
DÉROULEMENT DE LA GROSSESSE

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The Section of Early Detection and Prevention (EDP) conducts research on the efficacy, safety, and cost–effectiveness of cancer prevention and early detection interventions to guide rational cancer control policies, with a particular emphasis on low- and middle-income countries (LMICs). With the start of the new IARC Medium-Term Strategy 2021–2025 and the new organizational structure as of 1 January 2021, EDP became part of the newly created Early Detection, Prevention, and Infections Branch.

One of the principles that continue to guide EDP's work is the search for simplified, affordable technology adaptable to LMICs. EDP provides technical support to current and planned population-based prevention and screening programmes in LMICs in the context of cancer control, conducts clinical and screening trials, and carries out implementation and health economics research. In addition, EDP develops educational materials and conducts training activities for cancer control. EDP has established extensive networks involving highly skilled clinicians, epidemiologists, and other

personnel. These networks facilitate the transfer of research technology to the local researchers and often their students, who participate actively in study design and conduct, and data analysis. An important part of the work of EDP is the dissemination of the scientific evidence base and the provision of technical assistance to governments and policy-makers in countries developing cancer control programmes.

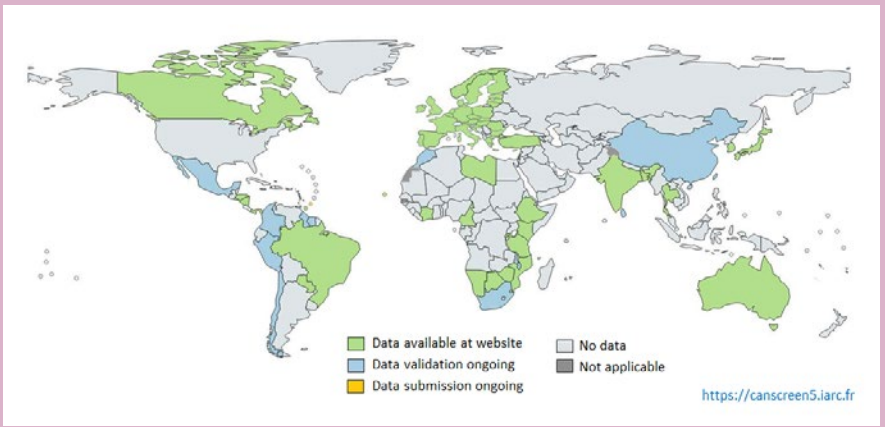
The multicentre and multidisciplinary studies of EDP are conducted within two separate Groups: the Prevention and Implementation Group (PRI) and the Screening Group (SCR).

Training of Trainers in CELAC within CanScreen5

The objective of the Screening Group project "Reduction of inequalities in cancer screening: a case study in the Community of Latin American and Caribbean States (CELAC)" is to examine policies in CELAC aimed at reducing inequalities in effective participation of the eligible population in cancer screening. The project, implemented in collaboration with the Centre for Global Health Inequalities Research (CHAIN) in Norway (supported by the Research Council of Norway) and the Pan American Health Organization (PAHO), also aims to enhance the capacity of the cancer screening programme managers in CELAC to implement quality-assured screening programmes. This has become an integral part of the IARC project Cancer Screening in Five Continents (CanScreen5) (https://canscreen5.iarc.fr).

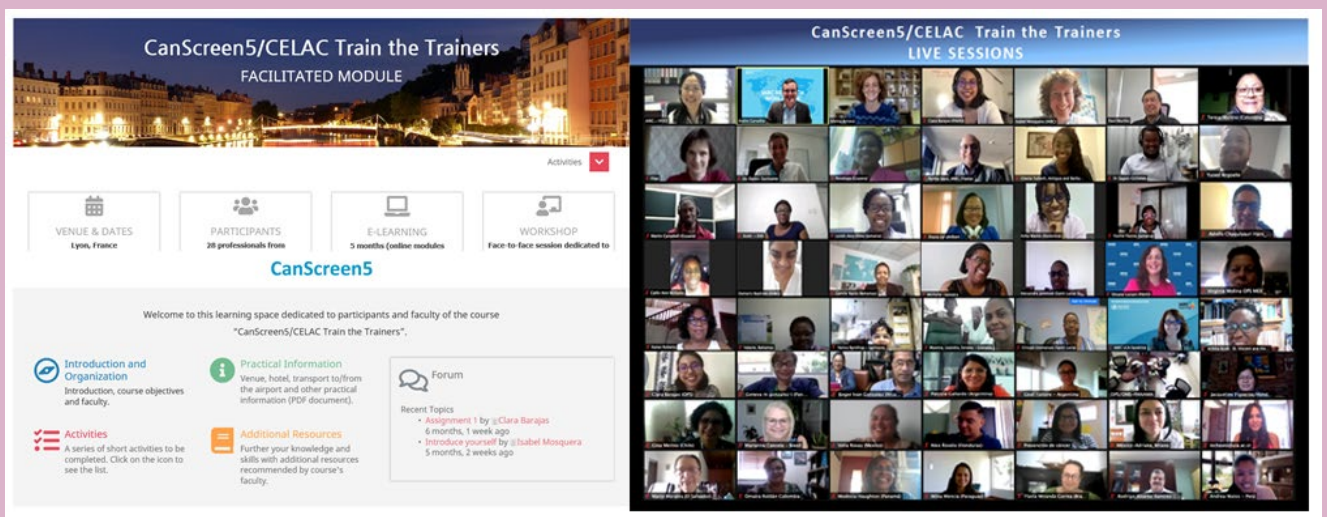
This Training of Trainers programme is a package of e-learning modules and live sessions. E-learning modules cover principles of cancer screening, planning and implementing screening programmes, and ensuring quality. Live sessions include keynote lectures and group discussions. Among other topics, lectures cover cancer control in the region, indicators in cervical cancer screening, social inequalities, and implementation science.

Countries contributing to the Cancer Screening in Five Continents (CanScreen5) initiative, with their stage in the process indicated. © IARC.



The first phase of Training of Trainers in CELAC has been carried out and involved 65 participants from 22 countries. After the training, participants reported that their knowledge had been increased by more than 50%, and this learning will be reinforced during face-to-face workshops. Using the CanScreen5 self-paced learning programme, participants will be able to train colleagues in their respective countries.

"Keep holding our hand" (quote from a Training of Trainers participant from Honduras). © IARC.



Prevention and Implementation Group (PRI)

HPV vaccine efficacy

In collaboration with the United States National Cancer Institute, the ESCUDDO randomized trial comparing one dose versus two doses of the bivalent and nonavalent human papillomavirus (HPV) vaccines among 20 000 adolescent girls (aged 12–16 years) is continuing in Costa Rica. Recruitment has been completed, and follow-up has been extended to 5 years to account for the possible impact of the COVID-19 pandemic, which may change exposure to HPV through changes in social interactions. In the Costa Rica HPV vaccine trial (CVT) study, the Prevention and Implementation Group (PRI) has demonstrated that one dose is still highly protective and immunogenic 11 years after vaccination (Kreimer et al., 2020a) and that three doses are protective against high-grade lesions during long-term follow-up (Porras et al., 2020).

Cervical screening in Latin America

Despite steady reductions in cervical cancer incidence and mortality in Latin America over the past decades, the incidence rates are still above the elimination threshold (age-standardized incidence rate of 4 cases per 100 000 women per year) (Figure 1) (Pilleron et al., 2020), highlighting the need for effective strategies to achieve the elimination goals.

The ASCUS-COL trial in Colombia investigated the efficacy to prevent precancerous cervical lesions of HPV testing compared with the usual care (immediate colposcopy and repeat Pap smear) in 2661 women with atypical squamous cells of undetermined significance (ASCUS) Pap results. HPV testing was found to reduce the burden of cervical lesions by 65% and colposcopy referral by 41% (Baena et al., 2020). No differences in health-related quality of life were observed by HPV positivity status (Urrea Cosme et al., 2020). When collected samples were used, the performance of the recently developed S5-methylation test (United Kingdom) to triage HPV-positive women (with ASCUS Pap results) highlighted the potential role of S5-methylation in HPV-based cervical screening (Ramirez et al., 2021).

The ESTAMPA study investigates cervical cancer screening and triage techniques in women (aged 30–64 years) in nine countries in Latin America. HPV-positive women receive colposcopy, biopsy, and treatment and a second screen after 18 months as needed. The main outcome is advanced cancer precursors (Almonte et al., 2020). More than 42 000 women have been recruited, and a high adherence to the screening process has been reported; 95% of

Figure 1. Distribution of age-standardized incidence rates of cervical cancer per 100 000 women per year in 2018 by country and subregion, compared with the elimination threshold defined by WHO of 4 per 100 000 women per year. Reproduced with permission from Pilleron et al. (2020), © John Wiley and Sons.

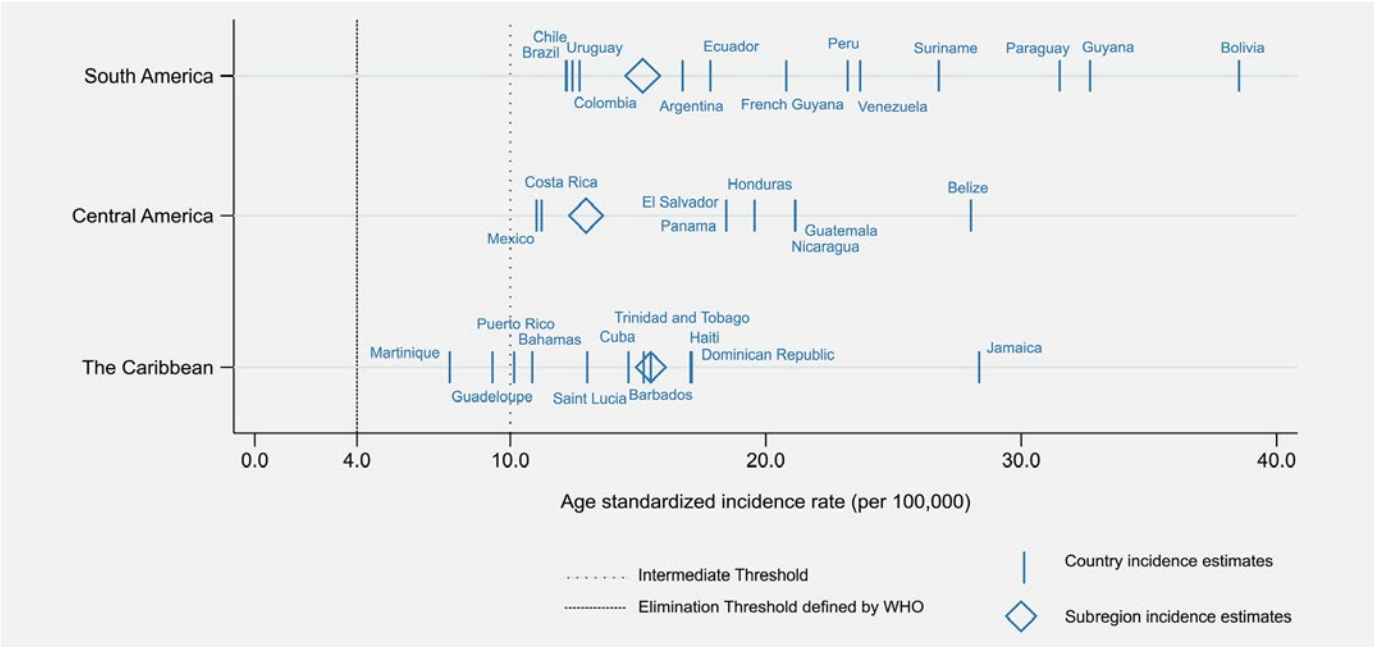
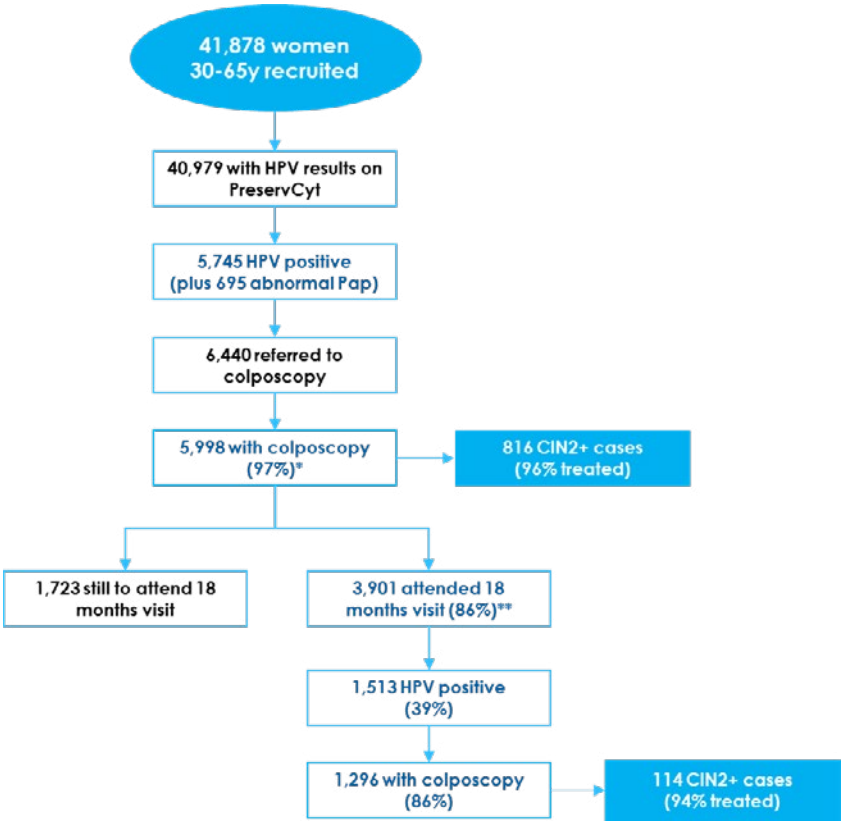


Figure 2. Progress of the ESTAMPA study as at July 2021. * Percentage computed after excluding 270 women who withdrew from the study. ** Percentage computed among women eligible to attend the 18-month visit (i.e. without cervical intraepithelial neoplasia grade 2 [CIN2] and in the study for at least 18 months). HPV, human papillomavirus. © IARC.



high-grade lesions detected have been treated (Figure 2). Results are supported by a study network promoting the sharing of experiences among more than 200 multidisciplinary professionals (Figure 3). In addition, the Psycho-ESTAMPA tool to assess the psychosocial impact of an HPV-positive screening result was developed and validated and will be used to measure the impact of various methods of communicating HPV test results (Arrossi et al., 2020).

To further support the implementation of HPV screening in the region, PRI is also conducting formative research on barriers to and facilitators of adoption of the WHO cervical screening guidelines, in the GUIDES project.

Cervical screening and treatment in Africa

The CESTA study compares the efficacy of cervical screening by (i) HPV detection with visual inspection with acetic acid (VIA) triage of HPV-positive women and ablative treatment of women who are both HPV-positive and VIA-positive, with (ii) HPV detection followed by ablative treatment of HPV-positive women. In Senegal, 18% of 350 HIV-negative women (aged 30–54 years) were HPV-positive, compared with 62% of 400 women living with HIV (aged 25–54 years) in South Africa; an additional 1200 women living with HIV are being recruited in South Africa to enable the evaluation of other, more suitable screening techniques.

A collaborative randomized trial in women living with HIV in Kenya previously reported that recurrent high-grade cervical disease (cervical intraepithelial neoplasia grade 2 or worse [CIN2+]) was lower after treatment by the loop electrosurgical excision procedure (LEEP) than after cryotherapy. Secondary data analyses demonstrated that endocervical curettage does not increase detection of CIN2+ (Chung et al., 2021a) and that the reduction in recurrence was associated with a decrease in HPV persistence in LEEP-treated women (Chung et al., 2021b).

Helicobacter pylori infection and gastric cancer

The HELPER study, a continuing collaboration with the National Cancer Center of Korea, has enrolled 11 799 participants, and 5269 participants who tested positive for *H. pylori* were randomized to eradication or placebo to investigate the reduction in the incidence of gastric cancer. All participants are being endoscopically followed up within the Korean National Cancer Screening Program.

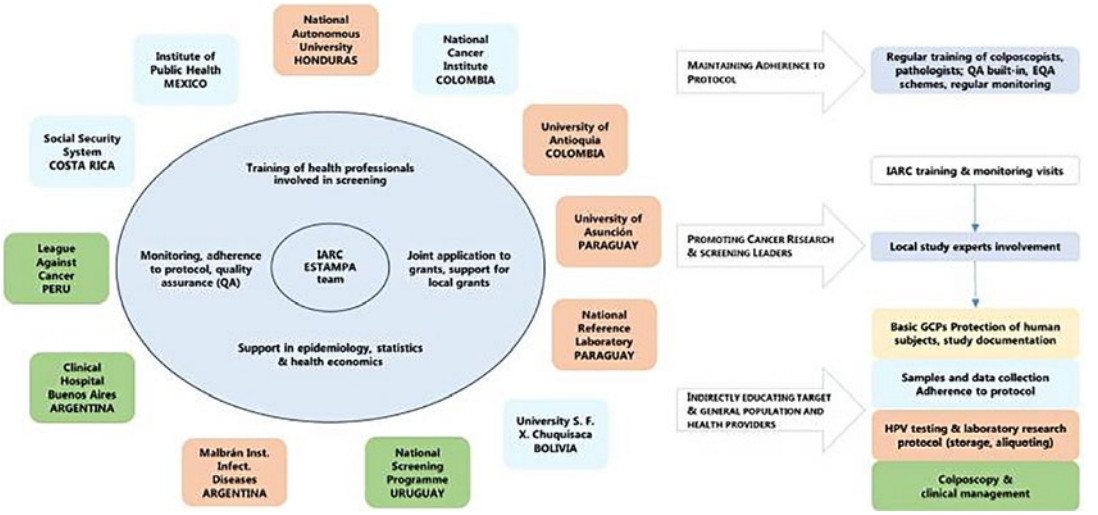
The GISTAR study, a collaboration with the University of Latvia, is investigating whether *H. pylori* test-and-treat and endoscopic follow-up of subjects with serological evidence of atrophic gastritis reduces gastric cancer mortality. Recruitment is continuing, with more than 10 000 participants included and followed up so far.

The prevalence of *H. pylori* and gastric lesions in low-risk and high-risk areas for gastric cancer is being investigated in the ENIGMA studies. In ENIGMA-Chile, the prevalence of serologically determined atrophic gastritis was significantly higher in the high-risk area, although comparable *H. pylori* prevalence is observed in both areas (Herrero et al., 2020).

Breast cancer screening in Belarus

Within the joint European Union and United Nations project BELMED (Preventing noncommunicable diseases, promoting healthy lifestyle, and support to modernization of the health system in Belarus), PRI supported the breast mammography screening component, particularly by ensuring the quality of the programme through training of healthcare professionals and the establishment of monitoring processes. The final report of the BELMED screening component is expected in early 2022.

Figure 3. The ESTAMPA study network. EQA, external quality assessment; GCPs, good clinical practices; HPV, human papillomavirus. © Almonte et al. (2020). Re-use permitted under CC BY. Published by BMJ. https://creativecommons.org/licenses/by/4.0/.



Screening Group (SCR)

Studies led by the Screening Group (SCR) during the 2020–2021 biennium have generated valuable evidence to support the development of resource-appropriate policies to deliver effective cancer prevention and early detection services in the following domains.

Evaluation of HPV vaccine

The SCR study under way in India recently reported that the vaccine efficacy of a single dose of quadrivalent HPV vaccine was as high as that of two doses and three doses at a median follow-up of 9.0 years. Vaccine efficacy against persistent HPV16/18 infection was 95.4% in recipients of a single dose, 93.1% in recipients of two doses, and 93.3% in recipients of three doses (Table 1) (Basu et al., 2021c).

SCR evaluated a new quadrivalent HPV vaccine produced by the Serum Institute of India (SII) in a phase II randomized trial that included female and male participants in two age cohorts: 9–14 years (n = 300) and 15–26 years (n = 300). The participants received either Gardasil or the SII vaccine (CTRI/2018/06/014601). Neutralizing antibody titre against vaccine-targeted genotypes (HPV6, HPV11, HPV16, and HPV18) was very high 7 months after vaccination, with 100% seroconversion irrespective of the vaccine type, indicating that the new vaccine is as immunogenic as Gardasil. A recommendation of a single dose and the use of a locally manufactured vaccine will significantly improve the affordability of vaccination programmes against HPV.

Cervical cancer screening and management of precancers

In a study in rural China, 9526 women (aged 30–65 years) were screened for cervical cancer on self-collected vaginal samples using the *care*HPV test (a signal amplification test) and a locally developed polymerase chain reaction (PCR)-based HPV test. The PCR-based test had significantly higher sensitivity in detecting high-grade precancers and/or cancers compared with the *care*HPV test (96.7% vs 72.5%) but lower specificity (82.1% vs 86.0%). Triaging with HPV16/18 genotyping considerably improved the specificity (97.0%), with some reduction in sensitivity (73.6%) (Zhao et al., 2020a).

In a study in Zambia aiming to evaluate thermal ablation for treatment of cervical precancer, 2456 VIA-positive women were randomized to be treated with thermal ablation, cryotherapy, or loop excision. Treatment success rates were similar for the three techniques, although they were significantly lower in HIV-positive women than in HIV-negative women (49% vs 83%). Data from the studies were shared with WHO for guideline development.

Oral cancer screening

SCR assessed a risk prediction model for oral cancer screening. The model showed that screening with visual examination of ever-users of tobacco and/or alcohol with no additional risk stratification would achieve a reduction of 23.3% in oral cancer mortality. Screening would be highly efficient, and the model indicated that screening of only 50% of ever-

Table 1. Efficacy of a single dose of quadrivalent human papillomavirus (HPV) vaccine compared with that of two doses and three doses (all vaccines given at age 10–18 years) for the prevention of incident and persistent HPV infections; 10-year follow-up data from IARC HPV vaccine study in India

	Unvaccinated	Single dose	Two doses (days 1 and ≥ 180)	Three doses (days 1, 60, and ≥ 180)
HPV incidence				
Number of women assessed	1479	2858	2166	2019
Incident HPV16 and/or HPV18 infections				
Observed events	138	92	59	59
Adjusted vaccine efficacy[a] (%) (95% CI)		63.5 (51.2 to 73.1)	67.7 (55.2 to 77.2)	66.4 (53.6 to 76.3)
Incident HPV31, HPV33, and/or HPV45 infections				
Observed events	148	136	89	86
Adjusted vaccine efficacy[a] (%) (95% CI)		43.5 (25.4 to 56.5)	54.0 (38.5 to 66.5)	54.6 (38.3 to 66.6)
HPV persistence				
Number of women assessed	1260	2135	1452	1460
Persistent HPV16 and/or HPV18 infections				
Observed events	32	1	1	1
Adjusted vaccine efficacy[a] (%) (95% CI)		95.4 (85.0 to 99.9)	93.1 (77.3 to 99.8)	93.3 (77.5 to 99.7)
Persistent HPV31, HPV33 and/or HPV45 infections				
Observed events	14	14	11	7
Adjusted vaccine efficacy[a] (%) (95% CI)		8.8 (–230.8 to 62.6)	8.4 (–239.3 to 65.7)	38.8 (–124.4 to 80.2)

CI, confidence interval; HPV, human papillomavirus.

[a] Adjusted through direct standardization on the five strata created from the disease risk score estimates.

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users of tobacco and/or alcohol would lead to a similar reduction in mortality (19.7%) (Cheung et al., 2021).

Screening and early diagnosis of breast cancer

To investigate the variability in the performance of screening mammography across the European Union, SCR estimated breast cancer detection rates adjusted by age, screening interval, and positive predictive value. For women aged 50–69 years, the detection rate of invasive cancers ranged between 3.8 and 7.4 per 1000 and that of ductal carcinoma in situ ranged between 0.7 and 2.7 per 1000 across countries (Armaroli et al., 2020). The remarkable heterogeneity was due to different background risk and differences in the quality and organization of programmes.

The SCR patterns-of-care study, involving 2120 patients with breast cancer registered during 2008–2017 at two publicly funded oncology centres in Morocco, reported a median delay of 6 months between symptom onset and physician consultation (Mrabti et al., 2021). A total of 45% of the patients presented with stage III or IV cancer. The median delay between registration at an oncology centre and the initiation of treatment was 1.5 months. Disparities in the quality of care between the two oncology centres resulted in a 25% difference in 5-year disease-free survival for early-stage breast cancers.

Colorectal cancer screening

SCR published comparative data on the performance of colorectal cancer screening programmes across the European Union. The participation rate was higher in countries that have adopted faecal immunochemical testing (FIT) (range, 22.8–71.3%) than in those using guaiac faecal occult blood testing (gFOBT) (range, 4.5–66.6%). Large variations in screening performance were observed. Compliance with referral for colonoscopy ranged between 64% and 92%. The detection rates of advanced adenomas and colorectal cancer were higher with FIT than with gFOBT, and higher in men than in women.

SCR implemented a demonstration project in Morocco to screen 9763 men and women for colorectal cancer using FIT through routine primary-care facilities. Of the 4.7% of participants who tested positive, only 62.6% underwent colonoscopy, highlighting the challenges of implementing colorectal cancer screening in the country. The detection rate of colorectal cancer was low (0.7 per 1000).

Impact of COVID-19 on cancer detection

SCR published a commentary on best practices to continue with cancer screening during the advancing and receding COVID-19 pandemic. SCR has also conducted studies to assess the impact of the pandemic on cancer screening programmes, especially in LMICs (Figure 4) (Basu et al., 2021a; Villain et al., 2021). These studies have also highlighted how some LMICs have leveraged the vertical investments made to mitigate the COVID-19 pandemic to improve the quality and reach of cancer screening programmes (Basu et al., 2021b).

Figure 4. IARC evaluated the impact of the COVID-19 pandemic on cancer screening programmes in several countries. The figure shows the significant decrease in the number of women screened for cervical cancer per month in Bangladesh in 2020 compared with previous years. The figure also shows how the programme recovered from the impact of lockdown within a few months as a result of planned measures. The bars indicate the number of COVID-19 cases detected by months in 2020. VIA, visual inspection with acetic acid. Reprinted from Basu et al. (2021b), © 2021, with permission from Elsevier.