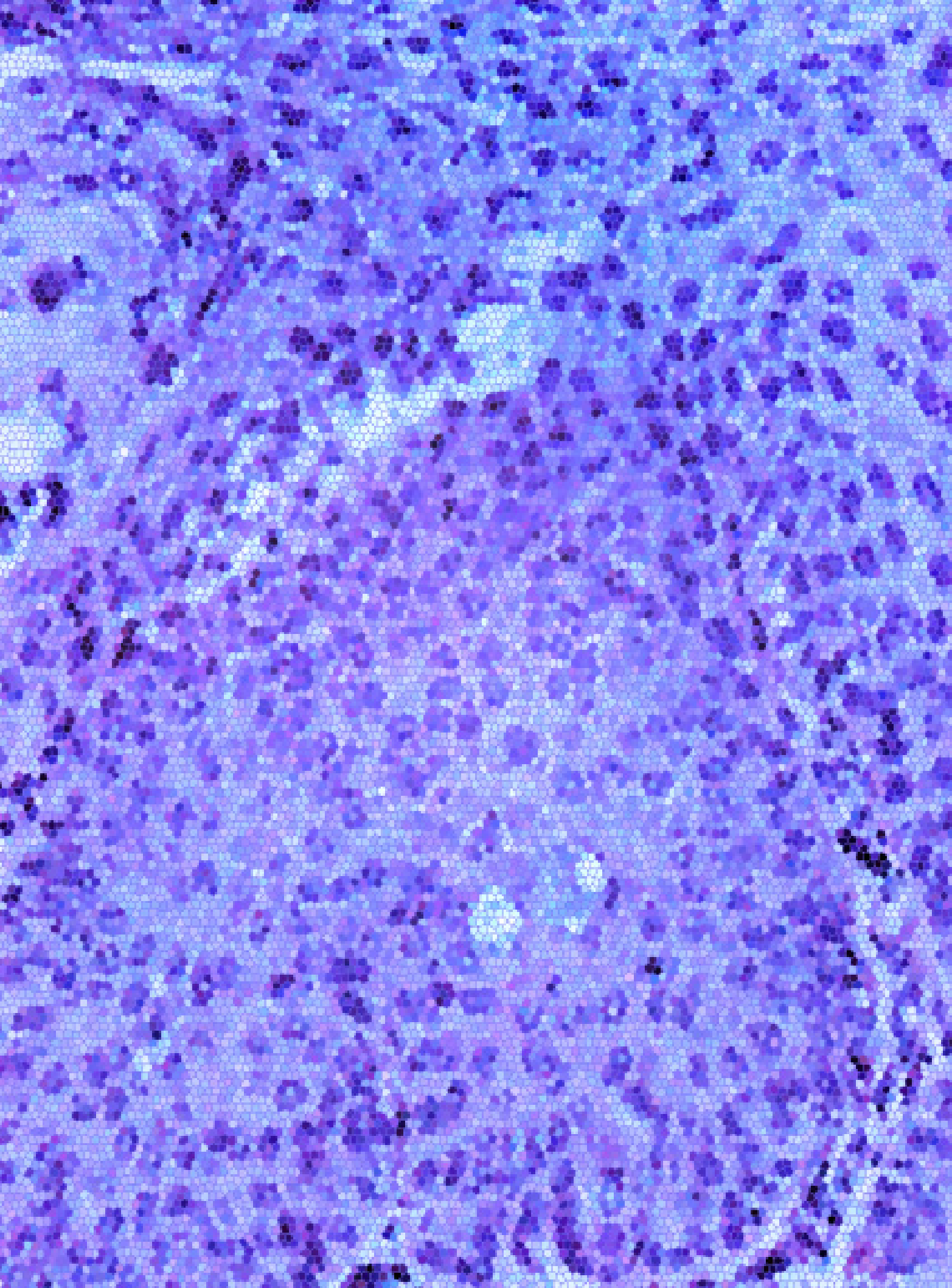
Section of Early Detection and Prevention (EDP)

Section head
Dr R. Sankaranarayanan

The Section of Early Detection and Prevention (EDP) conducts a range of studies to determine the feasibility, efficacy and cost-effectiveness of different primary and secondary prevention interventions for breast, cervical, colorectal and oral cancers in low- and middle-income countries, and to address quality assurance aspects of breast, cervical and colorectal cancer screening in national programmes conducted throughout the world. These studies aim to reduce cancer burden by prevention and screening and to reduce the wide disparities in the availability and access to affordable, quality-assured and effective early detection interventions around the world. Also addressed are the means by which the research activities can contribute to improving the capacity and infrastructure of health services to provide effective interventions.



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The objective of the Screening Group (SCR) is to guide the development of evidence-based public health policies for cancer screening and early diagnosis in a range of health care settings, particularly in low- and middle-income countries. This will lead to reduced burden of disease and improved quality of life and result in further development of health services and rational utilization of health care resources. To this end, our studies address the performance, efficacy, cost-effectiveness, harmful effects and quality assurance of different screening interventions for breast, cervical, oral and colorectal cancers in various health care settings, as well as the development of training resources in collaboration with national institutions in different countries.

Cervical cancer screening and prevention

Long-term follow-up of participants in the randomized trials of screening

To determine the long-term impact of a single round of human papillomavirus (HPV) screening, either by Pap smear or visual inspection with acetic acid (VIA), in preventing cervical cancer cases and deaths, around 210 000 women in the Dindigul and Osmanabad district screening trials in India have been followed-up. This has been achieved through linkage with population-based cancer registries, mortality registration systems and active follow-up by house visits. The 10-year follow-up results for the Osmanabad district cervical screening study are given in Table 1. There was a significant 35% reduction in cervical cancer mortality following a single HPV test as compared to the women receiving a single Pap smear; cervical cancer incidence following VIA was similar to that following cytology. Cervical cancer incidence in HPV-negative women was four times less than that of cytology-negative women, further indicating that HPV testing is a more effective approach than cytology in reducing cervical cancer burden (Table 2). The 11 year follow-up in the Dindigul district study indicates a 25% reduction in incidence and 27% reduction in cervical cancer mortality, documenting long-term protection following a single round of VIA screening in this cohort (Table 3 and

Table 1. Cervical cancer incidence and mortality during 2000-2009 using the cytology group as the reference in the Osmanabad District randomized controlled trial

Group	Cases	Person-yrs of follow-up (PYO)	Rate per 100 000 PYO	Hazard ratio (95% CI)
Incidence of all cervical cancer				
Cytology	162	311 480	52.0	1.00
HPV	147	332 150	44.3	0.85 (0.67 - 1.09)
VIA	181	331 360	54.6	1.05 (0.85 - 1.30)
Incidence of stage II or higher cervical cancer				
Cytology	62	311 480	19.9	1.00
HPV	46	332 150	13.8	0.70 (0.49 - 0.98)
VIA	98	331 360	29.6	1.49 (1.10 - 2.00)
Cervical cancer mortality				
Cytology	69	312 290	22.1	1.00
HPV	48	332 820	14.4	0.65 (0.47 - 0.91)
VIA	77	332 160	23.2	1.05 (0.79 - 1.39)

HPV: human papillomavirus; VIA: visual inspection with acetic acid; CI: confidence interval

Table 2. Cervical cancer incidence during 2000-2009 among women screened HPV-negative at baseline in the Osmanabad District randomized controlled trial

Group	Cancer cases	Number of women	Incidence rate (per 100, 000 PYOs)	
			Crude	ASR
HPV	11	24 380	4.6	4.3
Cytology	27	23 762	11.6	15.0
VIA	40	23 032	17.7	20.1
Total	78	71 174	11.2	13.1

PYOs: person years of observation; ASR: age-standardized rate; HPV: human papillomavirus; VIA: visual inspection with acetic acid

Table 3. Cervical cancer incidence and mortality during 2000-2010 in the Dindigul District randomized controlled trial

Group	Cases	Person-yrs of follow-up (PYO)	Rate per 100,000 PYO	Hazard ratio (95% CI)
Incidence of all cervical cancer				
Control	205	235 031	87	1.00
VIA	217	366 563	59	0.74 (0.60 - 0.92)
Cervical cancer mortality				
Control	133	235 031	49	1.00
VIA	139	366 563	32	0.73 (0.56 - 0.95)

CI: confidence interval; VIA: visual inspection with acetic acid

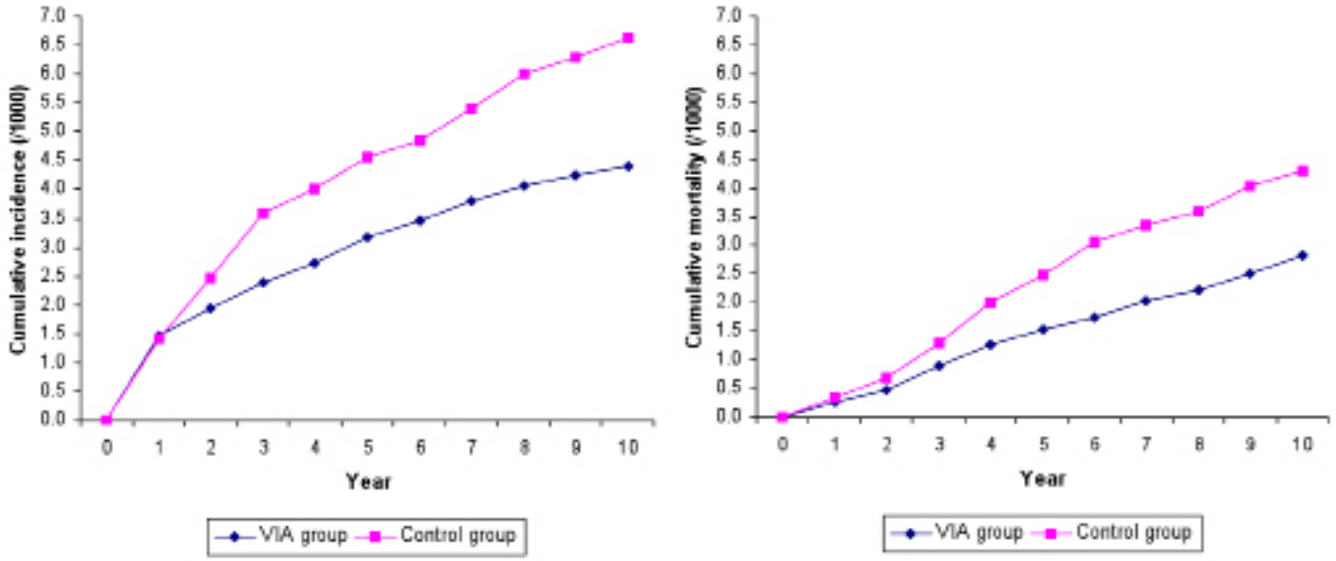

Figure 1. Cumulative cervical cancer incidence and mortality during 2000-2010 in the Dindigul District randomized controlled trial

Figure 1). VIA screening of the control group women has been completed in the Dindigul district study, and HPV testing of the control group women in the Osmanabad study is in progress and will be completed in 2012.

Multicentre randomized HPV vaccination trial

In collaboration with nine national institutions in India, SCR is conducting a randomized clinical trial comparing the efficacy of two versus three doses of HPV vaccination in preventing HPV infection and cervical neoplasia. HPV vaccination was initiated in September 2009. The entire course of vaccination of 20 000 girls would have been completed by the end of August 2010 had the Government of India not temporarily suspended all HPV vaccination trials in India effective April 2010. This followed reports of four deaths in vaccinated cohorts of two programmes of HPV vaccination conducted by another group of investigators in India. As of April 2010, we had vaccinated 17 696 girls partially or fully as per protocol: 8622 had one dose on day 1; 5598 had two doses on days 1 and 60; 1415 had two doses on days 1 and 180 as per protocol in the 2-dose group; 2061 with three doses on days 1, 60 and 180 as per protocol in the 3-dose group. Thus allocated vaccination schedules were interrupted for 14 220 girls while 3476 girls were administered vaccines as per protocol. Blood specimens were collected from 2773 participants at baseline; from 3391 girls at month 7, from 1691 girls at month 12 and from more than 9000 girls in month 18. Preliminary results on the antibody levels at baseline and at 7 months (1 month from the last dose of vaccination as per protocol) indicates that the immunogenicity in the 2-dose group was found to be non-inferior to the 3-dose group with respect to antibodies to HPV 16, 18, 6 and 11. A total of 1799 adverse events, including 68 severe adverse events (none related to HPV vaccination), have been reported. The serology and cervical samples were analysed for antibodies and HPV types at the Rajiv Gandhi Centre for Biotechnology, Trivandrum.

Evaluation of ongoing cervical cancer screening programmes and training initiatives

A descriptive evaluation of ongoing cytology screening programmes in Thailand (Deerasamee *et al.*, 2007; Kuhaprema *et al.*, 2011) and VIA screening initiatives in Bangladesh (Nessa *et al.*, 2010), Mali (Teguete *et al.*, 2011), Angola (Muwonge *et al.*, 2010) and United Republic of Tanzania (Ngoma *et al.* 2010) were carried out. Seven training courses in cervical cancer screening and prevention (four in India, two in China and one in Egypt) were conducted and around 300 doctors and nurses from Asian and African countries were trained. Our collaborative cervical cancer prevention schools in India, Angola, Guinea, United Republic of Tanzania, Brazil and Peru are active in educating human resources in their respective regions.

Breast cancer screening

In January 2006, a cluster randomized controlled trial was initiated in the Trivandrum district, India, to evaluate whether three rounds of triennial clinical breast examination (CBE) can reduce the rate of advanced disease incidence and breast cancer mortality. A total of 115 652 healthy women, aged 30-69 years, were randomly allocated to intervention or control groups. After completion of the first round of screening in May 2009, results were reported in terms of frequency of stage distribution, tumour size, lymph node involvement and breast conservation surgery in the intervention and control groups (Table 4). CBE had 52% sensitivity, 94% specificity, 6% false-positive rate, and 1% positive predictive value in detecting breast cancer. The age-standardized incidence rates for early stage (stage IIA or lower) breast cancer were 18.8 and 8.1 per 100 000 women, and the rates for advanced stage (stage IIB or higher) breast cancer were 19.6 and 21.7 per 100 000 women, in the intervention and control groups, respectively (Sankaranarayanan *et al.*, 2011a). The second round of screening is in progress.

Table 4. Comparison of intermediate outcome measures and treatment modalities in the study groups of Trivandrum breast cancer screening trial

	Intervention group		Control group		P-value
	No.	% (95% CI)	No.	% (95% CI)	
Breast cancers	80		63		
Size of primary tumour, ≤2cm	15	18.8 (10.2 to 27.3)	4	6.3 (0.3 to 12.4)	0.030
Negative pathological node	40	50.0 (39.0 to 61.0)	22	34.9 (23.1 to 46.7)	0.071
Early stage breast cancers (stages I and IIA)	35	43.8 (32.9 to 54.6)	16	25.4 (14.6 to 36.1)	0.023
Advanced stage breast cancers (stages IIB-IV)	36	45.0 (34.1 to 55.9)	43	68.3 (56.8 to 79.7)	0.005
Estrogen receptor-positive breast cancers	28	35.0 (24.5 to 45.5)	23	36.5 (24.6 to 48.4)	0.852
Treatment received					
Surgery	61	76.3 (66.9 to 85.6)	50	79.4 (69.4 to 89.4)	0.657
Radiotherapy	39	48.8 (37.8 to 59.7)	27	42.9 (30.6 to 55.1)	0.483
Chemotherapy	61	76.3 (66.9 to 85.6)	46	73.0 (62.1 to 84.0)	0.658
Hormone therapy	24	30.0 (20.0 to 40.0)	20	31.7 (20.3 to 43.2)	0.822
Received breast conservative surgery	14	17.5 (9.2 to 25.8)	3	4.8 (-0.5 to 10.0)	0.019

Table 5. Oral cancer incidence/mortality rates by number of times screened among individuals with tobacco and alcohol habits in the Trivandrum oral cancer screening trial

Number of times screened	Cases/deaths	Person-yrs of follow-up (PYO)	Incidence/mortality rate per 100 000 PYO	Incidence/mortality hazard ratio (95% CI)
		Oral cancer incidence		
Control	214	252 870	84.6	1.00
Intervention				
0	13	14 250	91.3	1.02 (0.60 - 1.74)
1	68	48 730	139.5	1.61 (1.14 - 2.29)
2	60	71 130	84.3	0.98 (0.73 - 1.32)
3	62	91 030	68.1	0.78 (0.54 - 1.13)
4	37	79 220	46.7	0.53 (0.35 - 0.81)
		Oral cancer mortality		
Control	109	250 700	43.5	1.00
Intervention				
0	9	14 230	63.2	1.73 (0.97 - 3.08)
1	45	48 810	92.2	2.50 (1.81 - 3.46)
2	24	71 250	33.7	0.77 (0.60 - 0.99)
3	15	91 240	16.4	0.35 (0.17 - 0.72)
4	2	79 410	2.5	0.05 (0.01 - 0.28)

Efforts are underway to evaluate the impact of breast cancer awareness in reducing mortality in large population-based studies. The efficacy of transillumination breast screening in detecting breast lumps and breast cancer is being evaluated in India and China.

Oral cancer screening

The cohort (200 000 subjects) of the Trivandrum oral cancer screening study have now been followed-up for 15 years. Results after four rounds of screening indicate a significant (47%) reduction in oral cancer incidence and a 95% reduction in mortality among subjects with tobacco and/or alcohol habits (Table 5). The screening of subjects in the control group has been completed.

Colorectal cancer screening

The goal of the Thailand Colorectal Cancer Screening Pilot Demonstration Project in Lampang Province, Thailand, jointly organized with SCR and the National Cancer Institute, is to evaluate the acceptability, feasibility, organization, implementation, monitoring and effectiveness of colorectal cancer (CRC) screening using a faecal occult blood test (FOBT) followed by a colonoscopy in those with a positive FOBT. By integrating this screening effort into the existing public health services, we intend to inform and guide the eventual large-scale CRC screening programme covering the entire country. This study aims to recruit around 150 000 subjects aged 50-65 years.

Cancer survival in Africa, Asia, the Caribbean and Central America

Population-based cancer survival data, a key indicator for monitoring progress against cancer, are not widely available in low- and middle-income countries. Survival of cancer-specific patients diagnosed in 1990–2001, and followed-up to 2003, in 25 population-based cancer registries from 12 countries in sub-Saharan Africa, Central America and Asia, were analysed by actuarial method. The five-year age-standardized relative survival (ASRS) and observed survival by clinical extent of disease varied drastically between countries. Five-year survival ranged from 76–82% for breast, 63–79% for cervix, 71–78% for bladder and 44–60% for large bowel cancers in China, Singapore, Republic of Korea and Turkey. Survival rates were the lowest, not exceeding 22% for any cancer site, in The Gambia in West Africa. Locally advanced disease ranged from 22–66% for different cancers and survival decreased with advanced stages. Survival variations correlate well with the early detection initiatives and development of health services. The wide disparity in cancer survival between countries and regions observed emphasizes the need for planned, urgent investments in improving awareness, population-based cancer registration, early detection programmes, health services infrastructure and human resources. (Sankaranarayanan *et al.*, 2010; Sankaranarayanan *et al.*, 2011b; Sankaranarayanan & Swaninathan, 2011; Sankaranarayanan *et al.*, 2011c).

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Publications

Arrossi S, Paolino M, Sankaranarayanan R (2010). Challenges faced by cervical cancer prevention programs in developing countries: a situational analysis of program organization in Argentina. *Rev Panam Salud Publica,* 28:249–257.doi:10.1590/S1020-49892010001000003 PMID:21152712

Deerasamee S, Srivatanakul P, Sriplung H *et al.* (2007). Monitoring and evaluation of a model demonstration project for the control of cervical cancer in Nakhon Phanom province, Thailand. *Asian Pac J Cancer Prev,* 8:547–556. PMID:18260727

Ferlay J, Héry C, Autier P *et al.* (2010). Global Burden of Breast Cancer. In: Li CI (ed). *Breast Cancer Epidemiology.* Springer, pp. 1–19.

Hashibe M, Ferlay J, Sankaranarayanan R (2010). Chapter 3: Descriptive Epidemiology, International Patterns. In: Olshan AF (ed). Epidemiology, Pathogenesis and Prevention of Head and Neck Cancer. New York: Springer, pp. 41–63.

Herrero R, Wacholder S, Rodriguez AC *et al.* (2011). Prevention of Persistent Human Papillomavirus Infection by an HPV16/18 Vaccine: A Community-Based Randomized Clinical Trial in Guanacaste, Costa Rica. *Cancer Discovery,* 1:408–419. doi:10.1158/2159-8290.CD-11-0131

Johnson NW, Warnakulasuriya S, Gupta PC *et al.* (2011). Global oral health inequalities in incidence and outcomes for oral cancer: causes and solutions. *Adv Dent Res,* 23:237–246. doi:10.1177/0022034511402082 PMID:21490236

Karsa LV, Lignini TA, Patnick J *et al.* (2010). The dimensions of the CRC problem. *Best Pract Res Clin Gastroenterol,* 24:381–396.doi:10.1016/j.bpg.2010.06.004 PMID:20833343

Kuhaprema T, Attasara P, Srivatanakul P *et al.* (2011). Organization and evolution of organized cervical cytology: a national screening program in Thailand. *Asian Pac J Cancer Prev.* In press.

Lambert R (2010). Colorectal cancer in inflammatory bowel disease. *World Gastroenterology News,* 15:7–10.

Lambert R (2010). Oral and pharyngeal cancer. *World Gastroenterology News,* 15:5–10.

Lambert R (2010). Prevention of gastrointestinal cancer by surveillance endoscopy. *EPMA Journal,* 1:473–483 doi:10.1007/s13167-010-0023-4.

Lambert R (2010). Accreditation in digestive endoscopy. *Acta Gastroenterol Latinoam,* 40:278–282. PMID:21049772

Lambert R (2010). Gastric and rectal carcinoids. *Endoscopy,* 42:661–663. doi:10.1055/s-0030-1255592 PMID:20669077

Lambert R (2011). Revolution by Epigenetics expected in digestive oncology. *World Gastroenterology News.,* 16:8–10.

Lambert R, Partensky C (2011). Cancers de l'œsophage, de l'estomac et du colorectum: la révolution épigénétique. *Cancerodigest*, 3:29–35.

Lambert R, Sauvaget C, de Camargo Cancela M, Sankaranarayanan R (2011). Epidemiology of cancer from the oral cavity and oropharynx. *Eur J Gastroenterol Hepatol,* 23:633–641.doi:10.1097/MEG.0b013e3283484795 PMID:21654320

Lambert R, Tanaka S, Ponchon T (2011). Laterally spreading colorectal neoplastic lesions. Endoscopy Journal. In press.

Missaoui N, Hmissa S, Sankaranarayanan R *et al.* (2010). [p16INK4A overexpression is a useful marker for uterine cervix lesions]. *Ann Biol Clin (Paris)*, 68:409–414. PMID:20650735

Muwonge R, Manuel MdaG, Filipe AP *et al.* (2010). Visual screening for early detection of cervical neoplasia in Angola. *Int J Gynaecol Obstet,* 111:68–72.doi:10.1016/j.ijgo.2010.04.024 PMID:20570259

Namujju PB, Waterboer T, Banura C *et al.* (2011). Risk of seropositivity to multiple oncogenic human papillomavirus types among human immunodeficiency virus-positive and -negative Ugandan women. *J Gen Virol,* 92:2776–2783. doi:10.1099/vir.0.035923-0 PMID:21832008

Nessa A, Hussain MA, Rahman JN *et al.* (2010). Screening for cervical neoplasia in Bangladesh using visual inspection with acetic acid. *Int J Gynaecol Obstet,* 111:115–118.doi:10.1016/j.ijgo.2010.06.004 PMID:20674919

Ngoma T, Muwonge R, Mwaiselage J *et al.* (2010). Evaluation of cervical visual inspection screening in Dar es Salaam, Tanzania. *Int J Gynaecol Obstet,* 109:100–104.doi:10.1016/j.ijgo.2009.11.025 PMID:20152973

Pimple S, Muwonge R, Amin G *et al.* (2010). Cytology versus HPV testing for the detection of high-grade cervical lesions in women found positive on visual inspection in Mumbai, India. Int *J Gynaecol Obstet,* 108:236–239.doi:10.1016/j.ijgo.2009.10.005 PMID:19945105

Quirke P, Risio M, Lambert R *et al.* (2011). Quality assurance in pathology in colorectal cancer screening and diagnosis—European recommendations. *Virchows Arch,* 458:1–19.doi:10.1007/s00428-010-0977-6 PMID:21061133

Ramadas K, Sauvaget C, Thomas G *et al.* (2010). Effect of tobacco chewing, tobacco smoking and alcohol on all-cause and cancer mortality: a cohort study from Trivandrum, India. *Cancer Epidemiol,* 34:405–412.doi:10.1016/j.canep.2010.04.006 PMID:20444665

Rey JF, Lambert R, Aabakken L *et al.* (2011). Proceedings of a preliminary workshop at Gastro 2009–narrow banding imaging in digestive endoscopy: clinical outcome of classification (Omed-Jges Educational Meeting held on 22 November, 2009). *Dig Endosc,* 23:251–266.doi:10.1111/j.1443-1661.2010.01083.x PMID:21699571

Rubio CA, Törnblom H, Lindh C *et al.* (2010). Colon carcinomas arising in gut-associated lymphoid tissue in a patient with Lynch syndrome. Am J Clin Pathol. In press.

Sankaranarayanan R (2011). Prevention of mortality to cervical cancer in rural India. The value of an HPV test. (Interview). In: *Newsletter on Human Papillomavirus,* No. 23 pp. 1–3.

Sankaranarayanan R, Boffetta P (2010). Research on cancer prevention, detection and management in low- and medium-income countries. *Ann Oncol,* 21:1935–1943.doi:10.1093/annonc/mdq049 PMID:20231304

Sankaranarayanan R, Esmy PO, Thara S *et al.* (2011). Cervical cancer screening in the developing world. In: Rajaraman S *et al.*, editors. Cervix cancer, prevention, early diagnosis and management. Oxford University Press. In press.

Sankaranarayanan R, Ferlay J (2011). Global Burden of Gynaecological Cancer. In: Ayhan A, Gultekin M, Dursun P, editors. Gynaecological Oncology. Gunes Publishing. In press.

Sankaranarayanan R, Parimal J, Joshi S (2011). HPV vaccination in primary prevention of cervical cancer. In: Rajaraman S *et al.*, editors. Cervix cancer, prevention, early diagnosis and management. Oxford University Press. In press.

Sankaranarayanan R, Ramadas K, Thara S *et al.* (2011a). Clinical breast examination: preliminary results from a cluster randomized controlled trial in India. *J Natl Cancer Inst,* 103:1476–1480. doi:10.1093/jnci/djr304 PMID:21862730

Sankaranarayanan R, Sauvaget C, Ramadas K *et al.* (2011b). Clinical trials of cancer screening in the developing world and their impact on cancer healthcare. *Ann Oncol,* 22 Suppl 7;vii20–vii28. doi:10.1093/annonc/mdr422 PMID:22039141

Sankaranarayanan R, Swaminathan R (2011). Cancer survival in Africa, Asia, the Caribbean and Central America. *IARC Sci Publ*, 162:1-291.

Sankaranarayanan R, Swaminathan R, Brenner H *et al.* (2010). Cancer survival in Africa, Asia, and Central America: a population-based study. *Lancet Oncol,* 11:165–173.doi:10.1016/S1470-2045(09)70335-3 PMID:20005175

Sankaranarayanan R, Swaminathan R, Lucas E (2011c). Cancer survival in Africa, Asia, the Caribbean and Central America. *IARC Sci Publ*, 162:1-291.

Sankaranarayanan R, Thara S, Ngoma T *et al.* (2011). Cervical Cancer Screening in the Developing World. In: Finkel, M, editor. Public Health in the 21st Century, Volume 2, Disease Management, pp. 231–244.

Sauvaget C (2011). Bodymass index and mortality in India. In: Preedy, VR, editor. Handbook of Anthropometry. In press.

Sauvaget C, Fayette JM, Muwonge R *et al.* (2011). Accuracy of visual inspection with acetic acid for cervical cancer screening. *Int J Gynaecol Obstet,* 113:14–24.doi:10.1016/j.ijgo.2010.10.012 PMID:21257169

Sauvaget C, Nene BM, Jayant K *et al.* (2011). Prevalence and determinants of high-risk human papillomavirus infection in middle-aged Indian women. *Sex Transm Dis*, 38:902–906.doi:10.1097/OLQ.0b013e318223be5f PMID:21934560

Sauvaget C, Ramadas K, Fayette JM *et al.* (2011). Socio-economic factors & longevity in a cohort of Kerala State, India. *Indian J Med Res,* 133:479–486. PMID:21623031

Sauvaget C, Ramadas K, Thomas G *et al.* (2010). Prognosis criteria of casual systolic and diastolic blood pressure values in a prospective study in India. *J Epidemiol Community Health,* 64:366–372. doi:10.1136/jech.2008.086777 PMID:19692728

Stock EM, Stamey JD, Sankaranarayanan R *et al.* (2011). Estimation of disease prevalence, true positive rate, and false positive rate of two screening tests when disease verification is applied on only screen-positives: A hierarchical model using multi-center data. *Cancer Epidemiol.* In press. doi:10.1016/j.canep.2011.07.001 PMID:21856264

Swaminathan R, Sankaranarayanan R (2010). Under-diagnosis and under-ascertainment of cases may be the reasons for low childhood cancer incidence in rural India. *Cancer Epidemiol,* 34:107–108.doi:10.1016/j.canep.2009.11.006 PMID:20022839

Swaminathan R, Shanta V, Ferlay J *et al.* (2011). Trends in cancer incidence in Chennai city (1982–2006) and statewide predictions of future burden in Tamil Nadu (2007–16). *Natl Med J India*, 24:72–77. PMID:21668047

Teguete I, Muwonge R, Traore C *et al.* (2011). Can visual cervical screening be sustained in routine health services? Experience from Mali, Africa. *BJOG*. In press. PMID:21895956

Vieth M, Lambert R (2010). Nicht polypoide (serratierte) Läsionen des Kolon. Verdauungskrankheiten, 28:125–130.

Vieth M, Quirke P, Lambert R *et al.* (2011). Annex to Quirke *et al.* Quality assurance in pathology in colorectal cancer screening and diagnosis: annotations of colorectal lesions. *Virchows Arch,* 458:21–30.doi:10.1007/s00428-010-0997-2 PMID:21061132

Welton ML, Lambert R, Bosman FT (2010). Tumours of the anal canal. In: WHO Classification of Tumours of the Digestive System. Bosman FR, Carneiro F, Hruban RH, Theise ND, editors. *IARC Sci Publ*, 9:184–193.

Winawer SJ, Krabshuis J, Lambert R *et al.*; World Gastroenterology Organization Guidelines Committee (2011). Cascade colorectal cancer screening guidelines: a global conceptual model. *J Clin Gastroenterol,* 45:297–300.doi:10.1097/MCG.0b013e3182098e07 PMID:21301355

Zheng W, McLerran DF, Rolland B *et al.* (2011). Association between body-mass index and risk of death in more than 1 million Asians. *N Engl J Med,* 364:719–729.doi:10.1056/NEJMoa1010679 PMID:21345101

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Quality Assurance Group

The Quality Assurance Group (QAS) aims to expand and disseminate information essential to maximizing the benefit and minimizing the harm of population-based cancer prevention programmes. Previous projects have dealt with secondary prevention through cancer screening. In recent years, complementary primary prevention, such as vaccination against human papillomavirus infection and promotion of healthy lifestyle, have also been addressed. The focus of population-based programmes is to give each eligible individual an equal chance of benefiting from an intervention. This makes the benefits of cancer prevention accessible to the widest number of people and thereby maximizes the positive impact on overall control of cancer and other chronic diseases.

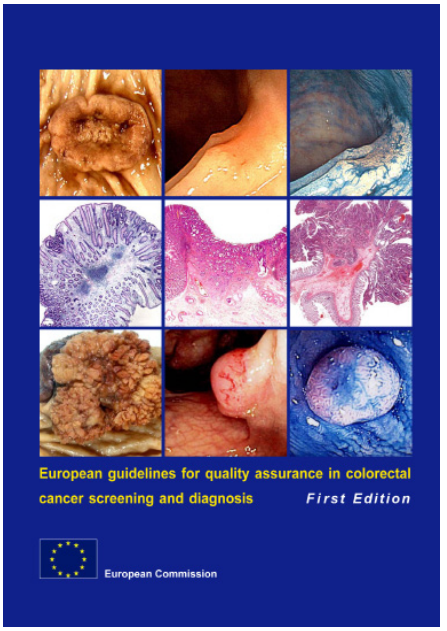


Figure 1. European Guidelines for Quality Assurance in Colorectal Cancer Screening and Diagnosis

The population-based approach to programme implementation is also recommended because it provides an organizational framework conducive to effective management and continuous improvement of health services, such as through linkage with population and cancer registries for optimization of invitation to screening and/or vaccination, and for evaluation of programme performance and impact.

The quality-assured process of population-based cancer screening not only includes identification, information and invitation of the eligible population to attend screening, but it also involves high-quality diagnosis and treatment of individuals with lesions detected through screening. Nationwide implementation of population-based screening programmes, according to evidence-based guidelines, makes high standard diagnostic and therapeutic services accessible to the entire population eligible for screening. Because large numbers of professionals undertake further specialization to meet the screening standards, they also deal with symptomatic patients. Consequently, these nationwide efforts also contribute to widespread improvement in diagnosis and management of cancers which are detected outside of screening programmes.

The activities of the Group are conducted in the framework of international collaborative projects with many experts in a wide range of health care settings, primarily in high, but increasingly also in low- and middle-income settings.

Development and updating of guidelines for quality assurance in cancer screening and diagnosis

Breast, cervical and colorectal cancers account for nearly one fifth of the 7.5 million cancer deaths per year worldwide (Ferlay *et al.*, 2010). Screening people of average risk for these cancers can lower the burden of disease in the population (IARC, 2002; IARC, 2005; Sankaranarayanan *et al.*, 2009; Lansdorp-Vogelaar & von Karsa, 2010). However, screening large segments of the population affects many predominantly healthy individuals and consumes considerable resources. Hence, quality assurance is required to maintain an appropriate balance between benefit and harm (Lansdorp-Vogelaar & von Karsa, 2010; von Karsa *et al.*, 2010).

Colorectal cancer screening

During the biennium, comprehensive evidence-based European Guidelines for Quality Assurance in Colorectal Cancer Screening and Diagnosis (Segnan *et al.*, 2010) (Figure 1) have been developed and published in a multi-year project coordinated by the QAS Group. The project involved 49 countries in four continents, primarily in Europe, but also in North and South America, Asia and Australia. Experts from all IARC Participating States contributed.

The 400-page evidence-based Guidelines cover the entire screening process from invitation and organization through diagnosis and management of any abnormalities detected through screening. They provide guiding principles, standards and procedures of quality assurance and best practice, which should be taken into account when establishing and running a colorectal cancer (CRC) screening programme in any resource setting. Although only the non-invasive faecal occult blood test is currently recommended for CRC screening by the EU, the new EU Guidelines also deal with endoscopic screening by colonoscopy or flexible sigmoidoscopy. In total, over 250 recommendations, graded according to the strength of the recommendation and the supporting evidence, are provided.

The new EU Guidelines are the first internationally developed, comprehensive procedures dealing with the entire process of CRC screening. They are also unique in the extensive documentation of the key clinical questions and the respective review that has been conducted to develop the standards and recommendations. Given the broad scope and depth of the Guidelines, only a few important aspects can be mentioned here.

The recommendations dealing with non-polypoid colorectal lesions, particularly in the serrated pathway, some of which are difficult to detect due to their non-polypoid morphology, is a prime example (Chap. 7 in Segnan *et al.* 2010) of the important contribution of the EU Guidelines. Although the existence of these lesions has been previously reported, their high prevalence was only recently recognized in the Western literature (Kudo *et al.*, 2008; Soetikno *et al.*, 2008). The first European protocol for surveillance of people found through screening to be at elevated risk for future development of CRC (Figure 2) is another important example of the innovative character of

the new Guidelines. Surveillance on an inappropriate scale has the potential to expose patients to unnecessary risks and to prohibit implementation of nationwide CRC screening programmes due to unnecessary consumption of limited colonoscopic resources (Chap. 9 in Segnan *et al.*, 2010; Winawer *et al.*, 2006).

The Guidelines also include the first comprehensive classification for histology of lesions detected in screening that is applicable worldwide (Table 1) (Chap. 7 in Segnan *et al.*, 2010; Quirke *et al.*, 2011). The detailed recommendations on communication, particularly on the essential elements to be included in invitation letters and informational brochures for CRC screening, are an additional resource that can help to reduce barriers to participation and therefore help to make high-quality screening available to all who may benefit (Chapters 2 and 10 in Segnan *et al.* 2010).

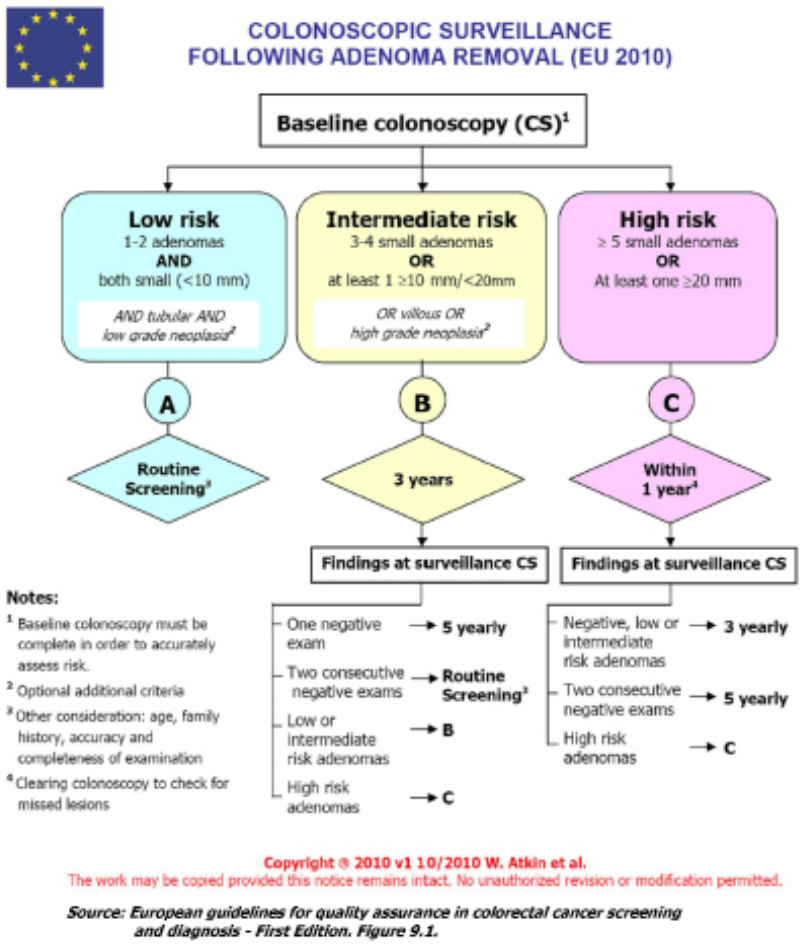
Breast cancer screening

Supplements dealing with histopathology, physico-technical quality control and digital mammography have been developed for the current fourth edition of the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis (Perry *et al.*, 2006). Publication is expected in 2012. These international collaborative efforts have been conducted in the framework of a project coordinated by QAS and co-financed by the EU Health Programme (European Cooperation for development and implementation of Cancer screening and prevention Guidelines (ECCG)).[1]

Cervical cancer screening and vaccination

In the framework of the above-mentioned EU project (ECCG), supplements on HPV testing and vaccination have also been prepared for the current second edition of the European Guidelines for Quality Assurance in Cervical Cancer Screening (Arbyn *et al.*, 2008). This work is currently ongoing with publication expected in 2012.

Figure 2. First protocol for monitoring screened individuals at risk of CRC



Source: European guidelines for quality assurance in colorectal cancer screening and diagnosis - First Edition. Figure 9.1.

Collaboration with WHO in development and implementation of cancer screening guidelines and in promotion of high-quality cancer registration

QAS has also collaborated with WHO headquarters (Departments of Reproductive Health and Research, Chronic Diseases Prevention and Management) and McMasters University in Canada in an ongoing effort to update the current WHO Guide to Essential Practice in Comprehensive Cervical Cancer Control (C4-GEP) (Figure 3) (WHO, 2006). Co-financing has been provided by WHO through a grant from the French National Cancer Institute. Publication of the final revised volume is expected in the next biennium.

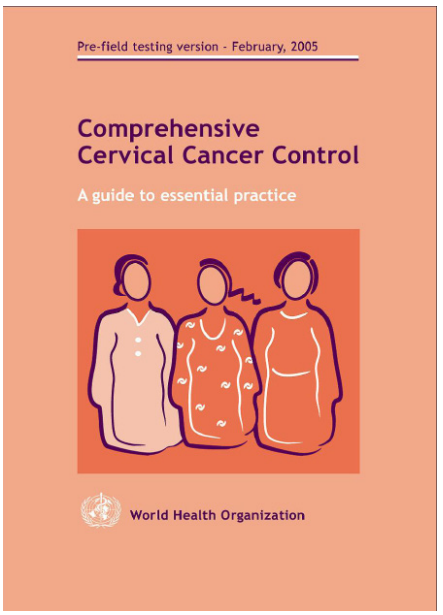


Figure 3. WHO Guide to Essential Practice in Comprehensive Cervical Cancer Control

In collaboration with the same departments at WHO headquarters, the European Regional Office (Director of Programme Management) and the respective WHO country offices, QAS has led joint WHO/IARC missions and workshops in Albania and Belarus. In these workshops, collaborating experts, IARC and WHO staff have assisted researchers and responsible authorities

Table 1. Adaptation of the revised Vienna classification[1] for colorectal cancer screening

1. No neoplasia[2]
Vienna Category 1 (Negative for neoplasia)
2. Mucosal low-grade neoplasia
Vienna Category 3 (Mucosal low-grade neoplasia
Low-grade adenoma
Low-grade dysplasia);
Other common terminology
Mild and moderate dysplasia;
WHO: low-grade intra-epithelial neoplasia
3. Mucosal high-grade neoplasia
Vienna: Category 4.1–4.4 (Mucosal high-grade neoplasia
High-grade adenoma/dysplasia
Non-invasive carcinoma (carcinoma in situ)
Suspicious for invasive carcinoma
Intramucosal carcinoma);
Other common terminology
Severe dysplasia;
High-grade intraepithelial neoplasia;
WHO: high-grade intraepithelial neoplasia
TNM: pTis
4. Carcinoma invading the submucosa or beyond:
4a. Carcinoma confined to submucosa
Vienna: Category 5 (submucosal invasion by carcinoma);
TNM: pT1
4b. Carcinoma beyond submucosa
TNM: pT2-T4

[1] For revised Vienna classification see Dixon (2002), for WHO classification see WHO (2000), for TNM see (TNM Classification of Malignant Tumours, 5th edition 1997; TNM Classification of Malignant Tumours, 6th edition 2002; TNM Classification of Malignant Tumours, 7th edition 2009).
[2] Category 2 of the Vienna Classification (indefinite) is not recommended for screening.
Source: European guidelines for quality assurance in colorectal cancer screening and diagnosis - First Edition. Table 7.1

in the development of plans for integrating population-based programmes for breast and cervical cancer screening into comprehensive efforts to improve cancer control.

Collaboration with cancer registries

A key outcome of the national workshops, conducted in collaboration with WHO, has been unanimous consensus on the need for fully functional cancer registries and effective and reliable linkage between screening data and cancer registry data to assure high-quality cancer screening programmes. The importance of collaboration between cancer screening registries and cancer registries in monitoring and evaluation was also highlighted. Priorities for future efforts were identified at a pan-European network meeting organized by QAS in collaboration with the work package on screening (Figure 4) in the EUROCOURSE[1] project and the Division of Epidemiology & Cancer Prevention in the Cancer Center & Institute of Oncology in Warsaw in May 2010 (Figure 5). The meeting was attended by 120 cancer screening and registration experts from across Europe and from Japan. The meeting was co-financed by the EU through the ECCG and EUROCOURSE projects.

Accreditation

At the request of the European Commission (Directorate Generals for Health and Consumers, and for Enterprise and Industry), the Group has continued an ongoing collaboration with the European cooperation for Accreditation (EA). Activities focused on planning a multi-year project for piloting an EU system for voluntary accreditation of breast cancer screening facilities. Useful experience in this area was also derived from missions of QAS staff and collaborators to Estonia and Malta to assess the progress of and exchange ideas about implementation of national breast cancer screening programmes. A mission to the Kielce region in Poland was also undertaken to prepare a pilot project implementing HPV testing in cervical cancer screening. This investigation was conducted in collaboration with the Division of Epidemiology and Cancer Prevention, Cancer Center and Institute of Oncology in Warsaw, the Holy Cross Cancer Centre and the regional cervical cancer screening programme in Kielce, Poland.

Discussions were also conducted with the Programme for Action in Cancer Therapy (PACT) of the International Atomic Energy Agency, to explore collaboration in the implementation of the accreditation project and to develop a joint proposal. Given the financial scope of the multi-year project, substantial external financing will be required to cover the 40% institutional contribution generally required for Directorate General for Health and Consumer Affairs (DG SANCO) grants.

European Code Against Cancer

The initial phase of a project to update the European Code Against Cancer (Boyle *et al.*, 2003) was completed during the biennium. At the request of DG SANCO, a project proposal to provide co-financing for the next phase of activities has been submitted to the Executive Agency for Health and Consumers.

European partnership for Action Against Cancer

During the biennium, QAS coordinated the development and submission of the application for the work package on cancer screening in the new Action Against Cancer in the framework of the EU Health Programme. Subsequent to approval of the proposal, the Group has provided core scientific and technical support for the work package coordination.

[1] The EUROCOURSE project (EUROpe against Cancer: Optimization of the Use of Registries for Scientific Excellence in research) is funded by the Seventh Framework Programme of the EU. The focus of the activities in work package 5 is developing and improving the interface of cancer registries with cancer screening programmes.

Figure 4.

Global screening report

At the request of DG SANCO, a project proposal has also been developed for updating and expanding the previously published report on implementation of cancer screening in the EU. Similar to the development and updating of the European Guidelines for quality assurance in cancer screening, international experts outside the EU will also be involved in the preparation of the next screening report. Additional funding will be sought during the next biennium to expand these efforts to encompass other regions of the world.

Figure 5.

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Publications

Arbyn M, Anttila A, Jordan J *et al.*, editors (2008). European guidelines for quality assurance in cervical cancer screening - second edition. Office for Official Publications of the European Communities, Luxembourg.

Arbyn M, Anttila A, Jordan J *et al.* (2010). European Guidelines for Quality Assurance in Cervical Cancer Screening. Second edition–summary document. *Ann Oncol,* 21:448–458.doi:10.1093/annonc/mdp471 PMID:20176693

Boyle P, Autier P, Bartelink H *et al.* (2003). European Code Against Cancer and scientific justification: third version (2003). *Ann Oncol,* 14:973–1005. doi:10.1093/annonc/mdg305 PMID:12853336

Ferlay J, Shin HR, Bray F *et al.* (2010). GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. IARC, Lyon, France.

IARC (2002). IARC Handbooks of Cancer Prevention, Vol.7: Breast Cancer Screening. IARC, Lyon, France.

IARC (2005). IARC Handbooks of Cancer Prevention, Vol.10: Cervix Cancer Screening. IARC, Lyon, France.

Kudo S, Lambert R, Allen JI *et al.* (2008). Nonpolypoid neoplastic lesions of the colorectal mucosa. *Gastrointest Endosc,* 68 Suppl;S3–S47. doi:10.1016/j.gie.2008.07.052 PMID:18805238

Lansdorp-Vogelaar I, von Karsa L (2010). Chapter 1: Introduction, in European guidelines for quality assurance in colorectal cancer screening and diagnosis - First edition, Segnan N, Patnick J & von Karsa L, (eds.). European Commission, Publications Office of the European Union, Luxembourg: 1–32.

Lynge E, Törnberg S. von Karsa L *et al.* (2011). Determinants of successful implementation of population-based cancer screening programmes. EJC. In press.

Perry N, Broeders M, de Wolf C *et al.*, editors (2006), European guidelines for quality assurance in breast cancer screening and diagnosis. Fourth edition. Office for Official Publications of the European Communities, Luxembourg.

Quirke P, Risio M, Lambert R *et al.* (2011). Quality assurance in pathology in colorectal cancer screening and diagnosis—European recommendations. *Virchows Arch,* 458:1–19. doi:10.1007/s00428-010-0977-6 PMID:21061133

Quirke P, Risio M, Lambert R, von Karsa L & Vieth M (2010). Chapter 7: Quality assurance in pathology in colorectal cancer screening and diagnosis, in European guidelines for quality assurance in colorectal cancer screening and diagnosis - First edition, Segnan N, Patnick J & von Karsa L (eds.). European Commission, Publications Office of the European Union, Luxembourg: 205–232.

Sankaranarayanan R, Nene BM, Shastri SS *et al.* (2009). HPV screening for cervical cancer in rural India saves women's lives. *N Engl J Med,* 360:1385–1394.doi:10.1056/NEJMoa0808516 PMID:19339719

Segnan N Patnick J & von Karsa L, editors (2010). European guidelines for quality assurance in colorectal cancer screening and diagnosis - First edition. European Commission, Publications Office of the European Union, Luxembourg.

Soetikno RM, Kaltenbach T, Rouse RV *et al.* (2008). Prevalence of nonpolypoid (flat and depressed) colorectal neoplasms in asymptomatic and symptomatic adults. *JAMA*, 299:1027–1035. doi:10.1001/jama.299.9.1027 PMID:18319413

Vieth M, Quirke P, Lambert R *et al.* (2011). Annex to Quirke *et al.* Quality assurance in pathology in colorectal cancer screening and diagnosis: annotations of colorectal lesions. *Virchows Arch,* 458:21–30.doi:10.1007/s00428-010-0997-2 PMID:21061132

Vieth M, Quirke P, Lambert R *et al.* (2010). Chapter 7 Annex: Annotations of colorectal lesions, in European guidelines for quality assurance in colorectal cancer screening and diagnosis - First edition, Segnan N, Patnick J & von Karsa L, editors. European Commission, Publications Office of the European Union, Luxembourg: 233–250.

von Karsa LV, Lignini TA, Patnick J *et al.* (2010). The dimensions of the CRC problem. Best Pract *Res Clin Gastroenterol,* 24:381–396.doi:10.1016/j.bpg.2010.06.004 PMID:20833343

von Karsa L, Arrossi S (2011). Development and implementation of guidelines for quality assurance in breast cancer screening – the European experience. Mexican Journal of Public Health. In press.

Winawer SJ, Zauber AG, Fletcher RH *et al.*; US Multi-Society Task Force on Colorectal Cancer; American Cancer Society (2006). Guidelines for colonoscopy surveillance after polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society. *Gastroenterology*, 130:1872–1885. doi:10.1053/j.gastro.2006.03.012 PMID:16697750

World Health Organization (2006). Comprehensive cervical cancer control: a guide to essential practice. WHO Department of Reproductive Health and Research and the Department of Chronic Diseases and Health Promotion. Geneva.

Prevention and Implementation Group (PRI)

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Every year more than 7 million people die from cancer, with the majority (75%) of cases occurring in developing countries. This proportion is rapidly increasing with population ageing in those areas. Using what we already know about cancer etiology and effective interventions, it is possible to prevent over 30% of premature deaths from cancer and to cure or prolong survival in another 30% with early detection and proper treatment.

Some examples of preventive interventions include: smoking cessation efforts; promotion of healthy diets, exercise and weight control programmes; and vaccination against hepatitis B to control liver cancer and human papillomavirus to prevent cervical, anal and possibly oropharyngeal cancer. In addition, screening for cervical, colorectal, breast, oral and stomach cancer have been shown to be effective when widely implemented. In the case of cervical cancer, for example, important advances in both primary and secondary prevention have been made in recent years. Several new preventive interventions offer enormous hope for reducing incidence and mortality from this disease, which has been extremely difficult to control in developing countries and remains one of the leading causes of cancer death.

For many cancers, there is still a need to develop safe and affordable preventive interventions. In the case of stomach cancer, another common malignancy, despite ample knowledge about the role of *Helicobacter pylori* in its etiology and the success of expensive endoscopy-based programmes, there is a clear need to investigate the potential of more affordable interventions, like screening with markers of atrophic gastritis or eradication of *Helicobacter pylori,* for example. For most interventions, there is a need to conduct research on how best to implement interventions in different socioeconomic and cultural settings.

It is important to disseminate information on how to apply current knowledge to cancer prevention, to generate new data to improve available interventions, and to investigate new approaches for control of the major cancers.

The objectives of the newly created Prevention and Implementation Group (PRI) are to: evaluate new preventive strategies with particular emphasis on the use of new technologies, including molecular markers; to engage in research on methods to implement existing strategies taking into account social, economic and cultural differences; and to collaborate with decision-makers to implement already available preventive interventions against cancer, particularly in developing countries where the need is highest. An additional objective is to foster technology transfer and generate educational processes for clinicians, public health decision-makers and the public, to make sure the available technology and information is available where it is needed most.

Natural history studies of cervical cancer

The Guanacaste, Costa Rica HPV natural history study (NHS) is a prospective, population-based cohort study with participation of a random sample of more than 10 000 women in a high risk area for cervical cancer, who were recruited, screened and followed for more than seven years beginning in 1993-1994. The study has generated a large series of publications and has clarified multiple aspects of the natural history of the disease, including epidemiologic, virologic, immunologic and genetic variables. In addition, it has provided extensive information on the validity of different screening methods in the region. A series of ancillary studies are being conducted to further investigate the reasons for the high prevalence of HPV infection in older women, to evaluate fluctuations of cervical antibody levels with the menstrual cycle and to define the long-term outcome of treatment of precancerous lesions.

HPV vaccine trial in Guanacaste, Costa Rica

A randomized clinical trial to evaluate the efficacy of the bivalent (HPV 16/18) vaccine was initiated in 2004 as a continuation of the NHS. A total of 7466 women, ages 18–25, were recruited and randomized to receive the HPV vaccine or a hepatitis A vaccine as control. Women were screened at yearly intervals and followed for four years. At the end of follow-up, all women received the vaccines they did not receive at recruitment (crossover) plus a hepatitis B vaccine as an additional benefit. The study confirmed the efficacy of the bivalent vaccine against HPV 16 and 18 and described its cross-protection against HPV 31, 33 and 45 (Herrero *et al.*, 2011). In addition, in stratified analyses, it showed the decline in vaccine efficacy at the population level with increasing age. One of the most interesting findings was the observation that HPV vaccine efficacy against HPV 16 and 18 was equally good among women who received one, two and three doses (Kreimer *et al.*, 2011), while there was no efficacy among women who were positive at the time of vaccination (Hildesheim *et al.*, 2007). Current plans include long-term follow-up of the vaccinated cohort. Given the fact that all women have now received the HPV vaccine, a new unvaccinated control group of about 2500 women was recruited recently to continue the evaluation of efficacy and safety over 10 years. During the Costa Rica HPV vaccine trial, we observed a high prevalence of anal HPV infection among young women. HPV-positive women will be followed with periodic virologic and cytologic examinations to investigate the natural history of anal infections and their relation to anal intraepithelial neoplasia.

Also in the framework of the Costa Rica HPV vaccine trial, we have evaluated and demonstrated high efficacy of the bivalent vaccine against anal infection (Kreimer *et al.*, 2011). These results will be followed over time to ascertain their potential as anal cancer prevention tools. Furthermore, we obtained an oral specimen for HPV testing from all women at their four year visit. Despite the lack of baseline oral HPV results, it will be possible to evaluate vaccine efficacy against prevalent infections in a randomized fashion. Further follow-up of study cohorts will establish efficacy of this intervention to reduce the burden of cervical neoplasia.

ASCUS triage project in Medellín, Colombia

The Atypical Squamous Cells of Unknown Significance (ASCUS) project in Antioquia, Colombia is conducted in collaboration with the Cancer and Infection Group at the University of Antioquia in Colombia. It is a randomized clinical trial of three different approaches to triage women with cytologic diagnosis of ASCUS and is underway in Medellín, Colombia. Approximately 3000 women with an ASCUS are being recruited and randomized to immediate colposcopy, repeat cytology or HPV testing. It is anticipated that the study will provide information on how to manage this frequent diagnosis in the context of the Colombian health system.

Multicentre study of triage methods for HPV-positive women

A screening investigation is being planned to define the best triage strategy for HPV-positive women in screening programmes based on HPV testing as the primary modality. There is now a trend for screening programmes to transition from cytology to HPV testing as the primary screening method, but the positive predictive value of the HPV test remains limited because many women with HPV infection do not develop disease, even when programmes are targeted to women over 30 years of age. It is therefore necessary to investigate the usefulness of a series of triage techniques, including visual inspection and cytology and a series of new biomarkers based on detection of DNA, RNA, proteins or other markers of transformation. The plan is to recruit nearly 100 000 women from several countries initially in Latin America, collect appropriate specimens, and obtain descriptive definitions of their cervical diagnosis in order to evaluate currently available and future triage methods.

Support of screening or vaccination initiatives in Latin America

Argentina is one of the countries that is starting to vaccinate young women with the HPV vaccine and at the same time is implementing HPV testing as the primary screening modality. The initial step in this process is the organization of a large pilot project in the Province of Jujuy, with the collaboration of PRI staff. Similarly, several countries in Latin America are considering or have started implementation of vaccination or HPV testing as their primary strategy (e.g. Mexico, Panama and Chile) with active participation of PRI staff.

Clinical trial of *Helicobacter pylori* eradication

In collaboration with the US Southwest Oncology Group and several centres in Latin America, PRI staff participated in a multicentre trial to evaluate the best option as an eradication treatment against Helicobacter pylori (Greenberg *et al.*, 2011). The eradication rate for the different treatments at six weeks has been published. In the near future the results for one year will be reported, in addition to a series of reports incorporating several biomarkers.

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Publications

Bottalico D, Chen Z, Dunne A *et al.* (2011). The oral cavity contains abundant known and novel human papillomaviruses from the Betapapillomavirus and Gammapapillomavirus genera. *J Infect Dis,* 204:787–792.doi:10.1093/infdis/jir383 PMID:21844305

Campos NG, Rodriguez AC, Castle PE *et al.* (2011). Persistence of concurrent infections with multiple human papillomavirus types: a population-based cohort study. *J Infect Dis,* 203:823–827.doi:10.1093/infdis/jiq131 PMID:21257737

Castle PE, Rodríguez AC, Burk RD *et al.*; Proyecto Epidemiológico Guanacaste Group (2011). Long-term persistence of prevalently detected human papillomavirus infections in the absence of detectable cervical precancer and cancer. *J Infect Dis,* 203:814–822.doi:10.1093/infdis/jiq116 PMID:21343148

Chaturvedi AK, Katki HA, Hildesheim A *et al.*; CVT Group (2011) Human papillomavirus infection with multiple types: pattern of coinfection and risk of cervical disease. *J Infect Dis,* 203:910–920. doi:10.1093/infdis/jiq139 PMID:21402543

Chen D, Truong T, Gaborieau V *et al.* (2011). A sex-specific association between a 15q25 variant and upper aerodigestive tract cancers. *Cancer Epidemiol Biomarkers Prev,* 20:658–664.doi:10.1158/1055-9965.EPI-10-1008 PMID:21335511

Chen Z, Schiffman M, Herrero R *et al.* (2011). Evolution and taxonomic classification of human papillomavirus 16 (HPV16)-related variant genomes: HPV31, HPV33, HPV35, HPV52, HPV58 and HPV67. *PLoS One,* 6:e20183.doi:10.1371/journal.pone.0020183 PMID:21673791

Greenberg ER, Anderson GL, Morgan DR *et al.* (2011). 14-day triple, 5-day concomitant, and 10-day sequential therapies for Helicobacter pylori infection in seven Latin American sites: a randomised trial. *Lancet*, 378:507–514.doi:10.1016/S0140-6736(11)60825-8 PMID:21777974

Herrero R, Wacholder S, Rodriguez AC *et al.* (2011). Prevention of Persistent Human Papillomavirus Infection by an HPV16/18 Vaccine: A Community-Based Randomized Clinical Trial in Guanacaste, Costa Rica. *Cancer Discovery,* 1:408–419. doi:10.1158/2159-8290.CD-11-0131

Hildesheim A, Herrero R, Wacholder S *et al.*; Costa Rican HPV Vaccine Trial Group (2007). Effect of human papillomavirus 16/18 L1 viruslike particle vaccine among young women with preexisting infection: a randomized trial. *JAMA*, 298:743–753. doi:10.1001/jama.298.7.743 PMID:17699008

Kemp TJ, Hildesheim A, Safaeian M *et al.* (2011). HPV16/18 L1 VLP vaccine induces cross-neutralizing antibodies that may mediate cross-protection. *Vaccine*, 29:2011–2014.doi:10.1016/j.vaccine.2011.01.001 PMID:21241731

Kreimer AR, González P, Katki HA *et al.*; for the CVT Vaccine Group (2011). Efficacy of a bivalent HPV 16/18 vaccine against anal HPV 16/18 infection among young women: a nested analysis within the Costa Rica Vaccine Trial. *Lancet Oncol,* 12:862–870.doi:10.1016/S1470-2045(11)70213-3 PMID:21865087

Kreimer AR, Rodriguez AC, Hildesheim A *et al.*; for the CVT Vaccine Group (2011)). Proof-of-Principle Evaluation of the Efficacy of Fewer Than Three Doses of a Bivalent HPV16/18 Vaccine. *J Natl Cancer Inst,* 103:1444–1451. PMID:21908768

Kreimer AR, Schiffman M, Herrero R *et al.* (2011) Long-term risk of recurrent cervical HPV infection and precancer and cancer following excisional treatment. *Int J Cancer.*doi:10.1002/ijc.26349 PMID:21823117

Louie KS, Castellsague X, de Sanjose S *et al.*; International Agency for Research on Cancer Multicenter Cervical Cancer Study Group (2011). Smoking and passive smoking in cervical cancer risk: pooled analysis of couples from the IARC multicentric case-control studies. *Cancer Epidemiol Biomarkers Prev,* 20:1379–1390.doi:10.1158/1055-9965.EPI-11-0284 PMID:21610224

Lubin JH, Muscat J, Gaudet MM *et al.* (2011). An examination of male and female odds ratios by BMI, cigarette smoking, and alcohol consumption for cancers of the oral cavity, pharynx, and larynx in pooled data from 15 case-control studies. *Cancer Causes Control,* 22:1217–1231.doi:10.1007/s10552-011-9792-x PMID:21744095

McKay JD, Truong T, Gaborieau V *et al.* (2011). A genome-wide association study of upper aerodigestive tract cancers conducted within the INHANCE consortium. *PLoS Genet,* 7:e1001333. doi:10.1371/journal.pgen.1001333 PMID:21437268

Porras C, Wentzensen N, Rodríguez AC *et al.* (2011) Switch from cytology-based to human papillomavirus test-based cervical screening: Implications for colposcopy. *Int J Cancer,* n/a. doi:10.1002/ijc.26194 PMID:21607948

Rodríguez AC, García-Piñeres AJ, Hildesheim A *et al.* (2011). Alterations of T-cell surface markers in older women with persistent human papillomavirus infection. *Int J Cancer,* 128:597–607.doi:10.1002/ijc.25371 PMID:20473864

Smith B, Chen Z, Reimers L *et al.* (2011). Sequence imputation of HPV16 genomes for genetic association studies. *PLoS One,* 6:e21375. doi:10.1371/journal.pone.0021375 PMID:21731721

Vaccarella S, Franceschi S, Herrero R *et al.* (2011). Clustering of multiple human papillomavirus infections in women from a population-based study in Guanacaste, Costa Rica. *J Infect Dis,* 204:385–390.doi:10.1093/infdis/jir286 PMID:21742837

Wentzensen N, Rodriguez AC, Viscidi R *et al.* (2011). A competitive serological assay shows naturally acquired immunity to human papillomavirus infections in the Guanacaste Natural History Study. *J Infect Dis,* 204:94–102.doi:10.1093/infdis/jir209 PMID:21628663