



EPIET REPORT

Summary of work activities

Anneke Steens

European Programme for Intervention
Epidemiology Training (EPIET), 2011 cohort

Background

Pre-fellowship short biography

Prior to EPIET, Anneke Steens worked for two years as an infectious disease epidemiologist at the Epidemiology and Surveillance unit of the Centre for Infectious Disease Control, Dutch National Institute for Public Health and the Environment (RIVM), working on influenza and serological surveys. Before that, she worked three years as a researcher on the role of the central nervous system in fatigue in multiple sclerosis patients at the medical physiology department of the University Medical Centre Groningen, the Netherlands. She has a master in Biology and a master in Clinical and Psychosocial Epidemiology.

EPIET assignment

In September 2011, Anneke Steens started as an EPIET fellow at the Department of Infectious Disease Epidemiology at the Norwegian Institute of Public Health, Norway.

Fellowship projects

Surveillance project

What are the most important infectious diseases among those 65 years of age and older? A comprehensive analysis on notifiable diseases, Norway, 1993–2011^{1,2}

Background: Due to the aging population, the burden for the healthcare system might increase and require changed public health priorities. As infections occur more frequently and are often more severe at older age, we inform priorities by describing the incidence and trends of infectious diseases (ID) among the 65+ population in Norway.

Methods: We included all eligible cases of the 58 IDs notifiable to the national notification system between 1993 (case definitions established) and 2011. We calculated current incidences of IDs by averaging annual incidences over the last five years (2007–2011) in order to get stable estimates for ranking. We determined trends by the change in

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Stockholm, May 2014

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incidence from 1993 onwards. We used incidence rate ratios (IRRs) to compare results of those aged 65 and over with those aged 20–64 years.

Results: Pneumococcal invasive disease was the most common ID among people aged 65 and over (incidence 58/100 000), followed by pertussis (54/100 000) and campylobacteriosis (30/100 000). For most IDs the incidence did not change over time, although the incidence of MRSA infections increased from 1/100 000 in 1995 (first year of notification) to 14/100 000 in 2011.

Overall, fewer cases were notified among people aged 65 and over compared to 20–64-year-olds (IRR=0.73). The IRRs of each of the invasive bacterial diseases and antibiotic resistant infections were above 1.5 (i.e. more common in people aged 65 and over than in 20–64-year-olds), while the IRRs for each food- and waterborne disease, blood-borne disease/STI and (non-invasive) vaccine-preventable disease were below 1, with the exception of tetanus.

Conclusions: Our results of a broad number of diseases over a long time span indicate that focusing public health efforts on preventing invasive bacterial disease and antibiotic-resistant infections would ensure a greater impact on the incidence of IDs among persons 65 years of age or older.

Status: Article published in BMC Infectious Diseases

Quality control of TB surveillance. A study to evaluate tuberculosis surveillance (MSIS) in Norway by linking MSIS data to the National Patient registry³

Background: This study assessed the completeness of tuberculosis (TB) surveillance in Norway and assessed whether linkage of the TB surveillance register (MSIS) with the Norwegian Patient register (NPR) can replace the current system in which MSIS collects data from hospital pharmacies to increase completeness of MSIS.

Methods: We linked data from MSIS with NPR, using the personal identifier unique to every Norwegian citizen, and compared the result for completeness and similarity. For a selection of cases registered in NPR but not in MSIS, we checked the hospital journals to determine the correctness of the TB diagnosis in NPR.

Results: First, as most TB cases are immigrants to Norway who often have a temporary identifier not registered in MSIS, linkage of MSIS with NPR would be difficult. Second, deficiencies in coding of tuberculosis in hospitals with erroneous use of the ICD-10 code lead to errors in the NPR. Third, the ICD-10 system does not distinguish between latent tuberculosis not requiring treatment and latent tuberculosis requiring treatment, making it impossible to distinguish between these two forms of latent tuberculosis in NPR data. In contrast, only treatment-requiring latent tuberculosis is notifiable to MSIS and comparisons between registries are difficult.

Conclusions: Overall, linkage of NPR and MSIS cannot replace the quality assurance using data from hospital pharmacies. A higher degree of detail in the ICD-10 system with a specific code for treatment-requiring latent tuberculosis would improve the utility of NPR data in this context. To enhance the possibility for other diseases to link MSIS with NPR, MSIS should register the temporary identification in addition to the personal identifier.

Implementation of our recommendations: From the next revision of MSIS onwards, the temporary identification number will be collected for all TB notifications. Furthermore, from January 2014 onwards, a new ICD-10 code will be used for latent tuberculosis (Z22.30).

Status: Internal report (in Norwegian) completed. Results are communicated further through an annual report.

Outbreaks

Suspected food poisoning outbreak in a canteen in Stavanger^{4,5}

Background: On 27 June 2012, several people reported to be ill after having eaten in a canteen in Stavanger that serves 200 people daily. The food safety authorities decided to assess the extent of the outbreak and identify possible risk factors. The Norwegian Institute of Public Health assisted with an analysis of the study.

Methods: In a cohort design, 200 employees were invited to fill out a questionnaire. We determined the number of people exposed, the number of ill people among those exposed and unexposed, attack rate (AR) and risk ratios (RR), with 95% confidence intervals (95% CI) for all different food items. The odds ratio (OR) for becoming ill was calculated using multivariable logistic regression analysis in Stata.

Results: 69 people responded to the questionnaire (response rate=33%). Thirty-two of the respondents reported gastrointestinal disease during the specified time period. The pasta salad with chicken served on the buffet on 20 June 2012 had the highest OR (3.8 95% CI 1.3–11.8); 55% of cases ate the salad. In a second analysis with a narrower (time-wise) case-definition, illness was also associated with pepper mackerel (7.8 95% CI 1.6–37.4; 38% of cases exposed). The median duration of illness among the cases that ate chicken pasta salad was significantly longer (8.5 versus 2.5 days) than among the cases that did not eat chicken pasta salad.

In addition to the cohort study, the food authorities visited the canteen and found some deviations from the protocols. The temperature control log, for example, showed that the temperature of the buffet where the food was presented, had been too high on some occasions.

Conclusions: The pasta salad with chicken most likely caused the outbreak. Most cases ate the salad, and it was served one day before most became sick, thereby fitting well the time of onset of the outbreak. It was produced the day before serving, and was stored in the fridge overnight. The difference in reported symptoms between those cases who ate the chicken pasta salad and those who did not indicates that symptoms could have also been caused by other factors. Status: Outbreak report completed

Outbreak investigation of suspected food poisoning at a pre-confirmation camp⁶

Background: During a youth camp in week 32 (6–10 August 2012), several participants became ill with gastroenteritis. As more youth camps would be held at the same location, the cause of the outbreak was investigated.

Methods: We conducted a retrospective cohort study investigation by inviting 198 participants to fill out a questionnaire. We determined the number of people exposed, the number of ill people among those exposed and unexposed, the attack rate (AR) and risk ratios (RR) with 95% confidence intervals (95% CI) for all food items. The OR for becoming ill was calculated using multivariable logistic regression analysis in Stata.

Results: 96 participants responded to the questionnaire (response rate=48%). Of these, 34 reported symptoms of gastroenteritis. Two participants reported symptoms starting on Wednesday morning/afternoon; the rest reported symptom onset ranging from Thursday evening to Saturday morning, with one later case. Potatoes served on Wednesday had the highest RR (9.8, 95% CI 1.4–67.7) and could explain most of the cases (97%). The reported symptoms suggest a norovirus outbreak.

The food safety authorities visited the camp location and did not find serious objections of the cleanliness or hygienic routines in the kitchen. The water supply was tested and showed good bacteriological/physical quality.

Conclusions: Boiled potatoes are not a common source for gastroenteritis outbreaks, but they may have been infected during self-serving/food-handling by already ill persons as some participants were already ill before the large outbreak started. The potatoes could explain most of the cases; they were served one day before most became ill, which fits well temporally with the estimated period of exposure assuming a norovirus outbreak.

Status: Outbreak report completed

Norovirus outbreak during a Christmas dinner in a hotel in Oslo, December 2012⁷

Background: On 13 December 2012, the Food Safety Authority (FSA) regional office in Oslo notified the Norwegian Public Health Institute (FHI) of 30 persons who fell ill after a Christmas dinner on 7 and 8 December at a hotel in Oslo. The hotel suspected oysters as the cause of the outbreak, based on reports from guests, and norovirus was suspected to be the infectious agent. At the same time, two other outbreaks linked to Christmas parties (one in another hotel of the same chain) were reported elsewhere in the country. FHI assisted the municipal health officer and the FSA with the investigation.

Methods: In a retrospective cohort design, we invited all guests who ate at the hotel on the weekend of 7–8 December, 2012 to fill out a questionnaire on gender, age, illness, symptoms, and consumed food items. We determined the number of people exposed to the various food items, the number of ill people among those exposed and unexposed, the attack rate (AR) and risk ratios (RR) with 95% confidence intervals (95% CI) of all different food items. ORs were determined using multivariable logistic regression. A case was defined as someone having suffered from at least one of the following gastrointestinal symptoms between 7 December 2012 and 12 December 2012: diarrhoea, vomiting, nausea, and/or abdominal pain for more than 12 hours, and who ate from the buffet.

The regional food safety authority traced back the oysters.

Results: Of 170 persons who responded to the questionnaire, 41 reported illness (AR 24%). Cases occurred both after the dinner on Friday (17/92; AR 18%) as well as after dinner on Saturday (20/71; AR 28%). The incubation period ranged between 6 and 112 hours (median 36 hours). Most cases recovered within 2 days, but some (7=19%) remained ill for 4 days or more. Reported symptoms included abdominal pain (76%), diarrhoea (70%), nausea (59%), fever (49%), and/or vomiting (43%). The analytical analyses indicated that oysters were the likely cause of the outbreak, with a relative risk of becoming ill after having eaten oysters being 10.2 [5.3–19.8]. The attack rate among those who ate oysters was 74%, and 76% of the cases had eaten oysters.

The importer of the oysters did not have any oysters of the same batch left, but oysters from two later batches from the same importer tested positive for norovirus.

Conclusions: Epidemiological evidence suggested that oysters served on 7 and 8 December caused the norovirus outbreak. Oysters still available at the importer were destroyed. The company recalled all oysters of the infected batch, and an international message was sent through the Rapid Alert System for Food and Feed (RASFF) as oysters had been distributed to various countries.

This outbreak was unrelated to the other outbreaks that occurred simultaneously in Norway, as they were caused by other infectious agents (data not shown).

Status: Outbreak report completed

Investigating an increase in hepatitis A patients without travel history: a domestic investigation and a multi-strain multi-state investigation⁸⁻¹²

The Nordic countries faced a food-borne outbreak of hepatitis A that started in October 2012 and was ongoing with 103 reported cases as of 27 June 2013. A case-control study in Denmark, Finland, Norway and Sweden, combined with trace-back investigations, identified frozen strawberries as the likely cause of the outbreak. The origin of the berries is still being investigated.

Status: Two articles have been published in Eurosurveillance (co-author)

Investigating a cluster of hepatitis A patients with travel history to Egypt¹³

Starting in November 2012, an increase in cases of hepatitis A in tourists returning from Egypt was reported from several European countries. By 24 April 2013, 80 HAV cases in travellers with symptom onset after 1 November 2012 visiting different areas in Egypt were reported. Four cases from Norway, six cases from the Netherlands and five cases from England shared an identical hepatitis A viral RNA sequence. This increase in cases suggests that vaccination recommendations for travellers to hepatitis A endemic countries should be reinforced.

Status: The outbreak has been published in Eurosurveillance (co-author)

Analysis of a cohort investigation of an outbreak among hotel guests in Turkey

Background: The Norwegian media reported a gastroenteritis outbreak with at least 34 children hospitalised among guests of a hotel in Alanya, Turkey. *Shigella sonnei* and *Salmonella* enteritica were found in patients from Norway, Finland, Sweden and Denmark.

Methods: A cohort study was performed among Norwegians who had been staying at the hotel at the end of July. About 400 persons were invited to fill out an online questionnaire. Based on the answers, we defined a case as a person who stayed at the hotel between 15–31 July and suffered from diarrhoea for two days or longer between 19 July 2013 and 10 August 2013. We excluded individuals who were ill for 13–24 hours.

Results: 144 persons responded to the questionnaire (response rate=36%). Of the 137 respondents who met the case definition (attack rate=35%). The first case became ill on 20 July, the outbreak peaked on 27–29 July and the last case occurred on 9 August, suggesting a point source outbreak with subsequent secondary cases. The (multivariable) regression analysis focussing on those cases that were ill during the peak showed the highest RR for slush (7.8 [1.9–31.4]), with an attack rate (AR) of 34%. The association increased as the dose increased. Swimming in the baby pool was also significantly associated with becoming a case (RR 3.3 [1.5–7.2], AR 41%).

Conclusions: Epidemiological evidence suggested that the outbreak of gastroenteritis among guests of the hotel at the end of July 2013 was caused by contaminated slush, but subsequent secondary transmission is also likely. Our study could not exclude the baby pool as a cause of the outbreak.

Status: Outbreak report completed. Summary of the report sent to the Turkish authorities and to the public health institutes of the other Nordic countries.

Research

Prompt effect of replacing the 7-valent pneumococcal conjugate vaccine with the 13-valent vaccine on the epidemiology of invasive pneumococcal disease in Norway¹⁴

Background: The introduction of PCV7 in the childhood immunisation programme in Norway in 2006 decreased the vaccine-type (VT) invasive pneumococcal disease (IPD) incidence in all age groups, and increased the non-vaccine-serotype (NVT) IPD incidence. The last phenomenon suggests serotype replacement. As the 13-valent pneumococcal conjugate vaccine (PCV) replaced the 7-valent PCV in 2011, further changes in epidemiology are expected. Close monitoring of IPD therefore remains important in order to quickly detect changes.

Methods: In this observational retrospective population-based cohort study we used data notified nationally between 1 January 2004 and 31 December 2012 to determine age-specific VT- and NVT-IPD incidences. The diversity in serotype distribution per year was analysed by using the Simpson's diversity index. PCV vaccine coverage and information on vaccine failure were obtained from the vaccination registry.

Results: The incidence of VT-IPD decreased in both the targeted and non-targeted age groups since PCV7 introduction and further after PCV13 introduction. Since introduction, there have only been two IPD cases with vaccine failure. The decrease in PCV7-incidence in non-targeted age groups became larger in later years, indicating a lag phase for the indirect protection and suggesting that the indirect protection of PCV13 will increase in coming years. The incidence of some NVT increased after PCV13 introduction. As this coincided with an increase in Simpson's diversity index in the targeted age group, it suggests that serotype replacement occurs again.

Conclusion: Our results indicate a very high effectiveness of the 2+1 vaccine schedule and suggest indirect protection of the non-targeted population. Since serotype replacement seems to occur again, it is important to continue monitoring of IPD so that adaptations to recommendations can be promptly issued.

Status: Article published in *Vaccine*

Predictions of serotype distribution after introduction of the 13-valent pneumococcal vaccine in the national immunisation programme in Norway

Background: Childhood immunisation with 7-valent pneumococcal conjugate vaccine (PCV7) since 2006 led to a decrease in vaccine-type (VT) invasive pneumococcal disease (IPD) and an increase in non-vaccine type (NVT)-IPD, also in non-targeted age groups. A 13-valent PCV (PCV13) replaced PCV7 for childhood immunisation in 2011. We aimed to predict how this would change VT and NVT IPD among people aged 50 and over in order to inform decisions on vaccination strategy.

Methods: We determined the monthly number of IPD caused by serotypes included in PCV13 (VT-PCV13), not included in PCV13 (non-PCV13) or included in PPV23 (VT-PPV23) in the people aged 50 and over between 1 January 2004 and 30 June 2013. We defined segmented quasi-Poisson models to characterise the recent trend (2004–June 2013) in monthly IPD counts, and used these models to predict expected seasonal counts for July 2013–June 2017.

Results: Preliminary results indicate that IPD with VT-PCV13 will decrease from 191 in 2012–2013 to 76 (95% PI 47–104) in 2016–2017. Non-PCV13 IPD will increase from 297 to 369 (95% PI 326–412). This will lead to a net decrease in VT-PPV23 IPD from 372 to 333 cases (95% PI 289–377). Overall, IPD among the people aged 50 and over will decrease until 2015–2016 and then stabilise at 445 (95% PI 391–499) if no change in vaccination policy occurs.

Conclusion: These results call for increased uptake of PPV23 among older adults. There is need for pneumococcal vaccines conferring broader protection against IPD.

Status: Preliminary results presented at the International Symposium on Pneumococci and Pneumococcal Diseases in Hyderabad, March 2014.

Scientific communication

- Two poster presentations and one oral presentation at ESCAIDE 2012 ¹
- Presentations of the South Sudan mission at Epicentre in Paris, at the Scientific Teleconference for European Epidemiology and Public Health Microbiology fellows (TEAM), at the Division of Communicable diseases at FHI and at the infectious diseases surveillance department (SMAO) at FHI
- Presentation of the evaluation of the TB surveillance system at the National Health Registers meeting in Norway
- Four interviews by telephone with national newspapers about outbreaks ^{5,10-12}
- Three manuscripts published as first author ^{2,14,16}; co-authored three rapid communications for Eurosurveillance ^{8,9,13}

Teaching experience

Lecture on time series analysis during the EPIET meeting

One-hour oral presentation, presented at the EPIET meeting at the FHI. It covered a summary of the time-series analysis (TSA) course of EPIET and explanation on why and how to create a TSA model.

Lecture on malaria at the Summer School of the University of Oslo

Three-hour lecture for the Summer School Program on International Community Health: Global Health at the University of Oslo. The lecture covered global malaria prevention and control strategies, and Millennium Development Goal 6 and malaria control: current global achievements and challenges. The audience was international with strong participation from developing countries; most participants worked in public health (medical doctors, nurses and policymakers).

Oral lecture and workshops for public health nurses at the Nordic School of Public Health NHV, Göteborg, Sweden

One lecture of 45 minutes and two three-hour workshops (including a short presentation, plenary discussions and facilitation during exercises). The audience was Scandinavian and worked in public health (e.g. infectious disease nurses). The material that was used was already available, but presentations were customised for this event.

Lecture at the department of infectious disease epidemiology – analysis of an outbreak

This lecture, written by the lecturer herself, covered outbreak analysis. An oral presentation of 20 minutes was given to colleagues at the Department of Infectious Disease Epidemiology.

International missions

Participation in an international mission in South Sudan with Epicentre

Tasks included obtaining surveillance data, making graphs of the surveillance data, performing rapid diagnostic screening at different clinics, and writing a report.

The mission investigated an increase in the number of malaria cases in the maternal and childhood departments run by MSF-OCP in Aweil State Hospital, South Sudan. The investigation was performed together with Epicentre, for MSF-OCP, and included collection of available surveillance data, rapid diagnostic testing in several clinics, and support for the development of an operational plan to control the increase of cases. Results indicated an increase in malaria in all age groups, both for long-time residents and those who recently relocated to the area. Mobile clinics were set up in those areas that reported the highest number of cases.

Status: Completed

Miscellaneous

Participation in the working group on revised recommendations on the use of pneumococcal vaccines in risk groups^{15,16}

Background: For decades, vaccination with the 23-valent polysaccharide pneumococcal vaccine (PPV23) has been recommended to risk groups in Norway to prevent invasive pneumococcal disease (IPD). In autumn 2011, a 13-valent pneumococcal conjugated vaccine (PCV) was licensed for use in adults, which might have a higher effectiveness than PPV23 due to different immunogenic properties. This called for a revision of vaccine recommendations for risk groups.

Methods: We searched the literature for (medical) conditions that make people more at risk for IPD, vaccine effectiveness (VE), and safety in risk groups. The percentage of IPD cases in 2012 caused by vaccine serotypes was determined on the basis of national surveillance data. We quantified the risk per risk group and elaborated step-wise recommendations on the need for vaccination, choice of vaccine, and timing of revaccination.

Results: Based on the 187 reviewed articles, medical conditions and vulnerability for IPD were heterogenic in most risk groups, with asplenic patients at highest risk. The coverage of serotypes that caused IPD was higher for PPV23 (79%) than PCV13 (46%). VE of both vaccines depends on the level of immunosuppression. Only for HIV/AIDS patients, sufficient data were available to show an additional effect of PCV13 when used in combination with PPV23.

Conclusion: The need for vaccination should be based on a risk assessment either for entire risk groups, or following individual assessment. If vaccination is needed, PPV23 is recommended, as PCV13 covered a small percentage of cases. Additional use of PCV13 is recommended for individuals with HIV/AIDS and asplenia. However, PCV13 should be considered in other risk groups depending on the severity of risk conditions, degree of risk for IPD, VE, and timing related to immunosuppressive therapy.

Status: Article published in *Epidemiology and Infection*

Supervisor's conclusion

During her two-year fellowship at Folkehelseinstituttet, Anneke Steens was involved in multiple outbreak investigations, surveillance and research activities, and has developed a broad understanding of communicable diseases and public health. She has collaborated closely with the Vaccinology and Microbiology departments as well as within the Infectious Disease Epidemiology department. With her scientific and analytical skills she has contributed substantially to the field of pneumococcal infections and vaccination policy in Norway. Anneke quickly learned Norwegian, and her enthusiasm and positive attitude was highly valued by her colleagues. We are happy to continue our collaboration with Anneke after her EPIET fellowship has ended.

Next steps

In mid-September 2013, Anneke Steens started as a researcher at FHI and works, among others, on a study on the prevalence of carriage of pneumococci and the distribution of pneumococcal serotypes carried by children attending day-care centres in Norway. She had submitted a grant-application to the Norwegian Research Council for a PhD project on Implications of different pneumococcal dynamics among groups with and without underlying illness following changes in vaccination. Despite the fact that she did not get funded through the Norwegian Research Council, she can continue working on the PhD project at FHI. This project will include collaboration between FHI (Norway) and the RIVM (the Netherlands).

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