



# ISSUES RELATED TO HPV VACCINE ACCEPTANCE: LESSONS FROM THE DANISH HPV VACCINE EXPERIENCE

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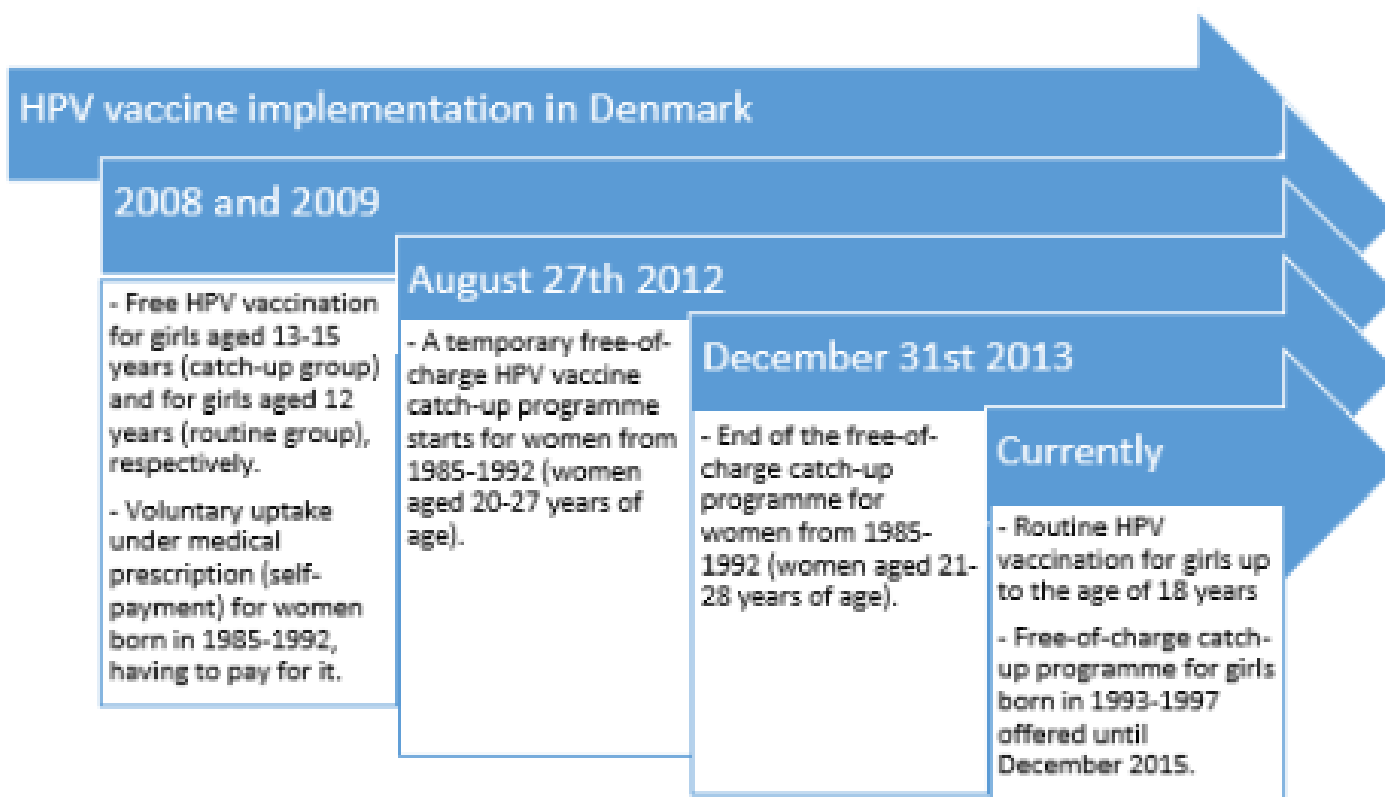
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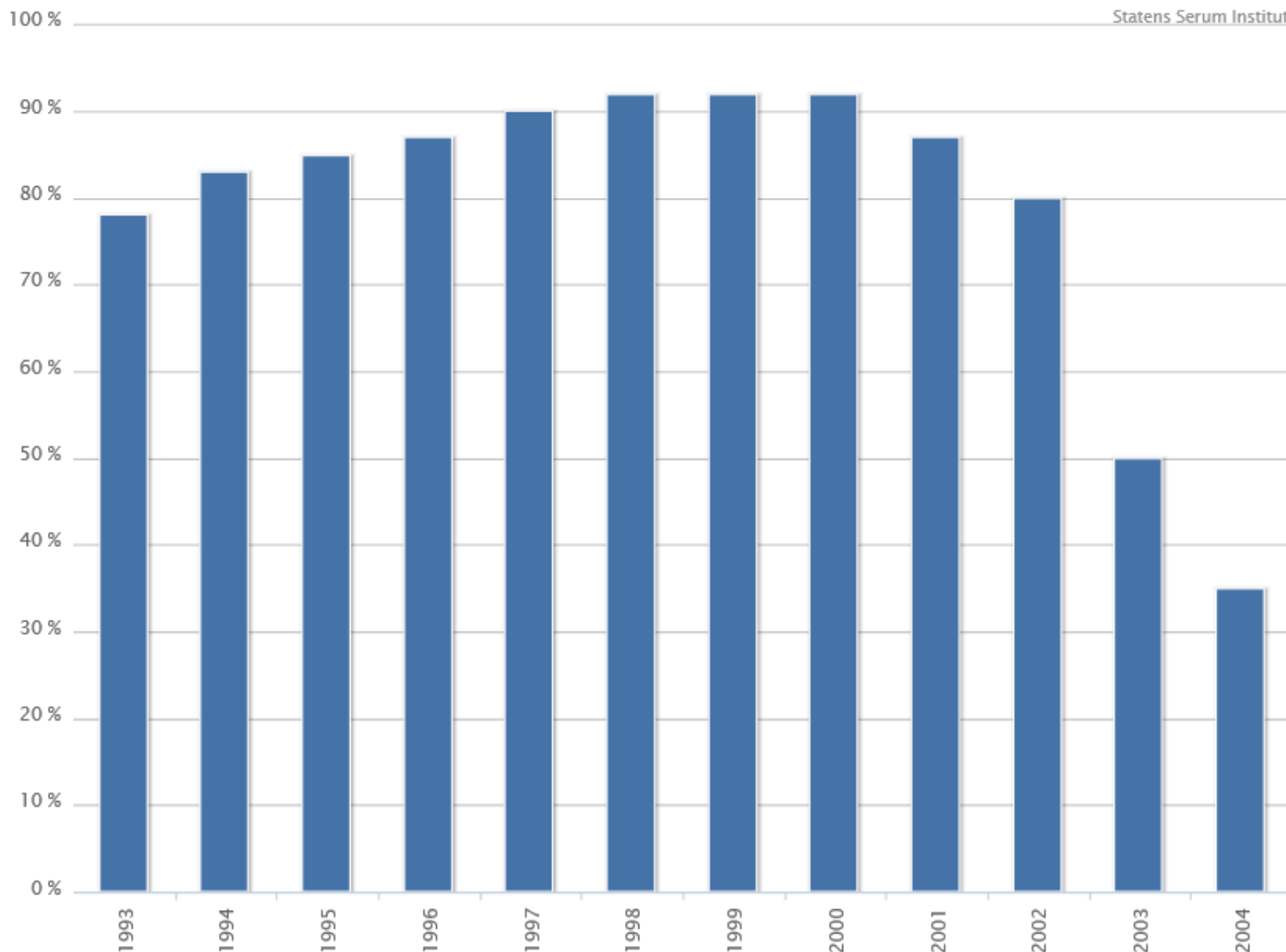
**BUILDING TRUST, MANAGING RISK: VACCINE CONFIDENCE AND  
HUMAN PAPILLOMAVIRUS VACCINATION**

**7-8 June 2017 - LSHTM, London**



# HPV VACCINE UPTAKE OF FIRST DOSE BY BIRTH COHORT

Statens Serum Institut



## TIMELINE

**Summer 2013:** Report of seven cases of POTS to Danish

Medicines Agency (DMA), A signal is raised with EMA

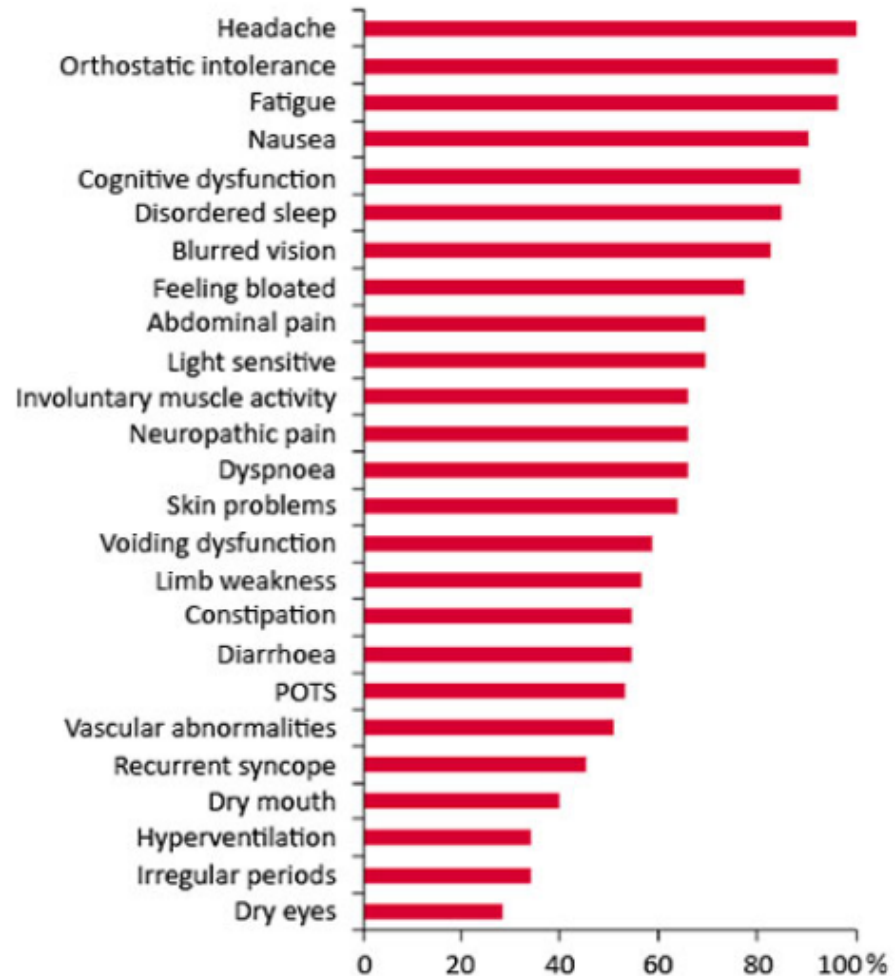
**December 2014:** EMA concludes that a causal relationship between Gardasil and POTS could neither be confirmed nor rejected.

**February 2015:** Case series consisting of 53 persons referred to the syncope unit in Copenhagen was published

**March 2015:** participates in "The vaccinated girls" – a TV documentary. Recommends a suspension of the programme and notes that especially physically active girls are at risk.

**June 2015:** Clinics in the five Danish Regions where girls who suspects HPV side effects can be referred to are established

Symptoms suspected to be side effects to vaccination against human papilloma virus. The frequency of the symptoms is given as percentages of patients reporting the given symptom out of all patients included in the descriptive analysis.



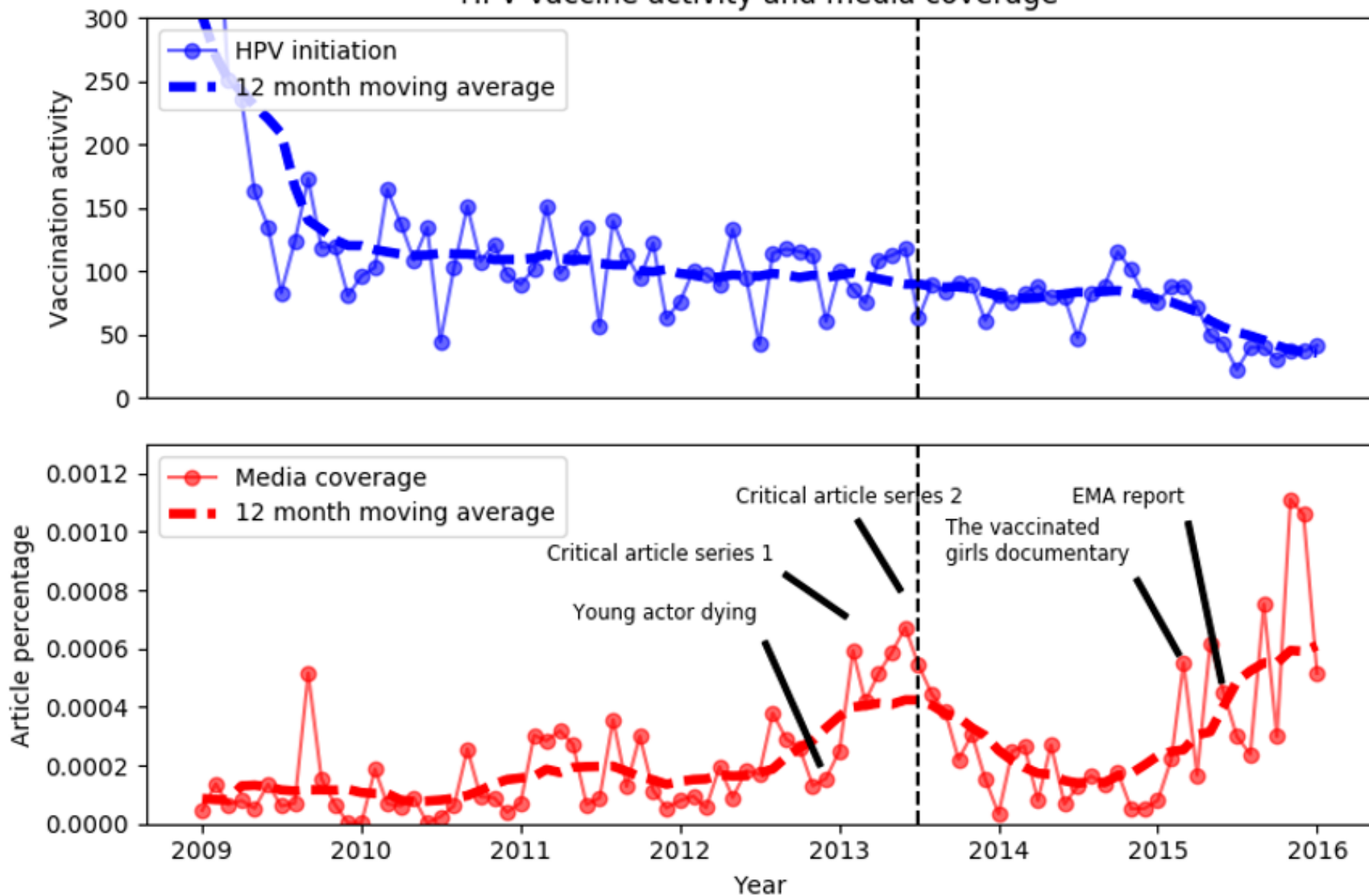
POTS = postural orthostatic tachycardia syndrome.

*Reporting of adverse events: Stimulated by the programme “The Vaccinated Girls” broadcasted 26 March 2015, by TV2*

Features interviews with families and vaccinated girls with medically unexplained symptoms .



## HPV vaccine activity and media coverage



# ADVERSE EVENT REPORTS RECEIVED PER YEAR IN DK

An adverse event report is received for 0,4% of the vaccinated (4 per 1000)

In 2016, only 17 non-serious reports related to vaccinations done in 2016 were received.

	2009	2010	2011	2012	2013	2014	2015	2016	Total
<b>Total reports</b>	288	66	43	96	511	224	822	307	<b>2326</b>
<b>Serious reports *</b>	25	5	6	18	177	91	475	182	<b>1005</b>

*\* Seriousness defined according to ICH and EMA criteria: Results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.*

16.06.2017



## TIMELINE CONTINUED

**July 2015:** DMA makes a referral to EMA/PRAC

regarding POTS and CRPS

**November 2015:** EMA concludes that these conditions are not more common in vaccinated compared to unvaccinated. Head of Parliament health committee response to the EMA-report: The doctors in the committee have connections to the industry and can't be trusted. The programme should be stopped. She believes that the HPV vaccines causes the reported adverse reactions.

**December 2015:** Public hearing in the Danish Parliament.

**June 2016:** 1 million Euro for research projects investigating the alleged side effects: More than half of the these funds were awarded to the syncope unit.

# Pre-Vaccination Care-Seeking in Females Reporting Severe Adverse Reactions to HPV Vaccine. A Registry Based Case-Control Study

Kåre Mølbak<sup>1\*</sup>, Niels Dalum Hansen<sup>2,3</sup>, Palle Valentiner-Branth<sup>1</sup>

## Results

The study included 316 cases who received first HPV vaccine between 2006 and 2014. Age range of cases was 11 to 52 years, with a peak at 12 years, corresponding to the recommended age at vaccination, and another peak at 19 to 28 years, corresponding to a catch-up programme targeting young women. Compared with 163,910 controls, cases had increased care-seeking in the two years before receiving the first HPV vaccine. A multivariable model showed higher use of telephone/email consultations (OR 1.9; 95% CI 1.2–3.2), physiotherapy (OR 2.1; 95% CI 1.6–2.8) and psychologist/psychiatrist (OR 1.9; 95% CI 1.3–2.7). Cases were more likely to have a diagnosis in the ICD-10 chapters of diseases of the digestive system (OR 1.6; 95% CI 1.0–2.4), of the musculoskeletal system (OR 1.6; 95% CI 1.1–2.2), symptoms or signs not classified elsewhere (OR 1.8; 95% CI 1.3–2.5) as well as injuries (OR 1.5; 95% CI 1.2–1.9).

## Conclusion

Before receiving the first HPV vaccination, females who suspected adverse reactions has symptoms and a health care-seeking pattern that is different from the matched population. Pre-vaccination morbidity should be taken into account in the evaluation of vaccine safety signals.

September  
2016

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## Baseline for immune mediated adverse events and cohort study among vaccinated and unvaccinated



Vaccine

Volume 27, Issue 22, 14 May 2009, Pages 2954–2958



BMJ

BMJ 2013;347:f5906 doi: 10.1136/bmj.f5906 (Published 9 October 2013)

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### Human papillomavirus immunisation of adolescent girls and anticipated reporting of immune-mediated adverse events

Torbjörn Callréus<sup>a</sup>, Henrik Svanström<sup>b</sup>, Nete Munk Nielsen<sup>b</sup>, Sigrid Poulsen<sup>c</sup>, Palle Valentiner-Branth<sup>d</sup>, Anders Hviid<sup>b</sup>  

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<http://doi.org/10.1016/j.vaccine.2009.02.106>


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#### Abstract

Determining incidence rates of potential adverse events before and after an immunisation programme is initiated, provides a useful framework for the evaluation of vaccine safety concerns. Human papillomavirus vaccination (HPV) of adolescent girls has recently been introduced in Denmark. Using a nationwide hospitalisation registry we estimated incidence rates of immune-mediated disorders before HPV vaccination in a cohort of 418,289 Danish girls aged 12–15 years. We further estimated the expected number of cases of immune-mediated disorders occurring in temporal relationship to a hypothetical HPV vaccination schedule purely by chance. Our results and analytical approach provides a framework for the evaluation of adverse event reports following immunisation of adolescent girls.

### RESEARCH

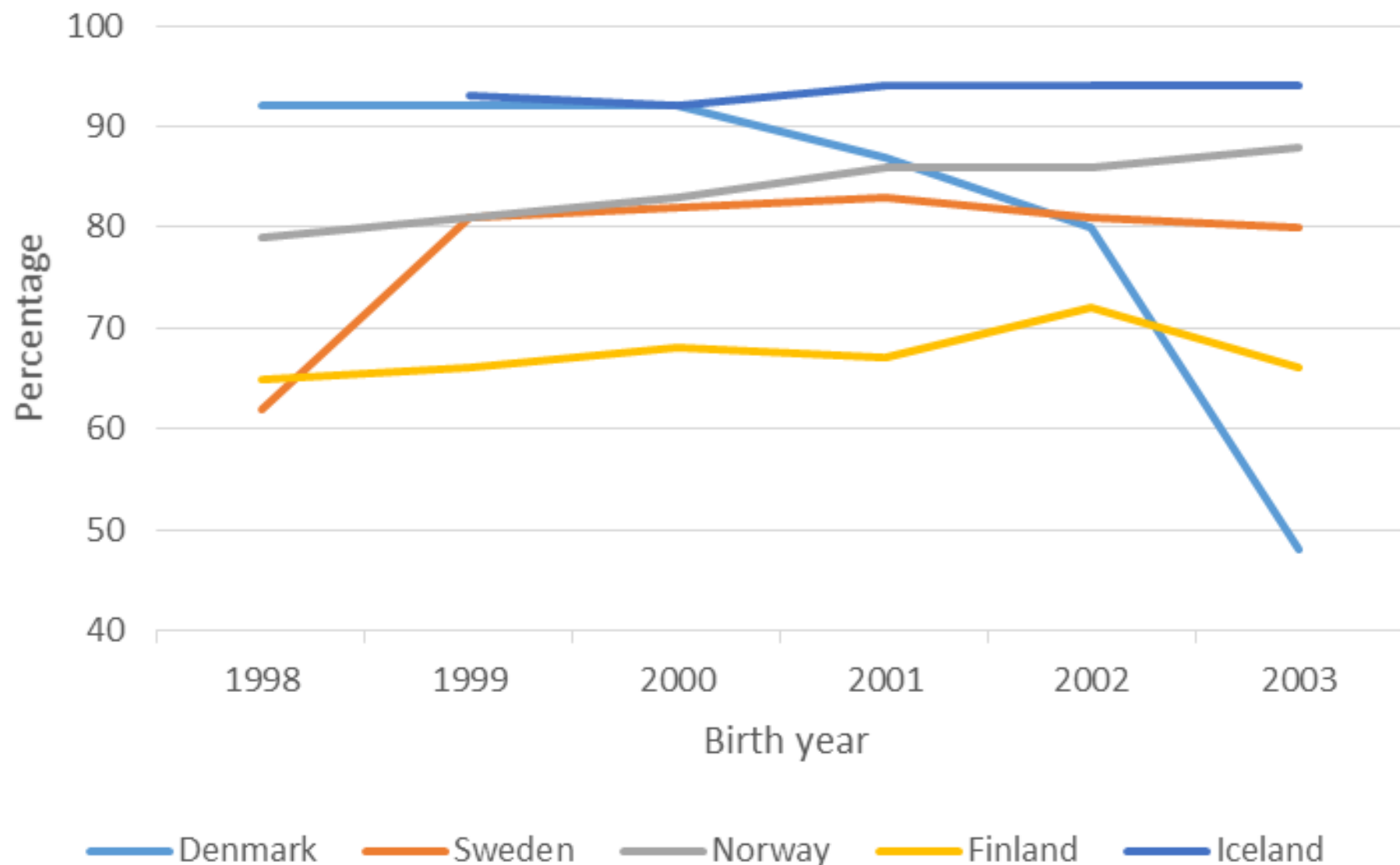
### Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study

 OPEN ACCESS

Lisen Arnheim-Dahlström *associate professor*<sup>1</sup>, Björn Pasternak *postdoctoral fellow*<sup>2</sup>, Henrik Svanström *statistician*<sup>2</sup>, Pär Sparén *professor*<sup>1</sup>, Anders Hviid *senior investigator*<sup>2</sup>

**Conclusions** This large cohort study found no evidence supporting associations between exposure to qHPV vaccine and autoimmune, neurological, and venous thromboembolic adverse events. Although associations for three autoimmune events were initially observed, on further assessment these were weak and not temporally related to vaccine exposure. Furthermore, the findings need to be interpreted considering the multiple outcomes assessed.

# TRENDS OF HPV VACCINE UPTAKE OF FIRST DOSE BY BIRTH COHORT IN THE NORDIC COUNTRIES BY END 2016





- ❖ The signal consisted mainly of medically unexplained physical symptoms in vaccinated girls
- ❖ No evidence from analytical studies
  - No studies have demonstrated an increased risk among vaccinated girls compared with unvaccinated

- ❖ Difficult to analyse in epidemiological studies
  - CFS/ME and POTS are ill-defined conditions

- ❖ Reporting has been stimulated by media attention, social media and "infostorms"

Data from passive adverse events surveillance are biased

- ❖ Females with suspected adverse reactions has symptoms and a health-care seeking pattern that is different from a matched population. Pre-vaccination morbidity should be taken into account in the evaluation of vaccine safety signals

- ❖ Next steps planned:

A large part of the target population, i.e. mothers of the 12 year old girls are hesitant regarding HPV vaccination. They are affected by histories of adverse events and news media. Many gets all information from social media where the authorities are not very active

Information campaign led by Danish Health Authority is now launched

# Ny informationsindsats om forebyggelse af livmoderhalskræft og HPV-vaccination

Sundhedsstyrelsen står sammen med Kræftens Bekæmpelse og Lægeforeningen bag en informationsindsats, der skal levere information til borgere og sundhedsprofessionelle om forebyggelse af livmoderhalskræft og HPV-vaccination.

## Vi bakker op om HPV-vaccination:



STATENS  
SERUM  
INSTITUT



LÆGEMIDDELSTYRELSEN  
DANISH MEDICINES AGENCY

DANSKE  
REGIONER

LÆGE  
VIDENSKABELIGE  
SELSKABER



PRAKTISERENDE  
LÆGERS  
ORGANISATION



Dansk Selskab for Kønssygdomme  
DSKO

Dansk Pædiatrisk Selskab  
Danish Paediatric Society



Fagligt Selskab for  
Sundhedsplejersker



SEX  
SAMFUND

KIU  
Kræft i underlivet



PRAKTISERENDE GYNÆKOLOGER  
DSG - DANISH SOCIETY OF GYNÆCOLOGICAL SPECIALISTS

dsam  
Dansk Selskab for Almen Medicin

Duration two years, facebook, youtube, short movies, homepage, information material to GP's. HPV vaccination is supported by a broad group of health persons and patient groups



# THANK YOU TO

✿ SWEDEN (TIIA LEPP)

✿ NORWAY (LILL TROGSTAD)

✿ FINLAND (HANNA NOHYNEK)

✿ ICELAND (THOROLFUR GUDNASSON)

