

Formidlingsmøde om forskning i mulige bivirkninger ved HPV-vaccinen

Onsdag d. 11. december 2019 kl. 15-17 i Lægemiddelstyrelsen



Program

Kl. 15:00 Velkomst og kort oprids af proceduren for tildeling af puljemidler samt kort beskrivelse af de udvalgte projekter

Ved Ib Valsborg, formand for følgegruppen og tidligere departementschef i Sundhedsministeriet.

Præsentation af forskningsresultaterne ved de tre forskere som modtog satspuljemidler med spørgsmål fra salen efter hver præsentation:

Kl. 15:15 • Reimar Thomsen, overlæge, lektor, ph.d., Aarhus Universitetshospital

Kl. 15:45 • Jesper Mehlsen, speciallæge samt seniorforsker, Rigshospitalet

Kl. 16.15 • Anders Hviid, seniorforsker, Statens Serum Institut

Kl. 16:45 Afrunding

Ved Pierre Quartarolo, Chef i Lægemiddelstyrelsens enhed for Lægemiddelovervågning & Medicinsk Udstyr

Følg os



Satspuljeforskning: Er der øget risiko for kontakt til skadestuer, hospitalsambulatorier eller indlæggelser med forskellige symptomer blandt HPV-vaccinerede piger?

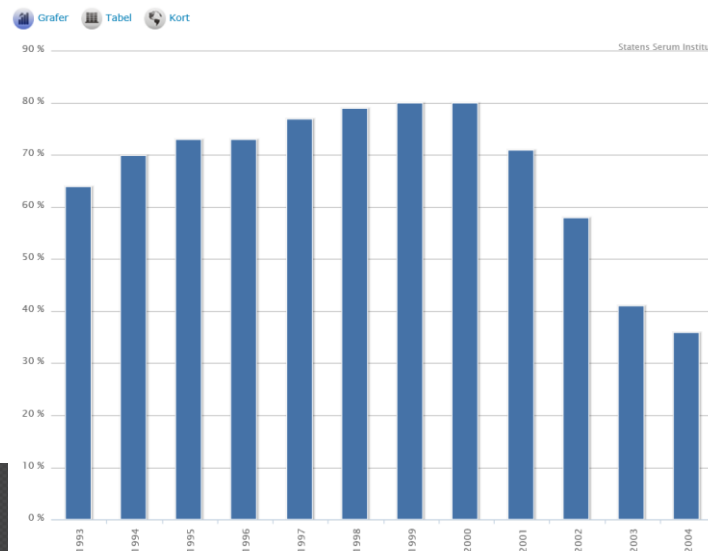
Reimar W. Thomsen, overlæge, lektor, ph.d.
Klinisk Epidemiologisk Afdeling
Aarhus Universitetshospital & Aarhus Universitet



Baggrund: HPV vaccinen og mistanken om bivirkninger

- HPV vaccination blev introduceret i børnevaccinations-programmet i 2009
- Beskytter mod HPV infektion i livmoderhalsen, som kan medføre kræft¹
- Fra 2013 tiltagende fokus på mulige bivirkninger blandt HPV vaccinerede piger: hovedpine, svimmelhed, træthed, kredsløbs-symptomer, CFS og POTS lignede symptomer²
- Kraftigt fald i vaccinations-tilslutning fra 2014³

Andel vaccineret med Human papillomavirus-vaccine (HPV) færdigvaccineret, Fødselsår: 1993-2004, Køn: Kvinder



¹Drolet et al, Lancet 2019; 394(10197): 497-509;
Palmer et al, BMJ 2019; 365: l1161.

²Brinth et al, Dan Med J 2015; 62(4): A5064;
Jefferson et al, Indian J Med Ethics 2017; 2(1): 30-37.

³Amdisen et al, Vaccine 2018; 36(38): 5747-5753.

Baggrund: HPV vaccinen og mistanken om bivirkninger

- Systematisk gennemgang af eksisterende studier har *ikke* fundet nogen sammenhæng mellem HPV vaccination og alvorlige bivirkninger: HPV vaccinen ser ud til at være *meget sikker*¹
- Mange tidligere studier har dog primært set på *specifikke*, veldefinerede diagnoser efter HPV vaccination²



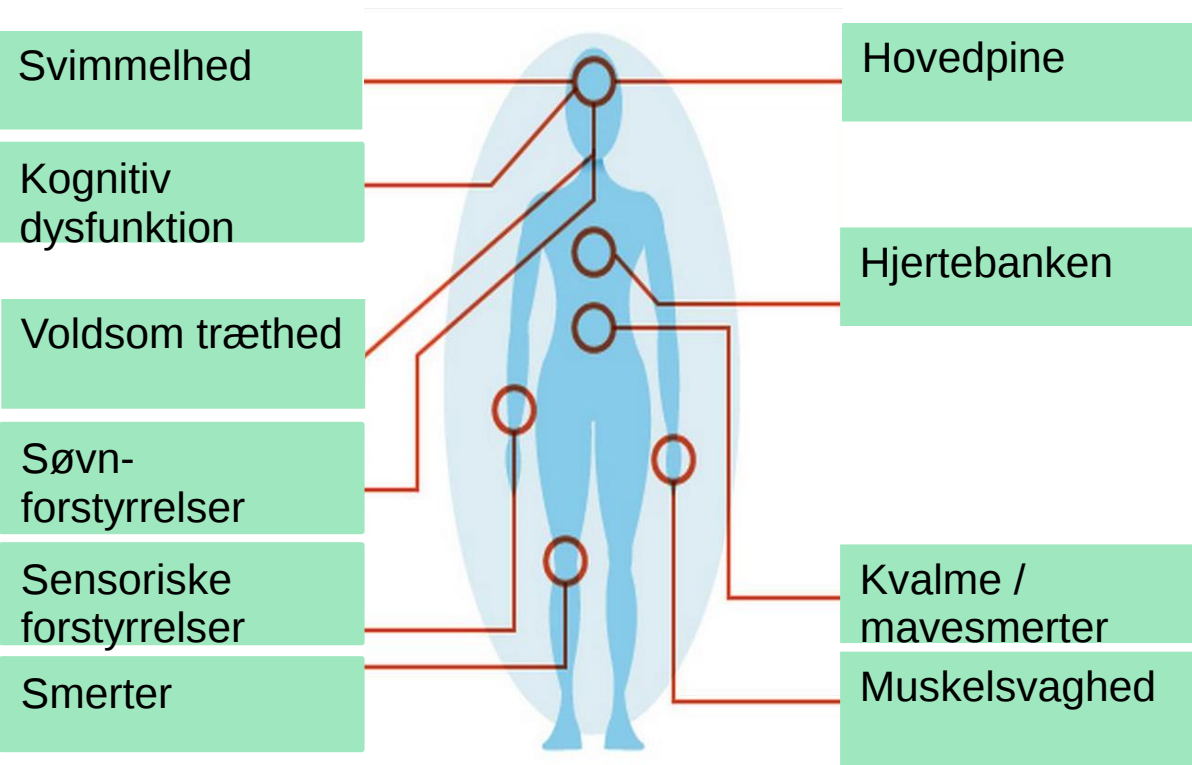
¹Arbyn et al, Cochrane Datab Syst Rev 2018;
5: CD009069;
Harder et al, BMC Med 2018;16(1):110.

²Arnheim-Dahlström et al, BMJ 2013;347:f5906;
Donegan et al, Vaccine 2013;31(43):4961-4967;
Scheller et al, JAMA 2015;313(1):54-61;
Feiring et al, Vaccine 2017;35(33):4203-4212;
Miranda et al, Vaccine 2017;35(36):4761-4768;
Jørgensen et al, BMJ 2018;362:k3694.

Overordnet forsknings-hypotese

Vores hypotese: der kan være en sammenhæng mellem HPV vaccination og bivirkninger, der ikke nødvendigvis viser sig som *specifikke* diagnoser.

Bivirkninger kan vise sig som kontakter til sygehus med *symptom-diagnoser*, fx træthed, svimmelhed, hovedpine, hjertebanken, smerter, m.v.





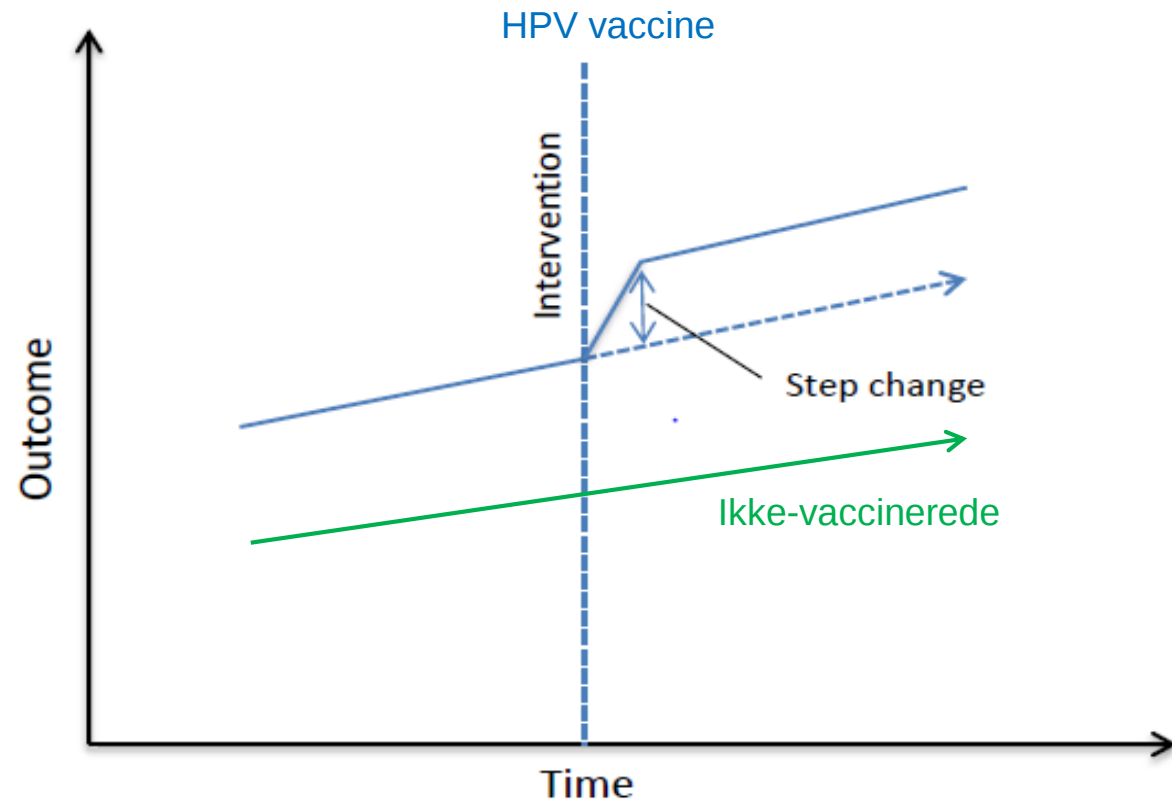
3 forskellige hypoteser / analyser

- Hvis det er HPV-vaccinationen, der er årsag til de mistænkte bivirkninger, så vil risikoen for symptomer:

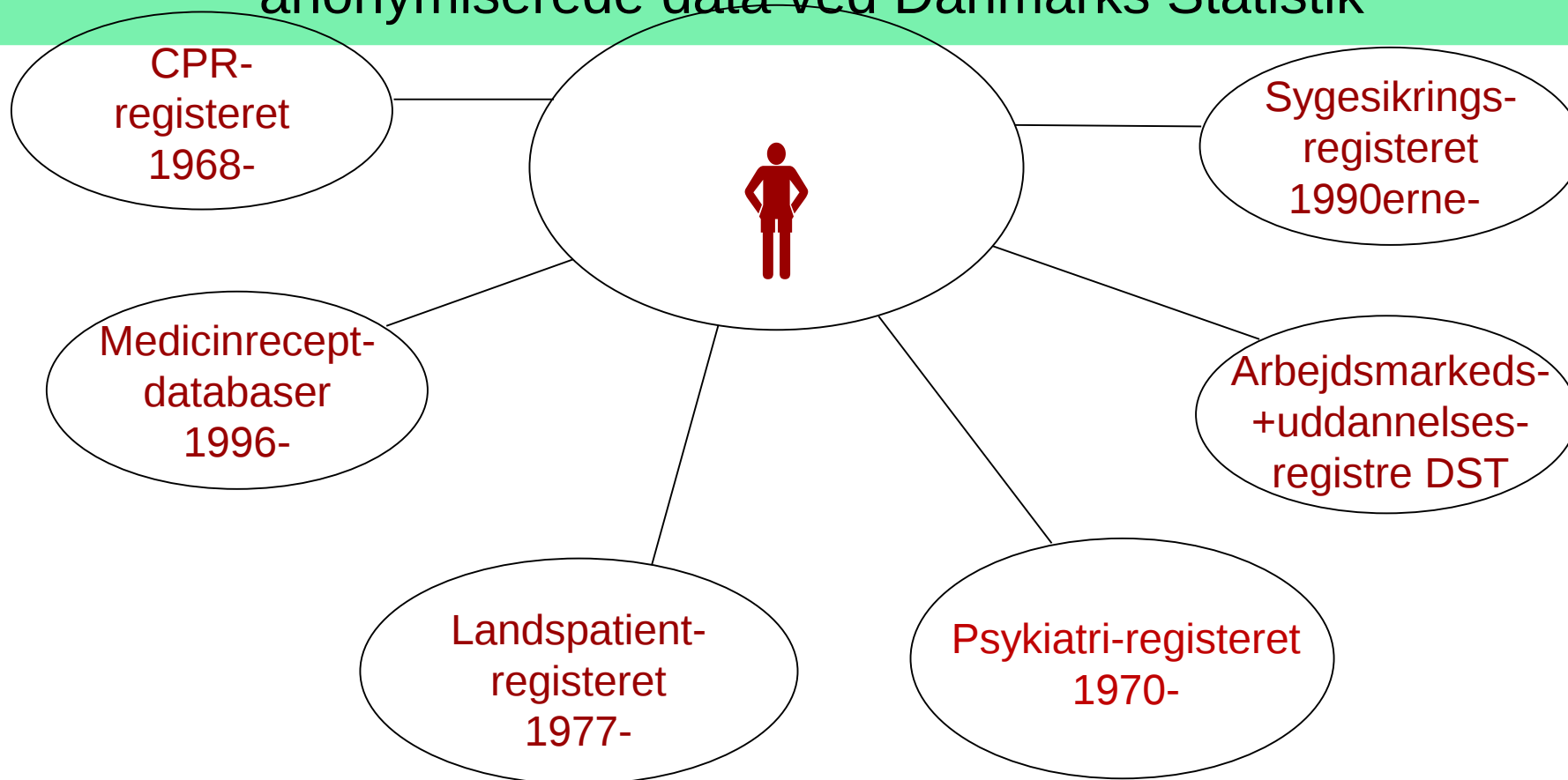
1. Være højere hos HPV-vaccinerede piger end hos ikke-HPV-vaccinerede piger

2. Være højere i tiden lige efter HPV vaccination, blandt piger der fik symptomer

3. Stige tydeligt blandt piger i forhold til drenge i befolkningen, efter man begyndte at HPV-vaccinere pigerne



Forskningsmetode: omfattende kobling og analyse af landsdækkende anonymiserede data ved Danmarks Statistik





Definition af symptomer

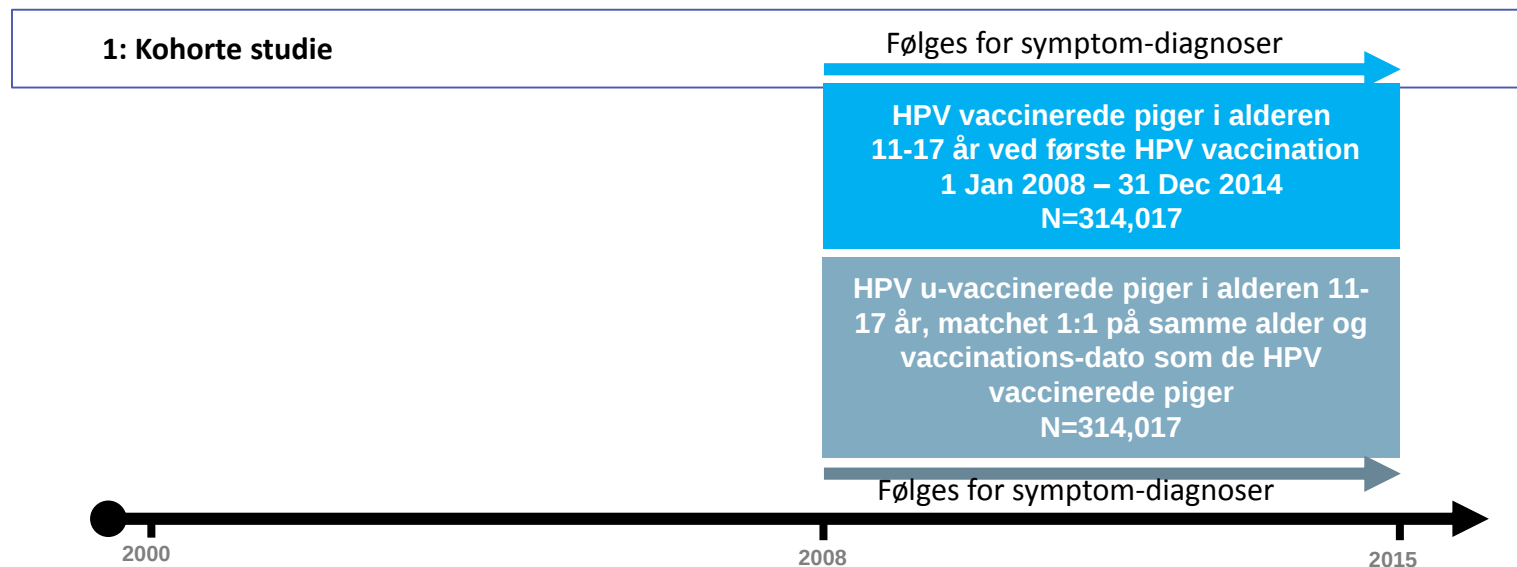
- Pigerne følges 1 år efter deres HPV vaccinationsdato for sygehus-kontakt med:
 - Mavesmerter
 - Uspecifik smerte
 - Hovedpine
 - Utilpashed og træthed
 - CFS
 - Hjertebanken
 - POTS
 - Lavt blodtryk eller besvimelse



Resultater

- De følgende resultater er uddrag af samlede analyseresultater, der er blevet fagfælle-bedømt (peer-reviewed), og i november 2019 accepteret til publikation som originalartikel i det videnskabelige tidsskrift *American Journal of Epidemiology*
- Artiklen med de samlede analyseresultater er i trykken, og forventes at udkomme i *American Journal of Epidemiology* inden for de nærmeste uger

Resultater: Analyse 1 – HPV vaccinerede vs. ikke-vaccinerede piger



	HPV vaccinerede piger (N=314,017)	HPV u-vaccinerede piger (N=314,017)
<i>Pigernes sygdoms-historie før vaccinationsdato:</i>		
Asthma	5.4%	5.7%
Hospitalskrævende infektion	7.5%	8.2%
Diabetes	0.34%	0.41%
Psykatrisk diagnose	2.3%	3.2%
Tidligere besøg hos psykolog/psykiater	1.8%	2.1%
Tidligere psykometrisk test eller samtaleterapi	3.6%	3.9%
>50 tidligere kontakter til praktiserende læge	25.8%	23.3%
<i>Pigernes forældre:</i>		
Længerevarende uddannelse (universitet)	14.1%	13.7%
Begge forældre i arbejde	72.0%	65.4%
Indkomst forældre over gennemsnit (>650.000 DKR)	53.1%	46.8%
Forældre gift	64.0%	59.1%
Dansk etnicitet	90.8%	88.4%

Diagnose	HPV vaccineret			HPV u-vaccineret			Relativ risiko* (95% konfidens-interval) for HPV vaccinerede vs. u-vaccinerede piger
	N	Person-år	rate/1.000	N	Person-år	rate/1.000	
Mavesmerter	2,303	296,133	7.78	2,465	295,414	8.34	0.91 (0.86 ; 0.97)
Hovedpine	618	310,708	1.99	583	310,593	1.88	1.09 (0.96 ; 1.22)
Uspecifikke smerter	265	312,825	0.85	269	312,736	0.86	0.95 (0.79 ; 1.14)
Lavt blodtryk/besvimelse	908	310,128	2.93	938	309,937	3.03	0.96 (0.88 ; 1.06)
Hjertebanken	122	313,296	0.39	109	313,243	0.35	1.14 (0.87 ; 1.50)
POTS	6	313,880	0.02	10	313,871	0.03	0.54 (0.19 ; 1.53)
Utilpashed/træthed	112	313,560	0.36	124	313,514	0.40	0.90 (0.68 ; 1.17)
CFS	<5	313,879	≤0.00	9	313,859	0.03	0.12 (0.02 ; 0.99)

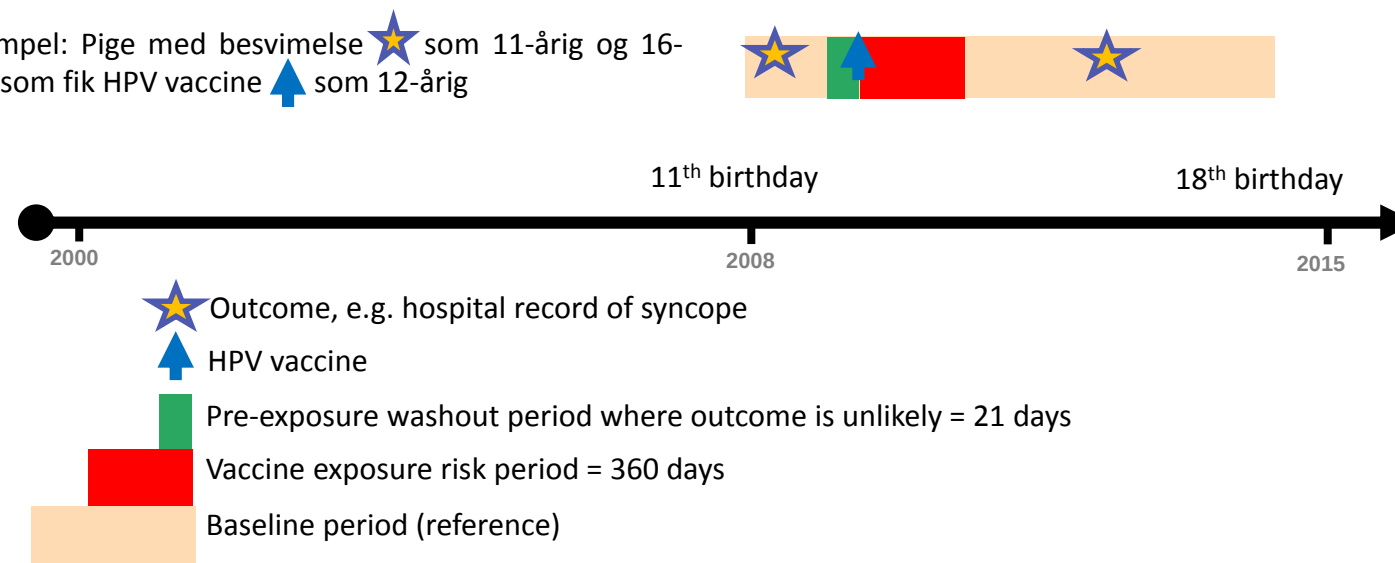
* Relativ risiko justeret for: alder, kalenderår (2008-2014), astma, diabetes, tidligere infektioner, psykiske lidelser, hyppighed af praktiserende læge kontakter sidste 5 år, tidligere psykometrisk undersøgelse eller samtaleterapi, tidligere behandling hos psykolog eller psykiater, forældres uddannelsesniveau, arbejdsmarkedstilknøytning, indkomst, civilstand, og etnicitet



Resultater: Analyse 2 – "Self-controlled" = pigers risiko i tiden omkring HPV vaccine

Self-controlled case series (SCCS) studie for alle 11.817 piger der oplevede symptom-diagnoser

Eksempel: Pige med besvimelse ★ som 11-årig og 16-årig, som fik HPV vaccine ▲ som 12-årig





Resultater: Analyse 2 – "Self-controlled" = pigers risiko i tiden omkring HPV vaccine

Diagnose	Relativ risiko* (95% konfidens-interval)
Mavesmerter	
Hovedpine	1.14 (0.99-1.32)
Uspecifikke smerter	0.85 (0.68-1.06)
Lavt blodtryk/besvimelse	1.02 (0.92-1.14)
Hjertebanken	0.93 (0.70-1.24)
POTS	
Utilpashed/træthed	1.09 (0.83-1.45)
CFS	0.82 (0.16-4.16)

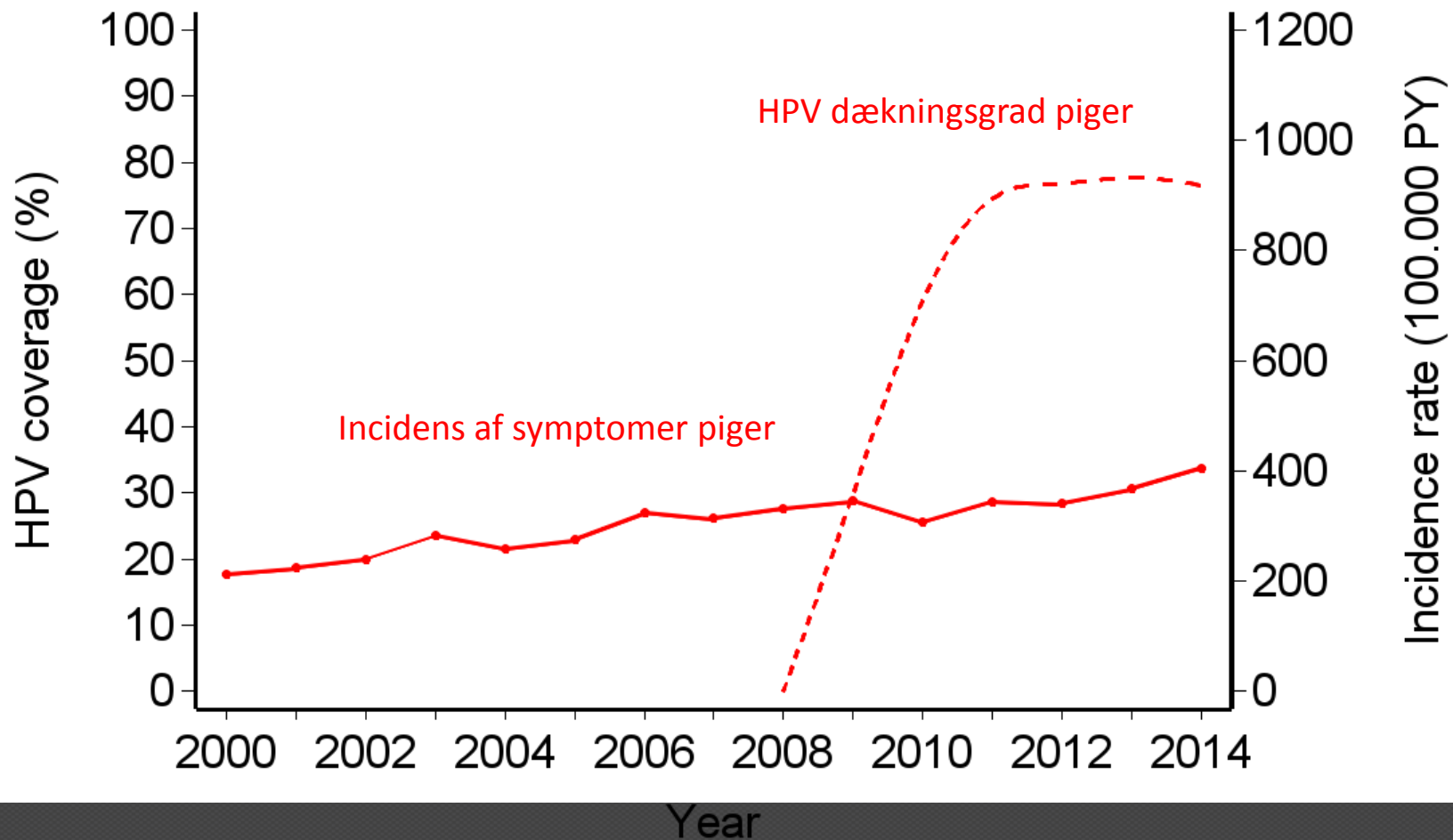
* Relativ risiko justeret for: alder, kalenderår



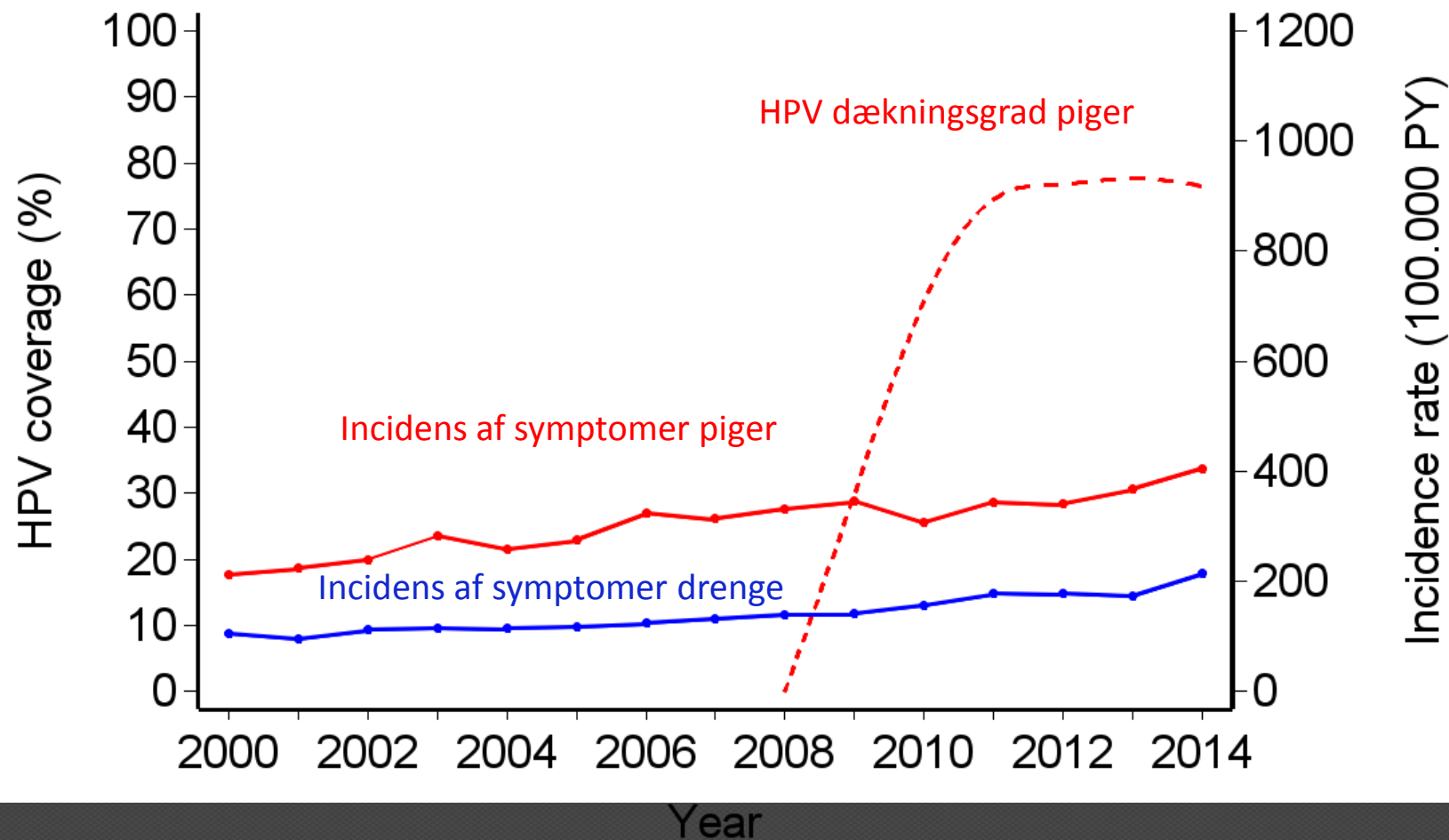
Resultater: Analyse 3 – årlig forekomst af symptom-diagnoser blandt piger i forhold til drenge i befolkningen

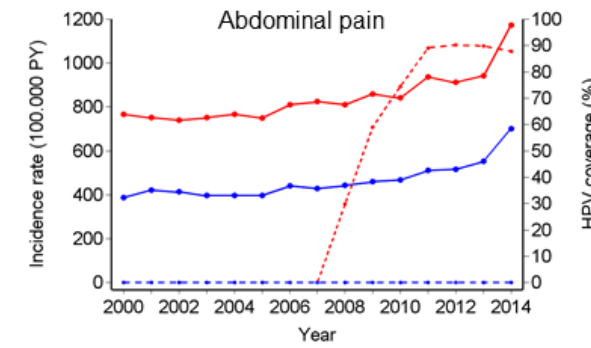
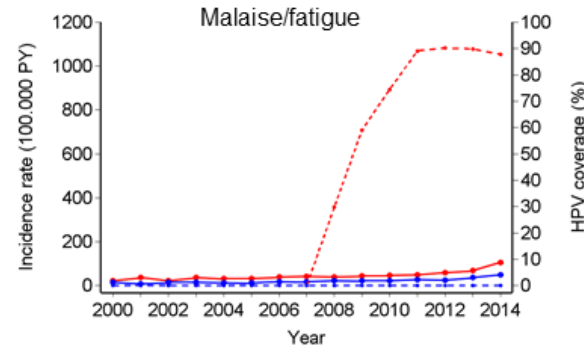
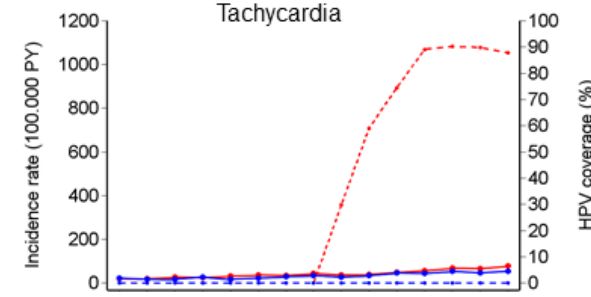
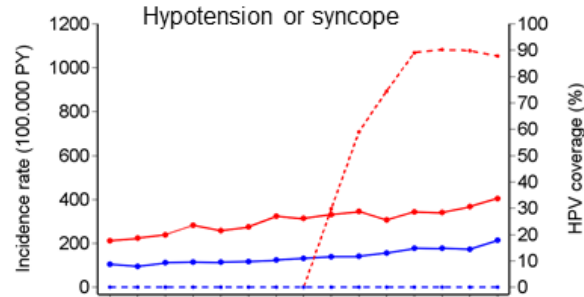
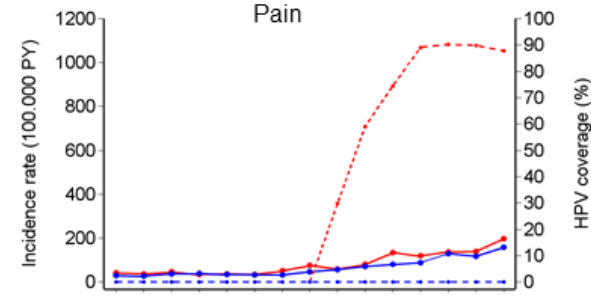
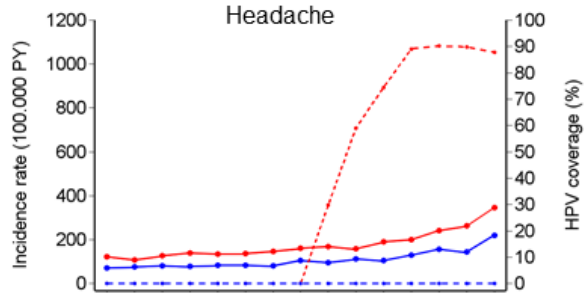


Årlig forekomst hospitalskontakt m. lavt blodtryk eller besvimelse



Årlig forekomst hospitalskontakt m. lavt blodtryk eller besvimelse





Styrker og begrænsninger i vores studie

BEGRÆNSNINGER

- Vi har kun undersøgt symptomer diagnosticeret på sygehus = formentlig de sværeste tilfælde
- Vi kender ikke den præcise kvalitet af diagnoserne for smerter, svimmelhed, træthed, kredsløbs-symptomer etc.
 - Men korrekthed af kodning afhænger næppe systematisk af, om pigerne er HPV-vaccineret eller ej
 - Og en eventuel "øget opmærksomheds bias" med mere komplet diagnose-kodning hos HPV-vaccinerede piger ville give en *øget* forekomst af symptomer (og det fandt vi *ikke*)
- Det præcise "risiko-vindue" for biologisk plausible bivirkninger efter HPV-vaccination er ukendt

STYRKER

- Vi har udført et stort, omfattende, populations-baseret, videnskabeligt studie i et sundhedsvæsen med fri adgang til lægehjælp
- Vi har haft mulighed for at koble komplette højkvalitets registerdata fra dagligdags klinisk praksis
- Vi har i analysen kunnet tage højde for en lang række forskelle blandt HPV vaccinerede og ikke-vaccinerede piger – og har derudover undersøgt piger med symptomdiagnoser internt
- Vi har anvendt "triangulering", hvor 3 forskellige analysemetoder - med hver deres styrker og svagheder - konsistent har givet samme resultat. Det styrker vores konklusion.



Konklusion

- Der er *intet* i vores store, landsdækkende studie, der giver mistanke om en sammenhæng mellem HPV vaccination og øget hyppighed af sygehuskontakter med symptomer som træthed, svimmelhed, hovedpine, hjertebanken, besvimelse, eller smerter
- Vores studie bidrager til evidensen for, at HPV vaccination har en sikker bivirkningsprofil mht. symptomer der kræver sygehuskontakt

Slut og tak!

Tak til medarbejderne på projektet:
Statistikere Buket Öztürk og Sia Kromann
Nicolaisen, og Professorer Lars Pedersen, Irene
Petersen, Jørn Olsen, og Henrik Toft Sørensen,
Aarhus Universitetshospital, Aarhus
Universitet, og University College London.



Aarhus Universitetshospital

HPV Vaccine Safety in Denmark

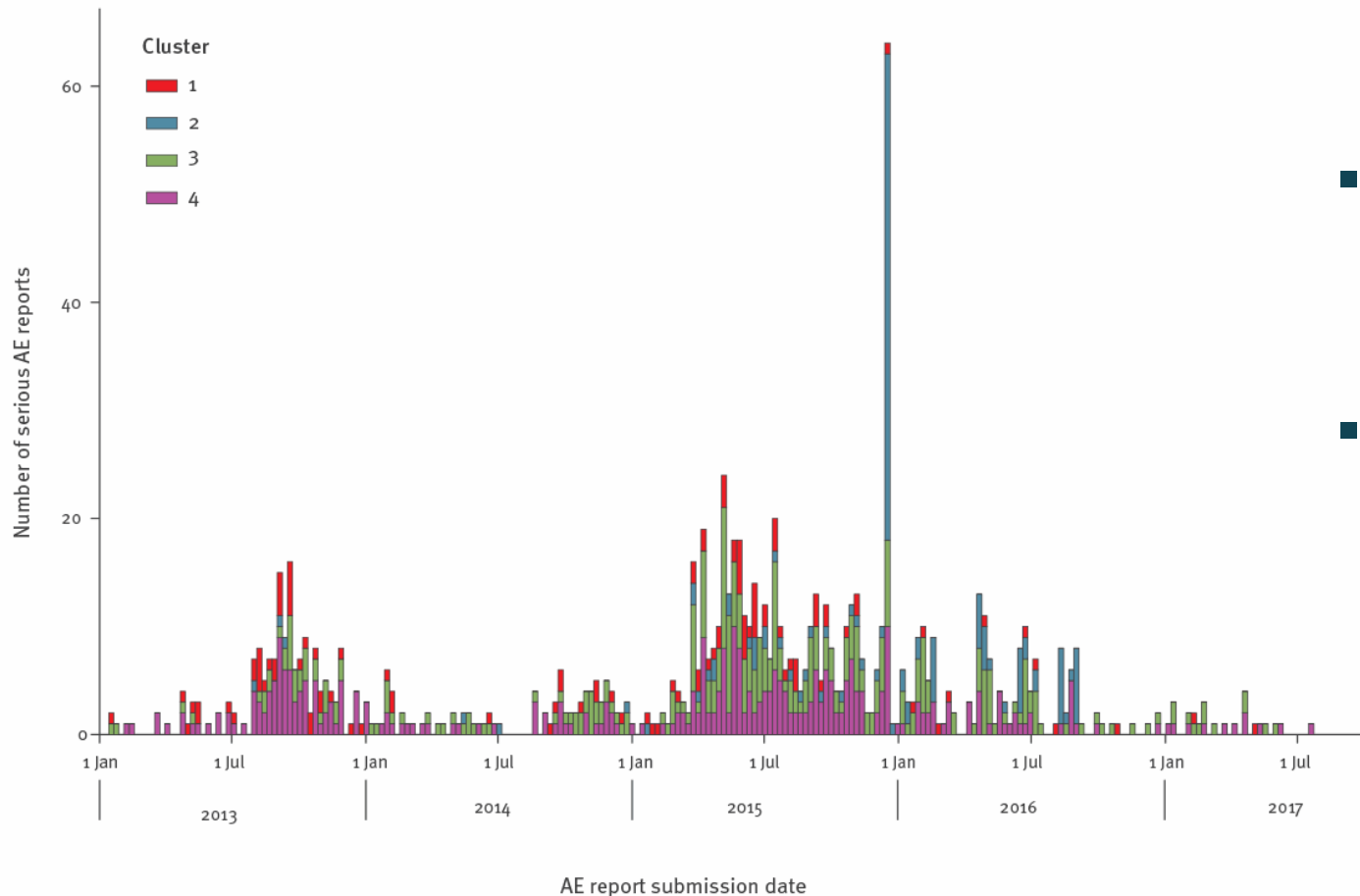
Anders Hviid, Morten Frisch,
Palle Valentiner-Branth,
Kåre Mølbak.

Statens Serum Institut.



1

"The Danish signal" – Temporal patterns



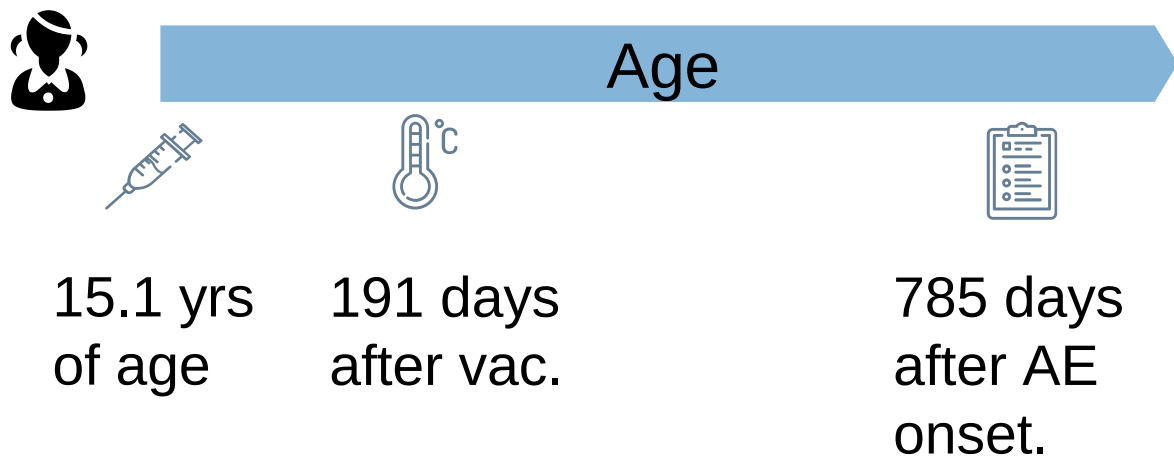
- Sep 2009-Aug 2017:
963 serious adverse event reports.
- Very few reports prior to 2013.
- Stimulated reporting?

(Ward. *Euro Surveill* 2019.)

1

"The Danish signal" – Report characteristics

- 963 reports with a median of 13 AE terms.



- Clusters? (Latent Class Analysis)

Cluster	#Reports	#AE terms
1	120	42
2	130	20
3	329	16
4	384	5

1

"The Danish signal" – Cluster composition

Ten most common adverse event (AE) terms within clusters of reports of serious AE following human papillomavirus vaccination in females, Denmark, 12 September 2009–17 July 2017 (n = 963)

Rank	Cluster 1 (120 reports)			Cluster 2 (130 reports)			Cluster 3 (329 reports)			Cluster 4 (384 reports)		
	AE term	n	%	AE term	n	%	AE term	n	%	AE term	n	%
1	Fatigue	114	95	Fatigue	120	92	Fatigue	294	89	Headache	142	37
2	Dizziness	113	94	Dizziness	118	91	Dizziness	248	75	Fatigue	126	33
3	Headache	107	89	Headache	111	85	Headache	242	74	Dizziness	104	27
4	Nausea	101	84	Cognitive disorder	102	78	Nausea	186	57	Syncope	71	18
5	Arthralgia	100	83	Abdominal pain	100	77	Arthralgia	149	45	Nausea	53	14
6	Disturbance in attention	99	83	Nausea	98	75	Disturbance in attention	143	43	Arthralgia	47	12
7	Memory impairment	88	73	Muscular weakness	94	72	Abdominal pain	118	36	Disturbance in attention	35	9
8	Muscular weakness	80	67	Palpitations	92	71	Syncope	110	33	Sensory disturbance (tied with 9)	34	9
9	Myalgia	75	63	Dysuria (tied with 10)	78	60	Muscular weakness	101	31	Abdominal pain (tied with 8)	34	9
10	Palpitations	73	61	Sleep disorder (tied with 9)	78	60	Myalgia/memory impairment ^a	100	30	Paraesthesia/ pain/migraine ^a	26	7

(Ward. *Euro Surveill* 2019.)

2

Explaining the "Danish signal" – Predicting AEs

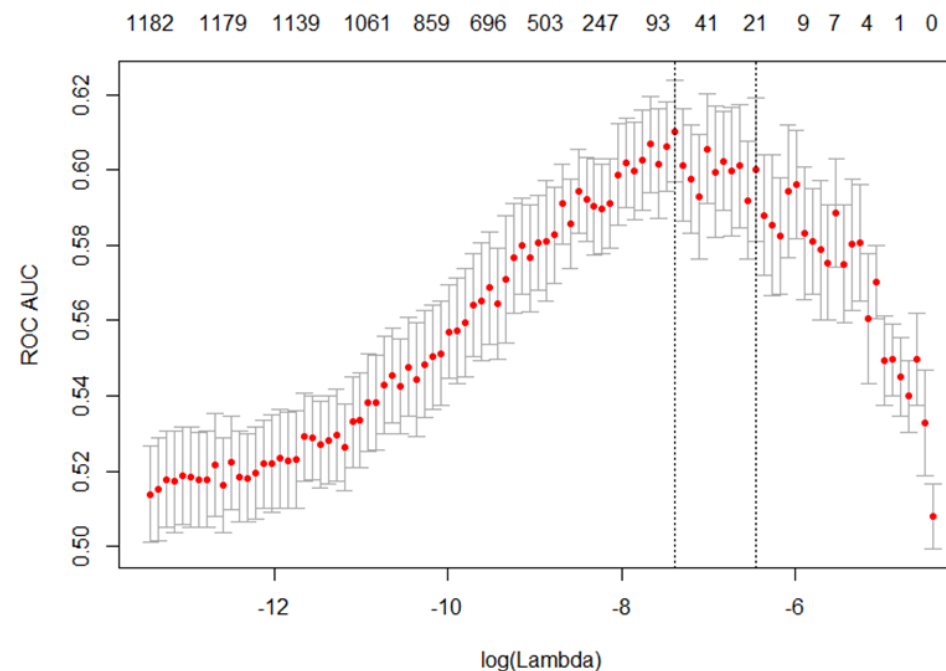
- Pre-vaccination health-care seeking behaviour is increased.
- Is this a valid explanation for the "Danish signal"?

	Cases	Controls
ICD-10 chapters		
Z00-Z99: Factors influencing health status and contact with health services	521 (60%)	1932 (45%)
S00-T99: Injury, poisoning and certain other consequences of external causes	503 (58%)	1859 (43%)
R00-R00: Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	184 (21%)	460 (11%)
O00-O99: Pregnancy, childbirth and the puerperium	120 (14%)	428 (10%)
M00-M99: Diseases of the musculoskeletal system and connective tissue	117 (14%)	346 (8%)
K00-K95: Diseases of the digestive system	95 (11%)	235 (5%)
F00-F99: Mental, Behavioral and Neurodevelopmental disorders	88 (10%)	223 (5%)
N00-N99: Diseases of the genitourinary system	82 (10%)	273 (6%)
J00-J99: Diseases of the respiratory system	73 (8%)	205 (5%)
E00-E89: Endocrine, nutritional and metabolic diseases	56 (6%)	184 (4%)
A00-B99: Certain infectious and parasitic diseases	44 (5%)	118 (3%)
G00-G99: Diseases of the nervous system	42 (5%)	92 (2%)
L00-L99: Diseases of the skin and subcutaneous tissue	33 (4%)	134 (3%)
C00-D49: <u>Neoplasms</u>	22 (3%)	102 (2%)
Q00-Q99: Congenital malformations, deformations and chromosomal abnormalities	21 (2%)	119 (3%)
H00-H59: Diseases of the eye and adnexa	19 (2%)	76 (2%)
I00-I99: Diseases of the circulatory system	17 (2%)	61 (1%)
H60-H95: Diseases of the ear and mastoid process	16 (2%)	81 (2%)
V00-Y99: External causes of morbidity	7 (1%)	19 (0%)
D50-D89: Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	2 (0%)	25 (1%)
P00-P96: Certain conditions originating in the perinatal period	0 (0%)	4 (0%)

2

Explaining the "Danish signal" – Machine Learning

- LASSO regression.
- Hospital contacts 5-yrs prior to vaccination for cases and controls.
- ICD-10 codes at different levels of granularity.
- Training/Test split 75%/25% with 10-fold cross-validation of hyperparameter.



2

Explaining the "Danish signal" – Conclusion

Model	<u>Lambda selection criteria</u>	ROC AUC	PR AUC	<u>Recall</u>	Precision	<u>Non-zero coef</u>
Model 1	<u>Accuracy</u>	0.65	0.28	0.07	0.52	75
Model 1	<u>Parsimony</u>	0.64	0.29	0.05	0.58	21
Model 2	<u>Accuracy</u>	0.64	0.27	0.07	0.47	78
Model 2	<u>Parsimony</u>	0.65	0.30	0.01	0.67	10
Model 3	<u>Accuracy</u>	0.64	0.27	0.08	0.55	20
Model 3	<u>Parsimony</u>	0.64	0.26	0.14	0.36	5
Model B	-	0.64	0.28	0.01	1.0	24

Table 2: Performance metrics of the predictive models. For each model we report the results for the lambda value maximizing the ROC AUC on the training data (Accuracy), and for the model with the highest lambda where the ROC AUC is within one standard deviation of the maximum (Parsimony). In addition to the ROC AUC, PR AUC, recall, and precision, we also report the number of non-zero coefficients in each model. Precision and recall are reported for the prediction threshold maximizing the precision.

- Pre-vaccination health-care seeking behavior **does not** explain the “Danish signal”.

Human Papillomavirus Vaccination Safety in Boys (10-17 yr old)



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Original article



Miscellaneous

Quadrivalent human papillomavirus vaccination in boys and risk of autoimmune diseases, neurological diseases and venous thromboembolism

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Editorial decision 3 December 2017; Accepted 15 December 2017

Abstract

Background: In recent years, human papillomavirus (HPV) vaccination of boys has been added to childhood vaccination programmes in several countries but, so far, no systematic population-based assessment with long-term follow-up has been undertaken of the relative incidence of adverse outcomes following HPV vaccination in this group. We investigated if quadrivalent HPV (qHPV) vaccination of 10–17-year-old boys is associated with any unusual risk of autoimmune diseases, neurological diseases or venous thromboembolism.

Methods: We conducted a national cohort study of 568 410 boys born in Denmark 1988–2006 and followed for 4 million person-years during 2006–16, using nationwide registers to obtain individual-level information about received doses of the qHPV vaccine and hospital records for 39 autoimmune diseases, 12 neurological diseases and venous thromboembolism. For each outcome, we estimated incidence rate ratios (RRs) with 95% confidence intervals (CIs) according to qHPV vaccination status.

Results: Altogether 7384 boys received at least one dose of the qHPV vaccine at age 10–17 years. Overall, RRs were close to unity for the combined groups of autoimmune diseases (RR = 0.96; 95% CI: 0.71–1.28, $n = 46$ cases in qHPV-vaccinated boys) and neurological diseases (RR = 0.67; 0.41–1.10, $n = 16$), as well as for venous thromboembolism (RR = 0.88; 0.33–2.35, $n = 4$). After taking multiple testing into account, none of the 52 individual outcomes studied appeared to occur in excess among qHPV-vaccinated boys.

Conclusions: Although additional large-scale epidemiological studies are warranted, our findings provide population-based reassurance that qHPV vaccination of 10–17-year-old boys is unlikely to be associated with an elevated risk of autoimmune diseases, neurological diseases or venous thromboembolism.

Key words: Human papillomavirus, vaccine safety, epidemiology, autoimmune diseases, neurological diseases, venous thromboembolism

Downloaded from https://academic.oup.com/ije/article-abstract/47/2/634/4040712 by Statens Serum Institut user on 28 November 2019

- HPV vaccination of boys is increasingly being implemented.
- Primarily based on safety in females.
- Is HPV vaccination in boys associated with autoimmune diseases, neurological diseases or venous thromboembolism?

3

HPV Vaccination Safety in Boys - Results

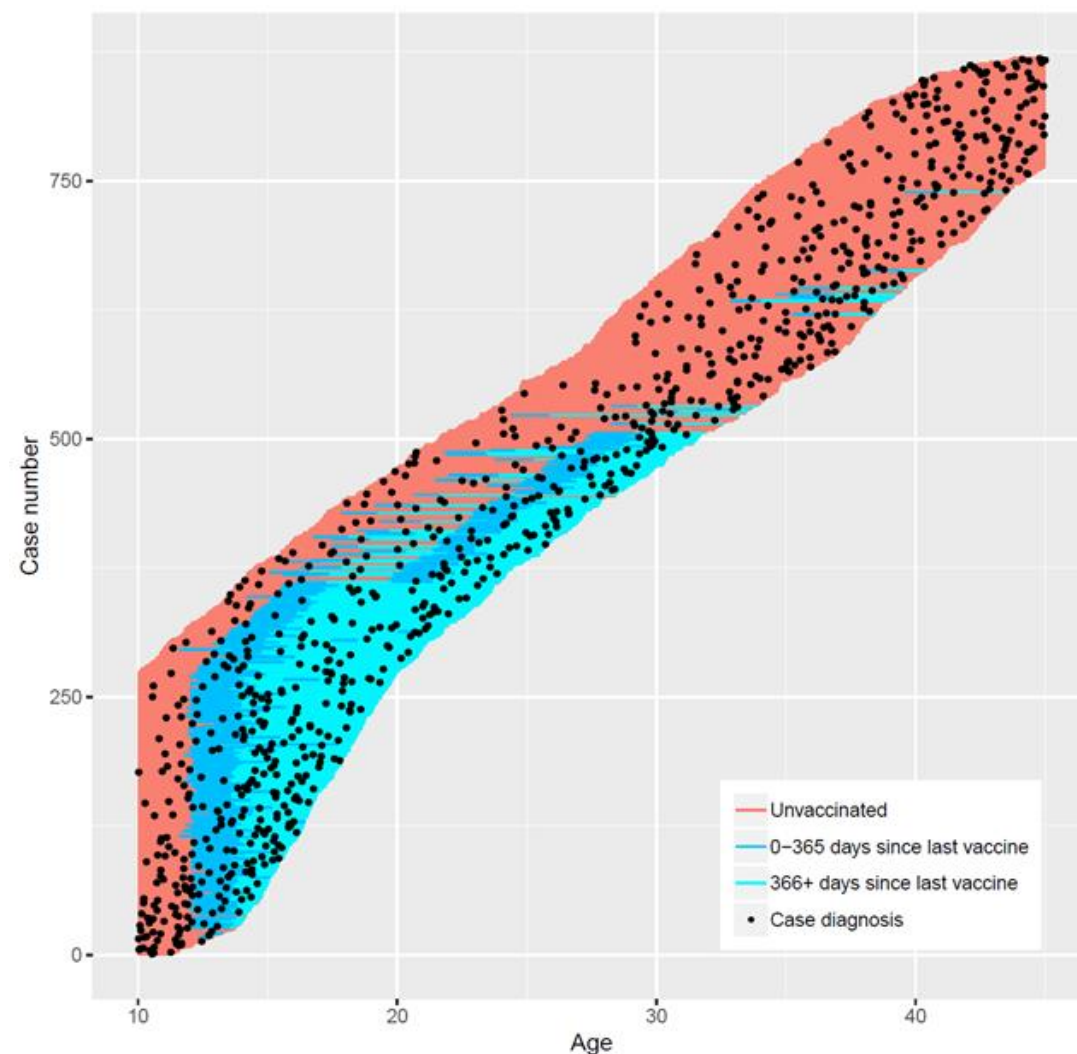
- 568,410 boys born 1988 – 2006.
- 4 million years of follow-up 2006-2016.
- 39 autoimmune diseases, 12 neurological diseases and VTE.
- 7384 boys with at least 1 dose of qHPV.

	Vaccinated Cases	RR (95% CI)
AID	46	0.96 [0.71-1.21]
ND	16	0.67 [0.41-1.10]
VTE	4	0.88 [0.33-2.35]

4

HPV Vaccination and autonomic dysfunction syndrome.

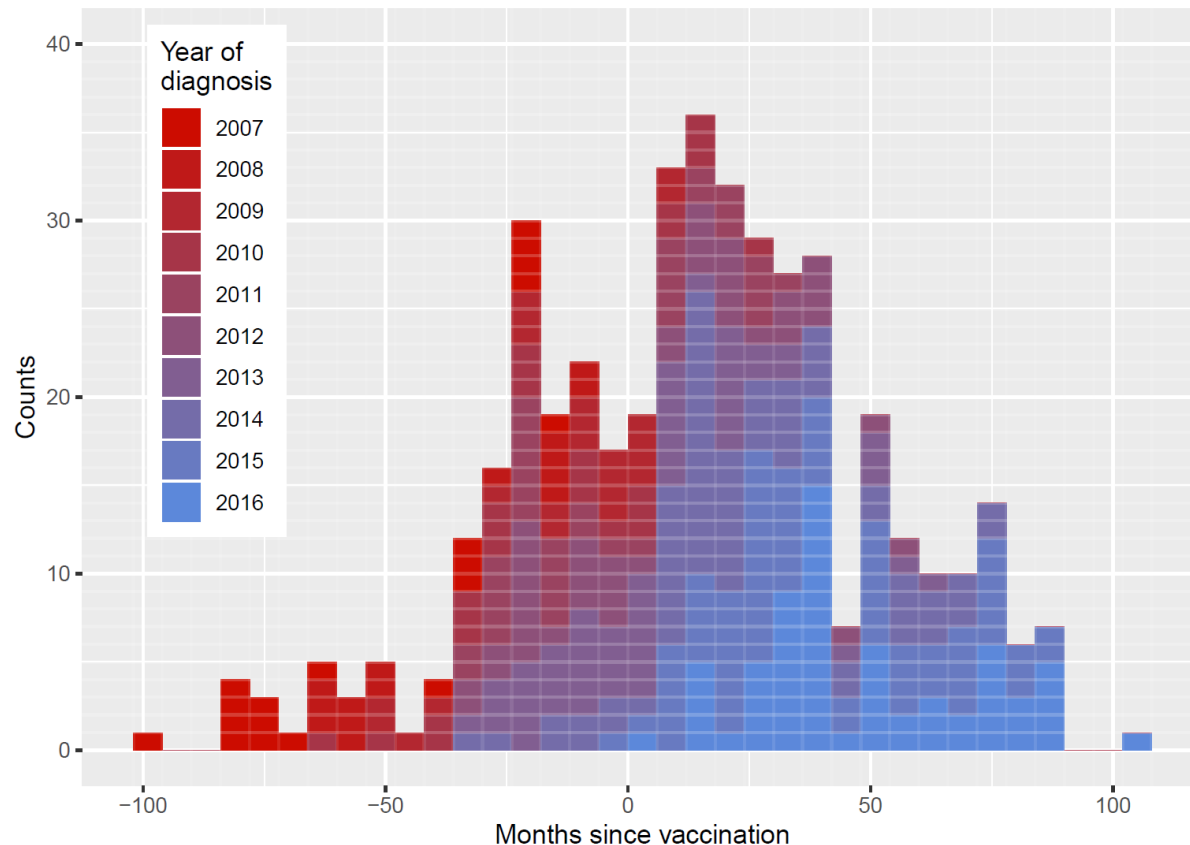
- Self-controlled case series analysis (1-year risk period) of CFS, CRPS & POTS diagnoses.
- 1,375,737 Danish-born females 10-44 years of age during the 2007-2016 study
- 869 cases.



(Hviid. Submitted 2019.)

4

HPV Vaccination and autonomic dysfunction syndrome.



- 433 vaccinated cases.
- 535 CRPS (median age, 29.3)
- 198 POTS (16.9)
- 136 CFS (28.4)

4

HPV Vaccination and autonomic dysfunction syndrome.

	Risk period count	RR (95% CI)*
CFS	4	0.38 [0.98-1.03]
CRPS	49	1.31 [0.91-1.90]
POTS	19	0.86 [0.48-1.54]
ALL	72	0.99 [0.74-1.32]

* 0-365 days post vac vs. unvac & 366 days+.

(Hviid. *Submitted* 2019.)

5

Innovative approaches
to study outcomes

School-absence records

	Person	Absence	School
Day 0	"143"	0	"Skolen"
Day 1	"143"	0	"Skolen"
Day 2	"143"	III	"Skolen"
Day 3	"143"	0	"Skolen"

- Repeated “measures” of absence.
- Mixed effects Poisson regression.
- Fixed: Grade, season, calendar.
- Random: Individual, class, school.

5

HPV Vaccination and All-Cause Morbidity

**14,068 Danish girls,
5th-9th grade, 2013-2018,
Copenhagen.**

“Forty-two percent of all medically certified long-term sickness absence was ascribed to ME/CFS, this figure being well in excess of all other causes.”

(Dowsett EG, Colby J. Long-Term Sickness Absence Due to ME/CFS in UK Schools. *J Chronic Fatigue Syndr.* 1997;3(2):29-42. doi:10.1300/J092v03n02_04)

	Absence Rate	Time in study
Unvax	3.5%	2.8 mil. days
HPV vax	3.4%	3.4 mil. days
RR	1.00	[0.98-1.03]

(Hviid. Submitted 2019.)

Litterature

2019: Human Papillomavirus Vaccination and All-Cause Morbidity in Adolescent Girls. [Submitted](#).

2019: Association between [quadrivalent](#) human papillomavirus vaccination and selected syndromes with autonomic dysfunction in Danish females: population-based self-controlled case series analysis. Submitted.

2019: Predicting who will report adverse events after HPV vaccination based on pre-vaccination healthcare utilization. Submitted.

2019: A Cluster Analysis of Serious Adverse Event Reports after Human Papilloma Virus Vaccination in Danish Girls and Young Women. [Euro Surveill](#). 2019 May;[24](#)(19).

2018: [Quadrivalent](#) human papillomavirus vaccination in boys and risk of autoimmune diseases, neurological diseases and venous thromboembolism. [Int J Epidemiol](#). 2018. Doi:10.1093/[ije](#)/dyx273.

2018: Human papillomavirus vaccination of adult women and risk of autoimmune and neurological diseases. [J Intern Med](#). 2018 Feb;[283](#)(2):154-165.

2017: [Quadrivalent](#) HPV Vaccination and the Risk of Adverse Pregnancy Outcomes. [N Engl J Med](#). 2017 Mar 30;[376](#)(13):1223-1233.

2014: [Quadrivalent](#) HPV vaccination and risk of multiple sclerosis and other demyelinating diseases of the central nervous system. [JAMA](#). 2015 Jan 6;[313](#)(1):54-61.

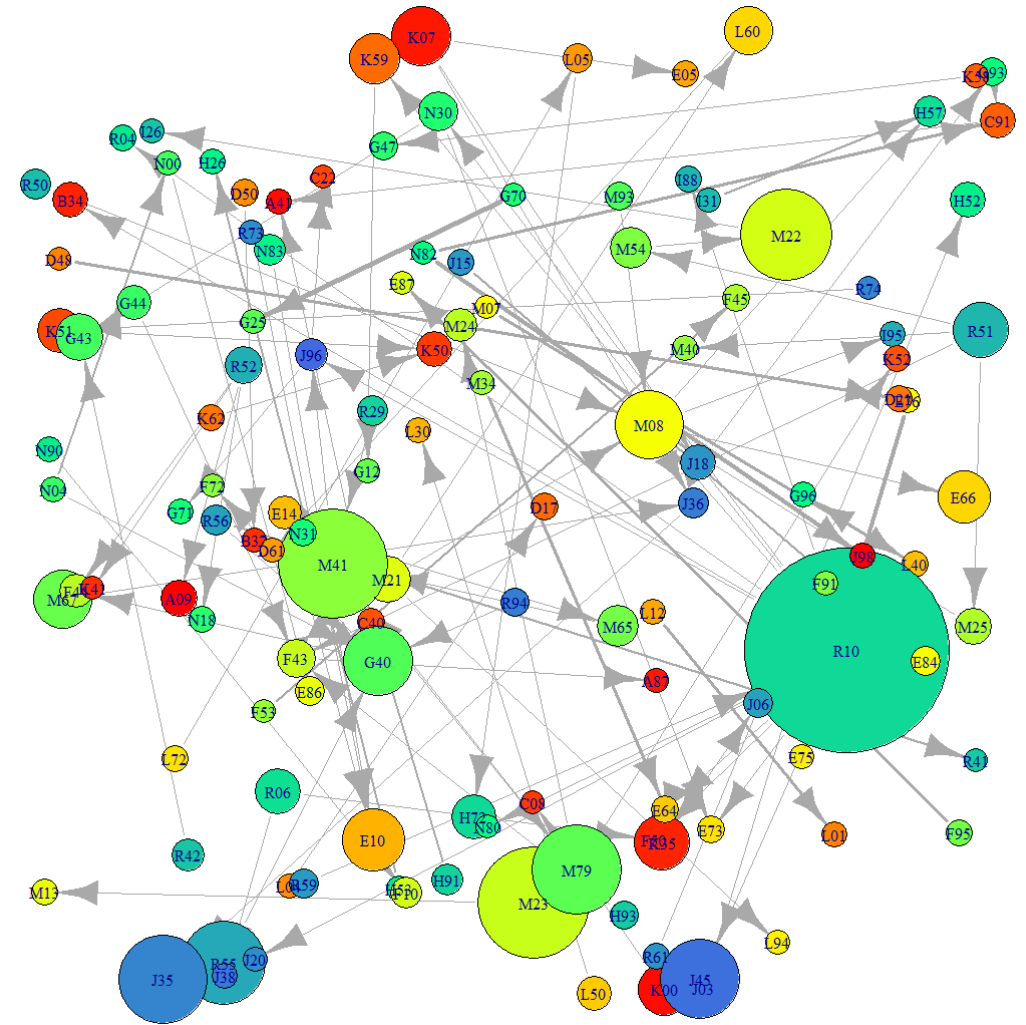
2014: [Quadrivalent](#) human papillomavirus vaccine and the risk of venous thromboembolism. [JAMA](#) 2014;[312](#):187-8.

2013: Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. [BMJ](#) 2013;[347](#):f5906.

2009: Human papillomavirus immunisation of adolescent girls and anticipated reporting of immune-mediated adverse events. [Vaccine](#) 2009;[27](#):2954-2958.

Future perspectives

- Boys and nHPV. New safety aspects?
- Novel approaches are needed.
- The HPV vaccines appear to be safe!



Formidlingsmøde om forskning i mulige bivirkninger ved HPV-vaccinen

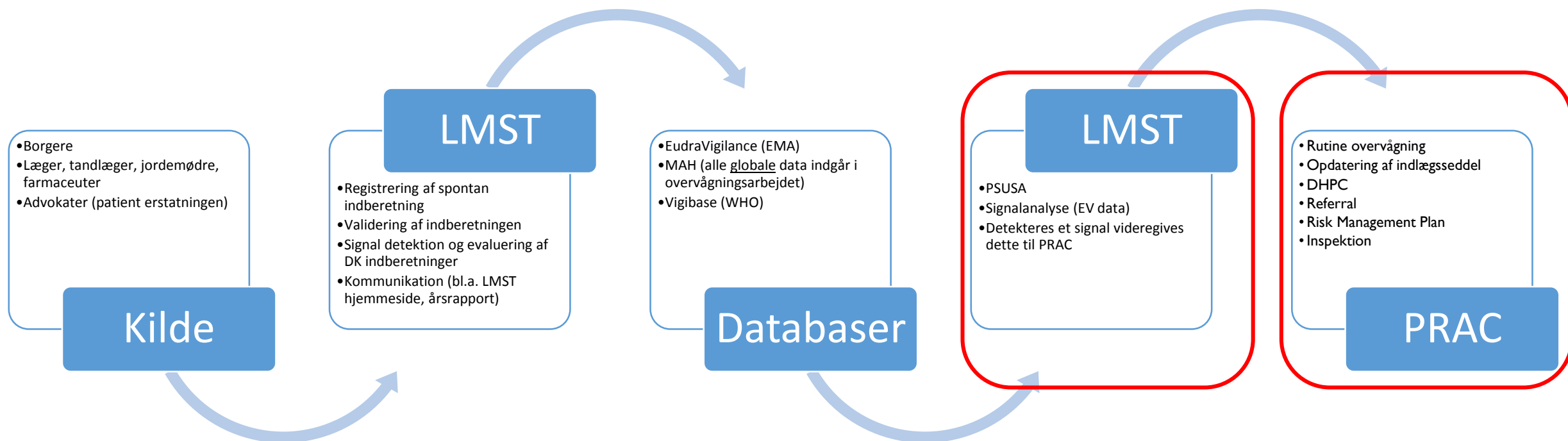
Pierre Quartarolo, Enhedschef for Lægemiddelovervågning & Medicinsk Udstyr



Sikkerhedsovervågning af HPV-vaccinen

- Lægemiddelstyrelsen overvåger fortsat sikkerheden ved HPV-vaccinen i samarbejde med det europæiske lægemiddelagentur, EMA, og myndighederne i de andre lande
- Resultaterne i de tre indsendte afrapporteringer har **ikke** ændret på Lægemiddelstyrelsens vurdering af sikkerheden ved HPV-vaccinen
- Lægemiddelstyrelsen vil informere EMA om resultater fra forskningsprojekterne
- Gardasil9 er sat på listen over lægemidler med skærpet indberetningspligt som følge af, at HPV-vaccination af drenge nu også er en del af børnevaccinationsprogrammet. Dermed har læger pligt til at indberette **alle** bivirkninger, de får formodning om.

Den spontane indberetnings "rejse" gennem systemet



Periodiske sikkerhedsopdateringer (PSUR)

- Balancen mellem fordele og ulemper vurderes løbende
- PSUR indsendes af virksomheden og vurderes kritisk af bivirkningskomiteen, PRAC, under EMA
- Indeholder globale data, herunder:
 - Bivirkningsindberetninger
 - Resultater fra nye kliniske studier
 - Publikationer, der omhandler nye aspekter om lægemidlets sikkerhed
- Frekvensen for indsendelse af rapporterne afhænger af typen af medicin, sikkerhedsprofilen og hvor længe, det har været på markedet
- Aktuelt indsendes der PSUR for Gardasil9 hvert år.
- Igangværende PSUR afsluttes i januar 2020
- Næste PSUR indsendes august 2020.

Følg os

