



# FIRST EVIDENCE FROM A RANDOMISED TRIAL THAT SCREENING REDUCES ORAL CANCER MORTALITY:

## THE TRIVANDRUM ORAL CANCER SCREENING STUDY (TOCS), KERALA, INDIA

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### Background

Oral cancer accounted for **274,300** new cases and **145,500** deaths annually in the world around 2002, two-thirds of which occurred in developing countries. Tobacco use in any form and alcohol drinking are major risk factors for oral cancer. Most invasive oral cancers are preceded by precancerous lesions and preclinical early invasive cancers that can be identified by visual inspection of the oral cavity. Oral cancer is thus potentially amenable to primary and secondary prevention. We describe here the findings after 3 rounds of oral screening at 3-year intervals in a cluster randomised controlled trial in Kerala, India.

### Study location-Trivandrum, Kerala, India



Notional map showing Trivandrum, Kerala, India

### Objectives

- To evaluate the efficacy of screening by visual inspection of the oral cavity in detecting early stages of oral cancer and in reducing mortality
- To evaluate the cost-effectiveness of intervention



### Methodology

- 13 clusters randomised to intervention (N=7) and control (N=6) groups
- 96,517 in the intervention and 95,356 in the control group
- Information on socio-demographic factors and habits collected for both intervention and control cohorts
- Education on the harmful aspects of tobacco/alcohol use for the intervention and control cohorts
- Between 1996-2004, 3 rounds of oral visual inspection at 3-year intervals provided to eligible individuals ( $\geq 35$  years) in the intervention group by trained health workers
- Screen positive cases referred for physician confirmation/biopsy
- Precancer cases were advised cessation of habits and were prescribed medication or surgical excision
- Oral cancer cases were treated by radiation and/or surgery according to the stage at diagnosis

### Criteria for screen positivity

Presence of one or more of the following lesions:

- White, red, nodular lesions suggestive of leukoplakia/erythroplakia
- Lesions suggestive of lichen planus
- Oral submucous fibrosis
- Suspicious ulcer/growth



### Referral investigations:

- Clinical examination by dentist or clinical oncologist
- Histological examination

### Monitoring and Evaluation:

#### Process measures:

- Participation in screening
- Screen (test) positivity
- Compliance with referral for reference investigators



### Intermediate outcomes:

- Detection rates of precancers and cancer
- Programme sensitivity
- Positive predictive value of screening test to detect both precancers and invasive cancer
- Stage distribution of cancers
- Survival/case fatality rate

### Final outcome:

- Reduction in mortality from oral cancer
- Sources of data:**
- Study database
  - Population-based cancer registry
  - Mortality registration offices
  - Death records from churches/mosques
  - Active follow-up by home visits and telephone inquiries

### Results:

#### Distribution of personal habits by sex and study groups:

	Males			Females		
	Intervention	Control	P-value	Intervention	Control	P-value
Number enumerated	41 540	41 954		54 977	53 402	
No habits (%)	26.5	33.4	0.15	72.6	79.3	0.20
Chewing (%)	29.7	25.2	0.78	26.5	20.1	0.15
Smoking (%)	62.9	55.5	0.046	2.9	1.1	0.06
Alcohol (%)	42.7	36.9	1.00	0.2	0.2	0.12

### Screening history:

Screening history	Total
Persons invited	96 517
Not screened	8 862 (9.2%)
Screened once	34 343 (35.6%)
Screened twice	24 210 (25.1%)
Screened thrice	29 102 (30.2%)
Subjects with referable lesions	5 145
Subjects complied with referral	3 218 (62.5%)*

\* Percentage of subjects with referable lesions



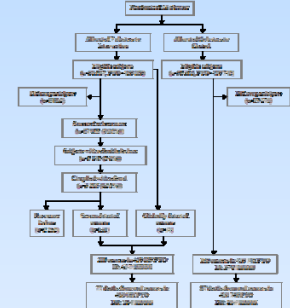
### Stage distribution of incident cases of oral cancer by study cases

Stage	Intervention group				Control
	Screened	Not screened	Prevalence	Risk	
I	48 (48.0%)	1 (1.0%)	1 (0.002%)	0.02	28 (12.5%)
II	23 (23.0%)	2 (2.0%)	1 (0.002%)	0.04	17 (7.5%)
III	22 (22.0%)	12 (12.0%)	1 (0.002%)	0.04	27 (12.0%)
IV	35 (35.0%)	24 (24.0%)	2 (0.002%)	0.07	38 (16.5%)
Unknown	5 (5.0%)	4 (4.0%)	4 (0.002%)	0.16	17 (7.5%)
Total	133 (133.0%)	50 (50.0%)	12 (0.002%)	0.23	127 (55.0%)

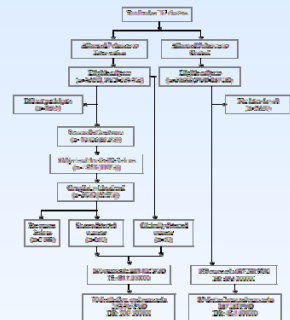
Person-years of observation (PYO), oral cancer cases, deaths, incidence and mortality rates, and rate ratios (RR) among all eligible subjects, eligible subjects with or without tobacco/alcohol drinking habits

Group	Intervention		Control		PYO (PYO/G)
	Screened	Not screened	Screened	Not screened	
Overall	271 155	271 155	271 155	271 155	10 000 000
With tobacco/alcohol	271 155	271 155	271 155	271 155	10 000 000
Without tobacco/alcohol	271 155	271 155	271 155	271 155	10 000 000
With tobacco/alcohol	271 155	271 155	271 155	271 155	10 000 000
Without tobacco/alcohol	271 155	271 155	271 155	271 155	10 000 000

### Study profile of all eligible subjects



### Results among persons with tobacco/alcohol habits



### Conclusions

- Good participation for screening (~ 90%)
- Moderate compliance to referral (~62%)
- A significant early detection of oral cancer (stage I & II) by visual inspection (**41.5% vs. 23.5%**)
- Significant (**34%**) reduction in oral cancer mortality among individuals with tobacco/alcohol habits
- Risk of disease extremely low among persons with no tobacco/alcohol habits
- Potential to prevent **37,000 oral cancer deaths** world-wide

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Sankaranarayanan R, Ramadas K, Thomas G, Muvonge R, Thara S, Mathew B, Rajan B. Trivandrum Oral Cancer Screening Study Group. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. *Lancet*. 2005 Jun 21; 365(9475): 1927-33.

### Chart for Visual inspection of the oral cavity:

Quick Clinical Reference Chart for Visual Inspection of the Oral Cavity to Detect Precancerous Lesions and Invasive Cancers

