Cost-effectiveness of population-based screening for oral cancer in India: an economic modelling study

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The Lancet Regional Health - Southeast Asia 2023;■: 100224

Published Online XXX
https://doi.org/10.1016/j.lansea.2023.100224

Summary

Background Oral cancer screening reduces mortality associated with oral cancer. The current study evaluated the cost-effectiveness of commonly used screening techniques, namely conventional oral examination (COE), toluidine blue staining (TBS), oral cytology (OC), and light-based detection (LBD) in the Indian scenario.

Methods The study used a Markov modelling approach to estimate the cost and health outcomes of four different approaches (COE, TBS, OC, and LBD) for screening oral cancer over time from a societal perspective. The discount rate was assumed as 3%. The outcomes estimated were oral cancer incident cases, deaths averted, and quality-adjusted life years (QALYs). To address the high burden of risk factors (tobacco and/or alcohol) in India, two Markov models were developed: Model A adopted a mass-screening strategy, whereas Model B adopted a high-risk screening strategy versus no screening. Probabilistic sensitivity analysis (PSA) was undertaken to address any parameter uncertainty.

Findings Mass-screening using LBD at three years had the least incident cases (3271.68) and averted the maximum number of oral cancer deaths (459.76). High-risk screening using COE at ten years interval incurred the least lifetime cost of 2,292,816.21 US$ (182,794,468.26 INR). The high-risk strategies (US$/QALY), namely COE 5 years (–29.21), COE 10 years (–90.68), TBS 10 years (–60.54), and LBD 10 years (–13.51), were dominant over no-screening.

Interpretation The most cost-saving approach was the conventional oral examination at an interval of 10 years for oral screening in high-risk populations above 30 years of age.

Funding Department of Health Research, Ministry of Health & Family Welfare, Government of India.

Keywords: Oral cancer; Oral screening; Markov model; High-risk screening; Mass screening; Cost-effectiveness analysis; Health system cost; Out-of-pocket expenditure

Introduction

In 2020, WHO South-East Asia region reported an age-standardised incidence rate of 8.0 and a mortality rate of 4.5 for oral cancer, which were highest among all WHO regions.[1] GLOBOCAN 2020 estimates showed that the annual number of incident cases of lip and oral cavity cancer was more than 100,000 in India.[1] As most oral cancer patients in India present in an advanced stage of the disease and require expensive and aggressive combined modality treatment,[2] early detection of oral cancer is important.

Commonly used techniques for early detection of precancerous and cancerous lesions of the lip and oral cavity are: conventional oral examination (COE), toluidine blue staining (TBS), oral cytology (OC), light-based detection (LBD) devices like Velscope, ViziLite plus.[3] Tobacco and alcohol use are main risk factors for oral cancer.[4,5] A study by Sankaranarayanan and

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Research in context

Evidence before this study

Oral cancer is the second and third most cancer in India in terms of incidence and mortality respectively. The late diagnosis and treatment in advanced stages increase the economic burden associated with oral cancer (on individual and government support for healthcare). The optimal use of resources currently available for critical healthcare expenditure is the way forward. Most of the previous cost-effectiveness studies regarding oral cancer screening were done in high-income countries due to which estimates are not generalisable to low-income and middle-income countries including India. Subramanian and colleagues did a cost-effectiveness study in India related to oral visual examination. However, the lifetime costs for the screening strategy and associated health outcomes quality-adjusted life years (QALYs) were not estimated. Hence, there is limited evidence to suggest the cost-effectiveness of oral cancer screening strategy in India.

Added value of this study

This economic modelling study was done to estimate the lifetime costs incurred on screening, diagnosis, and treatment of oral cancers, and to estimate the health outcomes associated with oral cancer in terms of QALYs gained in the Indian setting. Our study showed high-risk oral cancer screening (tobacco and/or alcohol users) was more cost-effective than the mass-screening strategy. Considering the cost-effectiveness, high-risk screening by conventional oral examination (COE) is the preferred strategy for oral cancer in India.

Implications of all the available evidence

Health policy decisions are becoming increasingly important as the opportunity costs of choosing the wrong strategies continue to be a threat. COE requires fewer resources in terms of training, equipment, and time, making it a desirable option for large-scale implementation in the developing world. Of all the screening techniques studied, screening using COE of high-risk individual at an interval of 10 years is the recommended screening strategy for Indian population under National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases and Stroke (NPCDCS). The current study will provide evidence for policymakers to draw guidelines to suggest an appropriate strategy for oral cancer screening in India.

colleagues in Kerala, India, showed that oral visual screening significantly reduced oral cancer mortality in high-risk individuals (users of tobacco and/or alcohol).[6]

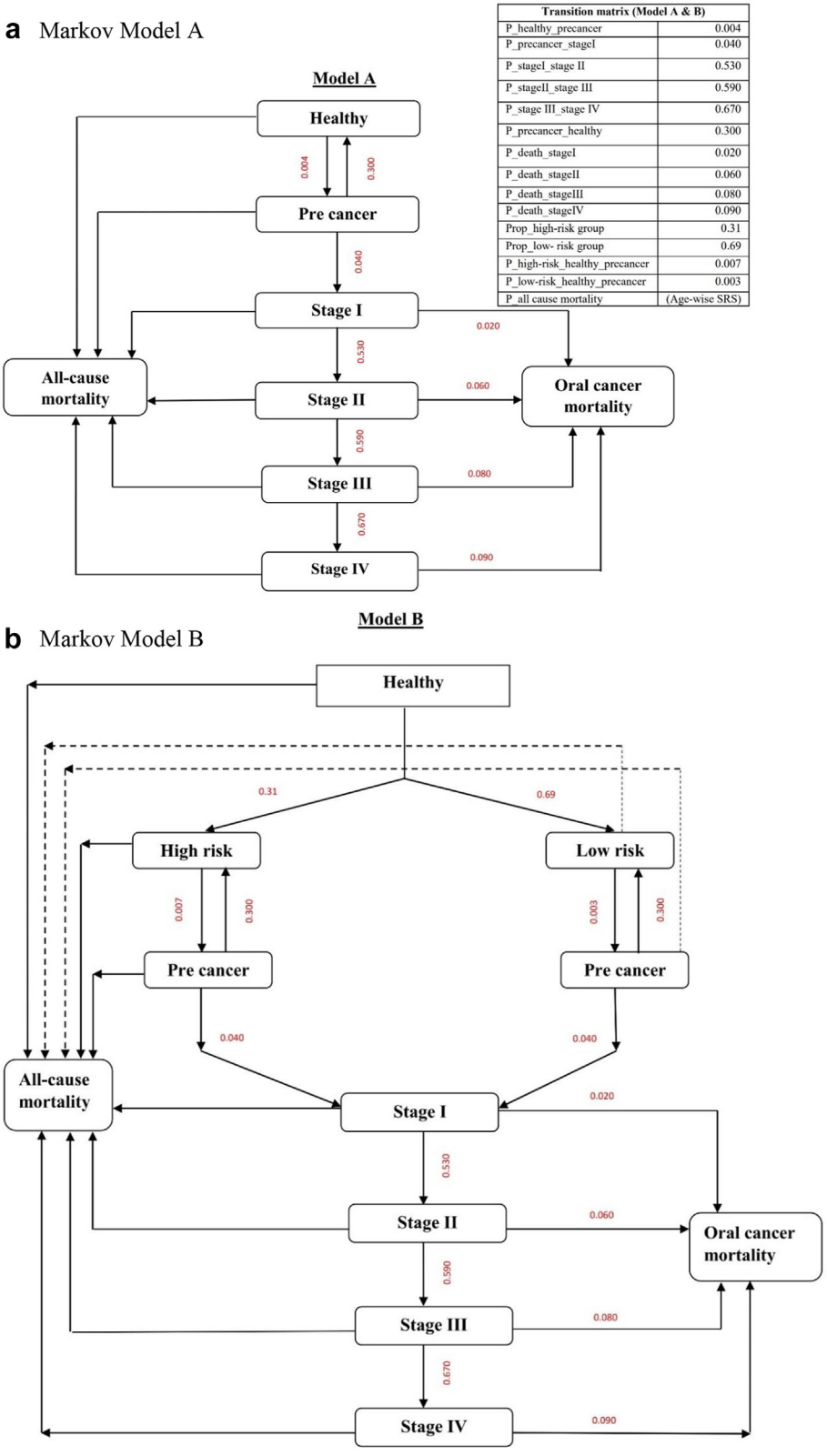
For a resource-constrained country like India, the economic burden related to oral cancer screening needs to be addressed.[7] Most of the previous cost-effectiveness studies regarding oral cancer screening were done in high-income countries,[8,9] due to which the estimates are not generalisable to low-income and middle-income countries including India. Hence, it is necessary to estimate the cost-effectiveness of oral cancer screening in the Indian setting. Subramanian et al. did a cost-effectiveness study in India related on oral visual examination. However, the lifetime costs for the screening strategy and associated health outcomes (quality-adjusted life years [QALYs]) were not estimated.[10] Thus, the current study was planned to estimate the lifetime costs incurred on screening, diagnosis, and treatment of oral cancers and the health outcomes associated with oral cancer in terms of QALYs gained in the Indian setting.

Methods

Economic modelling was done using the societal perspective in the Indian population (> age 30 years) to assess the cost-effectiveness of four commonly used oral cancer screening techniques, COE, TBS, OC, and LBD, compared to no-screening by estimating lifetime costs and health outcomes. According to National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases and Stroke (NPCDCS), the eligible age for population-based screening is above the age of 30 years. Hence, as per the programmatic guidelines, the starting age for our modelling study was assumed as 30 years.[11]

Model overview

Markov models are useful to model environments and-problems involving sequential, stochastic decisions over time. Markov model is also an ideal approach for a futuristic time-horizon.[12] As the current study tried to compare of mass/high-risk screening versus no-screening, the use of such a model is of paramount importance. In the current study, we estimated cost and health outcomes for a future time period (lifetime time horizon). We developed a probabilistic Markov model (Fig. 1 a and b) using Microsoft Excel based on the natural history of oral cancer progression from one health state to another. The microsimulation was in annual cycles. One cycle was for one year, and it was run for 70 cycles. Using a societal perspective, this model was utilised to estimate lifetime cost and health outcomes in a hypothetical cohort of men and women above 30 years of age. Estimating lifetime cost and health outcomes were done for both the screened and unscreened groups. For the screening group, screening strategies were COE, TBS, OC, and LBD, with screening intervals taken at 3 years, 5 years, and 10 years for each screening strategy. For the no-screening group, the cohort followed the



Transition matrix (Model A & B)	
P_healthy_precancer	0.004
P_precancer_stageI	0.040
P_stageI_stage II	0.530
P_stageII_stage III	0.590
P_stage III_stage IV	0.670
P_precancer_healthy	0.300
P_death_stageI	0.020
P_death_stageII	0.060
P_death_stageIII	0.080
P_death_stageIV	0.090
Prop_high-risk group	0.31
Prop_low- risk group	0.69
P_high-risk_healthy_precancer	0.007
P_low-risk_healthy_precancer	0.003
P_all cause mortality	(Age-wise SRS)

Fig. 1: (a) Markov Model A. (b) Markov Model B.

natural history of disease progression; was diagnosed and treated based on their health-seeking behaviour. This study is exempt from ethical review and approval as it is an economic evaluation study.

Markov models

Due to the high prevalence of tobacco and/or alcohol use in the Indian population and its established relation with the causation of oral cancer, high-risk individuals were defined as users of tobacco and/or alcohol.[6] Hence, two Markov models: Model A adopted a mass screening strategy versus no screening, whereas Model B adopted a high-risk (HR) screening strategy versus no screening (Fig. 1 a and b).

Model parameters

A literature search was performed on PubMed toextract event probabilities, health utility state values, and cost parameters to serve as model inputs. Following keywords were used for the search - oral cancer, natural history, progression, regression, incidence, prevalence and mortality of oral cancer.[13–18] (Tables 1 and 2. Pre-cancer incidence in the total population was estimated from already published literature.[6] Pre-cancer incidence in high-risk and low-risk was estimated using the incidence of pre-cancer in total population and the distribution of high-risk and low-risk individuals. The stage-wise prevalence was estimated based on detection rate of oral cancer, pre-cancer and stage distribution extracted from already published literature.[19] The probability of age-specific all-cause mortality was obtained from the census of India sample registration system (SRS) life tables for the population, including both males and females.[20] The probability of death due to oral cancer was estimated from stage-wise 5-yearly survival rates obtained from the literature.[21] The sensitivity and

S. No	Data required	Base value (S.E)	Distribution	Alpha (Parameters of distribution)	Beta (Parameters of distribution)	Data source
1	**Incidence of pre-cancer**					
	Total population	0.004	N/A			Estimated from Sankaranarayanan et al., 2005 (Details given in Supplementary section 1).[6]
	High-risk group	0.007	N/A			Estimated based on the incidence of pre-cancer and percentage of the population with habits and with no habits.
	Low-risk group	0.003				
2	**Prevalence of stage-wise oral cancer and precancer (Number of prevalent cases in 100,000 population)**					
	Pre-cancer	2660.06	N/A			Estimated based on the detection rate of oral cancer and precancer, and stage distribution derived from Sankaranarayanan et al., 2000. (Details given in Supplementary file S1 D).[19]
	Stage I	5.80				
	Stage II	3.16				
	Stage III	2.30				
	Stage III	1.05				
3	**Annual probability of death due to oral cancer**					
	Stage I	0.028	Beta	0.94	32.54	Estimated from Thavarool et el 2009[21].(Details of estimation of annual probability of death due to oral cancer given in the Supplementary file S1 F)
	Stage II	0.062	Beta	0.88	13.35	
	Stage III	0.093	Beta	0.81	7.99	
	Stage III	0.087	Beta	0.83	8.72	
4	**Annual probabilities progression/regression and health utility values**					
	Precancer to Stage I	0.04 (0.01)	Beta	15.32	367.68	Kumdee et al. 2018[13]
	Stage I to stage II	0.53 (0.27)	Beta	1.28	1.14	
	Stage II to Stage III	0.59 (0.25)	Beta	1.69	1.18	
	Stage III to Stage IV	0.67 (0.25)	Beta	1.70	0.84	
	Precancerous lesion to healthy	0.30 (0.10)	Beta	1.99	10.45	
5	**Utility value**					
	Perfect health	1.00	Beta			
	Precancerous	0.830 (0.020)	Beta	291.78	59.97	Kumdee et al., 2018.[13]
	Stage I	0.698 (0.086)	Beta	19.20	8.31	Prinja et al., 2021.[14]
	Stage II	0.594 (0.061)	Beta	37.90	25.91	
	Stage III	0.639 (0.042)	Beta	82.92	46.85	
	Stage IV	0.357 (0.041)	Beta	48.39	87.16	

Note: N/A: Not applicable.

Table 1: **Parameters of Model A.**

	Cost data	Costs (Base value and S.E)	Distribution	Formula for distribution parameter	Probabilistic value	Source of data
1	**Screening costs in INR**					
	Conventional oral examination	254.23	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	197.08	Estimated cost. Detailed in Supplementary file Table S2 A
	Toluidine blue staining	261.87	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	107.62	Estimated cost. Detailed in Supplementary file Table S2 B
	Oral cytology/Brush biopsy	690.67	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	290.35	Estimated cost (as per CGHS 2014 and 2015)[14-16]
	Light-based detection	402.75	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	96.14	Estimated cost. Detailed in Supplementary file Table S2 D
2	**Diagnostic costs (INR)**					
	Clinical oral examination + Oral biopsy	565.00	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	286.13	Estimated cost. Detailed in Supplementary file Section 2
3	**Treatment costs in (INR)**					
	Precancerous	12,280.00	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	6826.91	Estimated cost. Detailed in Supplementary file Tables S6 and S7
	Stage I/II	90,293.30	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	68063.80	Estimated cost. Detailed in Supplementary file Tables S6 and S7
	Stage III	98,272.95	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	110645.20	Estimated cost. Detailed in Supplementary file Tables S6 and S7
	Stage IV	90,689.43	Uniform	*RAND () ∗ Base value+(S.E – Base value)*	92000.77	Estimated cost. Detailed in Supplementary file Tables S6 and S7
4	**GDP per capita, India (INR)**	132,750.55	N/A			https://tradingeconomics.com/india/gdp-per-capita2021.[24]

Table 2: **Parameters of Model B.**

specificity of COE were taken from the meta-analysis conducted by the authors, and sensitivity and specificity for the remaining strategies were extracted from the literature.[22,23] In the screened arm, the annual probabilities of progression of one health state to another were adjusted for the screening coverage, treatment coverage, and sensitivity of the four screening strategies. In the screening arm, false positive cases were estimated using the specificity of the concerned screening tests to avoid overestimated costs. In the no-screening arm, the annual progression probabilities were adjusted for treatment coverage and the proportion of individuals showing symptoms and health-seeking behaviour in each health state. For the second model, for the high-risk group, the transition probabilities were adjusted for the distribution of high-risk and low-risk individuals, the sensitivity of screening strategies, screening coverage, and treatment coverage. In the low-risk group, the proportion of individuals showing symptoms in each stage and treatment coverage were considered for adjusting the raw transition probabilities. Details of estimation of model parameters and adjustments done top them have been given in Section 1 of Supplementary file Table S1 (A–F).

Cost data

The cost of screening strategies was estimated using the monthly salary and working hours of auxiliary nurse midwifery, the time required for screening one individual, the number of screenings per day, and the cost of material used for the screening. Support activities costs were also added, which included invitation and organisation for the screening, administration, registration, training, supervision, and miscellaneous activities required for the screening process. The cost of diagnosis was estimated considering the standard protocol of oral examination, i.e., the cost of consultation during outpatient department visits and the biopsy cost. The cost of stage-wise treatment was estimated for both public and private facilities.[15–18] (Supplementary file Tables S2–S7).

Outcomes

The outcomes were measured regarding oral cancer incident cases, averted oral cancer deaths, total costs incurred, QALYs gained, and incremental cost-effectiveness ratio (ICER). A discount rate of 3% was used to discount future costs and health outcomes.[25]

Statistical analysis

Using Microsoft Excel, these model parameters were then used to conduct a cost-effectiveness analysis. The total number of incident cases was calculated for each stage of oral cancer in each cycle by using the probabilities of progression and regression from one health state to another. Oral cancer deaths in each cycle were calculated by multiplying the stage-wise probability of death due to oral cancer with the population in each

health state of the Markov model (healthy, precancer and oral cancer stages I to IV). The incremental cost was calculated by subtracting the lifetime cost in the no-screening arm from that in each screening technique for different screening intervals. QALY was calculated using the length of life and quality of health i.e., utility scores of each health state. The utility score for healthy was considered as 1 and 0 for death. Stage-wise utility scores for oral cancer were extracted from the literature.[13,14] The number of individuals in each health state was estimated using transition probabilities. These numbers of individuals (in every health state) were multiplied by the utility values of each stage to estimate QALYs. A similar process was repeated in every cycle to estimate lifetime QALYs and this process was repeated for 70 cycles. The total amount of QALYs gained in each health state and cycle was added to get the QALYs gained for that specific arm (same process was repeated for both the control arm and intervention arm). The incremental QALY was calculated by subtracting the lifetime QALY in the no-screening arm from that in each screening technique for different screening intervals. The ICER was calculated as the division of incremental cost and the incremental effect.[25] Threshold analysis was conducted to observe the variation of ICER at different levels of screening coverage from (1%–5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%). In this process we kept all other parameters as fixed and varied only the screening coverage to see the variation in the ICERs over the period of time.[25]

Sensitivity analysis

To address the uncertainty in model parameter values, probabilistic sensitivity analysis (PSA) was done. Each parameter was given specific distribution according to the methodology by Briggs and colleagues[12,26] where they suggested that the normal distribution is a 'candidate distribution for representing the uncertainty in any parameter in the model'. Furthermore, Briggs and colleagues suggested the beta distribution for binomial outcomes, where parameters can vary between zero and one, for example annual probabilities.[26,27] In this microsimulation study, annual probabilities of progression and regression, health utility values, oral cancer mortality, and all-cause mortality were given beta distribution. Sensitivity and specificity of diagnostic techniques were given normal distribution whereas the costs were given uniform distribution. Using Monte Carlo Simulation, 1000 iterations were done to derive the Net Monetary Benefit (NMB) for all the screening techniques.[25] The probability of cost-effectiveness for all screening strategies was calculated at different willingness-to-pay thresholds (WTP).[24]

Budget impact analysis

A budget impact analysis (BIA) was done to estimate the financial consequences of implementing oral cancer screening in India. The BIA was done for two cycles, where 1 cycle = 1 year. The total cost of intervention for population above age 30 years in India was estimated for each screening strategies at various screening intervals. The annual health budget of India 2022–2023 was considered for the analysis. The impact of the cost of intervention on health care budget of India was estimated and presented as percentage of total health budget of the financial year 2022–2023. The annual healthcare budget of India for financial year 2022–2023 was (862,006.5 Million INR).[28,29]

Role of the funding source

The study sponsor had no role in study design; collection, analysis, and interpretation of data; in writing of the report; or in the decision to submit the paper for publication.

Results

The results of this economic modelling study are discussed in the following subsections: incidence of oral cancer, oral cancer deaths averted, the total cost incurred, total QALYs gained, and ICER for various screening techniques and at different intervals.

Incidence of oral cancer

The total number of new cases of oral cancer in a cohort of 100,000 population in various screening techniques (mass screening, high-risk screening, and no screening strategy) was estimated. The no-screening arm had the maximum number of new cases (5673.59). Mass-screening techniques (number of incident cases), namely LBD - 3 years (3271.68) had the least number of incident cases, followed by OC - 3 years (3276.92), and COE - 3 years (3309.91).

Oral cancer deaths averted

The maximum number of oral cancer deaths was observed in the no-screening arm (1180.45 oral cancer deaths) as compared to the mass/high-risk strategy. Mass screening/high-risk screening averted a higher number of oral cancer deaths compared to no screening. Mass screening using techniques, namely LBD and OC, at 3-year intervals averted the higher number of oral cancer deaths (459.76) (Table 3).

Lifetime cost incurred

The no-screening arm incurred lifetime cost of 2,677,683.84US$ (21,34,93,287.27 INR) per 100,000 population. Among mass and high-risk screening strategies, high-risk screening incurred lesser costs across all comparisons. Amongst various screening techniques, COE HR 10 years incurred the least lifetime cost 2,292,779.25US$ (182,794,468.26 INR), and OC 3 years 7,284,185.66US$ (580,751,021.64 INR) incurred the maximum lifetime cost. The high-risk screening

Screening Strategy	Cost (INR)	QALYs	Incremental cost (INR)	Incremental QALYS	ICER (INR per QALYs gained)	Death due to oral cancer	Death averted	Oral cancer incident cases
No Screening	213,493,287.27	1,777,201.71				1180.45		5673.59
COE								
3yr	325,531,121.20	1,783,762.19	112,037,833.93	6560.48	17,077.70	728.76	451.69	3309.91
3yr HR	225,651,433.66	1,782,840.02	12,158,146.39	5638.31	2156.35	768.29	412.16	3599.55
5yr	278,628,112.12	1,781,569.17	65,134,824.85	4367.46	14,913.66	840.30	340.15	3923.18
5yr HR	202,780,688.58	1,781,796.62	(10,712,598.69)	4594.91	**–2331.41(D)**	793.64	386.81	3811.77
10yr	252,389,378.34	1,780,197.68	38,896,091.07	2995.97	12,982.82	954.50	225.95	4550.84
10yr HR	182,794,468.26	1,781,457.48	(30,698,819.01)	4255.77	**–7213.46(D)**	815.00	365.46	3984.32
TBS								
3yr	405,390,056.25	1,783,459.80	191,896,768.98	6258.09	30,663.80	749.15	431.30	3403.39
3yr HR	244,711,064.67	1,783,104.70	31,217,777.40	5902.99	5288.47	764.02	416.43	3583.81
5yr	332,097,814.83	1,781,948.80	118,604,527.56	4747.08	24,984.71	858.29	322.16	4009.21
5yr HR	223,935,608.11	1,781,595.62	10,442,320.84	4393.91	2376.54	805.62	374.83	3865.98
10yr	276,596,675.49	1,780,469.49	63,103,388.22	3267.78	19,310.79	967.70	212.75	4613.27
10yr HR	193,806,328.95	1,781,289.71	(19,686,958.32)	4088.00	**–4815.80 (D)**	824.56	355.89	4026.57
OC								
3yr	580,751,021.64	1,783,881.01	367,257,734.37	6679.29	54,984.51	720.70	459.76	3276.92
3yr HR	290,412,200.01	1,782,926.02	76,918,912.74	5724.30	13,437.25	762.69	417.76	3573.95
5yr	411,105,295.12	1,782,321.41	197,612,007.85	5119.70	38,598.36	819.81	360.64	3889.13
5yr HR	264,719,039.27	1,781,876.29	51,225,752.00	4674.58	10,958.36	788.90	391.55	3790.32
10yr	340,632,976.45	1,780,753.03	127,139,689.18	3551.32	35,800.69	949.23	231.22	4527.76
10yr HR	229,559,511.34	1,781,524.49	16,066,224.07	4322.77	3716.65	811.18	369.28	3967.46
LBD								
3yr	511,575,807.73	1,783,881.01	298,082,520.46	6679.29	44,627.85	720.70	459.76	3271.68
3yr HR	268,133,691.67	1,782,926.02	54,640,404.40	5724.30	9545.34	762.69	417.76	3573.95
5yr	461,969,593.21	1,782,321.41	248,476,305.94	5119.70	48,533.38	833.18	347.28	3889.13
5yr HR	231,572,958.72	1,781,876.29	18,079,671.45	4674.58	3867.66	788.90	391.55	3790.32
10yr	312,176,859.58	1,780,753.03	98,683,572.31	3551.32	27,787.86	949.23	231.22	4525.92
10yr HR	208,845,581.77	1,781,524.49	(4,647,705.50)	4322.77	**–1075.17(D)**	811.18	369.28	3967.46

Note: HR: High-risk strategy and D: Dominant (The ICER value in negative denotes strategies dominant over no-screening). QAYL: quality-adjusted life years; ICER: incremental cost-effectiveness ratio; COE: conventional oral examination; TBS: toluidine blue staining; OC: oral cytology; LBD: light-based detection. The significance of bold is to mark the dominant strategies.

***Table 3*: Outcome indicator in cost and consequences in a cohort of 100,000 population among various screening scenarios versus no screening.**

strategy was cost-saving compared to the mass-screening strategy (Table 3).

QALYs

On comparing screening and no-screening, it was observed that mass-screening/high-risk screening yielded a greater number of QALYs. The no-screening arm yielded (1,777,201.71 QALYs). Amongst various techniques, mass-screening techniques, namely OC and LBD at 3-year intervals, yielded a greater number of QALYs (1,783,881.01 QALYs) with incremental QALYs of (6679.29) (Table 3).

ICER

Amongst the screening techniques, it was observed that high-risk screening was cost-saving compared to the mass-screening strategy. The high-risk screening techniques (ICER values) namely COE 5 years (–2331.41 INR/QALY) (–29.21 US$/QALY), COE 10 years (–7213.46 INR/QALY) (–90.68 US$/QALY), TBS 10 years (–4815.80 INR/QALY) (–60.54 US$/QALY), and LBD 10 years (–1075.17 INR/QALY) (–13.51 US$/QALY) were dominant over no-screening (no screening was costlier and less effective). The high-risk screening by COE at ten years was the most cost-saving approach (Fig. 2, Table 3).

Threshold analysis

At less than five per cent of screening coverage, high-risk strategies COE 5 and 10 years, TBS, and LBD 10 years are cost-saving. At 10% screening coverage, mass screening with COE at three years and high-risk screening with COE, TBS, OC, and LBD at 3, 5, and 10 years are cost-saving. The high-risk techniques COE 5 and 10 years, TBS 10 years, and LBD 10 years are cost-saving at all levels of screening coverage (1%–5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%) (Supplementary file Table S8).

Sensitivity analysis

The CE plane and cost-effectiveness acceptability curve (CEAC) were plotted for mass and high-risk screening

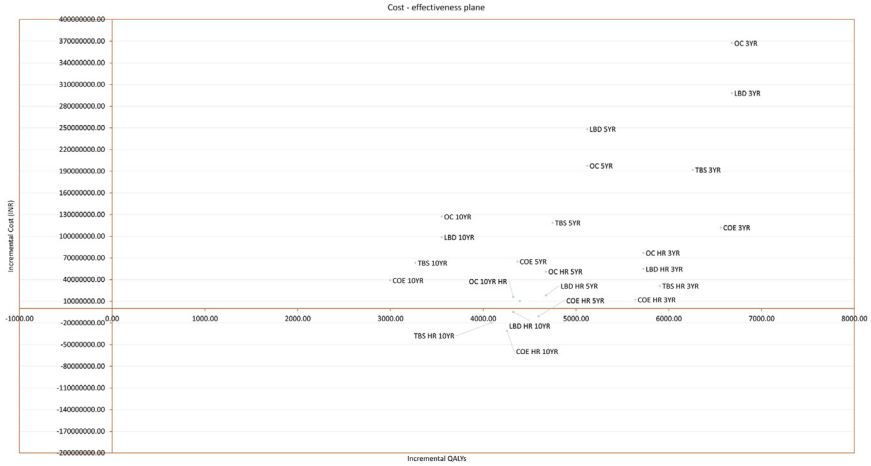


Fig. 2: Cost-effectiveness plane for mass-screening and high-risk screening strategies base case. HR: high-risk strategy; YR: year; COE: conventional oral examination; TBS: toluidine blue staining; OC: oral cytology; LBD: light-based detection.

strategies (Supplementary file Figures S1 and S2). Most of the ICER values from PSA fall on the southeast quadrant in the CE plane for the high-risk screening strategy by COE 10 years (Fig. 3 a). For different WTPs, among the high-risk screening techniques majority had more than an 80% probability of being cost-effective (Supplementary file Table S9). At the WTP of 1880.77 US$ (150,000 INR), the high-risk screening techniques, namely COE 10 years, had (91.1%) (Fig. 3 b), the highest probability of being cost-effective followed by TBS 10 years (90.2%), COE 5 year (90.1%), and LBD 10 year (90%).

Budget impact analysis

The budget impact analysis showed that oral screening using COE for high-risk population at 10-year interval would cost Rs. 25,727,541,030.81 for the first year, which is 0.03% of annual healthcare budget of India (862,006.5 million). For the second-year implementation, it would cost 28,300,295,133.90 INR which is 0.03% of annual healthcare budget of India (862,006.5 million). Thus, the budget impact analysis indicates that the implementation of nationwide oral screening using conventional oral examination for high-risk population above 30 years of age at 10-year interval would account for only 0.03% of annual healthcare budget of India in the year 2022–2023.

Discussion

Our CEA analysis revealed that mass-screening/high-risk screening had a lesser number of oral cancer incident cases and oral cancer deaths as compared to no-screening. Among the screening strategies, it was observed that high-risk screening was cost-effective compared to the mass-screening at various intervals.

Our findings were similar to the cost-effectiveness study regarding oral cancer screening in India by Subramanian and colleagues.[10] However, our results differ from the community-based early oral cancer screening program by trained health workers for the population aged over 40 years in USA. The study concluded that the no-screen arm was dominant, indicating a poor value for money.[8] However, they stated in their study that if changed to high-risk males over 40, the program is likely to be cost-saving. Another study by Kumdee and colleagues on oral cancer screening in Thailand stated that the screening was not cost-effective.[13] Kumdee and colleagues stated that screening could be cost-effective only if: 1) the sensitivity and specificity of mouth-self-examination (MSE) are more than 60%, 2) the sensitivity and specificity of visual examination by trained dentists (VETDN) are greater than 90%, or 3) the low accuracy steps like MSE or VETDN are removed from the screening program. This could be because the age-standardised incidence rate (ASIR) of Thai population was very low compared to the target population in India, especially in males (3.9 vs 12.6 per 100,000). In a study by Speight and colleagues in the UK, the ICER for the whole population (aged 49–79 years) ranged from £15,790 to £25,961 per QALY, which suggested no screening was always the cheapest option, and opportunistic screening by general dental practitioners may be cost-effective.[9] This study slightly differed from our study, as in our study, we had cost-saving screening strategies when compared to the no-screening arm.

Clinical utility

Through our study, it was evident that oral visual screening significantly reduced the number of incident cases when compared to no screening. Mass-screening at 3-year intervals and screening of high-risk

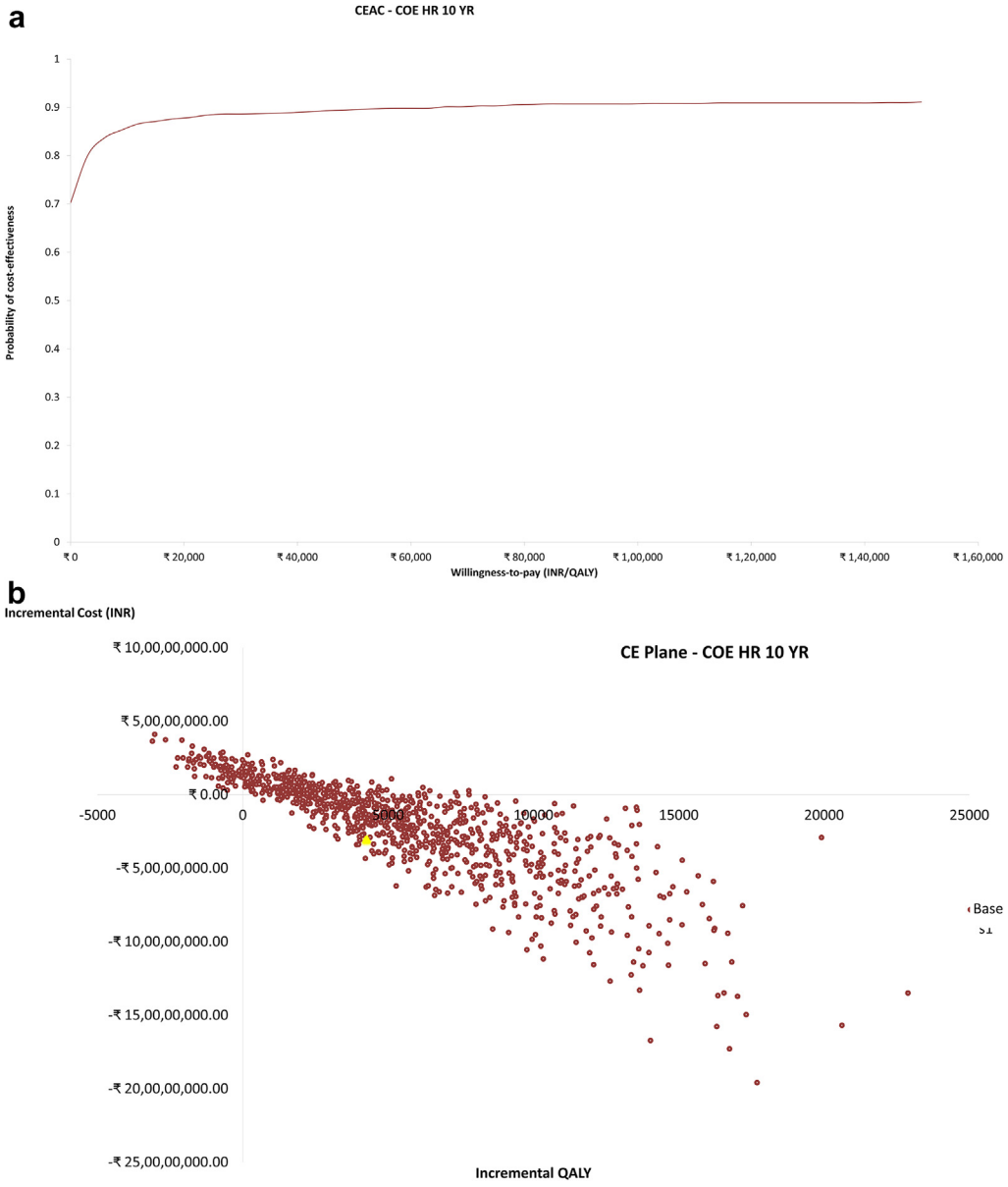


Fig. 3: (a) Cost-effectiveness plane and (b) cost-effectiveness acceptability curve of the conventional oral examination among high-risk at a 10-year interval screening. HR: high-risk strategy; YR: year; CE: cost-effectiveness; CEAC: cost-effectiveness acceptability curve; COE: conventional oral examination.

individuals at 5-year and 10-year intervals observed a lesser number of incident cases as compared to no-screening. This implies that fewer oral cancer incident cases will decrease the requirement of resources for treatment and management, as well as the associated economic burden. It was also observed from our analysis that mass-screening/high-risk screening resulted in a lesser number of oral cancer deaths as compared to no-screening. A previous study by Sankaranarayanan and colleagues in Kerala, India, has demonstrated that groups specialised for screening high-risk individuals can potentially reduce oral cancer mortality.[6] Thus, it was evident from our study that screening high-risk individuals could be the ideal approach for a resource-constrained country like India.

The commonly used techniques for oral cancer screening are COE, TBS, OC, and LBD.[3] TBS screening technique requires the application of toluidine blue dye or stain to the suspected mucosa and then visualisation to detect the suspected lesion.[3,30] OC requires the

scrapping of cells from the oral mucosa with a brush, preparing cytological sample from the collected material, and finally assessed by pathologists.[3,31] LBD is done using commercially available equipment for illumination like Velscope and ViziLite plus to detect precancerous and cancerous lesions.[3,32] These techniques are resource-intensive and need evaluation by specialists. Hence, they are not widely used for screening in a developing country like India.

On the other hand, COE requires less training, equipment, and time resources, making it a desirable option for large-scale implementation in the developing world. The time and workforce thus spared can be utilized for other national programs in our country to combat other public health issues. Thus, making oral screening by COE in high-risk individuals the most favourable approach.

In our study, across various intervals, screening of high-risk individuals by COE at an interval of 10 years was the most cost-saving approach. However, the current recommendation for oral cancer screening interval under the National programme for prevention of control of cancer, diabetes, cardiovascular diseases, and stroke (NPCDCS) is 5 years.[11] The current screening coverage in India is poor (women-1.2% and men-1.0%), as reported by the latest National Family Health Survey-5 (NFHS-5) survey data.[33] In our study, we assumed the screening coverage to be 80%. This is much higher than the current screening coverage in India. To address this uncertainty, we did a threshold analysis to see the variation of ICERs at different levels of screening coverage. And we found that the high-risk techniques COE (every 5 years and 10 years), TBS (every 10 years), and LBD (every 10 years) are cost-saving at all levels of screening coverage. Implementing a nationwide screening programme is a long process involving various steps, including invitation and organising for screening, registration, administration, training, supervision, and other miscellaneous activities. This requires consistent effort and commitment from all the stakeholders of the healthcare delivery system in our country.

The current study has several strengths. Most importantly, our study was the first of its kind for the Indian population, where we estimated lifetime cost and health outcomes of oral cancer screening, followed by diagnosis and treatment in either public or private setting. Our study also provides insight for both the government and the patient regarding the overall expenditure to be expected and planned in accordance. Second, our cost analysis captures the practical programmatic guidelines of the NPCDCS program. Third, while estimating the cost of cancer treatment, both the health system cost, as well as out-of-pocket expenditure was estimated following standard methodologies of costing. Fourth, we addressed parameter uncertainties in our results by performing sensitivity analysis.

Our study has some limitations. The values of transition probabilities were derived from international literature because of a scarcity of progression data for the Indian population. However, Thailand is closer to India regarding development and socio-economic status. Therefore, we used values from a study by Kumdee and colleagues on the Thai population.[13] In our study, we made some assumptions and estimations based on previously published literature which could affect the outcomes of our study, for example, starting age of the participants in our study was 30 years which differed from the reference study where the starting age was 35 years. Likewise, in our study, we used reimbursements rates of the Central Government Health Scheme (CGHS) to estimate various screening costs. However, we tried to address the uncertainty around these values by performing a sensitivity analysis in our study. For the sensitivity analysis certain parameters like incidence and prevalence of pre-cancer were not varied but kept fixed, whereas parameters like progression probabilities, mortality and cost were varied to its upper and lower limit.

Oral cancer screening of high-risk individuals (tobacco and/or alcohol users) was more cost-effective than the mass-screening strategy. High-risk oral screening of the population above 30 years of age using conventional oral examination at ten years intervals was the most cost-saving strategy for the Indian population. Considering the cost-effectiveness, high-risk screening is India's preferred strategy for oral cancer. Of all the screening techniques studied, screening using COE of HR individuals at an interval of 10 years is the recommended screening strategy for the Indian population under NPCDCS. The current study provides evidence for policymakers to draw guidelines to suggest an appropriate strategy for oral cancer screening in India.

Contributors

Conceptualisation: AL, PD. Data curation: PD, AS, DS. Formal analysis: PD, AL, PB, AS, DS. Funding acquisition: AL, KR. Investigation: PD, AL, PB, AS, DS. Project administration and resources: AL, MKS, KR. Software: PD, PB, SAR. Supervision: AL, MKS, SAR, KR. Validation: PD, AL, PB, SAR. Visualisation: PD, PB, AL. Methodology and Writing - original draft: PD, AL, DS. Writing -review and editing: PD, AL, PB, AS, DS, MKS, KR, SAR.

Data sharing statement

The data underlying this article are available in the article and in its online Supplementary Material.

Declaration of interests

None. The current study was supported by funding from Department of Health Research, Ministry of Health & Family Welfare, Government of India.

Acknowledgments

We are thankful to the authors of the studies from which we have extracted parameter values to conduct the cost-effectiveness analysis.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lansea.2023.100224.

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