Can India hit the target ? Cervix Cancer Control Program in Tamil Nadu State as a case study

MALLIGA J S MD

ASSOCIATE PROFESSOR

GYNEC ONCOLOGY/PREVENTIVE ONCOLOGY

prevonco@gmail.com, js.malliga@cancerinstitutewia.org

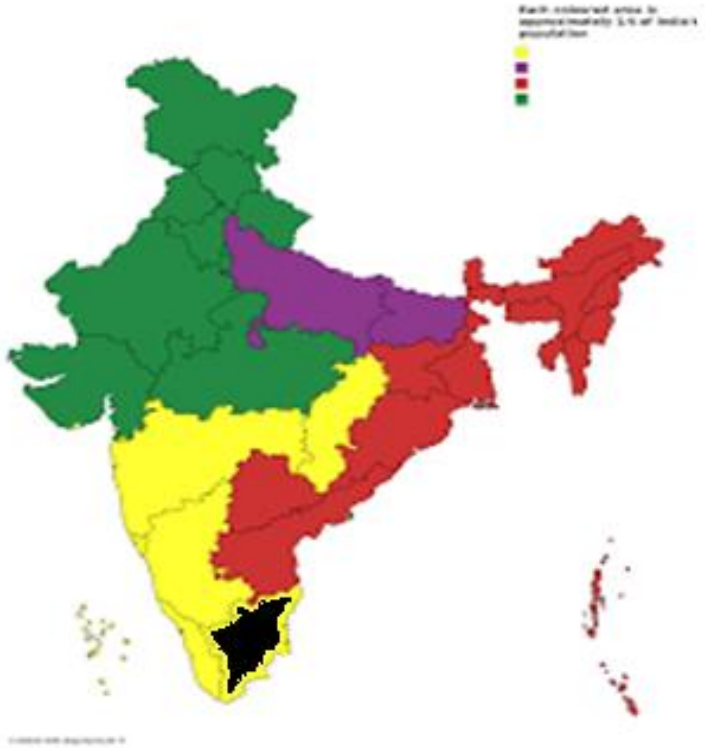
NO CONFLICTS OF INTEREST

INDIA

- SA country- most populous country in the world with one-sixth of the world's population.
- 2022 estimates stood at over 1.42 billion with 0.7 B female population
- 28 states and 8 Union territories

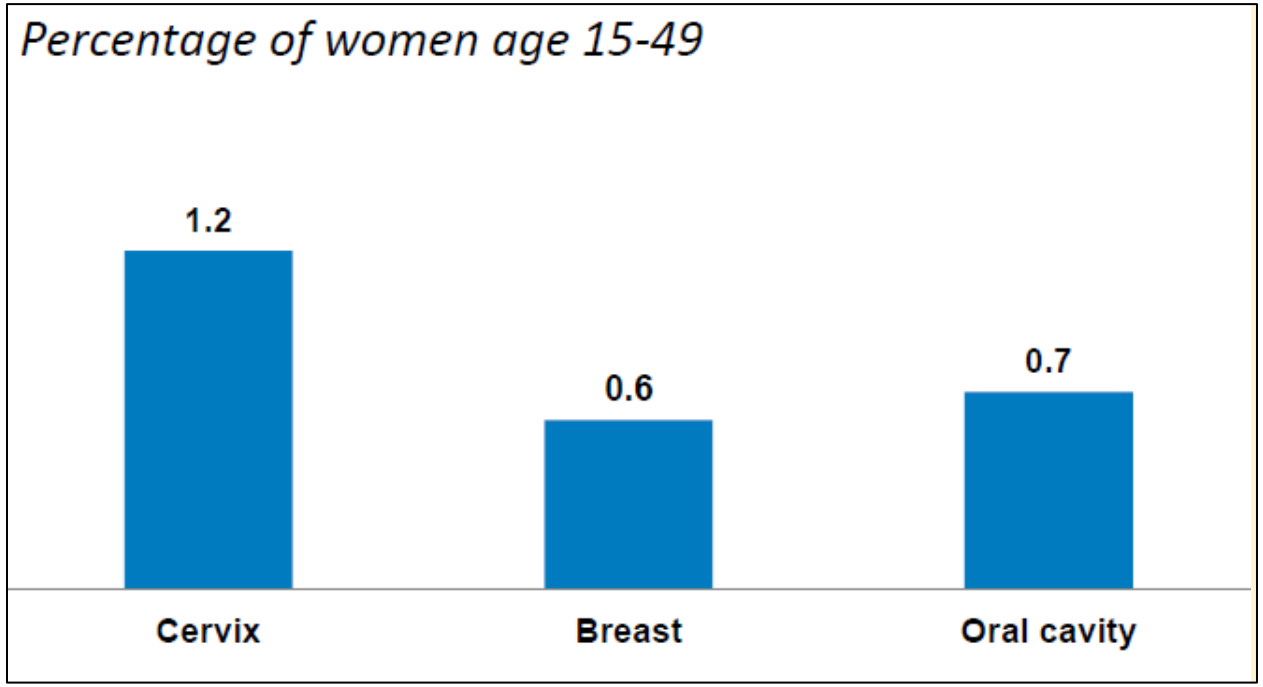
TamilNadu Southernmost State –

7.21 million



National Family Health Survey (NFHS-5) 2019-21

Provides information on population, health, and nutrition for India and each state/union territory (UT).



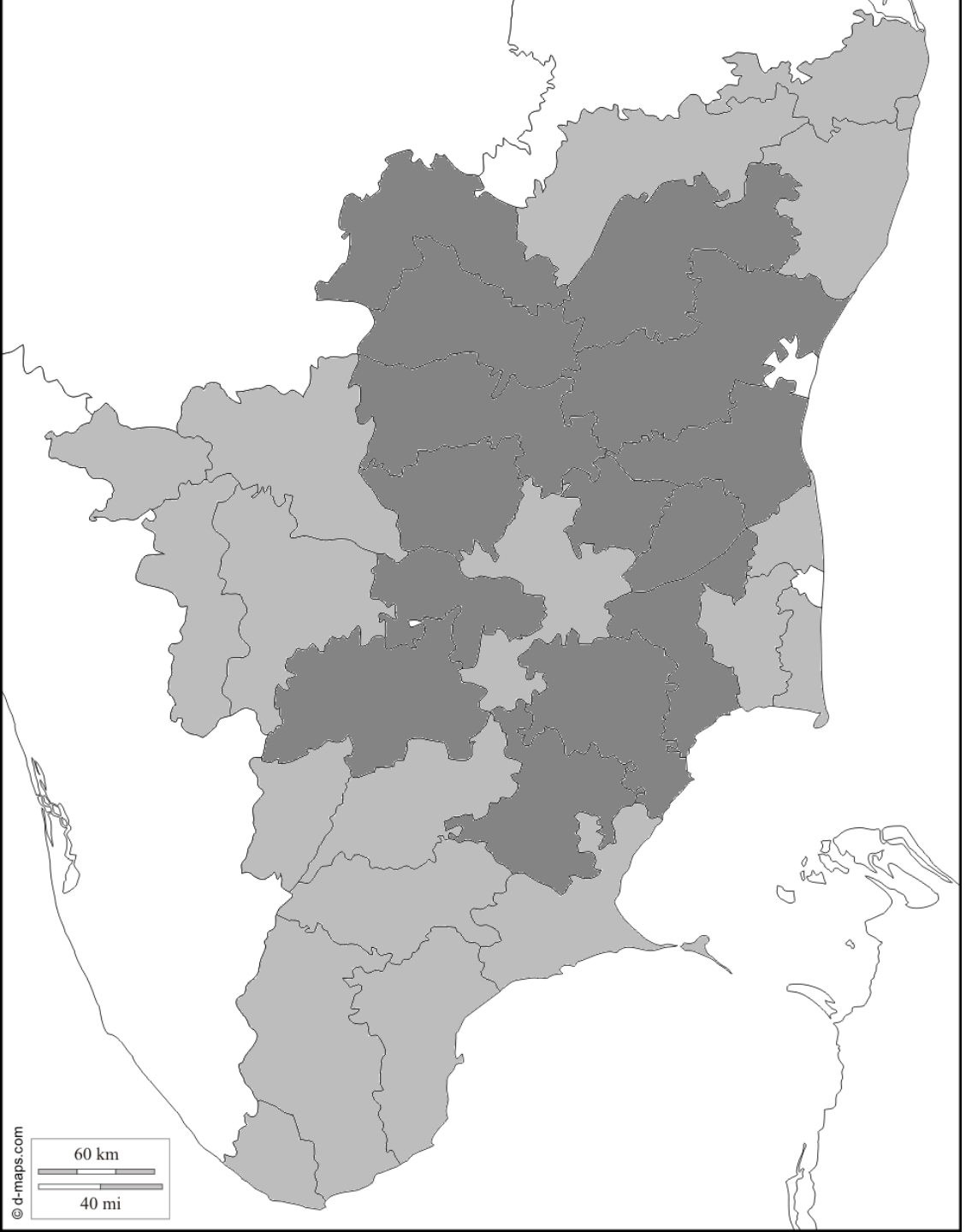
https://main.mohfw.gov.in/sites/default/files/NFHS-5_Phase-II_0.pdf

Table 12.8 Screening tests for cancer by state/union territory

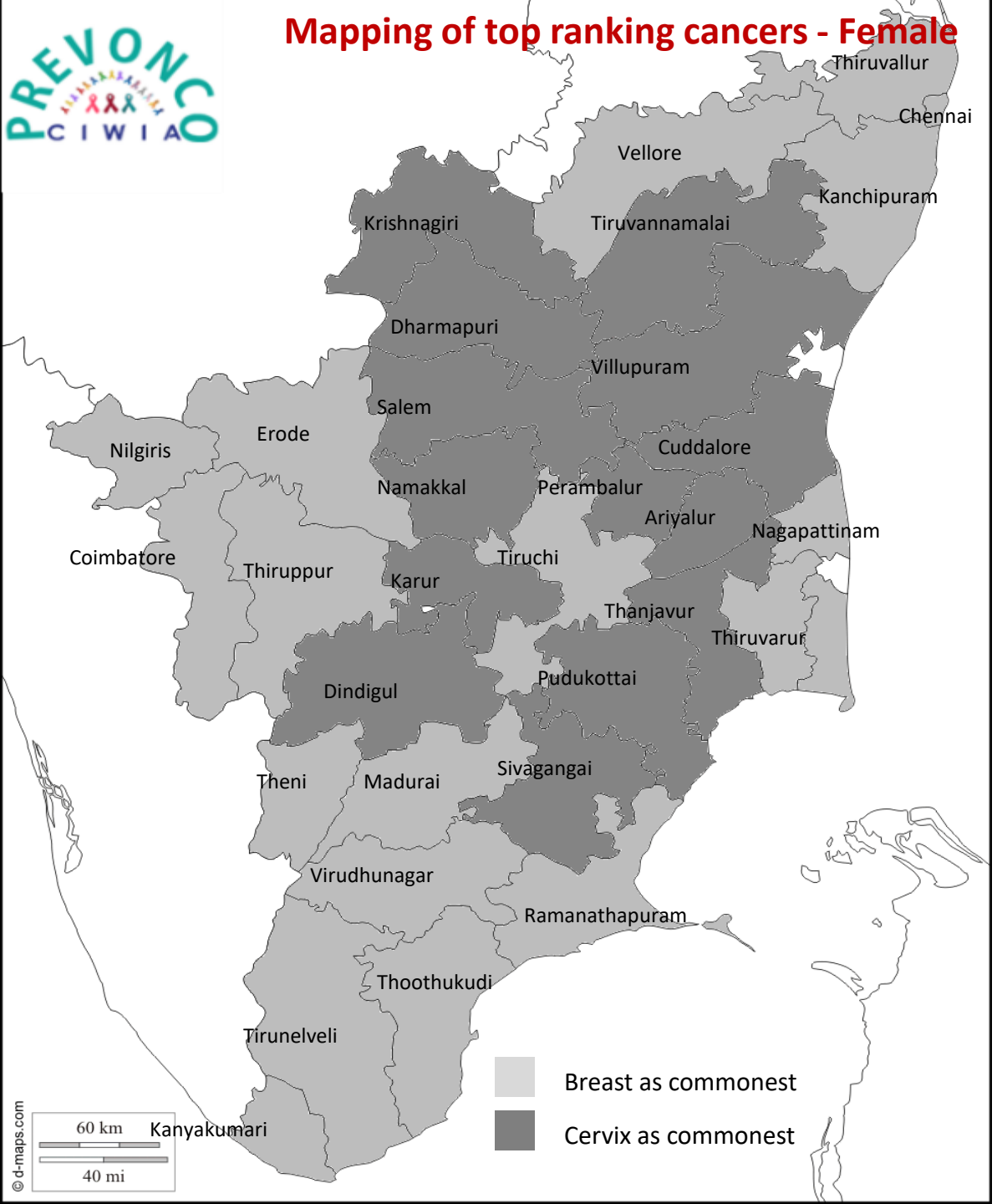
Percentage of women age 15-49 who have ever undergone specific screening tests for cancer, and percentage of men age 15-49 who have ever undergone an oral cavity screening test for oral cancer, by state/union territory, India, 2019-21

State/union territory	Type of examination undergone			Oral cavity screening test for men
	Cervix	Breast	Oral cavity	
India	1.2	0.6	0.7	0.2
North				
Chandigarh	0.9	0.0	0.2	0.1
Delhi	0.4	0.2	0.7	0.1
Haryana	0.5	0.2	0.3	0.2
Himachal Pradesh	0.7	0.3	0.3	0.1
Jammu & Kashmir	0.3	0.2	0.6	0.1
Ladakh	0.2	0.2	0.1	0.0
Punjab	1.9	0.3	0.4	0.1
Rajasthan	0.3	0.1	0.2	0.1
Uttarakhand	0.3	0.1	0.3	0.1
Central				
Chhattisgarh	0.3	0.2	0.2	0.2
Madhya Pradesh	0.7	0.5	0.7	0.1
Uttar Pradesh	1.0	0.3	0.6	0.2
East				
Bihar	0.5	0.2	0.3	0.2
Jharkhand	0.4	0.1	0.2	0.1
Odisha	0.7	0.1	0.2	0.1
West Bengal	0.1	0.1	0.1	0.1
Northeast				
Arunachal Pradesh	0.7	0.3	0.4	0.2
Assam	0.2	0.2	0.2	0.3
Manipur	1.3	1.0	0.6	0.1
Meghalaya	0.4	0.3	0.4	0.1
Mizoram	3.8	1.6	0.7	0.1
Nagaland	0.2	0.2	0.3	0.1
Sikkim	0.5	0.2	0.6	0.3
Tripura	0.4	0.3	0.4	0.0
West				
Dadra & Nagar Haveli and Daman & Diu	0.4	0.1	0.1	0.1
Goa	0.9	1.0	0.5	0.3
Gujarat	0.2	0.1	0.2	0.1
Maharashtra	1.7	1.0	1.0	0.1
South				
Andaman & Nicobar Islands	1.9	1.3	9.5	0.7
Andhra Pradesh	3.2	0.6	5.0	0.8
Karnataka	0.5	0.2	0.4	0.1
Kerala	2.3	1.5	0.5	0.1
Lakshadweep	1.2	0.3	0.2	0.1
Puducherry	5.3	2.9	1.2	0.2
Tamil Nadu	7.0	3.8	0.9	0.2
Telangana	2.1	0.3	1.8	0.4

Note: The questions on screening tests for cancer were asked in the biomarker questionnaire, so they include some respondents who were eligible for the biomarker questionnaire, but who may not have completed the individual women's or men's questionnaire.


60 km
40 mi
© d-maps.com

Mapping of top ranking cancers - Female



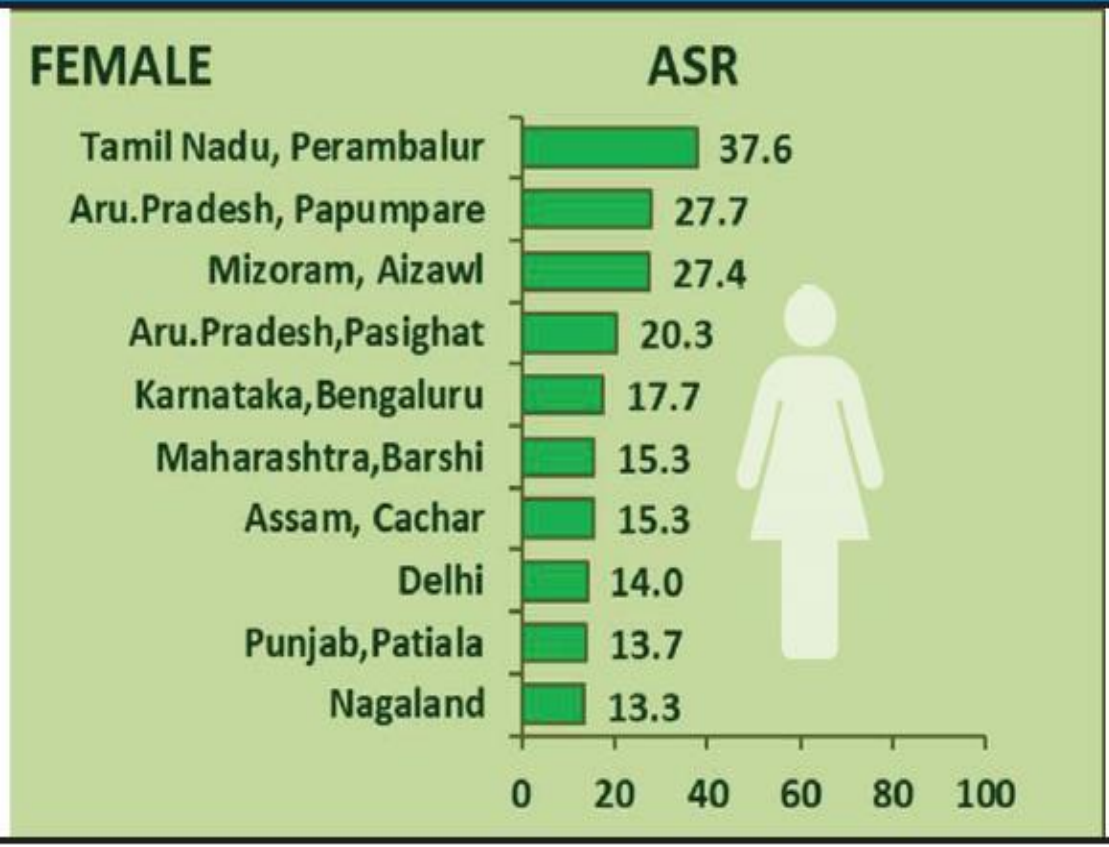
YEAR 2016

Incidence Statistics, Tamil Nadu	
	Female
New Cases	7545
% to all cancers	20.6
C.I.R	19.4
C.R%	1.989
A.S.R	17.3

Top Ranking States/Registries: Comparison of National and TNCRP 201

Source: National Cancer Registry Program, 2012-2016

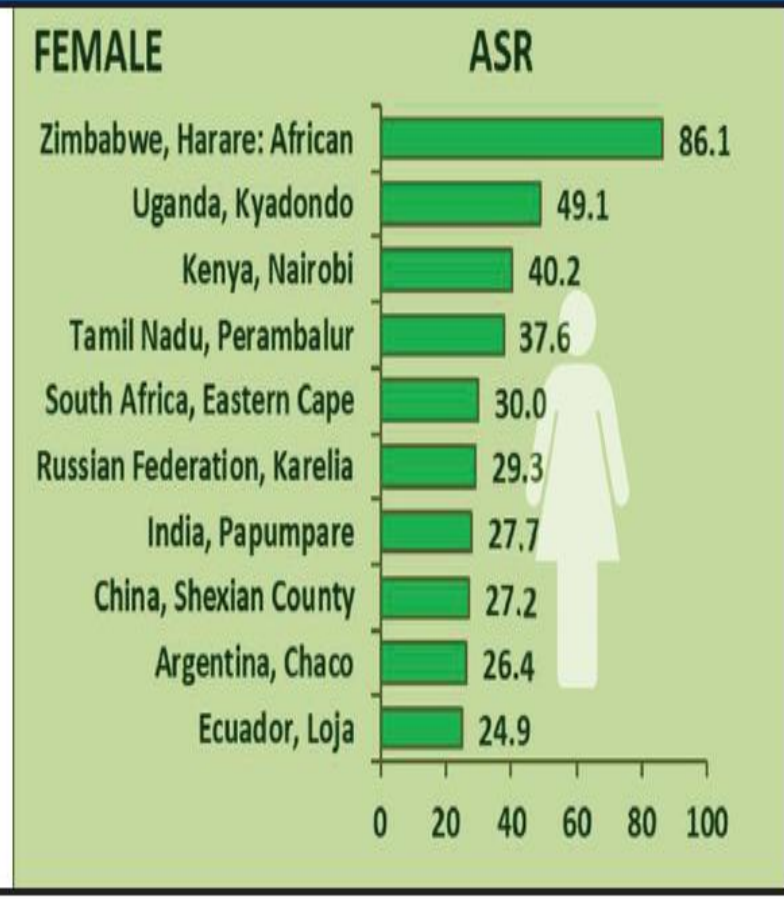
(period varies for individual registries)



Top Ranking Countries/Registries: International (2008-12) vs. TNCRP 2016 data

Source: IARC Scientific Publications No. 162, Cancer Incidence in Five Continents, Vol XI

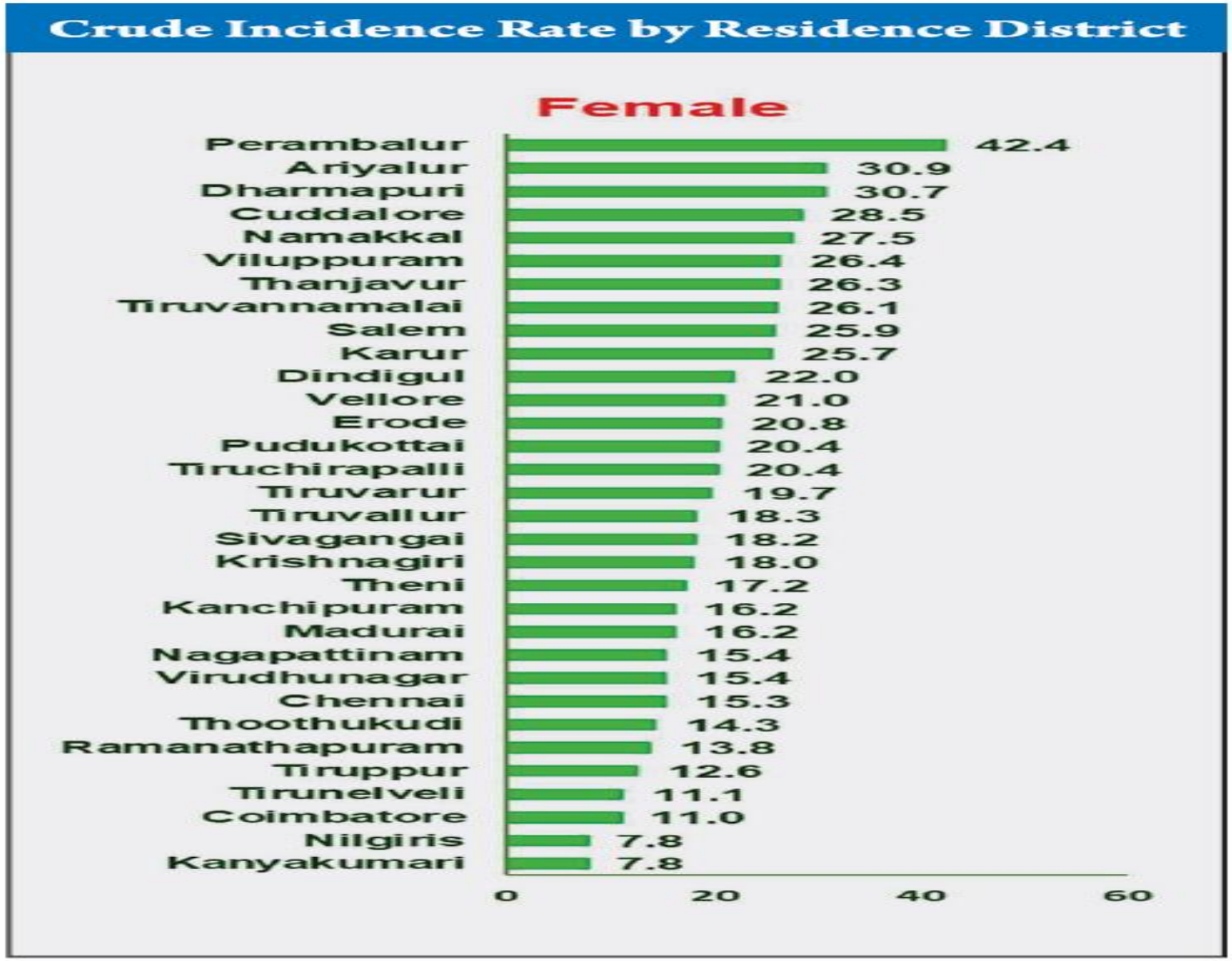
https://ci5.iarc.fr/CI5-XI/Pages/summary_table_site_sel.aspx



Trend - Cervix cancer, Tumour Stage, Cancer Institute (WIA), Chennai

Stage	1980-89 (n=5310)	1990-99 (n=5113)	2000-06 (n=3884)	2007-12 (n=2603)
	%	%	%	%
I	6.9	8.7	10.8	14.5
II	42.8	45.6	53.2	58.8
III	47.7	42.5	32.8	22.7
IV	0.4	1.1	1.3	1.9
SNP	2.2	2.1	1.9	2.1
TOTAL	100.0	100.0	100.0	100.0

Downstaging observed over time: Stage I has more than doubled in 25-30 years



CIR, ASR and Rates are per 1,00,000 population

Evidence on Screening

Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial

Rengaswamy Sankaranarayanan, et al *The Lancet*, August 4, 2007.

Comparative efficacy of visual inspection with acetic acid, HPV testing and conventional cytology in cervical cancer screening: a randomized intervention trial in Osmanabad District, Maharashtra State, India

Sankaranarayanan *et al*., N Engl J Med 2009;360:1385-1394

Effect of VIA Screening by Primary Health Workers: Randomized Controlled Study in Mumbai, India

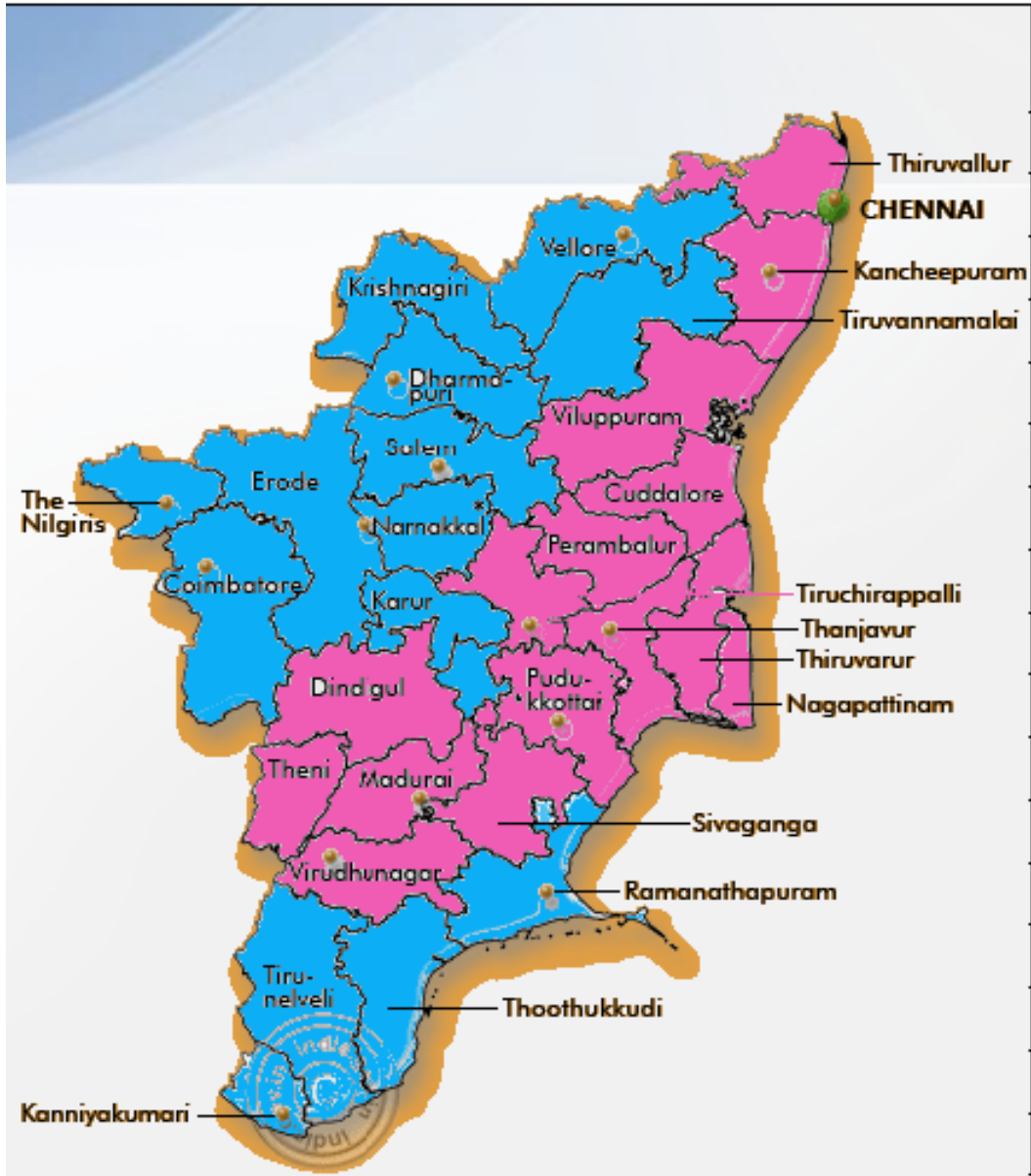
Surendra Shastri et al JNCI 2014 Mar; 106(3)

District level Pilot initiated in February 2007 by World Bank Supported Tamil Nadu Health Systems Project (TNHSP) in two districts –Theni and Thanjavur (Cervical cancer 2007-2010).

Key lessons learnt in the pilot and Gaps identified were carefully examined and incorporated in the scaling up strategy developed for state wide implementation.

https://www.capam.org/files/2016IIApresentations/ScalingUpCervicalCancerScreening-India.pdf

Scaling up to all 32 districts in a phased manner ; four NCDs



Phase I (16 districts) - 2012	Phase II (16 districts) - 2013
Thanjavur	Thiruvallur
Virudhunagar	Thiruvannamalai
Sivagangai	Vellore
Theni	
	Salem
Chennai	Namakkal
Cuddalore	Krishnagiri
Kanchepuram	Dharmapuri
Villupuram	Karur
Trichy	Coimbatore
Perambalur	Tirupur
Dindigul	Niligiris
	Erode
Nagapattinam	
Madurai	Tirunelveli
Thiruvarur	Thoothukkudi
Pudukottai	Kanniyakumari
	Ramanathapuram

TNHSP

An opportunistic screening program for cancer cervix and cancer breast was initiated in India since 2011 Tamil Nadu, (TNHSP)

Organised Screening Program for NCDs – since 2017 –

Phase I Pudukkottai, Krishnagiri, Perambalur

DM,HT, Common Cancers – Oral (VE&TCC), Breast (CBE), Cervix (VIA)

Senthilkumar& Kaur -2015

- *"surveyed 240 women with mean age of 44 years. Only 70 (29%) and 83 (35%) women agreed to undergo cancer cervix and cancer breast screening respectively. Overall, 167 (70%) had ever heard of cancer."* ***Clinical Epidemiology and Global Health*** *Volume 3, Supplement 1, 2015, Pages S63-S68*

Outcome of Screening (July 2012 - June 2016)

Target Population	Number screened	Screened (%)	Number positive	Positivity Rate (%)
1,44,49,595	1,17,33,084	81% of Target	3,87,691	3.30% Screened

Women who are VIA /VILI positive are followed up with Colposcopy and confirmed with Biopsy.

Staging and treatment based on Biopsy results

PROGRAMS IN THE PIPELINE 2023

NHM – 3 DISTRICTS –VISUAL TESTS

JICA – 3 DISTRICTS –HPV PILOT

BIVALENT VACCINE –SINGLE DOSE IN SELECTED POPULATION

ORGANISED CERVIX CANCER SCREENING: HPV DNA TESTING AS PRIMARY SCREENING TEST IN LIMITED RESOURCE SETTING

HPV SCREENING TEST AS A PRIMARY METHOD OF POPULATION BASED CERVICAL CANCER SCREENING –FEASIBILITY AND IMPLEMENTATION CHALLENGES, AMONG RURAL POPULATION OF VILLUPURAM

a. To study the feasibility of training health workers to collect and analyze cervix samples for HRHPV DNA

b. To study the effectiveness of combined HPV and visual tests in cervix cancer control in a limited resource setting

TOTAL POPULATION
697569

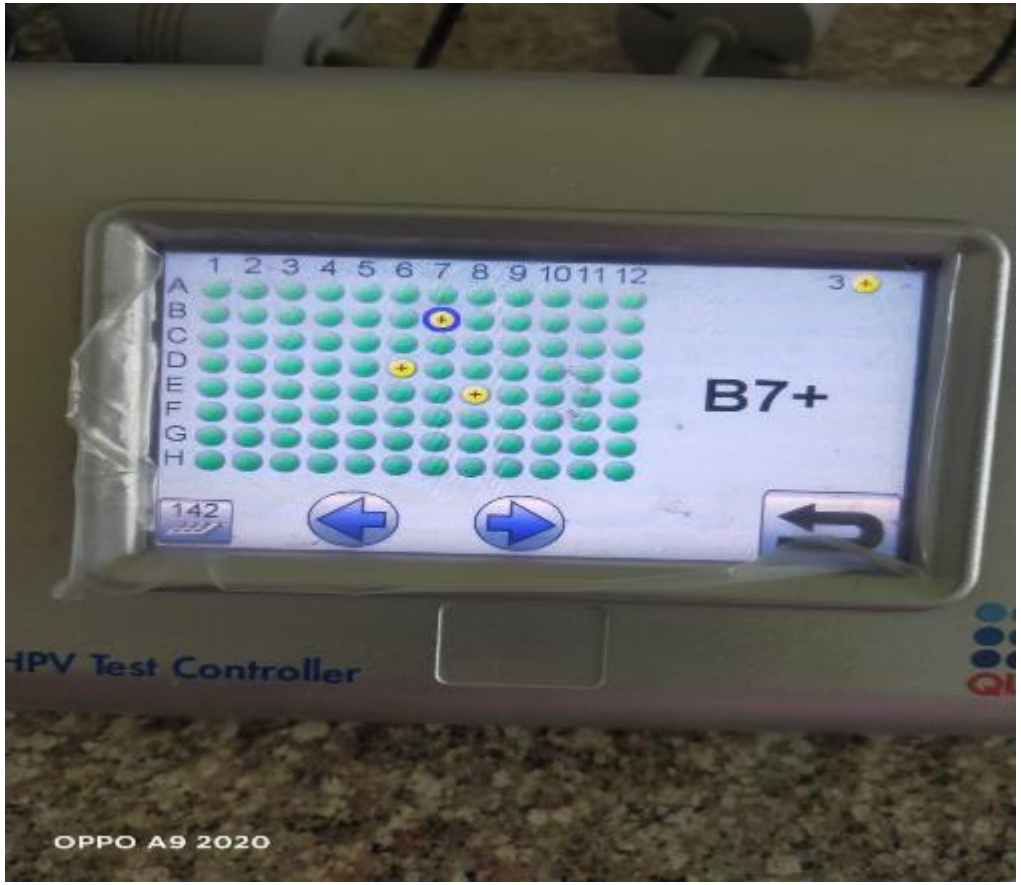
(2011 CENSUS)

VILLUPURAM SUBDISTRICT(TALUK)

WOMEN -
348163

TARGET
WOMEN (30-59
yrs) -104449

HPV DNA Testing –Rural Center



ALL THREE SCREENING TESTS

TOTAL SCREENED WOMEN	14565	PERCENT
HR- HPV+	1128	7.74
CYTOLOGY (ASC US+)	103	0.70
VISUAL TESTS –VIA/VILI	2708	18.59
CIN 2+	111	7.6/1000

TEST PERFORMANCE -TRIAGING

SEQUENTIAL/CO-TESTING	Sensitivity	Specificity	PPV	NPV
HR-HPV& ASC US	**92.79%** (86.29% to 96.84%)	**99.91%** (99.85% to 99.95%)	88.79% (81.60% to 93.90%)	99.94% (99.89% to 99.98%)
HR-HPV & ASC-H	**90.09%** (82.96% to 94.95%)	**99.93%** (99.87% to 99.97%)	90.91% (83.92% to 95.55%)	99.92%(99.86% to 99.96%)
HR-HPV & VISUAL TESTS	**64.86%** (55.23% to 73.69%)	**98.52%** (98.31% to 98.71%)	25.17% (20.25% to 30.62%)	99.73%(99.6 % to 99.81%)
HR-HPV/ ASCUS	**99.10%** (95.08% to 99.98%)	**92.92%** (92.49% to 93.33%)	9.70% (8.04% to 11.57%)	99.99%%(99.96% to 100.00%)
HR-HPV/VISUAL TESTS	**98.20%** (93.64% to 99.78%)	**76.19%** (75.49% to 76.89%)	3.07% (2.53% to 3.69%)	99.98% (99.93% to 100.00%)

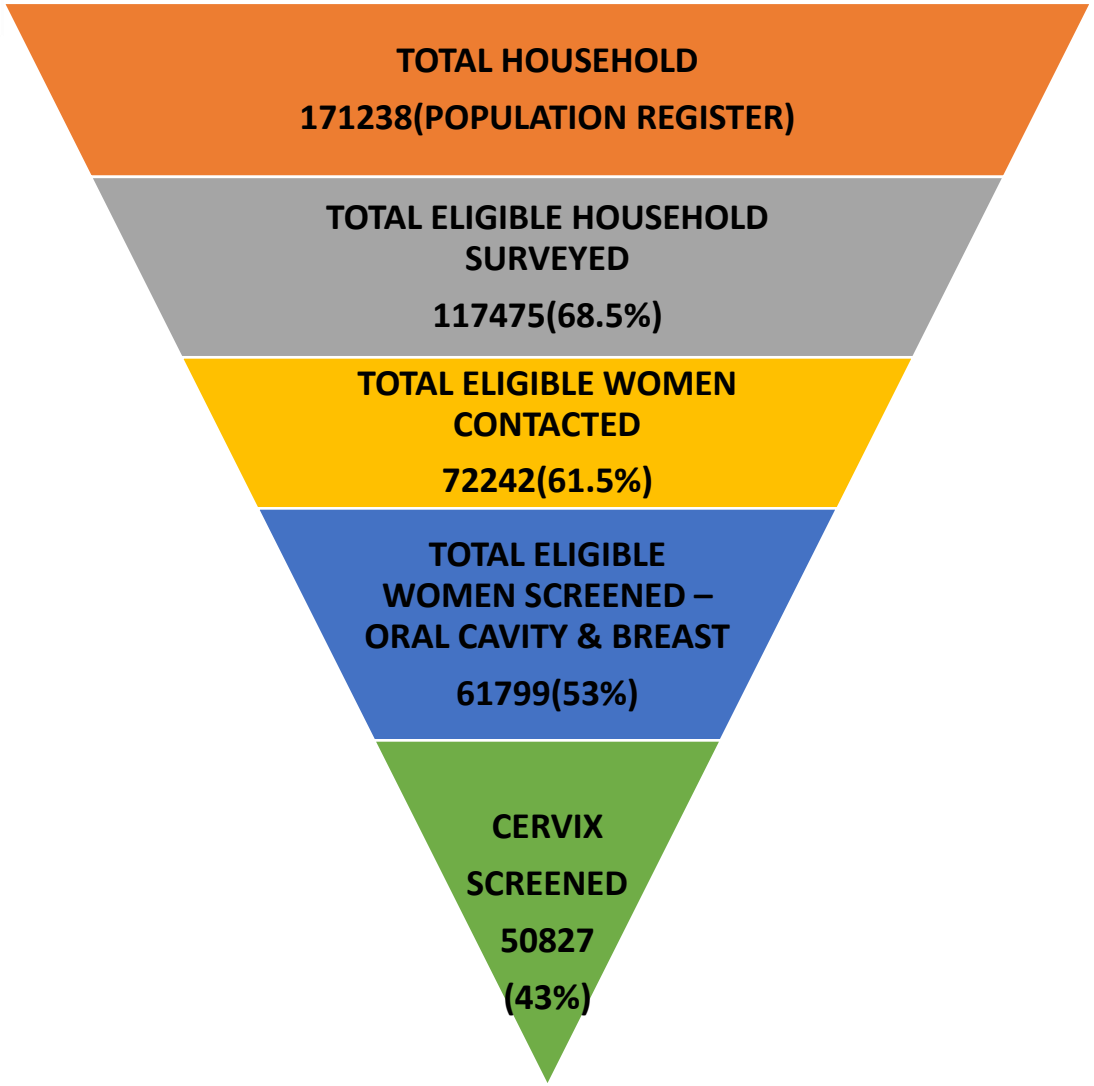
TRIAGING – VISUAL TESTS PICKED 66% OF CASES DIAGNOSED BY ASCUS +

HPV RUN DETAILS – 2015 TO 2022

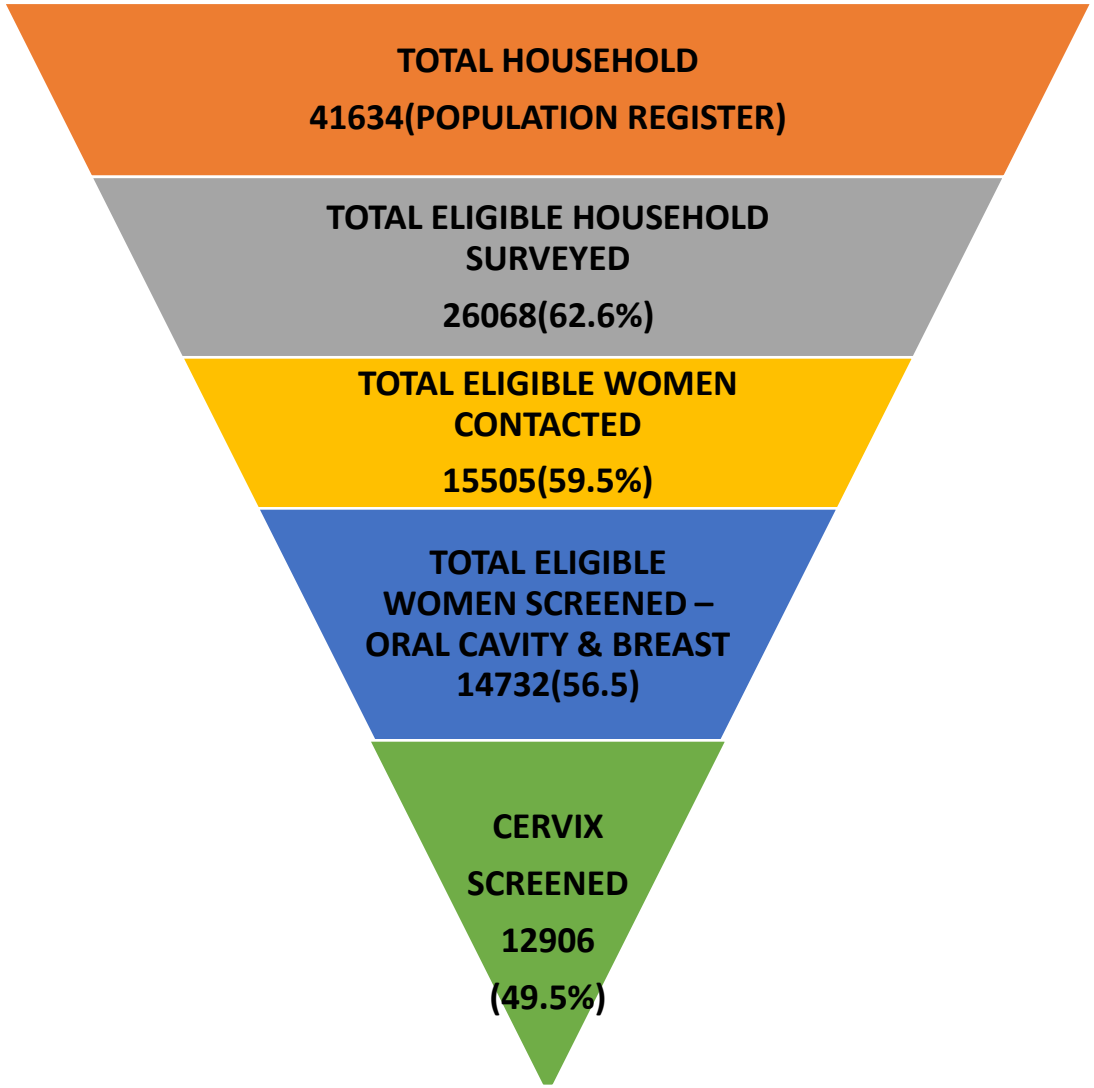
YEAR	TOTAL RUN	SUCCESS RUN	HIGH POSITIVE	ERROR
2015	42	26	07	09
2016	109	81	09	19
2017	143	137	02	04
2018	112	102	01	09
2019	111	104	03	04
2020	16	16	-	-
2021	43	38	03	02
2022 - 2023	58	51	05	02
TOTAL	634	555 (87.53%)	30 (4.73%)	49 (7.72%)

POPULATION SCREENING - CERVIX CANCER

VPM – 2015 TO 2022



TVM 2018 TO 2023(JAN)



Self sustainable, Low cost HPV testing

SI NO	PROJECT NAME	YEAR	TOTAL CERVIX SCREENED	HPV POSITIVE RATE	PRE CANCER	CANCER
1	VILLUPURAM	2015-2022	49860	3190 (6.4 %)	211	69
2	PUDUKKOTTAI	2018-2022	12108	915 (7.6 %)	33	14
3	TIRUVANNAMALAI	2019-2022	11682	934 (8.0 %)	47	14
4	SIVAGANGAI	2022	1598	119(7.4 %)	3	1
5	TOTAL		75248	5158(6.8 %)	294	98

CENTRALISED HPV TESTING (CRT –PHYSICIAN VS SS)

CHENNAI JUL 2019 – AUG 2022 N= 5779 (HPV Positive - 5.3%)

HPV GENO TYPE		BIOPSY						
		NORMAL	CIN I	CIN II	CIN III	CA INSTU	INVASIVE	REMARKS
HPV 16	32 (72)	11	6	5	6	1	3	
HPV 18	11 (30)	9	-	2	-	-	-	
OTHER HR HPV	61 (202)	30	13	6	5	-	1	5 (not done) 1 (Inconclusive)
HPV 16+18	2 (2)	-	1	1	-	-	-	
Total	106 (306)	50	20	14	11	1	4	6

IMPLEMENTATION PTP

	POINT OF CARE	CENTRALISED
COMPLIANCE TO TRIAGE	85-90%	50-70%
REPORT TAT	4-7 DAYS	10-15 DAYS
TREATMENT COMPLETION	48%	33%

16.10.2022 to 15.03.2023 -5 months		
	Care HPV Brush	Floq Swab
No of villages	17	14
Total Samples	1418	1218
HR-HPV Positive	93(6.5%)	67 (5.5%)

UNIVERSAL STM, UNIVERSAL SAMPLING BRUSH, RAPID TESTS WITH EFFECTIVE TRIAGING TESTS

SUMMARY- INTRODUCING HPV TESTS IN INDIA FOR POPULATION SCREENING

- Implementation Design – Test Availability
  Sampling Method
  Triaging
- Strengthening The Existing Resources – Training Of Personnel
  Linkage To Treatment Follow Up
  Data Capturing Monitoring
- Costs – Indigenous HPV Tests
  Universal Collection Medium
  Universal Collection Kit

Changing Dynamics

HR-HPV Prevalence Rate, Genotype

Triaging – Biomarkers

?Artificial Intelligence

HTA - Cost of screening

Screening strategy	Per patient screened			
	Sample collection/visual inspection	Laboratory processing	Support activities	**Total**
VIA	103	-	241	**344**
Pap test	118	293	241	**652**
HPV DNA	162	578	241	**980**

Prinja et al HTA Report Cx Ca Screening 2019

VACCINATION PLUS VIA ONCE IN FIVE YEARS

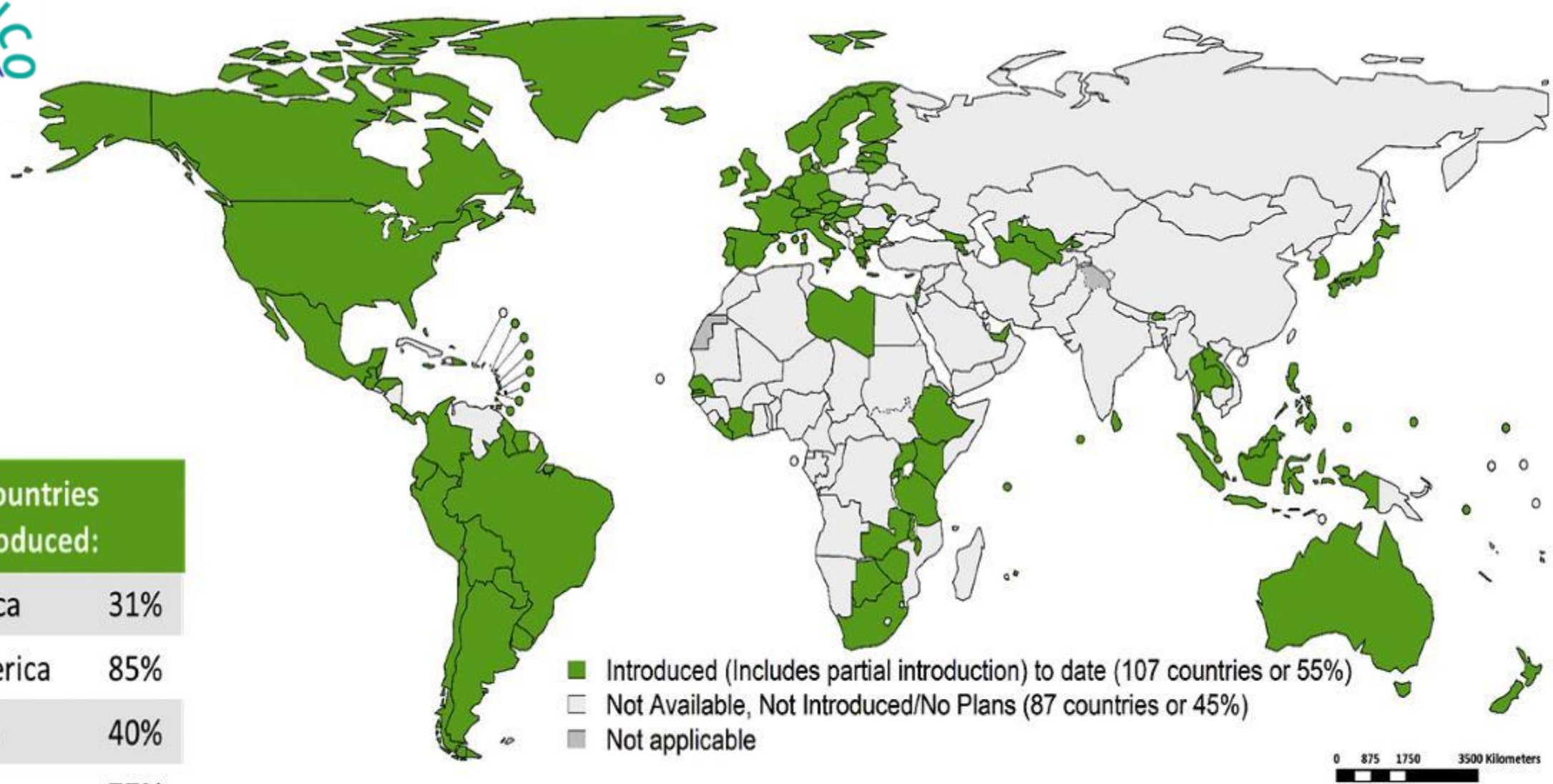
RESEARCH ARTICLE

Cost effectiveness of strategies for cervical cancer prevention in India

Akashdeep Singh Chauhan[1], Shankar Prinja[1]*, Radhika Srinivasan[2], Bhavana Rai[3], JS Malliga[4], Gaurav Jyani[1], Nidhi Gupta[5], Sushmita Ghoshal[3]

1 Department of Community Medicine and School of Public Health, Post Graduate Institute of Medical Education and Research, Chandigarh, India, 2 Department of Cytology and Gynaecological Pathology, Post Graduate Institute of Medical Education and Research, Chandigarh, India, 3 Department of Radiation Oncology, Post Graduate Institute of Medical Education and Research, Chandigarh, India, 4 Department of Preventive Oncology, Cancer Institute (WIA), Adyar, Chennai, India, 5 Department of Radiation Oncology, Government Medical College and Hospital, Chandigarh, India

PLOS ONE | https://doi.org/10.1371/journal.pone.0238291 September 1, 2020



% countries introduced:	
Africa	31%
America	85%
Asia	40%
Europe	77%
Oceania	56%

EVIDENCE AT HOME…….

Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study

Basu P, Malvi SG, Joshi S, Bhatla N, Muwonge R, Lucas E, et al Lancet Oncol, Published online 8 October 2021; https://doi.org/10.1016/S1470-2045(21)00453-8

- Systematic 10-year follow-up of a cohort of about 17 000 female participants who received the quadrivalent HPV vaccine at age 10–18 years demonstrated that the protection offered by a single dose of quadrivalent vaccine against persistent infection with HPV16 and HPV18 (the types responsible for nearly 80% of cervical cancers in low- and middle-income countries) was as high as that offered by two doses or three doses of the vaccine.

- The vaccine efficacy of a single dose against persistent HPV16/18 infection was 95.4%, which was not significantly different from the efficacy of two doses or three doses of the vaccine.

HPV vaccination appears to be a very cost-effective strategy for Punjab state, and is likely to be cost-effective for other Indian states.

Shankar Prinja et al Cancer 2017;123:3253-60.

Impact of human papillomavirus vaccination, Rwanda and Bhutan

Baussano I et al Emerg Infect Dis, Published online 21 Dec 2020

The prevalence of vaccine-targeted HPV types decreased sharply in consecutive surveillance studies, between the two surveys; the prevalence of other alpha-9 HPV types also decreased significantly, suggesting cross-protection.

Effectiveness of HPV vaccination against the development of high-grade cervical lesions in young Japanese women

Shiko Y, Konno R, Konishi H, Sauvaget C, Ohashi Y, Kakizoe T.
BMC Infect Dis, Published online 5 November 2020

The burden of cervical cancer can be decreased through HPV vaccination and cervical cancer screening.

HPV vaccination programs are the cornerstone to the WHO Global Strategy on Cervical Cancer Elimination

80% coverage of vaccination and screening of respective target groups can eliminate cervical cancer – WHO

Modelling Studies

- Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020–99: a modelling study
  Simms KT, et al. Lancet Oncol, Published online 19 February 2019;https://doi.org/10.1016/S1470-2045(18)30836-2

Widespread coverage of both HPV vaccination and cervical screening from 2020 onwards has the potential to avert up to 12·5–13·4 million cervical cancer cases by 2069, and could achieve average cervical cancer incidence of around four per 100 000 women per year or less, for all country HDI categories, by the end of the century

- Modelling based on existing HPV program in Finland shows that vaccination with moderate coverage eradicates oncogenic human papillomaviruses if a gender-neutral strategy is applied
  Vänskä S et al J Infect Dis, Published online 11 March 2020;

National Human Papilloma Virus (HPV) Vaccination Program (4vhpv) in Australia Since 2007, Initially For Girls Only Extended To Boys In 2013

Patel C, Euro Surveill. 2018 Oct;23(41):1700737. doi: 10.2807/1560-7917.ES.2018.23.41.1700737. PMID: 30326995; PMCID: PMC6194907.

- Decline in high-grade cervical disease and genital warts among vaccine-eligible women
- Reductions in genital warts incidence and HPV prevalence among heterosexual men

9vHPV vaccine is expected to prevent up to 90% of cervical and 96% of anal cancers.

WHO GOAL TO ELIMINATE – WHAT IT MEANS FOR INDIA?

- NATIONAL LEVEL - NP-NCD given impetus -NON COMMUNICABLE DISEASE CONTROL PROGRAMS –since 2010
- HPV Vaccination Programs – Indigenous – Towards Policy adoption
- Medical and Oncology Societies like FOGSI, AOGIN, ISCCP –Country-wide initiatives, focus on capacity building
- State-level initiatives to introduce HPV Screening and Vaccination pilot programs

CERVIX CANCER CONTROL GONE VIRAL

MAY NOT BE A BULL'S EYE FOR US

- Measurable impact in a decade, may take two decades for a complete picture
- Setting multiple revised targets for MDIs and LDIs may be necessary – to maintain the enthusiasm and the fever of action

WE ARE ON THE TRACK GRADUALLY INCREASING OUR PACE!!!

ACKNOWLEDGEMENT

Science without social relevance has little to it - M Gandhi

DR V SHANTA

THANK YOU!