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Abstract

Systematic literature review to evaluate and characterize the health economics and outcomes research studies in India

Aim: This systematic literature review was conducted to identify, evaluate, and characterize the variety, quality, and intent of the health economics and outcomes research studies being conducted in India. **Materials and Methods:** Studies published in English language between 1999 and 2012 were retrieved from Embase and PubMed databases using relevant search strategies. Two researchers independently reviewed the studies as per Cochrane methodology; information on the type of research and the outcomes were extracted. Quality of reporting was assessed for model-based health economic studies using a published 100-point Quality of Health Economic Studies (QHES) instrument. **Results:** Of 546 studies screened, 132 were included in the review. The broad study categories were cost-effectiveness analyses [(CEA) 54 studies], cost analyses (19 studies), and burden of illness [(BOI) 18 studies]. The outcomes evaluated were direct and indirect costs, and incremental cost-effectiveness ratio (ICER), quality-adjusted life years (QALYs), and disability-adjusted life years (DALYs). Direct medical costs assessed cost of medicines, monitoring costs, consultation and hospital charges, along with direct non-medical costs (travel and food for patients and care givers). Loss of productivity and loss of income of patients and care givers were identified as the components of indirect cost. Overall, 33 studies assessed the quality of life (QoL), and the WHO Quality of Life-BREF (WHOQOL-BREF) was the most commonly used instrument. Quality assessment for modeling studies showed that most studies were of high quality [mean (range) QHES score to be 75.5 (34-93)]. **Conclusions:** This review identified various patterns of pharmaco-economic studies and good-quality CEA studies. However, there is a need for better assessment of utilization of healthcare resources in India.

Key words: Cost analysis, health economics, India, outcomes research, pharmaco-economic

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INTRODUCTION

Health economics is a branch of economics that assesses the issues related to efficiency, effectiveness, and value of resources in health and healthcare. Such evaluations are important in understanding the economic aspects of health and disease and the limitations to procurement of adequate healthcare. This aids in decision making, not

only for policy makers and health administrators but also in clinics, for providers and care givers.^[1,2]

Health economic evaluations are more evolved in societies having reimbursement systems. India still lags behind in terms of healthcare financing and implementation of policies.^[3] The health scenario in India is mired by increasing industrialization coupled with changes in lifestyle and continued lack of disease awareness among the masses. The urban population is at a higher risk of chronic diseases such as diabetes mellitus, cardiovascular disease, cancer, and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS).^[4] In the rural parts of the country, infectious and waterborne diseases and reproductive tract infections continue to predominate, though the risk of developing chronic diseases is also increasing.^[5] It is, therefore, a challenge for healthcare providers to promote health using improved and cost-effective modalities for the prevention, diagnosis, and therapy of various diseases and ailments.

The disparity in health services provision across the country, along with burgeoning healthcare expenditure underlines the need for effective utilization of healthcare resources. The rapid growth of the pharmaceutical sector too has brought forth a need for clinical as well as economic evidence generation for drugs, medical devices, procedures, and diagnostics to enable an objective evaluation of their value to various stakeholders faced with multiple choices. Presently, there are small numbers of studies evaluating the cost of healthcare in India.

This systematic literature review was conducted with the objective to identify, evaluate, and characterize the variety, quality, and intent of the health economics and outcomes research studies being conducted in India. To the best of our knowledge, this is the most recent and comprehensive review of such studies and was planned to fill the evidence gap in published literature.

MATERIALS AND METHODS

Search strategy

The Embase and Medline (through PubMed) databases were searched for English language studies published between 1999 and 2012. The search criteria used a combination of terms such as “health economics,” “healthcare cost,” “economic burden,” “costs and cost analysis,” “drug cost,” “cost benefit analysis,” “cost of illness,” “cost-effectiveness analysis,” “quality of life,” “patient reported outcomes,” and “India.”

Selection criteria

Studies were included if they assessed health economics, cost analysis (CA), cost-effectiveness analysis (CEA), cost benefit analysis (CBA), cost of illness (COI), burden of illness (BOI), quality of life (QoL), and patient reported outcomes. All included studies were conducted in India only. All prospective and retrospective studies were included except for case studies and case reports. References from systematic review and meta-analyses were screened for potential relevant studies.

Data collection and analysis

Following the decision on inclusion/exclusion of studies, a two-stage data extraction process was used to capture the necessary information, with discrepancies resolved by a third reviewer. The main outcomes were type of pharmacoeconomic evaluation, disease type, cost outcomes, and QoL. Quality of reporting in model-based health economic studies was assessed using a published 100-point Quality of Health Economic Studies (QHES) instrument;^[6] the criteria for categorizing the quality are summarized in Table 1.

RESULTS

In total, 546 studies were identified for screening from all databases and 132 studies were included in the review. The flow of studies as per Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) is presented in Figure 1. Overall, 75% of studies were published in or after 2007. In general, studies were conducted as prospective or retrospective observational studies or as survey. A few prospective randomized studies also evaluated costs. Most of the studies were conducted from societal perspective, including both provider and patient costs. The included studies represented different disease areas such as infectious and tropical diseases (28 studies), chronic diseases (19 studies), cancer (6 studies), HIV/AIDS (6 studies), mental health and psychiatric illness (6 studies), maternal and child health (3 studies), and miscellaneous (64 studies). There were 19 studies assessing various outcomes in pediatric patients.

All the included studies assessed costs due to disease, and were broadly categorized into CEA (54 studies),

Table 1: Criteria for quality of health economic studies using instrument

QHES score	Quality of study
0-24	Poor
25-50	Low
51-74	Average
75-100	High

QHES: Quality of health economic studies

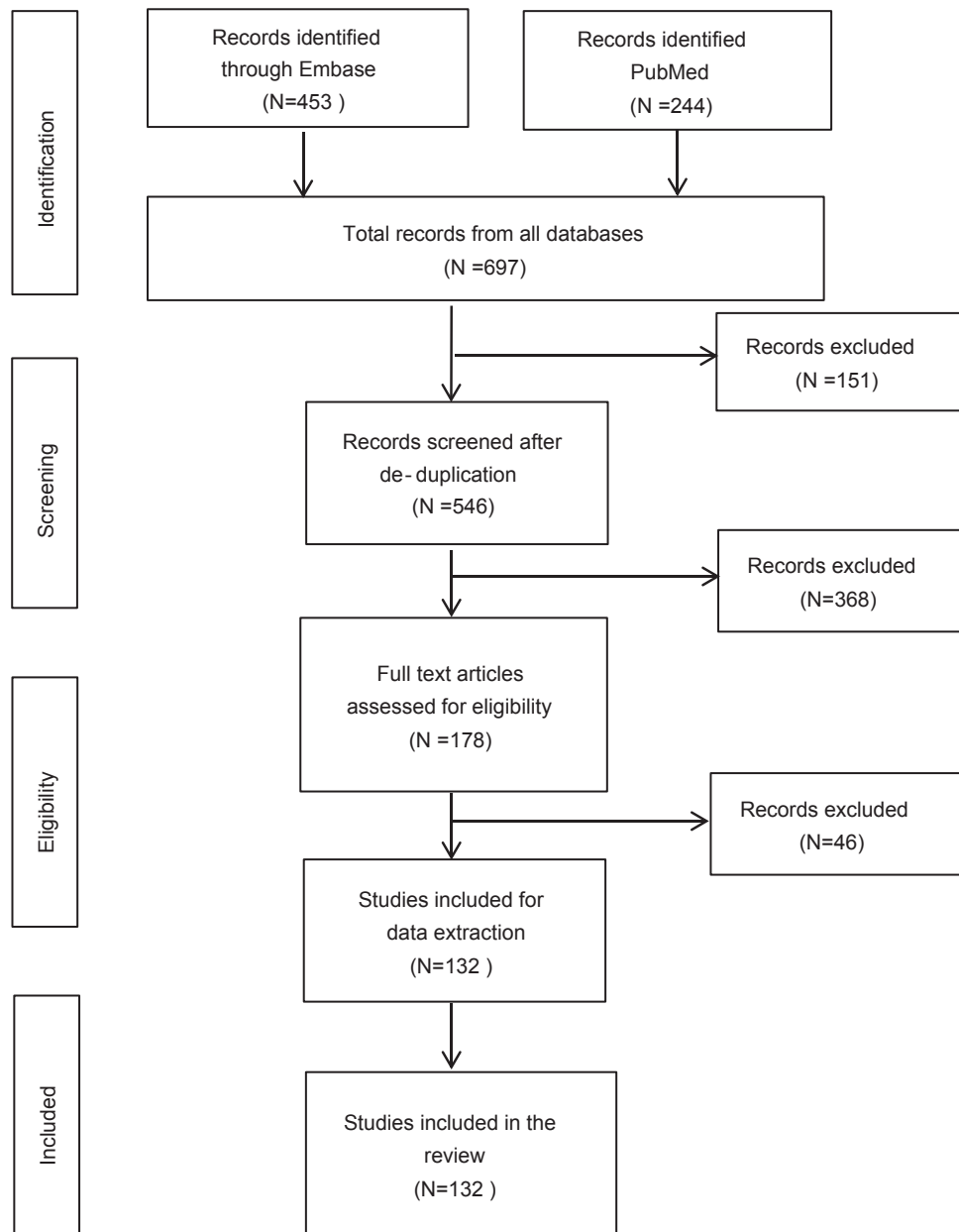


Figure 1: Flow of studies as per PRISMA flow diagram

CA (19 studies), and BOI (18 studies). The graphical depiction of all included studies is given in Figure 2. Only 35 studies adopted modeling approaches to estimate costs. Economic evaluation and QoL assessments were commonly estimated in patients with HIV/AIDS, carcinomas, or tuberculosis (TB). Studies also evaluated CEA of vaccines for immunization of children.

The outcomes evaluated in cost studies [Table 2] were direct and indirect costs, and incremental cost-effectiveness ratio (ICER), quality-adjusted life years (QALYs), and disability-adjusted life years (DALYs). A study conducted CEA of universal hepatitis B (HB) immunization in India using the Markov model (with or without costs of

treatment of long-term complications of HB infection) for calculation of marginal cost of every life year and QALY gained with universal HB vaccination.^[7] The immunization program increased the expected life of a birth cohort by 0.173 years (61.072 vs. 60.899 years) and the expected QALY lived per child by 0.213 years (61.056 vs. 60.843 years). This resulted in highly cost-effective universal HB immunization with intermediate endemicity rates in low-income population.^[7] The burden of disease can be quantified using DALY. A study estimated the burden of disease due to cancer for both genders and found that the DALY would increase from 4,598,976 in 2001 to 6,904,358 by 2016. Premature mortality was identified as a major contributor to disease burden in this study.^[8]

Economic evaluation is also involved in comparison of procedures. The CA and QoL were assessed in a prospective, randomized trial to compare mesh fixation techniques with and without tacks in patients undergoing laparoscopic repair of incisional and ventral hernia repair.^[9] The two groups were equally effective for recurrence rates, complications, hospital stay, chronic pain, and patient satisfaction. However, there was a statistically significant difference in the mean cost per patient in the suture group (\$521) as compared to the tacker group (\$1097) ($P < 0.001$).^[9]

Direct costs assessed medical costs including cost of medicines, monitoring costs, consultation and hospital charges, along with direct non-medical costs (travel and food for patients and care givers). In HIV patients, resource utilization and costs were estimated from Y. R. Gaitonde Centre for AIDS Research and Education (YRG CARE) in Chennai, India and from National AIDS Control Organization (NACO) (for HIV anti-retroviral therapies).^[10] In another study for cost-effectiveness of visceral leishmaniasis, the average drug cost per patient for each strategy (treatment) was estimated using the anthropometric database.^[11] Many studies conducted in India were sponsored by large institutions, and most of the studies on infectious and tropical diseases and maternal and child health were funded or supported by international organizations such as the World Health Organization (WHO), the United Nations Development Programme (UNDP), and the United States Agency for International Development (USAID).

Indirect cost components included loss of productivity

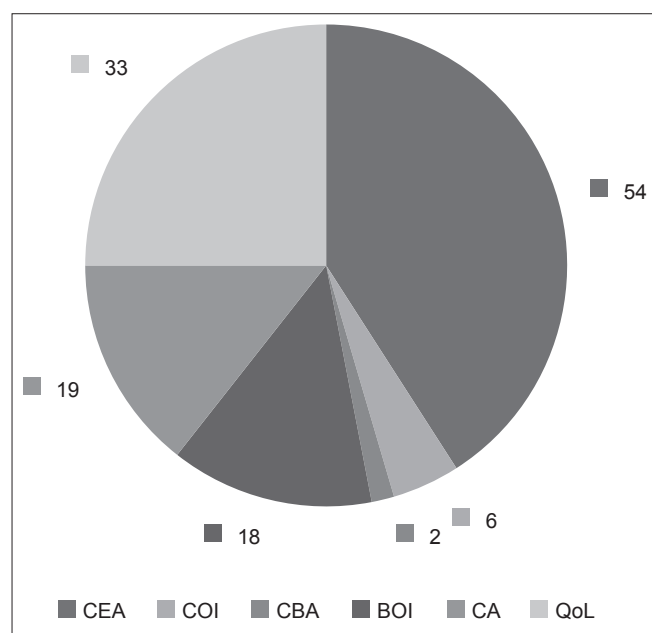


Figure 2: Categorization of included studies. BOI = Burden of illness, CA = Cost analysis, CBA = Cost benefit analysis, CEA = Cost-effectiveness analysis, COI = Cost of illness, QoL = Quality of life

and loss of income of patients and care givers. However, one prospective randomized study included the cost of materials (instruments used, sterilization process, electrical costs), manpower (surgeons, anesthetists, nurses, and other staff), and hospital rents (operating room and stay in hospital until the patient is deemed fit for discharge) as indirect costs.^[9] These costs were calculated by the institutional database. A few of the studies obtained indirect cost estimates by direct patient interview.

For quality assessment, the QHES instrument was used, which is a reliable instrument for assessing quality of health economic evaluations. The QHES scores were estimated for quality assessment of full economic studies (35 studies). The assessment of quality for these studies showed that most studies were of high quality [mean (range) QHES score to be 75.5 (34-93)] as presented in Figure 3. There were 24 studies out of 35 with QHES score >75. Decision tree analysis or Markov model was mostly used in these pharmacoeconomic studies. None of the studies met all the criteria of the QHES instrument.

Overall, 33 studies assessed QoL, and the WHO Quality of Life-BREF (WHOQOL-BREF) was the most commonly used instrument in these studies [Table 3]. The WHOQOL-BREF was used in a study assessing changes in QoL in widows of injecting drug users (HIV-related deaths).^[12] In HIV-infected children, health-related QoL (HRQoL) was assessed using the Pediatric Quality of Life Inventory™ (PedsQL™) in two studies.^[13,14] A 40-item Health Utilities Index (HUI) was used for assessment of HRQoL in children with cancer from their physicians' perspective.^[15] There were no differences in the patterns observed between cancer types for the child's HRQoL. However, a wide variation was seen in the total HRQoL scores among the children.

DISCUSSION

This systematic review provides the current overview of health economic studies in India. Most studies that were

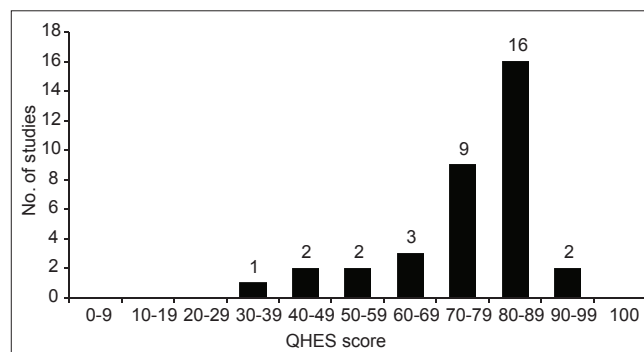


Figure 3: Quality of Health Economic Studies (QHES) total score for model-based studies ($n = 35$)

Table 2: Overview of cost-effectiveness studies

Study name	Type of evaluation/model	Disease/condition	Perspective	Year of cost; currency	Main cost outcomes	Cost input source/institution
Pho, 2012	CEA/ Cost-effectiveness of preventing AIDS Complications (CEPAC) model	Tuberculosis (in HIV patients)	NR	2009; USD	ICER (\$/YLS) - isoniazid and ethambutol (6 months): 1490, isoniazid (36 months): 3120	National institute for research in tuberculosis (Chennai), NACO, YRG CARE
Gupta, 2012	CEA/mathematical model (used MS-Excel spreadsheet software)	Haemophilus influenzae type b [Hib] vaccination]	Indian health system (government and societal)	2010; USD	IC: US \$81.4 million (government), US \$27.5 million (societal); ICER of Hib vaccination/ DALY averted: \$819 (government), US \$277 (societal)	UNICEF, National Family Health Survey (NFHS) and District Level Household Survey (DLHS)
Rheingans, 2012	CEA/rotavirus impact and cost-effectiveness model	Rotavirus (vaccination for children)	NR (study conducted in 25 GAVI countries including India)	2010; USD	CER/DALY averted: US \$82.98; rotavirus deaths averted/1000 births: 1.20	Medical treatment costs from WHO-CHOICE
Chandrashkar, 2011	CEA/dynamic transmission models of HIV and STI transmission	HIV (prevention for female sex workers)	NR	NR; USD	IC/infection averted (median range): US \$876 (370, 3040) to US \$2574 (1344, 7132); IC/DALY averted: US \$49 (20 171) to US \$143 (74 388)	NR
Dowdy, 2011	CEA/decision analytical model	Tuberculosis (serological testing vs. other strategies for diagnosis)	Indian TB control sector (including public RNTCP and private health care sector)	2010; USD	IC/DALY averted: \$19 (sputum smear microscopy) vs. US \$213 (MGIT culture); total cost: US \$11.9 million (sputum smear microscopy) vs. US \$27.6 million (MGIT culture)	Costs were estimated using data from private laboratories in India
Dranitsaris, 2011	CEA/ pharmacoeconomic model	Metastatic colorectal cancer (mCRC)	NR (study conducted in Canada, Spain, Malaysia, South Africa, and India)	2010; USD	A cost of \$98 for a new drug in first-line treatment of mCRC that would prolong patient survival by 3 months (considered cost effective)	Cost data were collected from local cancer centers and from the international oncology literature
Dranitsaris, 2011a	CEA/decision model	Metastatic colorectal cancer	Indian public healthcare	2010; USD	IC/QALY gained: >US \$200,000 to administer new treatment as first-line for mCRC	Costs were obtained from both public and private hospitals in India
Guerriero, 2011	CEA/Markov model	Bleeding trauma	UK health service perspective (study conducted in Tanzania, India, and the UK)	NR; USD	Cost of drug (tranexamic acid, TXA): US \$19 550/1000 patients; IC of TXA vs. no TXA: US \$20,670; Incremental cost per life year gained: US \$66	Cost data were obtained from hospitals of each country, WHO database, and UK reference costs
Kim, 2011	CEA/Companion Excel-based model	Rotavirus vs. HPV (vaccination)	Societal (study conducted in 72 GAVI-eligible countries including India)	2005; international dollars (I\$)	Vaccination cost/ individual (rotavirus vs. HPV), ICER (I\$/DALY averted)-I\$ 25 (base case): I\$ 212 vs. I\$ 293; treatment costs (rotavirus vs. HPV), ICER (I\$/DALY averted)-75% (base case): I\$ 220 vs. I\$ 324, 100% (base case) I\$ 212 vs. I\$ 293, 125% (base case): I\$ 204 vs. I\$ 262	Treatment cost data was taken from WHO-CHOICE

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Lohse, 2011	CEA/Gestational Diabetes Intervention Cost-Effectiveness Analysis model (GDM)	Gestational diabetes mellitus (GDM) and type 2 diabetes	NR (study conducted in India and Israel)	2011; USD	For GDM-estimated DALYs averted: 2.33; for type 2 diabetes-cost/DALY averted: US \$11.32	Cost data were collected from both public and private facilities in Chennai, Pune, and Ludhiana
Prinja, 2011	CEA/Markov model	HIV (prevention for female sex workers)	Indian health system	2008; USD	ICER (discounted @3%): Cost/HIV infection averted- US \$105.5 (INR 4748); Cost/DALY averted- US \$10.9 (INR 490). Targeted interventions for female sex workers were found to be very cost effective	Unit cost guidelines were taken from NACO and AVAHAN (Bill and Melinda Gates Foundation) and the Karnataka Health Promotion Trust (KHPT)
Vassall, 2011	CEA/decision analytical model	Tuberculosis (diagnosis)	Health service (study conducted in India, South Africa, and Uganda)	2010; USD	Cost/test of Xpert as a diagnostic technology: US \$22.63; mean ICER/DALY averted (compared to the base case): Xpert "in addition to" smear microscopy: US \$55, Xpert "as a replacement of" smear microscopy: US \$68, Xpert as "a replacement of" smear microscopy compared to "in addition to" smear microscopy: US \$343	Unit costs for outpatient visits and hospitalization sourced from WHO-CHOICE
Meheus, 2010	CEA/decision analytical model	Visceral leishmaniasis	Societal	2008; USD	CE of miltefosine–paromomycin combination: US \$92/death averted; liposomal amphotericin B with paromomycin: ICER- US \$652/death averted	The average drug cost per patient for each strategy was estimated using the anthropometric database. The value used was derived from WHO-CHOICE estimates for the South Asian region
Bender, 2010	CEA/state-transition model (first-order Monte Carlo simulation)	HIV (use of first-line ART)	Societal	2005; USD	Lifetime medical costs with no ART: US \$610; ranged from US \$5560 with stavudine-containing ART to US \$5720 with zidovudine-containing ART; ICER: \$670/year of life saved	Costs of ART were derived from the Clinton Foundation HIV/AIDS Initiative price list
Dandona, 2010	CEA/Monte Carlo simulations	HIV (prevention interventions)	NR	Cost in INR was converted to USD using the average exchange rate of INR 44.27 for a USD in the 2005–2006 fiscal year	Cost/DALY saved was <US \$50 (for blood banks, voluntary counseling and testing centers, prevention of parent to child transmission clinics); between US \$50 and US \$100 (for truckers and migrant laborer programs); more than US \$100 and up to US \$410 (for composite, street children, condom promotion)	The Andhra Pradesh State AIDS Control Society (APSACS)
Goldie, 2010	CEA/Global Maternal Health Policy Model	Maternal mortality	NR	2006; USD	Cost-effectiveness ratios <US \$500 per year of life saved (YLS)	UNICEF; UNFPA; Reproductive Health Costing Tools Model (RHCTM)

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Schulman-Marcus, 2010	CEA/Markov model	Acute coronary syndrome	Societal	2007; USD	ECG strategy cost an additional US \$12.65 per QALY gained compared to no ECG; cost of the ECG, cost of thrombolytic, and referral accuracy of the GP yielded ICERs for the ECG strategy ranging between cost-saving and US \$1124/QALY	Drug costs were from the International Drug Price Indicator Guide and local costing data; WHO-PREMISE survey
Taylor, 2010	CEA/Markov model	Open angle glaucoma and ocular hypertension	Payer (study conducted in India and Malaysia)	NR; INR, USD	Over a 5-year period, travoprost/timolol treatment sequence with a cost saving of INR 11,184 (US \$243) against latanoprost/timolol fixed combination	Unit costs were obtained from list prices
Sutherland, 2010	CEA/MonteCarlo Simulation	Postpartum hemorrhage	Indian health sector (decision maker)	2009; USD	Standard care: total cost: US \$20,000; misoprostol treatment: total cost: US \$21,212; DALYs saved: 215.9; ICER/DALY: US \$6; misoprostol prevention: total cost: US \$26,933; DALYs saved: 33.6; ICER/DALY: US \$170	Cost data were taken from one large community in India (involving training of rural volunteer health workers). Misoprostol price (average) was from international Drug Price Indicator Guide
Cook, 2009	CBA/Monte Carlo Simulation	Typhoid (vaccination)	Societal	2007; USD	Total COI avoided; net social cost/DALY provided-enrolled children (5-14.9 years): US \$10,671; US \$147; eligible children (2-15 years): US \$20,832; US \$166; adults+all eligible children: US \$88,885; US \$454	United Nations Educational, Scientific and Cultural Organization
Dabral, 2009	CEA/state-transition model	Measles (immunization)	Indian providers	NR; INR	Total cost of the SIA campaign: INR 25,177,095; cost per measles vaccine: INR 30; ICER/DALY: INR 430; cost/measles vaccine dose delivered: INR 30; cost to avert death: INR 15,381; cost/case averted: INR 385	A cohort reported by the WHO office for the National Polio Surveillance Program for an Indian district was used to determine total costs
Frick, 2009	CEA/decision tree	Visual acuity	Indian urban and rural healthcare system	2007; USD	Direct medical costs (urban India): age 5-15 years: school-based screening: cost: US \$1420; DALY averted: 2.5; CE ratio: US \$574; primary eye care: US \$4343; DALYs averted: 3.5; CE ratio: US \$2759; age 7-15 years: school-based screening: cost: US \$1910; DALY averted: 8.6; CE ratio: US \$221; primary eye care: US \$5888; DALYs averted: 12.3; CE ratio: US \$1075	Cost data were from a previously published study conducted in Delhi

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					Direct medical costs (rural India): age 5-15 years: school-based screening: cost: US \$1235; DALY averted: 1.0; CE ratio: US \$1211; primary eye care: US \$3760; DALYs averted: 1.5; CE ratio: US \$5775; age 7-15 years (local to Hyderabad): school-based screening: cost: US \$1561; DALY averted: 5.0; CE ratio: \$307; primary eye care: US \$4788; DALYs averted: 7.3; CE ratio: US \$1482	
Jeuland, 2009	CEA/ cost-effectiveness model	Cholera (oral vaccination)	Public Sector Financial (study conducted in Bangladesh, India, Indonesia, and Mozambique)	2007; USD	Cost effective (3*GDP/ cap): \$2613; very cost effective (GDP/cap): \$486	Vaccine cost derived from the estimated production costs of the Vietnamese vaccine
Rose, 2009	CEA/ individual-based Markov model; analyzed using Monte Carlo microsimulation methods with TreeAge Pro 2008 software	Rotavirus gastroenteritis (impact of vaccine)	Societal	2007; INR	Direct medical costs: vaccination cost: INR 8023 (about £100, €113, \$165) per life year saved; ICER with vaccination: INR 8023	Based on cost of vaccine to Brazilian Government, which was converted to INR
Olliaro, 2009	CEA/model unclear	Visceral leishmaniasis	Indian public health	2007; USD	Direct cost: cost of monotherapies per averted YLL for paromomycin: US \$2; AmBisome: US \$20-22; costs/death averted for paromomycin: US \$53-54; AmBisome: US \$523-527; combinations ranged US \$5-8/YLL averted and US \$124- 213/death averted	Costs of drugs were obtained both locally and from WHO
Sutherland, 2009	CEA/the simulation was designed to reflect the delivery outcomes of 10,000 women in India	Maternal mortality (interventions in home births)	NR	2008; USD	Median cost of misoprostol: US \$1401; median cost of prenatal iron supplementation: US \$2241; cost of iron supplementation/10,000 deliveries: US \$29,032, cost of misoprostol/10,000 deliveries: US \$30,232	Costs of birth attendant training, misoprostol use, and a prenatal iron supplementation program were taken from the literature
Esposito, 2008	CEA/decision-tree model of a birth cohort for a 5-year period	Rotavirus (vaccination program in children<5 years)	Indian healthcare system	2008; USD	Total DALYs lost: 4,564,545 without vaccination and 3,203,135 with vaccination; treatment costs: US \$65.4 million without vaccination and US \$44.8 million with vaccination	The costs of vaccine administration were from WHO

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Diaz, 2008	CEA/ individual-based stochastic model	Cervical cancer (impact of HPV 16 and 18 vaccination)	Societal	2005; I\$ (international dollars)	Cost/vaccinated girl: I\$ 10 (I\$ 2 per dose); CER for combined vaccination and screening strategy with single-visit visual inspection with acetic acid (VIA) increased from I\$ 290/YLS at I\$ 10/vaccinated girl to I\$ 7230/YLS at I\$ 360/ vaccinated girl	Cost estimates were based on data from a previously published analysis of screening in India
Chow, 2007	CEA/Dye and Floyd's transmission model for TB, dynamic compartmental simulation model for the HIV-1, Markov state-transition model for cardiovascular diseases, state-transition model for diabetes, static model of a cohort of smokers, state-transition model of breast cancer, state-transition model in blindness	Diarrhea, tuberculosis, acute lower respiratory infections, maternal mortality, neonatal mortality, malaria, HIV, vitamin A deficiency, iodine deficiency, cardiovascular disease, diabetes, epilepsy, tobacco attributable deaths, breast and cervical cancer, blindness	NR	2001; USD, INR	Diarrhea: (oral rehydration therapy, facility care, other costs): INR 20,000/ DALY averted; TB: avertable DALYs (ss+): 67,300,000; (ss-): 22,700,000; acute lower respiratory infection: INR 38,900/DALY; maternal mortality: INR 20,000/ YLL; avertable maternal YLLs: 1,413,000; neonatal mortality: 385,000-7,830,000 avertable YLLs; malaria: ICER (INR/DALY averted) for in-home residual spraying with insecticide: 1,290,000; for insecticide-treated bed net: 760,000; measles: INR 1900/YLL averted; Hep B; 1100; Hib: 2500, Diphtheria- tetanus-pertusis Diphtheria-tetanus- pertusis (DTP)-Hep B: 1500; DTP-Hep B-Hib: 3000, rotavirus: 52; streptococcus: 620; HIV (adhere): INR 6640/YLL averted; HIV (MTCT+): INR 9050/YLL averted; HIV (below poverty line): INR 12,700/YLL averted; vitamin A deficiency: DALYs: 2,723,000- 3,354,000 (% attributable risk mortality averted); iodine deficiency: cost per person INR 0.45: INR 85-92/DALY; cost per person INR 18: INR 3400-3700/DALY; cardiovascular disease: US \$11; diabetes: INR 5100-5900/DALY averted; epilepsy: phenobarbital- lamotrigine combination treatment: INR 126,000/DALY averted; surgery+phenobarbital: INR 125,000/DALY averted	Costs were taken from literature, UNICEF, RNTCP, International Drug Price Indicator Guide (MSH 2005)

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Fung, 2007	CEA/deterministic mathematical model	HIV (among commercial sex workers)	Providers	2004; USD, INR	Financial cost/CSW/month: US \$86; economic cost per CSW reached/month: US \$240; CER: US \$33.7-133.4/HIV infection averted, ICER with peer educator costs: US \$55.6-218.5/HIV infection averted; costs/DALY saved range: US \$1.9-7.5 and US \$3.1-12.3	Cost collection was based on the Costing Guidelines for HIV Prevention Strategies. Cost/HIV infection averted treatment of STI for CSWs in WHO South East Asia Region (Sear-D region)
Freedberg, 2007	CEA/The Cost-Effectiveness of Preventing AIDS Complications (CEPAC) International model	HIV (prevention using ART)	NR	2005; USD	Direct cost: lifetime medical costs: US \$530 (no ART)- US \$5430 (two ART regimens)/person; ICER: US \$430/YLS-US \$550/YLS; ICER for two lines of therapy: US \$1880/YLS vs. first-line therapy	Costs were obtained from literature, WHO, YRG CARE
Aggarwal, 2003	CEA/Markov model	Hepatitis B (immunization)	Societal	NR; USD	HB immunization increased the expected life of a birth cohort by 0.173 years (61.072 vs. 60.899 years); expected QALY lived/child by 0.213 years (61.056 vs. 60.843 years); CE of immunization: \$16.27/life-year gained and CU \$13.22/QALY gained	Costs of treatment of sequelae of chronic HB were from physician estimates
Prakash, 2003	CEA/Markov model (decision tree)	Hepatitis B (immunization)	Societal	1993; INR converted to USD	Direct costs: CER: US \$27.36/DALY	Costs were calculated based on a household survey conducted by the National Council of Applied Economic Research
Aggarwal, 2002	CEA/Markov transitional probability model	Chronic hepatitis B	NR	NR; INR, USD	Direct costs: QALY (treated group): 23.69 years; QALY (untreated group): 22.75 years; cost (IFN-treated group): INR 300,000; cost (untreated group): INR 40,700	For cost analysis, estimates were from Indian prices of IFN and medical treatment
Ghoshal, 2002	CEA/decision analysis	Achalasia cardia	Patients	NR; INR	Direct cost: Botulinum toxin: INR 18,520/patient; pneumatic dilation: INR 4568/patient; ICER: 13,952/patient	Cost data was obtained from SGPGI

ART=Anti-retroviral treatment, CBA=Cost benefit analysis, CEA=Cost-effectiveness analysis, CER=Cost-effectiveness ratio, COI=Cost of illness, CSW=Commercial sex worker, CU=Cost utility, DALY=Disability-adjusted life year, EPI=Expanded Program on Immunization, HIV=Human immunodeficiency virus, HPV=Human papillomavirus, IC=Incremental cost, ICER=Incremental cost-effectiveness ratio, INR=Indian rupees, MGIT=Mycobacteria growth indicator tube, NACO=National AIDS control organization, NR=Not reported, QALY=Quality-adjusted life year, RNTCP=Revised national tb control program, SGPGI=Sanjay Gandhi postgraduate institute of medical sciences, UNFPA=United nations population fund, USD=United States dollar, WHO=World health organization, YLL=Years of life lost, YRG CARE=Y. R. Gaitonde centre for aids research and education

identified could not be classified as full-fledged health economic studies. This is perhaps a reflection of the lack of understanding of standard concepts of health economics in India. A systematic review (Desai *et al.*) published in 2012 looked at the quality of 29 model-based studies from India.^[16] Our literature review being more recent assesses the quality and tabulates the results of 35 studies along with the source of cost inputs across those studies. Most studies were sponsored by or conducted in collaboration with major institutes in India. This brings forth the fact that sponsorship

and motivation are the major factors in conducting such evaluations in India. In addition, we report on the diversity of other health economics and outcomes research studies from India, including QoL or patient reported outcomes studies.

Most of the model-based studies included CEA and the perspective was societal. However, we also found studies that used modified societal perspective,^[17] hospital perspective,^[18] provider's perspective,^[19] and patient's perspective.^[20] In the study assessing costs incurred by

Table 3: Overview of QoL studies

Study name	Disease	QoL scale	QoL outcomes
Chhabra, 2011	Bronchial asthma	Asthma Control Questionnaire , Asthma Quality of Life Questionnaire, Baseline Dyspnoea Index, Oxygen Cost Diagram	BDI and OCD scores were significantly lower in female patients indicating greater dyspnea and a poorer QoL, especially in the symptoms and emotional domains of the AQLQ
Jindal, 2011	Chronic stable asthma in women	AQLQ	A statistically significant negative correlation between years of exposure and various AQLQ domains including activity limitation, symptoms and total AQLQ values. Overall, QoL and asthma control were poor in asthmatic women
Kumar, 2011	Oral caries in children	Oral Health-Related Quality of Life	Children without parents presented poor scores for OHRQoL compared to those having parents. Caries status was significantly related to OHRQoL and its domains; no caries related to good OHRQoL
Mathew, 2011	Musculoskeletal (MSK) pain	Modified Indian Health Assessment Questionnaire (HAQ) (CRD, Pune)	Among the clinical diagnoses, non-specific MSK pain scored a high HAQ-DI. MSK pain, both due to specific and non-specific disorders, showed an important impact on HRQoL
Patil, 2011	Autistic disorder in children (QoL assessed for mothers)	Symptom check list-90-revised (SCL-90-R); Mechanisms of Coping; QoL	Parents were seen to have high psychopathology on SCL-90-R. The General Symptomatic Index (measure of general distress) was high in about 70.7% of the mothers; 39% of the mothers had poor QoL. Autism in children affects the psychological health and QoL of the mothers
Roopalekha, 2011	Dementia (QoL assessed for female caregivers)	Brief Cope, Zarit burden scale, Beck depression inventory	Female caregivers suffered from moderate to severe burden of 70%, moderate to severe depression of 50%, physical co-morbidity of 52.7%
Sankpal, 2011	Hepatitis	QoL	Higher scores of QoL ($P<0.001$) correlated with prescription of alternative medicines. Life span/QoL of hepatitis sufferers depended on appropriate palliative care
Sindhvani, 2011	Chronic obstructive pulmonary disease	Clinical COPD Questionnaire (CCQ scoring)	Statistically significant clinical CCQ scores in experimental and control groups from the 4 th month (group I vs. group II: 14.9 vs. 21.4, $P=0.002$ and 13.9 vs. 20.9, $P=0.001$ at the end of 4 and 6 months, respectively)
Varghese, 2011	Voice restoration in laryngectomies	European organization for research and Treatment of cancer qol questionnaire (QLQ-C30 and QLQ-HandN-35)	QoL scores were significantly higher among voice rehabilitated patients as compared to nonrehabilitated laryngectomies
Vikas, 2011	Obsessive-compulsive disorder (OCD) (patients and caregivers of OCD compared to depressed patients)	World health organization quality of life questionnaire-BREF version, Yale brown obsessive-compulsive Disorder Scale, Hamilton depression rating scale	Patients with OCD had the lowest scores in the psychological health domain of the WHOQOL-BREF. Patients with OCD had a better QoL and were less disabled than the depressed subjects. Caregivers of OCD patients experienced burden in several areas and had to accommodate to the patient's behavior as compared to the caregivers of depressed patients
Wortmann, 2011	Mild to moderate dementia (QoL for both patients and caregivers)	QoL	A significant reduction of general health and neuropsychiatric symptoms and non-significant reduction in caregiver burden
Banerjee, 2010	HIV-infected children	Pediatric quality of life inventory 4.0 (PedsQL™ 4.0)	HIV infection was associated with a negative impact on QoL among children with lower scores for physical, school, and emotional functioning and health symptoms
Das, 2010	HIV-infected children	PedsQL™ 4.0	HIV-infected children demonstrated a better QoL in physical health domain (76.8 ± 12.47) than those suffering from cystic fibrosis (70.50 ± 16.4 and 70.35 ± 16.2)
John, 2010	Intermediate anorectal malformations in children	Self-structured disease impact questionnaires and Achenbach's Child behavior check list	The average QoL scores in children increased from 8.1 to 12. There was a direct correlation between institution of the BMP and increase in the QoL score ($P<0.001$)
Chirivella, 2009	Children with cancer (11 types of cancer)	Health utilities index (2 and 3)	Mean HUI2 and HUI3 scores were 0.71 and 0.62, respectively. No differences in the patterns between cancer types for the child's HRQoL, but wide variation in the total HRQL scores among the children

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Bai Kirubha, 2009	Dermatophytosis	Dermatology life quality index for adults and Children's dermatology life quality index-cartoon version for children	The overall QoL score [mean CDLQI score: 9.14±4.94 (SD) before treatment vs. 1.71±1.36 (SD) after treatment] [mean DLQI score: 7.62±4.27 (SD) before treatment vs. 1.49±1.70 (SD) after treatment] improved significantly following treatment with griseofulvin ($P<0.0001$)
Kumar, 2009	Dental anxiety and oral HRQoL	Corah dental anxiety scale, Oral health-related quality of life-UK (W) questionnaire	Poor OHQoL reported in female patients than in males. People with high dental anxiety were 2.34 times more likely to present poor OHQoL than those having low anxiety
Pandey, 2009	Head and neck cancer	Distress Inventory for Cancer (version 2) (DIC2), Functional assessment of cancer treatment-head neck questionnaire (v4)	Mean distress score: 24.6; mean FACT-HN score: 114.5. There was a negative correlation between distress and QoL scores (patients with higher distress had poor QoL)
Wadasadawala, 2009	Early breast cancer	EORTC QLQ-C30, breast cancer-specific BR23 modules	The scores for social functioning and financial difficulties in QLQ-C30 showed better outcome in the APBI group ($P=0.025$ and 0.019 , respectively), and body image in breast cancer-specific BR23 modules was significantly better in the APBI group as compared with the WBRT group ($P=0.005$)
Nagpal, 2008	Postpartum mothers (women who delivered in the last 6 months)	Mother generated index questionnaire for postpartum QoL; physical morbidity and Edinburgh postnatal depression scale for validation	Overall adjusted mean primary score index: 3.6; secondary score index: 2.9; EPDS score: 10.9. A trend toward lower primary and secondary score index in lower socioeconomic stratum was observed (lower, middle, and higher strata)
Kermode, 2008	Mental health among widows of injecting drug users (IDU)	WHOQOL-BREF questionnaire, The General Health Questionnaire (GHQ12), Health and Well-being Questionnaire	Women experienced significant improvement in physical and psychological health and their interaction with the environment was positive after participating in the intervention (peer-facilitated participatory action groups) ($P\leq 0.05$), although the patterning of these improvements varied by state
Sachin, 2008	Epilepsy in women	WHO-QOL (BREF), Coping checklist, Burden assessment schedule	Women with epilepsy rarely used constructive coping strategies and this contributed to their poor psychosocial status and adjustment within the family and society
Shore, 2008	Disability	Survey questions from International Classification of functioning, disability, and health (ICF)	In India, 31% of recipients could use the wheelchair independently for mobility. The impact on health and QoL was generally viewed as positive
Dhuria, 2007	Tuberculosis (category I, II, and III)	WHO-QOL (BREF)	Overall score, mean (SD): TB cases, 10.98 (1.40); controls, 14.21 (1.00); TB patients had significantly lower mean scores than the controls for overall QoL and its domains
Bhattacharya, 2007	Menopausal women	The Menopause rating scale (MRS II)	Significant improvement in HRQoL was found after 3 months, and further improvement was obtained 12 months after receiving tibolone in menopausal women
Jacob, 2007	Mental health in elder patients	Mini mental status examination, Revised clinical interview schedule, WHO-QOL (BREF)	Significant reduction in psychiatric morbidity and improvement in QoL scores at 3 months for subjects who attended the day-care program
Ramachandran, 2007	Heart failure	Kansas City Cardiomyopathy Questionnaire (KCCQ)	Significant improvement in the QoL and functional capacity of patients in the telephonic disease management (intervention group) [mean (SD): from 60.0 (23.6) to 76.3 (17.3)] compared with controls [mean (SD): from 62.2 (22.6) to 63.4 (21.9)] over a 6-month period
Sridhar, 2007	Type 2 diabetes	ATT39, ATT19, barriers to self-care, social support, QoL and well-being questionnaires	Gender differences in all the parameters studied: men had better adjustment with disease, coped better, integrated better, and had better QoL and well-being than women
Menon, 2005	Extrahepatic portal hypertension in children (QoL after surgery)	QoL (changes in scholastic ability, physical activity, social interaction, and economic effects on the family)	Growth parameters improved significantly in children after surgical intervention for portal hypertension. Overall improvement in scholastic abilities, physical activity, and social interaction was also noted
Patel, 2005	Sickle cell hemoglobinopathy in children	QoL (interview-based multidimensional disease-specific scale)	All domains, physical, psychosocial, cognitive, and morbidity, were affected. QoL was affected in children with sickle cell disease (SCD) and to a lesser extent in sickle cell trait

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Saxena, 2004	Range: common cold to cancer	WHOQOL-100	Hindi and English versions of WHOQOL-100 had some equivalence, but conceptual and scalar concerns remained regarding the application of a language version to subjects from another culture
Steffen, 2004	Travelers' diarrhea (TD)	QoL (using a 10-item questionnaire in relation to contracting TD)	QoL was considerably affected and was directly related to the severity of diarrhea
Vijayakumar, 2004	Blindness	QoL questionnaire	Self-care score range: 24.6-30.0%; mobility score range: 37.6-44.3%. Overall QoL scores were not significantly different between those who did and did not receive economic rehabilitation ($P=0.1$)

APBI=Accelerated partial breast irradiation, BMP=Bowel management program, MNJIO=Mehdi Nawaz Jung institute of oncology and regional cancer centre, QoL=Quality of life, WBRT=Whole breast radiotherapy, ACQ=Asthma control questionnaire, AQLQ=Asthma quality of life questionnaire, BDI=Baseline dyspnoea index, OCD=Oxygen cost diagram, OHRQoL=Oral health-related quality of life, EORTC=European organization for research and treatment of cancer, WHOQOL-BREF=World health organization quality of life questionnaire-BREF version, YBOCS=Yale brown obsessive-compulsive disorder scale, HDRS=Hamilton depression rating scale, CBCL=Child behavior check list, HUI=Health utilities index, COPD=Chronic obstructive pulmonary disease, DLQI=Dermatology life quality index, CDLQI=Children's dermatology life quality index-cartoon, OHQoL=Oral health-related quality of life, FACT-HN=Functional assessment of cancer treatment-head neck, EPDS=Edinburgh postnatal depression scale, MGI=Mother generated index, MRS=Menopause rating scale, CCL=Coping checklist, BAS=Burden assessment schedule

pulmonary TB patients in rural India,^[20] the financial burden for TB treatment was imposed on the patients, despite the provision of free smears and drugs by The Revised National TB Control Programme (RNTCP) in India. The single greatest cost was time lost during admission; the total patient costs represented 193% of the estimated monthly income of a manual laborer. One of the reasons for the high expenditure was treatment at private healthcare centers. Another study estimating expenses for chemotherapy, side-effect management, and best supportive care in patients with metastatic colorectal cancer found significantly lower cost of care in public healthcare centers as compared to the private centers in India. This may be a reflection of the modest level of care offered to patients in public hospitals and the ability of the private sector to mark up the cost of goods and health services.^[21]

An understanding of the true cost measures including all direct and indirect cost components is necessary while formulating national policies. CEAs are more appropriate for similar outcomes measures for interventions. When assessing dissimilar outcomes of interventions or comparing different health states, CBA and cost-utility analysis (CUA) are more useful. The cost-effectiveness of any procedure or intervention reflects the proper utilization of the available resources. As healthcare resources are scarce, it is necessary to analyze the cost of treatment modalities that have the same therapeutic potential and to identify the alternatives that are most efficient and cost-effective to derive the same benefit.^[9] For example, estimation of DALY combines information on morbidity, mortality, and disability to provide an indicator of the burden of disease. Thus, the estimation of burden of cancer by DALY shows that there is a need to initiate measures for prevention and control of cancers.^[8] The modern cancer medicines are often out of reach to a broader population due to their high costs.

Therefore, in countries like India that have no central healthcare costs evaluation process, the WHO criteria for cost-effectiveness may be applied for estimation of appropriate and affordable prices.^[21]

Another obstacle in the implementation of adequate healthcare in India is the existence of multiple health practices and policies across the Indian subcontinent. This disparity of health systems across India was highlighted in a study assessing COI across five resource-poor locations in India. The study concluded that there is no uniform model to establish the cost of healthcare across the subcontinent.^[22] Therefore, a central mechanism of disease control is not applicable, as resource availability differs between the urban and rural parts of India. It is difficult to devise and implement a single healthcare policy for the entire country. The optimal way of handling this issue is to have specific health policy in each state, considering the factors such as health state, income, education, and climatic conditions.

The pharmacoeconomic studies published from India have been few but the trend has increased since 2007. Most studies from India were published in foreign journals and the authors of most model-based studies were from outside India. These studies utilized appropriate model parameters and analyses, and were therefore categorized to be of high quality as per the QHES instrument. There is still a paucity of health economic studies conducted in India by Indian healthcare providers. The evidence from literature is best published in Indian journals, so that they are readily accessed by the medical community in India.

This systematic review has several strengths. To the best of our knowledge, this is the most recent systematic review on this important topic, particularly in the Indian context. Our review identified different health economic studies conducted across India. This review focused on utilization

of healthcare resources in India and the measures to be taken to provide better healthcare for a broader population. Government agencies and industry play a key role toward achieving this goal. The present review has included a broad range of evidence across different studies, but the heterogeneity of data on pharmacoeconomic studies, different study designs, and varying disease types has limited the comparability across studies. One possible limitation of this review could be the quality of studies included. Majority of the studies were retrospective in nature, and such studies are prone to bias. However, as with any review of literature, a balance has to be found between having too stringent search criteria and too loose a search strategy to fulfill the question of interest, and we have attempted to sketch a baseline understanding of the situation in India for this pertinent area through this systematic review.

In conclusion, this review identified various patterns of health economic studies in India. Majority of the CEA studies conducted in recent years were of high quality, but overall, the model-from studies were limited and conducted by researchers based outside India. Utilization of healthcare resources in India is inadequately assessed and needs to be relevant to the different healthcare settings in India.

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