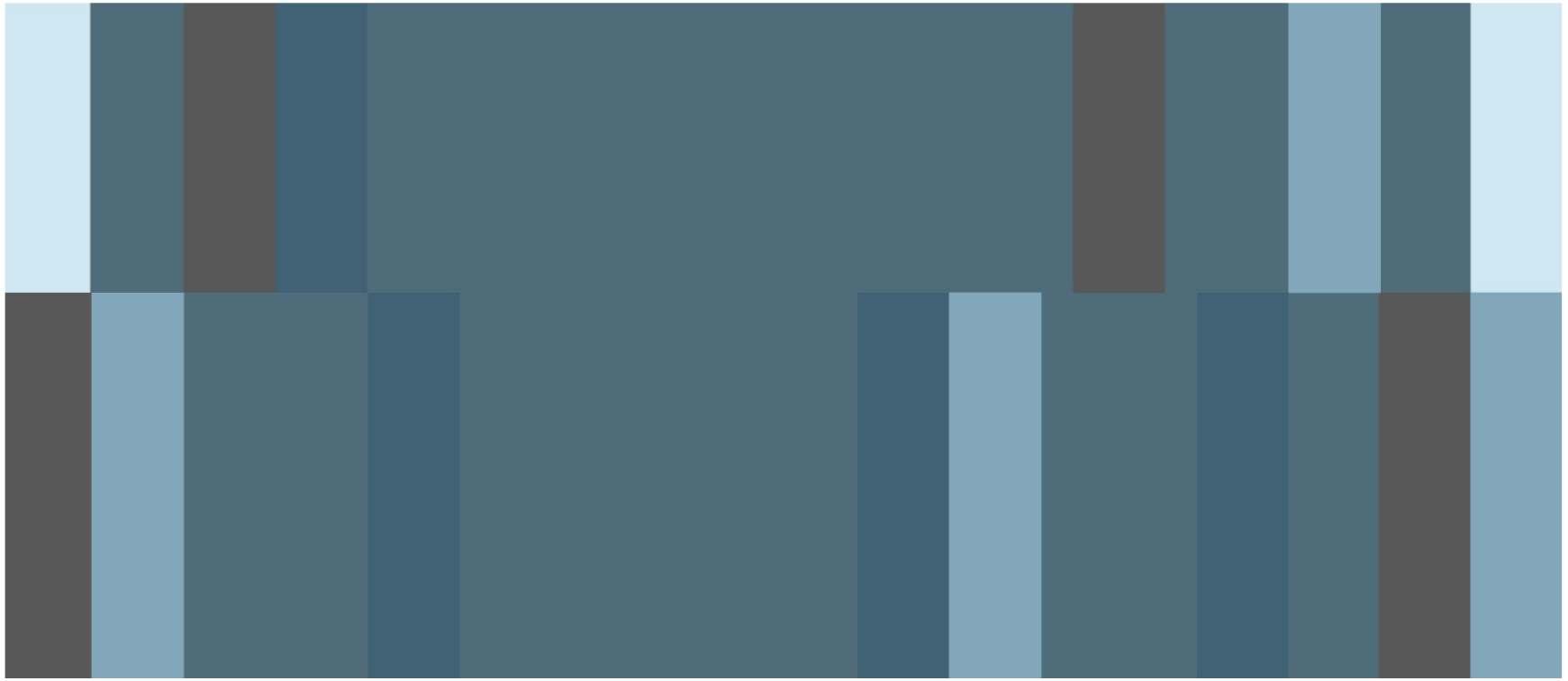

Børnevaccinationer

Søren Brostrøm
Enhedschef, overlæge, ph.d., MPA

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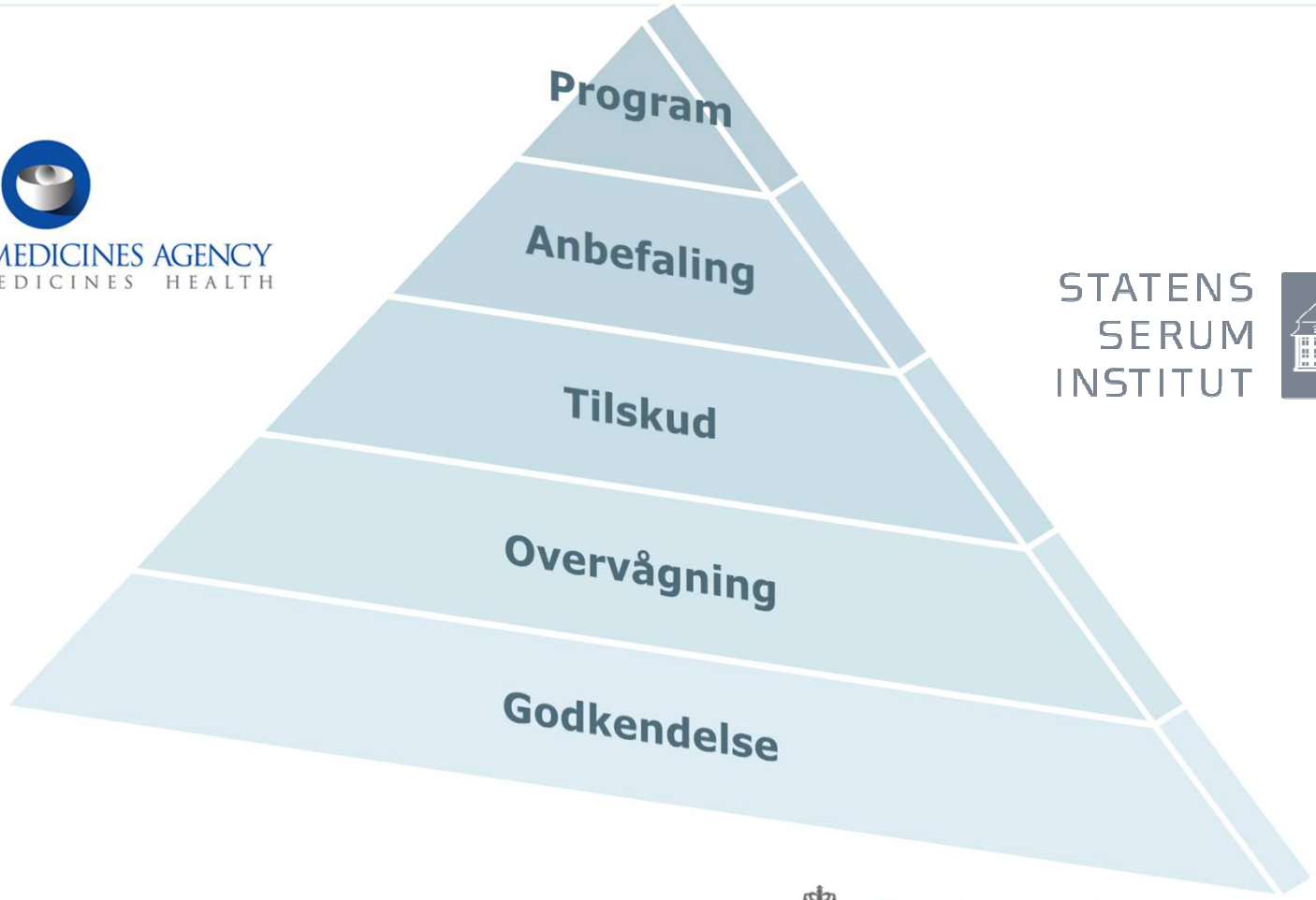
Danish Health and Medicines Authority

Sundhedsstyrelsens rolle



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STATENS SERUM INSTITUT

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Godkendelse

Oftest central procedure

- Europæiske Lægemiddelagentur (EMA)
- Lande på skift ansvarlig for faglig vurdering

Eksempel: Gardasil® 9

- Kliniske undersøgelser igangsat 2007
- 7 studier, 11 lande, > 15.000 personer
- 2008 + 2011: EMA 'scientific advice' til producent
- Marts 2015: positiv vurdering fra EMAs eksperter (CHMP)
- Afventer EU Kommissionen

Sundhedsstyrelsen
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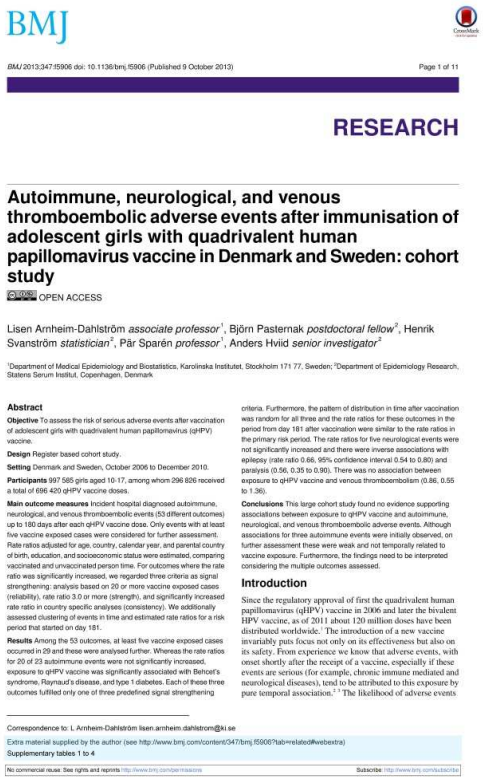
Overvågning - bivirkninger

Sundhedsstyrelsen

- Indberetning: læger, patienter, virksomheder m.v.
- Første 2 år: alle formodede bivirkninger
- Daglig gennemgang af alvorlige bivirkninger
- EMA underrettes, fælles database
- EUs bivirkningskomité (PRAC)
- Vaccinationspanel
- Balance fordele/ulemper
- Produktresumé og indlægsseddel
- Information ('Nyt om Bivirkninger' m.v.)

Faglige miljøer

- Forskning



BMJ

BMJ 2013;347:f5906 doi: 10.1136/bmj.f5906 (Published 9 October 2013) Page 1 of 11

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

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Abstract

Objective To assess the risk of serious adverse events after vaccination of adolescent girls with quadrivalent human papillomavirus (qHPV) vaccine.

Design Register based cohort study.

Setting Denmark and Sweden, October 2006 to December 2010.

Participants 997 585 girls aged 10-17, among whom 296 826 received a total of 696 420 qHPV vaccine doses.

Main outcome measures Incident hospital diagnosed autoimmune, neurological, and venous thromboembolic events (53 different outcomes) up to 180 days after each qHPV vaccine dose. Only events with at least five vaccine exposed cases were considered for further assessment. Rate ratios adjusted for age, country, calendar year, and parental country of birth, education, and socioeconomic status were estimated, comparing vaccinated and unvaccinated person time. For outcomes where the rate ratio was significantly increased, we regarded three criteria as signal strengthening: analysis based on 20 or more vaccine exposed cases (reliability), rate ratio 3.0 or more (strength), and significantly increased rate ratio in country specific analyses (consistency). We additionally assessed clustering of events in time and estimated rate ratios for a risk period that started on day 181.

Results Among the 53 outcomes, at least five vaccine exposed cases occurred in 29 and these were analysed further. Whereas the rate ratios for 20 of 23 autoimmune events were not significantly increased, exposure to qHPV vaccine was significantly associated with Behcet's syndrome, Raynaud's disease, and type 1 diabetes. Each of these three outcomes fulfilled only one of three predefined signal strengthening criteria. Furthermore, the pattern of distribution in time after vaccination was random for all three and the rate ratios for these outcomes in the period from day 181 after vaccination were similar to the rate ratios in the primary risk period. The rate ratios for five neurological events were not significantly increased and there were inverse associations with epilepsy (rate ratio 0.66, 95% confidence interval 0.54 to 0.80) and paralysis (0.56, 0.35 to 0.90). There was no association between exposure to qHPV vaccine and venous thromboembolism (0.86, 0.55 to 1.36).

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.

Introduction

Since the regulatory approval of first the quadrivalent human papillomavirus (qHPV) vaccine in 2006 and later the bivalent HPV vaccine, as of 2011 about 120 million doses have been distributed worldwide.[1] The introduction of a new vaccine invariably puts focus not only on its effectiveness but also on its safety. From experience we know that adverse events, with onset shortly after the receipt of a vaccine, especially if these events are serious (for example, chronic immune mediated and neurological diseases), tend to be attributed to this exposure by pure temporal association.[2 3] The likelihood of adverse events

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Supplementary tables 1 to 4

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Sundhedsstyrelsen

Danish Health and Medicines Authority

Overvågning – tilslutning og effekt

Ydelseskoder (gratis vacciner)

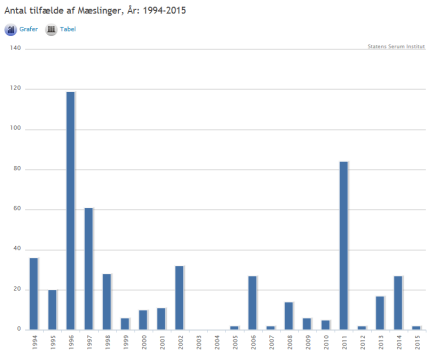
Det Danske Vaccinationsregister

Meldesystemet (epidemiloven)

Landspatientregisteret

Kvalitetsdatabaser (livmoderhalskræft)

Videnskabelige undersøgelser



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Børnevaccinationsprogrammet

Hyppige + alvorlige + epidemier = kopper, polio, mæslinger m.v.
Ingen behandling = dødelighed og senfølger
Flokimmunitet
Global eliminering

1993: *Hæmophilus influenzae* grp. B (HiB)
    Alvorlig sygdom, men ej epidemisk
    120/år invasiv infektion (80 HiB-meningitis)
2007: Pneumokok
2008: HPV til piger

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Kriterier

Alvorlighed og hyppighed

Erfaring fra store børnepopulationer

Gavnlige virkninger overstiger potentielle skadevirkninger

Etik: intervention ift. raske børn

Forældres accept, indpasning i program

Interaktioner og økologiske effekter

Samfundsøkonomi

Sundhedsstyrelsen
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HPV

Cervarix® og Gardasil®

7 store lodtrækningsforsøg

> 40.000 personer

Beskyttelse mod svære celleforandringer

Globalt 55 mio vaccinerede

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Hepatitis B

WHO 1997

- Anbefaling

SST 2005

- Akut HBV faldet fra 250 til 40
- Bærertilstand fra 0,15% til 0,03%.
- Risikogrupper: narkomaner, MSM, indvandrere, børn af do.
- Effektiv risikostrategi
- Genindføre screening af gravide

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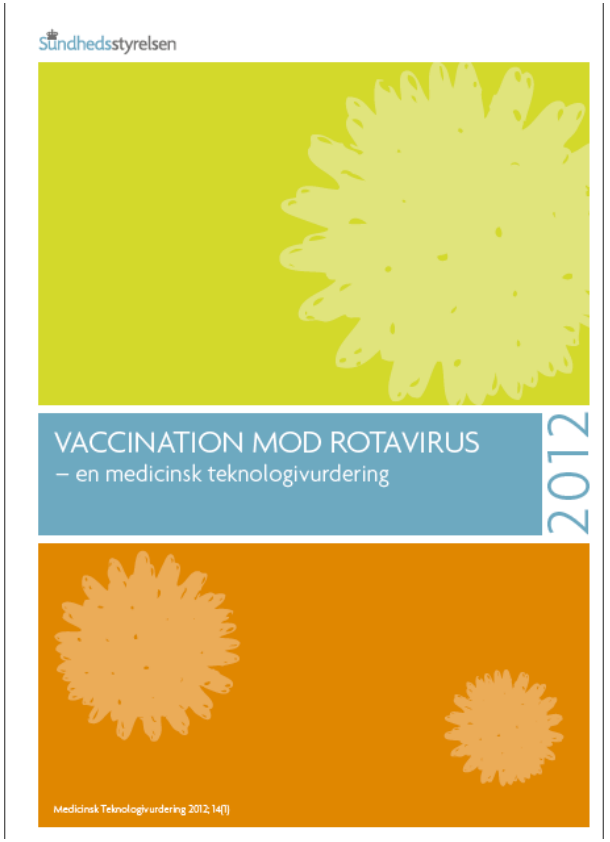
Rotavirus

WHO 2007

- Anbefaling for Europa

SST 2012

- Ingen dødelighed
- 30.000 diaré, 9.000 lægebesøg og 1.100 indlæggelser
- Samfundsøkonomi: forældres fravær
- Fokus på risikogrupper



Sundhedsstyrelsen
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Udfordringer

Tilslutning

Bivirkninger

Forsyningssikkerhed

Nye vacciner, nye indikationer

Nye sygdomme

Justering af programmer

Sundhedsstyrelsen
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