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Poster Abstracts

New Technologies and Comparative Effectiveness

The Danish Lung Cancer Screening Trial

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Background: Randomized controlled trials of the effect of lung cancer screening with CT scanning are now being performed both in the U.S. and in Europe. In the U.S., the National Lung Screening Trial includes 53.461 participants and compares annual CT screening with chest x-ray. The trial finished recruitment in 2004 and is expected to have a final analysis in 2009 or 2010. In Europe, several randomized trials are being performed in different countries; in most, CT screening is compared with no screening in the control arm of the trials. The largest trial is the NELSON trial, which is being performed in the Netherlands and Belgium and includes 15.523 participants. In Denmark, the Danish Lung Cancer Screening Trial (DLCST) started recruitment in 2004, has included 4104 participants, will complete screening by March 2010, and plans to pool results with the NELSON trial. The results of baseline screening have been reported. In Italy, two different randomized trials are conducted: the ITALUNG trial includes 3206 participants, and the DANTE trial includes 2472 participants. In Germany, a randomized trial including 4000 participants has started but not yet finished recruitment.

Results: At baseline, 179 persons showed noncalcified nodules larger than 5 mm, and most were rescanned after 3 months. The rate of false-positive diagnoses was 7.9%, and 17 individuals (0.8%) turned out to have lung cancer. Ten of these had stage I disease. The preliminary results from the DLCST of the following screening rounds will be presented.

Psychosocial Consequences of Cancer Screening: Development and Validation of a Questionnaire

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Background: In cancer screening, thousands have to be screened several times to prevent one death from the cancer screened for. To obtain this reduction in mortality, hundreds of healthy participants will inevitably have false-positive screening results.

Objective: Firstly, to develop different condition-specific questionnaires measuring psychosocial consequences of abnormal and false-positive cancer screening results; secondly, to test if the different questionnaires encompassed a common core questionnaire; and, thirdly, to statistically validate the questionnaires using primarily the Item Response Theory Rasch model.

Methods: Focus group interviews with participants from breast, cervical, and lung cancer screening programmes were conducted. The psychosocial consequences of abnormal and false-positive screening results were discussed. The face and content validity of the draft version of the questionnaires were tested in the focus groups. Survey data from breast, cervical, and lung cancer screening programmes have been analysed using primarily Rasch analysis. Classical Test Theory analyses have also been conducted.

Results: A core questionnaire, Consequences of Screening (COS), encompassing two parts, has been found relevant and valid for screening participants for breast, lung, and cervical cancer. The COS Part I consists of 26 items; Part II consists of 22 items. Part II of the COS is a universal questionnaire for long-term psychosocial consequences. In order to achieve high content validity, breast, cervical, and lung cancer screening-specific items and dimensions must be added to the COS.

Conclusion: The reliability and the construct validity of a core questionnaire have been established. The COS has been translated into several languages and is used in ongoing surveys.

Integrating Digital Mammography in a Decentralised Breast Cancer Screening Programme

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Purpose: The implementation of digital mammography in a decentralised screening programme requires adaptations in image transmission, reconciliation with previous mammograms, storage, on-screen reading and reporting, and workflow. This conversion is an informatics challenge for both the radiology cabinet and the screening programme.

Methods and Materials: Eight public/private radiology cabinets with four different Mx devices (two Sectra devices, three GE devices, two Lorads, and one Fuji/Siemens CR system) collaborated with the breast screening programme in canton Fribourg. For image transmission, each centre installed a KISANO server, which assured high security level image transmission over the Internet on a peer-to-peer basis. After acquisition, the image is sent to the KISANO server and reconciled with the previous Mx (received from the central archive, if available). The first radiology reading is done following the work list on the local workstation. The Web-based electronic screening reporting form follows the work list, and when validated, the information is transmitted to the screening centre with the current and prior images. There, the second reading takes place on a multi-modality workstation. All communications between the radiology cabinets, the screening centre, and the archive are provided by a central hosted communication centre.

Results: Automated DICOM image transmission and reconciliation with previous mammograms using the KISANO server modality proved to be a robust system in a multi-vendor environment. Electronic reporting decreased the number of incomplete reports.

Conclusion: Integration of multi-vendor digital mammography devices in a decentralised screening programme has been implemented successfully.

Evaluation of Lung Cancer Screening: The Japanese Guidelines for Lung Cancer Screening

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Background: Lung cancer is the leading cause of death from cancer in Japan. In 2007, there were 65,602 deaths from lung cancer, accounting for 19.5% of the total cancer deaths.

Methods: The guidelines for lung cancer screening were developed based on the established method. The efficacy of chest radiography, sputum cytology, and low-dose computed tomography (CT) was evaluated. Based on the balance of the benefits and harms, recommendations for population-based and opportunistic screening were formulated.

Results: Based on the analytic framework involving key questions, 1,576 articles published from January 1985 to July 2005 were selected using MEDLINE and other databases. After the systematic review, 72 articles were confirmed. For evaluation of chest radiography and its use in combination with sputum cytology, four randomized controlled trials (RCTs) and five case-control studies were found. All RCTs were conducted in the 1970s and 1980s. These results did not suggest that lung cancer screening reduced mortality. However, treatment for lung cancer has

been improved since these studies were conducted. Mortality reduction from lung cancer was shown in four out of five case-control studies conducted after the late 1990s in Japan. No studies have evaluated the effect of CT screening on mortality from lung cancer.

Conclusions: Considering the improvement in treatment for lung cancer and based on the results of five case-control studies conducted in Japan, we recommended a combination of chest radiography and sputum cytology (limited to the high-risk group). CT screening is not recommended for population-based screening due to insufficient evidence.

Rising Chemotherapy Costs Make Colorectal Cancer Screening Cost-Saving

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Background: Colorectal cancer (CRC) not only causes high morbidity and mortality, but also generates a considerable burden of treatment costs that increases explosively because of newer, more expensive chemotherapies.

Objective: To examine whether CRC screening would become cost saving with the widespread use of the newer chemotherapies.

Methods: We used the MISCAN-Colon microsimulation model to assess whether widespread use of new chemotherapies would affect the treatment savings of CRC screening in the general population. We considered three scenarios for chemotherapy use: the past, the present, and the near future. We assumed that survival improved and treatment costs for patients diagnosed with advanced stages of CRC increased over the scenarios.

Results: Compared with no screening, the treatment savings from preventing advanced CRC and CRC deaths by screening more than doubled with the widespread use of new chemotherapies. The lifetime average treatment savings were larger than the lifetime average screening costs for screening with Hemoccult II, immunochemical FOBT, sigmoidoscopy, and the combination of sigmoidoscopy and Hemoccult II (average savings versus costs per individual in the population: Hemoccult II, $1398 versus $859; immunochemical FOBT, $1756 versus $1565; sigmoidoscopy, $1706 versus $1575; sigmoidoscopy and Hemoccult II, $1931 versus $1878). Colonoscopy did not become cost saving, but the total net costs of this strategy decreased from $1317 to $296 per individual in the population.

Conclusions: With the increase in chemotherapy costs for advanced CRC, screening becomes a desirable approach not only to reduce CRC incidence and mortality but also to control the costs of CRC treatment.

Cost-Effectiveness of Stool DNA Testing to Screen for Colorectal Cancer in the Medicare Population

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Background: The Centers for Medicare and Medicaid Services (CMS) considered whether to reimburse stool DNA testing for colorectal cancer screening among Medicare enrollees.

Objective: To evaluate the conditions under which stool DNA testing could be cost-effective compared with the colorectal cancer screening tests currently reimbursed by CMS.

Methods: We used two independently developed microsimulation models to compare effects and costs of stool DNA testing every three years and every five years to those of the currently reimbursed CRC screening strategies.

Results: Strategies of stool DNA testing every three or five years gained fewer life-years at higher costs than the currently recommended colorectal cancer screening strategies and were therefore dominated. Screening with the stool DNA test would be cost-effective at a per-test cost of $40 to $60 for 3-yearly stool DNA testing, depending on

the simulation model used. Threshold costs of the stool DNA test at 3-year intervals were $140 to $167, with 50% better test characteristics and $302 to $364 with a perfect test. If the stool DNA test were able to increase screening adherence to 75%, while adherence for other strategies remained at 50%, the threshold costs could increase to $314–$391.

Conclusion: Future stool DNA test development should not only focus on improving test characteristics but also on reducing test costs, because even with perfect test characteristics, stool DNA screening is not cost-effective at the current test cost.

Type of Hormone Therapy and Risk of Misclassification at Mammography Screening

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Background: The accuracy of screening mammography is known to be lower in current hormone therapy (HT) users than in never users.

Objective: To investigate how the risk of misclassification at mammography screening depends on type of hormone, administration, regime, and dose of the therapy.

Methods: We linked data from the Mammography Screening Register from Fyn with the Drug Prescription Register from Fyn to identify current and never HT users among screening participants. We compared the false-positive risk and the interval cancer proportion between current users of different HT preparations, taking women's age, breast density, screen number, and age of comparison mammogram into account.

Results: Oestrogen-only users had a significantly higher false-positive risk when administered by injection instead of oral (RR 2.37, 95% CI 1.37–4.09]). Women using sequential oestrogen-progestogen had a significantly higher false-positive risk (RR 1.94, 95% CI 1.16–3.26) and a non-significantly higher interval cancer proportion (RR 4.29, 95% CI 0.69–26.53), when administration of both hormones was transdermal instead of oral. Tibolone use resulted in a non-significantly lower false-positive risk and a non-significantly higher interval cancer proportion compared with comparable hormones.

Conclusions: Our data showed an increased risk of misclassification at mammography screening among oestrogen-only users when administered via injection and among sequential oestrogen-progestogen users when the administration is transdermal for both hormones. A possible explanation is that these two HT preparations lead to a raised concentration of oestrogen or progestogen in the plasma for several days, followed by a period of non-raised concentration. Tibolone seems not to offer an advantage regarding accuracy of screening mammography.

Effectiveness of Population-Based Service Screening With Mammography for Women Aged 40–49 Years

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Background: Though consensus has been reached that mammography screening can reduce mortality for women age 50–69, the effectiveness for women age 40–49 is still questioned, and few studies of the effectiveness of service screening for the age group have been made.

Objective: The aim of this study was to estimate the effectiveness of service screening in the age group 40–49 on breast cancer mortality for women invited to and attending mammography screening.

Methods: All Swedish counties were included in the study. Breast cancer mortality was compared between areas

with screening for women 40–49 years (study group) and areas where women below age 50 were not invited (control group). The mortality measure used was incidence-based mortality with breast cancer as underlying cause of death. The average followup was 16 years in both the study and control groups. The numbers of person-years were 7.3 and 8.8 million for the study group and control group, respectively. Individual data were collected to adjust for women not invited and for non-compliance.

Results: The estimated relative risk for the reference period 1970–1985 (i.e., before the start of service screening), was 0.94 (95% CI: 0.85 to 1.05). The numbers of breast cancer deaths were 803 and 1238 in the study group and control group, respectively, during the followup 1986–2005. The RR was 0.75 (0.67–0.84) when adjusting for non-invitation and 0.72 (0.64–0.81) when adjusting for non-compliance.

Conclusions: In this large study, mammography screening for women aged 40–49 is clearly shown to be efficient for reducing breast cancer mortality.

Effectiveness of Cervical Cancer Screening: Patients' Understanding of Screening for the Cancer in Major Hospitals in Malaysia

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Background/Objective: We studied women with cervical cancer to determine whether they had had a Pap smear within the 3 years preceding cancer development and their understanding of screening for this cancer.

Methods: The study had two parts: (1) Pathology Data and (2) Survey Data. For pathology data, all cases of cervical cancer diagnosed in 2000–2006 were retrieved from eight hospitals. The Pap smear history was obtained from clinical records. For the survey data, patients who were still undergoing treatment in some of these hospitals and three others were administered structured questionnaires to determine their awareness about screening.

Results: The results showed 1431 cases of cervical cancer in women aged 25–85 were diagnosed in these hospitals. Most had not had a Pap smear within 3 years before cancer development. The percentage of patients who had had Pap smears ranged from 0% to 12%. Questionnaires were returned by 221 patients; 56.3% had no or only primary education and 61.1% had a household income of RM1000 or less. Level of education and household income were strongly associated ($p<0.05$) with knowledge of and having had a Pap test. The main reasons cited for not having had a Pap smear were "Never heard about it" (36.2%), "Shy" (10.4%), "Afraid to do it" (13.1%), "Think the test is not important" (8.1%), and "No encouragement from family" (4.5%). A large majority (95.9%) of the patients did not know the optimal interval for screening.

Conclusion: In conclusion, a large number of cervical cancer patients had not had a Pap smear within 3 years preceding cancer development and most had inadequate knowledge about this screening test.

Net Direct Costs for Treating Colorectal Cancer in Ontario

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Background: As the Canadian Institute for Health Research Team in Population Based Colorectal Cancer (CRC) Screening, we investigate the comparative effectiveness of policy options and the net direct costs of treating CRC for cost-effectiveness analysis of these options.

Objective: Estimate net direct costs of treating CRC in Ontario.

Methods: We estimated all direct health care costs to the universal public payer among all Ontario residents receiving a first diagnosis of CRC from 1996 to 2007 (ages 50 to 75), identified from the population-based cancer registry, using linked administrative data. We compared these costs to those of age- and sex-matched controls. Records were extracted from the diagnosis date of CRC and the index date of controls, to death or last followup. We included direct costs for physician, hospital, home care, diagnostic, laboratory and prescription drug services, and

radiotherapy and chemotherapy (including new agents). Costs were assigned to initial care (12 months following CRC diagnosis), continuing care (cases and controls), and terminal care (12 months preceding death, stratified by cause of death for cases and controls). Average costs per control were subtracted from average costs per CRC case to obtain net costs of treating CRC.

Results: Net costs of treatment increased with higher stages, younger ages, male gender, and deaths due to CRC compared with other causes. These will be compared with international results, and implications for population-based CRC screening and control will be examined.

Conclusion: Complete net direct costs of treatment are mandatory for planning population-based CRC screening and control.

Evolution and Early Results From Ontario's Province-Wide Colorectal Cancer Screening Program

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Background: Ontario, Canada is implementing Canada's first province-wide, organized, colorectal cancer (CRC) screening program (ColonCancerCheck).

Objective: To describe the implementation, evolution, and early results from the ColonCancerCheck Program (the "program").

Methods: Descriptive, using data from ColonCancerCheck and the Ontario Health Insurance Plan database.

Results: The program involves: (1) biennial guaiac fecal occult blood test (gFOBT) for asymptomatic men and women 50–74 years (with colonoscopy for FOBT+) and (2) colonoscopy as the initial screening test for those who are at increased risk (family history of >1 first-degree relative(s) with CRC). Eligible persons are invited to participate by their Family Physicians (FPs). FPs are paid by the universal public payer for their performance in CRC screening of their patients. Beginning in April 2007 and each fiscal year thereafter, Ontario public hospitals were contracted to deliver additional colonoscopies to support the program. Hospitals report monthly on all colonoscopies performed (volumes, indications, wait times, etc.). In April 2008, the program-branded gFOBT kit was introduced. FOBT kit results are reported to the program and to the FPs. Program results (population FOBT participation rate, program FOBT positivity rate, program CRC detection rate, etc.) for 2008 will be presented. In addition, results from a letter of invitation feasibility pilot and the outcomes of pay for performance will be presented.

Conclusions: Remarkable progress has been achieved since the launch of ColonCancerCheck in Ontario. Methods of colonoscopy reporting can serve as a model for other jurisdictions.

Strategies to Manage HPV DNA-Positive Women: Nested Studies in the NTCC Randomised Controlled Trial

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Background: HPV DNA testing is more sensitive but less specific than cytology.

Objectives: Evaluating different management procedures for HPV-positive women.

Methods: In the NTCC randomised trial, women were tested by HybridCapture2 (HC2) or cytology. For HC2-positive women (who had immediate colposcopy), we performed viral genotyping on stored samples (by reverse line blot hybridisation after GP5+/GP6+ PCR) and evaluated the overexpression of p16INK4A by immunostaining. We estimated the relative (versus cytology) cross-sectional sensitivity for CIN2+ histology and the relative referral rate to immediate colposcopy. We also computed the cumulative incidence of CIN3 after enrolment.

Results: Among women aged 35–60 years, the relative cross-sectional sensitivity and relative immediate referral rate were 1.53 and 1.08, respectively, for HC2 testing with triage by p16. These values were 0.96 and 0.83, respectively, for infection by HPV types 16 or 18 (group A); 1.18 and 0.99, respectively, for group B (group A or types 33, 35, and 52); and 1.33 and 1.21, respectively, for group C (group B or HPV31). The relative cumulative incidence of CIN3 at 3.5 years for p16-negative versus p16-positive women was 0.18 (95% CI 0.04–0.83). Any bipartition based on HPV genotype provided lower prognostic value.

Conclusions: At age 35 or more, p16INK4A immunostaining seems more efficient than viral genotyping for choosing which HPV DNA-positive women to immediately refer to colposcopy. In addition, p16-negative women are at low risk of CIN3 for 3.5 years. Therefore, they could be safely retested just after 3 years without need of short-interval repeats.

Comparative Effectiveness of Colorectal Cancer Screening Tests: How Do We Ensure Optimal Allocation of Limited Resources?

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Background: Numerous tests are available to screen for colorectal cancer, including many new technologies. These screening tests differ in their test performance, cost, and recommended screening schedule; therefore, comparative assessment of the tests across all these dimensions is required to select the optimal test.

Objective: To assess the effectiveness and cost of the screening tests incorporating real-world patient compliance and to evaluate which test provides the most benefit under conditions of fixed budget allocations.

Methodology: We built an agent-based model to assess the impact of compliance and budget constraint for the average risk population. We obtained rates for compliance with initial screening and follow-up diagnostic testing from a review of the peer-reviewed literature. The number of individuals screened and life-years gained were based on a hypothetical screening program with $1 million in funding. We assessed the comparative effectiveness of fecal tests, sigmoidoscopy, and optical and virtual colonoscopy.

Results: With 100% compliance with screening and diagnostic testing, average life-years gained per person is 26 days for low-sensitivity fecal tests, 28 days for sigmoidosocpy, and about 32 days for high-sensitivity fecal tests and colonoscopy. Fecal tests have the largest decline in effectiveness as compliance decreases. Under scenarios of fixed levels of funding, high-sensitivity fecal tests provide more benefit than other screening tests if at least 40% compliance can be achieved.

Conclusion: Inclusion of patient compliance has significant impact on test cost-effectiveness, and understanding potential funding constraints is important in assessing the optimal test for colorectal cancer screening.

National Colorectal Cancer Screening Programme in the Czech Republic

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Background: The Czech Republic, with 10.5 million inhabitants and 4.8 million over age 50, occupies the top position in world statistics of colorectal cancer incidence and mortality. In 2007, this malignancy was diagnosed in 7,826 people, and 4,154 died because of this disease. Although the organized screening program has currently been running for nearly a decade (introduced July 1, 2000), the incidence and mortality of colorectal cancer have been stable over recent years. This could be caused by the very high prevalence (51,489 cases) of colorectal cancer, with no reduction in predictive models. Moreover, no noticeable shift in rates or proportions of clinical stages has been recorded since the launch of the program. Advanced stages (III and IV) still represent more than 50% of all colorectal cancers diagnosed.

Objective: To determine the current status of program implementation, its monitoring and reporting, and results from years 2006–2009.

Methods: In years 2000–2008, guiac fecal occult blood test (gFOBT) was offered to asymptomatic individuals over age 50, followed by colonoscopy in case of its positivity. In the beginning of 2009, the design of the program was changed, introducing primary screening colonoscopy and immunochemical FOBT as another screening modality. To asymptomatic individuals aged 50–54, guiac or immunochemical FOBT has been offered, followed by screening

colonoscopy, if positive. For those aged 55, there is a choice of either FOBT biannually or primary screening colonoscopy in 10-year intervals.

Results: Since the beginning of online individual data management in 2006 until December 2009, there were 30,008 screening colonoscopies (FOBT+) and 1,331 primary screening colonoscopies performed. The ratio of cancers found during screening colonoscopy (indicated by positive FOBT) was much higher than in primary screening colonoscopy. Contrariwise, the ratio of adenomas diagnosed was nearly the same for both of these screening methods. The proportion of advanced cancers was 21% and advanced adenomas, 49%. Most of the cancers were found in the sigmoid colon (35%) and rectum (27%). A positivity rate of 3.7 % (intervals 3.1–5.0%) of FOBTs was achieved. Twelve cases of perforations in diagnostic procedure (0.04 % of all colonoscopies) and 15 cases of perforation and 129 cases of major bleeding during endoscopic polypectomy (0.10% and 0.89% of all therapeutic colonoscopies) have been reported.

Conclusion: The organized colorectal cancer screening program in the Czech Republic is equipped with a highly functional information system. Participation of the target population has been intensively rising every year since the beginning of online individual data management. This trend could be caused by the broad offer of screening modalities, especially primary screening colonoscopy, introduced in the beginning of 2009.

Comparative Effectiveness of Breast Cancer Screening: The Copenhagen Organised Screening Programme 1991–2007

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Background: Copenhagen has the longest running organised screening programme for breast cancer in Denmark. The programme started in 1991.

Objective: We have evaluated the impact of specific structural/technical changes to the programme with regard to quality indicators of the European guidelines for quality assurance in breast cancer screening and diagnosis.

Methods: The mammography programme supplied information on structural/technical changes and data on all invited women and screening test results. Oncological data were retrieved from the National Cancer Register. Data were linked using the Danish unique personal identity number.

Results: Major changes during the period were the appointment of a new chief executive (primo 1997), centralization of assessments to one hospital and increased use of ultrasound (1997), and the introduction of high-frequency ultrasound (2001) and stereotactic-guided biopsies (2002). The recall rate dropped from 4.6% to 3.2%, and the false-positive rate dropped from 3.9 to 2.5 from 1994–95 to 1996–97. The detection rate increased from 5.8/1000 in 1999/2001 to 8.7/1000 in 2003/05, while the benign to malign ratio changed from 1:5.0 to 1:11.4. The interval cancer rate increased from 2.7/1000 to 3.2/1000 in the same period.

Conclusions: The arrival of a new chief was followed by a decrease in false-positive tests. Even though the recall rate declined, the introduction of combined high-frequency ultrasound and stereotactic-guided biopsies resulted in an increase in detection rate without an increase in benign surgical biopsies. The concomitant increase of interval cancer is, however, of concern.

For additional information on this topic, see *New Technologies and Comparative Effectiveness* in **Abstracts** and **References**.

Stoppage Rules in Older Populations

Performance Indicators of Breast Cancer Screening in Elderly Women

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Background / Purpose: The Czech Breast Cancer Screening programme was launched in September 2002. The target population includes women aged 45–69 years who are invited for an examination by a GP or gynaecologist every other year. To improve participation rates, the General Health Insurance Company carried out the pilot project of centralised non-attendees invitation. Another objective of the project was to assess the performance of screening in women aged 70–74 years who were included in the invited cohort.

Objective: To estimate performance indicators of mammography screening in a population of women aged over 70 years compared to younger women.

Methods: Performance indicators will be estimated for women aged 70–74 years (elderly) screened within the pilot project between July 2007 and February 2008 and compared with those for women aged 45–69 (younger) attending the programme in 2007.

Results: The pilot project was attended by 26,130 elderly women. Further assessment rates for initially screened women were 10.1% (compared to 17.7% for younger women) and 5.5% for subsequently screened women (10.2% in younger women). In total, 355 tumours were detected in elderly women. Detection rates were 14.3 per 1000 initially screened women (6.5 in younger women) and 7.3 per 1000 subsequently screened women (3.7 in younger women). Similar proportions of invasive tumours less than 10 mm in size were observed in both age groups.

Conclusion: This screening process in elderly women yields very favourable performance indicators, combining high detection with low referral rates. Estimated parameters should be employed in further analysis assessing costs and effectiveness of cancer screening for elderly women.

For additional information on this topic, see *Stoppage Rules in Older Populations* in **Abstracts** and **References**.

HPV Vaccine in Cervical Cancer Screening

HPV Vaccination Program in Rural Northern Greece

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Background / Purpose: "Panagia Philanthropini" will utilize proven outreach developed for screening of breast and cervical cancer, in order to implement an HPV vaccination program for underprivileged, rural, minority, and immigrant teenagers. Utilizing the present human network, the center will raise HPV vaccination and cervical screening awareness among middle-aged and teenage women. Implementation will be achieved in cooperation with health workers, ensuring patients' comfort.

Methods: Raising of public awareness was undertaken using interactive teaching tools (i.e., poster competition, pamphlet development, Web-based outreach, and meetings in high schools so that youth could meet experts and discuss HPV vaccination). The vaccination protocol will be reviewed by the Scientific and Ethics Committee. Upon ratification, a daily inoculation clinic will be developed.

Objective: The Center has a high screening cross-generational return rate (>75%) given that school girls, recruited in the early '90s to sensitize their mothers and grandmothers for screening, are currently participants themselves. Based upon the screening of 7,000 women annually, the teenage target population is 700–1,000 per year, over a 5-year period, inoculating up to 5,000 girls.

Results and Conclusion: For each woman screened and teenage girl vaccinated, data on socioeconomic and educational status, environmental exposures, and other women's health issues will be systematically documented, enabling correlation of the efficacy of the outreach and the vaccine with these data. The comparison will enhance insight regarding effectiveness of mass HPV vaccination in underprivileged populations in 5-, 10-, 15-, and 20-year increments, providing valuable data to the scientific community.

For additional information on this topic, see *HPV Vaccine in Cervical Cancer Screening* in **Abstracts** and **References**.

Can Overdiagnosis and/or Overtreatment Be Reduced by Individualized Screening?

Overdiagnosis in a Breast Cancer Screening Programme in the Czech Republic

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Background / Purpose: There were 1,611,582 examinations performed in 1,067,836 women attending the organized breast cancer screening programme in the Czech Republic during the period 2002–2007. A total of 7,835 cases of breast cancer were detected.

Objective: To estimate the extent of overdiagnosis for different age groups.

Methods: Overdiagnosis of ductal carcinoma in situ (DCIS) only was assumed. A certain proportion of DCIS is non-progressive and represents the overdiagnosed tumours. Markov models with variable number of states were used. Simultaneous estimation of $\lfloor_1$ (transition rate to preclinical screen-detectable phase, where no signs of the disease are present, but it could be detected by mammography), $\lfloor_2$ (transition rate from preclinical screen-detectable phase to clinical phase) and μ (incidence of overdiagnosed tumours) was performed. The estimation procedure was performed using Bayesian methods implemented in WinBUGS software.

Results: The incidence of overdiagnosed tumours was from $3x10^{-6}$ to $9x10^{-6}$, according to age group examined, and was slightly higher for older women.

Conclusion: Overdiagnosis does not seem to be a significant problem in the organized breast cancer screening programme in the Czech Republic.

Breast Screening Outcomes Among Relatives of Women With Breast Cancer

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Background: Evidence on the impact of screening on women with a family history of breast cancer is required for developing definitive breast cancer screening guidelines.

Objectives: To compare breast screening behaviours and outcomes among women with high and moderate risk of breast cancer.

Methods: The study design is a retrospective cohort of female relatives of cases of invasive breast cancer (probands) in the Ontario Familial Breast Cancer Registry who were diagnosed between 1996 and 1998. Eligible women (1514 women, 848 families) were 20 to 69 years of age and were not affected by breast cancer at the time of their relatives' diagnoses. The cohort has been followed for two years to collect data on any changes in screening practices or diagnoses of benign breast disease or breast cancer.

Results: Of the 1305 eligible women contacted, 1113 women (85%) were telephone interviewed at baseline and 976 women have been followed for two years. Of these women, 45 had an invasive breast cancer or ductal carcinoma in situ and 66 had a benign breast disease. Women at highest risk were more likely to have had a screening mammogram and more likely to have a breast cancer diagnosis (relative risk [RR]=2.01; 95% confidence interval [CI]=1.07–3.8) or benign breast disease (RR=1.46; 95% CI=0.88–2.43) than women at moderate risk.

Conclusions: Preliminary analyses suggest that risk of breast cancer influences screening behaviours and outcomes. The results of this study may suggest screening guidelines among high-risk women.

Cost-Effectiveness of Cervical Cancer Screening: Vaccinated Versus Unvaccinated Populations

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Background: In countries where HPV vaccination is introduced, vaccinated women will be invited to attend cervical cancer screening in the future. To reduce inefficient screening and risk of overdiagnosis in vaccinated women, information on HPV vaccination status could be used for tailored screening.

Objective: To know what the optimal screening policy for cervical cancer is in vaccinated versus unvaccinated women.

Methods: We used the microsimulation model MISCAN and considered eight different screening scenarios: (a) cytological testing with repeat cytology for borderline/mildly abnormal (BMD) smears; (b) three scenarios of primary HPV testing with cytological triage for HPV positive tests; and (c) four scenarios of primary cytological testing with HPV triage for BMD smears. For all scenarios, we considered both conventional and thin-layer cytological testing and compared 171 screening policies that varied by frequency, interval, and initiation age. We estimated the numbers of (quality-adjusted [QA]) life-years (QALY) gained and the costs of the different screening policies and determined the efficient screening programs for the vaccinated versus the unvaccinated population. Finally, we performed extensive sensitivity analyses.

Results and Conclusion: Vaccination resulted in an increase in the number of colposcopies per gained life with a factor of 1.9 (20.6 per gained life) and the number of triage tests per gained life, with a factor 3.2. The incremental cost-effectiveness ratio increased from €23,552 to €118,714 per QALY gained. The only cost-effective policy considering the €20,000 per QALY gained threshold is one screen-test per lifetime, optimal at age 40. Vaccination did not affect the optimal primary screening and triage tests to be recommended.

Cancer Screening Rates Among Hispanic Subgroup Populations

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Background and Significance: Hispanics/Latinos represent 15% of the U.S. population and the largest minority group. Cancer is the second leading cause of death among Latinos, with lower survival rates and more advanced disease at diagnosis.

Objectives: The goal of the CMS-Cancer Prevention and Treatment Demonstration (CMS-CPTD) project of New Jersey is to reduce disparities in cancer care for Latinos through the use of patient navigation.

Methods: The CMS-CPTD is a randomized trial comparing patient navigation (intervention) to education (control) for cancer screening. We analyzed data for 509 participants who completed the CMS-CPTD baseline questionnaire to identify the presence of significant differences among the four most prevalent subgroups (Hispanics/Latinos from Cuba, Ecuador, Puerto Rico, and the Dominican Republic) regarding cancer screening behavior and attitudes.

Results: There were no statistically significant differences in cancer screening behaviors between the four Hispanic subgroups, but differences in attitudes towards cancer screening and vulnerability were identified. There was a statistically significant difference ($p<.05$) between the Cuban and Dominican subgroups toward perceived self-vulnerability to cancer. Cubans were also statistically less worried about getting cancer than the other three subgroups.

Conclusion: Despite differences in perceived vulnerability to cancer, there were no differences in cancer screening behavior in this population. This finding contradicts previous studies that indicated that equal access to care is not sufficient to bridge the gaps in cancer screening. An updated analysis of cancer screening practices among Hispanics would be useful to identify new challenges and solutions to increasing cancer screening among this population.

Is It Cost-Effective to Intensify Colorectal Cancer Screening for Obese Smokers?

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Background / Purpose: It is recognized that offering more intensive screening to high-risk individuals based on risk factors such as a high body mass index (BMI) and smoking may be beneficial. However, the presence of such risk factors may also limit the benefits of intensifying screening, because besides affecting CRC incidence they also affect the risk for other diseases such as lung cancer and cardiovascular disease.

Objective: To determine the optimal colonoscopy screening schedule for obese current-smokers and normal weight never-smokers and to evaluate the effect of using risk-specific life tables that take into account the effect of BMI and smoking on other-cause mortality.

Methods: We used the MISCAN-Colon micro-simulation model of CRC to estimate costs and effects of colonoscopy screening in obese current-smokers and normal weight never-smokers for screening schedules with different screening ages and intervals. From these model outcomes, we have determined the optimal CRC screening schedule for obese current-smokers and compared it with optimal screening in normal weight never-smokers from a cost-effectiveness perspective. We conducted this analysis once with general life tables and once with risk-specific life tables.

Results: The optimal screening schedule for obese current-smokers is more intensive than that for normal weight never-smokers when using a general life table. Using a risk-specific life table, the higher other-cause mortality for obese current-smokers reduces the difference in optimal screening intensity.

Conclusions: The impact of risk factors on other-cause mortality should not be ignored because this will result in too intensive screening recommendations in, for example, obese current-smokers.

The Cost of CIN Detection in Cervical Screening: The Impact of a Definition of a Positive Screening Test

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Background: Several studies from RCTs comparing primary cervical screening with HPV and cytology testing suggested HPV strategies that appeared to have similar PPV for high-grade CIN as cytology testing. These studies counted only women referred for colposcopy in the denominator of the PPV.

Objective: To measure the impact of the definition of a positive screening test on estimating costs of CIN detection through PPV.

Methods: We compared the reported relative PPVs for the suggested HPV screening strategies versus cytology screening with the relative PPVs when including all women with positive screening tests in the denominator.

Results: When all women with positive screening tests were included in the denominator, the relative PPV of HPV strategies reacting to HPV viral load ≥1pg/ml decreased from the reported 0.87 (95% CI: 0.60–1.26) to 0.44 (0.30–0.64) for ≥CIN3 in the Swedish RCT and from 0.78 (0.52–1.16) to 0.51 (0.33–0.79) for ≥CIN2 in the Italian Phase 1 RCT (25–34 years). On the contrary, for a strategy recommending to react to HPV viral load ≥2pg/ml for women aged 35–60 screened in the Italian RCT, the relative PPV for ≥CIN2 slightly increased from 0.85 (0.66–1.09) to 1.07 (0.81–1.39), whereas it increased from 0.27 (1.15–0.50) to 1.84 (0.99–3.41) for ≥CIN3 for a strategy reacting to HPV viral load ≥10pg/ml as suggested from the Finnish RCT.

Conclusion: The definition of positive screening tests had a decisive impact on the relative PPVs of recommended HPV screening strategies. The reported PPVs failed to account for part of the costs of CIN detection.

Characteristics of Screen-Detected and Interval Cancers Among Participants of Organized Screening Programs: Overdiagnosis or Early Diagnosis?

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Background: Early diagnosis of breast cancer through regular mammography is essential to reduce morbidity and mortality; however, diagnosis of DCIS may result in unnecessary treatment.

Objectives: To compare the characteristics of cancers detected at screening to those diagnosed during the interval between screen events.

Methods: Women aged 50 to 69 who participated in a population-based screening program during 2000 and 2001 (n = 1,054,409) and were diagnosed with breast cancer within 15 months (n = 3,825) were included. Cancers were categorized as screen detected (n = 3,110) or interval (n = 719), and multivariate logistic regression was used to make comparisons on tumour size, nodal status, and TMN stage.

Results: A smaller proportion of screen-detected breast cancers were considered large (> 20 mm: 19.6% versus 36.8%), node positive (23.3% versus 34.3%), and late stage (TMN stage III+: 2.4% versus 6.9%) compared to interval cancers. In addition, a larger proportion of screen-detected cancers were classified as DCIS (19.7% versus 9.9%). These relationships persisted when adjusted for age and family history.

Conclusions: Small, node-negative, and early-stage tumours found at screening compared to those arising during the interval between screens suggest that organized screening programs are successful in achieving early diagnosis. However, the increased proportion of tumours categorized as DCIS suggests that some overdiagnosis may be occurring. Future analyses should be population based and target biomarkers and disease grade to further clarify the early detection-overdiagnosis debate.

For additional information on this topic, see *Can Overdiagnosis and/or Overtreatment Be Reduced by Individualized Screening?* in **Abstracts** and **References**.