

# Evaluating Health Expenditure Trends and Disease Burden in India: A Cost per DALY Approach

Bhavani Shankara Bagepally <sup>\*</sup>, Sajith Kumar S <sup>\*</sup>, Akhil Sasidharan 

Health Technology Assessment Resource Centre, ICMR-National Institute of Epidemiology, Chennai, India

\*These authors contributed equally to this work

Correspondence: Bhavani Shankara Bagepally, Email [bagepally.bs@gov.in](mailto:bagepally.bs@gov.in)

**Background:** Efficient allocation of healthcare resources requires a comprehensive evaluation of healthcare spending and its impact on disease burden. This study aims to estimate the costs-per disability-adjusted life years (DALY) in India. Data from 2010 to 2019 on DALYs and health expenditure per capita (HEp) for individual states in India were utilised.

**Design and Methods:** We followed the CHEERS statement 2022 to present our study's methodology and outcomes. Pearson's product-moment correlations were used to analyse associations between DALYs and HEp. A panel regression analysis was conducted using a log regression model to estimate changes in DALYs due to health expenditure changes. All costs are reported in Indian rupee (₹) along with its 95% CI, with a conversion factor of 1 US\$ = ₹82.4 applied.

**Results:** The costs-per-DALY were estimated for each state and India. DALY was negatively correlated with HEp. The estimated mean cost-per-DALY for India was ₹82,112 (₹55,810 to ₹1,08,413) [\$997 (\$667 to \$1316)]. The mean cost per-DALY varied across states, with value of ₹27,058 (₹22,250 to ₹31,866) [\$328 (\$270 to \$387)] for states in the first quartile based on Human Development Index (HDI) and ₹2,69,175 (₹1,05,946 to ₹4,32,404) [\$3267 (\$1286 to \$5248)] for those in fourth HDI quartile. States such as Gujarat (0.16), Karnataka (0.17) and Maharashtra (0.22) have lower, and Arunachal Pradesh has the highest cost-per-DALY to Gross state domestic product per-capita ratio (2.41), followed by Nagaland (1.45).

**Conclusion:** Higher healthcare investment has a lower disease burden; however, reduction in DALY varies across states. Study findings provide evidence to aid the setting up of differential willingness-to-pay thresholds across Indian states for efficient and equitable healthcare resource allocation.

**Keywords:** disease burden, DALY, cost per DALY, health expenditure

## Introduction

Health is a crucial component of human development and well-being.<sup>1</sup> Poor health outcomes can lead to lower productivity, decreased economic growth, and higher healthcare costs.<sup>2</sup> Despite the progress made in India's healthcare sector, the disease burden remains a major concern. Effective resource allocation for improving health outcomes is essential for promoting sustainable economic and social development in India.<sup>3</sup> Despite many government-funded programs and insurance systems, healthcare spending has recently varied from 1.2% to 1.6% of gross domestic product (GDP).<sup>4</sup>

Quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs) are two commonly used general metrics of health effectiveness.<sup>5</sup> DALY quantifies health loss arising from both fatal and non-fatal disease burdens, encompassing the sum of years of life lost due to premature mortality and years of life lived with disability. One DALY denotes the equivalent of one year of healthy life lost, and analysis of DALY levels and trends facilitates efficient comparisons between various diseases and injuries.<sup>6-8</sup> In India, the cost of treating illnesses is considerable and results in a significant financial burden on patients who are required to cover the majority of these costs out of their own pockets.<sup>9,10</sup> To ensure optimal spending, it is crucial to comprehend how health expenditure affects the burden of disease and disability in the population.

GDP is a metric to capture the annual value of goods and services produced within a nation's borders, serving as the conventional indicator for evaluating economic progress and development. Variations in GDP per capita are utilized to analyse the effects of improved health, portraying the mechanism by which enhanced health contributes to increased income, notably through factors like elevated productivity.<sup>11,12</sup> Previous studies have reported a significant association between GDP per capita and DALYs among individual states in India, indicating that disease burden and economic performance are related.<sup>13,14</sup>

The aim of this study is to assess the cost per DALY in India by analysing trends in disease burden and health expenditure spanning 2010 to 2019. Through this analysis, we seek to evaluate the state-specific economic burden of disease and the efficiency of healthcare expenditure. Utilizing health expenditure per capita (HEp) data allows for the evaluation of how changes in health expenditure correspond to the changes in disease burden among different states. Our hypothesis posits that incorporating Cost per DALY as a supplementary metric provides a comprehensive approach to assessing healthcare outcomes. Assessing cost per DALY against established GDP-based thresholds will aid policymakers in prioritizing high-value interventions, optimizing state-level resource allocation, and supporting equitable decision-making criteria. Our study contributes to the existing literature by applying the Cost per DALY methodology to the Indian context, providing valuable insights for policymakers and researchers.

## Design and Methods

We analysed data from 2010 to 2019 on the DALYs per 100,000 population and the health expenditure per capita (HEp) for various states in India. The Global Burden of Disease (GBD) Injuries and Risk Factors Study, published by the Institute for Health Metrics and Evaluation (IHME),<sup>8</sup> provides a comprehensive estimate of the disease burden in terms of DALY in India and other countries. The data on DALYs was obtained from the "India State-Level Disease Burden Initiative" as a part of the GBD injuries and risk factors study<sup>7</sup> published by IHME.<sup>8</sup> The GBD estimates provide a comprehensive estimate of the disease burden in terms of DALY for all the individual states in India. The data on state-level actual health expenditure was obtained from multiple sources, which provides information on the healthcare spending by various states.<sup>10,12,15–17</sup> The health expenditure data for a particular year is obtained from previous budget documents, the annual report of the controller general of accounts, the economic survey, and the annual reports of the national health authority. However, due to reporting discrepancies, notably in certain states (primarily in the northeastern region) where data was missing, we conducted a comprehensive data compilation from various sources spanning multiple years. To account for private spending, we collected data on the proportion of out-of-pocket expenditures and incorporated it as an adjustment factor when estimating the cost per DALY.<sup>10,18</sup> In instances where OPE data for states was unavailable, we used national averages. Additionally, to generate more comprehensive insights for individual states, the human development index (HDI),<sup>19</sup> gross state domestic product (GSDP) per capita,<sup>15</sup> and population,<sup>20,21</sup> were utilised in further calculations. Using a standardised measure of health outcomes, such as the DALY per 100,000 population, allows us to compare the disease burden of states with different sizes and characteristics. HEp and DALY per-capita were estimated using the population data.

The HDI is a widely accepted measure of overall development, and it includes the three components of education, income, and health. The state-wise HDI values were used to categorise individual states into four HDI quartiles, with the ones having the lowest HDI value falling into the first quartile, followed by those in the second and third quartiles, and the states with the highest HDI value being placed in the last quartile. The use of the HDI quartiles allowed us to examine whether this relationship holds in the context of disease burden and health expenditure in India. The cost per DALY in each of these quartiles was estimated separately. To estimate the state-specific cost per DALY, we followed the methods suggested by Daroudi et al<sup>5</sup> and revised methods suggested by Ochalek et al.<sup>22</sup> We have used crude DALY to account for the population difference across different states in India and further updated the model and analysis using the most recent Indian data. Given the potential impact of the COVID-19 pandemic on disease burden and gross productivity, and due to data constraints, this study focused solely on a more recent pre-pandemic period.

## Data Analysis

Pearson's product-moment correlations were independently estimated to determine the associations between the DALYs per 100,000 population and HEp during 2010–2019. To establish a causal relationship between DALYs per 100,000 population and HEp in Indian states from 2010 to 2019, we conducted a panel regression analysis and used the following log regression model to estimate the change in DALYs due to a change in health expenditure.

$$\log\text{DALY}_{it} = \alpha + \beta \log\text{HE}_{it}$$

Where,

$\log\text{DALY}_{it}$  = natural logarithm of the DALY (per 100,000 population) for state  $i$ , and year  $t$

$\log\text{HE}_{it}$  = the natural logarithm of HEp for the state  $i$ , and year  $t$ .

$\beta$  is the regression coefficient that quantifies the change in DALY (per 100,000 population) associated with a unit change in HEp, holding all other variables constant. The selection between a fixed effects model and a random effects model in panel regression was made using the Hausman test. The estimated panel regression vector ( $\beta$ ) was used to adjust the change in HEp for calculating the cost per DALY for all states. The regression model was estimated for states with different HDI categories separately, as well as for all states combined. This approach allowed us to investigate the relationship between the cost per DALY and HEp within each HDI category, as well as across all states.

To estimate the cost per DALY for Government health expenditure (GHE), we used the formula, Cost per DALY = HE per capita / ( $\beta$  \* DALY per capita), and subsequently, using the adjustment factor (OOPE for states), we estimated the cost per DALY for total health expenditure (THE).

The cost per DALY estimate provides a measure of the cost-effectiveness of health expenditure in reducing the burden of disease and disability in India. The cost per DALY estimate provides a measure of the resources needed to gain one additional healthy year of life in a population. In this study, the cost per DALY estimate is used to evaluate the efficiency of health expenditure in reducing the burden of disease and disability in India. The lower the cost per DALY, the more cost-effective the health expenditure is in improving health outcomes. All costs are reported in Indian rupee (₹), and a conversion factor of 1 US\$ = ₹82.4 was applied.<sup>23</sup>

We used graphical representations, including maps and violin plots, to further visualise the relationship between DALYs and health expenditure in India. The maps provided a visual representation of the distribution of cost per DALY and the ratio of cost per DALY to GSDP among individual states in India. Cost per DALY based on HDI quartiles was plotted using the Violin plots. All analyses were performed using Stata V.17,<sup>24</sup> and statistical tests were considered significant at a  $p$ -value < 0.05. All values are reported as the mean with a 95% confidence interval (CI) and the median with the interquartile range (IQR). We adhered to the CHEERS Statement 2022 to ensure a concise and thorough presentation of our study's methodology and findings and included the CHEERS checklist as [Appendix 1](#).

## Validation

All DALY data were sourced from the “India State-Level Disease Burden Initiative”, a component of the GBD injuries and risk factors study<sup>7</sup> published by IHME.<sup>8</sup> Health expenditure data were compiled from various sources, including budget reports, NHA reports, and the Economic Survey.<sup>10,12,15–17</sup> Additional information such as HDI values<sup>19</sup> gross state domestic product per capita,<sup>15</sup> and population,<sup>20,21</sup> was collected for subsequent calculations. The methodology for estimating Cost per DALY was adapted from two prior studies conducted by Daroudi et al<sup>5</sup> and Ochalek et al.<sup>22</sup>

## Results

### Correlation Analysis

The results of a pairwise correlation between DALY per 100,000 population and HEp for ten years indicate a significant negative correlation between these variables ( $r = -0.65$ ,  $p < 0.01$ ). State-wise analysis shows every state, except for Andhra Pradesh, Goa, and Kerala, demonstrated a negative correlation between DALY and HEp. The correlation coefficient ranged from  $-0.52$  in Himachal Pradesh to  $-0.99$  in Chhattisgarh. The negative correlation can primarily be attributed to the decline in disease burden, as all states except Goa and Kerala experienced a decrease in DALY numbers from 2010 to 2019.

### Panel Regression Analysis

The Hausman test was conducted for all panel regression models, and random effects were found to be preferred over fixed effects ( $p > 0.05$ ). The regression analysis revealed a significant negative association between the logarithm of HEp and the logarithm of the DALY per 100,000 population. For every unit increase in HEp, there was a corresponding

**Table 1** Panel Regression Results

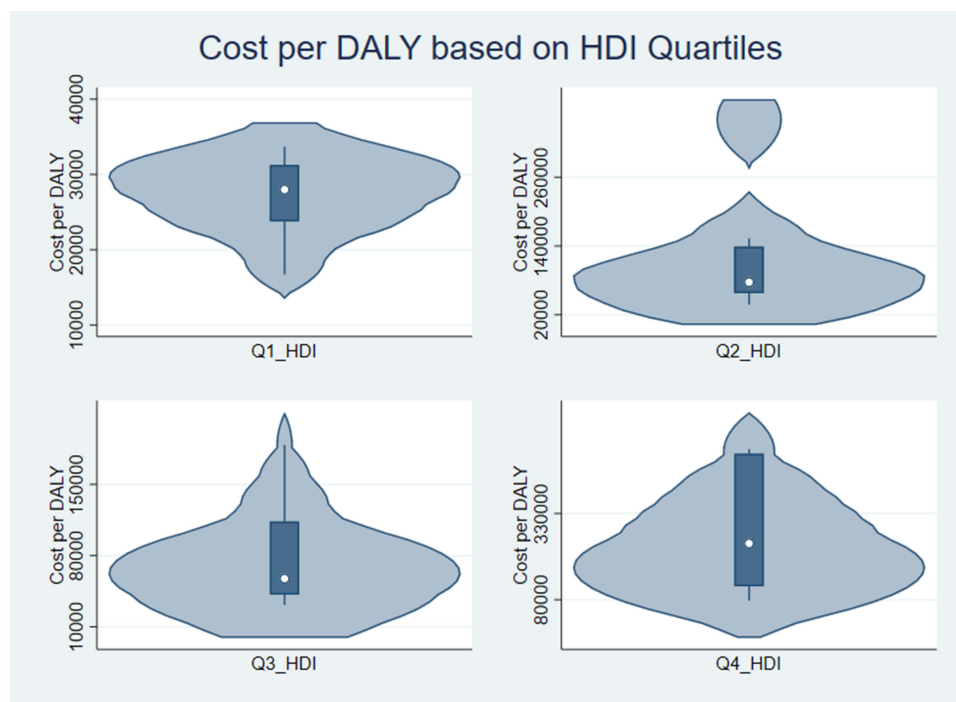
		HDI Q1 (SE)	HDI Q2 (SE)	HDI Q3 (SE)	HDI Q4 (SE)	Overall (SE)
Constant*		12.23 (0.109)	11.51 (0.121)	11.74 (0.093)	11.052 (0.158)	11.84 (0.062)
Log HEp*		-0.2530 (0.016)	-0.1570 (0.016)	-0.1831 (0.012)	-0.0950 (0.020)	-0.1971 (0.008)
R <sup>2</sup>	Between	0.11	0.50	0.37	0.65	0.57
	Overall	0.12	0.52	0.43	0.59	0.59

**Notes:** Dependent variable: Log DALY per 100,000 population \*All values are significant at  $p < 0.01$ .

reduction in the DALY rate across different HDI quartile states. The magnitude of this reduction varied across different HDI quartiles, ranging from 0.09 to 0.25 units per 100,000 population. Furthermore, an overall one unit (one rupee) increase in HE per capita was associated with a 0.19 unit reduction in DALY per 100,000 population. The panel regression results are presented in Table 1.

## State-Wise Cost per DALY

The  $\beta$  value from the panel regression analysis was used to estimate the cost per DALY for each HDI quartile and India overall. The estimated mean cost per DALY (95% CI) for states in the first HDI quartile was ₹27,058 (₹22,250 to 31,866) [\$328 (\$270 to \$387)] with a median (IQR) of ₹ 27,994 (7466) [\$340 (\$91)]. Similarly, the mean (95% CI) and median (IQR) values for states in the second quartile were ₹1,18,023 (30,203 to 2,05,843) [\$1432 (\$367 to \$2494)] and ₹76,801 (80,659) [\$932 (\$979)], respectively. For states in the third quartile, the corresponding values were ₹80,819 (29,799 to 1,31,838) [\$981 (\$362 to \$1600) and ₹57,402 (71,619) [\$697 (\$869)] for the mean (95% CI) and median (IQR), respectively. The states in the fourth quartile of the HDI were found to have the highest mean (95% CI) cost per DALY, with a value of ₹2,69,175 (1,05,946 to 4,32,404) [\$3267 (\$1286 to \$5248)] and a median (IQR) of ₹ 2,43,106 (3,84,355) [\$2950 (\$4665)] (Figure 1).



**Figure 1** Cost per DALY based on HDI quartiles. [The Y-axis represents the estimated cost per DALY for states in each HDI quartile. The box in the plot represents the interquartile range, with the top and bottom edges representing the 3rd and 2nd quartiles, respectively. The center line represents the median (Q2) of the data. The violin shape portrays the kernel density plot, where the width of the plot at each point indicates the density of data points in that specific area].

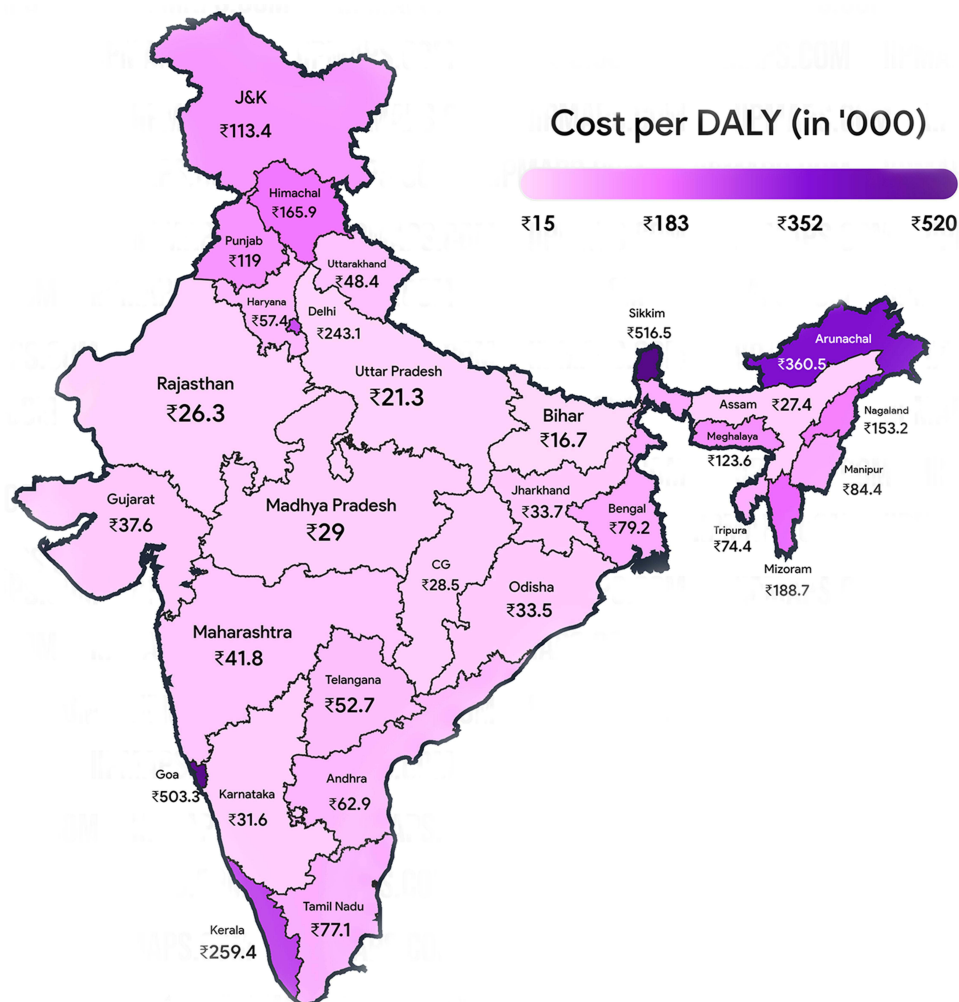
Similarly, the estimated mean (95% CI) and median (IQR) cost per DALY for India overall were ₹82,112 (55,810 to 1,08,413) [\$997 (\$667 to \$1316)] and ₹ 51,700 (\$68,198) [\$627 (\$828)], respectively.

The individual state-wise estimation found that the cost per DALY was highest in Sikkim [₹5,16,489 (\$6268)], Goa [₹5,03,300 (\$6108)], and Arunachal Pradesh [₹3,60,488 (\$4375)], followed by Kerala [2,59,447 (\$3149)] (Figure 2).

All these states belong to the fourth HDI quartile except Arunachal Pradesh, which belongs to the second quartile (Figure 3). Similarly, the lowest cost per DALY was observed among states within the first HDI quartile, with Bihar [₹16,725 (\$203)], Uttar Pradesh [₹21,327 (\$259)], and Rajasthan [₹26,251 (\$319)] having the lowest values (Supplementary Table 1).

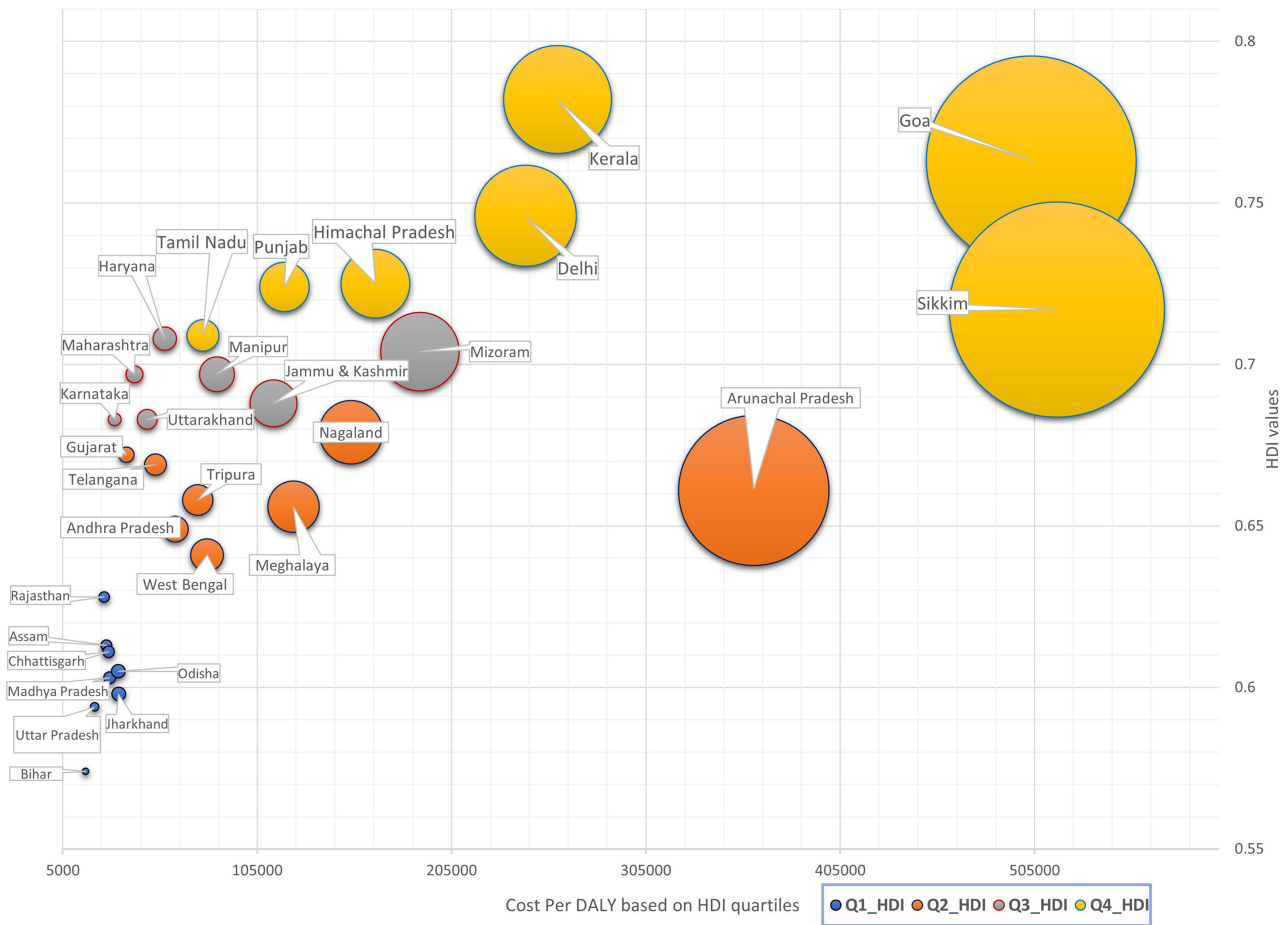
## Cost per DALY to GSDP Ratio

Further, we have estimated the cost per DALY to GSDP ratio for individual states in India during 2019. States such as Gujarat (0.16), Karnataka (0.17) and Maharashtra (0.22) have the lowest cost per DALY to GSDP ratio in India. On the other hand, Arunachal Pradesh has the highest cost per DALY to GSDP ratio (2.41), followed by Nagaland (1.45) and Meghalaya (1.26) (Supplementary Figure 1). Within states, in the first HDI quartile, Jharkhand has the highest (0.68), and Rajasthan has the lowest cost per DALY to GSDP ratio (0.38). Among states in the second quartile, Arunachal Pradesh (2.41) has the highest value and Gujarat in the other end (0.16). Similarly, for the third quartile, Manipur has the highest



**Figure 2** State-wise cost per DALY in India. [The figure displays the estimated cost per DALY (in thousands) for individual states in India. States with lighter colors indicate a lower cost per DALY, while darker blue represents a higher cost per DALY value].





**Figure 3** State-wise cost per DALY based on HDI values. [The scatter plot illustrates the relationship between the cost per DALY and state HDI values, categorized into four HDI quartiles. Each data point is represented by a bubble, with the x-axis indicating the cost per DALY and the y-axis representing the state HDI values. The bubbles are color-coded to represent the four HDI quartiles, and the size of each bubble reflects the corresponding cost per DALY value. Larger bubbles indicate higher costs per DALY, while smaller bubbles indicate lower costs per DALY].

(1.18) and Karnataka (0.17) has the lowest. However, among the fourth quartile, HDI states Sikkim has the highest value (0.84), followed by Kerala (0.77) and lowest for Tamil Nadu (0.22).

## Discussion

We have analysed the trends and relationships between the disease burden and HEP in individual states in India from 2010 to 2019 period. Panel regression analysis was used to estimate the elasticity of DALY per 100,000 population to HEP within the four different HDI quartiles. The results showed that increased health expenditure is associated with a reduction in the disease burden in most states, except for Andhra Pradesh, Goa, and Kerala. The observed positive correlation between DALY and HEP in Andhra Pradesh, Goa, and Kerala can be attributed to the fluctuations in DALY and HEP across different years. In the case of Andhra Pradesh, there has been a consistent decrease in DALY over the years, suggesting improvements in health outcomes. Conversely, Goa demonstrates a slight increase in DALY across the years, indicating a potential worsening of the disease burden. Notably, Kerala initially exhibited a decreasing trend in DALY, indicating positive health outcomes, but experienced an increase in DALYs in 2019, suggesting a potential reversal of progress. These trends highlight the dynamic nature of disease burden within these states a topic extensively explored in prior studies.<sup>25–27</sup> Furthermore, the HEP in these states also displays an uneven trend over the years, further influencing the correlation with DALY. It is important to note that the observed positive correlation does not imply a consistent causal relationship between DALY and HEP in these states. Rather, the correlation is driven by the intricate interplay of varying DALY and HEP levels across different years. The cost per DALY for

individual states in India showed that the metric is much lower in states belonging to the first three quartiles of HDI than in high HDI states.

The study found that in most states, there is a negative association between DALY and HEP which explains that as health expenditure per capita increases, the number of years lost due to ill health, disability, or premature death decreases. The regression analysis results indicate a significant negative association between the logarithm of HEP and the logarithm of the DALY per 100,000 population. This suggests that as HEP increases by one unit, there is a corresponding reduction in the DALY rate across different HDI quartiles. This finding highlights the importance of investing in healthcare and the potential impact of doing it to improve health outcomes and a reduction in the burden of disease. The magnitude of the reduction in the DALY rate varies across different HDI quartiles, with the reduction ranging from 0.09 to 0.25 units per 100,000 population. This indicates that the impact of investing in healthcare may be greater in states with lower levels of human development.

The estimated mean cost per DALY for states in the fourth quartile was almost tenfold higher than the cost per DALY in the first HDI quartile. The findings imply that, on average, it costs 10-fold extra money to prevent or treat a DALY in high HDI states compared to states in the first quartile. States with high HDI values may have reached a threshold of diminishing returns when more health spending will not result in meaningful gains in health outcomes. However, states with a low HDI, on the other hand, have greater room for growth and improvement since they may lack proper funding and have a higher disease burden. Understanding the marginal efficiency of healthcare spending will ensure that resources are spent effectively and efficiently. The variation in cost per DALY among states is influenced by socioeconomic factors, healthcare policies, and funding. Higher per capita income and healthcare spending are associated with higher costs per DALY, as observed in states like Goa, Arunachal Pradesh, Mizoram, and Sikkim. These states, except for Goa, receive special funding from the central government through the Ministry of Development of the North-Eastern Region (DoNER). Conversely, states like Uttar Pradesh, Bihar, Gujarat, and Karnataka, with lower per capita health expenditure, show lower costs per DALY. Differences in healthcare policies, funding, and resource allocation also contribute to variations in cost per DALY. Therefore, the observed variations in cost per DALY in our study are influenced by a combination of socioeconomic factors, healthcare policies, and funding that differ across states. The study by Daroudi et al,<sup>5</sup> reports a similar result as the cost per DALY averted in high HDI nations was significantly higher compared to low HDI countries. They found that the average cost required to prevent one DALY in high HDI nations was approximately 70 times more than in low HDI nations. Thus, the cost of averting one DALY in very high HDI nations is around \$70,000, while the same amount of funding can avert approximately 70 DALYs in low HDI countries.

The estimated cost per DALY in states belonging to the first three quartiles of HDI is much lower than India's existing GDP-based WTP threshold value. Similarly, the states in the lower HDI quartiles have a lower cost per DALY than those in the higher quartiles. This highlights the importance of considering the level of human development when allocating healthcare budgets as the policies and programs that work well in high-HDI states may not be as effective or efficient in low HDI and vice versa. Similarly, for states in the lower HDI quartiles, like Assam, it costs about ₹27,451 to avoid one DALY, which was about 0.51 of the GSDP per capita of the state. At the same time, the cost per DALY to GSDP per capita was nearly 0.8 in very high HDI states like Kerala (0.77) and Sikkim (0.84). Against this backdrop, it is important to note that the GDP-based WTP threshold of 1 GDP per capita for cost-effectiveness may not be acceptable for all settings and health conditions. This criterion may not accurately reflect the disease burden, healthcare capacity, and resource constraints in Indian states.

Studies have reported that the often-accepted criterion of 1–3 times GDP per capita is excessively high, especially for lower and middle-income countries with tight resource constraints. Due to socio-cultural, resource, and data availability disparities, threshold and valuation estimates should not be equal across economies.<sup>5,28</sup> Several studies have highlighted the disadvantages of using the WTP threshold in healthcare decision-making, particularly in low and middle-income countries where resources are limited.<sup>29,30</sup> For instance, a study by Marseille et al argues that reliance on these thresholds reduces the value of cost-effectiveness analyses and makes such analyses too blunt to be useful for most decision-making in public health.<sup>29</sup> Another study by Woods et al suggests an opportunity cost-based cost-effectiveness threshold for LMICs compared to the WTP threshold.<sup>30</sup> These findings suggest exploring the cost per DALY metric to provide more accurate and reliable estimates of the cost-effectiveness of healthcare interventions, particularly in resource-limited settings.

Similarly, differential spending and cost-effectiveness threshold based on the HDI status of the states is advocated to improve efficiency and achieve better health outcomes. This approach allows for a more nuanced understanding of each

state's unique challenges and opportunities. It can help to guide healthcare policy and investment decisions towards improving health outcomes and achieving greater value for money.

Previous literature has already demonstrated the economic cost of rising disease burden.<sup>13,26</sup> The projected increment in the allocated health budget is out of step with the growing disease burden.<sup>25</sup> Thus, the present study analyzing the cost per DALY based on disease burden and budget expenditure provides a more subtle understanding of the economic cost of rising disease burden as well as the burden of disease on individuals and society. By examining the cost per DALY for different states and different diseases, policymakers can prioritise disease control and prevention efforts based on their cost-effectiveness. This might lead to improved health outcomes and more efficient use of healthcare resources in the long run.

Our study uses the methods suggested by Daroudi et al.<sup>5</sup> The study estimates the cost per DALY averted for 176 nations using different HDI and GDP per capita levels. The analysis included data on the global burden of disease from 2000 to 2016 and was based on opportunity cost. However, in our study, we examined state-level disease burden and per capita health expenditure trends (both government and total) for the years 2010 to 2019 to calculate the cost per DALY in various Indian states. Similarly, while Daroudi et al employed age-adjusted DALY numbers, we used crude DALY data to account for population heterogeneity between states. Our study takes advantage of more recent data and offers state-specific conclusions relevant to India.

The findings of the study suggest that investing in health expenditure is an essential strategy for reducing disease burden and improving health outcomes. However, it is important to consider certain limitations when interpreting the study results. It is essential to note that our findings are based on secondary data gathered from the GBD study, which comes with inherent assumptions and limitations.<sup>7,26</sup> Another limitation of this study is the possible underestimating of health expenditure, which is due to a lack of state-specific statistics on health spending by departments such as railways, defense, etc. We also did not consider differences in disease epidemiology, functional status, and policies across states, which may affect the cost per DALY estimates. Additionally, the study is based on cross-sectional data, limiting the ability to establish causality between the variables studied. Further, the relationship between GDP and DALYs is likely to be complex, and we acknowledge the possibility of reverse causality between the two variables. Thus, the generalizability of our findings to other settings, populations, or healthcare systems must be done with careful consideration. Therefore, while the cost per DALY estimate is a useful measure of cost-effectiveness, it should not be the sole factor used in decision-making. Furthermore, the absence of DALY estimates data from the GBD study beyond 2019 limited our ability to fully assess the influence of the COVID-19 pandemic on cost per DALY trends in Indian states.

## Conclusion

The cost per DALY is crucial in identifying cost-effective healthcare interventions for each state. Our study found a significant negative association between health expenditure per capita and DALY rates across different HDI quartiles, suggesting that increased healthcare investment can reduce disease burden. Moreover, the cost per DALY was found to be significantly higher in states with high HDI as compared to those with low HDI. These findings underscore the need for differential spending and cost-effectiveness thresholds based on the HDI status of states to achieve better health outcomes and improve the efficiency of healthcare spending.

## Data Sharing Statement

All data files from the current study are publicly available. If necessary, the same data can be obtained from the corresponding author upon prior request.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.



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## Disclosure

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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