

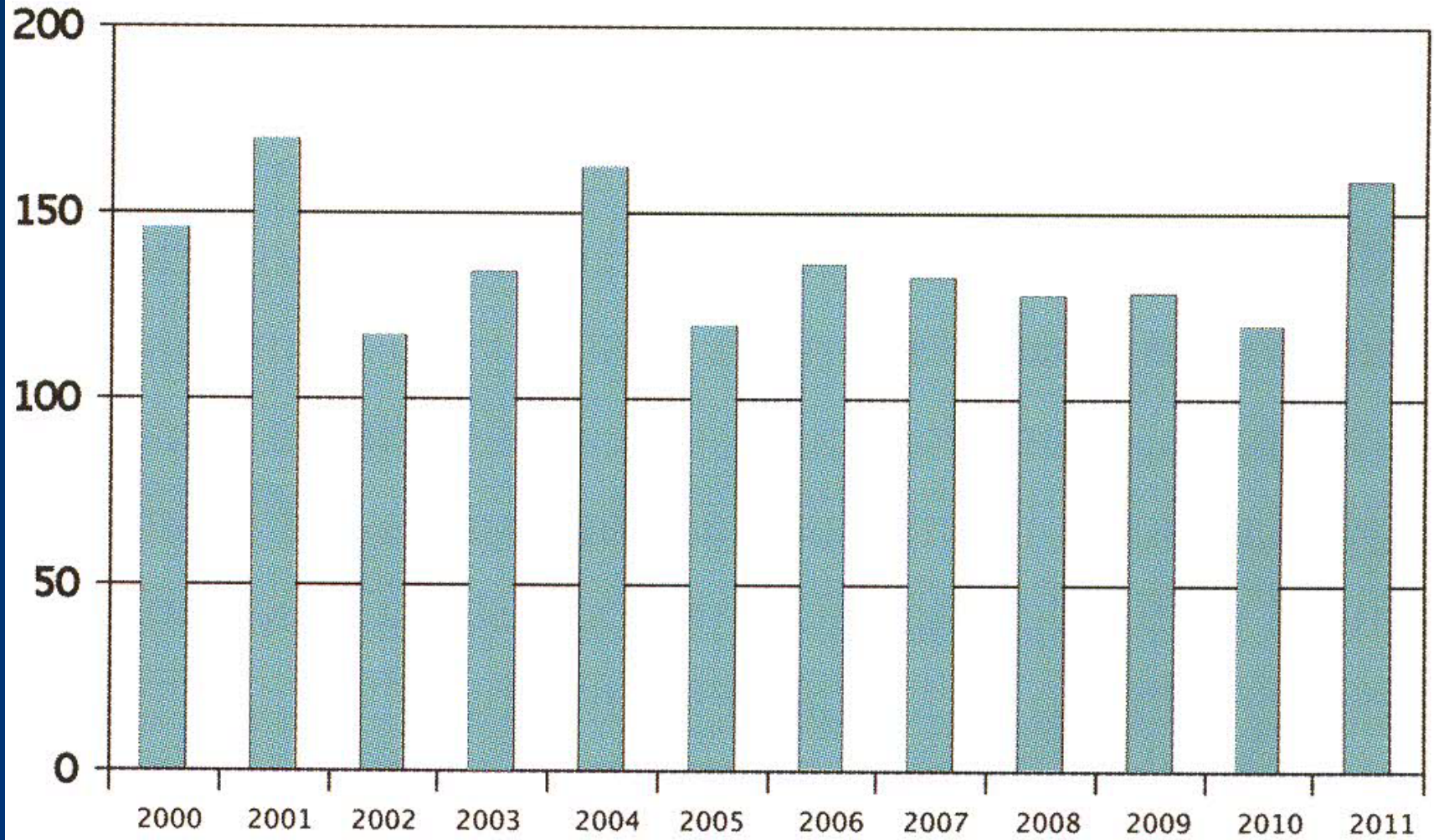
Research, teaching, and clinical work



Department of Obstetrics and Gynecology, University Hospital

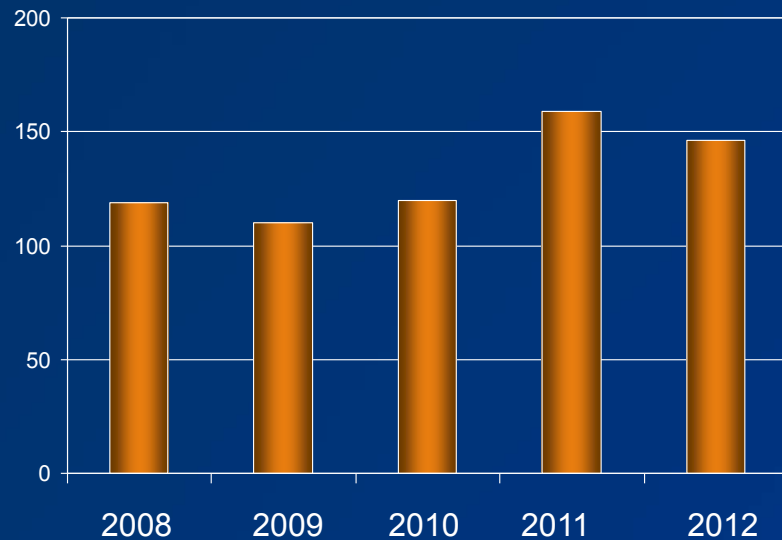


Research productivity: Department of Obstetrics and Gynecology

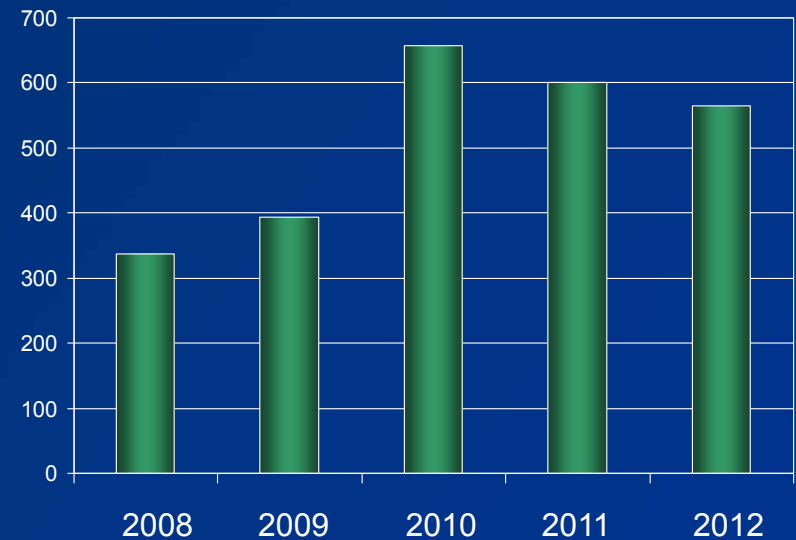


Publications and impact factors

Publications/year



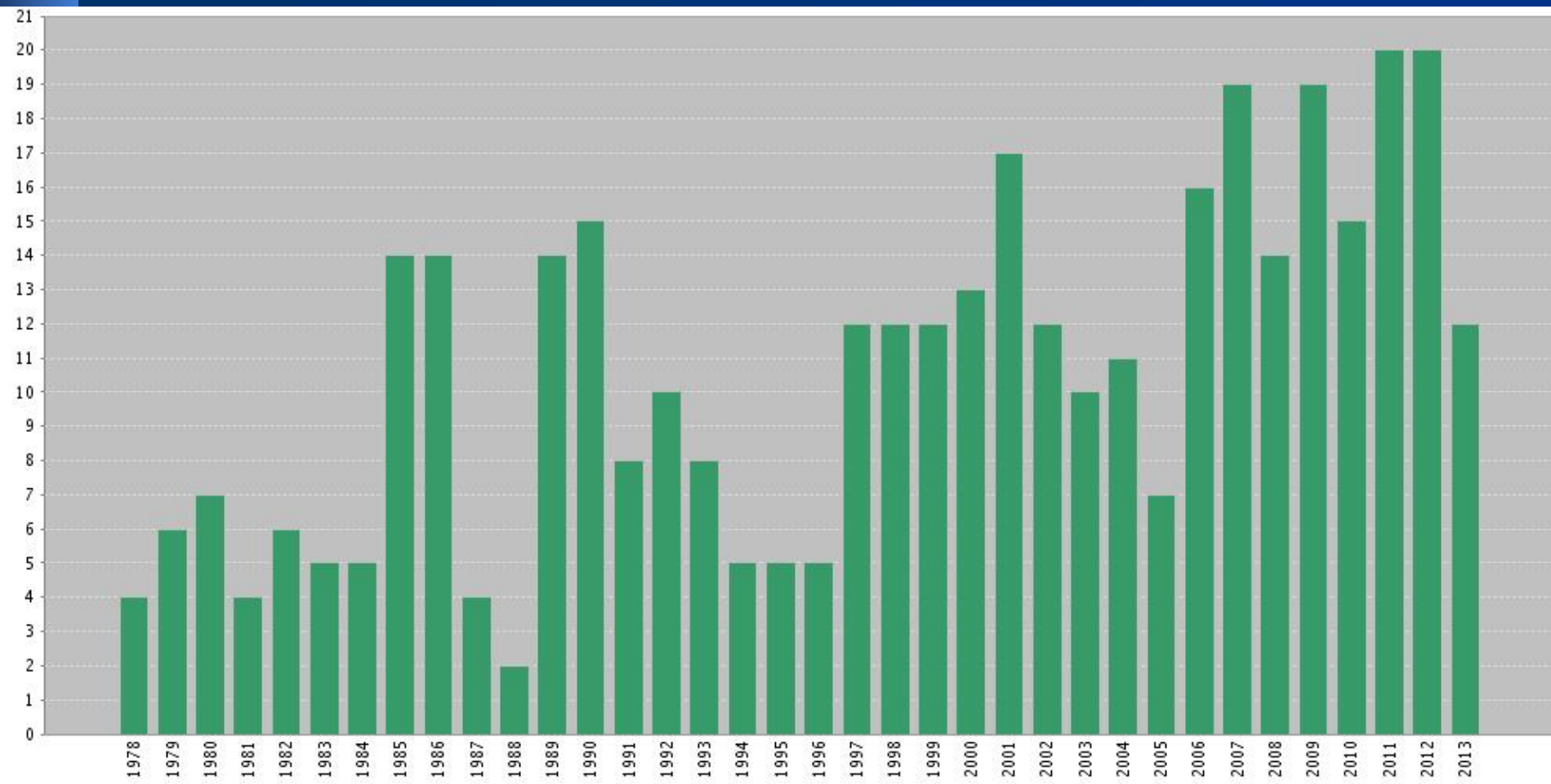
Impact factors



Academic dissertations 2012 (N=8)

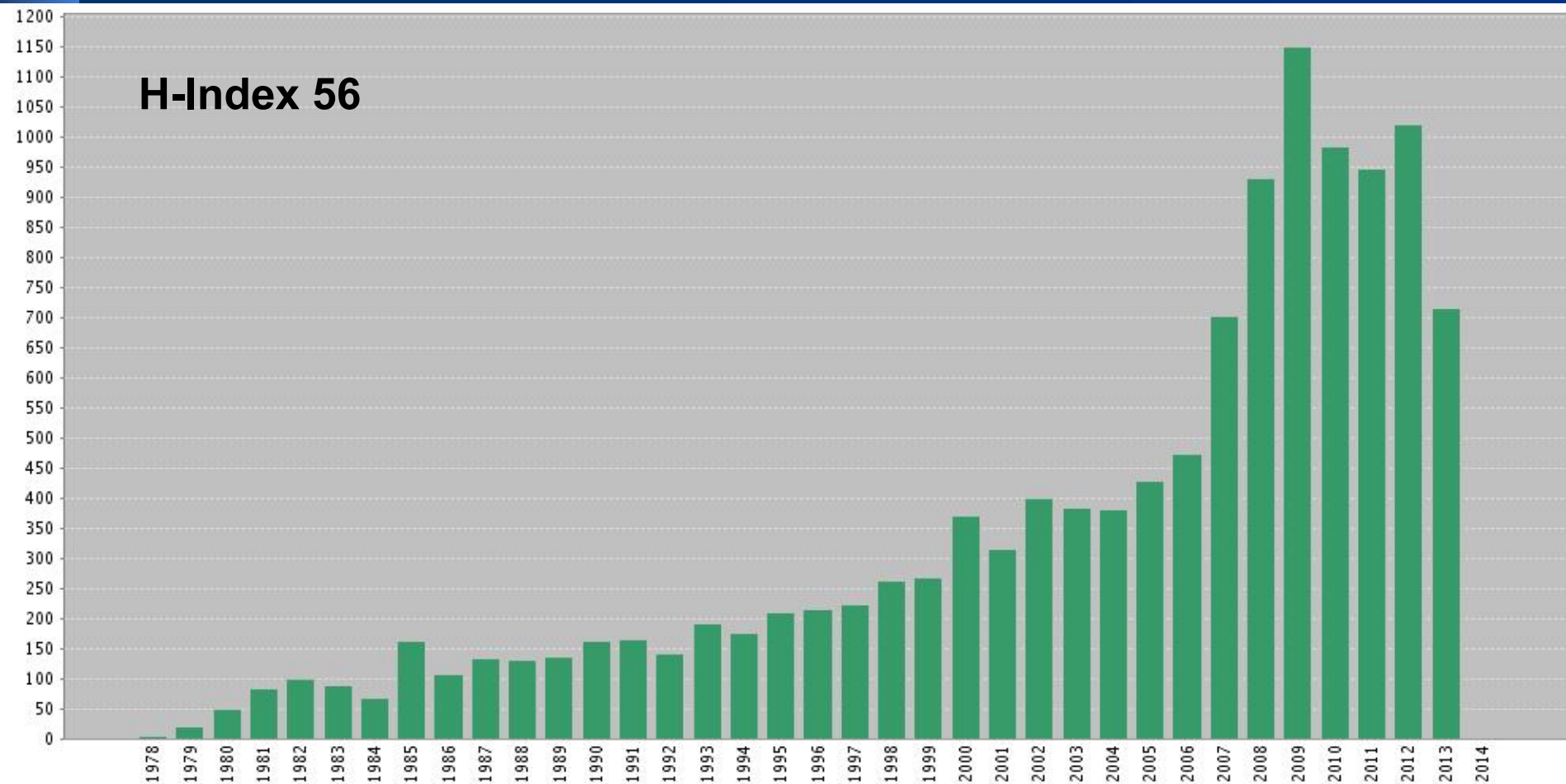
- Brummer T: *Hysterectomy* for benign indications in Finland
- Färkkilä A: Molecular studies on pathogenesis, prognostic factors, and new treatment options for *ovarian granulosa cell tumors*
- Heliövaara-Peippo S: Hysterectomy and levonorgestrel-releasing intrauterine system in the *treatment of menorrhagia* – a 10-year randomized comparative trial
- Jaakkola S: *Postmenopausal hormone therapy* and the risk for uterine cancers
- Koivisto-Korander R: *Uterine carcinosarcoma*, leiomyosarcoma and endometrial stromal sarcoma: epidemiological, clinical and prognostic aspects
- Mentula M: Second trimester *medical termination of pregnancy*: procedure, immediate complications and the risk of repeat termination
- Öhman H: Immunogenetic risk factors of *Chlamydia*-induced *tubal factor infertility*
- Lönnberg S: Case-control studies for the evaluation of performance and age-specific outcome of organised *cervical cancer screening*

Publications (JP)



Citations (JP)

H-Index 56



1979

Klamydia
on tippuria
kavalampi.

Käytetään kondomia.

RFSU
intercare



NATIONAL INSTITUTE
FOR HEALTH AND WELFARE

2012

Hanna Öhman

Immunogenetic risk factors
of *Chlamydia*-induced tubal
factor infertility

2013

OULU 2013
D 1207

ACTA

UNIVERSITATIS OULUENSIS

Erika Wikström

EPIDEMIOLOGY OF
CHLAMYDIA TRACHOMATIS
INFECTION IN FINLAND
DURING 1983–2009

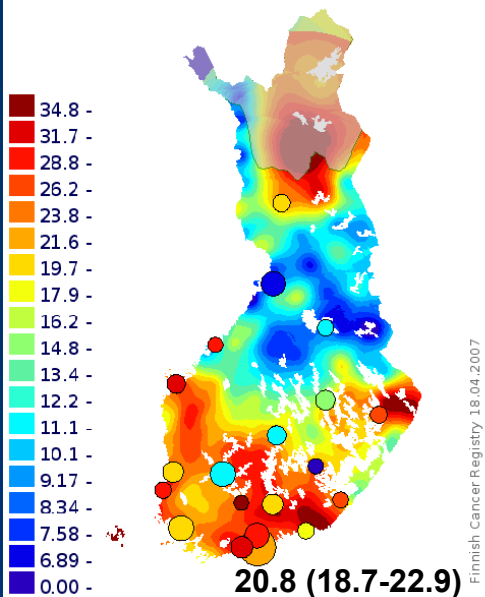
UNIVERSITY OF OULU GRADUATE SCHOOL,
UNIVERSITY OF OULU, FACULTY OF MEDICINE,
INSTITUTE OF CLINICAL MEDICINE,
DEPARTMENT OF DERMATOLOGY AND VENEREOLOGY,
OULU UNIVERSITY HOSPITAL, DEPARTMENT OF DERMATOLOGY,
NATIONAL INSTITUTE FOR HEALTH AND WELFARE,
UNIVERSITY OF HELSINKI, FACULTY OF MEDICINE,
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY,
UNIVERSITY OF TAMPERE, SCHOOL OF HEALTH SCIENCES



Age
<23

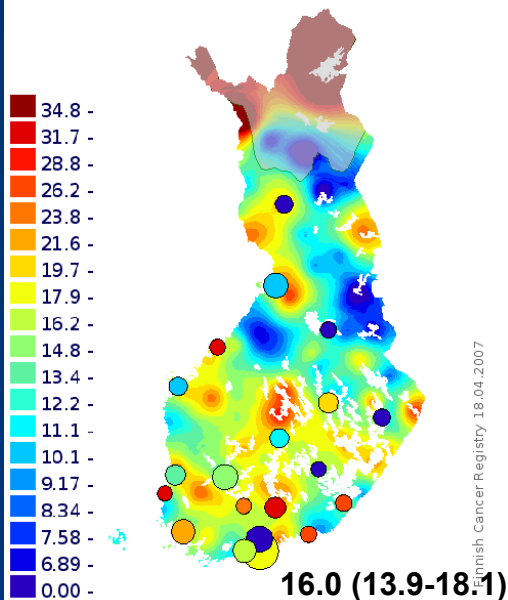
Prevalence of Chlamydia

Females < 23 years, 1983-1989



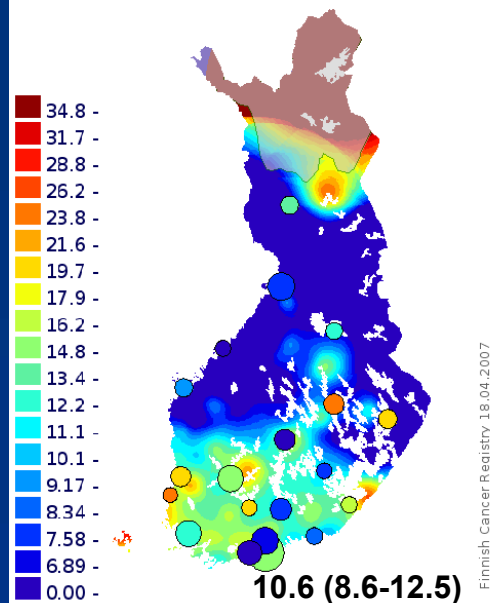
Prevalence of Chlamydia

Females < 23 years, 1990-1996



Prevalence of Chlamydia

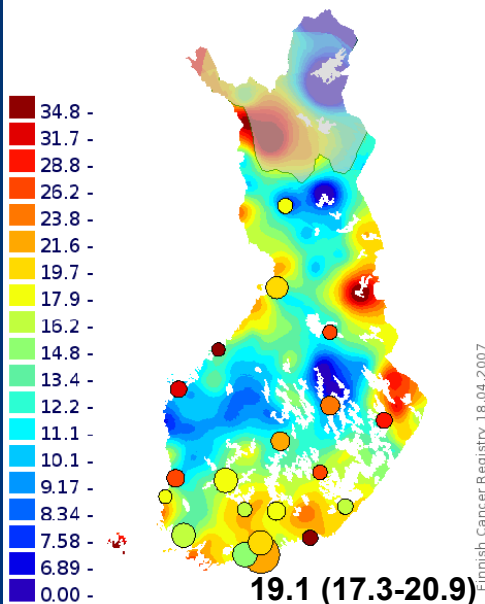
Females < 23 years, 1997-2003



Age
23-28

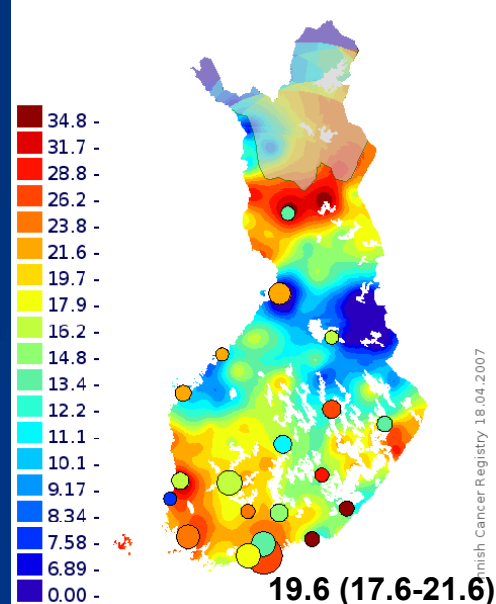
Prevalence of Chlamydia

Females 23-28 years, 1983-1989



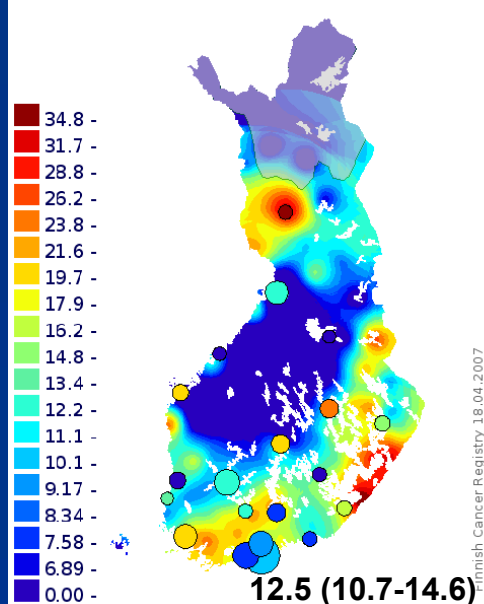
Prevalence of Chlamydia

Females 23-28 years, 1990-1996

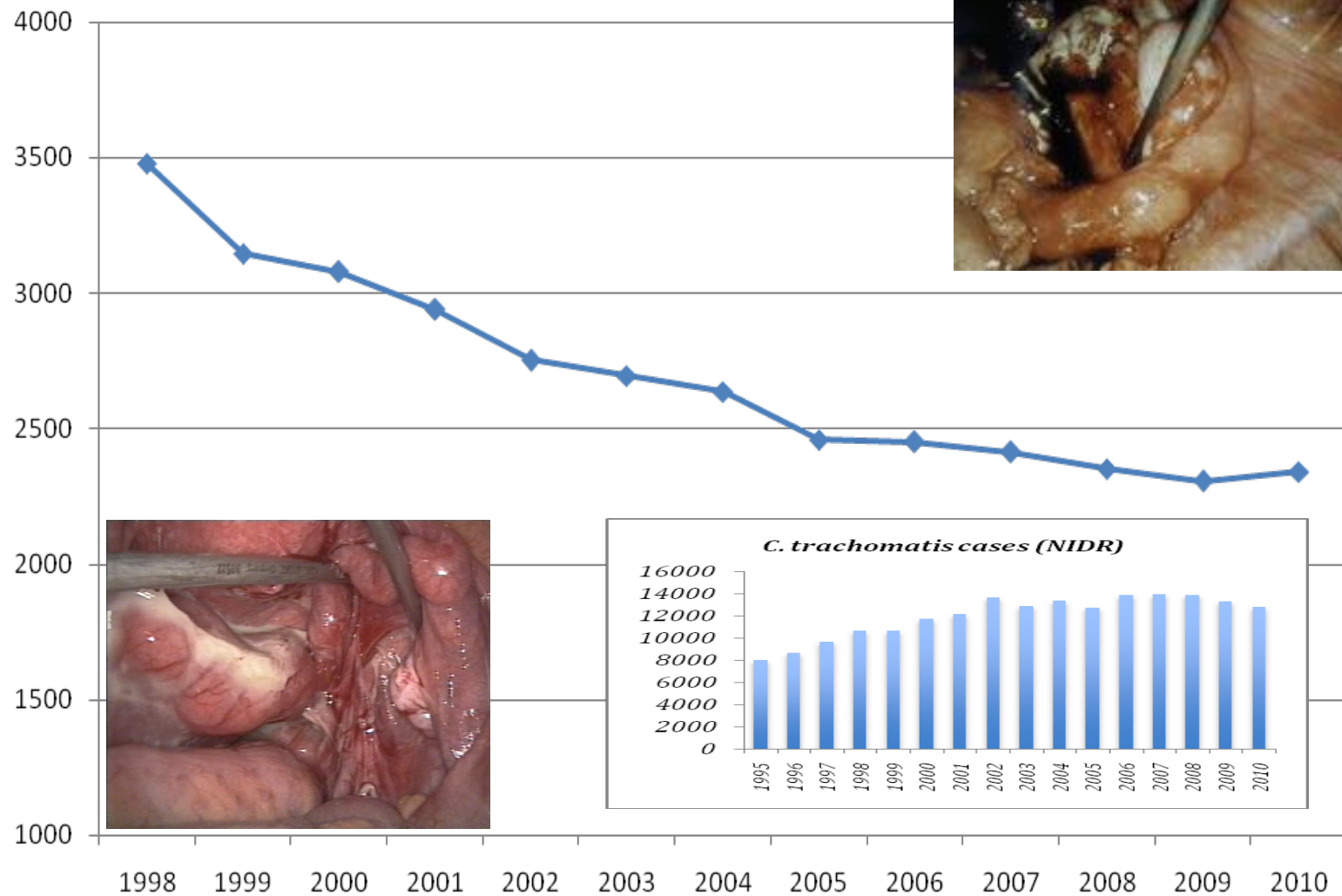


Prevalence of Chlamydia

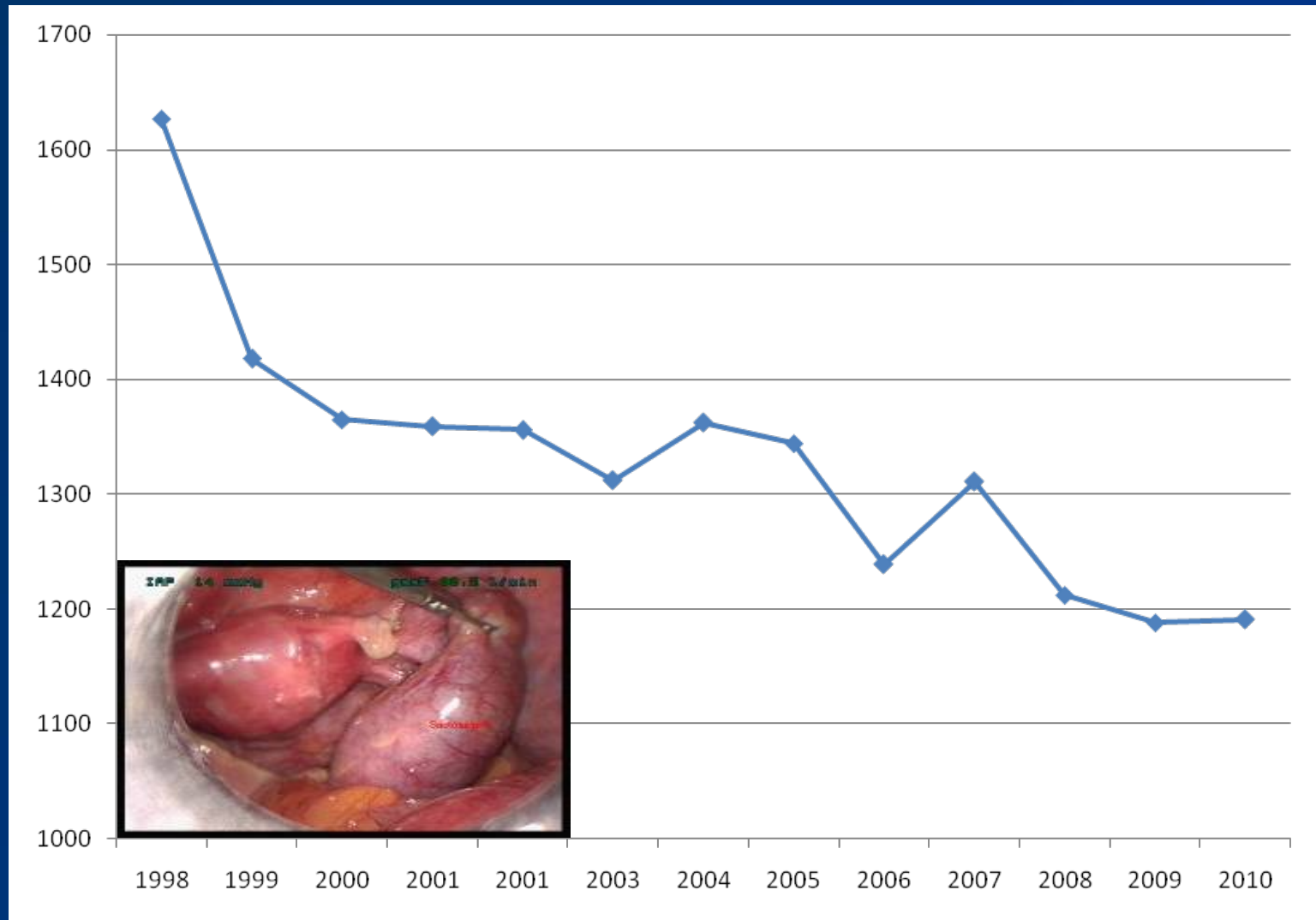
Females 23-28 years, 1997-2003



PID rate 1998-2010*

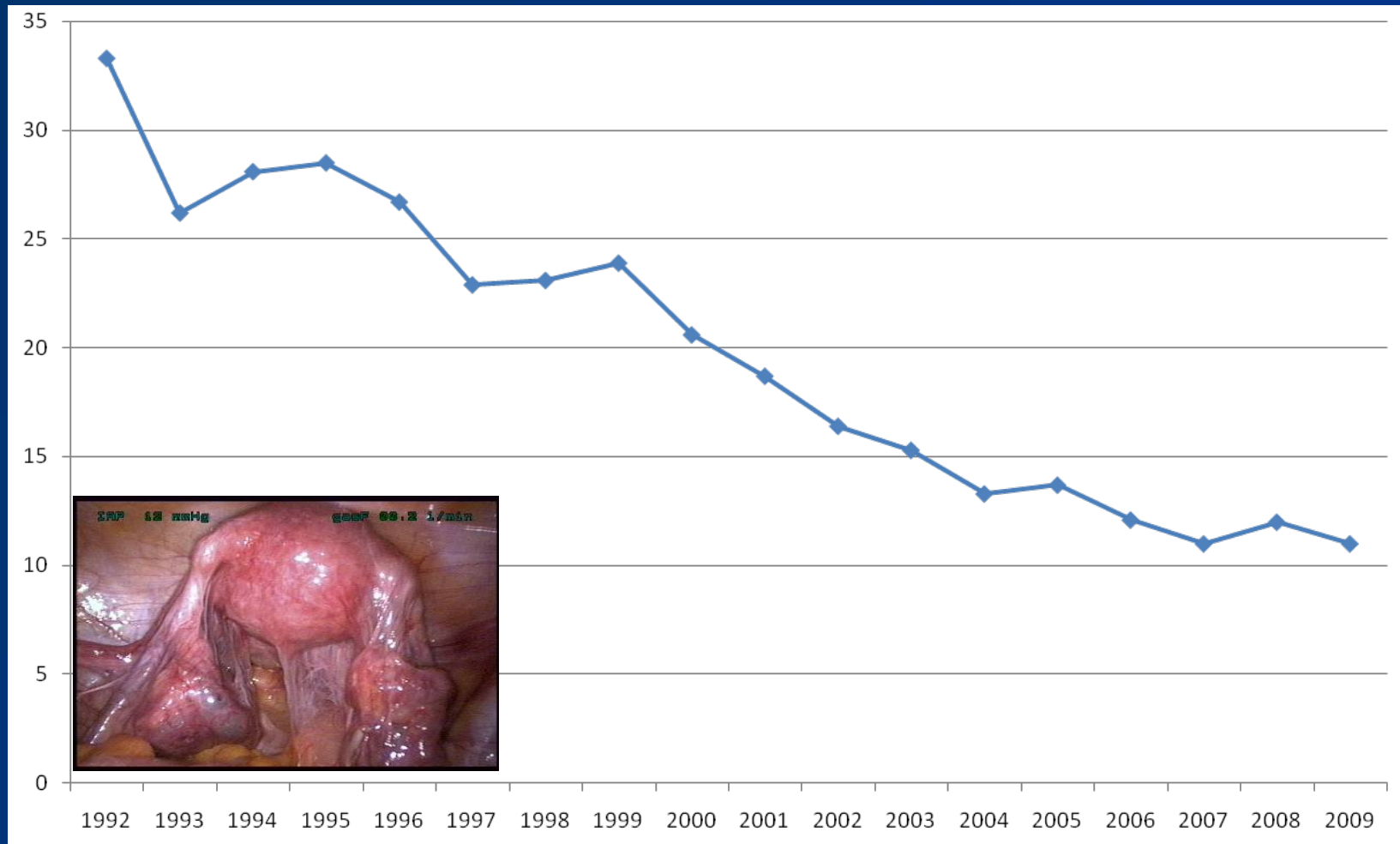


Tubal pregnancy rate 1998-2010



Proportion of tubal factor infertility of all infertility 1992-2009

Percent



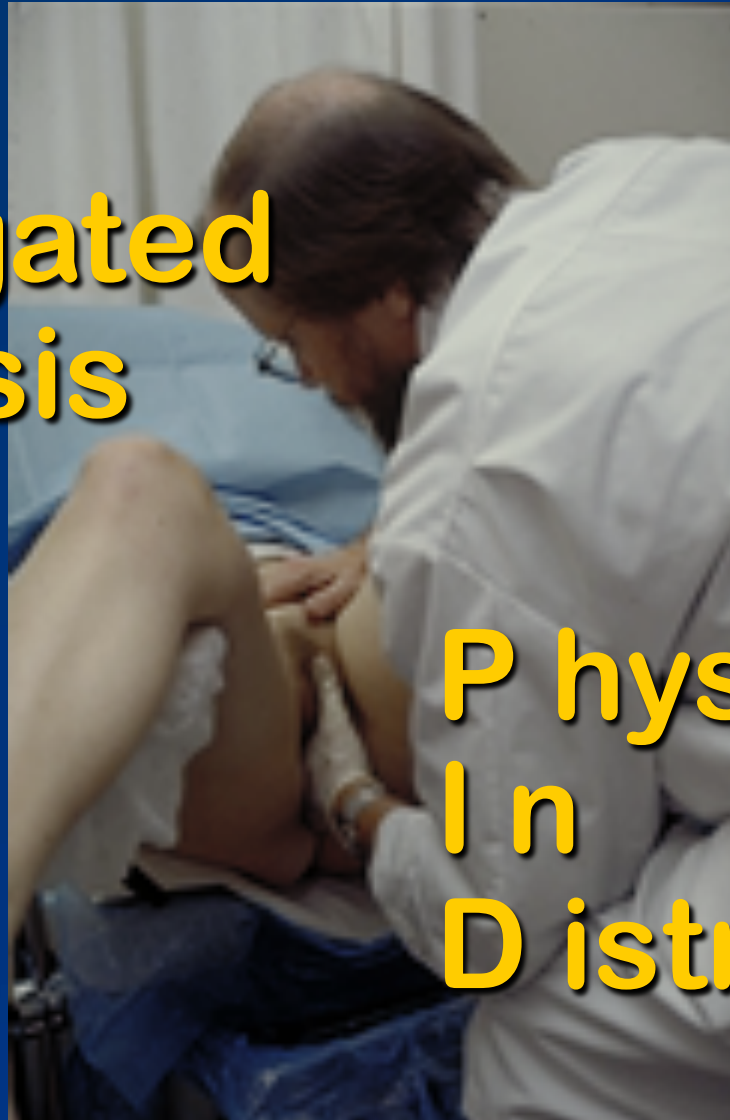
THL, 2011

PID-Identifying research gaps

- Defining PID
- Cellular infiltrates in the endometrium which best correlate with PID/TFI
- Development of a noninvasive biomarker reflecting UGT infection
- Accuracy of TVS or MRI to detect early tubal inflammation in women with LGT infection
- Causal role of BV-associated organisms and M.genitalium
- Improve mechanisms to prevent reinfection

Pretty Inadequate Diagnosis

P oorly
I nvestigated
D iagnosis



P hysician
I n
D istress

A photograph of four men in dark suits and ties standing in a hallway. From left to right: a man with short brown hair, a man with short grey hair, an older man with white hair and glasses, and a man with a full grey beard and glasses. They are all looking towards the camera. In the background, there is a glass door, a clock on the wall, and a blue directional sign with white text. The sign has arrows pointing left and right, with text in Finnish and English: 'Lähdetietä • Press' (left), 'Näytteliasettajakloppi' (right), and 'Exhibitors' Lounge' (right).

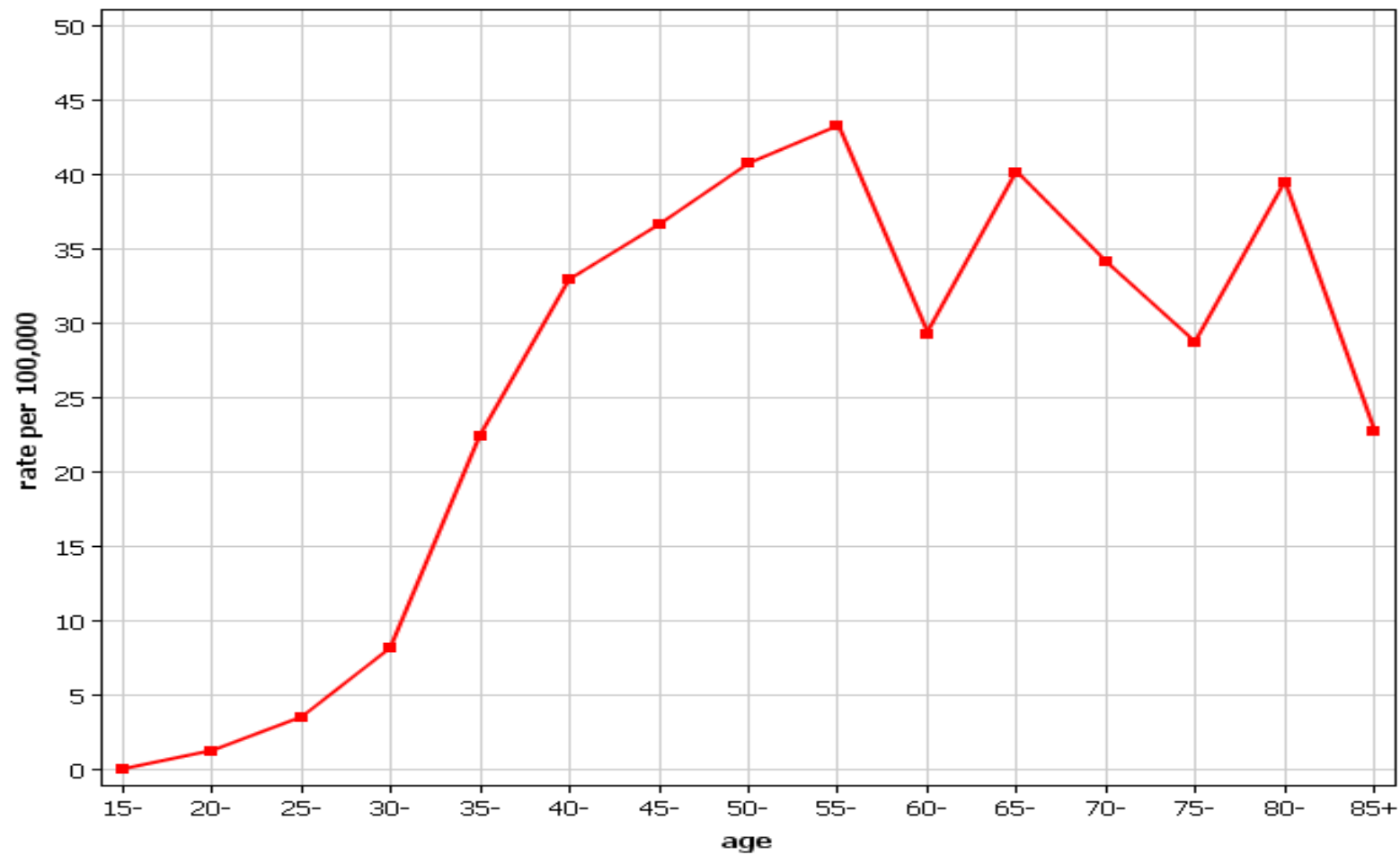
natureOUTLOOK

HUMAN PAPILLOMAVIRUS

30 August 2012 / Vol 488 / Issue No. 7413

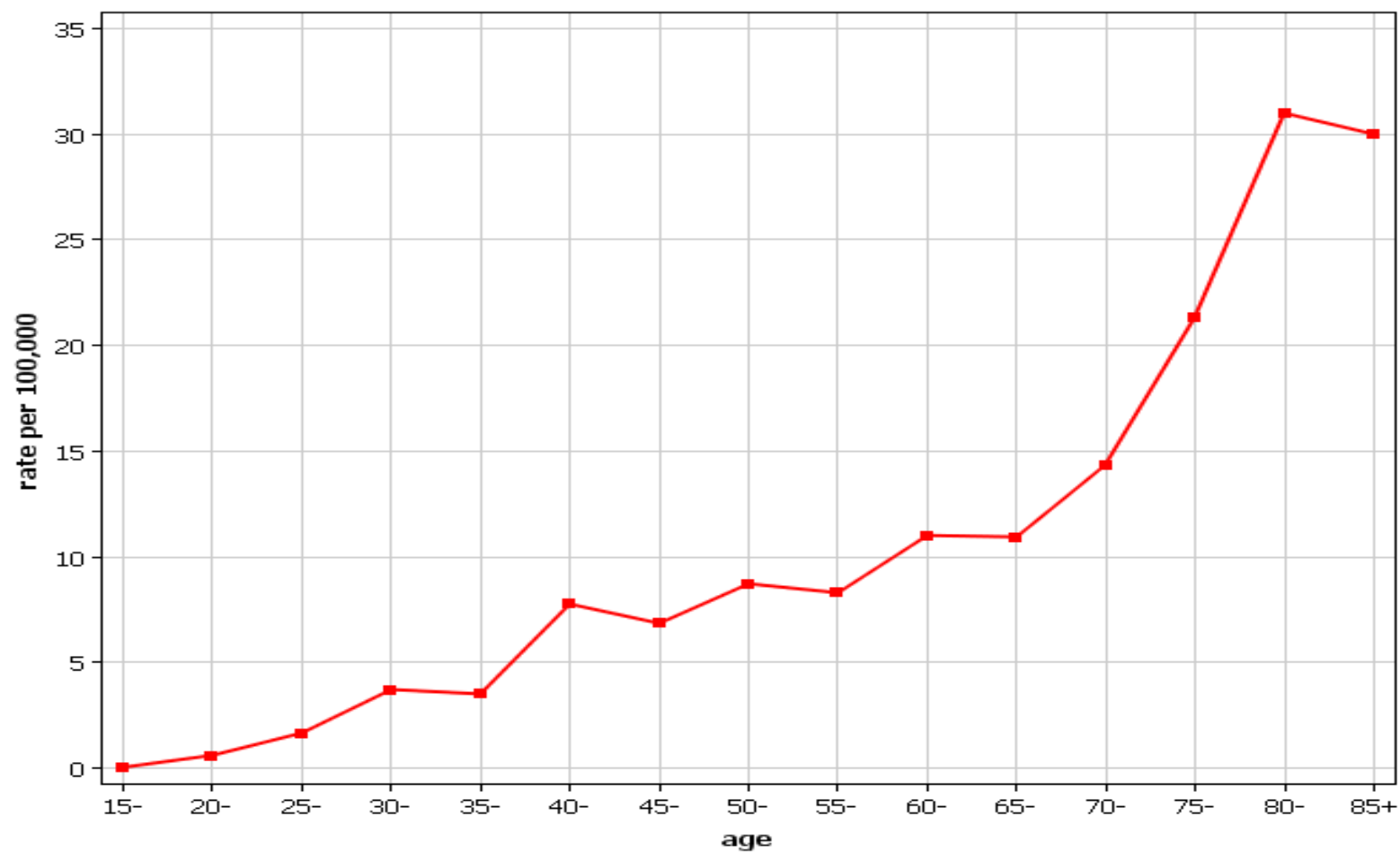
Finland-Incidence (1963)

Cervix uteri



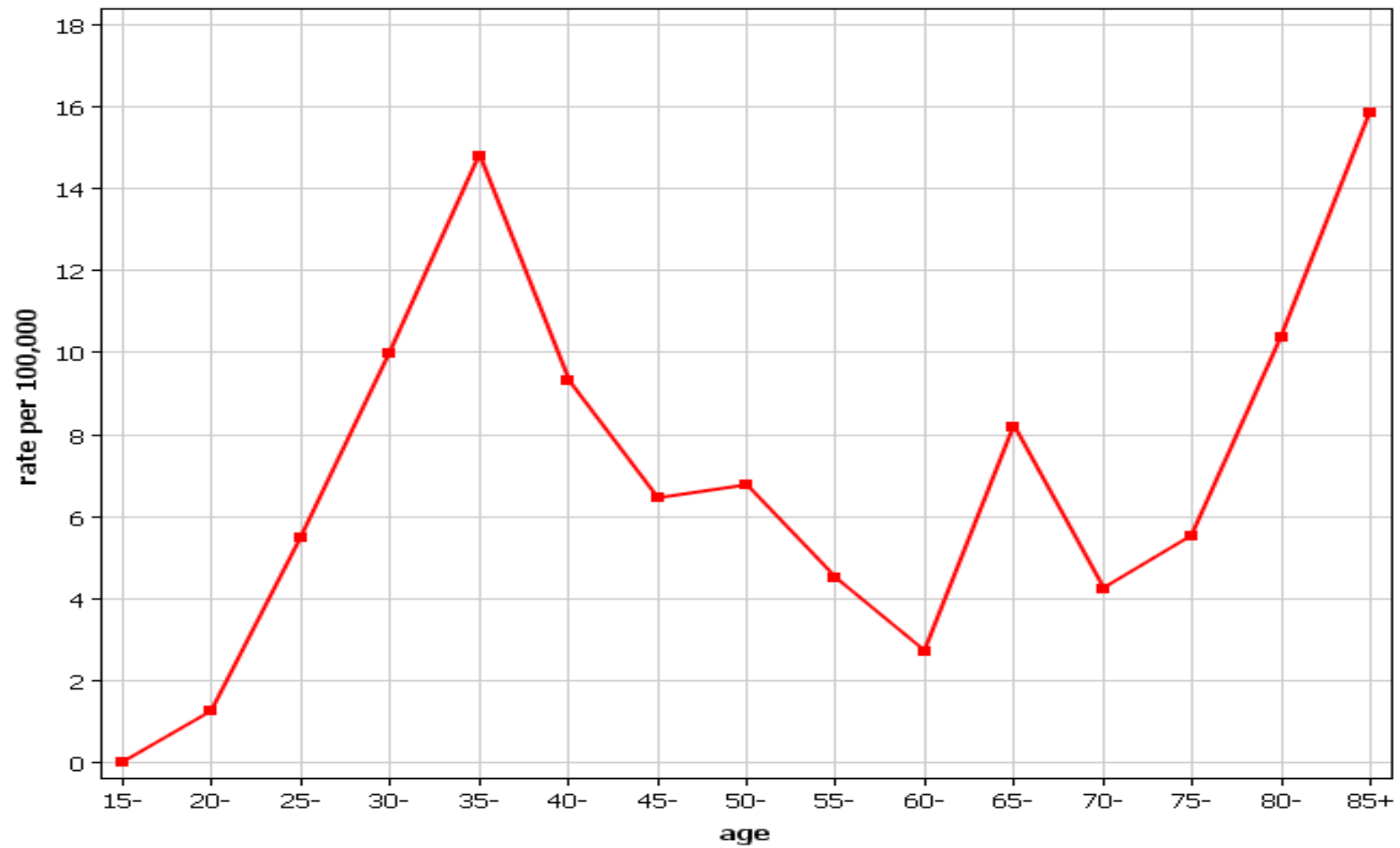
Courtesy by Nieminen P

Finland-Incidence (1989) Cervix uteri



Courtesy by Nieminen P

Finland-Incidence (2008) Cervix uteri



Courtesy by Nieminen P

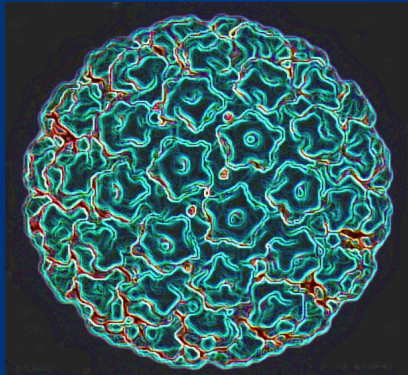
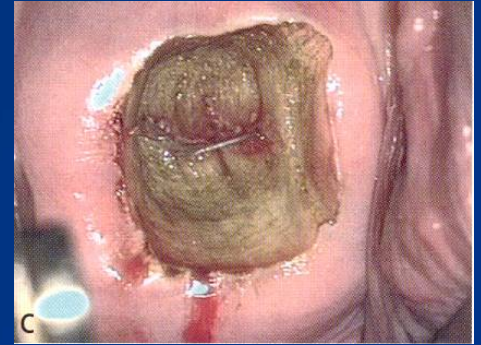
HPV disease burden in Finland*

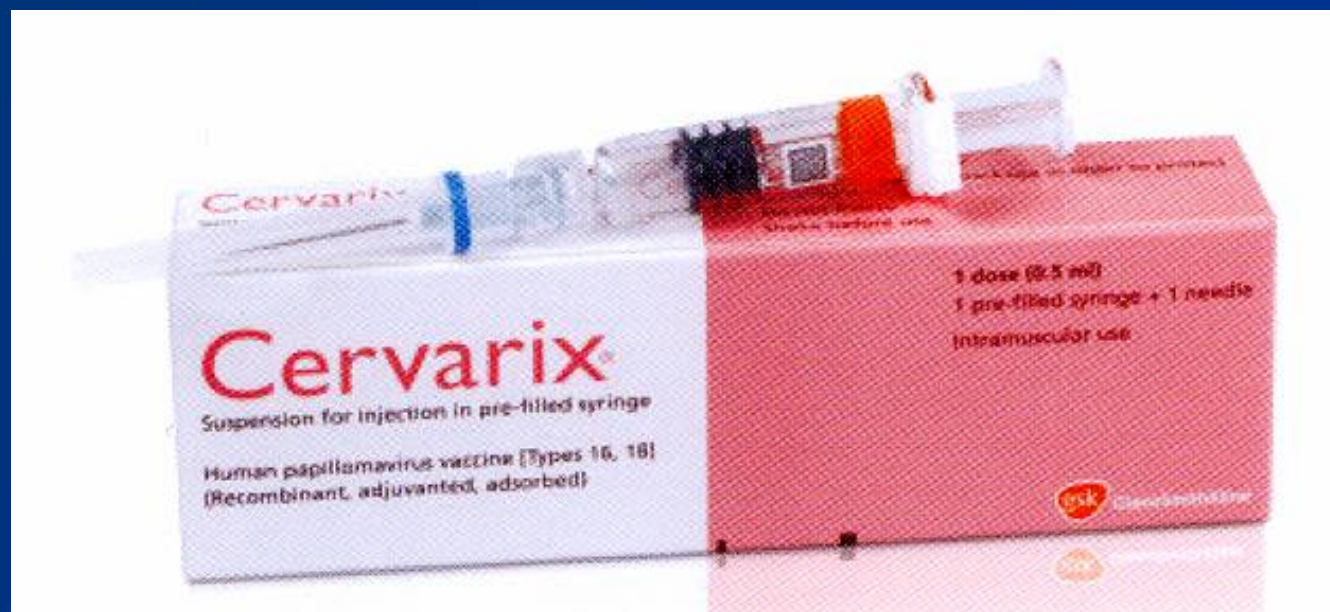
- 500 000 Pap tests
- 6 400 condyloma cases
- 16 300 colposcopies
- 3 000 conizations
- 160 cervical cancers
- 100 oropharyngeal and other anogenital cancers

Total health care costs 45 M€

Prevention of cervical cancer

- Secondary prevention
 - Early detection by screening
 - Disease burden has shifted to management of CIN
- Primary prevention
 - Vaccination
 - Eradication of disease





Efficacy of both vaccines against HPV16/18 related CIN3+

HPV naive*	Vaccine No./Total	Control No./Total	VE (%) 95%CI
▪ Quadrivalent	0/4,616	34/4,680	97.2 (91.5-99.4)
▪ Bivalent	0/5,466	27/5,452	100 (85.5-100)

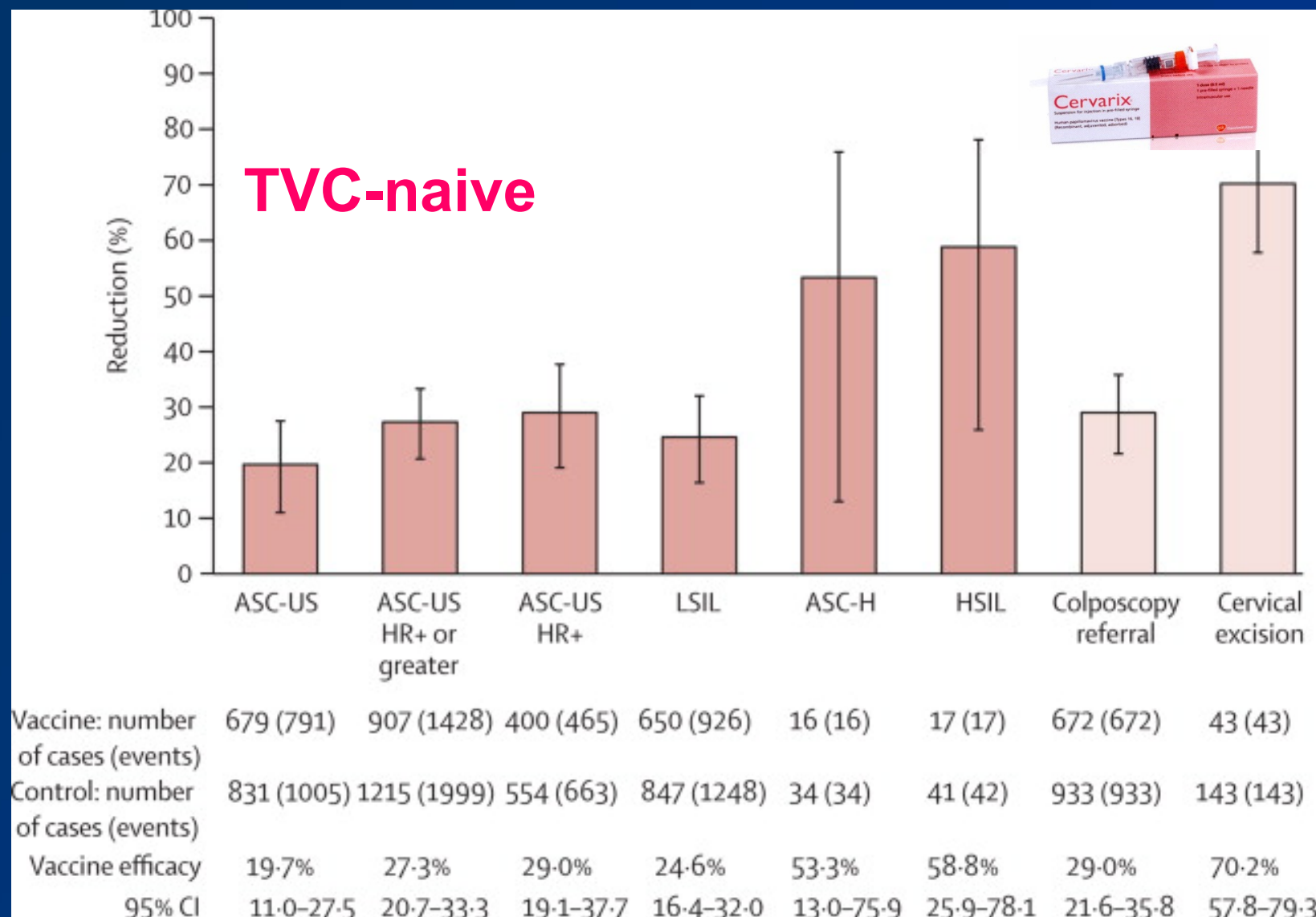
Intention-to-treat (ITT)**

▪ Quadrivalent	100/8,562	177/8,598	43.5 (27.3-56.2)
▪ Bivalent	51/8,694	94/8,708	45.7 (22.9-62.2)

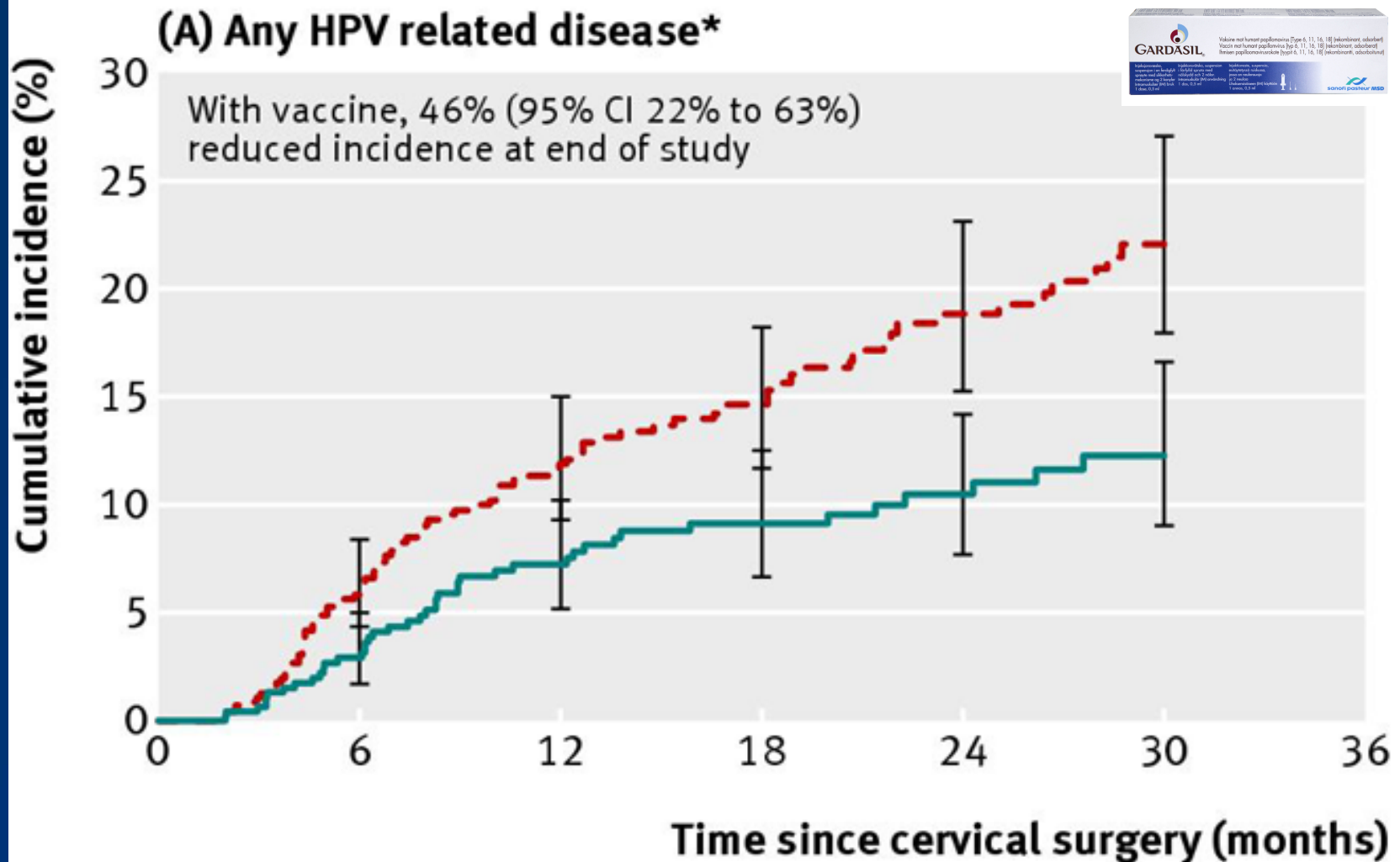
*HPV naive population: Subjects received at least 1 vaccination, were seroneg and DNA neg to HPV6/11/16/18 and DNA neg to 10 non-vaccine types and had normal Pap test;
**All subjects who received at least 1 vaccination and had follow-up regardless of the presence of HPV infection or HPV-related disease at enrollment

Lehtinen M, et al: Nat Rev Clin Oncol 2013

Reduction in cytological atypias, colposcopy referrals and cervical procedures



Impact of Quadrivalent Vaccine on new Cervical Disease after Definitive Therapy



587 vaccineo recipients; 763 placebo recipients;
Joura E, et al: BMJ 2012;344:e1401

Community Randomised Trial: What is the Best Vaccination Strategy?



Study arm	Girls	Boys
	Recruited/Invited (%)	Recruited/Invited (%)
■ A (N=33)	6,468/12,247 (52.8)	2,734/12,464 (21.9)
■ B (N=33)	7,364/14,856 (49.6)	4,885/15,446 (31.6)
■ C (N=33)	6,682/12,612 (53.0)	4,042/12,932 (31.3)



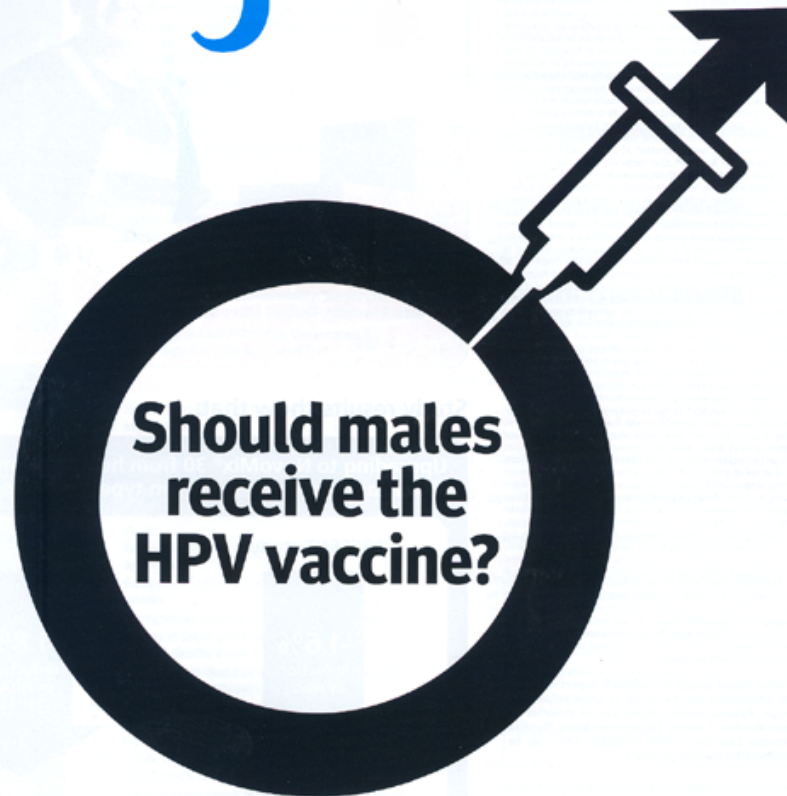
- A: 90% of girls and boys received HPV16/18 vaccine, 10% of girls and boys received HBV;
- B: 90% of girls received HPV16/18 vaccine, 100% of boys received HBV;
- C: 100% of girls and boys received HBV

Total 32,000 vaccinated; Total 35,000 volunteers not vaccinated

Lehtinen M, et al: Unpublished

BMJ

339.871-926 No 7726 ISSN 1759-2151
17 October 2009 | bmj.com



**Should males
receive the
HPV vaccine?**

PLUS Disclosing competing interests
Economic sanctions towards North Korea
Lessons from the Ribena girls

**BMJ Group Awards
ENTER NOW**

**HPV-related
disease
burden:
Not just
a women's
issue!**

Questions remain

- The efficacy of HPV vaccines in preventing cervical cancer has not yet been demonstrated
- There is no evidence that HPV vaccination reduces the rate of cervical cancer beyond what cytologic screening has achieved



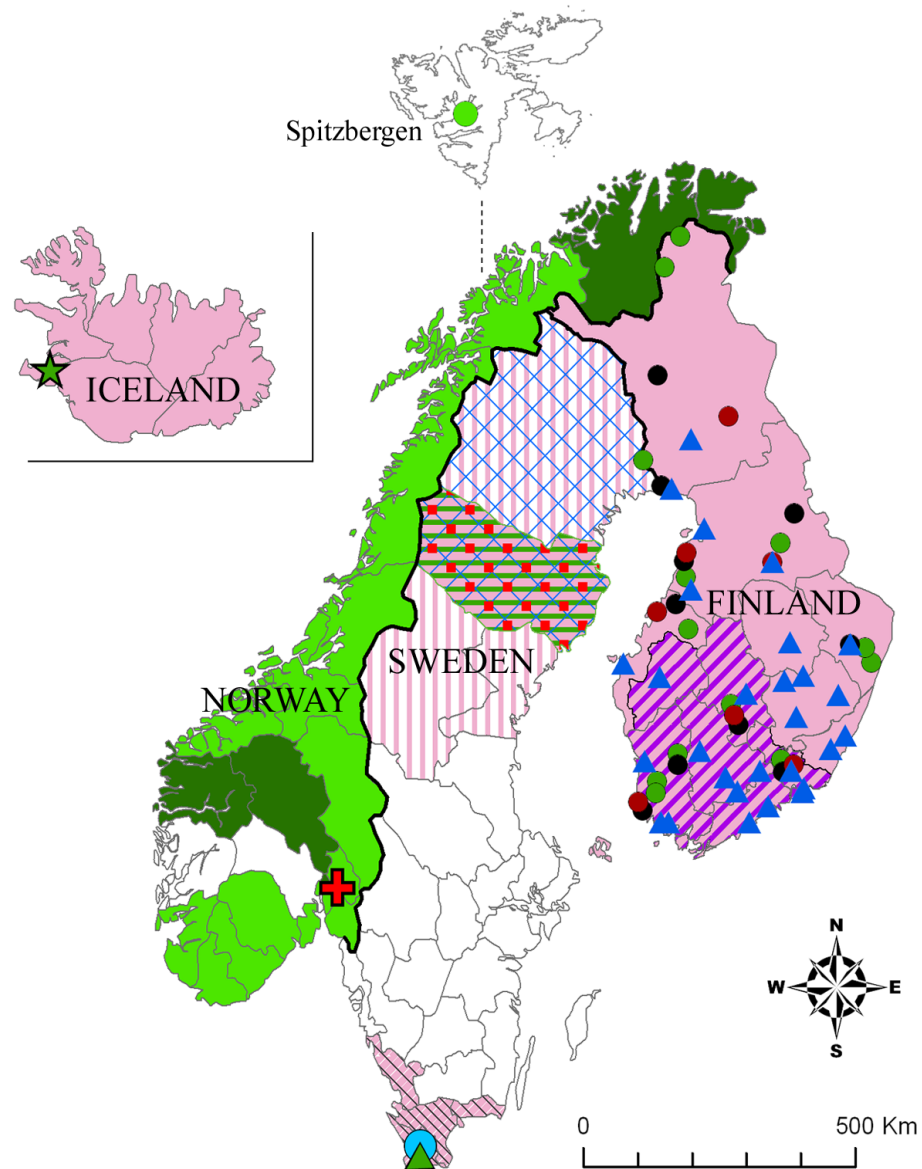
Cancer Registry Based Passive Follow-up

Group	No.	Yrs of F/U	CIN3+ Incidence	
■ Vaccine	866	3,464	0	0 (0-106.4)
■ Placebo	861	3,444	3	87.1 (17.9-254.5)
■ Unvacc	15,719	62,876	59	93.8 (71.4-121)

Cancer Registry follow-up started 6 months after active trial follow-up (FUTURE II);
Incidence per 100,000 (95% CI); Unvacc=Unvaccinated control cohort

Rana MM, et al, Int J Cancer 2013;132:2833

Network of biobanks

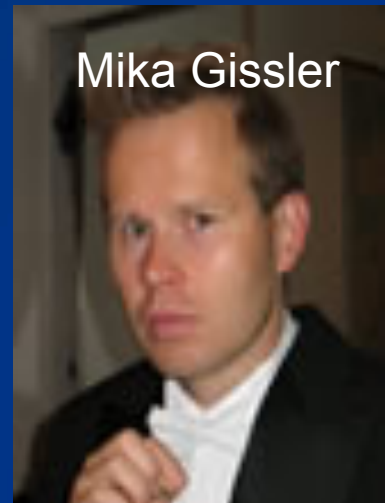


Finland is a paradise of biobanks and health registries...



Eero Pukkala

Eero Pukkala



Mika Gissler

Mika Gissler

Cervical procedures for treatment of CIN increase the risk for preterm delivery

- 25,827 women, of whom 5,835 had subsequent singleton deliveries
- **Risk for preterm delivery (<h.37)**
 - **Excisional Rx** **OR 1.99 (95%CI 1.8-2.2)***
 - **Ablative Rx** **OR 1.60 (95%CI 1.4-1.8)***



*Adjusted for maternal age, parity, and smoking; Jakobsson M, et al, Obstet Gynecol 2007;109:309

Disease burden of placental abruption

Material

- Cases (N=7,951) and controls (N=23,852) 1969-2005

Registry linkages

- Birth registry
- Hospital Discharge Registry
- Cancer Registry
- Cause of death-registry
- **Congenital Anomalies Registry**



Tikkanen M, et al: Placental abruption-Studies of incidence, risk factors and potential predictive biomarkers, University of Helsinki 2008;
AOGS 2010; AOGS 2011; Prenat Diagn 2011; AOGS 2012a; AOGS 2012b; AOGS 2013a; AOGS 2013b; Obstet Gynecol 2013; Prenat Diagn 2013; **Obstet Gynecol 2013;122:268**



Outcomes and Costs with LNG-IUS or Hysterectomy for Treatment of Menorrhagia

598 Women Screened



362 Excluded
184 Not Eligible
178 Refused to Participate



Ritva Hurskainen

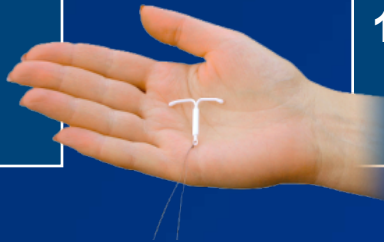
Satu Heliövaara-Peippo

236 Randomized

119 Assigned to LNG-IUS
117 Received Treatment
as Assigned

116 Included in 1-Year Primary
End Point Analysis

117 Included in 5-Year Primary
End Point Analysis



117 Assigned to Hysterectomy
109 Received Treatment
as Assigned

112 Included in 1-Year Primary
End Point Analysis

115 Included in 5-Year Primary
End Point Analysis

Lancet 2001; 357:2733; JAMA 2004; 291:1456; AOGS 2009; BJOG 2010; Maturitas 2011; Am J Obstet Gynecol, 2013 (in press);
PhD Theses: Ritva Hurskainen 2001, Karoliina Halmesmäki 2007, Satu Heliövaara-Peippo 2012

GENERAL GYNECOLOGY

Quality of life and costs of levonorgestrel-releasing intrauterine system or hysterectomy in the treatment of menorrhagia: a 10-year randomized controlled trial

Satu Heliövaara-Peippo, MD, PhD; Ritva Hurskainen, MD, PhD; Juha Teperi, MD, PhD; Anna-Mari Aalto, PhD; Seija Grénman, MD, PhD; Karoliina Halmesmäki, MD, PhD; Markus Jokela, PhD; Aarre Kivelä, MD, PhD; Eija Tomás, MD, PhD; Marjo Tuppurainen, MD, PhD; Jorma Paavonen, MD, PhD

OBJECTIVE: Menorrhagia is a common problem impairing the quality of life (QOL) of many women. Both levonorgestrel-releasing intrauterine system (LNG-IUS) and hysterectomy are effective treatment modalities but no long-term comparative studies of QOL and costs exist. The objective of this study was to compare QOL and costs of LNG-IUS or hysterectomy in the treatment of menorrhagia during 10-year follow-up.

STUDY DESIGN: A total of 236 women, aged 35-49 years, referred for menorrhagia to 5 university hospitals in Finland were randomly assigned to treatment with LNG-IUS ($n = 119$) or hysterectomy ($n = 117$) and were monitored for 10 years. The main outcome measures were health-related QOL (HRQOL), psychosocial well-being, and cost-effectiveness.

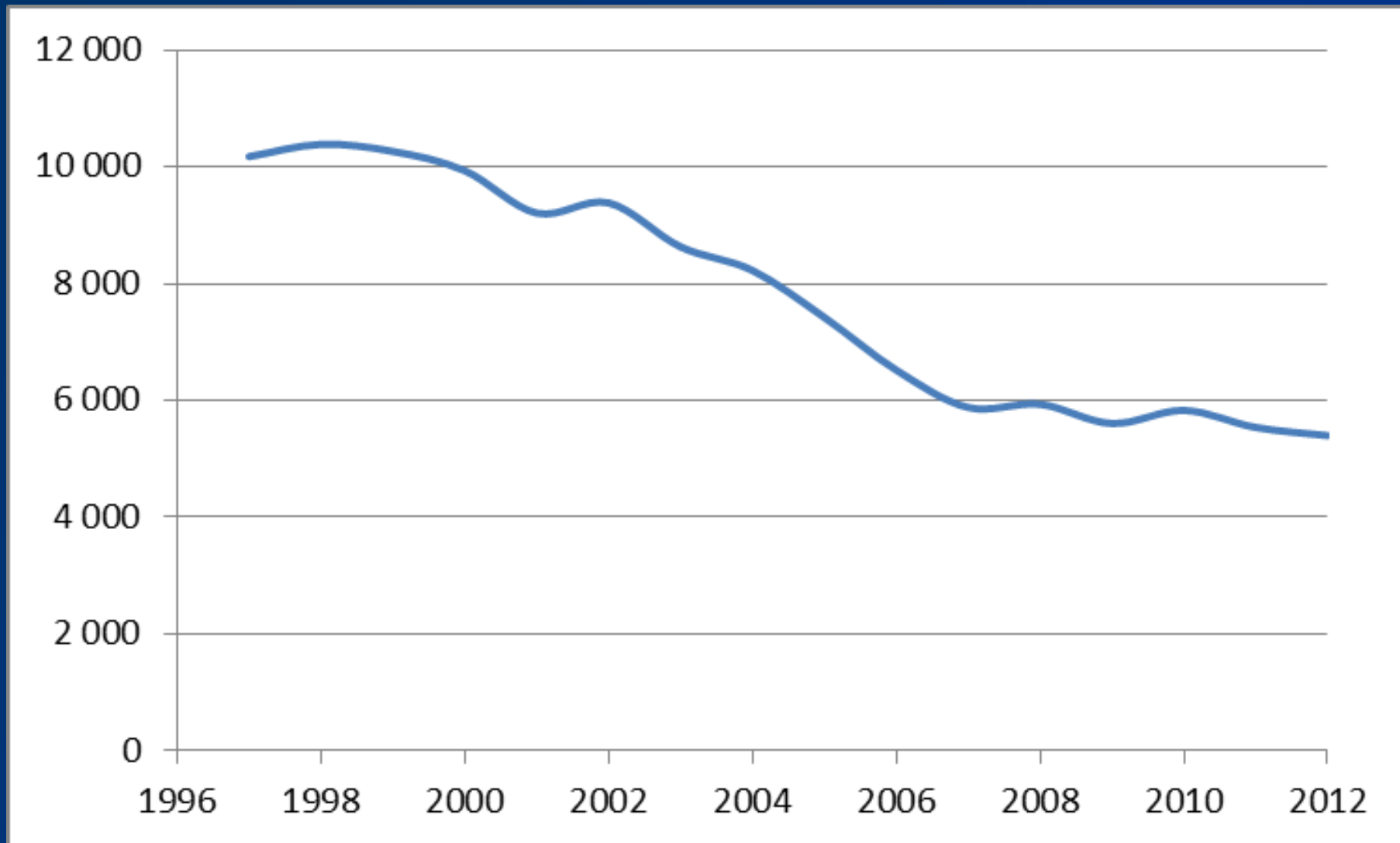
RESULTS: A total of 221 (94%) women were followed for 10 years. Although 55 (46%) women assigned to the LNG-IUS subsequently

underwent hysterectomy, the overall costs in the LNG-IUS group (\$3423) were substantially lower than in the hysterectomy group (\$4937). Overall, levels of HRQOL and psychosocial well-being improved during first 5 years but diminished between 5 years and 10 years and the improved HRQOL returned close to the baseline level. There were no significant differences between LNG-IUS and hysterectomy groups.

CONCLUSION: Both LNG-IUS and hysterectomy improved HRQOL. The improvement was most striking during the first 5 years. Although many women eventually had hysterectomy, LNG-IUS remained cost-effective.

Key words: cost-effectiveness, health-related quality of life, hysterectomy, levonorgestrel-releasing intrauterine system, menorrhagia

Hysterectomy rate in Finland



Challenges in acute and emergency obstetrics: From practice guidelines development to clinical effectiveness

- Amniocentesis in the diagnosis of subclinical intra-amniotic infection
- Prediction of preterm delivery by new biomarkers
- Abnormally invasive placentation: EU-collaboration with practice guidelines development
- Management of retained placenta: medical or surgical?
- New treatment for massive postpartum hemorrhage: Bakri balloon
- The disease burden associated with placental abruption
- Amniotic fluid EPO in the diagnosis of fetal asphyxia
- Foley catheter balloon for cervical ripening and labor induction



Subclinical IAI and preterm birth

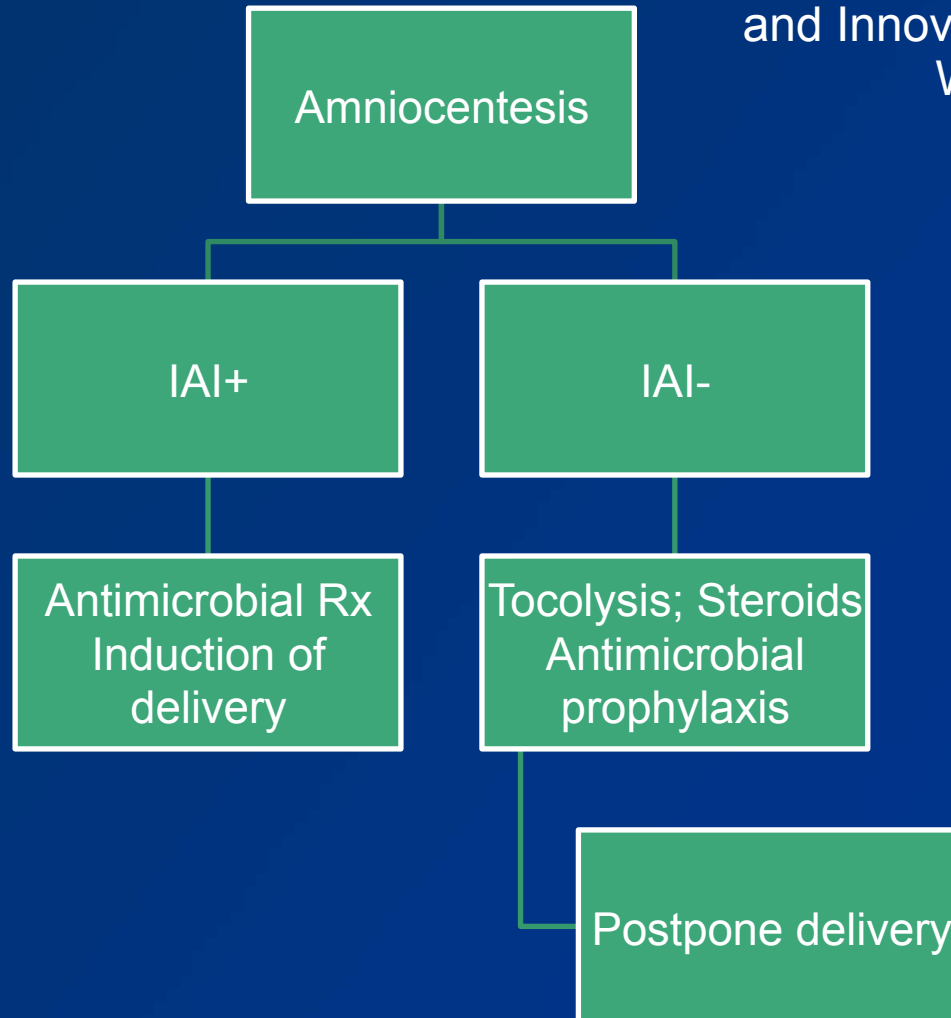
- Amniocentesis in early diagnosis of intra-amniotic infection
- Evaluation of new biomarkers
- Development of a bedside point-of-care test (SalWe)



Subclinical IAI

SalWe Ltd.

SalWe Ltd. is a Strategic
Centre for Science, Technology
and Innovation in Health and
Well-being.

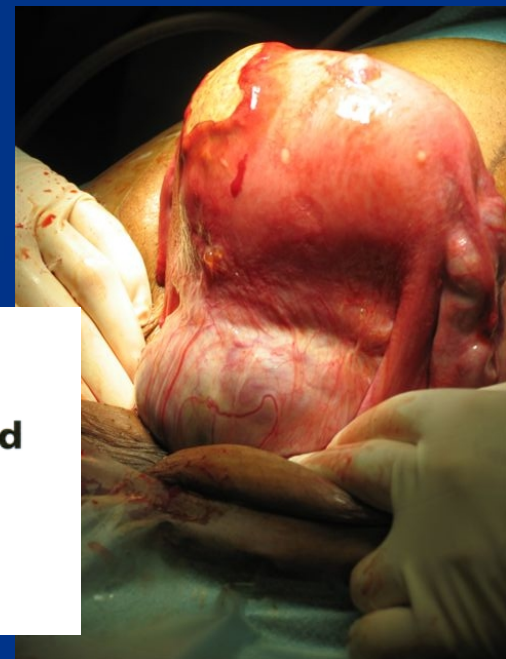
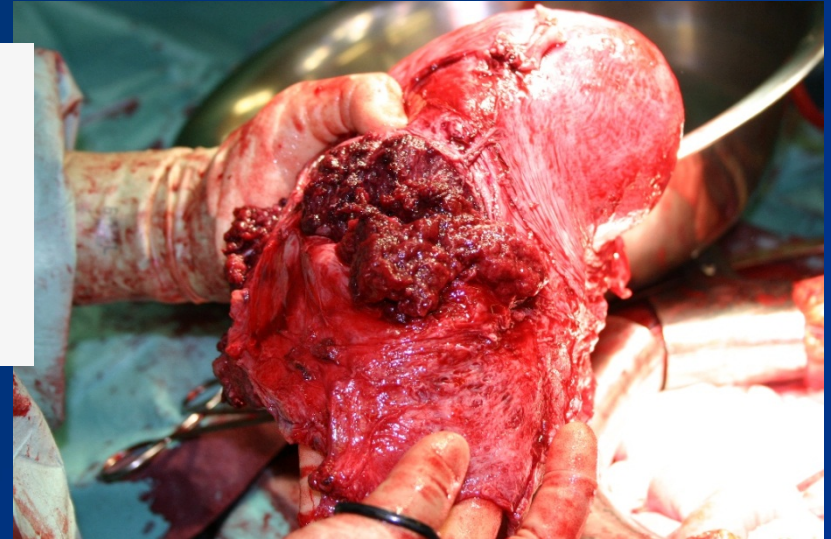
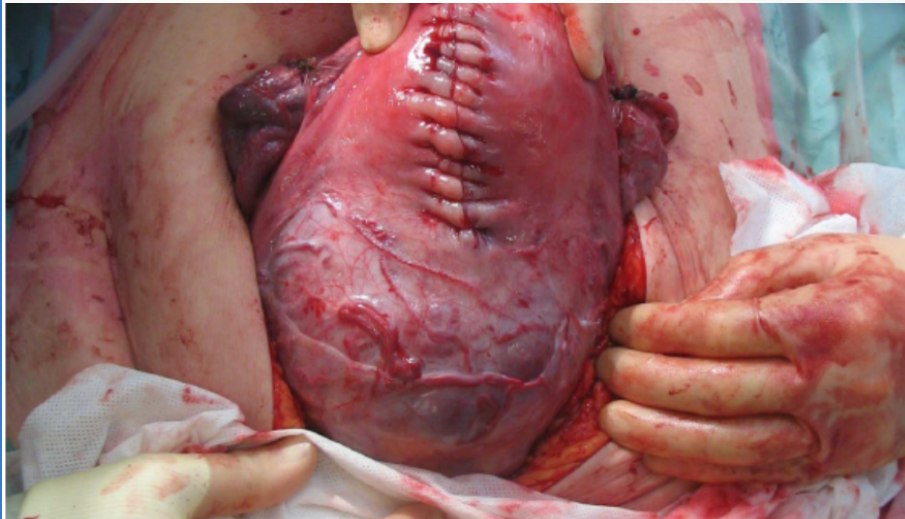


Abnormally Invasive Placenta (AIP)



EW-AIP

European Working group on Abnormally Invasive Placenta

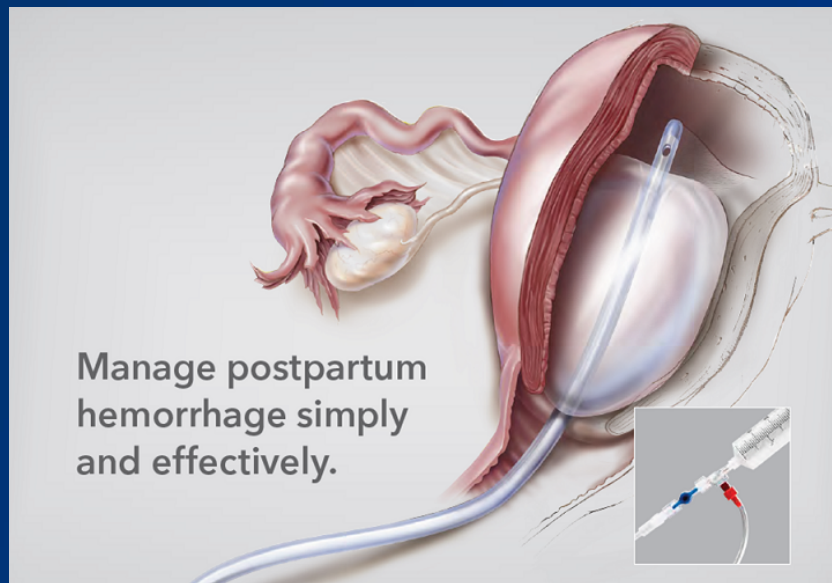


MAIN RESEARCH ARTICLE

Antenatal diagnosis of placenta accreta leads to reduced blood loss

MINNA TIKKANEN, JORMA PAAVONEN, MIKKO LOUKOVAARA & VEDRAN STEFANOVIC

Department of Obstetrics and Gynecology, University Central Hospital, Helsinki, Finland



AOGS MAIN RESEARCH ARTICLE

Use of Bakri balloon tamponade in the treatment of postpartum hemorrhage: a series of 50 cases from a tertiary teaching hospital

MAIJU GRÖNVALL, MINNA TIKKANEN, ERIKA TALLBERG, JORMA PAAVONEN & VEDRAN STEFANOVIC

Department of Obstetrics and Gynecology, University Central Hospital, Helsinki, Finland

86%!

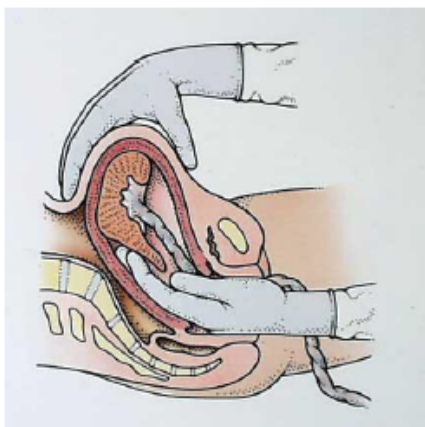
Grönvall M, et al: AOGS 2013;92:433;

Grönvall M, et al: Pelvic arterial embolisation in severe obstetric hemorrhage. A case series from a tertiary teaching hospital. AOGS (submitted)

Manual Removal of Retained Placenta

Cohort of 108 Cases at Teaching University Hospital

Mathias Thylin
Graduation Thesis, May 2010
Student number: 012849408



Supervised by Doc. Vedran Stefanovic, MD, PhD, Clinical teacher
Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Finland

Table 1. Incidence trends of retained placenta in Helsinki University Hospital^{*}.

Year	Total deliveries	Cesarean deliveries (%)	Vaginal deliveries	Retained placenta (% of all vaginal deliveries) ^{***}	Manual removal of placenta	Expulsion of placenta with sulprostone infusion
2007	5025	1329 (26.4)	3696	85 (2.29)	80	5 [*]
2008	5426	1293 (23.8)	4133	121 (2.51)	104	17
2009	5437	1253 (23.0)	4184	117 (2.79)	108	9
2010	5624	1373 (24.4)	4251	126 (2.96)	107	19

^{*}The study started in October 2007.

^{***}The increase in the incidence trend is not significant ($p = 0.086$).

AOGS MAIN RESEARCH ARTICLE

Intravenous sulprostone infusion in the treatment of retained placenta

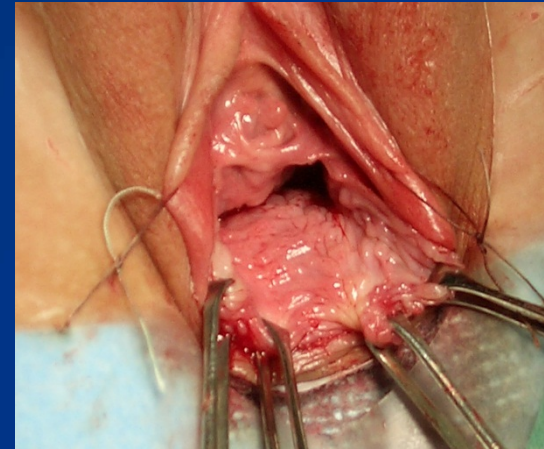
VEDRAN STEFANOVIC, JORMA PAAVONEN, MIKKO LOUKOVAARA, ERJA HALMESMÄKI,
JOUNI AHONEN & MINNA TIKKANEN

Department of Obstetrics and Gynecology, University Central Hospital, Helsinki, Finland

40%!

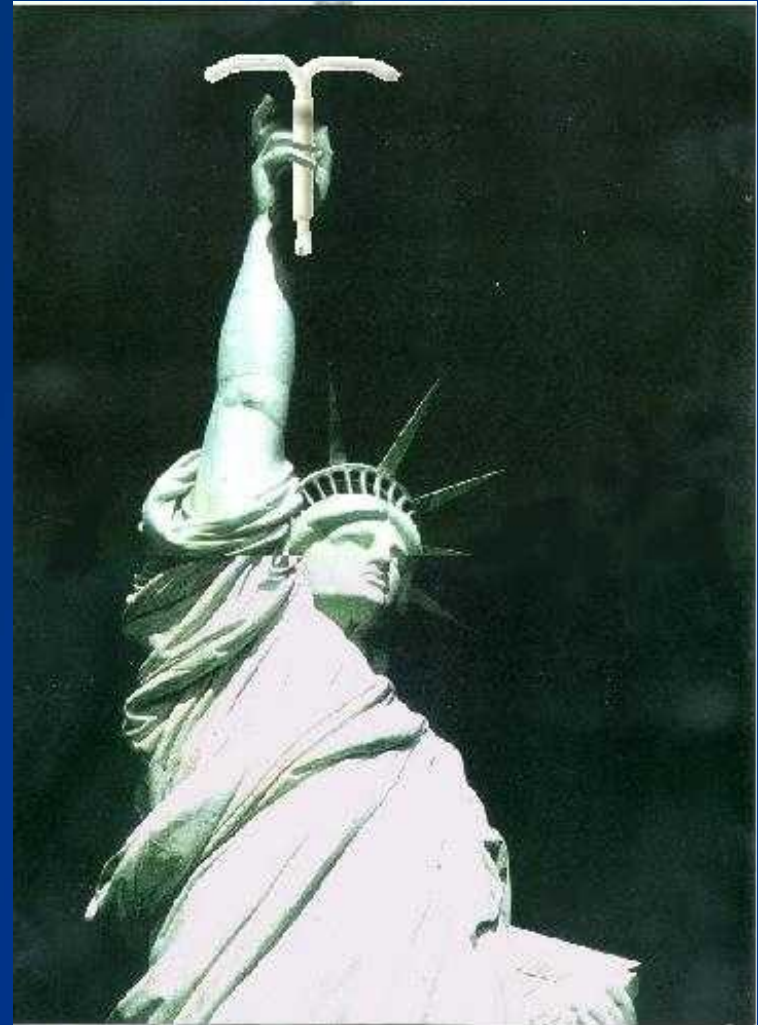
Vestibulectomy in the treatment of severe vulvar vestibulitis syndrome

- Day surgery
 - Short-term F/U
 - Long-term F/U
 - QoL
- Pragmatic management guidelines
- Tommola P: PhD Thesis program*
 - VALT; a new entity
- National and international visitors
- Site visits



Take home message

- Research, teaching, clinical practice go together
- Today's research translates into better clinical practice tomorrow!
- Increasing number of residents or acting consultants are actively doing research
- Networking is the key
- The future of clinical research is looking good!



Acknowledgements

- Dan Apter
- Sture Andersson
- Mika Gissler
- Päivi Joki-Korpela
- Maija Jakobsson
- Ritva Hurskainen
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- Seppo Meri
- Marjo Metsäranta
- Pekka Nieminen
- Mika Nuutila
- Mirja Puolakkainen
- Eero Pukkala
- Vedran Stefanovic
- Heljä-Marja Surcel
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- Lutz Gissmann
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- King K. Holmes
- Mohsin Rana
- Frank Struyf
- Heather Sings