

Exploring incidence rates of Guillain Barré (GBS), Chronic Fatigue (CFS/SEID) and Postural Orthostatic Tachycardia Syndrome (POTS) prior to HPV vaccine introduction among adolescent girls in Finland

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Disclosures

- Public health official for government
- Private practitioner at Aava
- Scientific coordination of ARIVAC consortium on phase III with PCV10; sanofi pasteur as one of members until 2010
- No personal payments from industry since 2011

National Institute for Health and Welfare



- Advices the Finnish government
- Emphasis on public health
- Collaborates in public-private partnerships with vaccine manufacturers to enhance public health



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- National vaccination program against human papillomavirus (HPV) was introduced in Finland in Nov 2013:
 - Target group: girls 11-12 years of age; catch-up 13-15 years (until 12/2015)
 - Mean coverage: 66% for the first dose (as of 4.June2016)
- Prior to introduction, strong criticism on HPV vaccine safety was spread by a small group of concerned health care professionals
- International concerns remain about safety of HPV vaccines, including GBS, CFS and POTS



As part of vaccine safety assessment, understanding baseline rates of medical conditions of interest within the target group are crucial for signal verification, comparison with rates after Immunization, and hypotheses testing

Aim of the study

Overall

Establishing the baseline rates of medical conditions of recent interest to study the safety of HPV vaccines post-introduction

Specific

Assessment of the age- and sex-specific incidence rates of GBS, CFS/SEID and POTS before HPV vaccine introduction late 2013 in Finland.

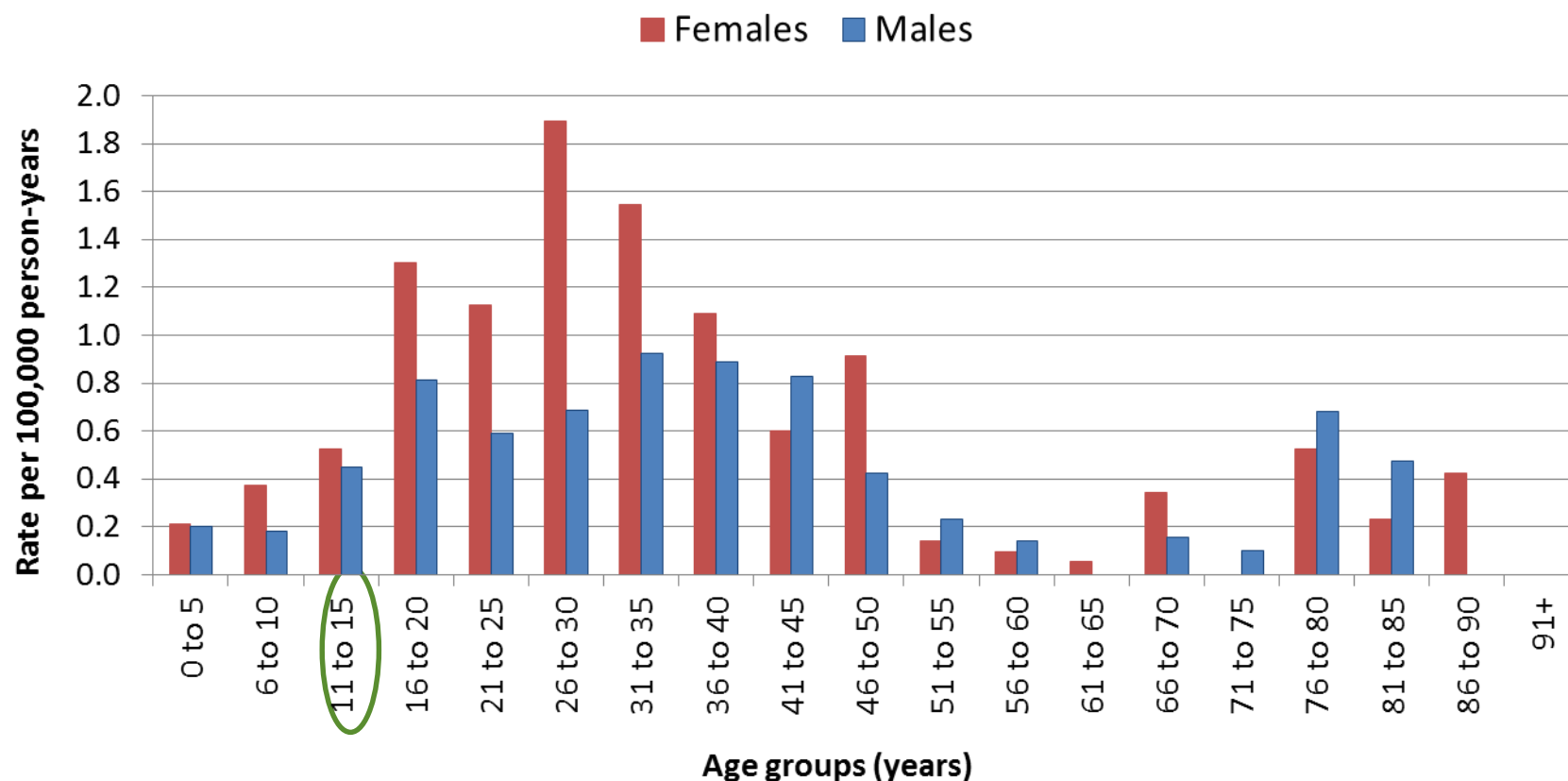
Methods

- **Design:** Register-based retrospective cohort
- **Study period:** 2002 to 2012 (-2014)
- **Population:** All population residing permanently in Finland (5,4 mi)
- **Cases** with first diagnosis of CFS/SEID, GBS, POTS registered in the Finnish National Hospital Discharge Register (HILMO) containing hospital inpatient and outpatient data
- **Special focus** on girls aged 11-15 years (age cohort appr 30 000)
- **Diagnoses classified by ICD-10 codes:**
 - CFS/SEID: G93.3
 - GBS: G61.0
 - POTS: G90.9, G90.8, G93.3, I49.8
- **Incidence rates** per 100,000 person-years with 95% confidence intervals (CI)

 **Relative increase** in incidence rate per year by Poisson regression

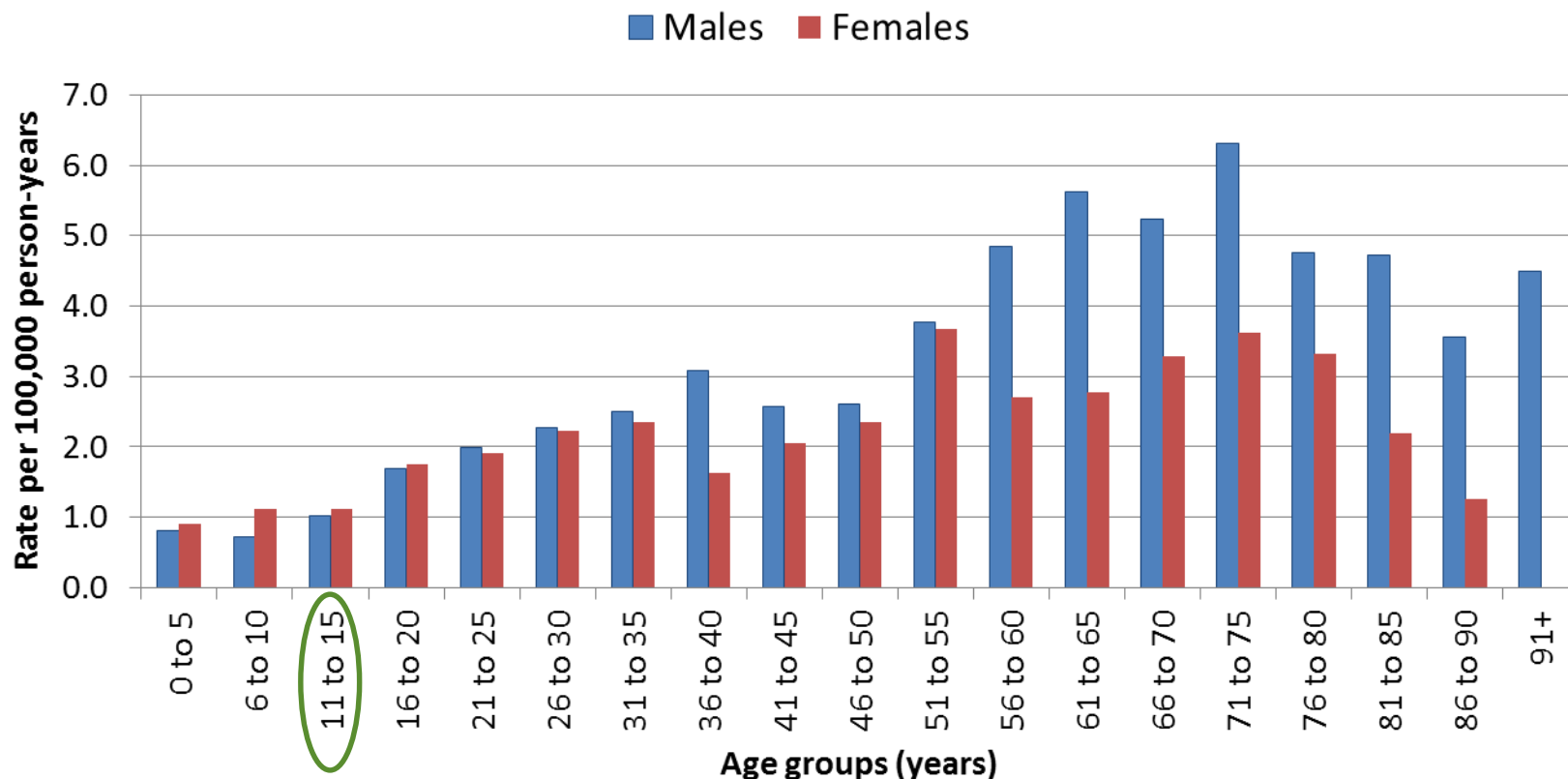
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Age-specific incidence rate of Chronic Fatigue Syndrome CFS/SEID per 100,000 person-years by age groups and sex, Finland, 2002-2012



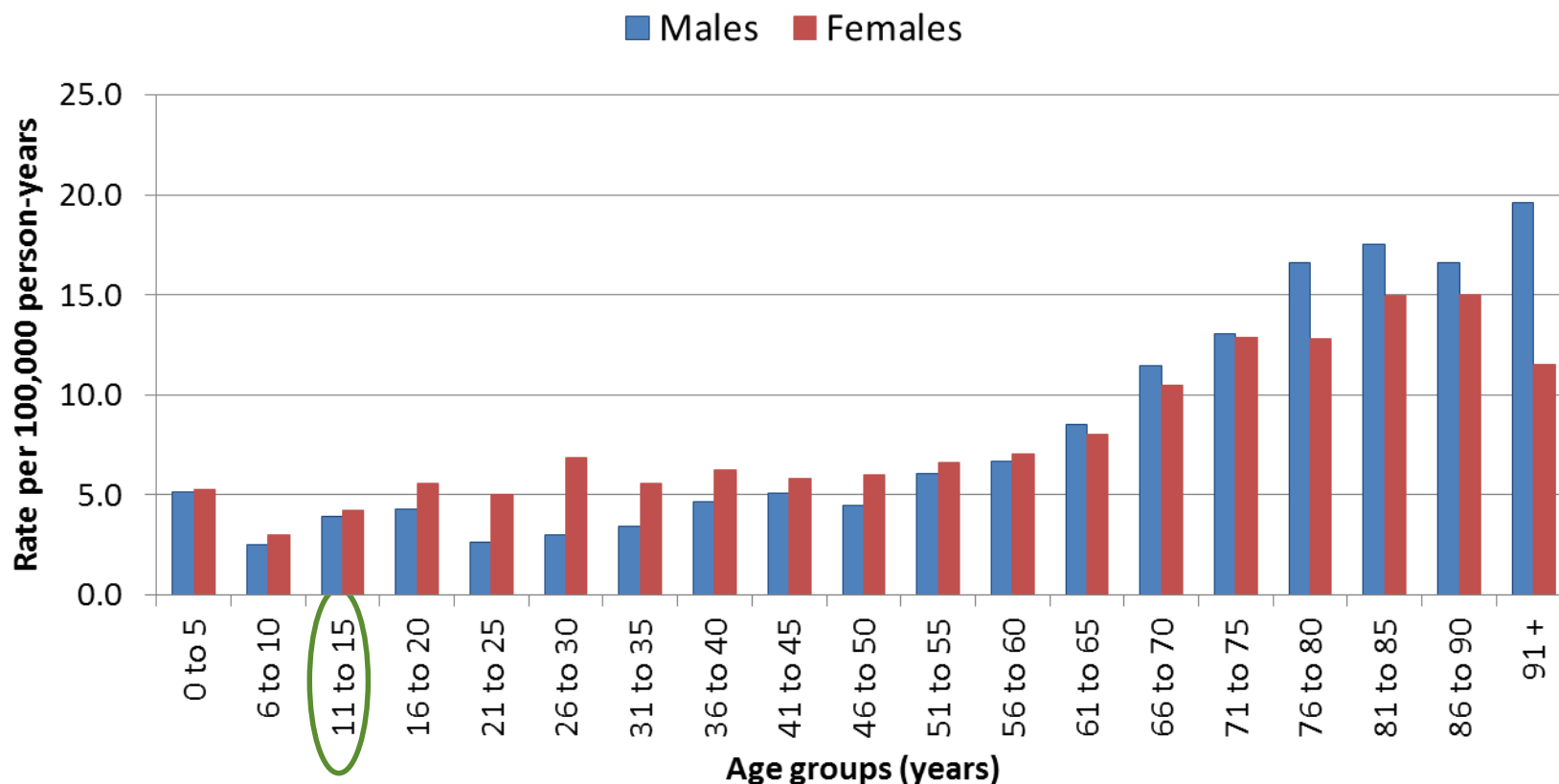
Females 11-15 years: **9 CFS cases**
Rate: 0.53 (95% CI: 0.27-1.01)

Age-specific incidence rate of Guillain Barré Syndrome GBS per 100,000 person-years by age groups and sex, Finland, 2002-2012



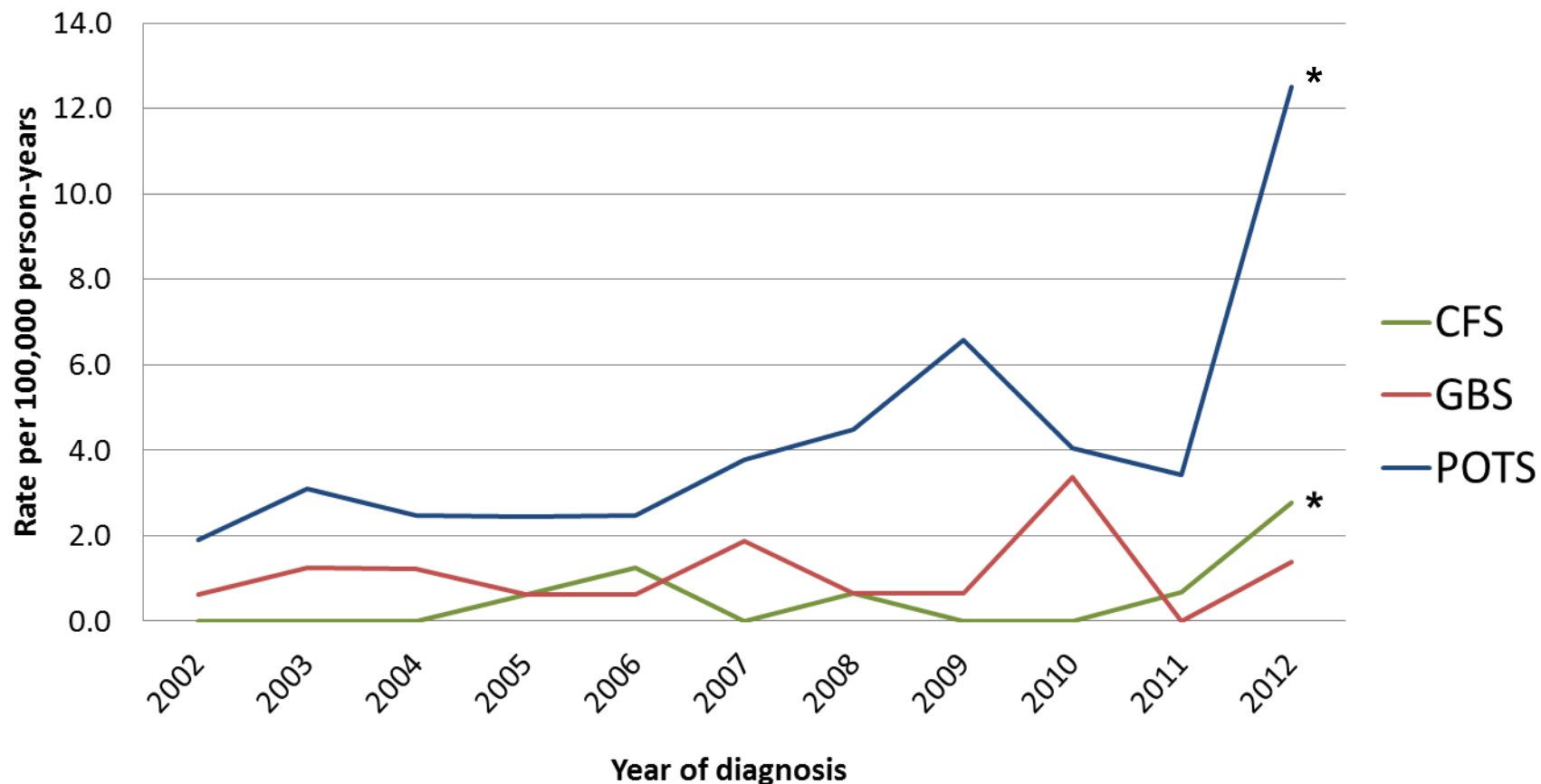
Females 11-15 years: 19 GBS cases
Rate: 1.11 (95% CI: 0.71-1.74)

Age-specific incidence rate of Postural Orthostatic Tachycardia Syndrome POTS per 100,000 person-years by age groups and sex, Finland, 2002-2012



Females 11-15 years: **72 POTS cases**
 Rate: 4.21 (95% CI: 3.34-5.30)

CFS/SEID, GBS and POTS rate per 100,000 person-years in females 11-15 years by year 2002-2012



* Significant increase

Summary

- CFS/SEID, GBS and POTS can be found in all distinct age- and sex-related diagnostic entities
- Significant increase in CFS/SEID and POTS rates over the years before HPV immunization was introduced
- No increase in GBS rates during the observation period
- Clinical case definition, and evidence based diagnostic and treatment guidelines for CFS/SEID and POTS are being formed

Limitations

- We must recognize difficulties in diagnosing and fully characterizing CFS/SEID and POTS; symptoms often overlap between POTS and CFS/SEID
- Increase in POTS and CFS/SEID rates might be true and/or partly due to multiple underlying contributing factors, such as increased awareness and trends in the preferred use of ICD-10 codes among the clinicians
- Data source HILMO (hospitalized, hospital outpatient visits in public care) is good for capturing the most serious cases; however, we may be underestimating the rates of less severe POTS and CFS/SEID cases

Conclusions

- Rates based on register data should be interpreted with caution, especially for non-specific diagnostic entities for which internationally and even nationally agreed criteria and case definitions are still being formed -> Brighton collaboration effort?
- To assess the associations with HPV vaccination, factors contributing to clinicians setting the diagnoses and using different ICD codes should be explored
- We will continue our analysis by register based linkage studies, i.e. national vaccination register vs. HILMO and PHC (AvoHILMO) register data but also
- Collaborate with the adult & child neurologist and pediatric infectious disease specialist to further understand these clinical entities and their association to HPV vaccination

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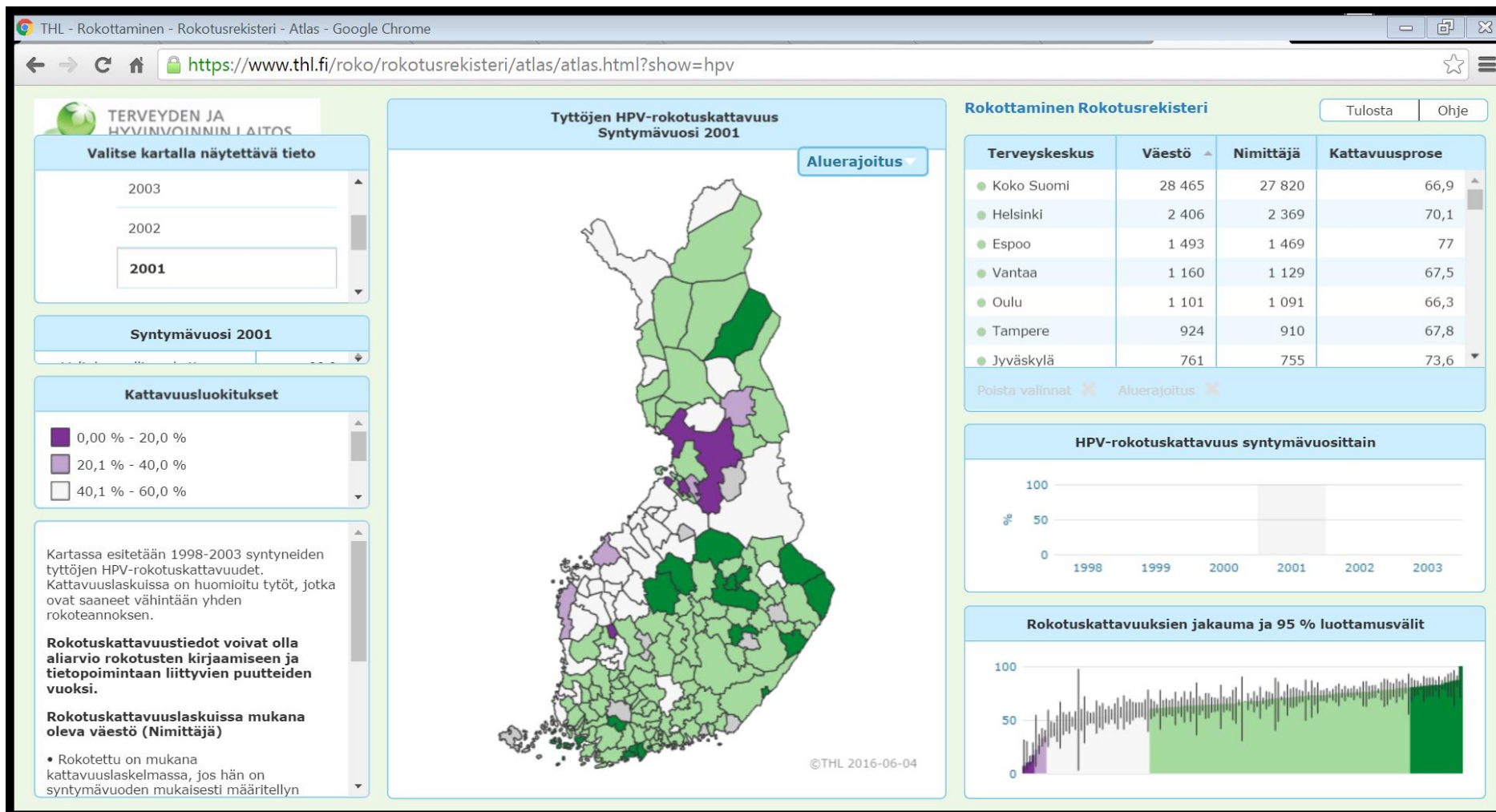
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KiiToS!



Mean coverage HPV I dose 66% - large geographic variations



HPV coverage by dose and birth cohort in Helsinki vs. Finland

