is considerably higher in magnitude to any of the mortality elasticity estimates from the extended Bokhari et al (2007) model. Another study, Andrews et al (2017) used an alternative approach to identification to directly estimate an all-cause mortality elasticity estimate for the UK NHS of -0.705. Once again, this is higher than the results from Bokhari et al (2007). Edney et al (2017) and Vallejo-Torres et al (2016) perform similar studies in the contexts of Australia and Spain. The overall results in terms of expenditure per QALY give similar results to these UK studies, but the elasticities cannot be directly compared. In the case of Edney et al. (2017), an elasticity, -1.602, is estimated on HRQoL-weighted YLL reflecting the percentage change in QALYs resulting from delayed mortality for a given percentage increase in expenditure. Vallejo-Torres et al. (2016) instead estimate an elasticity, -0.0681, reflecting the percentage effect on Quality Adjusted Life Expectancy (QALE) that results from a given percentage increase in expenditure in a given year, which would then need to be sustained over the lifetime period (Lichtenberg 2004).

Previous work has estimated cost per DALY averted for 123 low- and middle-income countries based on elasticities estimated from the Bokhari et al (2007) model but country-level data on health expenditure, epidemiology and demographics from GBD and the World Bank (Ochalek et al. 2018). Using these sources, which have been standardised to be internationally comparable, rather than Indian data would have resulted in slightly higher (5-33%) estimates of the DALYs averted for a 1% change in Indian health expenditure. If the health expenditure variable between the data sets was the same, this would result in a slightly lower cost per DALY averted estimates. However, the government health expenditure variable used in Ochalek et al (2018), a World Bank estimate, is slightly higher than what is reported in the National Health Accounts (National Health Accounts Technical Secretariat 2017). As a result, the range of cost per DALY averted for India from the current study (₹14,116 to 22,275) is very similar to that from Ochalek et al (2018) (₹16,793 to ₹23,046) (see Table 3). However, it is the larger differences due to alternative but plausible effects on mortality of changes in health expenditure illustrated in Table 4 which indicate the importance of further research to provide state specific elasticity estimates for India using within-country and within-state data.

Further research

Improving estimates of health opportunity costs for the Indian states could focus on the following issues: First and foremost, estimating under-5, adult male and adult female mortality elasticities for India as a whole or for each of the states using within-country data. Second, while estimated mortality effects do not appear to be a poor surrogate for morbidity effects from this analysis, it would also be of value to estimate the elasticity of health expenditure for outcomes beyond mortality using within-country data where possible. Third, given the vast heterogeneity across states in India, research to estimate state-specific elasticities would potentially be viable and useful.

Conclusions from this analysis, interpretation and next steps

The range of potential cost per DALY averted for India is ₹9,000 to ₹14,000 and for the states is in the region of ₹5,000 to ₹60,000 per DALY averted (see Table 3). Given the greater dangers of aggregation bias using country-level data and the difficulty of fully accounting for unobserved heterogeneity and endogeneity using the instruments for health expenditure that are available across countries this suggests that estimates based on within-country data may be lower. The range estimated here is also consistent with the range of implied cost per QALY gained for India based on the analysis in Woods et al 2016 (₹7,500 to ₹50,000 converted from 2013 US\$ to 2015 INR), which extrapolates the UK findings based on estimates of the income elasticity of demand for health and assumptions about the relative underfunding of HCS (i.e. the shadow price for public expenditure on health). Estimates based on this analysis have been adopted in Norway while further research using within-country data are explored. Nonetheless further research to provide updated Indian and/or state specific elasticity estimates using within-country and within-state data would be a priority.

Estimates of an updated all-cause mortality elasticity for India as a whole could exploit cross sectional variation in expenditure and outcomes, seeking potential instruments from socioeconomic variables and/or exogenous elements in how funding tends to be allocated, following Claxton et al (2017) and Andrews et al (2017) respectively. This would start to identify where in the range of estimates might be most plausible. However, it would still require that a single elasticity estimated at a national level be applied equally across all states. It would also mean that differences between states would be modest and may not reflect real differences in the marginal productivity for health care expenditure, i.e. insofar as states have similar health expenditure per capita and similar mortality rates, conditional life expectancies and population distribution, then the cost per DALY or QALY estimates will also be very similar. This could be relaxed by attempting to estimate all-cause elasticities for each state. Building on the approach taken in published studies reviewed here this might be possible using interaction terms for state when estimating a national all-cause model or estimating separate state specific all-cause models. The latter poses the challenge of finding units of analysis with sufficient variation in expenditure and outcomes within-state as well as suitable instruments.

However, in general, direct estimates of all-cause elasticities tend to be lower than those implied by estimates at disease area level because they are likely to be subject to some aggregation bias compared to those which are able to capture any heterogeneity of effect by disease area. Therefore, it would be an advantage to estimate elasticities (national and for states) by disease areas. However this would require expenditure by disease area as well as mortality outcomes to be available at the unit of analysis that will provide sufficient variation. Nonetheless updated estimates of all-cause elasticities for India and/or the states based on within-country data would be a significant improvement over existing estimates, whether or not they are directly estimated or implied by estimates at disease area level. They would start to identify where in the ₹5,000 to ₹60,000 range would be most plausible using the framework of analysis in this paper.

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Appendix A. Variables used to calculate DALYs averted

Variable	Measure used	Source	Year used
1-year probability of death for females, males and both for ages in a given five-year age category (n-n+4)	Where life table data is given by 1-year age group (e.g., 0-1): $P(annual\ mortality\ n\ to\ n+4) = \\ 1 - \left(\prod_{t=n}^{n+4}(1-p_t)\right)^{\frac{1}{5}}$ Where life table data is given by 5-year age group: $P(annual\ mortality\ n\ to\ n+4) = \\ 1 - (1-p_{n\ to\ n+4})^{\frac{1}{5}}$	Sample Registration System (SRS) Statistical Report 2015 life tables, Office of the Registrar General & Census Commissioner, India Ministry of Home Affairs, Government of India http://www.censusindia.gov.i	
Conditional life expectancy for females, males and both by five-year age category (n-n+4)	$e_x\;$ by age category 0-85+.	n/vital_statistics/SRS_Reports 2015.html (Office of the Registrar General & Census Commissioner 2016)	
Absolute number of death for females, males and by five-year age category (n-n+4)	Absolute deaths n to n + 4 = P(annual mortality n to n + 4) * population n to n + 4	Calculated from p(death) and population variables	2015
Population by females, males and both by five-year age category (n-n+4)	Population by 5-year age category 0-85+.	Total population in mid-year 2015 comes from (Civil Registration System (CRS) Vital Statistics of India, Statement 2). http://www.censusindia.gov.in/2011- Documents/CRS Report/crs report%202015 23062017.pdf (Office of the Registrar General 2015) % of population in each age group 2015 comes from Detailed Tables, Table 1, SRS Report, for each 5-year category. (Office of the Registrar General & Census Commissioner 2016)	

			,
		Because probability of death	
		data is further disaggregated	
		into <1 and 1-4, we augment	
		this with data from the 2011	
		Census about the distribution	
		of the population under-5 and	
		assume this distribution does	
		not change for each state	
		between 2011 and 2015. For	
		Telangana we use the	
		distribution from Andra	
		Pradesh as Telangana was still	
		in Andra Pradesh in 2011 so	
		there is no population data	
		for Telangana in census	
		2011.SRS report (see above	
		links); 2011 census - http://www.censusindia.gov.i	
		n/2011census/Age level data	
		/Age level data.html (Office	
		of the Registrar General &	
		Census Commissioner 2011)	
Per capita GDP	GDP at factor cost (Current Prices) / Total	Table 15. GDP at factor cost	2014-15
(2015 INR)	Population	(current prices), Handbook of	2014-13
(2013 11411)	ropulation	Statistics on Indian States.	
		(Reserve Bank of India 2017)	
		(Neserve Barik of Ilidia 2017)	
Government	Total value, current dollars	Table A.6: Key Health	2014-15
health	Total value, current donars	Financing Indicators for select	2011 13
expenditure		States: NHA Estimates 2014-	
(2015 INR)		15, National Health Accounts	
(2013 1111)		Estimates for India 2014-15.	
		https://mohfw.gov.in/newshi	
		ghlights/national-health-	
		accounts-estimates-india-	
		2014-15 (National Health	
		Accounts Technical	
		Secretariat 2017)	
		Note: Delhi and West Bengal	
		values are from 2013-14 NHA	
		as 2015-16 values were not	
		available.	
YLL	$YLL_{i}^{all\ ages} =$	Calculated from absolute	2015
	I DD _i	deaths and conditional life	
	$CLE_i^{0-4} * absolute deaths_i^{0-4} + CLE_i^{5-9}$	expectancy variables	
		, ,	
	$* absolute \ deaths_i^{5-9} + \cdots + CLE_i^{85 \ and \ over}$		
	$*absolute\ deaths^{85\ and\ over}_i$		
ı		1	

YLD	Total for all diseases by state	Institute for Health Metrics	2016
		and Evaluation Viz Hub	
		https://vizhub.healthdata.org	
		/gbd-compare/india	
		(Indian Council of Medical	
		Research et al. 2016)	
DALY	$DALY_i = YLL_i + YLD_i$	Calculated from YLL and YLD	2015-16
		variables	