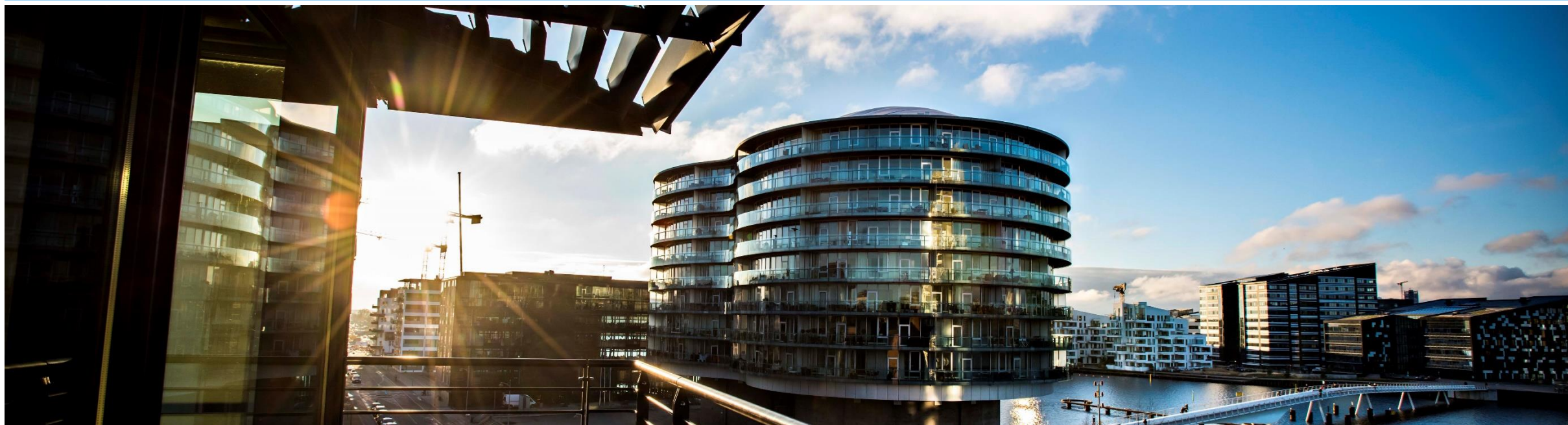


Monitoring Adverse events following immunization with HPV-vaccines in Denmark

Line Michan, Danish Medicines Agency



Adverse event reporting schedule for vaccines in Denmark

- Reporting by both health care professionals and consumers
- Legal obligation for health care professionals to report all suspected adverse drug reactions for new vaccines for the first 2 years.
- After than legal obligation to report serious or unexpected reactions
- Primarily by e-form, telephone or postal is also available
- Specific reporting scheme for vaccines – focus on batch numbers and other concomitant vaccinations

Bivirkning Vaccine Patient Indberetter Resumé

Information om bivirkningen

For at give os det bedste udgangspunkt for at vurdere bivirkningen, og for at minimere vores behov for at indhente supplerende oplysninger, beder vi dig venligst udfylde så mange felter som muligt.

De obligatoriske felter er markeret med en rød stjerne *

Angiv bivirkningens diagnose/symptom * ?

Her har du mulighed for at vælge en præcis diagnose/symptom fra et medicinsk opslagsværk, hvis du skriver på engelsk.

Hvornår startede bivirkningen? ?

Dag Måned År

DD MM ÅÅÅÅ

Er bivirkningen stoppet?

Ja

Er aftagende

Nej

Ophørt men med følger

Steps in surveillance

- Submission of reports to Danish Medicines Agency
- Reports are forwarded to the EMA, WHO, pharmaceutical company databases
- Causality assessment of individual ADR reports
- Assessment of potential signals

Adverse event reports received per year in DK

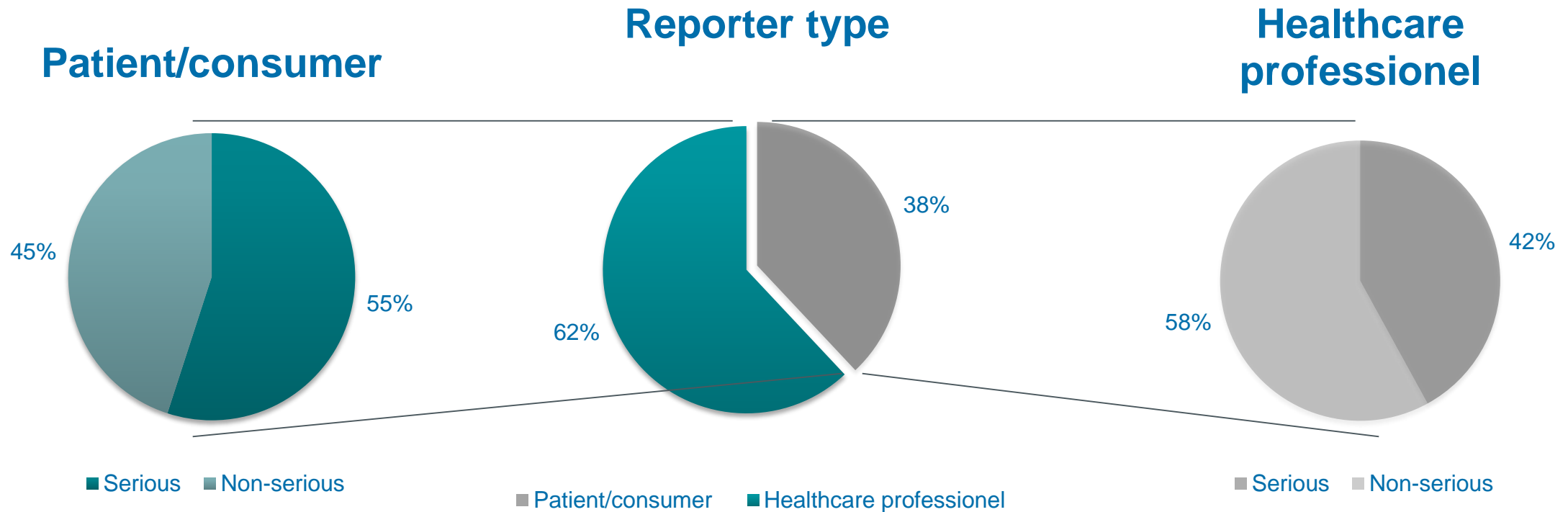
	2009	2010	2011	2012	2013	2014	2015	2016 Jan- jun	Total
Total reports	288	66	43	96	511	224	822	222	2241
Serious reports *	25	5	6	18	177	91	475	135	958
Vaccine doses sold	347.690	151.476	163.374	349.730	488.224	114.457	53.781	42.743	1.711.475

* 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.

Start year of adverse event (all reports until 2015)

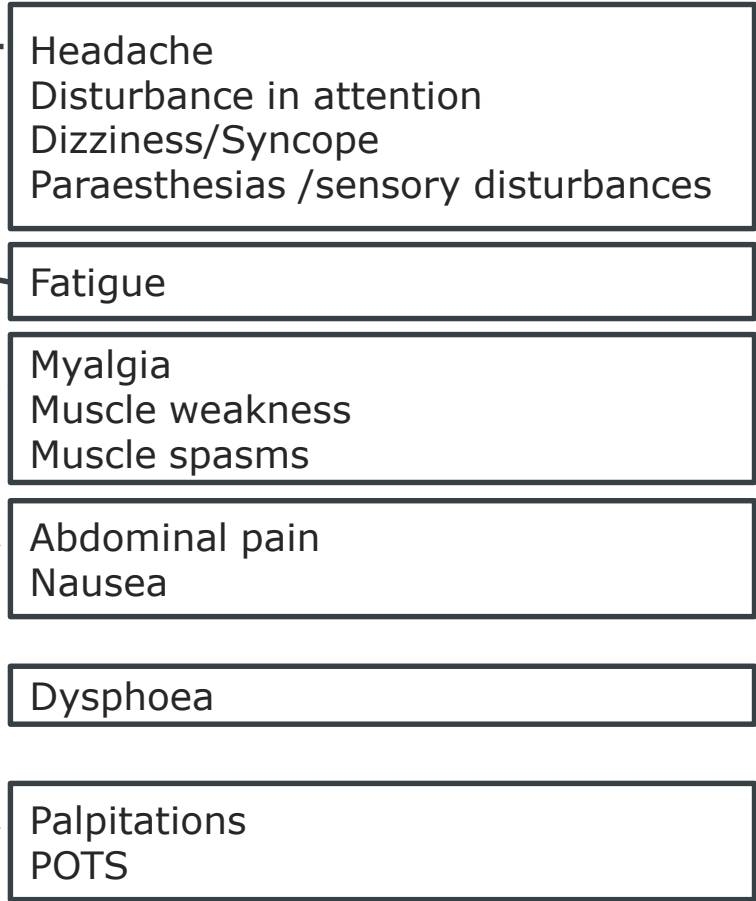
	2003-2008	2009	2010	2011	2012	2013	2014	2015
Reported start date for adverse event	211	334	145	148	360	587	153	81
Vaccine doses sold	?	347.690	151.476	163.374	349.730	488.224	114.457	53.781

Reported adverse events for HPV-vaccines



Most frequently reported reactions

Reported reactions according to MedDRA	Number of reactions
Nervous system disorders	5629
General disorders and administration site conditions	3112
Musculoskeletal and connective tissue disorders	2455
Gastrointestinal disorders	2226
Skin and subcutaneous tissue disorders	1522
Psychiatric disorders	1117
Eye disorders	911
Respiratory, thoracic and mediastinal disorders	713
Cardiac disorders	567
Infections and infestations	511



Causality assessment

Possible

- 1) Consistent temporal relationship between vaccination and symptoms, and there is documentation for the occurrence of the reported type of adverse reaction after vaccination.
- 2) Adverse events in connection to subscription, dose and vaccine administration
- 3) Reactions caused by vaccine quality defect
- 4) Anxiety reaction caused by vaccination

Insufficient documentation

- 1) Consistent temporal relationship between vaccination and symptoms, but there is no or indeterminate documentation for the occurrence of the reported type of adverse reaction after vaccination.
- 2) Data are conflicting

Less likely

Other known disease or other factors are more likely to explain the symptoms.

Unclassifiable

The information in the report is inadequate, and it cannot be assessed if the symptoms are related to the vaccine

2015 review:

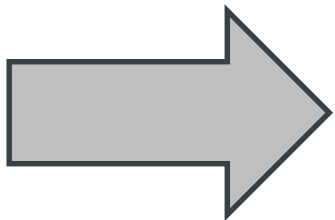
Review of the 363 serious reports for HPV-vaccines

Large proportion of the reports (34-43%) describe a symptom complex of headache, pain, fatigue, circulatory symptoms and neurological symptoms.

In most cases the patients are left undiagnosed. In some cases the patients fulfill criteria for POTS.

The disease diagnose encompassing most of the symptoms could be a CFS-like condition.

- Need for review of the world-wide data, comparative data on background incidences etc.



EMA referral

Public communications for Healthcare professionals

- Quartely overviews in Danish pharmacovigilance update – monthly bulleting for health care professionals – over 4000 subscribers
- Core data for all reported events following immunisation are publicly available on agency website.



Information to public on AEFI monitoring for HPV-vaccines: <https://www.youtube.com/watch?v=Qi-J-pMviDo>



Thank you