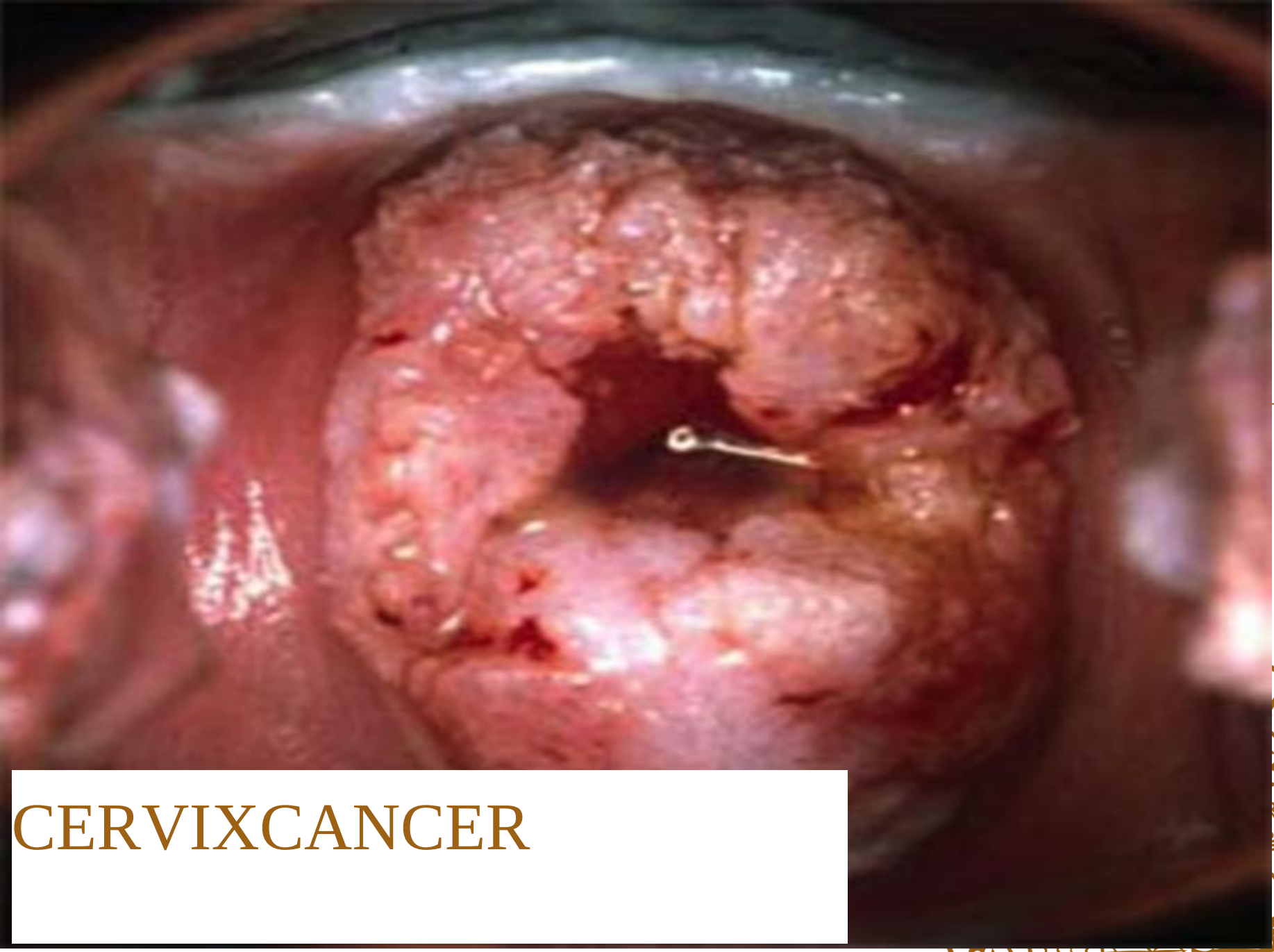
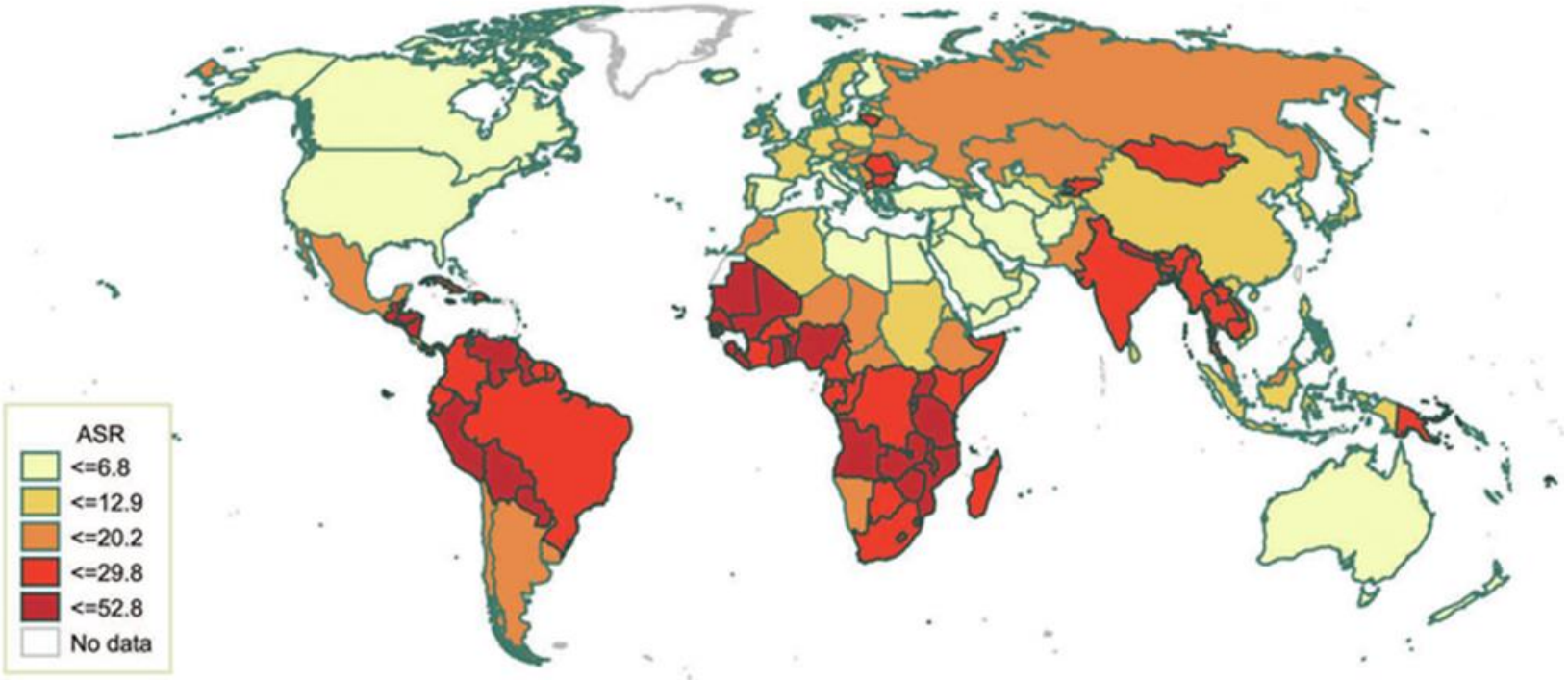
Cervical cancer -studies on prevention and treatment

LOTTEN DARLIN, DISSERTATION 131213, SFOG 140826



CERVIXCANCER

World age-standardized incidence rates of cervical cancer



ASR, age-standardized incidence rate; Rates per 100,000 women per year.
Data sources: IARC, Globocan 2008.

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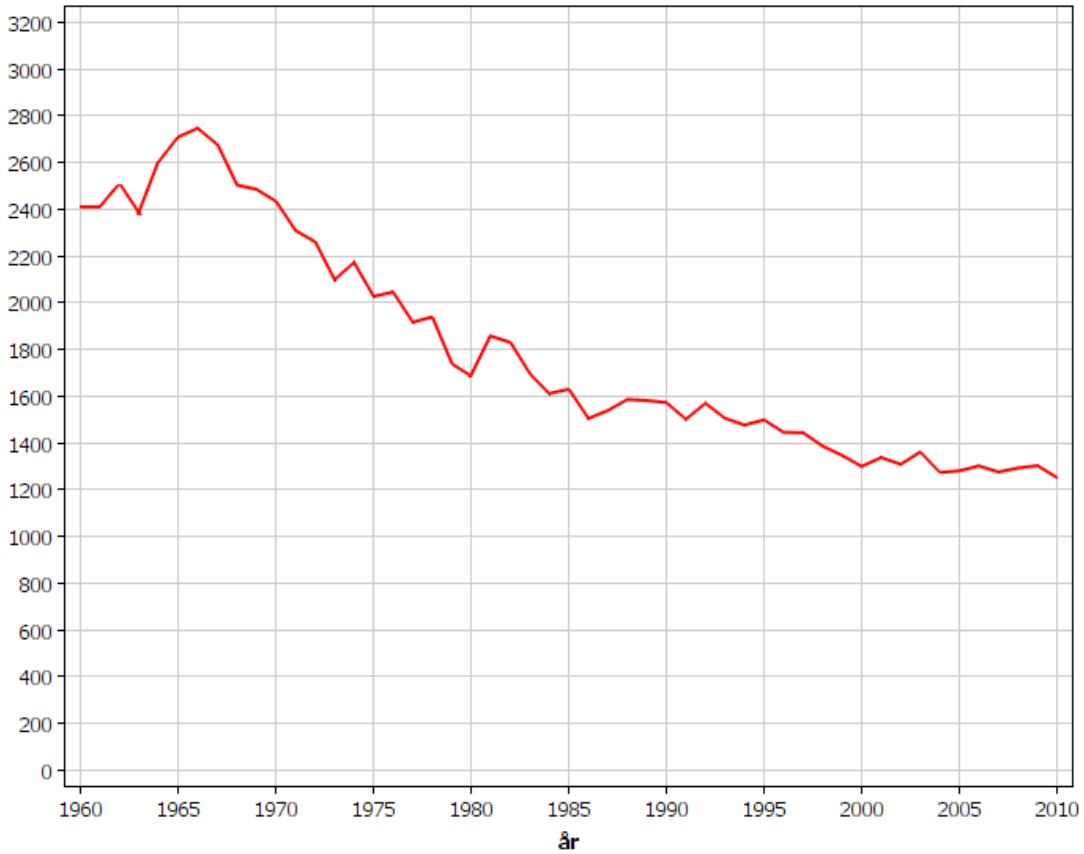
Incidens och mortalitet

CERVIXCANCER I VÄRLDEN

Nordiska länderna incidens livmoderhalscancer år 1960-2010



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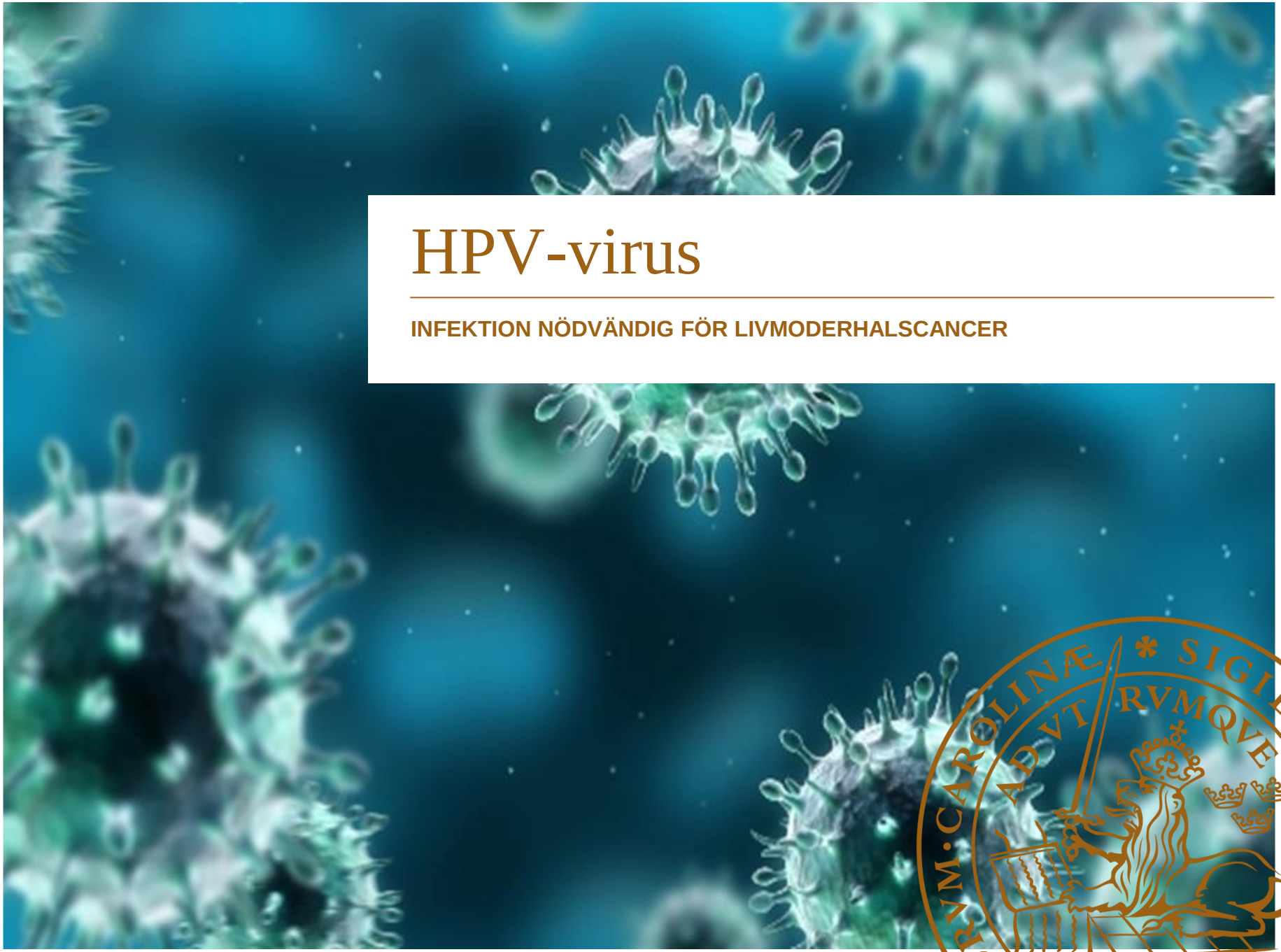
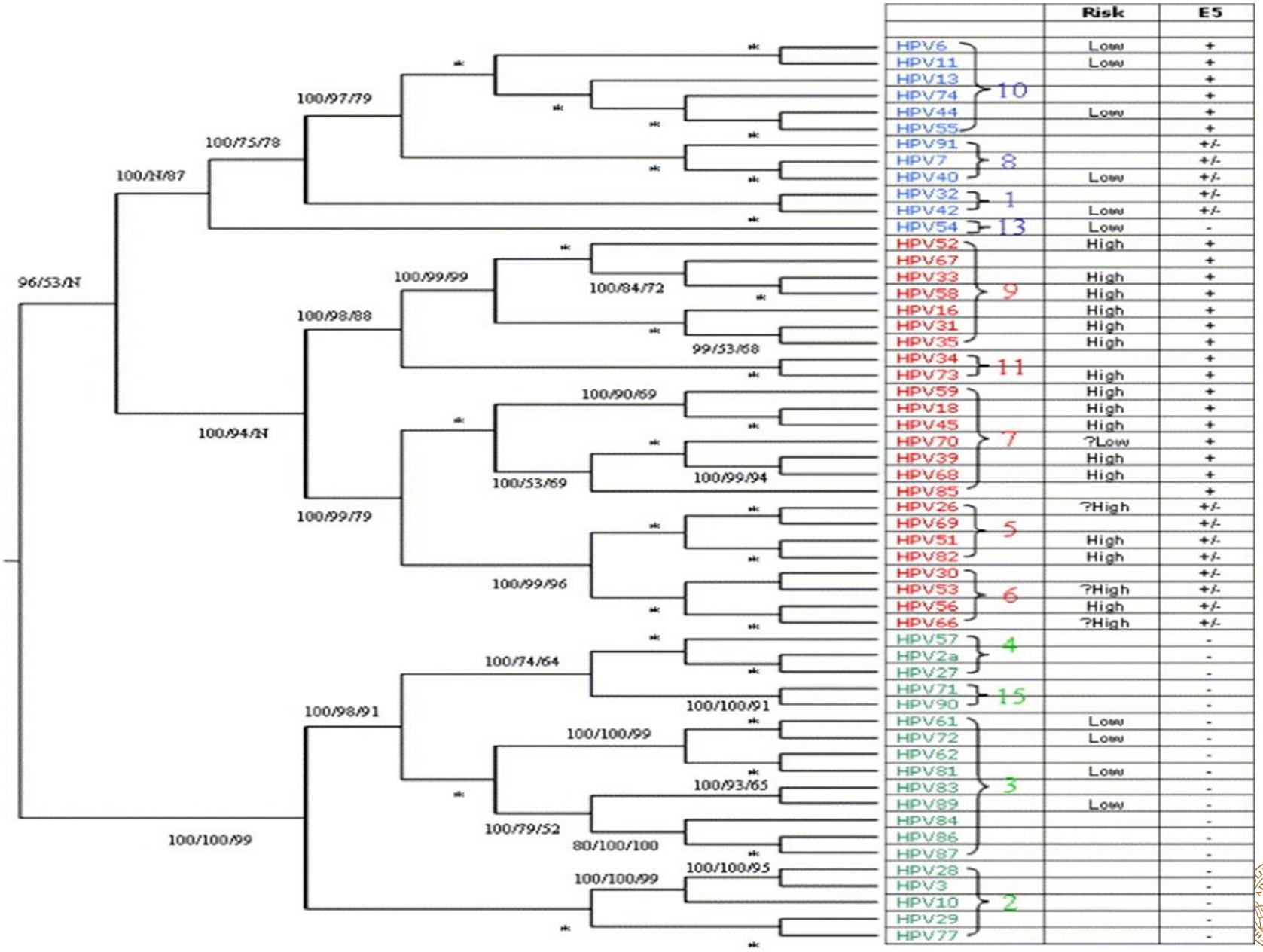
NORDCAN © Association of the Nordic Cancer Registries (26.11.2013)



HPV-virus

INFEKTION NÖDVÄNDIG FÖR LIVMODERHALSCANCER



Burke 2005

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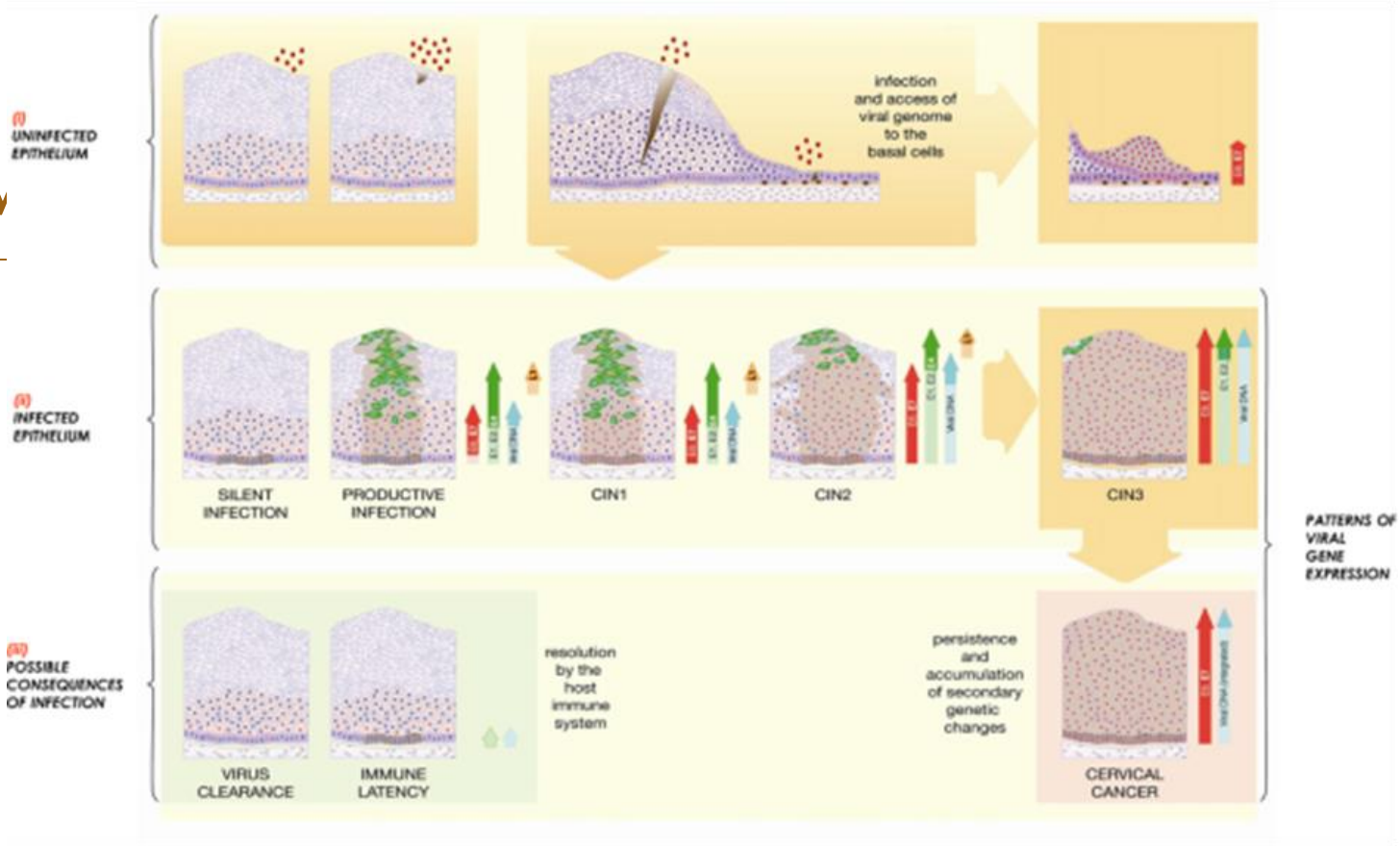
HPV



Doorbar et al 2012

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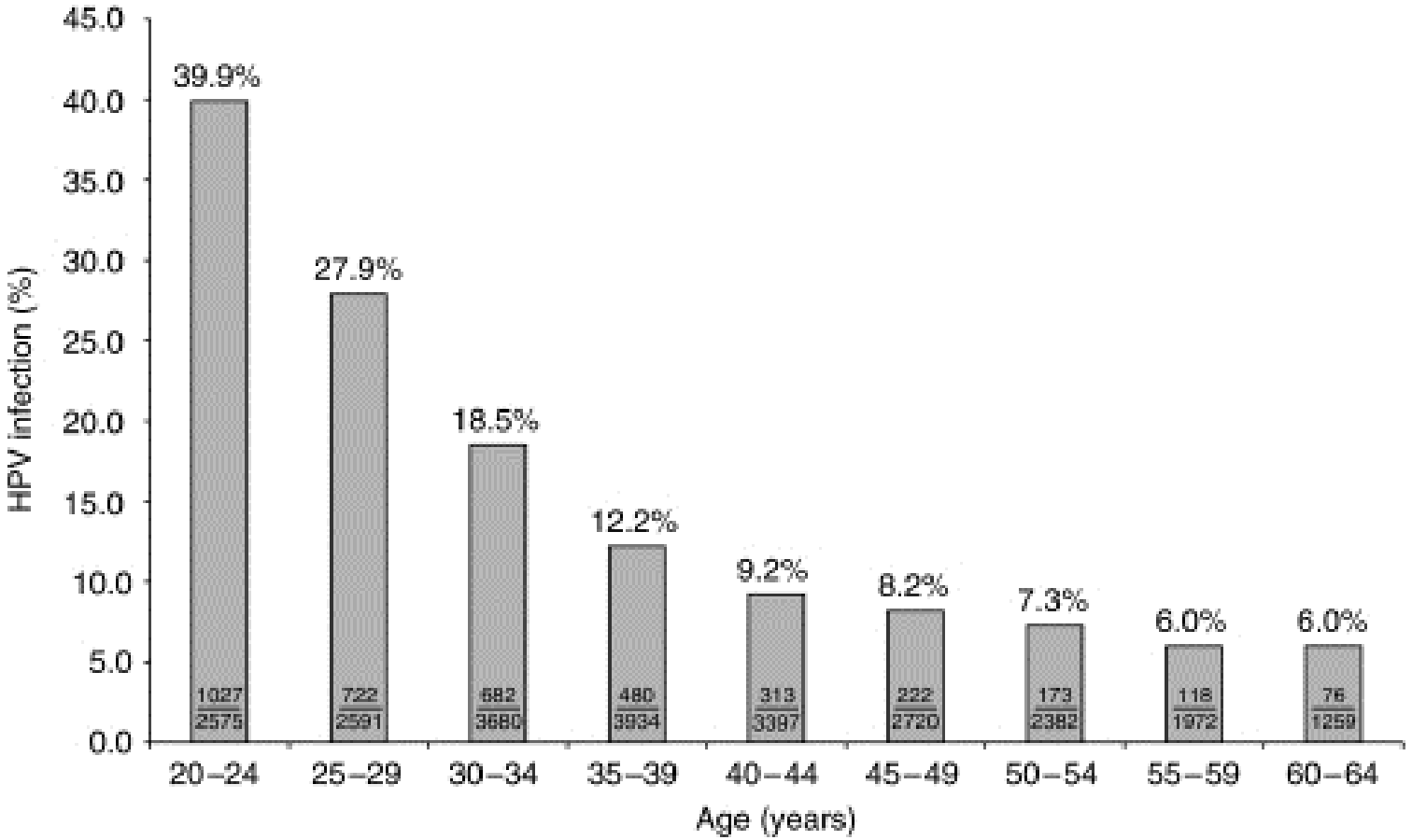
HPV-prevalens, åldersindelad



Cancer research UK; Kitchener et al 2006

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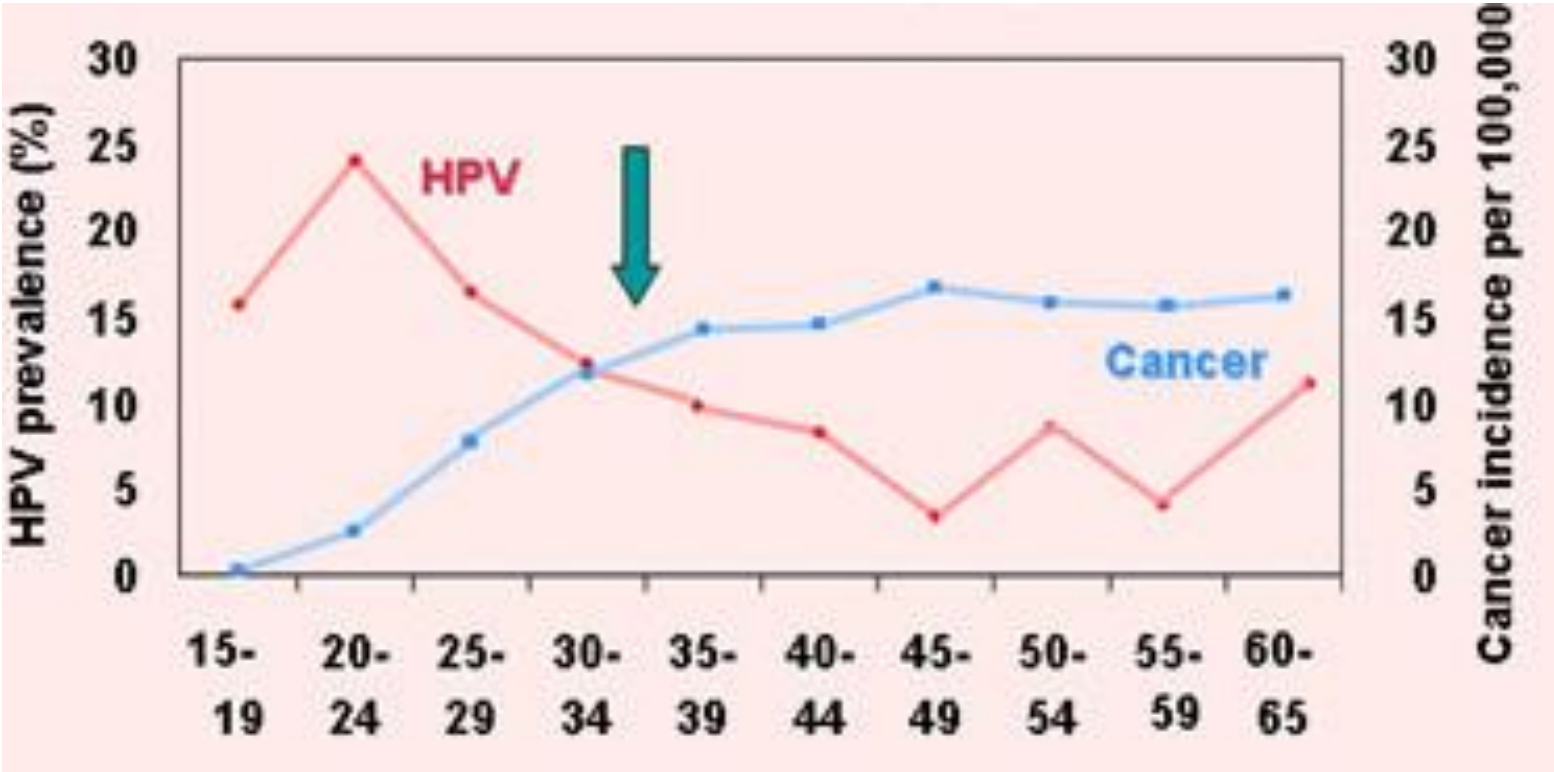
HPV-prevalens och cervixcancer-incidens, åldersuppdelad i år.



Sellots et al 2000 o 2002; Riots et al 1997

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Cellförändringar; risk att utveckla cancer

	Regress	Persist	Progress to CIN3	Progress to invasive cancer
CIN1	57%	32%	11%	1%
CIN2	43%	35%	22%	5%
CIN3/CIS	32%	<56%		>12%

Ostor et al 1993

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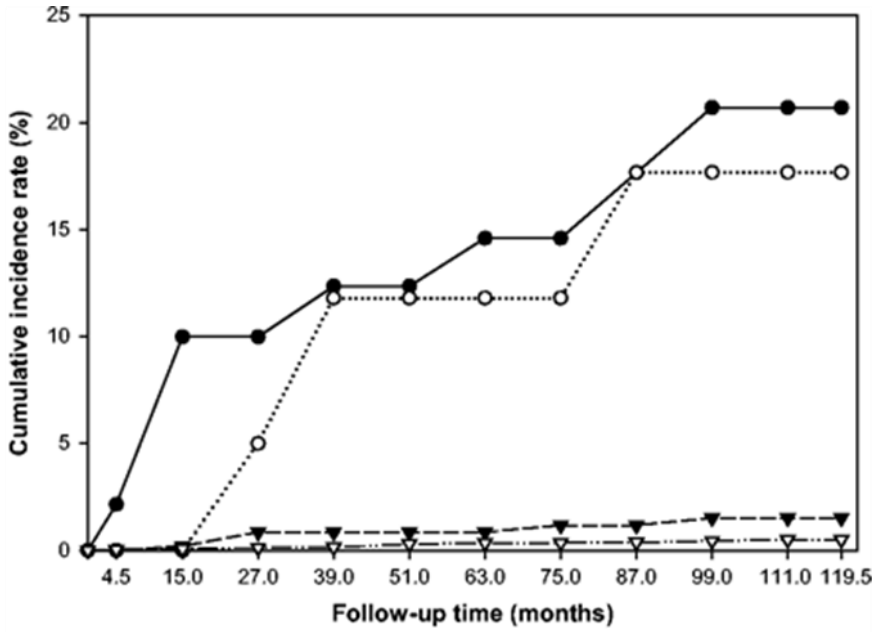
Risk att utveckla cervixcancer beroende på HPV-typ



Khan et al 2005

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section for this paper
- ☐ Experimental
- ☒ Clinical
- ☐ Epidemiological

Elderly Women Above Screening Age Diagnosed with Cervical Cancer Have a Worse Prognosis

LOTTEN DARLIN, CHRISTER BORGFELDT, EMELIE WIDÉN and PÄIVI KANNISTO

Department of Obstetrics and Gynaecology, Skane University Hospital, Lund University, Lund, Sweden

Abstract. *Aim: To analyse the cervical screening history in women with cervical cancer and their outcome. Design: All women diagnosed with cervical cancer between January 2009 and December 2010 in the South Sweden region were included in the audit. Materials and Methods: Cervical cancer was registered in 165 women in 2009 and 2010. Their screening history was analysed, and was classified as normal or imperfect. The method of discovering the cancer was either by symptoms or by screening. The main outcome measure was overall survival in cervical cancer related to cervical screening history. Results: Women above 65 years of age were more frequently diagnosed with advanced stage disease (The International Federation of Gynecology and Obstetrics II-IV) (n=36 out of 43; 84 %)*

1960s in order to detect and treat dysplastic lesions preceding cervical cancer (2). Not all invited women attend the recommended cervical screening program. Moreover, there is a lower and upper age-limit for the screening, which varies to some extent in the 20 counties in Sweden. In Skane, in the South Sweden region (Skane, Blekinge and Kronoberg), women are invited to screening tests every third year between the ages of 23 and 50, and every fifth year between the ages of 51 to 60, (in Skane to 65 years of age). The compliance with the screening program in South Sweden for women below 50 years of age varies between 68%-73% depending on where the women live. For the age-group 51-65 years, the compliance varies between 55-73%. Since cervical cancer can

Hypotes: Analysera cellprovshistoriken, och därigenom hitta sätt att förebygga cervixcancer.

- Aim: Analyse the screening history in women with cervical cancer 2009-2010, and see their outcome.

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Resultat

- Kvinnor över 65; mer avancerade stadier

- Alla patienter som diagnostiserats av screening-programmet levde fortfarande (30/30) vid median-uppföljningstiden (36 mån).

- Av alla kvinnor var en tredjedel över 60 år. Av dessa hade 42% normal screeninghistoria

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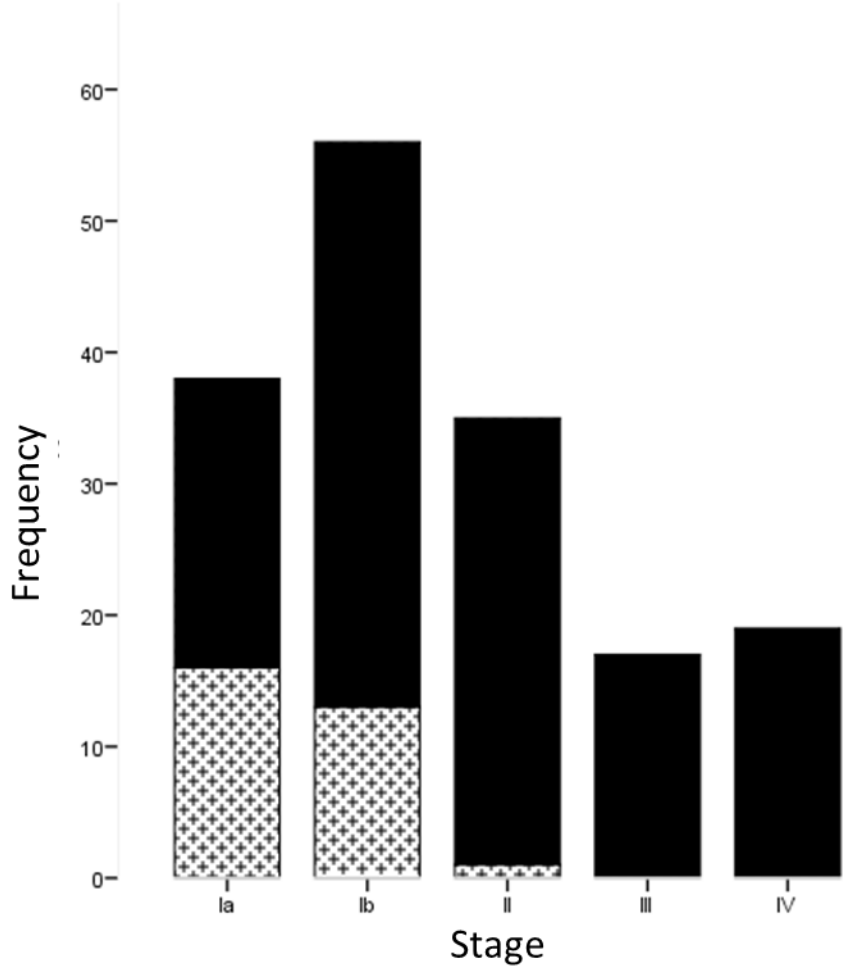
Screening-upptäckta vs symtomupptäckta



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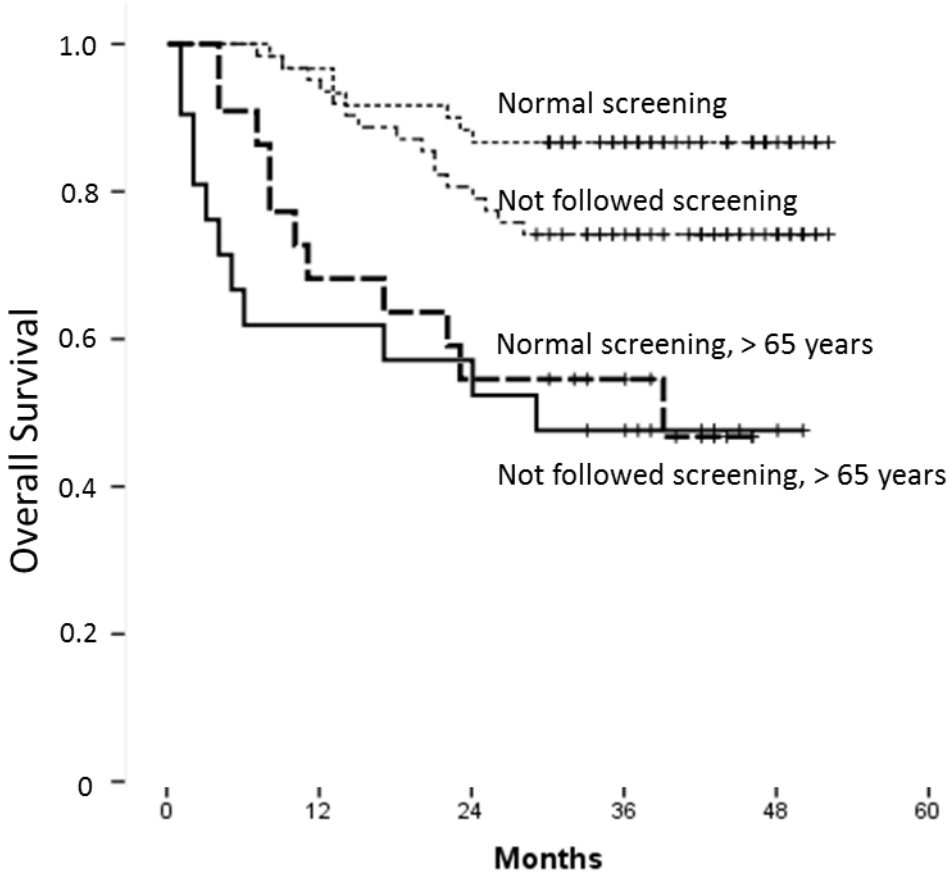

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Konklusion

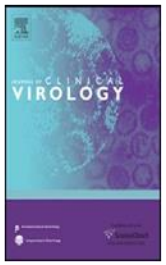
- Konklusion: Cervix cancer hos kvinnor över 65-årsålder upptäcks i avancerade stadier av sjukdomen, med dålig prognos.

Journal of Clinical Virology 56 (2013) 52–56

Contents lists available at SciVerse ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv



Vaginal self-sampling without preservative for human papillomavirus testing shows good sensitivity

Lotten Darlin [a,*], Christer Borgfeldt [a], Ola Forslund [b], Emir Hénic [a], Joakim Dillner [b,c,d], Päivi Kannisto [a,e]

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Article history:
Received 18 March 2012
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Keywords: HPV testing
Vaginal smear Cytology
Self-collected vaginal smear

abstract

Background: Several strategies have been used to reach non-attending women in organized cervical- cancer-screening programs, with varying success. Self-sampling (SS) for HPV is effective for increasing coverage in screening programs, but requires expensive commercial sampling kits.
Objective: We aimed to evaluate if vaginal SS, without commercial preservatives was adequate for HPV testing.
Study design: Women with abnormal cervical smears as determined from the organized screening pro- gram were invited to a colposcopy clinic. The 121 women were asked to insert a cotton swab into the vagina and rotate it, put the cotton swab into a sterile cryotube, break the upper part of the stick and put the cap on. Thereafter, the gynaecologist collected a liquid based cytology (LBC) sample. The presence of HPV-types in SS and LBC samples was analysed with PCR and luminex-based typing.
Results: High-risk-HPV (hr-HPV) DNA was found in 65 of the tested 108 SS (60%; 95% CI 0.50–0.69), whereas LBC found hr-HPV in 64/108 samples (59%; 95% CI 0.49–0.69). The agreement between sampling with SS and LBC was good, kappa value 0.67 (95% CI; 0.53–0.81). The sensitivity for SS with hr-HPV to find HSIL was 81% (95% CI; 67–95%), specificity 49% (95% CI; 37–60%) and the sensitivity for LBC with
hr-HPV to find HSIL was 90% (95% CI 80–100%), specificity 53% (95% CI; 42–65%).
Conclusions: This new vaginal self-sampling method detects hr-HPV-infections with similar sensitivity as a cervical smear taken by a gynaecologist. This self-sampling method is cost-effective and well tolerated, and the kit is suitable for regular mail transport.

Journal of Clinical Virology 58 (2013) 600

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Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Corrigendum

Corrigendum to "Vaginal self-sampling without preservative for human papillomavirus testing shows good sensitivity" [J. Clin. Virol. 56 (2013) 52–56]

Lotten Darlin [a,*], Christer Borgfeldt [a], Ola Forslund [b], Emir Hénic [a], Joakim Dillner [b,c,d], Päivi Kannisto [a,e]

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[c] Department of Laboratory Medicine, Karolinska Institute and Hospital, Stockholm, Sweden
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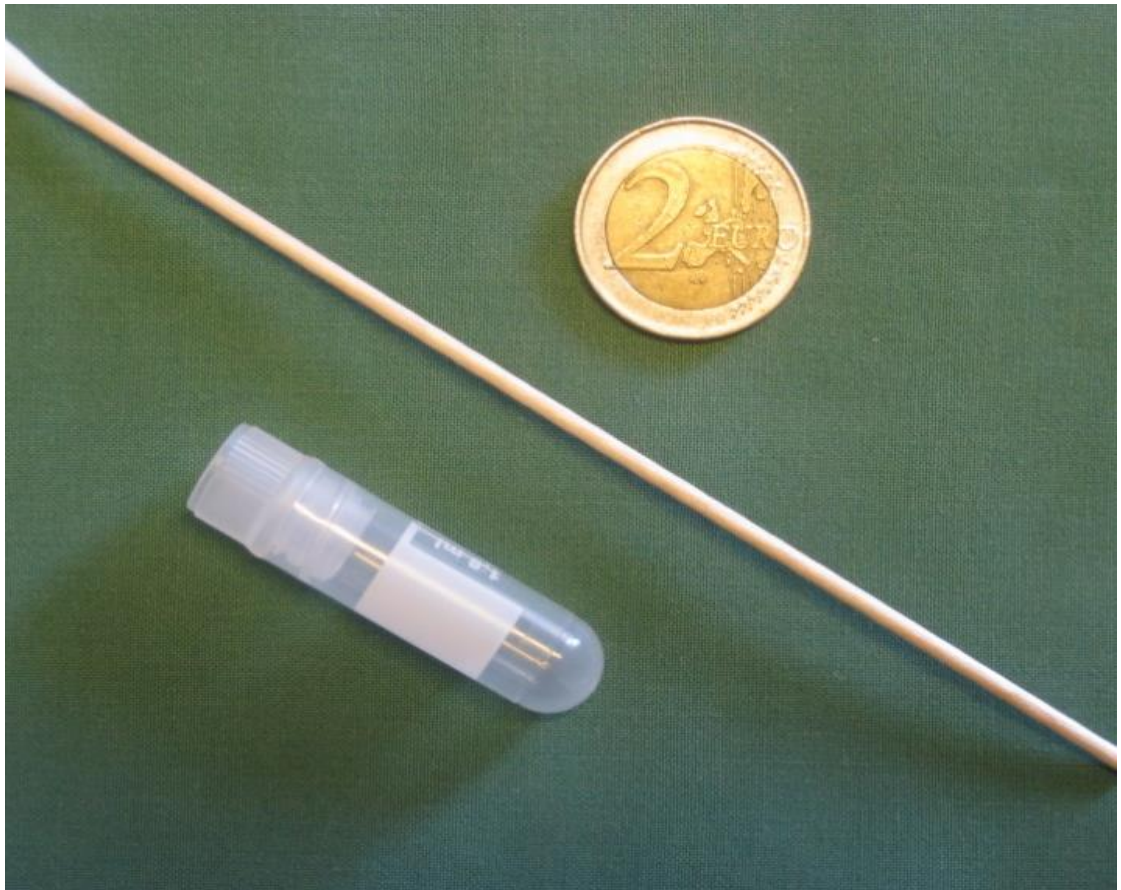
The authors regret that there were some errors in the above article. These errors are corrected below.
The authors would like to apologise for any inconvenience caused.

The results section within the abstract should have read:
The sensitivity for SS with hr-HPV to find HSIL was 77% (95% CI; 62–91%), specificity 47% (95% CI; 35–59%) and the sensitivity for LBC with hr-HPV to find HSIL was 79% (95% CI; 66–93%), specificity 50% (95% CI; 38–62%).

The last sentence of the results section in the main body of the article should have read:
The sensitivity for SS with hr-HPV to find HSIL was 77% (95% CI; 62–91%), with a specificity of 47% (95% CI; 35–59%) and the sensitivity for LBC with hr-HPV to find HSIL was 79% (95% CI; 66–93%), with a specificity of 50% (95% CI; 38–62%).

Hypotes: Vårt självtest är lika säkert som LBC HPV-test

Aim: att evaluera vårt HPV självtest



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Resultat

- Sensitiviteten att finna

  HSIL var hos självtestet 81%,

  med LBC HPV-test hade sensitiviteten 90%.

- Kappavärdet mellan de två testen är 0.67

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Konklusion

- Vårt självtest är lika säkert som ett läkar-taget HPV-test

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Journal of Clinical Virology 58 (2013) 155–160

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Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Comparison of use of vaginal HPV self-sampling and offering flexible appointments as strategies to reach long-term non-attending women in organized cervical screening

Lotten Darlin [a,*], Christer Borgfeldt [a], Ola Forslund [b], Emir Hénic [a], Maria Hortlund [b,c], Joakim Dillner [c], Päivi Kannisto [a,d]

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Keywords:
Screening
Non-attendance
HPV testing
Vaginal smear
Cytology
Self-collected vaginal smear

abstract

Background: Many cervical cancers occur among women who have not attended cervical screening. Strategies to reach non-attending women may improve the effectiveness of cervical screening programmes.

Objective: To compare the responses among long-term non-attending women to either (i) HPV-testing of a self-collected vaginal sample, or (ii) cytological screening with a flexible no-fee appointment for sampling at an outpatient clinic.

Study design: Among the 242,000 women aged 32–65 years in Southern Sweden, we identified 28,635 women who had not had any cervical smears taken for >9 years. We randomized 1000 women to invitation to HPV self-sampling, and 500 women to flexible outpatient clinic appointments. Responding women received a questionnaire about their reasons for previous non-attendance.

Results: The response rate to HPV self-sampling was three times higher than the flexible outpatient clinic invitations (147/1000 women (14.7%) compared to 21/500 (4.2%) $p < 0.0001$). High-risk (hr)-HPV was found in 10/147 self-sampled women (6.9%). 7/10 hr-HPV-positive women attended colposcopy, but no HSIL was found. Among the clinic-sampled women, 2/21 had hr-HPV and 1/21 had HSIL. Reasons for not attending were "uncomfortable with vaginal examination", "feel healthy", "lack of time" and "experience of unfriendly health workers".

Conclusions: Although the response rate was low for both interventions, the invitation to vaginal HPV self-sampling was more effective for increasing the coverage of the screening programme. The fact that "uncomfortable with vaginal examination" was the most common reason for non-attending suggests that self-sampling could be further explored as a strategy to increase the coverage of cervical screening programmes.

Hypotes: Ett HPV självtest ger fler svar än flexibel mottagning

Aim:

- Att jämföra två olika sätt att få ”non-attenders”(>9 år) att ta cellprov.
- Att ta reda på orsaker till tidigare ”non-attendance”

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Resultat

- 14,7 % Svarade på självtestet, av dem 6,9% hrHPV
- 4,2% Kom på öppen mottagning, 9,5% hrHPV
- Vanligaste orsaken till utebliven screening:
- Obehag vid vaginal undersökning
- Känner sig frisk
- Tidsbrist

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Konklusion

- Fler kvinnor svarar på HPV självtest än på kallelse till flexibla mottagningar
- Vanligaste orsaken till tidigare ”non-attendance” är obehag vid vaginala undersökningar

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Gynecologic Oncology 117 (2010) 266–269

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

The sentinel node concept in early cervical cancer performs well in tumors smaller than 2 cm

Lotten Darlin [a,c], Jan Persson [a,c], Thomas Bossmar [a,c], Bengt Lindahl [a,c], Päivi Kannisto [a,c], Anna Måsbäck [b,c], Christer Borgfeldt [a,c,*]

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article info

Article history:
Received 8 December 2009
Available online 18 February 2010

Keywords:
Sentinel node
Cervical cancer
Gamma probe
Lymphoscintigram
Human

abstract

Objective. The aim of the study was to evaluate the sentinel node (SLN) concept for lymphatic mapping in early stage cervical cancer.

Methods. 105 women with early stage (1a1–2a) cervical cancer were scheduled for the sentinel node procedure in conjunction with a complete pelvic lymphadenectomy. The day before surgery, 1–1.5 mL 120MBq Tc^{99} albumin nanocolloid was injected submucosally at four points around the tumor followed by a lymphoscintigram (LSG) to achieve an overview of the radiotracer uptake.

Results. During surgery, the overall detection rate (gamma probe) of at least one SLN was 90% (94/105 women) whereas at least one SLN was identified in 94% (61/65 women) with a tumor ≤ 2 cm. Bilateral SLNs were identified in 62/105 (59%) of the women.

Among 18 women with any metastatic lymph node 17 had a metastatic SLN (sensitivity 94%, 95% CI 73–100%). Among 61 women with a tumor ≤ 2 cm, all five women with any metastatic lymph node also had a metastatic SLN (sensitivity 100%). One woman with a 1.5-cm squamous epithelial carcinoma had metastatic positive SLNs on each side but also one metastatic bulky (≥2 cm) node without radiotracer uptake. The negative predictive value for patients with cervical cancers ≤ 2 cm was 100%.

Conclusions. The SLN-technique seems to be an accurate method for identifying lymph node metastases in cervical cancer patients with tumors of 2 cm or smaller. In case of a unilateral SLN only, a complete lymphadenectomy should be performed on the radionegative side. All bulky nodes must be removed.

Hypotes: Sentinel node är lika säkert som standardmetoden vid cervixcancer

- Aim: Utvärdera SLN istället för fullständig lymfkörtelutrymning vid tidig cervixcancer

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Resultat

- Minst en sentinel node hos 90% av patienterna
- Tumör< 2cm 94%
- 1 falskt negativ SLN hos tumör 3,5cm
- Sensitivitet hos alla 94%, hos patienter med tumör <2cm 100%

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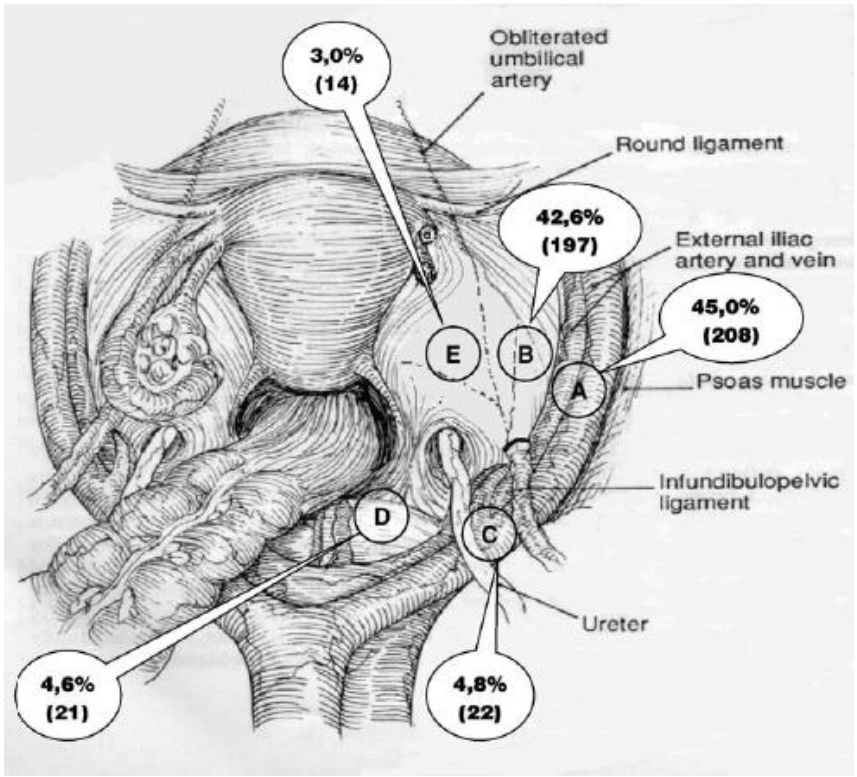
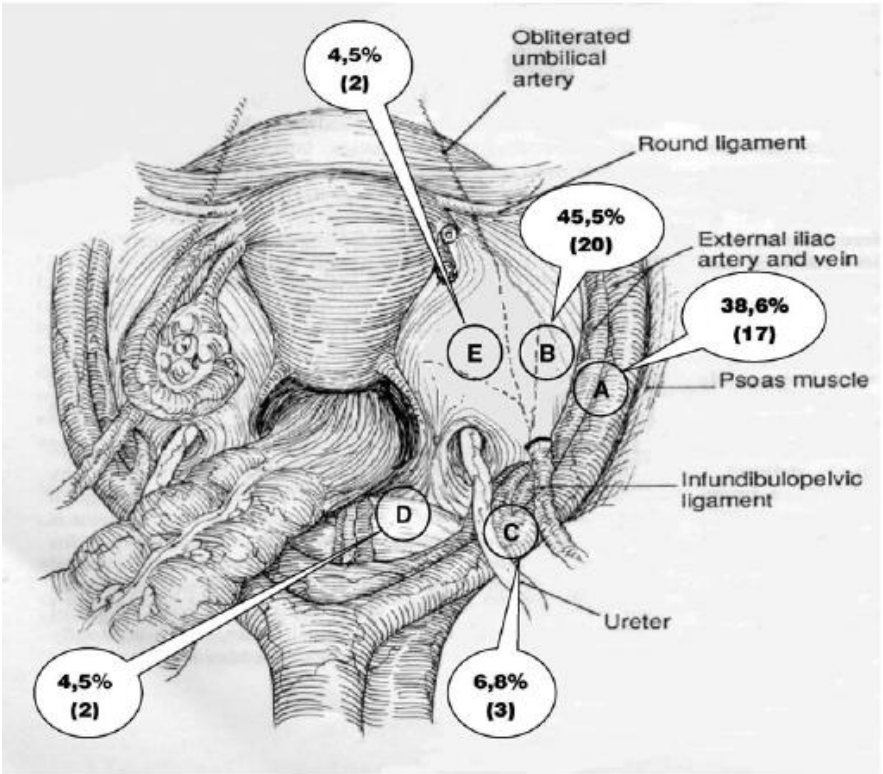
Sentinel node distribution



Sentinel nodes



Positive sentinel nodes

Rob et al 2005

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Varför sentinel node?

- Minska morbiditeten hos patienter
- Hitta metastaser bättre
- Hitta ovanligt belägna lymfkörtlar

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Konklusion

Sentinel node är säkert vid cervixcancer mindre än 2 cm.

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