

## EPIET REPORT

## Summary of work activities Bolette Søborg European Programme for Intervention Epidemiology Training (EPIET), 2011 cohort

## Background

### Pre-fellowship short biography

Prior to EPIET, Bolette Søborg worked as a medical doctor working in public health at the Department of Infectious Disease Epidemiology, Statens Serum Institut. Her education included an MSc in Medical Sciences and a PhD in Infectious Disease Epidemiology, both from the University of Copenhagen.

### **EPIET** assignment

In September 2012, Bolette Søborg joined EPIET as a Member State track fellow in the Department of Infectious Disease Epidemiology, Statens Serum Institut in Copenhagen, Denmark, under the supervision of Kåre Mølbak, Head of Department.

# **Fellowship projects**

### **Surveillance projects**

## Infectious disease notifications in Denmark, 2001–2011: Is gender difference an overlooked parameter in disease surveillance?

Background: Gender is rarely emphasised as a useful parameter in infectious disease surveillance. We aimed to explore gender differences in Danish infectious disease notification data with the wider aim to gain insights into possible different disease surveillance practices.

Methods: We examined gender differences for all notifiable infectious diseases and selected three as an example: syphilis, hepatitis B virus (HBV) infection and measles. Following Danish case definitions for each disease, we compiled the number of cases by gender and age and used total population denominators from Statistics Denmark (the central authority on Danish statistics) to calculate cumulative incidence. We then calculated cumulative incidence ratios (IR) as the ratio of males over females.

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Results: Among 1 771 syphilis notifications, cumulated incidence was higher among males (5.4 per 100 000 versus 0.5 per 100 000, IR 10.8). Overall, 80% of male cases were in men who have sex with men (MSM). Males had higher rates of acute HBV (0.8 per 100 000 versus 0.4 per 100 000, IR 2.1) whereas females had higher ratios of chronic HBV infection (3.0 per 100 000 versus 3.7 per 100 000, IR 0.8). Measles was more common among males (0.3 per 100 000 versus 0.2 per 100 000, IR 1.5), especially among infants <1 (IR 1.6).

Conclusions: Gender seems important for disease surveillance practices with regard to the presented diseases. Gender differences in syphilis notifications suggest increased awareness or high-risk behavior among MSM. The HBV notification difference suggests male underreporting of chronic HBV cases, as pregnancy screening assures notification of female cases. The increased measles notification rates among males and infant boys <1 year of age lack obvious explanations, but seem irrespective of vaccine administration, which is given at 15 months. Gender-stratified analysis may help reveal gaps and artefacts of surveillance data.

Status: Completed, report delivered. Data published in EPI-NEWS, a weekly newsletter [15].

#### Piloting the implementation of a varicella surveillance system in Denmark

Aim: To assess if and how data captured from the general practitioners' DAK-E system can be used in Danish public health surveillance using varicella as a case 'tracer condition'.

Specific objectives: Using varicella data obtained from the DAK-E system in order to measure the completeness and representativeness of the data captured in the system.

Status: Primary analysis of data completed and a summary of results delivered.

## Routine analysis of hepatitis A, B and C, syphilis and gonorrhoea, results published in weekly newsletters [11-21]

### **Outbreaks**

#### Investigation of Salmonella Strathcona outbreak [1]

In September 2011, SSI identified several cases of the very rare *Salmonella* serotype *S*. Strathcona that had not previously been diagnosed in Denmark. The Department of Epidemiology initiated an outbreak investigation. ECDC reported that Germany, Austria and Italy had also reported cases in the same period. The initial outbreak investigation identified that small, elongated 'Datterino' tomatoes may have been the source of the outbreak, which was later confirmed by an analytical study. The same type of tomatoes was also sold in Germany and Austria.

Status: Completed

#### Investigation of a hepatitis A outbreak

In March 2012, the Danish notification system for infectious diseases identified a cluster of six hepatitis A cases. Laboratory typing confirmed that cases had an identical subtype (1B) and identical sequences. An outbreak team was formed. Initial trawling questionnaires did not succeed in identifying any common links between cases, and as no new cases were reported, all further investigation was stopped.

Status: Completed, report delivered.

#### HUS-associated VTEC outbreak in Denmark, September–November 2012 [2]

Denmark faced an outbreak of verocytotoxin-producing *E. coli* (VTEC) O157:H7 infections in autumn 2012. Thirteen cases were diagnosed, eight of which had haemolytic uraemic syndrome (HUS). Epidemiological investigations suggested ground beef as the vehicle of the outbreak. The outbreak strain had a rare toxin gene subtype profile: *eae*, *vtx1a* and *vtx2a*, and a high proportion of HUS (62%) among cases, a finding previously linked with the outbreak subtype profile. Toxin subtyping can be useful to identify high risk VTEC strains [2].

Status: Completed; rapid communication manuscript published in Eurosurveillance, January 2013.

## Ongoing multi-strain, food-borne hepatitis A outbreak with frozen berries as suspected vehicle: four Nordic countries affected, October 2012–April 2013 [3, 4]

A food-borne outbreak of hepatitis A in Denmark was notified to other countries on 1 March 2013. A case–control study identified frozen berries eaten in smoothies as potential vehicle. In the following weeks, Finland, Norway and Sweden also identified an increased number of hepatitis A patients without travel history. Most cases reported having eaten frozen berries at the time of exposure. By 17 April 2013, 71 cases were notified in the four countries [3]. Case control studies in Denmark and Sweden pointed to strawberries as the most like vehicle. Product investigation analysis done in joint collaboration between the four Nordic countries pointed to strawberries originating from North Africa and processed by a Belgian company to be the most likely vehicle. Based on circumstantial evidence, the Nordic supermarket chain Coop recalled and withdrew strawberries originating from North Africa and processed in Belgium from their stores.

Status: Completed; rapid communication published in Eurosurveillance in April; rapid communication update published in the same journal in July [3, 4].

### Research

#### Tuberculosis incidence among immigrants in Denmark from 1992–2011

Background: In Denmark, immigrants comprise 8% of the population but account for 60% of annual tuberculosis (TB) cases. In 2011, 60% of immigrants to Denmark came from high-TB incidence countries, and two of the ten countries accounting for the largest number of immigrants faced high rates of multidrug-resistant TB. To determine whether post-entry screening should be initiated, we estimated the risk of TB among immigrants arriving in Denmark in 1992–2011 and measured it as a function of time since entry.

Methods: We cohorted immigrants included in the civil registration system (CRS) who had arrived in 1992–2011 and extracted time since entry and continent of origin. We used CRS identifiers to link cohort participants with TB cases identified through the Danish National Tuberculosis surveillance database. For 1997–2011, we obtained the immigration status from the Danish Immigration Register. We estimated incidence rate ratios (RRs) for TB using log-linear Poisson regression.

Results: In 1992–2011, 621 850 immigrants entered Denmark (Median age: 23 years; interquartile range: 19–29; 50% were male). We identified 2 442 TB cases (overall TB rate: 607 per 100 000 person-years for sub-Saharan Africans and 124 per 100 000 for Asians). Compared with others, immigrants who arrived in the last 12 months (RR: 2.7, 95% confidence interval (CI): 1.8–4.2) or from sub-Saharan Africa (RR: 103; 95% CI 77–140) were at a higher risk of TB. Also at a higher risk were asylum seekers (RR: 2.2, 95% CI: 1.5–3.34).

Conclusions: The groups that are at higher risk of TB are recently arrived immigrants, those arriving from highendemic countries and those seeking asylum. Post-entry TB screening, including an offer of free treatment and followup, could accelerate a decline in TB incidence.

Status: Ongoing, data analysis completed, article draft in progress. Abstract has been presented at the Society for Epidemiologic Research (SER) conference in Boston, June 2013, and at the European Congress of Epidemiology in Denmark, August 2013. Abstract Presented at ESCAIDE, November 2013.

### **Teaching experience**

#### Epidemiology for fourth-semester medical students at the University of Copenhagen

A methodology course in Epidemiology for medical students is mandatory to all fourth-semester medical students. I taught fifteen classroom lessons of 45 minutes in autumn 2012 and again in spring 2013. For detailed information on the course, please refer to: <u>http://kurser.ku.dk/course/smea09020u/2013-2014</u>.

Status: Completed

### Scientific communication

#### **Oral communication**

- Three oral communications delivered at ICCH15 conference, Fairbanks, Alaska USA in August 2012 [5, 6, 7].
- Oral presentation of the Nordic hepatitis A outbreak to clinicians at Hvidovre University Hospital, Copenhagen, and to the Food Authority Network meeting, Copenhagen.
- Communication on the hepatitis A outbreak through the Danish Medical Bulletin, available from: <u>http://www.ugeskriftet.dk/portal/page/portal/LAEGERDK/UGESKRIFT\_FOR\_LAEGER?public\_visningsType=1</u> <u>5&public\_modtager=5&public\_nyhedsId=89195</u>

#### Manuscripts

- Rapid communication on VTEC outbreak published in Eurosurveillance, January 2013 [2]
- Rapid communication on multi-state Hepatitis A outbreak published in Eurosurveillance, week 17 and 27, 2013 [3, 4]
- Regarding Greenlandic research: two manuscripts submitted and published in 2012.
- Please see reference list for details [8, 9]

I am the author and co-author of eleven weekly SSI newsletters (EPI-NEWS); please see reference list for details [11-21].

## **Publications and presentations**

1. Kjelso C, Ethelberg S, Dorleans F, Soborg B, Mølbak K, Muller L. European outbreak of *Salmonella* Strathcona caused by small tomatoes, August–November 2011. [Oral presentation by Kjelso C at ESCAIDE 2012 in Edinburgh]

2. Soborg B, Lassen SG, Müller L, Jensen T, Ethelberg S, Mølbak K, Scheutz F. A verocytotoxin-producing *E. coli* outbreak with a surprisingly high risk of haemolytic uraemic syndrome, Denmark, September-October 2012. Euro Surveill. 2013 Jan 10;18(2). doi:pii: 20350.

3. Gillesberg Lassen S, Soborg B, Midgley SE, Steens A, Vold L, Stene-Johansen K, et al. Ongoing multi-strain foodborne hepatitis A outbreak with frozen berries as suspected vehicle: four Nordic countries affected, October 2012 to April 2013. Euro Surveill. 2013 Apr 25;18(17):20467.

4. Nordic outbreak investigation team. Joint analysis by the Nordic countries of a hepatitis A outbreak, October 2012 to June 2013: frozen strawberries suspected. Euro Surveill. 2013;18(27):pii=20520.

5. Soborg B, Melbye M, Wohlfahrt J, Andersson M, Koch A. Genetic susceptibility to tuberculosis in Greenland – Use of the Greenlandic family relations database. Oral presentation at ICCH15, Fairbanks Alaska, USA, August 2012.

6. Soborg B, Børresen ML, Andersson M, Koch A, Nielsen NO. Cytokine responses in relation to BMI and chronic infections among Inuit in Greenland. Oral presentation at ICCH15, Fairbanks Alaska, USA, August 2012

7. Byberg S, Soborg B, Andersson M, Bjerregaard P, Jørgensen ME. Diabetes is a risk factor for tuberculosis in the Inuit population of Greenland. Oral presentation held by Bybjerg S at ICCH15, Fairbanks Alaska, USA, August 2012.

8. Byberg S, Soborg B, Andersson M, Bjerregaard P, Jørgensen ME. Diabetes is a risk factor for tuberculosis in the Inuit population of Greenland. Eur Respir J. 2012 Nov;40(5):1289-91. doi: 10.1183/09031936.00039612

9. Nielsen NO, Soborg B, Børresen ML, Andersson M, Koch A. Cytokine responses in relation to age, gender, body mass index, *Mycobacterium tuberculosis* infection, and otitis media among Inuit in Greenland. Am J Hum Biol. 2012 Oct 17.

10. Soborg B, Wohlfahrt J, Andersson M, Ethelberg S, Andersen P, Mølbak K. The tuberculosis incidence among immigrants in Denmark from 1992 – Is it time to screen? Abstract accepted to Annual Society of Epidemiologic Research meeting, Boston, USA, 2013 and to the European Congress of Epidemiology, 2013

#### Weekly newsletters

11. Soborg B, Cowan S. Hepatitis A yearly report 2010, week 40, 2011. Available from: http://www.ssi.dk/English/News/EPI-NEWS/2011/No%2040%20-%202011.aspx

12. Soborg B, Cowan S. Acute and chronic hepatitis B yearly report 2010, week 47, 2011. Available from: http://www.ssi.dk/English/News/EPI-NEWS/2011/No%2047%20-%202011.aspx

13. Andersen P, Soborg B. Selected vector-borne viral diseases, week 6, 2012. Available from: <u>http://www.ssi.dk/English/News/EPI-NEWS/2012/No%206%20-%202012.aspx</u>

14. Soborg B, Cowan S. Acute and chronic hepatitis C, 2011, week 9, 2012. Available from: <u>http://www.ssi.dk/English/News/EPI-NEWS/2012/No%209%20-%202012.aspx</u>

15. Soborg B, Ethelberg S, Mølbak K. Gender differences in notifiable diseases, 20012011, week 11, 2012. Available from: <u>http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2011%20-%202012.aspx</u>

16. Wojcik O, Cowan S, Christiansen A.H, Soborg B. Hepatitis B, HIV and syphilis screening of pregnant woman, 2011, week 14–15, 2012. Available from: <u>http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2014-15%20-%202012.aspx</u>

17. Soborg B, Hoffmann S, Cowan S. Gonorrhoea 2011, week 36, 2012. Available from: <u>http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2036%20-%202012.aspx</u> 18. Soborg B, Hoffmann S, Cowan S. Syphilis 2011, week 37, 2012. Available from: http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2037%20-%202012.aspx

19. Soborg B, Müller L, Lassen SG, Ethelberg S, Mølbak K, Scheutz F. VTEC O157 outbreak September–October 2012. Available from: <u>http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2045%20-%202012.aspx</u>20. Soborg B, Cowan S, Midgley S, Vestergaard HT. Hepatitis A yearly report 2011, week 49, 2012. Available from: <u>http://www.ssi.dk/English/News/EPI-NEWS/2012/No%2049%20-%202012.aspx</u>

21. Cowan S, Christiansen AH, Søborg B. Hepatitis B, HIV and syphilis screening of pregnant women, 2012. Lassen SG, Søborg B. Hepatitis A outbreak caused by frozen strawberries continues in Denmark – Cases observed across the Nordic countries. Available from: <u>http://www.ssi.dk/English/News/EPI-NEWS/2013/No%2022%20-%202013.aspx</u>

## Supervisor's conclusions

Bolette Søborg was part of the first round of 'Member-State track EPIET fellows', and her success has proven the value of this approach. Despite the fact that Bolette was already an experienced epidemiologist, the EPIET programme had a lot to offer to her: excellent training modules, qualified supervision, a strong focus on field epidemiology, a growing network, and a European perspective – factors which all contributed to the development of competencies that will not only benefit Bolette but also the Danish public health system.

During her two-year fellowship at the Department of Infectious Disease Epidemiology at SSI, Bolette was an integral part of the department and a highly productive member of staff. Bolette also showed herself as a highly positive, constructive and enthusiastic colleague, with whom it was always a pleasure to work. While still seeing to her core duties as a staff member, Bolette, in her function as an EPIET fellow, could engage in a number of projects and in three outbreak investigations: she took part in a *Salmonella* outbreak investigation and was the driving force in the investigations of an international outbreak of hepatitis A and a serious outbreak of HUS infection, which both led to publications in Eurosurveillance. Bolette conducted a complex TB study involving large-register datasets and complex statistical analysis. Much of Bolette's work during her fellowship had a clear and direct public health relevance. Two projects in particular deserve mentioning. Analysing surveillance data of hepatitis A, conducted the initial case interviews and was responsible for a case-control study which in effect solved the outbreak and later led to the retraction of the food vehicle in Scandinavia. Second, Bolette's work on the risk of TB associated with immigrants in Denmark convincingly identified short- and long-term risks associated with particular groups of the Danish population, a finding which has a strong prevention potential.

## **Next steps**

Upon completion of her fellowship, Bolette will finish her training in public health medicine. After graduating from the EPIET programme, she will work in the Danish Health and Medicines Authority, Department of Hospital Services and Emergency Management, advising the Danish Ministry of Health on issues related to infectious diseases.