



Fellowship portfolio

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Dr. Anna Kuehne MPH

PAE Cohort 2014, Robert Koch Institute (RKI), Berlin

Background

Pre-fellowship short bio

Prior to PAE, Anna Kuehne worked at the Surveillance Unit of the Department for Infectious Diseases Epidemiology of the RKI in the area of burden of infectious disease modelling and surveillance system evaluation and improvement. From the RKI she has been seconded to WHO Headquarters for several months to support the global MERS taskforce as an epidemiologist [1]. Previously she completed a medical doctoral thesis about health and access to health care for undocumented migrants in Germany at the University of Hamburg [2] and a Master in Public Health at the London School of Tropical Medicine and Hygiene. Anna Kuehne studied medicine at the University of Hamburg, Leipzig and Santiago de Cuba and worked as a clinician for critical care at the University Hospital of Leipzig prior to her change of career to epidemiology.

EPIET/PAE assignment

In September 2014, Anna Kuehne was assigned to the Respiratory Infections Unit of the RKI. Over the course of this two-year training fellowship, the goal is to gain experience in conducting outbreak investigations, analysing, implementing or evaluating surveillance systems, the planning, development and execution of a research project, presentation of results and teaching epidemiology.

Fellowship projects

Surveillance project

1. Find and treat or find and lose? Screening newly arrived asylum seekers for infectious pulmonary tuberculosis in Germany 2002-2014

Background: Tuberculosis (TB) is a notifiable disease in Germany. In Germany 5,865 cases of active tuberculosis were notified in 2015 and mark an end to the decreasing trend in annual TB case notifications. Demographic changes and migration influence TB incidence in Germany and the early detection with active case finding and their access to timely and complete treatment will determine possibilities to meet WHO TB elimination goals. While passive case finding, i.e. cases that consulted a physician with TB symptoms and were consecutively identified, is still the most common source of new cases in 2015, the proportion of cases identified by active case finding increased from 14% to 27% from 2002 to 2015. Among active case finding, the screening of asylum seekers is yielding most cases: Asylum seekers undergo compulsory chest x-ray screening at arrival centres in order to identify infectious pulmonary TB cases early and initiate timely treatment. We therefore aimed to assess

whether TB patients identified by screening for active pulmonary TB among asylum seekers had an equally successful and completely reported treatment outcome as TB patients diagnosed subsequent to clinical presentation in Germany.

Methods: We analysed characteristics and treatment outcomes of TB cases notified between 2002 and 2013 (as of 1 March 2015) in Germany stratified by the mode of case finding. We defined a successful treatment outcome as completed therapy (with or without bacteriological confirmation) and loss to follow-up as lack of information on outcome (missing, not-determined, transferred out). To adjust for demographic and clinical factors confounding the association between the mode of case finding on treatment outcomes and loss to follow-up, we conducted a multivariable logistic regression interpreting coefficients in terms of odds ratios (OR) and 95% confidence intervals (CI). The association of the mode of case finding with the outcomes and loss to follow-up was adjusted for age and sex, country of origin, drug resistance, infectiousness, previous TB and severity of the disease. It was furthermore adjusted for changes in the data plausibility checks introduced in 2006.

Results: TB cases diagnosed because of symptoms (N=46,885) had a median age of 50 years, pulmonary TB in 78% (36,699/46,885) and smear positive TB in 48% (17,790/36,699) of pulmonary TB cases. Successful treatment outcome was notified in 75% (35,370/46,885), outcome was not determined in 2.7% (1,295/46,885), and additional 4.8% (n=2,246/46,885) had no information on outcome. TB cases identified by asylum seekers' screening (N=1,219) had a median age of 28 years, pulmonary TB in 90% (1,100/1,219) and smear positive TB in 27% (74/1,100) of pulmonary TB cases. 59% (719/1,219) had a successful treatment outcome, 10% (122/1,219) had an undetermined outcome, and additional 12% (143/1,219) no information on outcome.

Multivariable analysis indicates 2.3-times higher odds of asylum seekers identified by screening compared to patients diagnosed because of TB symptoms for a non-successful treatment outcome. Investigating in more detail patients with known outcomes and excluding all patients with missing information on outcome from the model still indicates 1.3-times higher odds for a non-successful treatment outcome for patients identified by screening asylum seekers compared to patients identified with TB symptoms. Furthermore, OR for loss to follow-up indicates 2.6-times higher odds for loss to follow-up for patients identified by screening asylum seekers compared to patients identified with TB symptoms.

Conclusion: While the lower proportion of smear positive TB among screened asylum seekers compared to symptomatic cases indicate an earlier diagnosis, treatment outcomes were less often successful and patients more often lost-to-follow up. Increased efforts are needed to have complete information on this key monitoring parameter for TB elimination.

Improvements in linking TB patients to treatment facilities to ensure sufficient follow up will be critical to secure screening benefits for asylum seekers and the communities.

Role and output: Primary investigator

Development of study protocol, data preparation, data analysis, data presentation and communication, manuscript preparation. Abstracts accepted for oral presentation at the conference of the national public health services (BVÖGD) in Reutlingen, Germany, 2016 [3] and the EUPHA Conference on Migrant and Ethnic Minority Health in Oslo, Stockholm, 2016 [4]. Manuscript completed and planned to be submitted for peer review to Eurosurveillance.

Supervisor: Lena Fiebig (RKI)

2. Migration status in surveillance data

(Project started before PAE/EPIET)

Background: Migration is an important factor impacting on infectious disease epidemiology. The timely identification of groups at risk and prevention needs resulting from migration is indispensable to adequately design and implement public health measures. It remains to be assessed to which extent surveillance data for notifiable diseases can directly generate meaningful migration-specific information. The objectives of this study are to review indicators of migration background utilized in the German infectious disease surveillance, as well as to assess their limitations.

Methods: We describe the indicators of migration used for mandatorily notifiable diseases and pathogens and their legal basis in the Protection against Infection Act and conduct a descriptive analysis of surveillance data for tuberculosis (TB), HIV and syphilis from 2002-2013.

Results: Migration status is collected only for five infectious diseases and operationalization varies. For TB (country of birth) and HIV (country of origin) a foreign origin was more frequent than for syphilis (country of origin); namely 46, 30 and 13% of cases with available information, respectively. In all three examples, there are indications of risk profiles that are specific for particular groups of migrants.

Discussion: A standardization of indicators of migration in infectious disease surveillance is important to enhance data comparability between diseases and pathogens as well as across countries. Routine surveillance already partly allows migration sensitive analyses, yet further research is needed to guide interpretation of the complex relationship between migration and infectious diseases and plan public health measures adequately.

Role and output: Primary investigator

Study protocol, data analysis, literature review, manuscript writing. Peer-reviewed manuscript completed and published [5]

Supervisor: Andreas Gilsdorf (RKI)

3. Outbreaks of infectious diseases in shelters of asylum seekers

(Project started before PAE/EPIET)

Background: The German Asylum Act entitles asylum seekers (AS) to preventive healthcare, however, little data is available about preventable infectious diseases affecting AS and spread of infectious diseases within centralized homes for AS. The study aims to identify common causes of infectious disease outbreaks in centralized homes of AS notified according to German Infection Protection Act (GIPA) to inform measures of prevention.

Methods: Outbreaks of infectious diseases are notifiable according to GIPA when caused by a notifiable disease and/or when posing a health-threat to the general public. German national GIPA notification-data from 01.01.2001 to 13.11.2013 was systematically searched for outbreaks reported to have occurred within centralized homes for AS followed by descriptive analysis of pathogens causing the outbreaks, number of cases and hospitalization-frequency.

Results: 77 outbreaks affecting 397 cases in centralised AS homes were notified. 33.8% of the 77 outbreaks were caused by vaccine-preventable-diseases (chicken pox, measles, meningococcal meningitis), 19.5% by common gastrointestinal pathogens (norovirus, rotavirus, salmonella), 15.5% by tuberculosis, 7.8% by scabies, 6.5% by giardia, 5.2% by influenza and 11.7% by others. 44.1% of the

397 cases were caused by vaccine-preventable-diseases, 24.5% by common gastrointestinal pathogens and 6.8% by tuberculosis. 20.6% of cases involved in the outbreaks were hospitalized. Hospitalization was highest among cases of shigella (100.0%), tuberculosis (66.7%), salmonellosis (44.0%) and measles (39.3%).

Conclusions: Vaccine-preventable-diseases and diseases/pathogens that can be detected by screening including tuberculosis were most common causes for notified outbreaks in centralized AS homes. They account for more than half of affected cases and subsequent hospitalizations. Despite limited representativeness and comparability, available notification-data offers a unique insight into distribution of communicable diseases affecting AS in centralized homes. Provision of vaccinations, screening and early treatment can possibly prevent onward transmission of infectious diseases not only to AS but as well to host communities.

Role and output: Primary investigator

Study protocol, data analysis, manuscript writing. Oral presentation at the German national public health services conference (BVOEGD) 2015, Rostock, Germany [6] and the meeting of working groups of federal and national level public health authorities on surveillance (BLAG) 4. July 2015. Peer-reviewed manuscript submitted and published [7].

Supervisor: Andreas Gilsdorf (RKI)

Summary of routine surveillance activities

1. Routine surveillance of Hepatitis C September 2014- December 2015

Weekly control of completeness and coherence of data reported for Hepatitis C death cases and infections in children as well as trend and cluster monitoring of national surveillance data. Anna Kuehne assisted in the preparation of information material for federal and local health departments regarding the changes in Hepatitis C case definition for mandatory national notification. Furthermore, Anna Kuehne participated and prepared internal meetings with the surveillance and data management unit concerning improvement of data quality of reported HCV cases. Anna Kuehne wrote the annual Hepatitis C surveillance report 2015 published in the German Epidemiological Bulletin [8].

2. Routine biweekly TB Meetings

Biweekly meeting to discuss current trends and data as well as tasks and requests (for information, publications, presentations) to the TB team from outside and inside the RKI.

3. Evaluation of TB treatment outcome classifications within the German surveillance system and adaption of the German Protection against Infection Act (IfSG)

Anna Kuehne assisted in the revise and adaptation of TB treatment outcome categories and reporting guidelines for local public health authorities and identified current inconsistencies and areas for improvement in treatment outcome reporting categories. In addition, Anna Kuehne commented and advised with other members of the TB team on the suggestions by the German Ministry of Health for changes of the IfSG with regards to TB screening and reporting.

4. RASFF Monitoring

Monitoring of the Rapid Alert System for Food and Feed of the European Commission for two months per year and information of local health authorities in case of relevant infectious disease related danger from food in Germany.

5. EpiLag Infectious Disease Surveillance Conference Call at RKI

The EpiLag conference call is a scientifically- structured platform for weekly exchange of information about current events related to infectious disease epidemiology between national level and federal states. Exchanges include information relevant to both national and international events in Germany and Europe. All epidemiological content is derived from an established, weekly search protocol. Following the protocol, the German Epidemiological Bulletin, ProMed, EWRS-, CDTR- and IHR reports are screened for relevant information to present at EpiLag. The telephone conference is prepared and protocolled on a four-monthly-basis by Anna Kuehne.

6. Infectious disease epidemiology on call service

To assure 24/7 reachability of the RKI an ongoing on call duty is established to assist the national focal point and to provide timely information to international and national health authorities, ministries and physicians about infectious disease related public health threats. Anna Kuehne assists the on call surveys about two weeks per year, including Christmas 2014.

Outbreak investigation

1. Cluster of Ebola cases associated with funeral preparations in Freetown, 2015

Background: From March 2014 to April 2015, Sierra Leone reported more than 8,500 cases of Ebola virus disease (EVD) including 3,490 deaths. On 26/02/2015 Western Area Emergency Response Centre (WERC) in Freetown received an alert about a death of an herbalist and initiated case investigation to confirm EVD-aetiology and identify source and contacts.

Methods: We defined a confirmed EVD case as anyone with laboratory diagnosis by polymerase-chain-reaction. We identified and traced contacts to minimize further transmission.

Results: The herbalist's exposure stemmed from treating Ebola patients. He died 25/02/2015 and was confirmed positive post-mortem. The preparation of his body for the burial resulted in a cluster of 13 cases (31% female, median age 28 years, case-fatality-ratio 62%): The index case, 10 secondary and two tertiary cases. Nine known contacts of the herbalist were traced, all developed symptoms between 06/03/2015 and 12/03/2015 and were confirmed positive. Another herbalist also had attended the body preparation of the index case but evaded line-listing. He died 17/03/2015, his body was prepared for burial, following delayed alert and laboratory confirmation. Eight known contacts of the second herbalist were traced. One developed symptoms 28/03/2015 and was confirmed positive. Again one additional contact evaded line-listing, fell ill 24/03/2015 and presented at a health-centre where he was confirmed positive. No additional cases ensued.

Conclusion: In this cluster linked to unsafe funeral preparations, the transmission of Ebola virus was a consequence of late alerts of deaths and evasions from contact tracing. Secondary cases among those appropriately contact-traced were identified early, enabling prevention of further transmission. To stop the outbreak, we recommend involvement of the community and education of herbalists, who play an important role in healthcare provision and burials.

Role and output: Primary investigator

Under the supervision of the field coordinator, Anna Kuehne was in charge of the coordination of outbreak investigation, case identification and active case search, case isolation, contact tracing, source identification, descriptive epidemiology, identification of epidemiological link, communication to District Ebola Response Centre Western Area, social mobilisation team and communities. Findings and recommendations were communicated in the end-of-mission report for WHO and in a poster accepted at ESCAIDE conference in Stockholm, Sweden, 2015 [9].

Supervisor: WERC Field Coordinator Jeff Gilbert (WHO)

Applied epidemiological research

1. Mortality, morbidity and health-seeking behaviour in Monrovia during the Ebola outbreak 2014-2015 – result from a mobile phone survey

Background: Since the Ebola outbreak has been declared in Liberia in March 2014 more than 10,500 Ebola cases – including over 4800 deaths – occurred; the majority was identified in Monrovia. However, official numbers are thought to underestimate the size of the outbreak. It is assumed that closure of health facilities and mistrust in existing structures also had an impact non-EVD morbidity and on mortality. To quantify morbidity and mortality and to describe the health-seeking behaviour in Monrovia Médecins sans Frontières (MSF) conducted a cell phone survey.

Methods: We conducted a cell phone based survey considering a recall period from the 14th May 2014 to the day of survey (December 2014- March 2015). We draw a sample of households, where at least one person in the household was connected to a cell phone network in Monrovia within the 30 days prior to the survey. We conducted structured interviews, covering household size, morbidity, cause of death and health seeking behaviour. We defined an Ebola-related death as any death meeting the current Liberian case definition. We calculated all-cause and Ebola specific mortality rates.

Results: The sample consisted of 6813 household members in 905 households. 277 household members were reported to be sick in the 30 days prior to the survey, 54% reported to have been sick with malaria. During the recall period 17 Ebola cases were reported of which 10 died (case fatality rate: 59%). Overall 55 deaths occurred during the recall period (crude mortality rate of 0.33/10,000 persons per day; 95%-CI: 0.25-0.43). Ebola attributable deaths are 10 of 55, indicating an Ebola specific mortality rate of 0.06 (95%-CI:0.03-0.11). 16% of the sick household members tried to access health care in a government-run health facility, 41% in a private health facility, 43% sought healthcare outside health facilities.

Discussion and conclusion: CMR was estimated well below the emergency threshold of 1/10,000 persons per day. Non-EVD-associated mortality in Monrovia does not appear to be higher than previous estimates for Liberia. Our results suggest excess mortality in the population directly resulting from Ebola. Substantial reported health-seeking behaviour outside of health facilities may suggest the need for adapted health messaging and improved access to health care.

Role and output: Co-investigator to Etienne Gignoux (Epicentre)

Adaptation of the study protocol and design, training surveyors, facilitate implementation in the field, data analysis and preparation of the final report to Epicentre and MSF and a manuscript for peer review publication. Manuscript published at *PLOS Neglected Tropical Diseases* [10].

Supervisors: Etienne Gignoux and Klaudia Porten (Epicentre)

2. Evaluation of a mass drug administration of Artesunate/Amodiaquine as malaria chemoprevention during the Ebola outbreak in Monrovia, Liberia, 2014

Background: In October 2014, during the Ebola outbreak in Liberia, malaria transmission continued, while healthcare-services were limited. Médecins Sans Frontières (MSF) implemented a mass drug administration (MDA) of malaria chemoprevention (CP) in Monrovia, to reduce malaria-associated morbidity, palliate the decreased access to healthcare and reduce admissions to Ebola-treatment-units for malaria-associated fever.

Methods: MSF carried out two rounds of MDA of Artesunate/Amodiaquine (ASAQ) targeting all residents of four neighbourhoods of Monrovia. We describe the MDA's scale, side effects and their impact on adherence and estimate its effectiveness. We systematically selected every 200th household in the distribution area for follow-up using a standardized questionnaire. We calculated proportions, allowing for cluster effect. We calculated adjusted incidence ratios (IR) using Poisson regression and compared prevalence differences (PD) pre- and post-MDA using a z-test. We extrapolated the PD to the target population.

Findings: In total, 1,259,699 courses of ASAQ-CP were distributed. Of all study participants (n=1136) > 90% received ASAQ-CP in both rounds. 52% initiated ASAQ-CP in round 1 and 22% in round 2; >75% of those not starting the CP reported not feeling sick or saving ASAQ for later. Adherence to the full course of ASAQ after initiation exceeded 90% in both rounds. Side effects were frequent but mild; experiencing side effects in round 1 was not associated with treatment initiation in round 2 (IR 1.0, 95%CI 0.49-2.1). The prevalence of self-reported malaria decreased from 4.2% in the month prior to round 1 to 1.5% after round 1 (p<0.001), indicating that 14,821 (95%CI 4,801-24,840) malaria episodes were averted in the target population. Reduction of self-reported malaria was larger among household members completing ASAQ-CP (PD=4.9%) compared to those not taking ASAQ-CP (PD=0.6%) in round 1 (p<0.001).

Conclusions: The reduction in reported malaria cases following the intervention suggests that MDAs may be effective in reducing malaria incidence and thus fever cases during Ebola epidemics. Despite high coverage of the MDA in Monrovia, initiation of malaria CP was low, possibly due to ongoing lack of healthcare services. We recommend future studies using comparison communities and laboratory diagnostic to determine the reduction of malaria incidence attributable to MDAs. Combining MDAs with bednet-distributions and improvements in healthcare might reduce the proportion of participants saving their CP for future malaria episodes.

Role and output: Primary investigator

Adaptation of the study protocol, training surveyors and data entry staff, study implementation, supervision of data entry, data analysis, preparation of final report to Epicentre and MSF and manuscript for peer review publication. Oral presentations at TEPHINET conference, Mexico City, Mexico, 2015 [11] and ESCAIDE conference, Stockholm, Sweden, 2015 [12] and presentation as a poster at ESCAIDE conference, Stockholm, Sweden, 2015 [13]. Manuscript accepted for publication in *PLOS One* [14].

Supervisors: Amanda Tiffany and Klaudia Porten (Epicentre) and Kostas Danis (EPIET)

3. Sexual health among migrants from sub Saharan Africa (MiSSA) living in Berlin

Background: Migration has an impact on the epidemiology of viral Hepatitis (HEP) and HIV in Germany and migrants from sub-Saharan Africa (MisSA) in Germany are particularly affected by HIV. In the last 10 years a total of 10-15% of all newly diagnosed HIV cases are MisSA, and approximately one third of them acquired HIV in Germany. Prevalence of HEP among MisSA in Germany is not known, but Western Africa, where most MisSA in Germany originate from, reports the highest prevalence of hepatitis B worldwide. There is limited information on knowledge, attitudes, behaviors and practices (KABP) regarding HIV, HEP, sexually transmitted infections (STI) and sexual health, as MisSA are not reached with surveys targeting the general population. To determine HIV, HEP and STI -information and -prevention needs of MisSA a KABP-survey was initiated in six study regions in Germany, the study in Berlin was planned and implemented by Anna Kuehne.

Methods/Design: This was a cross-sectional KABP-survey regarding HIV, HEP and STI among MiSSA living in Berlin using convenience sampling. The study design was developed as a community-based participatory health research (CBPHR) project: persons working in HIV/STI prevention with MisSA, key-persons from MisSA-communities and HIV/STI researchers were involved in all steps of the research process. From October 2015-December 2015 trained peer researchers recruited participants in Berlin. Potential modes of survey administration were interview or self-completion, and questionnaire was available in English, French and German. Questions on knowledge about HIV, HEP and STI were presented as true statements; participants were asked if they had known information before.

Discussion: We chose working with peer researchers for data collection to get access to a diverse sample of MisSA and reach particularly vulnerable sub-groups, such as MisSA without legal status. Being able to reach hard-to-be-reached is one of the big advantages of CBPHR. The active inclusion of the persons under study has resulted in higher acceptance of the study in the target community and ultimately leads to increased accessibility and better quality of collected data. Furthermore, the participation of MisSA in the development of study design and data collection assures a better understanding of the interests, needs and living conditions of this group.

Role and output: Primary investigator

Study protocol amendment for Berlin context, identification of local partner organisation, training and of and ongoing support for peer researchers and study implementation. Communication with peer researchers, African community and stakeholders in HIV prevention; facilitation of networking between different actors in HIV prevention and African community. Data entry and data analysis. Preparation of report for local stakeholders. Responsibilities for implementation and networking were shared with Adama Thorlie. Abstract submitted to ESCAIDE conference 2016 and was accepted for oral presentation [15]. For her master thesis for the MSc. Applied Epidemiology at the Berlin School of Public Health Anna Kuehne performed a multilevel logistic regression with random effect to identify sociodemographic determinants associated with HIV knowledge and testing [16]. Anna Kuehne is co-author of a manuscript about the study design submitted for peer-review. Manuscript for peer review about impact of HIV, hepatitis and STI knowledge on testing uptake in progress.

Supervisor: Viviane Bremer and Claudia Santos-Hövenner (RKI)

4. Estimating true STEC incidence from HUS notifications

(Project started before PAE/EPIET)

Background: Shiga toxin-producing *Escherichia coli* (STEC) is an important cause of gastroenteritis (GE) and life-threatening haemolytic uremic syndrome (HUS). Incidence of STEC-illness is largely underestimated in notification data, particularly of serogroups other than O157 (“non-O157”) because of their mild symptoms, and complex and disproportionately underutilized diagnosis. We estimated true incidence of STEC-associated HUS and STEC-GE in Germany to inform diagnostic-, prevention-, and surveillance-strategies.

Methods: Using HUS national notification data (2008-2012, excluding 2011) as starting point, we modelled annual incidence of STEC-illness separately for O157 and non-O157 STEC, taking into account the groups’ different probabilities of causing bloody diarrhoea and HUS, and the resulting difference in their ascertainment. Uncertainty of input parameters was evaluated by stochastic Monte Carlo simulations.

Findings: Median annual incidence of STEC-associated HUS and STEC-GE was estimated at 0.11 (95% CI 0.08-0.20), and 34.6 (95% CI 12-145) per 100,000 population, respectively. Notification data underestimated STEC-associated HUS and STEC-GE incidences by factors of 1.8 and 32.3, respectively. Non-O157 STEC accounted for 78% of all STEC-GE, 51% of all bloody STEC-associated diarrhoea and 32% of all STEC-associated HUS cases. Estimates were most sensitive to the proportion of HUS among laboratory-confirmed non-O157 STEC cases.

Interpretation: Non-O157 serogroups dominate incidence of STEC-GE and contribute significantly to STEC-associated HUS in Germany. This might apply to many other countries considering European surveillance data on HUS. Non-O157 STEC should be considered in parallel to STEC O157 when searching aetiology in patients with GE or HUS, and accounted for in modern surveillance systems for STEC illness.

Role and output: Primary investigator

Study protocol, data analysis, development of stochastic model, conducting the mathematical modelling, data interpretation, manuscript writing. Poster presented at Global VTEC conference 2015 in Boston, USA [17]. Oral presentation at ESCAIDE conference 2015 in Stockholm, Sweden [18]. Manuscript prepared and research published in peer-reviewed journal *Epidemiology&Infection* [19].

Supervisor: Dirk Werber (RKI/LaGeSo Berlin)

5. Differentiating high and low suspect Ebola cases based on clinical presentation and history of contact

Background: The suspect Ebola case-definition aims to detect all cases with high sensitivity but low specificity to isolate cases early; since 02/2015 >90% of suspects have been tested negative. The risk of transmission between isolated patients before laboratory confirmation could be minimized by using a secondary case-definition to separate patients according to their probability of being confirmed Ebola cases.

Methods: We conducted a retrospective analysis of admissions to MSF Ebola Centre in Monrovia, Liberia (08/2014- 03/2015) to study the discriminative accuracy (sensitivity, attributable frequency,

diagnostic-test-odds-ratio, area-under-the-ROC-curve) of clinical signs, contact history and combinations thereof.

Results: Among 1832 suspect patients, history of contact, gastro-intestinal symptoms and illness-duration >3 days showed best test performance with a sensitivity 47-85%, attributable frequency 6-18%, diagnostic-test-odds-ratio 1.35-2.22 and an area-under-the-ROC-curve 0.53-0.59. Combining all the above yielded a tool with 20% sensitivity but 94.4% specificity. However positive predictive value decreased over time from 93% (08-09/2014, n=919: 79% tested positive) to 31% (01-03/2015, n=91: 11% tested positive) and negative predictive value increased from 23% to 90%.

Discussion and Conclusion: Standard patient-interview currently conducted at admission does not yield sufficient information to consistently discriminate high-risk from low-risk suspects in the West African outbreak. We recommend further studies to support development of an evidence-based tool for discrimination.

Role and output: Primary investigator

Study protocol development, data preparation, data analysis, preparation of report to MSF and poster presented at Targeting Ebola Conference 2015 in Paris, France [20].

Supervisors: Bernadette Gergonne (MSF) and Klaudia Porten (Epicentre)

Scientific communication during the fellowship

1. Manuscripts published in peer reviewed journals: 5

2 original research articles published in German peer-reviewed scientific journals [5][7]

3 original research articles published in international peer-reviewed scientific journals [10][14][19]

2. EpiBull publications: 1

1 situation report on Hepatitis C in Germany 2014 [8]

3. Posters at national and international scientific conferences: 4

1 poster at Targeting Ebola Conference, 28.-29.05.2015, Paris, France [20]

1 poster at Global VTEC Symposium, 13.-16.09.2015, Boston, USA [17]

2 posters ESCAIDE conference, 11.-13.11.2015, Stockholm, Sweden [9][13]

4. Oral presentations at national and international scientific conferences: 7

1 oral presentation at BVÖGD conference, 23.-24.04.2015, Rostock, Germany [6]

1 oral presentation at TEPHINET global conference, 7.-11.09.2015, Mexico City, Mexico [11]

2 oral presentations at ESCAIDE conference, 11.-13.11.2015, Stockholm, Sweden [12][18]

1 oral presentation at BVÖGD conference, 27.-30.04.2016, Reutlingen, Germany [3]

1 oral presentation at EUPHA conference on Migrant and Ethnic Minority Health, 23.-25.06.2016, Oslo, Norway [4]

1 oral presentation at ESCAIDE conference, 28.-30.11.2016, Stockholm, Sweden – accepted [15]

5. Presentations at PAE meetings: 4

Anna Kuehne: Epicentre Mission to Monrovia. 12/2014

Anna Kuehne, Andreas Gilsdorf: Ausbrüche von Infektionskrankheiten in Unterkünften für Asylbewerber 2001-2013. 02/2015

Anna Kuehne, Dirk Werber: Estimating true STEC incidence based on haemolytic uremic syndrome notification data. 08/2015

Anna Kuehne, Lena Fiebig: Find and treat or find and lose? Screening newly arrived asylum seekers for infectious pulmonary tuberculosis in Germany 2002-2014. 06/2016

Teaching experience

1. Training surveyors for cell phone survey in Monrovia, Liberia, November 2014

Anna Kuehne trained 19 surveyors to conduct interviews with participants of the mortality survey in Monrovia during a two-day-training. Topics covered were research ethics, epidemiology and survey methodology, general information about Ebola, introduction to MSF, introduction to the content of the questionnaire, difficult situations during interviews and strategies to avoid and react to them. Theoretical input on research ethics, surveys and MSF was provided by lectures. Ebola information was synthesized by summarizing collective knowledge of the surveyors on a flip chart. The interview was trained several times and difficult questions were discussed in groups and strategies to react to them were developed by group participants.

2. Training data management team of the district Ebola response centre (DERC) Western Area, Sierra Leone, March 2015

National and regional Ebola surveillance data in Sierra Leone and Western Area suffer from incompleteness as much as from duplication. Three sources of data are supposed to be entered and matched if appropriate by the data entry team into VHF-Epi-Info-database: a) information from the case investigation form - filled in by the district surveillance officer at first detection of the case, b) laboratory reports sent daily by Ebola laboratories, c) information from Ebola treatment units about the current status and outcome of the disease. However due to a small range of common first and last names, frequent misspellings and little consistency in the use of patient identification numbers, data – particularly from the initial phase of the outbreak – remained unmatched in the DERC data base.

Anna Kuehne was responsible to conduct training on data use, data entry and data maintenance for the DERC Western Area data management team. The training consisted of lectures and regular trainings of 30 minutes to 1 hour working directly with VHF-Epi-Info-database. To improve previously entered data, CDC developed an R-code that allows identification of possible datasets that belong to the same patient, Anna Kuehne conducted the training explaining the data management team the code output and how data could be improved from there. Training was performed by two lectures and two half-daily workshops in VHF-Epi-Info-database for the data management team.

3. Training peer researcher for the MiSSA study, Cologne/Berlin, Germany, August and October 2015

In August 2015 Anna Kuehne assisted the peer researcher training in Cologne with an input on STI, HIV and Hepatitis. In October 2015 Anna Kuehne conducted a two-day training for peer researchers in Berlin to explain the study purpose and design, map out places for recruitment, train recruitment strategies and give a background on HIV, Hepatitis and STIs. The methods used present a mix of frontal talks, summarizing collective knowledge and interactive training and simulations.

4. Training local public health authorities, Berlin/Meissen, Germany, October 2015

Anna Kuehne conducted two lectures for local public health authorities, each 20 minutes.

- I. Seminar for local health authorities in Saxony about outbreaks of infectious diseases in shelters of asylum seekers, October 2015
- II. Seminar for local health authorities about TB in Germany and TB screening among asylum seekers, October 2015. Audio-video-recording available
http://multimedia.gsb.bund.de/RKI/Video/Tuberkulose_Webinar_RKI_10_2015.mp4

5. Teaching at the rapid risk assessment module, Athens, Greece, June 2016

Anna Kuehne facilitated the course on data collection in the field with EpiCollect software and the case study on mortality surveys in the field.

6. Summer Academy on Tropical Medicine and International Health, Missionsärztliches Institut, Würzburg, Germany, July 2016

Anna Kuehne was holding lectures on tuberculosis epidemiology in Germany and tuberculosis among asylum seekers and Ebola surveillance and field epidemiology in West Africa. She also facilitated a seminar on careers in international health.

International assignments

1. Epicentre/MSF France mission to Monrovia, Liberia 27.10.-03.12.2014

Anna Kuehne provided epidemiological support to the MSF France mission in Monrovia for Epicentre. Her main task was the implementation of a mortality survey in Monrovia to identify mortality, morbidity and health seeking behaviour in Monrovia [7]. She also conducted the evaluation of the first mass drug administration of antimalarial drugs in an Ebola context [11]. Furthermore, she developed a study protocol for the differentiation of Ebola and non-Ebola cases based on data from ELWA3- the largest existing Ebola treatment unit [19]. In addition, she assisted in the assessment of the functioning and infection-prevention-practice of health facilities in the north of Monrovia.

2. GOARN/WHO mission to Freetown, Sierra Leone 05.03.-13.04.2015

Anna Kuehne served as a field epidemiologist in order to support WHO Western Area district response team in Sierra Leone and reported directly to the field coordinator.

Anna Kuehne was tasked with the epidemiological surveillance of seven wards in the Western District Region, these being 384, 385, 386, 389, 390, 391, 392. Within each ward Anna Kuehne supervised two

District Surveillance Officers (DSOs) and coordinated their work with the ward contact tracers, ward community monitors, quarantine officers and social mobilisation team. Anan Kuehne supervised the investigation of alerts called in by 117, the case investigation and line listing of contacts and their follow-up. Anna Kuehne visited on a daily basis the houses under quarantine for the purpose of ascertaining their state of health and any needs in terms of food supply or medical issues. To facilitate case finding and coordination in the field Anna Kuehne liaised with other partner organisations working in the field including MSF, CDC, Save the Children, SMAC, Plan International, Welthungerhilfe and the Red Cross. As part of her work she investigated a cluster of Ebola cases linked to funerals and herbalist treatments [6].

In addition to ward supervision Anna Kuehne was tasked with improving the VHF-data base for the Western Area and liaised for that purpose with CDC and WHO statistical support staff on national level to facilitate further training in data entry and supervise data cleaning

An oral presentation about Ebola response in Sierra Leone was given as part of the regular seminar of the Department of Infectious Disease Epidemiology in June 2015 together with Christina Frank.

A media article about the mission was prepared and published on the RKI website and an RKI booklet about RKI engagement in Ebola response [20] and a poster presentation prepared [21].

Summary of additional activities for the department of infectious disease epidemiology

1. Representative of the working group on migration of the Department for Infectious Disease Epidemiology at RKI

As the representative of the working group on migration, Anna Kuehne supported the development of recommendations for screening for infectious diseases among migrants and health of migrants and receiving communities [22]. In addition, the working group assisted the department with responses to ministry of health and the public.

2. Nominated expert for the scientific advisory group of the ECDC on screening newly arriving migrants for a duration of 2 years

The objective of the ECDC project in screening newly arrived migrants is to systematically review and synthesize the evidence on infectious diseases considering emergency public health and longer-term preventive actions for newly arriving migrants within existing EU/EEA health systems. Using the newly developed GRADE “evidence to decision” framework, ECDC is searching for evidence and update high quality systematic reviews on effectiveness, acceptability, feasibility, equity, resource use and cost effectiveness of migrant screening. This review will inform the deliberation of the evidence and subsequent development of an evidence-based guidance document, which will serve as a European guidance for key migrant health infectious diseases. Anna Kuehne is a member of the advisory group to oversee this process.

3. Feedback to GOARN for the Ebola-Coordination-Centre at RKI

Preparation of structured feedback to GOARN for the Ebola-Coordination-Centre at RKI and participation in GOARN telephone-feedback together with Thomas Kratz and Christina Frank. Participation in RKI/GIZ/GOARN workshop to discuss future areas of RKI commitment to GOARN.

EPIET/EUPHEM modules attended

1. **Introduction course, 29 September - 18 October 2014, Spetses, Greece**
2. **Outbreak module, 5-7 November 2014, Berlin, Germany**
3. **Multivariable analyses module, 25-29 March 2015, Vienna, Austria**
4. **Project review module, 24-28 August 2015, Lisbon, Portugal**
5. **Time series analyses module, 23-27 November 2015, Bilthoven, the Netherlands**
6. **Vaccinology module, 16-20 May 2016, Paris, France**
7. **Rapid risk assessment module, 20-25 June 2016, Athens, Greece**
8. **Project review module, 22-26 August 2016, Lisbon, Portugal**

Participation in further training

1. **Course on Rapid Assessment in Complex Public Health Emergencies. 24.-28 January 2015, Veyrier du Lac, France**
2. **Data Management System (DMS) Schulung, 22. July 2015, Berlin, Germany**

Supervisor's conclusions

During her EPIET fellowship, Anna was involved in a wide range of projects, undertook an impressive amount of work, and achieved a large amount of outputs including five peer-review publications. She was able to work independently and effectively and delivered high quality work. She was highly motivated and always focused on achieving the goals of the projects she was involved in. Although she had competencies and experiences in public health and statistical analysis before the EPIET training, she further enhanced her capacities and improved her epidemiological skills. She had a very positive attitude towards scientific review, and she was always ready to accept constructive criticism. Many of Anna's projects have important public health implications not only in Germany, but also internationally. She joined two international missions during the Ebola outbreak to Liberia and Sierra Leone, and her projects in Germany mainly focused on vulnerable populations in Germany, e.g. refugees, asylum seekers and migrants from Sub-Saharan Africa. She demonstrated her aptitude to efficiently work in different teams and has been a very valued member of staff in any team. I know Anna to be a highly motivated, dedicated, skilled and talented field epidemiologist, both at national and international level. I give her my highest recommendation for her future career in infectious disease epidemiology.

Personal conclusions

My motivation to apply for PAE training was to increase my skills in epidemiology, as an interest in this area developed during previous work and whilst undertaking a Master degree. Over the last two years, the programme has provided me with the opportunity to work on national and international level and it allowed me to further develop statistical and analytical skills, trained at EPIET modules.

Directly following the fellowship, I will apply these newly gained skills in the surveillance unit of the department for infectious diseases at the RKI.

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