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Research Article

Cost-utility Analysis of a Novel Oral Cancer Screening Model in Thailand

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Abstract

Purpose: Oral cancer rates have risen globally at an alarming rate. This is notable in Thailand, where oral cancer screening is crucial to reduce the government's health care burden. To this end, this study aimed to generate a novel oral cancer screening model for early detection and diagnosis, and to analyze its cost-effectiveness compared with a non-screening scenario.

Methods: We designed a model with three main screening processes, S1, S2, and S3, each involving an individual set of procedures, the last being a biopsy for definitive diagnosis. A simulation model was formulated to represent the screening scenario and was used to assess the costs and the subsequent quality-adjusted life years (QALYs). An incremental cost-effectiveness ratio (ICER) was also calculated based on a non-screening scenario.

Results: This novel model proved to have an 88% coverage level in oral cancer screening. The ICER calculation was 176,312.65 THB/QALY which was 0.80 times relative to gross domestic product (GDP) per capita in 2022.

Conclusion: This novel oral cancer screening shows the highest coverage level and the largest volume of targeted inhabitants that can be reached in Thailand which will be ultimately cost-effective compared with late diagnosis. Therefore, this model can be employed as a government policy for the more budget-efficient early detection and treatment of oral cancer.

Key points:

i.Development of a novel oral cancer screening model tailored for Thailand, addressing rising incidence rates and the need for early detection to reduce healthcare burdens.

ii.Comprehensive cost-utility analysis demonstrating the model's high coverage, cost-effectiveness, and potential to revolutionize oral cancer screening policies in Thailand.

iii.Contradiction of previous findings regarding the cost-ineffectiveness of screening through improvements in screening flow, increased cancer incidence rates, and adjustments to cost-effectiveness thresholds, ultimately supporting the model's effectiveness and feasibility.

Introduction

For Thailand in 2015, the incidence rates of oral cancer were 5.5 and 4.3 cases per 100,000 in men and women, respectively, accounting for an average of 4.9 cases per 100,000 persons [1]. In 2019, the incidence rate in men increased dramatically to 7.4 cases per 100,000 persons, while in women it decreased slightly to 3.0 cases per 100,000 persons, accounting for the total incidence rate increased to 5.2 cases per 100,000 persons [2]. The Tumor, Node, Metastasis (TNM) staging system classifies cancer into four stages, each with unique characteristics and varying five-year survival rates. Researchers have reported different survival rates for each stage, depending on the population and period analyzed. However, all studies observed a correlation between advanced stages and lower survival rates [3,4], with stage IV having a two to four times shorter five-year survival rate than stages I and II. Advanced stages of cancer incur greater treatment complexities and costs, posing a burden on public health strategies that are increasing year on year [1,5]. Aside from medical expenses, the quality of life for an oral cancer patient is significantly lowered in advanced stages.

This demonstrates the necessity of an oral cancer screening model enabling the early diagnosis of typical lesions. Implementing policy-level oral cancer screening in Thailand would minimize government-regulated medical costs and increase the quality of a patient's life via early detection. However, in 2018 a study claimed that this would be cost-ineffective due to procedural complexities [6]. In contrast to this conclusion, the current study contends that screening would improve the quality of life of the Thai population and should be included among the government-administered public-health policies. To this end, we constructed a novel oral cancer screening model with early detection and diagnosis performance that is superior to existing models. The cost-effectiveness of this model was analyzed through a simulation process and the results were compared to a non-screening scenario.

Methods

The study procedures were approved by the Institutional Review Board with COA. No. MU-DT/PY-IRB 2019/041.0307. All participants were fully informed of the procedures and objectives of this study, and each completed informed consent forms in advance of their participation. The first date of collection procedures began on September 5th, 2019 and the last date was August 28th, 2020.

Population

The targeted population was individuals 40 years or above because of the recorded demographic distributions of oral potentially malignant disorders (PMDs) and a lower incidence for under 40 years [7,8]. A total of 392,823 inhabitants were included in this oral cancer screening model. Demographic data of the targeted inhabitants are shown in Table 1.

Area of study

The public health structure of Thailand is geographically divided into 13 health regions. This study focused on the ninth health region comprising four provinces in the northeastern part of Thailand, namely Nakorn Ratchasima, Chaiyaphum, Buriram, and Surin, which fall under the Mahidol University and The Center of Excellence in Oral Cancer at Maharat Nakorn Ratchasima Hospital. Recent statistics on oral cancer in Thailand (2013-2015 and 2016-2018), reveal the number of oral cancer cases in the northeastern region of the country to exhibit a similar trend to other regions [1,5]. Therefore, the proposed model can be employed in this area as an appropriate representative pilot model.

Novel oral cancer screening model design

This oral cancer screening model comprised three main screening processes: Screening 1 (S1), Screening 2 (S2), and Screening 3 (S3), each of which occurred in sequence. Thailand's national public health policy provides universal healthcare coverage with three main levels of public hospitals, namely, the primary, the secondary, and the tertiary care units through which the Thai population can be served. Therefore, the design of our model was consistent with the country's health structure in terms of reduced screening processes, increased population coverage, and enhanced potential. The details of these three sequential processes are as follows (Figure 1):

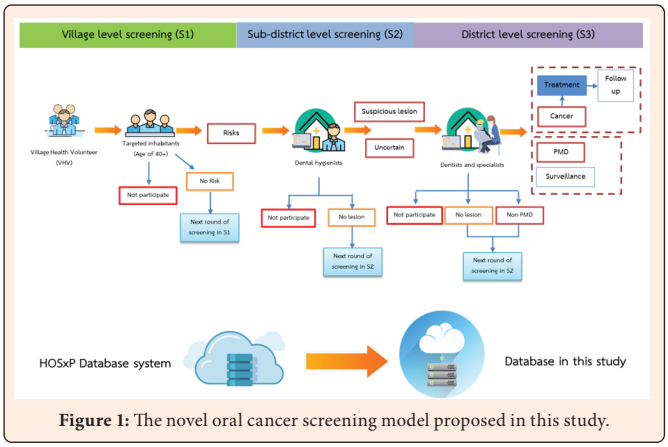

Figure 1: The novel oral cancer screening model proposed in this study.

S1 was a village-level screening process in which a village health volunteer (VHV) can attend to all those in the village via a primary care unit. We screened for the following eight risk factors of oral cancer: 1) tobacco use history, 2) smokeless tobacco use history, 3) alcohol consumption, 4) betel chewing history, 5) time spent outdoors, 6) denture use for at least one year, 7) symptoms of oral irritations, and 8) cancer history. The relationship between these risk factors and oral PMDs, we elucidate in our previous study (9). The conditions "no risk" and "did not appear for screening" were also provided at this level to avoid the neglect of screening or counterfeit results. The list of targeted inhabitants who registered in each village was delivered to the VHV for screening. It was generated from the database specifically developed for this oral cancer screening model by extracting the data from the central database called HOSxP – the public health database system in Thailand. Participants who exhibited at least one of the eight risk factors became the Risk group and were referred to S2 for oral lesion screening, while those who presented "no risk" and "did not appear for screening" waited for the next round of annual S1 screening.

S2 was a sub-district-level screening process in which primary-care-unit staff screened the Risk group. The primary-care-unit staff called dental hygienists had been trained to detect normal soft tissue in the oral cavity before their inclusion in this level and played key roles in the screening. Six areas involving lips, gingiva, buccal mucosa, tongue, palate, and floor of mouth were introduced as screening areas. The training process was conducted to reduce false negative detection. The dental hygienists received the screening sheet from VHV, then made an appointment for each person, took further history, and recorded those data in the database. They performed a conventional oral examination of the Risk group as a screening test. Concurrently, they presented the screening results as "did not appear for screening," "no lesion," "suspicious lesion," and "uncertain." With these types of answers, the dental hygienists did not require special and specific attributes that went beyond their normal job description and avoided different competencies in oral mucosal detection. This methodology can reduce the workload stress that is associated with the screening process and reduce the avoidance of duty. Moreover, it reduced the huge differences in consistency between dental health professionals and students [10]. The first two groups waited for the next round of annual S2 screening. The other groups became a Lesion group and were referred to S3 for the confirmation of the lesion. This process can reduce the gap of a competency [10] between the examiner within the S2 step.

S3 was a district-level screening process hosted by the secondary care unit. This level was designed to allow active screening by enhancing the performance of the secondary care unit through the participation of the tertiary care unit, the Center of Excellence, and the university hospital. Normally, general dental practitioners are the main responders in this area. However, at this level, oral medicine specialists, and oral and maxillofacial surgeons performed screening. This incorporation can be feasible in every healthcare region in Thailand because the same public health structure has been implemented throughout the country. The screening date was determined in advance, with only two days of screening for each secondary care unit. The Lesion group was asked to present within the appointment dates. All the cases were screened by specialists.

The Lesion group inhabitants were categorized into one of five main groups: "did not appear for screening," "no lesion," "non-PMD," "PMD," and "cancer." In this step, the targeted inhabitants were diagnosed via conventional oral examination only or via biopsy to confirm the presence of lesions. The biopsy was prescribed to targeted inhabitants solely upon the clinical impression of the specialists. The specimens obtained from the biopsy procedure were then sent back to Faculty of Dentistry, Mahidol University. Oral pathologist specialists in the Faculty of Dentistry, Mahidol University interpreted the specimens and gave the definitive diagnosis. All participants who presented lesions received primary treatment and follow-up plans. The follow-up plans were taken care of by general dentists at theeconddary care unit. The "did not appear for screening" and "no lesion" groups were sent back to S2 to wait for the next round of annual screening, while the "non PMD" group proceeded with S3 on an appointment basis. The "PMD" group received treatment and underwent a surveillance plan and follow-up, and the "cancer" group was referred to the tertiary care unit to receive advanced treatment and follow-up as their residential areas lay under the jurisdiction of the secondary care unit.

Cost-utility analysis

The number of inhabitants in Table 1 was accounted for in both screening and non-screening scenarios in the simulation process. The input parameters are displayed in Table 2. Mortality rates for the Targeted inhabitants, the Risk, and the Lesion groups were acquired from the Social Security area population which showed different mortality rates at each age point [11] and are exhibited in supplementary Table 1. A discount rate of 3% was applied.

Screening scenario

Following Table 1, all targeted inhabitants were distributed into seven different groups according to their age and based on ten-year intervals. Each group was represented by its lowest age point in the simulation process, i.e., in 40–49 years interval represented as 40 years. If inhabitants had reached 81 years of age, they were removed from the simulation. This is in line with the estimated life expectancy in Thailand of 80 years [12]. Therefore, inhabitants whose age were over 80 years old

were not included in the simulation. In total, 368,053 inhabitants were involved in the simulation. The simulation model of screening is shown in Figure 2a.

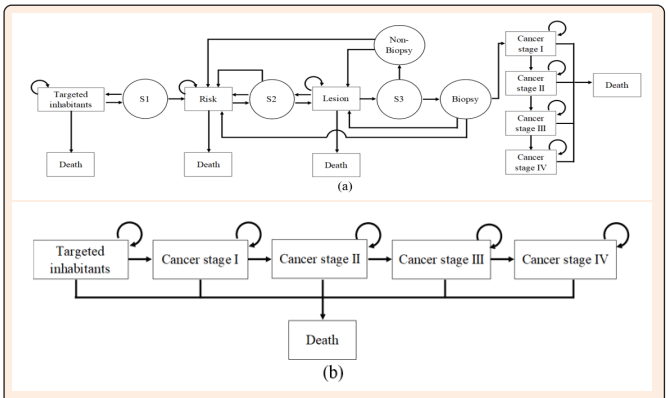

Figure 2: Simulation model. a.) Screening, b.) Non-screening.

Non-screening scenario

A non-screening scenario was conducted as a counterpart. The same number of inhabitants were involved. The same age intervals were accounted for; composed of participants aged from 40 to 79 years. The simulation itself was also implemented similarly and shown in Figure 2b.

Incremental Cost-Effectiveness Ratio (ICER)

To examine the effectiveness of this screening model, a cost-utility analysis was performed. Only cancer found in both screening and non-screening scenarios was registered but PMD occurrence was neglected due to the lack of available PMD statistics in Thailand. The ICER is a parameter that indicates the effectiveness of the model and was used in this study. In the screening scenario, all the costs accrued by this study were included, and the QALYs corresponding to the screening scenario were applied to enable the assessment of this scenario.

The cost-effectiveness threshold relied on WHO criteria [13], employing the ICER as the indicator, compared with the gross domestic product (GDP) per capita. This novel oral cancer screening model was considered highly cost-effective if ICER was <1 time the GDP per capita [13].

Table 1: Demographic data of targeted inhabitants included in this study.

Area	Targeted	Participated			
		Male		Female	Total
Area 1 (Nakhorn Ratchasima)	203,737	83,149		94,047	**177,241**
Area 2 (Chaiyaphum)	105,894	45,721		54,417	**100,138**
Area 3 (Buriram)	56,950	22,106		26,851	**48,957**
Area 4 (Surin)	26,242	10,285		12,563	**22,848**
Total	**392,823**	**161,306**		**187,878**	**349,184**
Age (years old)	**Area 1**	**Area 2**	**Area 3**	**Area 4**	**Total**
40 – 49	40,736	21,701	10,686	4,696	**77,819**
50 - 59	54,770	31,747	14,784	7,005	**108,306**
60 - 69	42,707	25,201	12,191	5,792	**85,891**
70 - 79	25,156	14,849	7,527	3,505	**51,037**
80 - 89	11,559	5,706	3,227	1,591	**22,083**
90 - 99	2,283	917	531	253	**3,984**
100 +	30	17	11	6	**64**
Total	**177,241**	**100,138**	**48,957**	**22,848**	**394,184**

Table 2: Parameters involved in the simulation process of both screening and non-screening scenarios.

Parameter	Value	S.E.	Distribution	Reference
Parameter for screening scenario				
Coverage of the screening model (Compliance of S1 level)	0.888909	0.000001	Beta	Data collection
Not found risk factor sending back to Targeted inhabitants group.	0.448345	-	-	Data collection
Found risk factor becoming Risk group.	0.551655	-	-	Data collection
Compliance of S2 level	0.457740	0.000003	Beta	Data collection
Not found lesion sending back to Risk group.	0.965432	-	-	Data collection
Found lesion becoming Lesion group.	0.034568	-	-	Data collection
Compliance of S3 level	0.572647	0.000162	Beta	Data collection
Non-biopsy ratio	0.711175	-	-	Data collection
Found neither cancer nor lesion sending back to Risk group	0.147462	-	-	Data collection
Found non-cancerous lesion, received treatment, and sending back to Lesion group.	0.852538	-	-	Data collection
Biopsy ratio	0.288825	0.000259	Beta	Data collection
Found non-PMD lesion, received treatment, and sending back to Risk group.	0.359127	-	-	Data collection
Found PMD lesion, received treatment, and sending back to Lesion group.	0.591270	-	-	Data collection
Found Cancer stage I	0.049603	0.000430	Beta	Data collection
Cancer incidence rate (Only for non-screening scenario)				
Cancer stage I incidence rate	0.203644	-	-	(5)
Cancer stage II incidence rate	0.203644	-	-	(5)
Cancer stage III incidence rate	0.263308	-	-	(5)
Cancer stage IV incidence rate	0.329403	-	-	(5)
Cancer progressive rate				
From cancer stage I to cancer stage II	0.53	0.27	Beta	(32)
From cancer stage II to cancer stage III	0.59	0.25	Beta	(32)
From cancer stage III to cancer stage IV	0.67	0.25	Beta	(32)
Mortality rate				
Mortality rate from non-cancer stage (Targeted inhabitant, Risk, and Lesion groups in screening scenario)	Supplementary Table 1	-	-	(11)
Mortality rate from cancer stage I	0.55	-	-	(3)
Mortality rate from cancer stage II	0.63	-	-	(3)

Mortality rate from cancer stage III	0.80	-	-	(3)
Mortality rate from cancer stage IV	0.86	-	-	(3)
Costs (both direct medical and direct non-medical costs)				
Only for screening scenario				
Cost of S1 level screening (THB per person)	10.00	-	-	Data collection
Cost of S2 level screening (THB per person)	20.00	-	-	Data collection
Cost of S3 level screening (THB per person)	20.00	-	-	Data collection
Cost of biopsy process in S3 level screening (THB per person)	450.00	-	-	Data collection
Cost of non-biopsy process in S3 level screening (THB per person)	200.00	-	-	Data collection
Both screening and non-screening scenarios				
Cost spent in cancer stage I found (THB per person)	82,006.00	11,694.42	Gamma	(6, 33)
Cost spent in cancer stage II found (THB per person)	144,649.00	21,444.14	Gamma	(6, 33)
Cost spent in cancer stage III found (THB per person)	133,049.00	13,323.25	Gamma	(6, 33)
Cost spent in cancer stage IV found (THB per person)	160,794.00	11,233.68	Gamma	(6, 33)
Utility				
Cancer stage I	0.61	0.05	Beta	(6)
Cancer stage II	0.61	0.05	Beta	(6)
Cancer stage III	0.34	0.09	Beta	(6)
Cancer stage IV	0.34	0.09	Beta	(6)
Thailand GDP				
GDP per capita in 2022 (USD)	6,278.20	-	-	(15)
Exchange rate (1 USD to THB)	35.23	-	-	(16)

Sensitivity analysis

One-way sensitivity analysis

Five parameters considered to affect the ICER value were the screening model coverage, the compliance of the S2 level, the compliance of the S3 level, the biopsy ratio, and the cancer ratio regarding the biopsy procedure, all of which were undertaken in the one-way sensitivity analysis. All parameters were altered at the lowest and the highest values in the range and relied on the estimated value within 95% confidence intervals. Any percentage change in ICER value was evaluated.

Probabilistic sensitivity analysis

Monte-Carlo simulation of 1,000 rounds was performed by varying those five parameters simultaneously with the costs of all cancer stages using their distributions. All random parameters were used in probabilistic sensitivity analysis. The cost-effectiveness acceptability curve was used to evaluate with respect to the typical 160,000 THB threshold for every cost-effectiveness analysis in Thailand. This was presented in a previous study [6] (Figure 3).

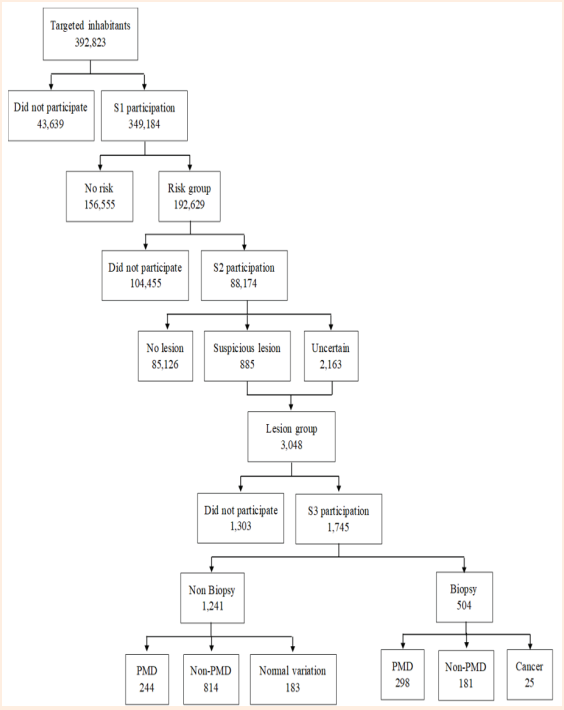

Figure 3: The diagram of the inhabitants in each screening step of the constructed oral cancer screening model's implementation.

Results

The employment of the proposed oral cancer screening model in the area of study

In total, 392,823 inhabitants were targeted in this study area; however, only 349,184 inhabitants participated, representing 88.89% of coverage. The largest volume was in the 50-59 years age range. Detailed demographic data of the targeted inhabitants were presented in Table 1.

The number of targeted inhabitants involved in each screening step is displayed in Figure 4. 349,184 targeted inhabitants participated in S1, and 192,629 of these participants exhibited at least one risk factor and became the Risk group.

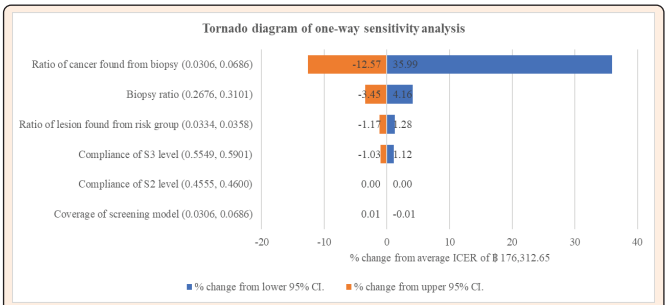

Figure 4: Tornado diagram of one-way sensitivity analysis. Changes of ICER in percentage upon ranges of individual parameters.

Only 88,174 of the Risk group participated in S2. However, 85,126 of the 88,174 inhabitants did not exhibit any oral lesions and were classified in the "no lesion" group. Thus, only 885 inhabitants were categorized into the "lesion found" group, with a further 2,163 inhabitants classified into the "uncertain" group. In total, 3,048 inhabitants became the Lesion group.

At S3, 1,303 of Lesion group did not participate in the procedure; thus, only 1,745 inhabitants attended this level. Among them, only 504 inhabitants required a biopsy to ensure a definitive diagnosis. The other 1,241 inhabitants did not require a biopsy as a definitive diagnosis could be made.

Of the 504 specimens biopsied, 298 were diagnosed as cases of PMD lesions; 181 were non-PMD lesions; and 25 were cancer lesions. Conversely, the 1,241 inhabitants that did not require a biopsy revealed 244 cases of PMDs, 814 of non-PMDs, and 183 normal variations (Table 3).

Table 3: Cancer lesions detected in this study based on ages and stages.

Age	Male	Female	Total
40 - 49	0	0	**0**
50 - 59	3	2	**5**
60 - 69	5	0	**5**
70 - 79	0	10	**10**
80 - 89	0	1	**1**
90 - 99	0	4	**4**
100 +	0	0	**0**
Total	**8**	**17**	**25**
Stage		**Amount**	
Stage I		24	
Stage II		0	
Stage III		1	
Stage IV		0	

Of the 25 biopsied cancer lesions, 24 lesions were diagnosed as stage I; only one lesion diagnosed as stage III. The details of the cancer cases detected are reported in Table 4 and in the literature [14].

Table 4: Costs and QALYs generated by the simulation process for both the screening and the non-screening scenarios. Incremental cost, and incremental QALYs were calculated by weight average in case of a combination between age intervals. The ICER was calculated owing to adjusted incremental cost and incremental QALYs.

Start age in simulation	Years in simulation	Cost (THB)		Incremental Cost	QALYs (Years)		Incremental QALYs
		Screening	Non-screening		Screening	Non-screening	
40	40	1,367,144.41	338,502.81	1,028,641.60	8.48	1.86	6.62
50	30	2,075,860.62	517,017.01	1,558,843.61	11.39	2.53	8.87
60	20	1,803,933.15	455,830.50	1,348,102.65	8.68	1.98	6.70
70	10	1,184,365.56	309,810.40	874,555.16	4.79	1.18	3.60
Weighted average of all age intervals							
	Cost (THB)			**QALYs (Years)**			
Age	**Screening**		**Non-screening**	**Screening**		**Non-Screening**	
40–70	1,648,839.14		412,653.36	9.03		2.01	
Incremental cost (THB)			1,236,185.77				
Incremental QALYs (years)			7.01				
ICER (THB/QALY)			176,312.65				
GDP per capita of Thailand in 2022 (THB)			221,180.99				
Ratio of ICER per GDP per capita			0.80				

Cost-utility analysis

Table 4 shows the estimated costs and QALYs of each of the different starting ages undergoing the simulation process. ICER was calculated using the incremental cost and the incremental QALY which were generated by a weighted average of each age interval by the number of inhabitants involved in each corresponding age interval. The estimated costs of 1,648,839.14 THB in the screening scenario and 412,653.36 THB in the non-screening scenario corresponding to the estimated QALYs of 9.03 years in the screening scenario and 2.01 years in the non-screening scenario.

ICER was 176,312.65 THB compared with the GDP per capita (6,278.20 USD) of Thailand in 2022 [15]. Employing the yearly average exchange rate of USD to THB in 2022, as availed by the Bank of Thailand [16], the GDP per capita of Thailand was 221,180.99 THB, resulting in an ICER/GDP per capita of 0.80. This was considered highly cost-effective according to the WHO criteria [13].

Parameters uncertainty analyses

One-way sensitivity analysis

Figure 4 presented a tornado diagram of one-way sensitivity analysis and showed that the ratio of cancer found from biopsy, the biopsy ratio, and the ratio of lesions found from the Risk group played keys role in changes in the ICER. However, the first two variables relied on specialists and oral surgeons who determined whether the inhabitants required a biopsy. Therefore, the key variable to enhance cost-effectiveness consequently became the ratio of lesions found from the Risk group. In this analysis, the corresponding values were 0.0334 to 0.0358, which were relatively low in percentage compared with the other parameters. However, if the percentage of lesions found in the Risk group becomes 20%, the change in the ICER decreases by 23.75%. (Data not presented).

Probabilistic sensitivity analysis

The cost-effectiveness acceptability curve is displayed in Figure 5. Three thresholds were focused on this analysis. They were composed of 1) a threshold of 160,000.00 THB as presented in Kumdee, et al. (2018) [6], which was written in 2017 and published in 2018 so the threshold of 160,000.00 THB was implemented in 2017; 2) a threshold of 176,312.65 THB which was this study's estimation; and 3) a threshold of 185,483.85 THB which was 160,000.00 THB adjusted for a constant inflation rate of 3% yearly based on compound interest from 2017 to 2022. The results revealed that at the threshold of 160,000.00 THB, merely 21.0% of cases were deemed cost-effective. At the threshold of 176,312.65 THB, it increased to 48.3%, and at the threshold of 185,483.85 THB, 62.0% was considered cost-effective.

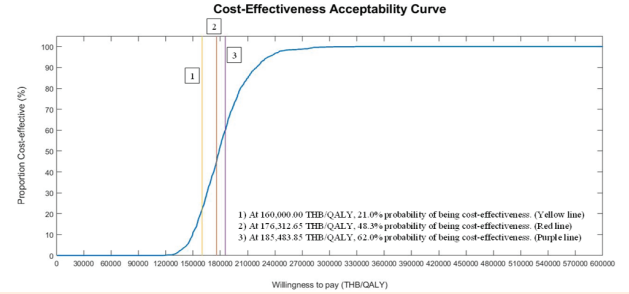

Figure 5: Cost-effectiveness acceptability curve of Monte Carlo simulation. The three lines indicate probability of cost-effectiveness using different thresholds. 1) Yellow line shows threshold of 160,000.00 THB/QALY indicating 21.0% cost-effectiveness, 2) Red line shows threshold of 176,312.65 THB/QALY indicating 48.3% cost-effectiveness, and 3) Purple line shows threshold of 185,483.85 THB/QLAY indicating 62.0% cost-effectiveness.

Discussion and Conclusion

Our novel oral cancer screening model shows the highest coverage level and the largest volume of targeted inhabitants that can be reached in Thailand. This will ultimately be more cost-effective than late diagnosis. Therefore, this model can be employed as a government policy for a more budget-efficient early detection and treatment of oral cancer. We generated this model based on the health region structure of Thailand in the ninth region which is representative of national oral cancer incidence. Additionally, we investigated the cost-effectiveness of this screening model utilizing collected data for the input parameters of the simulation. The results showed the ratio of ICER to GDP per capita in 2022, indicating that this oral cancer screening model is cost-effective according to WHO guidelines [13]. The strengths of the proposed screening model are cost-effectiveness in early-stage cancer detection with simple treatment and a decrease in the financial burden for late-stage cancer. The data showed that 24 of 25 cancers were found in stage I through the discovery of pre-cancer lesions in screening (96%). By contrast, with non-screening only 40% of cases are detected early. This increases government health burdens for treating late-stage cancer, the mortality rate remains high, and the quality of life is low. Thus, we conclude that our proposed oral cancer screening model is cost-efficient.

Our results contradict the 2018 study in Thailand [6] which showed that oral cancer screening was cost-ineffective. This is because several steps in the flow of our screening model were improved which we attribute to four key factors: (1) the reduction of unnecessary steps, (2) an increase in the incidence of oral cancer, (3) an increase in the GDP of Thailand, and (4) an increase in the cost-effectiveness threshold due to inflation. To explain further, first, we eliminated several ineffective steps in our screening model such as mouth self-examination, which simplified the process and lowered dropout rates, and incorporated existing health structures. Second, the incidence of oral cancer in Thailand increased from 4.9 cases per 100,000 persons in 2013-2015 (1) to 5.2 cases per 100,000 persons in 2019 (2). There were 6.4 cases per 100,000 persons found by our screening associated with increased incidence. As there may be concealed cancer patients who were never screened, this number is more realistic. Third, the increase in the GDP of Thailand made the cost-effectiveness threshold higher than that in 2018. Our study displays ICER calculated from simulation 0.8 times GDP per capita in 2023. Fourth, there was an increase in the cost-effectiveness threshold for the cost-effectiveness acceptability curve. According to the previous study in Thailand, in 2018, the willingness-to-pay cost-effectiveness threshold in Thailand was 160,000 THB indicating cost-ineffectiveness. However, the topic of a cost-effectiveness threshold is an ongoing discussion. A recent study in 2023 showed that there are two aspects for determining cost-effectiveness thresholds which are calculated from GDP per capita and determined by other factors [17]. England and Thailand determined their thresholds explicitly while other countries did not [18]. In 2007, Thailand determined the threshold as 100,000 THB/QALY which was 0.8 times GDP per capita [19]. In 2010, it was changed to 120,000 THB/QALY to maintain 0.8 times GDP per capita. In 2013, it was reconsidered as 160,000 THB/QALY. However, in 2015, a study on the cost-effectiveness threshold in Thailand suggested that 160,000 THB/QALY seemed to be lower than it should be. They suggested that around 240,000 THB/QALY was more suitable [20]. They also suggested that the willingness to pay was dependent on a patient's perception of the severity of the disease. We considered utilizing 160,000 THB/QALY as an optional threshold in this study but added a 3% yearly inflation rate from 2018. Around 185,000 THB/QALY was obtained, and this supported the cost-effectiveness of our model. This suggests that the 160,000 THB/QALY may be lower than it should be. Therefore, our screening model is considered cost-effective by the WHO criteria and the national threshold.

Typically, the efficacy of a screening model is based on 4C criteria, namely: coverage, completeness, compliance, and continuity. Given that our model was based on the healthcare structure in Thailand, we are in line with these criteria. For coverage, around 90% of the targeted inhabitants were captured in the implementation of this model. The VHVs are key as they can reach every targeted inhabitant directly and recruit them in a screening process. This study is the first to capture such a large number of targeted inhabitants and achieve this degree of coverage in oral cancer screening in Thailand. Our model can be used for oral cancer screening in other regions of Thailand as they have the same accessible healthcare structure and the same process of recruiting individuals for screening [21].

The reduction of screening model complexity, mouth self-examination, and taking benefits from the healthcare structure enhances the participation rate of targeted inhabitants. Active screening within the community and the facilitation of post-cancer treatment allowed our model to reach completeness. Each screening step was improved as follows: In S1, only one history of risk factor was used to recruit the targeted inhabitants in screening. In S2, dental hygienists perform conventional oral examinations. The difference in competency between dental health professionals and students in diagnosing oral mucosal lesions was lessoned (10) by providing the option of an 'uncertain' diagnosis in this step. We reduced workload stress in our design to prevent slacking from screening duty. To reduce false negatives, training for normal soft tissue detection was conducted with dental hygienists. Sensitivity and specificity evaluations were alleviated due to the inclusion of the targeted inhabitants into S3 and the addition of the 'uncertain' option. However, sensitivity and specificity of

conventional oral examination in detection of soft tissue change were evaluated in literature at 0.85 and 0.97, respectively [22]. Non-medical or non-dental and healthcare workers showed similar results [23-29]. In S3, specialists examined the oral cavity. A biopsy was prescribed by specialists due to clinical impressions and the specimens were interpreted by an oral pathologist specialist at Mahidol University. With this, more inhabitants were included in the screening, resulting in higher costs. However, it remained cost-effective as it decreases the long-term cost of treatment through early-stage cancer detection.

Decreasing the complexity of the model by eliminating mouth self-examination can enhance compliance indirectly due to drop-out rate reduction. Moreover, our model was designed to have an alert system to warn non-participating inhabitants and VHVs to track their participation. Compliance testing is a crucial step. The alert system is not in use owing to COVID-19 restrictions, but it is also cost-effective. For continuity, it is challenging to ensure sustainable screening without a stable public health policy. This study accordingly aimed to extend systemic screening to policymakers as we believe our model to be effective. Moreover, the real sustainability of this model regarding continuity is the direct transfer of knowledge and technology from the specialists and the tertiary care units to the secondary care unit. This ensures that they can adequately care for oral cancer and other related patients.

The limitations of our model are the lack of PMD in simulating both screening and non-screening scenarios as no PMD statistics are available; utility value obtained from literature was with the trade-off method. Further, we did not assess the long-term psychological effect. Our study shows that the proposed screening model is feasible to implement for oral cancer screening, but further developments are required. A remaining issue is evaluating the relationship between risk factors and their history to divide into high- and low-risk groups. Screening in high-risk group appears to be more cost-effective [30]. The evaluation of an alert system and effective tracking could also be implemented. Another important issue is the study of malignant transformation of PMD in both continuous treated and non-continuous treated groups which is the barrier to completely performing the cost-effectiveness of oral cancer screening model assessments [31-33]. These are areas for further research.

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Author Contributors

B.K., and N.J. conceptualized the overall study. B.K., S.P.K., and K.A. formulated the study aims and goals. B.K., and K.A. participated in this novel oral cancer screening model. B.K., S.P.K., K.A., and S.T. conducted the clinical examination process. B.K. collected the data. B.K., and N.J. extracted the data features. B.K., and N.J. formulated the mathematical model representing the oral cancer screening model and performed the simulation process. B.K., V.S., K.A., and N.J. participated and conducted all analyses in this study. N.J. drafted and revised the manuscript under critical review of S.P.K. The data was verified by B.K., V.S., S.T., and N.J. who enabled to access all data throughout the study.

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