



SECTION OF EARLY DETECTION AND PREVENTION (EDP)

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Prevention and early detection, including interventions to reduce exposure, screening, and early diagnosis, can decrease cancer incidence and mortality and improve quality of life. The Section of Early Detection and Prevention (EDP) is

composed of two groups: the Prevention and Implementation Group (PRI) and the Screening Group (SCR).

EDP carries out research on resource-appropriate public health policies and

feasible, quality-assured, and cost-effective prevention and early detection strategies for the control of common cancer types such as breast, cervical, colorectal, oesophageal, oral, and gastric cancer globally, with an emphasis

on low- and middle-income countries (LMICs). Prevention offers the most cost-effective long-term strategy for cancer control. The Section's main focus areas in primary prevention are the development and implementation of safe, effective, and affordable vaccination schemes for human papillomavirus (HPV)-related cancers and the evaluation of the impact of *Helicobacter pylori* eradication on gastric cancer. The major focuses of EDP's early detection research are assessing new technologies and alternative screening approaches, as well as the impact of improved awareness and access to health services for the

early detection of major cancer types such as breast, cervical, colorectal, and oral cancer.

The Section designs and conducts research studies in collaboration with investigators in national cancer organizations, health services, universities, and other key groups within and outside the Agency. EDP works closely with other international organizations to develop, implement, and promote effective strategies for preventing and controlling cancer in the context of national cancer control programmes. In the Section's studies, there is a

continuing emphasis on developing training resources, augmenting capacity for cancer prevention and early detection initiatives, and scaling up of prevention and early detection services within local health systems. The establishment of cancer research networks in LMICs to exchange experiences and enhance the local capacity is among EDP's priorities.

More recently, the Section has expanded its focus on implementation research, to support the efforts of national health systems to translate scientific findings into the well-being of the population.

PREVENTION AND IMPLEMENTATION GROUP (PRI)

The Prevention and Implementation Group (PRI) investigates cancer epidemiology and prevention, with a focus on HPV vaccines, *H. pylori* eradication for gastric cancer prevention, triage methods for HPV-positive women, and the promotion and evaluation of cervical cancer control programmes. Recently, PRI has included implementation research objectives in ongoing projects and national implementation activities, including consideration of the cost-effectiveness of preventive interventions.

CERVICAL CANCER STUDIES IN GUANACASTE, COSTA RICA

Given the demonstrated efficacy of the HPV vaccines against persistent infection with vaccine types regardless of the number of doses (one, two, or three) and stable antibody levels extending to 7 years, and considering the public health potential of one-dose vaccination, PRI is initiating a large randomized trial of the non-inferiority of one versus two doses of the bivalent and nonavalent vaccines. The ESCUDDO study will recruit 20 000 adolescent girls (ages 12–16 years) in Costa Rica, who will be randomized to receive the bivalent or nonavalent vaccine. At the 6-month visit, they will be randomized to a second dose of the same vaccine or a control vaccine (diphtheria–pertussis–tetanus). The study will evaluate the non-inferiority of one or

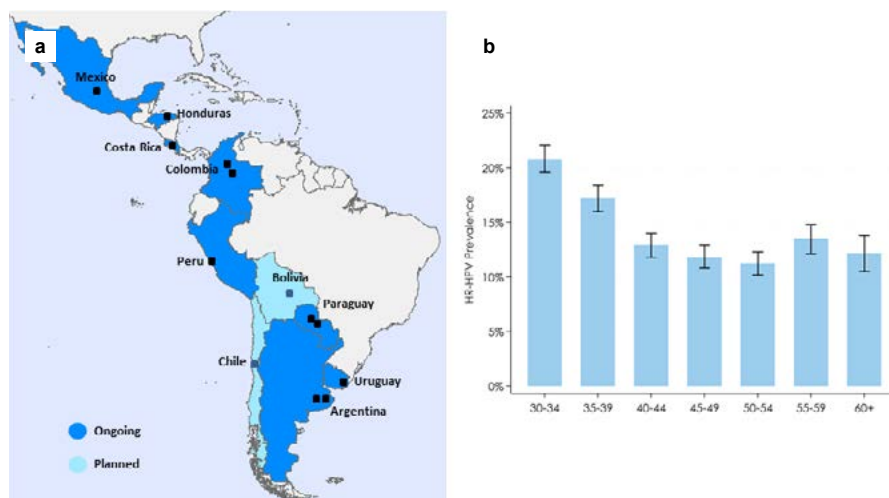
two doses for each of the two vaccines. In addition, approximately 4000 women aged 17–20 years will be recruited as a control group to estimate the efficacy of the vaccination schedules.

MULTICENTRE STUDY OF HPV SCREENING AND TRIAGE (ESTAMPA)

The ESTAMPA study investigates emerging cervical cancer screening and triage techniques in Latin America. About 50 000 women aged 30–64 years are being invited for HPV screening. All HPV-positive women receive colposcopy, biopsy, and treatment as needed, and are

recalled for a second screening after 18 months. The main outcome is precursors of advanced cancer. The performance of visual, cytological, and molecular triage methods will be evaluated. The study is under way in 11 centres (Figure 1a) (recruitment, ~23 500). Based on 22 390 study records, the global prevalence of high-risk HPV infection is 14.6% (95% confidence interval [CI], 14.2–15.1%), decreasing from 20.8% in those aged 30–34 years to 12.1% in those older than 60 years, and showing a second peak, of 13.5%, in women aged 55–59 years (Figure 1b).

Figure 1. The ESTAMPA study of HPV screening and triage: (a) map of study centres; (b) overall high-risk HPV prevalence by age group. © IARC.



The ENIGMA study investigates the prevalence of *H. pylori* infection, precancer, and cofactors in population samples from areas with high and low risks of gastric cancer. The study plans to assess age-specific infection prevalence as well as bacterial (including microbiome), host, and environmental factors that explain geographical patterns. ENIGMA has been completed in Chile and is under way in the Islamic Republic of Iran (Figure 2). Additional study sites include China, Colombia, Costa Rica, the Republic of Korea, and Uganda.

In collaboration with the National Cancer Center of the Republic of Korea, PRI is conducting a randomized controlled trial of *H. pylori* eradication for gastric cancer prevention (the HELPER study), which aims to recruit 11 000 subjects aged 40–65 years who are attending endoscopy within the National Cancer Screening Program (Park et al., 2017). *H. pylori*-positive subjects are randomized to quadruple eradication therapy or placebo. All participants (current recruitment, ~5000) will be routinely screened within the National Cancer Screening Program every 2 years for 10 years (Figure 3).

A randomized trial with the University of Latvia (GISTAR) aims to determine whether combined *H. pylori* and pepsinogen screening followed by eradication therapy in *H. pylori*-positive subjects and endoscopic follow-up of those with serological atrophic gastritis reduces gastric cancer mortality compared with standard care (Leja et al., 2017). The study aims to recruit 30 000 subjects aged 40–64 years in Latvia and neighbouring countries (current recruitment, ~5000).

CERVICAL CANCER PREVENTION IN AFRICA

PRI is collaborating with the World Health Organization (WHO) Department of Reproductive Health and Research (RHR) and the United Republic of Tanzania in a study with 1500 women

Figure 2. ENIGMA study coordination meeting in Ardabil, Islamic Republic of Iran, in August 2017. © IARC/Rolando Herrero.



Figure 3. The HELPER study team at the National Cancer Center, Republic of Korea, in July 2017. © IARC/Rolando Herrero.



to build HPV testing capacity and to assess the reproducibility, feasibility, and acceptability of rapid HPV testing at different levels of the health care system (the AISHA study). Also with RHR, PRI is planning a large trial of two screen-and-treat algorithms using HPV testing currently recommended by WHO (the CESTA study). The first CESTA pilot studies will be in Senegal and South Africa.

SUPPORT OF HPV VACCINATION AND SCREENING PROGRAMMES

PRI continues to provide support to cervical cancer screening programmes in Mongolia, Myanmar, Romania, and several countries in Latin America. PRI is collaborating with RHR to develop new guidelines on thermal ablation and other novel ablative treatments for cervical intraepithelial neoplasia (CIN)

beyond cryotherapy. Within the BELMED project, in collaboration with the WHO Regional Office for Europe and national offices, PRI is facilitating the preparation and implementation of pilot screening programmes for breast cancer to implement population-based screening in Belarus (Figure 4).

IMPLEMENTATION RESEARCH TO INCREASE HPV VACCINATION COVERAGE IN FRANCE

The PAPRICA project aims to evaluate whether an innovative educational intervention about HPV vaccination directed at doctors in Lyon can be effective in

increasing vaccination coverage. With the collaboration of academic groups in France, PRI has developed and piloted at Saint-Étienne an HPV educational intervention based on behaviour change theories, and will test this intervention through a randomized clinical trial in Lyon.

Figure 4. Training course on breast cancer epidemiology and screening in Belarus, in December 2016. Courtesy of the Belarus Project Management Team.



SCREENING GROUP (SCR)

The main focus of the Screening Group (SCR) is research on primary prevention and early detection of common cancers through interventions that are particularly relevant in LMICs. SCR contributes evidence to support resource-appropriate cancer control policy-making, and engages in producing training resources and organizing educational programmes.

HPV VACCINATION

The effectiveness of fewer than three doses of quadrivalent HPV vaccine in preventing cervical neoplasia is being evaluated among 17 729 participants in India (Figure 5). Two doses were reported to be as immunogenic as three doses against HPV 16 and 18; even recipients of a single dose demonstrated robust and sustained immune responses, albeit inferior to those of

Figure 5. HPV vaccination in girls 10–18 years old in India. © IARC/Partha Basu.



participants who received three or two doses (Sankaranarayanan et al., 2016a). Frequencies of cumulative incident and persistent HPV 16/18 infections over 7 years were low in all the vaccinated groups, including the recipients of a single dose, compared with the unvaccinated controls (Table 1).

CERVICAL CANCER SCREENING

SCR studies demonstrated the superior sensitivity of HPV testing over cytology in routine health-care settings in Thailand, and over visual inspection with acetic acid (VIA) in a demonstration project in India (Figure 6) (Mittal et al., 2017; Sangrajrang et al., 2017). The study in Thailand also demonstrated the high efficacy of liquid-based cytology in triaging the HPV-positive women (Sangrajrang et al., 2017). A point-of-care HPV 16/18 E6 test to triage the HPV-positive women was evaluated in China (Zhang et al., 2017a). Although the E6 test had a much lower test positivity (9.9%) compared with liquid-based cytology (48.4%) and VIA

Figure 6. Cancer screening mobilization in a rural area in India. © IARC/Eric Lucas.



(28.0%), E6-positive women had a much higher 10-year cumulative incidence rate (53.0%) of CIN of grade 3 or higher (CIN3+) compared with those who tested positive with cytology or VIA.

Table 1. Proportion (%) of one-time incident human papillomavirus (HPV) infections and persistent HPV infections in women in the IARC-India HPV vaccination study

HPV type	Dose received				Vaccinated group (total)	Unvaccinated group
	3 Doses (days 1, 60, and 180)	2 Doses (days 1 and 180)	2 Doses (days 1 and 60)	1 Dose		
	Incidence of HPV infection					
(Number of women assessed)	(1180)	(1179)	(1473)	(1823)	(5655)	(1481)
Vaccine-targeted types						
HPV 16/18	0.9	0.9	1.7	1.6	1.4	6.2
HPV 6/11	1.2	0.5	1.5	1.2	1.1	2.8
HPV 16/18/6/11	2.0	1.4	3.2	2.8	2.4	8.6
Non-vaccine-targeted types						
HPV 31/33/45	5.1	4.5	3.4	5.7	4.7	7.7
Other types excluding HPV 31/33/45 ^a	14.4	13.2	10.8	13.8	13.0	18.0
Any HPV type ^b	18.9	16.7	15.3	19.0	17.5	26.8
	Persistence of HPV infection					
(Number of women assessed)	(604)	(608)	(818)	(959)	(2989)	(1141)
Vaccine-targeted types						
HPV 16/18	0.2	0.0	0.4	0.0	0.1	1.2
HPV 6/11	0.0	0.0	0.1	0.1	0.1	0.0
HPV 16/18/6/11	0.2	0.0	0.5	0.1	0.2	1.2
Non-vaccine-targeted types						
HPV 31/33/45	0.2	0.2	0.2	0.7	0.4	0.5
Other types excluding HPV 31/33/45 ^a	2.2	0.8	1.1	1.6	1.4	2.3
Any HPV type ^b	2.8	1.2	1.8	2.3	2.0	3.8

^a HPV types HPV 26/35/39/51/52/53/56/58/59/66/68/70/73/82.

^b HPV types HPV 16/18/6/11/26/31/33/35/39/45/51/52/53/56/58/59/66/68/70/73/82.

The efficacy and safety of a new battery-powered portable thermocoagulator to treat cervical precancers is being evaluated in a randomized controlled trial (compared with cryotherapy and large loop excision of the transformation zone [LLETZ]) in Zambia, and in cross-sectional studies in Brazil, Bangladesh, China, India, Morocco, and Rwanda.

BREAST CANCER SCREENING

In a randomized trial involving 130 000 women in India, the third round of screening to evaluate clinical breast examination (CBE) is in progress. SCR implemented a study evaluating the impact of increased awareness and better access to early breast cancer detection in a cohort of 22 500 women in India (Gadgil et al., 2017). With breast awareness, the proportion of women with early-stage tumours increased from 74% to 81% and the proportion with lymph node-negative cancers increased from 46% to 53%. A study on the pattern of breast cancer care in oncology centres in Morocco has been initiated to document time intervals in care pathways from onset of symptoms to detection of disease and initiation of treatment.

ORAL CANCER SCREENING

The natural history of oral precancerous lesions is being addressed in the

randomized trial of oral visual screening in Kerala, India. There was a 38% reduction in oral cancer incidence (95% CI, 8–59%) and a 81% reduction in oral cancer mortality (95% CI, 69–89%) in users of tobacco and/or alcohol who adhered to four screening rounds, at 15 years of follow-up. The study participants in both intervention and control arms have been linked to the Trivandrum Cancer Registry, and a 20-year follow-up analysis is planned in 2020.

COLORECTAL CANCER SCREENING

SCR initiated a pilot study in 2017 to assess the feasibility and efficacy of colorectal cancer screening with immunochemical faecal occult blood testing (iFOBT) followed by triage colonoscopy in Morocco, in collaboration with the National Institute of Oncology, Rabat. A pilot study in Thailand that involved 130 000 people demonstrated that iFOBT-based colorectal cancer screening could be implemented successfully in routine health services.

COMPREHENSIVE SCREENING FOR NONCOMMUNICABLE DISEASES (NCDs)

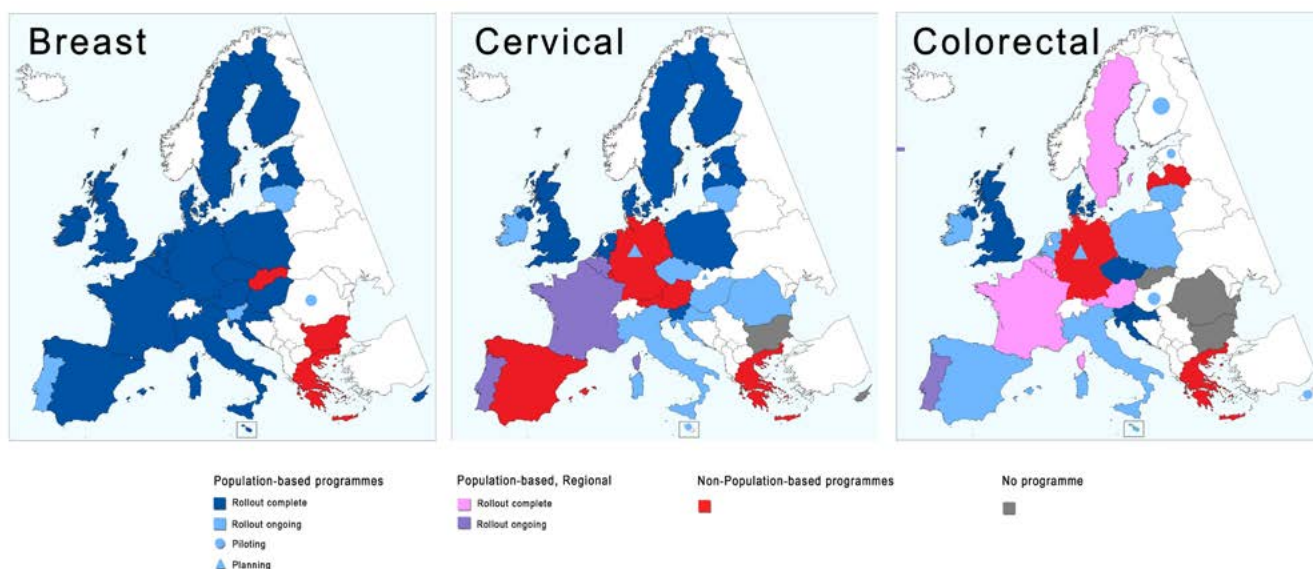
SCR is evaluating the feasibility and efficacy of a comprehensive NCD control package administered by trained community health workers in rural India. The community health workers check

people older than 30 years at their homes for body mass index, blood pressure, and blood sugar. Oral visual examination is performed on those who use tobacco and/or consume alcohol. Women are made aware of common symptoms of breast cancer, and they provide a self-collected vaginal sample for an HPV test for cervical cancer screening. The study is expected to recruit 13 000 individuals.

EVALUATION OF NATIONAL CANCER SCREENING PROGRAMMES

SCR prepared the second report on the implementation status of cancer screening in the European Union (Ponti et al., 2017). The report described implementation status, protocols, organization, screening coverage, and performance of breast, cervical, and colorectal cancer screening in the 28 European Union Member States (Figure 7). SCR evaluated the breast and cervical cancer screening programme of Morocco. In 2016, 1.6 million women were screened for breast cancer and 0.2 million women for cervical cancer. The programme was systematically evaluated and recommendations made to improve quality and performance. Evaluation of the breast and cervical cancer control programme in Japan demonstrated geographical disparities and the need to improve the participation rate (Sauvaget et al., 2016).

Figure 7. Status of implementation of the cancer screening programmes in the 28 European Union Member States. Figure reprinted from Basu P, Ponti A, Anttila A, Ronco G, Senore C, Vale DB, et al. (2018). Status of implementation and organization of cancer screening in the European Union Member States – Summary results from the second European screening report. *Int J Cancer*. 142(1):44–56. <http://dx.doi.org/10.1002/ijc.31043> PMID:28940326



TECHNICAL SUPPORT TO NATIONAL
CANCER CONTROL PROGRAMMES

SCR provided scientific advice and support to national cancer control programmes in Bangladesh, Belize,

Burundi, Congo, Kenya, Sierra Leone, Swaziland, Togo, Viet Nam, and other countries in collaboration with national governments, WHO, the International Atomic Energy Agency (IAEA), and the United Nations Population Fund

(UNFPA). SCR is supporting the ministries of health in Burkina Faso, Chad, Côte d'Ivoire, and Senegal to implement and evaluate the first pilot projects on cervical cancer screening.

TRAINING RESOURCES FOR CANCER SCREENING

The Screening Group has published a range of training resources for cancer screening, particularly relevant to trainees from low- and middle-income countries. All these resources are available on the newly designed website at <http://screening.iarc.fr>. The latest such publications are *Atlas of Colposcopy: Principles and Practice* and *Colposcopy and Treatment of Cervical Precancer*. Both of these publications, and many others, are freely accessible online.

The screenshot shows the IARC Screening Group website. At the top, it features the IARC logo and the World Health Organization logo. The main navigation bar includes links for HOME, RESEARCH PROJECTS, TRAINING, ONLINE LIBRARY, COLLABORATORS, and ABOUT THE GROUP. The TRAINING section is highlighted, listing resources such as Manuals, eLearning courses, Digital learning series, Video tutorials, Other useful screening videos, Audio presentations, and Quick clinical reference charts. Below this, a banner for 'Training' features two book covers: 'Colposcopy and treatment of cervical precancer' and 'ATLAS OF COLPOSCOPY PRINCIPLES AND PRACTICE'. Both books are marked as 'NOW AVAILABLE PRINT AND PDF'. The background of the banner shows a person using a colposcope.