
ROBERT KOCH INSTITUT



Department for
Infectious Disease Epidemiology

Evaluation Report – Public Version

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Department for Infectious Disease Epidemiology
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Unit AL3: Director's Office

Department Head: Prof. Dr. med. Gérard Krause

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1. Department 3

Head: Prof. Dr. Gérard Krause

Deputy: Dr. Osamah Hamouda

2. Tasks and Goals of the Department

2.1. Summary

The mission of the department is to prevent, detect and control infections in the population in Germany. In addition to the legally mandated duties in this context the department is also actively engaged in epidemiological research and training.

The department supports the local public health service by building up a comprehensive national surveillance system, maintaining a 24/7 on call duty system and the Epidemiological Situation Centre, providing scientific support for pandemic management, deploying epidemiological teams for outbreak investigations and offering special training for the respective target groups. The department hosts the majority of the national advisory committees affiliated at the RKI, was in charge of 54 % of all ministerial decrees directed to the 4 technical departments of the Robert Koch Institute 2009-2012, authors more than half of all RKI-reports in the epidemiological bulletin and coordinates all RKI- fact sheets for physicians (Ratgeber). The department executes the nation's reporting obligation with the European Union and the World Health Organization and represents Germany in many international networks.

The department's scientific activities have clearly increased in quantity and level of sophistication. All these activities are a result of joint contribution by all units of the department. Scientists of the department are renowned experts visible through publications, memberships in international advisory groups, and invited presentations. Furthermore the department has created the first Master of Science programme to be run by a federal institution and has initiated the instalment of the first joint professorship appointment in the remit of the Federal Ministry of Health, both indications for the scientific liaison between academia and the RKI.

In addition to strategic orientation, coordination and quality control of the above mentioned activities the director and staff of the director's office initiated or carried out a number of these activities directly.

2.2. Current status of the work and summary of relevant results

2.2.1 Service

The mission of the department is to prevent, detect and control infections in Germany's population (see 4.3., AL3) through

- Continuous surveillance and assessment of the epidemic situation
- Implementation and support of outbreak investigations
- Development and evaluation of strategies for prevention and intervention
- Research and method development in the field of infectious disease epidemiology
- Execution of legal duties in the field of infectious disease control
- Support and advice for other partners of the public health service and political decision makers
- Development of evidence-based recommendations for the public health service
- Information for the public
- Exchange with other national and international health authorities
- Qualification and further training in the field of public health with emphasis on infectious disease epidemiology

The legally mandated task and duties of the department include among others notifiable disease surveillance, complementary monitoring and surveillance of non-notifiable disease, international reporting obligations within the Early Warning and Response System (EWRS) of the European Union and the International Health Regulations (IHR) (see 2.5.2., AL3) and coordination of the response to public health emergencies of infectious origin (see 2.5.3-2.5.5., AL3). An important task of the department is the risk assessment and scientific advice for the government and policy

makers as reflected by the large and increasing number of ministerial decrees directed to the department (see 2.5.8., AL3). Six different national advisory committees are hosted and scientifically supported by respective units of the department. All units of the department contribute to the yearly epidemiological report (coordinated by unit 32) and together they have published more than half of all RKI-reports in the epidemiological bulletin. Additionally the department maintains a 24/7 on call duty service centrally for the whole institute. Upon request the department provides immediate technical support to the local public health service, ranging from scientific advice on the phone, to provision of technical tools up to the deployment of epidemiology teams on site (see 2.5.3., AL3). Although not formally a task of the institute the department engages in multiple activities of training (see Unit PAE and the respective chapters 2.6 of each unit) and capacity building in order to support dissemination of skills in the public health service, to strengthen liaison with academia and to generate a pool of qualified scientists for this field. The director and his office coordinate and supervise these activities. The director's office runs the network of national reference centres and consiliary laboratories and edits and co-authors a large portfolio of guidelines and recommendations for the public health service and for medical staff (see 2.5.6. and 2.5.7., AL3)

2.2.2. Research

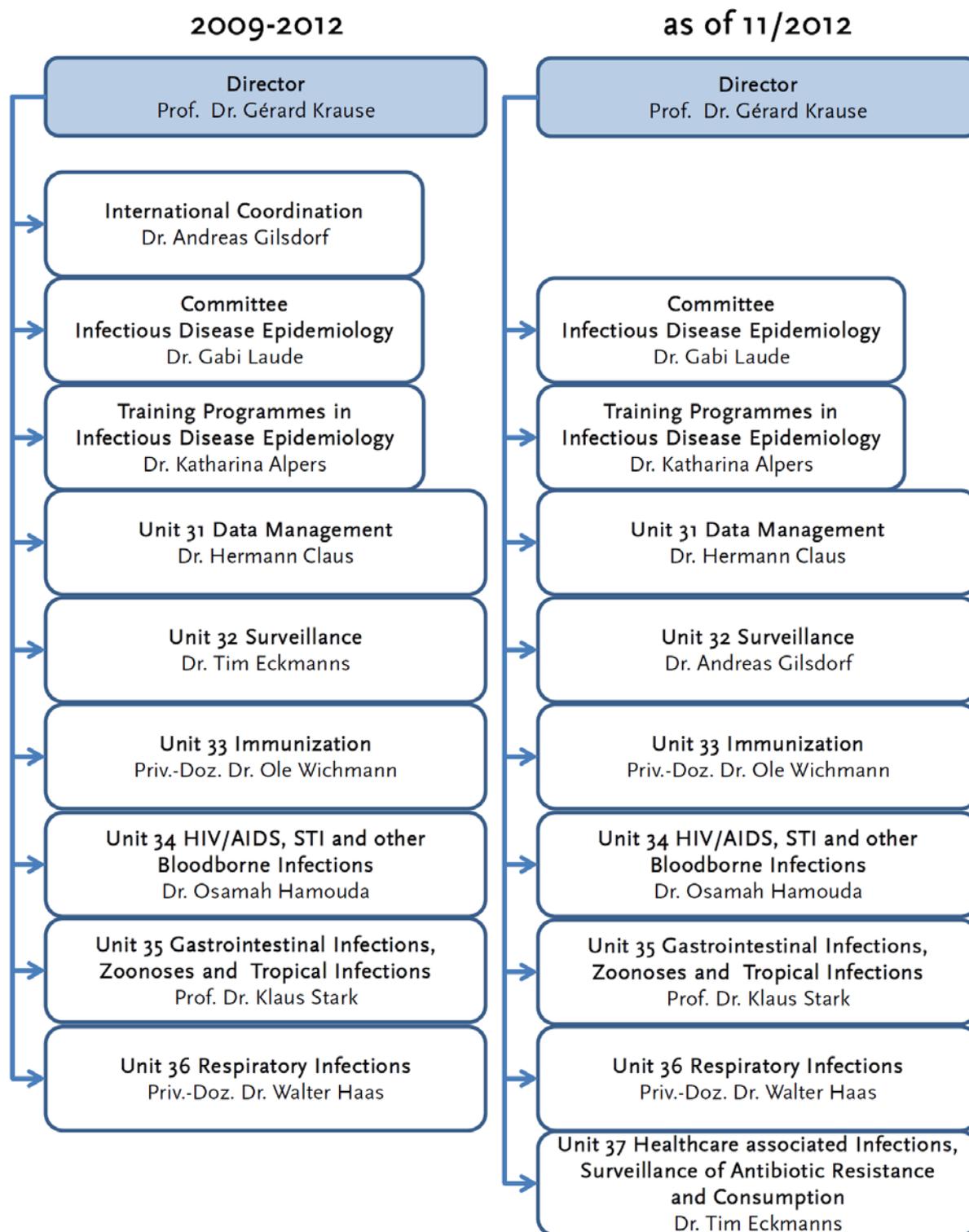
In order to provide the above described service at the best available scientific level the department engages in own epidemiological research. This research goes way beyond descriptive analysis of surveillance data, and is mostly funded by competitively acquired external funding. While most of this is being done by the respective units, the director himself and staff of the director's office are also personally engaged in initiation and execution of research projects and acquisition of external grants (e.g. REACT see 2.2.7., Unit 32, ARS see 2.2.4, Unit 32).

2.2.3. Organisation

The department was created in 2002 as successor of the former centre for infectious disease epidemiology (as part of Dept. 2) which was founded in consequence of the new infectious disease control law enacted in 2001. During the reporting period of this report the department contained a dedicated unit for surveillance related data management (Unit 31) and another for generic surveillance (Unit 32). In international comparison this set-up is unique and makes Germany one of the few large federal countries with a generic electronic surveillance platform comprising all notifiable diseases and all administrative levels of the public health service. This contributes to user friendliness, standardisation, data safety and efficiency. In 2006 the former unit for respiratory and vaccine preventable disease was divided up into one unit dedicated to vaccine preventable diseases (Unit 33) and another to respiratory infections (Unit 36) complementing the already existing disease specific unit for HIV AIDS and other blood transmitted infections (Unit 34), and the unit for gastroenteric and zoonotic infections (Unit 35). In 2009 with the creation of the postgraduate programme for applied epidemiology training (PAE) and its establishment as a masters of science programme at the Charité the PAE-unit was created reporting directly to the director of the department (see PAE).

While organisational substructures are essential to allow for the development of specialised expertise the above mentioned duties require a multidisciplinary approach across units. This is particularly true in outbreak situations during which extreme thematic flexibility and immediate reallocation of surge capacity is essential. The need for high level disease specific expertise on one hand and the ability to mobilise all staff for the investigation of unexpected public health emergencies on the other hand is a challenge for staff and management.

Figure 1: Organogram before and after reorganisation in 2012



2.3. Major goals and contribution to the goals of the department

In the recent years Germany has experienced some extraordinary challenges and also opportunities in the area of infectious disease epidemiology which result in the following emerging issues:

- a) The implementation of the New International Health Regulations (IHR) requires faster, more detailed and more reliable information exchange internationally.

- b) Public communication (e.g. through Web 2.0) has become increasingly decentralised, accelerated, and widespread resulting in dramatically reduced turn-around time for response and communication.
- c) Antimicrobial resistance and its respective public attention and regulations have gained importance.
- d) The attention to nosocomial infections particularly in vulnerable settings such as neonatology is rising.
- e) The potential but also complexity in the field of immunisations is increasing.
- f) The world first experience with a pandemic in the era of modern virological surveillance and pandemic vaccine availability has had a major impact on the societal expectations to public health response.
- g) Globalised market of food and other potential vehicles of infectious pathogens raise the risk for larger point source outbreaks with international implications.
- h) Social inequalities and public health programmes for difficult to reach populations are gaining attention also in the field of infectious diseases.
- i) The demand for fully evidence based recommendations is increasing including in areas for which conventional methods of evidence-based medicine are hardly applicable.
- j) Modelling, health economics and burden of disease assessments are gaining importance for health policy recommendations.
- k) There is an increasing societal demand for transparent, participatory recommendations with full control of conflicts of interest.
- l) Emerging issues in infectious disease prevention require increasing involvement of and coordination with scientific associations and other academic institutions, as the experience with 2009 influenza pandemic and the EHEC/HUS outbreak in 2011 has made evident.
- m) Increasing budgetary constraints and regulation in the health care sector lead to potential reduction of hygienic and microbiological laboratory capacity and expertise.
- n) The public health service, especially at local community level, is challenged by budgetary constraints and has difficulties to attract qualified staff.
- o) Appearance of new research networks in the field of infectious disease epidemiology such as the German Centre for Infection Research (DZIF) and the National Cohort have created new research opportunities as well as competitors in the field.

Following the implementation of the IHR, the experience with the 2009 influenza pandemic and the 2011 EHEC/HUS outbreak the director has initiated and conducted a variety of evaluations and has participated as invited expert in international evaluation activities. Those activities resulted in useful recommendations (e.g. Krause et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2010; Krause et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz*, 2013). These recommendations and the above listed challenges have been addressed in various ways. Those changes initiated by the director or executed throughout the department are exemplified by the following:

2.3.1. Reassigning the portfolio of the surveillance unit (addressing the emerging issues a, b, f, g, h, j, l)

After installing one dedicated expert for international scientific coordination reporting directly to the director in 2008, it was now decided to have all generic issues of international coordination including surveillance and IHR in the remit of unit 32. In addition the coordination of the epidemiological situation centre was also transferred from the director's office to the new surveillance unit in order to assure a critical mass of officers able to cover the task in high load situations (see 2.5.5., AL3). The former expert for international scientific coordination (Andreas Gilsdorf) was appointed head of the new surveillance unit (Unit 32), thus assuring full continuity and synergy. One of the future focus activities of the new unit will be work on burden of disease. This evaluation report covers past activities until September 2012; therefore activities only recently

transferred to the surveillance unit will not be presented in the Unit 32 chapter but under 2.5.2 and 2.5.5., AL3 below.

2.3.2. Instalment of the task force for DEMIS (German electronic notification system for infectious diseases) (addressing the emerging issues a, b, f)

In the aftermath of the EHEC/HUS outbreak in 2011 a law was drafted in which the RKI was requested to design a new surveillance system which integrates all relevant digital documentations from peripheral health care providers in order to reduce manual work load, reporting delay and transmission errors. For this task a consortium of a private consulting enterprise, the Fraunhofer Institute and the Robert Koch Institute was created to conceptualise a new information architecture which would liaise with the electronic health documentation system currently being developed at national level (e-card). In order to assure competent representation in this complex endeavour the department created a taskforce which is being coordinated by the deputy head of the data management unit 31 (G. Kirchner) and the deputy head of the surveillance unit 32 (J. Benzler).

2.3.3. Creation of a new unit for nosocomial infections and surveillance of antimicrobial resistance and usage (Unit 37) (to address emerging issues c and d)

The director of the department was member of the drafting group of the national strategic plan for the prevention of antimicrobial resistance which was officially adopted by the Germany government in 2008. In 2006 the director has acquired a large ministerial grant to build up a national laboratory based antimicrobial resistance surveillance system. The implementation of this grant was taken in charge by unit for surveillance (Unit 32) which was later staffed with regular positions created through the RKI2010 programme (see 2.2.4., Unit 32). Since then various pathogens with antimicrobial resistance have been made notifiable by law and a new committee is being installed to monitor the provision of scientific recommendations in this field. In light of the increased demand in and attention to this field the above named unit was installed in the department named unit for health care associated infections, and surveillance of antimicrobial resistance and consumption (Unit 37). The head of this unit is the former head of Unit 32 (T. Eckmanns), who was previously in charge of the topic, thus assuring best possible competency and continuity. Because this unit was founded November 1, 2012, all activities referring to antimicrobial resistance will be described under the chapter Unit 32, the unit in charge of this topic from 2006 up to the recent reorganisation.

2.3.4. Establishment of the Epidemiological Situation Centre (addressing emerging issues a, b, k, l)

In 2009, upon the move to the provisional facility in Weissensee the RKI has installed a special facility for the Epidemiological Situation Centre (ESC). This centre was designed and organised by the department based on the experience with the SARS outbreak 2003 and various pandemic preparedness exercises. It proved immediate utility during the 2009 H1N1 pandemic and the 2011 HUS/EHEC outbreak (see 2.5.5., AL3).

2.3.5. Initiating developments of evidence based methods for public health recommendations (addressing emerging issues e, f, i, k, l)

It is largely acknowledged that for population based public health interventions new methods of investigation but also of evidence grading must be developed. In 2006 the director of the department has started to address this challenge by organising a workshop of international experts and has remained collaborative expert of ECDC when it engaged in coordinating further developments in this field. In addition, the unit for immunisation in the department (Unit 33) organised several international workshops in this context with a particular focus on vaccinology. It was therefore decided to create a methodological nucleus for evidence based public health (EBPH) in the unit FG 33 and one of the last vacant scientist positions created by the RKI 2010 programme was dedicated for this function. Recently FG 33 acquired an ECDC sponsored tender for developing the methodology of evidence-based public health (EBPH) and has engaged in an number of research projects in the field of health economics (see 2.2., Unit 33).

2.3.6. Focusing on advanced study designs to assess effectiveness of interventions (addressing emerging issues e, f, g, i, j)

In the first years of its existence the research work of the department was dominated by descriptive analyses of epidemiological trends and investigations of outbreaks. In the recent years five additional types of study designs have gained importance in the department's research:

1. Interventional studies or prospective observational studies comparing the effectiveness of different kinds of public health interventions e.g. the role of masks for the prevention of influenza transmission in households (Suess et al., *BMC Infect Dis* 2012) or the effectiveness of the pandemic vaccine in the prevention of the 2009 pandemic influenza (Wichmann O et al., *Euro Surveill* 2010).
2. Study designs using secondary data analysis to validate data on surveillance or vaccination coverage (Böhmer MM et al., *Vaccine* 2011).
3. Customised population based surveys, behavioural surveillance and qualitative methods to study burden of disease, knowledge, attitude and behaviour towards prevention of infectious diseases e.g. attitude towards vaccines and adherence to recommendations (Böhmer MM et al., *BMC Public Health* 2012; Walter D et al., *Euro Surveill* 2012; Marcus U et al., *Sexual Health* 2011; Velasco E et al., *BMJ Open* 2012).
4. Epidemiologic modelling (see 2.3.7., AL3) to interpret acute epidemic phenomena such as pandemics as well as complex associations of risk factors for sporadic diseases (Meyer S et al., *Biometrics* 2012; Höhle M et al., *Epidem Infect* 2011; an der Heiden M et al., *PLoS One* 2009).
5. Serosurveys either custom designed for a specific research question or conducted with existing health surveys in cooperation with department 2 of the RKI (Dudareva S et al., *PLoS One* 2011; Bätzing-Feigenbaum J. et al., *HIV Medicine* 2009).

While the above mentioned publications represent only selected examples co-authored by the director's office, the diversity and the level of sophistication of research activities have increased throughout the department, which can be seen by the publication output of the respective units and also by the fact that the number of studies that required and received approval by the ethics committee has increased in the recent years (from less than 3 during 2005 -2008 to more than 13 during 2009-2012).

2.3.7. Creating a professorship and a project group for infectious disease modelling (addresses emerging issues i, j, l)

In January 2011 the director of the department jointly with the Humboldt University Berlin (HU) successfully applied for a grant of the Federal Ministry for Education and Research (BMBF) through which instalment of epidemiological professorships are being sponsored for a period of 5 years. In a highly competitive selection process Prof. Dirk Brockman from Northwestern University Evanston, USA was offered and has accepted the professorship in a joint appointment between RKI and HU. This will result in the creation of an independent research group within the RKI. Although organisationally not part of the department, this group will be physically located in the same facility as the department for infectious disease epidemiology to assure best possible interaction. The project description of the second phase of the BMBF tender will be jointly written by the director of the department and the newly installed professor. With this professorship the RKI will be the first federal institute in the remit of the Federal Ministry of Health to appoint a professorship jointly with a university.

2.3.8. Installing new advisory committees and strengthening scientific support of existing ones (addressing emerging issues c, e, f, i, k, l)

In the attempt to have a more external participation and quality control in public health recommendations and policy advice the following new external advisory committees have been installed (hosting/coordinating unit in parentheses): Committee for the Measles Elimination (Unit 33); Committee for Antimicrobial Therapy (Unit 32), Expert Advisory Group for Influenza and Pandemic Preparedness (Unit 36). At the same time the intensity of scientific support for the already existing external advisory committees has significantly increased in recent years, particularly for the National Standing Committee on Immunisations (Unit 33) and the Blood Safety Committee (Unit 34).

2.3.9. Strengthening evaluation and networking for national reference centres (addressing emerging issues l and m)

In order to strengthen the reference laboratory capacity the director's office has made the procedures for selection and evaluation of national reference centres (NRC) more stringent and has created monetary and organisational incentives for NRC and national consiliar laboratories (NCL) to create networks through which they can share access to patients and samples, exchange methodological expertise and have stronger interaction with the RKI (see 2.5.6., AL3)

2.3.10. Prioritisation of pathogens for surveillance and epidemiological research (addressing emerging issues m and n)

The director's office has developed a systematic, evidence based methodology to prioritise pathogens for surveillance and epidemiological research in order to address the challenge of budgetary constraints within the department and the public health service at large (see 2.4.2., AL3).

2.3.11. Foundation of Master of Science Programme for Applied Epidemiology and other improvements in the training offer (addressing emerging issue n, l)

Through various formats and initiatives the training activities in the public health service and in medical and public health schools has been continuously expanded and intensified. The most important mile stone in this context is the Masters of Science Programme for Applied Epidemiology founded and directed by the director of the department (see PAE). (Bremer et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009, Krause G et al., *Euro Surveill* 2009a, Krause G et al., *Euro Surveill* 2009b)

2.3.12. Co-appointment with the Helmholtz Centre for Infection Research and the Hanover Medical School (addressing emerging issues l, n, o)

In August 2011 the director of the department was appointed head of the newly founded department for epidemiology at the Helmholtz Centre for Infection Research (HZI) in Brunswick and chair for infectious disease epidemiology (W3) at the Hannover Medical School. Both institutions and the RKI as well as the two affected federal ministries propagated this multiple appointment while the director's duties at RKI are fully maintained. In the meanwhile HZI and RKI have signed a cooperation contract (December 2012). The director's multiple affiliation has also helped to assure access and participation of the RKI department for infectious disease epidemiology in the National Cohort (see 2.4.1, AL3) and the newly created German Centre for Infection Research (DZIF) (see 3.2., AL3).

2.4. Additional work and methods for investigations

2.4.1. National Cohort

The National Cohort is a prospective cohort study in Germany run by several Helmholtz centres, other public research centres and universities to study risk factors and etiologic mechanisms of widespread diseases at the population level. It is one of the few if not only large cohort studies of its kind that also addresses infectious diseases. A total of 200,000 adult individuals will be recruited through a network of 18 study centres within Germany. After four years, all participants will be re-invited for follow-up examinations. This will allow the correlation of the incidence of diseases of different aetiologies with clinical, socio-behavioural and laboratory findings from earlier examinations. Furthermore the cohort will serve as a population study for the association between infections and non-communicable diseases.

In 2008 the Helmholtz Association as initiator of the National Cohort has asked the department for infectious disease epidemiology at RKI to provide its expertise in the concept and design of the cohort. The director of the department then was given the task to coordinate the working group on immunity and infection within the national cohort. In this role the director's office has organised a number of workshops with participation of various relevant research institutions in Germany in order to conceptualise research priorities. Together with the Helmholtz centre for Infection Research (HZI) the department then developed the respective epidemiological instruments such as

questionnaires and study proposals. Now through his dual affiliation (see above) the director of the department is member of the epidemiological steering committee and delegate in the members' assembly. This assures linkage of first-hand information between RKI and HZI, together with B. Kurth (Dept. 2), who is a personally nominated representative of the RKI in the National Cohort. Through this liaison the department has had privileged participation in the methodological design and scientific analysis of the national cohort involving all units of the department. Already several joint projects in the context of the National Cohort have been initiated between the HZI and the department.

2.4.2. Prioritising pathogens for surveillance and epidemiological research

The large number of infectious agents to be potentially covered by the department for infectious disease epidemiology exceeds by far its capacity, thus it is necessary to prioritise the resources dedicated for surveillance and epidemiological research of infectious diseases. Since 2005 the director and staff (A. Gilsdorf and Y. Lenz) have developed a tool which would allow standardised, transparent and reproducible prioritisation and also involvement of all relevant stakeholders. This included a Delphi process with internal (RKI) and external experts and a metric-consensus approach to score pathogens according to ten three-tiered criteria. Additional experts were invited to weight each criterion, leading to the calculation of a median weight by which each score was multiplied. The 127 pathogens were ranked according to the total weighted score and divided into four priority groups. Twenty-six pathogens were ranked in the highest priority group (see 4.3., AL3); among those were pathogens with internationally recognised importance (e.g., Human Immunodeficiency Virus, *Mycobacterium tuberculosis*, Influenza virus, Hepatitis C virus, *Neisseria meningitidis*), pathogens frequently causing large outbreaks (e.g., *Campylobacter* spp.), and nosocomial pathogens associated with antimicrobial resistance. Other pathogens in the highest priority group included *Helicobacter pylori*, Respiratory Syncytial Virus, *Varicella zoster* virus and Hantavirus. While several pathogens from the highest priority group already have a high profile in national and international health policy documents, high scores for other pathogens (e.g., *Helicobacter pylori*, Respiratory syncytial virus or Hantavirus) have resulted in shifting more attention and resources towards those previously less acknowledged pathogens. The methodology and the results have been published in 5 international scientific publications and are being referred to by various research institutions within and outside Germany (Gilsdorf et al., *Euro Surveill* 2011a, Gilsdorf et al., *Euro Surveill* 2011b, Balabanova et al., *PLoS One* 2011).

2.5. Scientific advice and consulting services

2.5.1. 24/7 on call duty system

The department maintains a 24/7 on call duty system staffed with infectious disease epidemiologists (pool of approx. 35 volunteers coordinated by the director's office) to immediately respond to requests from the peripheral public health service or international public health agencies. The on call duty officer is supported by senior experts (usually director and heads of units), likewise available 24/7. The duty system is intended to assist local and state public health departments in infection control activities either by immediate consultation or by referral to more specialised units at the RKI. Another important function of the duty system is to assure continuous availability for notifications according to the International Health Regulations (IHR) and the European Early Warning and Response System (EWRS). The availability is assured through telephone, fax and e-mail and all communication by the duty system is being logged for documentation and quality control.

Next to the public health service, hospital emergency rooms, physician practices, fire departments, and ambulances also frequently request advice after regular working hours. Typical questions here include hygienic measures after transporting infectious patients, post exposure prophylaxis after exposures to blood, patients with meningococcal disease or rabies suspected animals.

On average the duty officer receives 8-10 telephone calls per week (300-500 calls per year) and spends an average of 5 hours per week of active duty responding to requests and notifications. At the beginning of public health emergencies or outbreaks this workload can temporarily increase drastically until the Epidemiological Situation Centre is being activated and takes over the service.

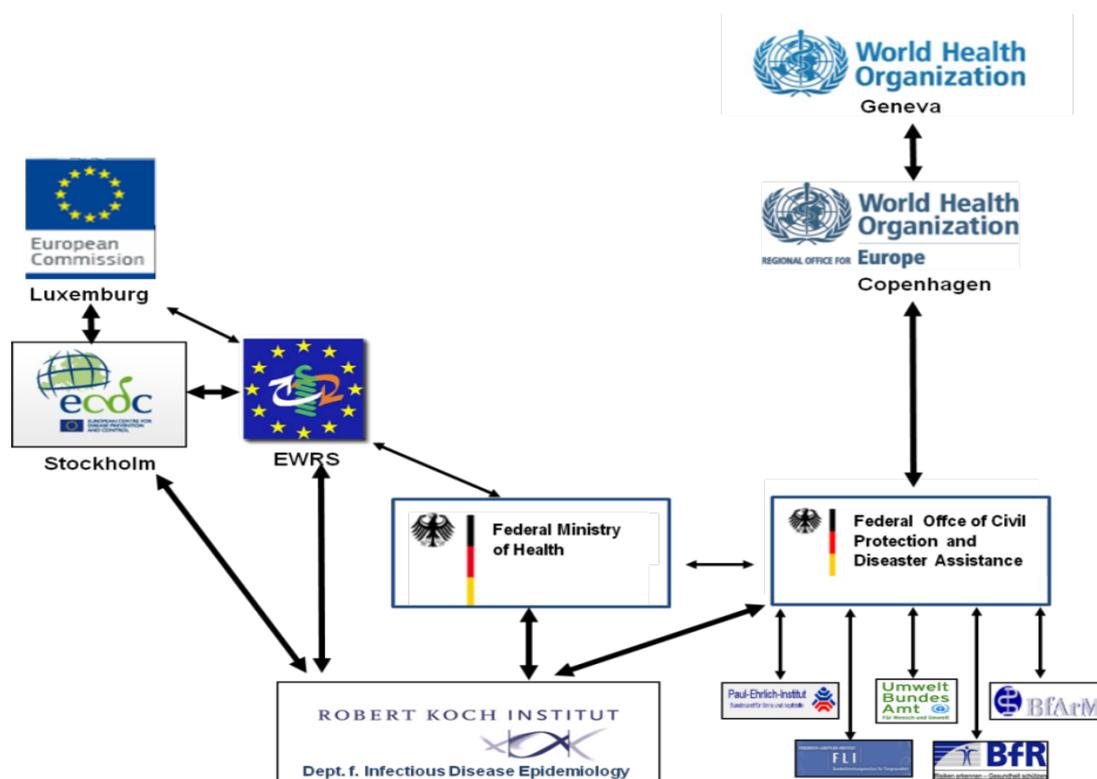
2.5.2. Early Warning and Response System and International Health Regulations

The department is focal point for the reporting and assessments of biological threats within the scope of the Early Warning and Response System (EWRS, EU) and International Health Regulations (IHR, WHO). All notifications made through the local and regional public health authorities that might constitute an international public health event are reported and followed up through these two reporting systems.

From 2009 to September 2012 747 events were notified by EU Member States through EWRS, not including respective follow-up notifications. For example the EHEC outbreak notification alone triggered 246 follow up notifications. All of these notifications are assessed by the on call duty officer and then managed by the respective unit in the department.

The German national focal point for IHR is the Situation Centre of the German Federal Office for Civil Protection and Disaster Assistance, which forwards all incoming international notifications to the respective federal agency in charge. For the vast majority of these notifications the RKI is the agency in charge, represented by the department for infectious disease epidemiology of the RKI.

Figure 2: The role of the department for infectious disease epidemiology at RKI in international reporting networks of the European Early Warning and Response System (EWRS, left) and the International Health Regulations (IHR, right)



2.5.3. Support or coordination of outbreak investigations

From 2009 to Sept. 2012 the department has responded to roughly 60 requests by the state health departments to assist or coordinate in outbreak investigations. In most of these, this involved deployment of a team of epidemiologists on site. In these situations RKI staff functions in the status of a seconded expert, and reports to the local health authority. Most deployments last several days and often require repeated field activities on site. An outbreak investigation team of the RKI generally consist of one or two senior epidemiologists and one to three PAE fellows (see PAE). The list containing selected documented outbreak investigations in which PAE fellows from RKI or the regional health authorities have participated can be found in 4.1.10, AL3.

2.5.4. Outbreak and Pandemic Response

During larger outbreak investigations or public health emergencies forces from all units of the department are gathered for epidemiological investigations, surveillance, support of the public

health service and communication. During the large EHEC/HUS outbreak in 2011 for example the department alone had the following workforce involved (FTE=full time equivalent):

- | | |
|--|---------------------------------------|
| • Situation room: 24(14)/7; 1-2 shifts/day | 5-15 Full Time Equivalent (FTE) / day |
| • Field teams: 18 teams; 1-4 day duration | 2-15 FTE /team |
| • Data entry: | 4-14 FTE/day |
| • Surveillance: | 5- 10 FTE/day |
| • Trace back, cluster and food liaison: | 2-6 FTE /day |
| • Study and analysis: | 6 - 10 FTE/day |
| • Lab-epi liaison: | 1-2 FTE /day |
| • Logistics: | 1-4 FTE/day |
| • Press-epi liaison: | 1 FTE /day |
| • International and federal liaison: | 2 FTE /day |

2.5.5. Epidemiological Situation Centre

When the department moved to the provisional facility in Weissensee in 2009 an Epidemiological Situation Centre (ESC) was installed (Lagezentrum). This proved to be very useful for the tremendous information management and also coordination of RKI investigation logistics during the 2009 influenza pandemic and also during the 2011 EHEC/HUS outbreak. The main function of the ESC is to collect epidemiologic information, to organise the national response, to triage all information requests, and to collate the case-reports for Germany. During the two EHEC /HUS outbreak and the 2009 flu pandemic the ESC was staffed mainly with personnel from all units of the department with some support from other departments of the RKI. As the workload diminished, functions of the ESC were continued in a “virtual ESC”, by staff working decentralized from their individual offices, which allowed to continue other duties. During the H1N1-pandemic 94 different persons were involved in the ESC, in 642 people shifts, including 127 weekend shifts resulting in 4500 person hours, or 560 person working days. During the EHEC/HUS outbreak the ESC was running for about 2 months with an average staffing of 5-15 daily fulltime equivalents.

The technical equipment of the ESC is fairly basic compared to similar structures in other organisations. Until 2012 the director's office had the organisational responsibility of the ESC and started closer cooperation with the ECDC, Stockholm and the Centres of Disease Prevention and Control (CDC), Atlanta to exchange best practices. In September 2012 the organisational responsibility of the ESC was transferred to the new surveillance unit (see 2.3.1., AL3).

2.5.6. National Reference Centres and Consiliary Laboratories

In 1995 the German Federal Ministry for Health started to fund National Reference Centres (NRC) for the laboratory surveillance of important pathogens and syndromes. Since then the selection and evaluation process has been gradually transferred to the RKI. Since 2009 the RKI is in charge of the management of the budget currently comprising 2.6 million Euros. The number of NRC has increased from 15 in 2009 to 19 in 2012. In addition there are now 49 (previously 47) nominated national consiliary laboratories (NCL) which cover additional aspects or pathogens with a special laboratory focus.

From 2009 to 2012 a number of important changes have been introduced to the system: The tendering and selection process has been made more transparent and competitive, following a strict prioritisation process upon need and not upon offer. The evaluation process also has become more rigorous, following a list of published criteria and involving not only the committee for infectious disease epidemiology but also topic specific external experts. In order to enhance the effectiveness and cooperation of the system, 10 National Reference Networks were launched in 2009 (see 4.4., AL3). The aim of these networks is to facilitate exchange on diagnostic methods and prevention concepts and to improve the geographic coverage of the services. In a competitive grant process, the RKI awards financial support for cooperation projects with networks. Scientific coordination and administration is executed by the director's office. The committee for infectious disease epidemiology - hosted by the director's office as well - plays a pivotal role in the quality assurance by being majorly involved in selection, evaluation and prioritisation of the NRC and CL (Laude G et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009, Laude G et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012.)

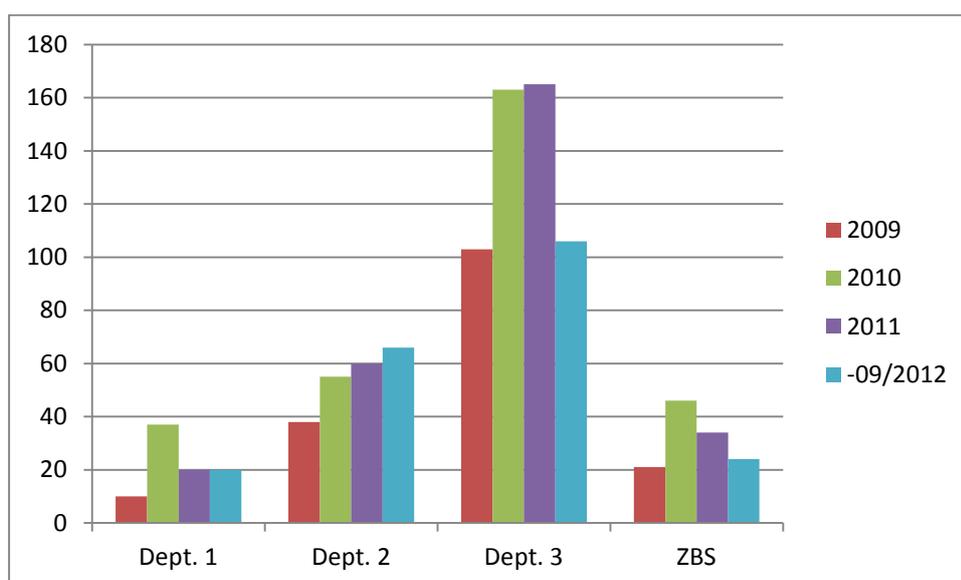
2.5.7. Fact sheets for physicians

The RKI fact sheets for physicians are a very popular source of information for clinicians and public health officers alike as they contain in a very brief format all the information necessary for the management of infectious diseases. They are coordinated and edited by the director's office (G. Laude) together with the editor of the Epidemiological Bulletin (J. Seedat) but are based on contributions of the departments' units, the national reference centres and consiliary laboratories, the respective scientific associations and other disease specific experts throughout Germany. They are published in the Epidemiologic Bulletin and updates can be accessed through the RKI homepage and on the RKI document server. From January to September 2012 the 48 fact sheets were downloaded 38,466 times from this server. This equals a proportion of 7.4% of all downloads, even though they only constitute 1.8% of the documents available on the document server, showing the high impact these fact sheets have. According to need the updating cycle of fact sheets ranges from every 4-5 years up to multiple times in one year (see 4.1.4., AL3).

2.5.8. Scientific advice to the Ministry of Health

The Ministry of Health is issuing decrees to RKI to ask for scientific advice. Reports to ministerial decrees range from brief assessments on specific epidemiological situations up to rather complex analysis which are similar to a scientific review as far as complexity and size is concerned. From January 2009 to September 2012 1,147 ministerial decrees have been directed to the four scientific departments of the RKI, of which 622 (54%) were primarily answered/reported by the department for infectious disease epidemiology. Figure 3 shows also that the number of decrees is increasing over the years.

Figure 3: Number of decrees, 2009-2012, by leading department of RKI, not including reports initiated by RKI



2.6. Training and teaching activities

2.6.1. Intensive course “Epi for action” for the Public Health Service

In 1996 a two week course in infectious disease epidemiology for public health officers has been established. While the first week of this course was dedicated to introduce basic concepts of infectious disease epidemiology the second week was dedicated to train the technical skills needed for outbreak investigations. This also includes the usage of Epi Info (until 2006) and Epi Data (since 2007). The course is characterised by a very participatory and intensively supervised format: A total of over 27 facilitator work days is being invested for the first and 32 work days for the second week of the course. Throughout the years 2006 to 2011 the participants satisfaction has always been 7 or above on a scale from 0 to 9. From 2001 to 2011 746 participants were trained with 22 to 61 participants per course; about 70% were from the public health service, 8% from the veterinary public health service and 22% form other professions and institutions. However the proportion of

participants from the public health service has diminished in recent years and the department has decided to reassess the current training need. A team of scientists of the department is now systematically evaluating the course using quantitative and qualitative methods. The results are going to be used to adapt or completely re-design the format and content of the course.

2.6.2. University-course „Infectious disease epidemiology“

Since 2011 the director's office (Y. Lenz) together with other colleagues of the department has established the university course „Infectious disease epidemiology“ for under- and postgraduate students of Humboldt University (within the ZIBI Graduate School “Research in Infection Biology and Immunology”). The course is a mandatory module within the programme of the International Research Training Group GRK1673 “Functional Molecular Infection Epidemiology” in Berlin. The course addresses the link between epidemiology, laboratory science and clinical practice. It covers key concepts of pathogen transmission dynamics, infectious disease surveillance, prevention and control strategies, as well as study design and the fundamentals of statistical analysis. The material is presented in 14 lectures and interactive seminars. The course is also open for guests.

2.6.3. License for board certified training in hygiene and environmental health

The Berlin Physicians Associations has renewed the license of the director for two years of the board certified training in hygiene and environmental health. This allows physicians working in the department to get up to two years of their work acknowledged for their medical board certification.

2.6.4. Other academic teaching activities

- Master of Science programme for applied epidemiology, member of examination committee (founded and directed by G. Krause, coordinated by K. Alpers)
- Lecture practical course “Hygiene”, 2nd semester, 18 hours per semester until 2010, Charité medical school (G. Krause)
- Lecture “outbreak investigation”, 5th semester, 1 hour per semester until 2009, obligatory lecture Charité medical school (G. Krause)
- Lecture “surveillance”, 3rd semester, 1 hour per semester, until 2009, obligatory lecture Charité medical school (G. Krause)
- Lecture “vaccinations”, 3rd semester, 1 hour per semester, until 2009, obligatory lecture Charité medical school (G. Krause)
- Lecture “waterborne infections” 1 hour per semester, continuously from winter semester 2008/2009 until summer semester 2009, obligatory lecture Charité medical school (G. Krause)
- Lecture “airborne infections” 1 hour per semester, continuously from winter semester 2008/2009 until summer semester 2009, obligatory lecture Charité medical school (G. Krause)
- Lecture “federal duties in public health”, 1 hour per year, until present, obligatory lecture for MSAE course since 2009 (G. Krause)
- Lecture “outbreak investigations”, “Surveillance” and “pandemic preparedness” total 4 hours per year, Bielefeld summer school “infectious disease epidemiology”, university Bielefeld (G. Krause)
- Supervisor for PhD/dissertations and master theses (currently 3 PhD/dissertation projects in the unit and 2 master thesis projects) (G. Krause).
- Course “International principles of TB and HIV control: modern laboratory diagnosis, management and surveillance.” Intensive Course for professionals from Eastern European countries, 5 hours teaching, 16 – 20 Feb 2009, National Mycobacterium Reference Laboratory, London (Y. Lenz)
- Lecture and facilitation of a seminar “Discussion, conclusions and recommendations of a scientific manuscript”, EPIET/PAE Module “Communication and Scientific writing”, 3 hours, 24 – 28 Jan 2011 (Y. Lenz)
- Lecture “Introduction to the infectious disease epidemiology”, ZIBI Summer School, Humboldt University, 1 hour, 24 Jun 2011 (Y. Lenz)

- "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universität, mandatory module within the GRK1673, winter semester 2011/2012, (established and coordinated Y. Lenz)
- Seminar "Introduction to the infectious disease epidemiology", teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673, 24 Oct 2011, 1.5 hours (Y. Lenz)
- Seminar "Link between laboratory and infectious diseases epidemiology", teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673, 31 Oct 2011, 1.5 hours (Y. Lenz)
- Seminar "Main principles of diagnostic trials and epidemiological/clinical study design", teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673, 21 Nov 2011, 1.5 hours (Y. Lenz)
- Seminar "Good epidemiological practice". How to report results properly: scientific writing and presenting, teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673, 5 Dec 2011, 1.5 hours (Y. Lenz)
- Lecture "Introduction to the aims and scope of infection epidemiology", ZIBI, Lecture Series „Infection Biology" (Ringvorlesung), Humboldt University, 2 Jan 2012, 1.5 hours (Y. Lenz)
- Lecture "Diagnostic accuracy studies: not to be biased about a bias", PAE/EPIET Laboratory Module, 1 Feb 2012, 1 hour (Y. Lenz)
- Lecture "Diagnostic accuracy studies: not to be biased about a bias", PAE/EPIET Laboratory Module, 21 Feb 2012, 1 hour (Y. Lenz)
- Lecture "Introduction to the infectious disease epidemiology", ZIBI, Summer School „Pathogen – Host Interplay“, Humboldt University, 15 Jun 2012, 1 hour (Y. Lenz)
- Lecture "Epidemiology of drug resistant tuberculosis", ZIBI, Scientific Symposium "Global Challenges of Acute and Chronic Tropical Infections", Humboldt University, 19 Jun 2012, 40 min (Y. Lenz)
- Established and organized the series; teaching of the following seminars: teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673, winter semester 2012/2013, (Y. Lenz)
- Seminar "Introduction to the aims and scope of infection epidemiology", teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673, 16 Oct 2012, 1.5 hours (Y. Lenz)
- Seminar "Link between laboratory and infectious diseases epidemiology", teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673, 27 Oct 2012, 1.5 hours (Y. Lenz)
- Seminar "Surveillance", teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673), 23 Oct 2012, 1.5 hours (A. Gilsdorf)
- Seminar "Types of epidemiological studies", teaching module "Infectious diseases epidemiology", conducted by RKI jointly with Humboldt and Freie Universities, mandatory module within the GRK1673, Nov 2011, 1.5 hours (A. Gilsdorf)
- Course "Introduction to epidemiology – IntoEpi", Annecy February 2009 and 2010, in cooperation with ECDC and EpiConcept, 3 weeks course: Concept and one week training (A. Gilsdorf)
- Facilitator in EPIET Module "Project Review", one week, August 2009 and 2010, Rome (A. Gilsdorf)

3. Cooperation with other scientists or research institutions

3.1. Internal (within RKI)

- Gérard Krause is member of various RKI internal committees.
- Andreas Gilsdorf is member of the strategic group on internationalization at the RKI.
- Yanina Lenz coordinated a serosurvey on EHEC jointly with ZBS. (Manuscript submitted)

For further cooperations see unit specific chapters

3.2. External / National

Epidemiological Steering Committee of the National Cohort

See 2.4.1., AL3

German Centre for Infection Research

The German centre for infection research (Deutsches Zentrum für Infektionsforschung, DZIF) is an integrated multi-centre structure bringing together selected universities, university hospitals, and non-university research institutes to link their research and clinical infrastructure. DZIF aims to foster translational efforts aiming at novel diagnostic, preventive and therapeutic measures against the most important infectious diseases. Although the Berlin consortium (of which RKI was part of) was not selected for the DZIF, the director of the department for infectious disease epidemiology at RKI is providing epidemiological expertise within the DZIF through his HZI and RKI affiliation. This has not yet resulted in integration of RKI as a full member of DZIF, but the liaison function will at least help to avoid redundancies or interferences of respective research activities (see 2.3.12., AL3).

Working Group on Infectious Disease Epidemiology of the German Society for Epidemiology (DG Epi)

The director is active member of the Working Group on Infectious Disease Epidemiology of the German Society for Epidemiology (DG Epi) and the department has organised various meetings of the working group.

Assembly of the Highest Health Administrations of the 16 federal states in Germany (AOLG) and Working Group on Infectious Disease Control (AGI) of the AOLG

The director represents the RKI in the assembly of the Highest Health Administrations of the 16 federal states in Germany (AOLG) and in a specific Working Group on Infectious Disease Control (AGI) of that assembly. Since public health management lies within the federal states, representation of the RKI in these groups and providing scientific advice is of particular importance.

- Gottschalk R et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009
- Krause G et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2010

Humboldt University and Free University, Berlin

The department cooperates with Humboldt University, Berlin and Free University, Berlin for the university-course „Infectious disease epidemiology“ (see 2.6.2., AL3).

Children Hospital University Hospital, Freiburg

Together with Prof R. Berner, Children Hospital University Hospital Freiburg (now University Hospital Dresden) the director is supervising a doctoral thesis on invasive group B streptococcal (GBS) infections in adults, Germany. In a national prospective active surveillance study during a 2-year period (2009-2010) monthly questionnaires were sent by the RKI to 111 participating

microbiological laboratories to report isolation of GBS in any sample obtained from a normally sterile site in patients aged > 1 year.

University Hospital Frankfurt

Together with Priv. Doz. Dr. S. Wicker, head of occupational health at the Frankfurt University Hospital and Prof. R. Gottschalk, head of the Frankfurt Health Department the director is working on concepts to improve influenza vaccination coverage in medical personnel

- Wicker S et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012
- Wicker S et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2010

Ministry of Health

In the aim to gather scientific evidence for the drafting of the national plan for the prevention for antimicrobial resistance the director was actively involved (e.g. as thesis supervisor) in studies on surveillance and on patients' and physicians' attitudes and behaviour with respect to antimicrobial resistance.

- Velasco E et al., *Infection* 2011
- Velasco E et al., *BMJ Open* 2012
- Schweickert B et al., *Eur J Clin Microbiol Infect Dis* 2012

Paul Ehrlich Institute and the Federal Institute for Drugs and Medical Devices

Particularly during the pandemic the director interacted very intensively with the Paul Ehrlich Institute and the Federal Institute for Drugs and Medical Devices to assure the best available evidence regarding medical counter measures and vaccination.

- RKI & PEI, *Epid Bull* 2009

Federal Office of Consumer Protection and Food Safety (BVL), Federal Institute for Risk Assessment (BfR)

During planning and managing of food borne outbreaks the cooperation with the Federal Office of Consumer Protection and Food Safety and the Federal Institute for Risk Assessment under the Ministry of Agriculture is very important to allow fast and competent outbreak investigations both from a public health and a food safety side. This cooperation is mainly dealt with in the respective unit, but high level interactions require the involvement of the director of the department.

- Frank C et al., *N Engl J Med* 2011
- Buchholz U et al., *N Engl J Med* 2011
- Stark K et al., *Euro Surveill* 2012

3.3. External / International

General aspects of cooperation within the European Union

Since 2008 the director's office had one epidemiologist (A. Gilsdorf) in charge of the scientific coordination of international cooperation. This was an important step to align the overall international cooperation between the RKI, the European Centre for Disease Prevention and Control (ECDC) in Stockholm, and the European Commission. The continuity in content and presence at these institutions assures a strong constructive contribution of Germany, especially in the Advisory Forum, the Competent Body Working Group at ECDC, as well as in the Early Warning and Response System network. The director is permanent member of the Advisory Forum at ECDC (alternate: A. Gilsdorf). A. Gilsdorf is also co-founder of a small informal group of international coordinators of the Public Health Institutes of France, the Netherlands, United Kingdom and Germany, facilitating a better exchange of best practice among the institutes.

- Gottschalk R et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009
- Hollmeyer H et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009
- Schreck S et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009

- Wiese-Posselt M et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009

World Health Organization

The director was invited expert in a working group on the International Health Regulations (IHR) by WHO and in the IHR Review Committee of WHO, which also reviewed the H1N1 Flu pandemic in 2009.

- Amato-Gauci A et al., *Euro Surveill* 2011
- van Kerkhove MD et al., *PLoS Med* 2011
- Devaux I et al., *Euro Surveill* 2011
- Krause G et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2010
- ECDC working group et al., *Euro Surveill* 2009

Risk Assessment Guidelines for Diseases transmitted on Aircraft (RAGIDA), Response to Emerging Infectious Disease: Assessment and Development of Core Capacities and Tools (REACT)

The director was scientific lead of the REACT Projekt and A. Gilsdorf was involved in the RAGIDA project. Both projects were executed by unit 32 (see 2.2.7., Unit 32).

- Leitmeyer K et al., *Euro Surveill* 2011
- Mohr O et al., *Euro Surveill* 2012
- Askar M et al., *Euro Surveill* 2012

European Programme for Intervention Epidemiology Training (EPIET), ECDC

As an important national training site the director's office is involved in the activities regarding EPIET (see PAE).

- Bremer V et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009;
- Krause G et al., *Euro Surveill* 2009a
- Krause G et al., *Euro Surveill* 2009b

4. Appendix

4.1 Overview on achievements of the director's office, 2009-2012

4.1.1. Scientific publications, 2009 – 2012

Number of peer-review publications co-authored by members of the director's office: 67

Impact factor (IF) according to JCR (for 2012 according to 2011)

2009: 26,1

2010: 18,0

2011: 199,9

2012: 42,7

Cumulative 2009-12: 286,8

A) Original research articles in peer-review journals

2012 (until Sept.)

Böhmer MM, Walter D, Falkenhorst G, Müters S, **Krause G**, Wichmann O: Barriers to pandemic influenza vaccination and uptake of seasonal influenza vaccine in the post-pandemic season in Germany. *BMC Public Health* 2012; 12(1):938.

Dehnert M, Fingerle V, Klier C, Talaska T, Schlaud M, **Krause G**, Wilking H, Poggensee G: Seropositivity of Lyme Borreliosis and Associated Risk Factors: A Population-Based Study in Children and Adolescents in Germany (KiGGS). *PLoS One* 2012; 7(8):e41321.

Klein S, Schöneberg I, **Krause G**: Vom Zwang zur Pockenschutzimpfung zum Nationalen Impfplan - Die Entwicklung des Impfwesens vom Deutschen Kaiserreich bis heute [The historical development of Immunisation in Germany : From compulsory smallpox vaccination to a National Action Plan on Immunisation]. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012, 55(11-12):1512-1523.

Laude G, Kist M, **Krause G**: Referenznetzwerke aus Nationalen Referenzzentren mit assoziierten Konsiliarlaboratorien in Deutschland. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012; 55(2):223–230.

Mohr O, Askar M, Schink S, Eckmanns T, **Krause G**, Poggensee G: Evidence for airborne infectious disease transmission in public ground transport – a literature review. *Euro Surveill* 2012; 17(35):pii=20255.

Schweickert B, Noll I, Feig M, Claus H, **Krause G**, Velasco E, Eckmanns T: MRSA-surveillance in Germany: data from the Antibiotic Resistance Surveillance System (ARS) and the mandatory surveillance of MRSA in blood. *Eur J. Clin Microbiol Infect Dis* 2012; 31(8): 1855-1865.

Stark K, Bauerfeind R, Bernard H, Eckmanns T, Ethelberg S, Flieger A, Giesecke J, Greiner M, Karch H, **Krause G**, Mielke M, O'Brien SJ, Pulz M, Scheutz F, Schielke A, Stahl RA, Takkinen J, Tarr PI, Tauxe RV, Werber D: Experiences from the shiga toxin-producing *Escherichia coli* O104:H4 outbreak in Germany and research needs in the field, Berlin, 28-29 November 2011. *Euro Surveill* 2012; 17(7):pii=20091.

Suess T, Remschmidt C, Schink SB, Schweiger B, Nitsche A, Schroeder K, Doellinger J, Milde J, Haas W, Koehler I, **Krause G**, Buchholz U: The role of facemasks and hand hygiene in the prevention of influenza transmission in households: results from a cluster randomised trial; Berlin, Germany, 2009–2011. *BMC Infect Dis* 2012; 12(1):26.

Velasco E, Ziegelmann A, Eckmanns T, **Krause G**: Eliciting views on antibiotic prescribing and resistance among hospital and outpatient care physicians in Berlin, Germany: results of a qualitative study. *BMJ Open* 2012; 2(1):e000398.

Walter D, Böhmer MM, Reiter S, **Krause G**, Wichmann O: Risk perception and information-seeking behaviour during the 2009/10 influenza A(H1N1)pdm09 pandemic in Germany. *Euro Surveill* 2012; 17(13):pii=20131.

Werber D, **Krause G**, Frank C, Fruth A, Flieger A, Mielke M, Schaade L, Stark K: Outbreaks of virulent diarrhoeagenic *Escherichia coli* – are we in control? *BMC Med* 2012; 10(1):11.

Wicker S, Gottschalk R, Wolff U, **Krause G**, Rabenau HF: Influenzaimpfquoten in hessischen Krankenhäusern. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012; 55(8): 932–936.

Wilking H, Götsch U, Meier H, Thiele D, Askar M, Dehnert M, Frank C, Fruth A, **Krause G**, Prager R, Stark K, et al.: Identifying risk factors for Shiga toxin-producing *Escherichia coli* by payment information. *Emerg Infect Dis* 2012; 18(01):169-170.

2011

Altmann M, Wadl M, Altmann D, Benzler J, Eckmanns T, **Krause G**, Spode A, an der Heiden M: Timeliness of surveillance during outbreak of Shiga toxin-producing *Escherichia coli*, Germany, 2011. *Emerg Infect Dis* 2011; 17(10):1906–1909.

Amato-Gauci A, et al., European Influenza Surveillance Network EISN (for Germany: **Gilsdorf A**, Schweiger B, Poggensee G, **Krause G**, Buda S, Eckmanns T): Surveillance trends of the 2009 influenza A(H1N1) pandemic in Europe. *Euro Surveill* 2011; 16(26): pii: 19903.

Askar M, Faber MS, Frank C, Bernard H, **Gilsdorf A**, Fruth A, Prager R, Höhle M, Suess T, Wadl M, **Krause G**, Stark K, Werber D: Update on the ongoing outbreak of haemolytic uraemic syndrome due to Shiga toxin-producing *Escherichia coli* (STEC) serotype O104, Germany, May 2011. *Euro Surveill* 2011; 16(22):pii=19883.

Balabanova Y, **Gilsdorf A**, Buda S, Burger R, Eckmanns T, Gärtner B, Groß U, Haas W, Hamouda O, Hübner J, Jänisch T, Kist M, Kramer MH, Ledig T, Mielke M, Pulz M, Stark K, Suttrop N, Ulbrich U, Wichmann O, **Krause G**: Communicable Diseases Prioritized for Surveillance and Epidemiological Research: Results of a Standardized Prioritization Procedure in Germany, 2011. *PLoS One* 2011; 6(10):e25691.

Böhmer MM, Walter D, Müters S, **Krause G**, Wichmann O: Seasonal influenza vaccine uptake in Germany 2007/2008 and 2008/2009: Results from a national health update survey. *Vaccine* 2011; 29(27):4492-4498.

Böhmer MM, Walter D, **Krause G**, Müters S, Gößwald A, Wichmann O: Determinants of tetanus and seasonal influenza vaccine uptake in adults living in Germany. *Hum Vaccin* 2011; 7(12):1317–1325.

Buchholz U, Bernard H, Werber D, Böhmer MM, Remschmidt C, Wilking H, Deleré Y, an der Heiden M, Adlhoch C, Dreesman J, Ehlers J, Ethelberg S, Faber M, Frank C, Fricke G, Greiner M, Höhle M, Ivarsson S, Jark U, Kirchner M, Koch J, **Krause G**, Luber P, Rosner B, Stark K, Kühne M, RKI HUS investigation team: German Outbreak of *Escherichia coli* O104:H4 Associated with Sprouts. *N Engl J Med* 2011; 365(19):1763-1770.

Dudareva S, Schweiger B, Thamm M, Höhle M, Stark K, **Krause G**, Buda S, Haas W: Prevalence of Antibodies to 2009 Pandemic Influenza A (H1N1) Virus in German Adult Population in Pre- and Post-Pandemic Period. *PLoS One* 2011; 6(6):e21340.

Frank C, Faber MS, Askar M, Bernard H, Fruth A, **Gilsdorf A**, Höhle M, Karch H, **Krause G**, Prager R, Spode A, Stark K, Werber D, on behalf of the HUS investigation team: Large and ongoing outbreak of haemolytic uraemic syndrome, Germany, May 2011. *Euro Surveill* 2011; 16(21):pii=19878.

Frank C, Werber D, Cramer JP, Askar M, Faber M, an der Heiden M, Bernard H, Fruth A, Prager R, Spode A, Wadl M, Zoufaly A, Jordan S, Stark K, **Krause G**, for the HUS Investigation Team: Epidemic Profile of Shiga-Toxin-Producing *Escherichia coli* O104:H4 Outbreak in Germany - Preliminary Report. *N Engl J Med* 2011; 365(19):1771-1780.

Gagliotti C, Balode A, Baquero F, et al., EARS-Net Participants (Disease Specific Contact Points for AMR; for Germany, Altmann D, **Gilsdorf A**, Noll I, Tille A, Witte W): *Escherichia coli* and

Staphylococcus aureus: bad news and good news from the European Antimicrobial Resistance Surveillance Network (EARS-Net, formerly EARSS), 2002 to 2009. *Euro Surveill* 2011; 16 (11): pii=19819.

Gilsdorf A, Krause G: Prioritisation of infectious diseases in public health: feedback on the prioritisation methodology, 15 July 2008 to 15 January 2009. *Euro Surveill* 2011; 16(18):pii=19861.

Gilsdorf A, Krause G: Authors reply: Prioritisation of infectious diseases in public health: feedback on the prioritisation methodology, 15 July 2008 to 15 January 2009. *Euro Surveill* 2011; 16 (27): pii=19912.

Leitmeyer K, (Participants from RKI, Schenkel K, Amorosa R, Mücke I, Dias-Ferrao V, Diercke M, **Krause G**, Eckmanns T, (RAGIDA Part 1), Interviewed experts, Brodhun B, Buchholz U, Buda S, Frank C, Haas W, Hellenbrand W, Koch J, Poggensee G, Sagebiel D, Siedler A, Stark K, et al. Participants for RAGIDA Part 2, Eckmanns T, **Gilsdorf A**, Grunow R, Hellenbrand W, Siedler A, et al.): European Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft – the RAGIDA project. *Euro Surveill* 2011; 16 (16): pii=19845.

Siedler A, Mankertz A, Feil F, Ahlemeyer G, Hornig A, Kirchner M, Beyrer K, Dreesman J, Scharkus S, Marcic A, Reiter S, Matysiak-Klose D, Santibanez S, **Krause G**, Wichmann O: Closer to the Goal: Efforts in Measles Elimination in Germany 2010. *J Infect Dis* 2011; 204(Suppl.1):S373-S380.

Ultsch B, Siedler A, Rieck T, Reinhold T, **Krause G**, Wichmann O: Herpes zoster in Germany: Quantifying the burden of disease. *BMC Infect Dis* 2011; 11:173.

van Kerkhove MD, et al. (for Germany, Buda S, **Krause G**, Haas W), on behalf of the WHO Working Group for Risk Factors for Severe H1N1pdm Infection: Risk Factors for Severe Outcomes following 2009 Influenza A (H1N1) Infection: A Global Pooled Analysis. *PLoS Med* 2011; 8 (7): e1001053.

Velasco E, Espelage W, Faber M, Noll I, Ziegelmann A, **Krause G**, Eckmanns T: A national cross-sectional study on socio-behavioural factors that influence physicians' decisions to begin antimicrobial therapy. *Infection* 2011; 39(4):289-297.

Wadl M, Rieck T, Nachtnebel M, Greutelaers B, an der Heiden M, Altmann D, Hellenbrand W, Faber M, Frank C, Schweickert B, **Krause G**, Benzler J, Eckmanns T, on behalf of the HUS surveillance and laboratory team: Enhanced surveillance during a large outbreak of bloody diarrhoea and haemolytic uraemic syndrome caused by Shiga toxin/verotoxin-producing *Escherichia coli* in Germany, May to June 2011. *Euro Surveill* 2011; 16(24):pii=19893.

Walter D, Böhmer MM, an der Heiden M, Reiter S, **Krause G**, Wichmann O (2011): Monitoring pandemic influenza A(H1N1) vaccination coverage in Germany 2009/10 - Results from thirteen consecutive cross-sectional surveys. *Vaccine* 2011; 29(23):4008-4012.

2010

Devaux I, Kreidl P, Penttinen P, Salminen M, Zucs P, Ammon A, on behalf of the ECDC influenza surveillance group, and the national coordinators for influenza surveillance (for Germany: **Gilsdorf A**, Schweiger B, Poggensee G, **Krause G**, Buda S, Eckmanns T): Initial surveillance of 2009 influenza A(H1N1) pandemic in the European Union and European Economic Area, April - September 2009. *Euro Surveill* 2010; 15(49):pii=19740. Erratum in: *Euro Surveill* 2011; 16(3): pii=19769.

Gilsdorf A, Poggensee G, Working Group Pandemic Influenza A(H1N1)v: Influenza A(H1N1)v in Germany: the first 10,000 cases. *Euro Surveill* 2010; 15(34):pii=19318.

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B) Overview articles or systematic reviews (incl. non peer-review articles)

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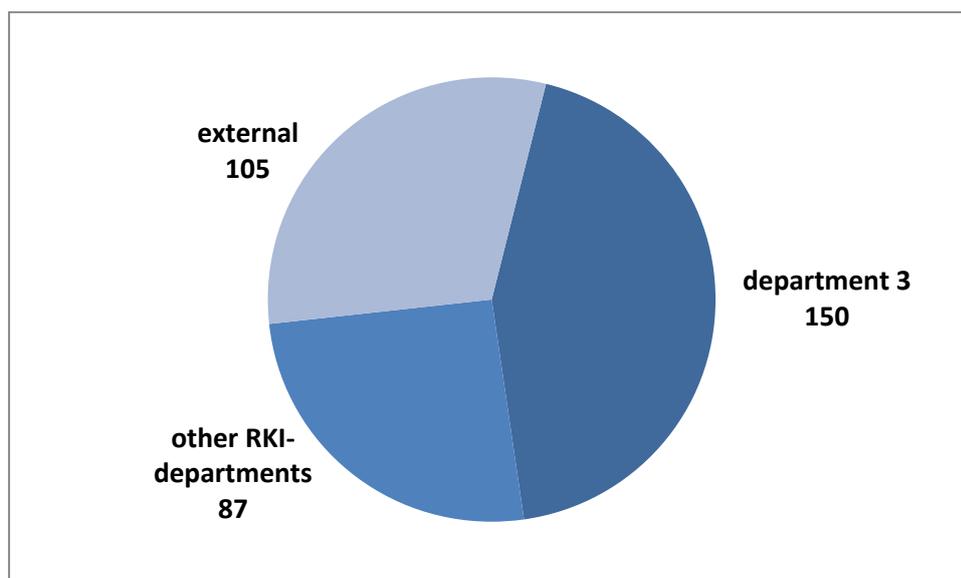
C) Book chapters

Krause G. *Electronic Reporting in Infectious Disease Surveillance*, In: M'ikanatha N, Lynfield R, Van Beneden C, de Valk H. *Infectious Disease Surveillance*. Blackwell, London, in print

D) Articles in the Epidemiological Bulletin

From issue 1, 2009 to issue 49, 2012 of the Epidemiological Bulletin, the department has contributed 150 of the 341 articles (not including fact sheets for physicians). This amounts to 43% of all and 63% of all RKI-contributions. The detailed list of Bulletin articles can be found under the respective unit chapters.

Figure 4: Number of articles contributed by department for infectious disease epidemiology, compared to other internal and external contributors 2009-2012 to the Epidemiological Bulletin (44%, fact sheets for physicians not included) (n=341)



Contributions to the Epidemiological Bulletin by the director's office alone:

Priorisierung übertragbarer Infektionserreger unter dem Aspekt der Surveillance und epidemiologischen Forschung. *Epid Bull* 2011; 44:397-404.

Aktuelle Initiativen zur Bewertung der im Verlauf der Pandemie geleisteten Arbeit. *Epid Bull* 2010; 19: 171-173.

Etablierung von Referenznetzwerken aus Nationalen Referenzzentren mit assoziierten Konsiliarlaboratorien in Deutschland. *Epid Bull* 2009; 44:455-458'.

4.1.2. Selected relevant publications

Five important publications for the scientific community 2009–2012

1. Velasco E, Ziegelmann A, Eckmanns T, **Krause G**. Eliciting views on antibiotic prescribing and resistance among hospital and outpatient care physicians in Berlin, Germany: results of a qualitative study. *BMJ Open* 2012; 2(1):e000398.
2. Frank C, Werber D, Cramer JP, Askar M, Faber M, an der Heiden M, Bernard H, Fruth A, Prager R, Spode A, Wadl M, Zoufaly A, Jordan S, Kemper MJ, Follin P, Müller L, King LA, Rosner B, Buchholz U, Stark K, **Krause G**; Epidemic profile of Shiga-toxin-producing *Escherichia coli* O104:H4 outbreak in Germany. *N Engl J Med* 2011; 365(19):1771-1780.
3. **Balabanova Y, Gilsdorf A**, Buda S, Burger R, Eckmanns T, Gärtner B, Groß U, Haas W, Hamouda O, Hübner J, Jänisch T, Kist M, Kramer MH, Ledig T, Mielke M, Pulz M, Stark K, Suttorp N, Ulbrich U, Wichmann O, **Krause G**: Communicable Diseases Prioritized for Surveillance and Epidemiological Research: Results of a Standardized Prioritization Procedure in Germany, 2011. *PLoS One* 2011; 6(10):e25691.
4. Suess T, Buchholz U, Dupke S, Grunow R, an der Heiden M, Heider A, Biere B, Schweiger B, Haas W, **Krause G**; Shedding and transmission of novel influenza virus A/H1N1 infection in households--Germany, 2009. *Am J Epidemiol* 2010;171(11):1157-1164.
5. Wichmann O, Siedler A, Sagebiel D, Hellenbrand W, Santibanez S, Mankertz A, Vogt G, **Krause G**. Further efforts needed to achieve measles elimination in Germany: Results of an outbreak investigation *Bulletin of the World Health Organization* 2009; 87(2):108-115.

Five important publications for the public 2009–2012

1. RKI & PEI: Vorläufige Empfehlungen des Paul-Ehrlich-Instituts und des Robert Koch Institutes zur Anzahl der benötigten Teildosen des pandemischen Impfstoffs Pandemrix® (GSK) zum Schutz gegen die Neue Influenza A (H1N1) und zu dessen Anwendung in der Schwangerschaft. *Epid Bull* 2009; 41:425-426.
2. Vorläufige Ergebnisse der EHEC/HUS-Studie. EHEC O104:H4-Ausbruchsgeschehen in Deutschland aufgeklärt: Auslöser waren Sprossen von aus Ägypten importierten Bockshornkleesamen. Gemeinsame Pressemitteilungen von BfR und RKI 25.5.2011 und vom BfR, BVL und RKI am 5.7.2011
3. **Krause G, Gilsdorf A**, Becker J, Bradt K, Dreweck C, Gärtner B, Löwer J, Marcic A, Nicoll A, Pott E, Schaade L, Schoeller A, Stollorz V, Träger C, Razum O. Erster Erfahrungsaustausch zur H1N1-Pandemie in Deutschland 2009/2010. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2010; 53:510-519.
4. **Krause G**, Frank C, **Gilsdorf G**, Mielke M, Schaade L, Stark K, Burger R, Der HUS-Ausbruch 2011 in Deutschland - Herausforderungen für den Infektionsschutz: Was sollte verbessert werden? *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2013;
5. 48 Fact sheets physicians:
http://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/merkblaetter_node.html

4.1.3. List of disease specific fact sheets for physicians (Ratgeber) N=48

	First publication	Updates
Influenza	1999	2001; 2004; 2006; 2008; 5/2009; 7/2009; 10/2009; 2011
Meningococcal disease	1999	2002; 2003; 2004; 2007; 2009; 2010; 2011
Early summer meningoencephalitis	1999	2001; 2003; 2004; 2007; 2009; 2010; 2011
Lyme borreliosis	1999	2001; 2007
Hepatitis A	1999	2001; 2006; 1/2008; 3/2008; 9/2008
EHEC	1999	2001; 2007; 2008; 2011
Campylobacter	1999	2001; 2005
Rabies	1999	2002; 2005; 1/2009; 4/2009; 2010

Measles	1999	2002; 2004; 2009; 4/2010; 9/2010
Legionella	1999	2001; 2006
Norovirus	2000	2002; 2005; 2007; 2008
MRSA	2000	2003; 2007; 2009
Tuberculosis	2000	2002; 2009
Listeria	2000	2003; 2010
Malaria	2000	2003; 2006; 2012
Poliomyelitis	2000	2004; 2008; 2009; 2011
Hepatitis B	2000	2002; 2004; 2011
Abdominal typhoid, paratyphoid	2000	2005; 2007; 2008
Scarlet fever	2000	2008
Varicella	2000	2002; 2004; 2010
Diphtheria	2001	2007; 2009
Chlamydia trachomatis	2001	2009
Chlamydia psittaci, pneumoniae	2001	2009
Rubella	2001	2003; 2010
Yellow fever	2001	2010
Shigellosis	2001	2007; 2012
Mumps	2001	2003
Pertussis	2001	2006; 2008; 3/2010; 9/2010
Trichinellosis	2002	-
Rotavirus	2002	2007; 2010
Tetanus	2002	2004; 2010
Q Fever	2002	2003; 2009
Lassa fever	2002	2011
Epidemic keratoconjunctivitis	2003	2004; 2010
Syphilis	2003	2004; 2007
Head lice	2003	2007; 2008
RSV	2004	2011
Hepatitis C	2004	2011; 2012
Cryptosporidiosis	2004	-
Brucellosis	2005	2008
Echinococcosis	2005	-
HIV/AIDS	2006	2011
Hantavirus	2006	-
Toxoplasmosis	2007	12/2007; 2009
Salmonellosis	2009	-
Scabies	2009	-
Clostridium difficile	2009	-
Anthrax	2012	-

4.1.4. Overview on collaborations in networks

See 3. AL3

4.1.5. Memberships and participation in Advisory Boards

Dr. Andreas Gilsdorf

- Advisory Forum of the ECDC, Deputy
- EWRS Focal Points at European Commission
- Network Committee Generic Preparedness Section

Prof. Dr. Gérard Krause

- Advisory Forum of the ECDC
- Competent body for Threat Detection of the ECDC
- Competent body for Response of the ECDC

- Competent body for Preparedness of the ECDC
- Competent body for Preparing Guidelines of the ECDC
- Competent body for Scientific Advice of the ECDC
- Expert group for evidence based public health recommendations at ECDC
- External expert in the IHR review committee at WHO
- Coordinator of the infectious disease working group of the National Cohort
- Member of Scientific Advisory Board of the German Association for Infectiology (DGI)
- Member of Advisory Board for the National Reference Centres in Belgium
- Steering committee for the European Programme for Intervention Epidemiology Training (EPIET), chairman: 2006-2007
- Member of EPIET training site forum 2005 - 2007
- German Society for Epidemiology (DGepi)
- EPIET Alumni network
- EIS Alumni Network
- Representative of founding member of national cohort association
- Member of epidemiological steering committee of national cohort
- Member of steering committee of HZI
- Member of scientific committee of HZI

4.1.6. List of completed dissertation or master theses in the director's office, 2009 – 2012

Year	Title	Name	Degree	University/ Supervisor RKI
2012	Population based serial cross-sectional surveys on influenza H1N1 vaccination coverage 2009/2010	Dietmar Walter	Dr. rer. medic.	Charité / Krause
2012	Prescribing habits for antimicrobial treatment in Germany	Edward Velasco	Dr. rer. medic.	Charité / Krause
2012	Polio eradication Analysis of enterovirus surveillance in Germany	Katrin Neubauer	Master of Science in Epidemiology	Berlin School of Public Health / Krause
2012	Prevalence of primary resistant HIV	Fabia zu Knyphausen	Master of Science in Epidemiology	Berlin School of Public Health / Krause
2012	Das Landesgesundheitsamt als Schnittstelle zwischen Gesundheitsämtern und Robert Koch Institute im öffentlichen Gesundheitsdienst in Deutschland. Ausgewählte Aufgaben des niedersächsischen Landesgesundheitsamt (NLGA) am Beispiel von wissenschaftlichen Studien im Bereich der angewandten Epidemiologie	M. Diercke	Master of Science in Epidemiology	Berlin School of Public Health / Krause, Dreesmann (Federal Health Authority Lower Saxony)
2011	Das Erkennen, Bekämpfen und Verhüten von Infektionskrankheiten	C. Adlhoch	Master of Science in Epidemiology	Berlin School of Public Health / Krause, Eckmanns
2009	Identification of risk factors for antimicrobial resistance in Escherichia Coli	Kirstin Heckenbach	Master of Public Health	Berlin School of Public Health / Krause
2008	Epidemiological Methods in Infectious Disease Control	Annette Schrauder	Dr. med.	Charité / Krause

4.1.7. Reports and written scientific advice to the Ministry of Health

There were 211 reports and written scientific advice to the Ministry of Health between 2009 and 30.09.2012. The overall number of reports varies from the sum of reports in the respective unit sections due to the contribution of multiple units to many reports.

4.1.8. Presentations as invited speaker, 2009-2012

Staff from the Director's Office were invited to speak at 55 conferences.

4.1.9. Outbreak investigations with on site participation of staff of the department (including PAE fellows of the department assigned to the regional health authorities) 2009-2012

Title	Place	Year
RSV outbreak	Heidelberg, Baden-Wuerttemberg	2012
Investigation of a pointsource gastroenteritis outbreak in a canteen	Berlin	2012
<i>Salmonella</i> Muenchen outbreak	Bavaria	2012
<i>Salmonella</i> Typhimurium outbreak	Lauenburg	2012
Gastrointestinal outbreak in a kindergarten	Rhineland-Palatinate	2012
Adenovirus outbreak in Germany	Baden-Wuerttemberg	2012
Nosocomial outbreak of resistant <i>Klebsiella</i> spp	Leipzig	2012
Nosocomial outbreak of <i>Salmonella aureus</i>	Berlin	2012
<i>Legionella</i> spp. outbreak	Rhineland-Palatinate	2012
Risk assessment in a training and research institute for animal husbandry affected by Q fever	Schleswig-Holstein	2012
Measles outbreak	Landau	2012
CA-MRSA-cases in a asylum seeker shelter	Neumünster, Schleswig-Holstein	2011
Gastroenteritis outbreak after a scientific workshop	Berlin	2011
Shiga-toxin-producing <i>Escherichia coli</i> O104:H4 outbreak	Northern Germany plus exported cases	2011
Recipe-based restaurant cohort study of ten groups of diners during a large STEC-outbreak	Lübeck	2011
Investigation of a satellite outbreak within a large Shiga-toxin-producing <i>Escherichia coli</i> (STEC) O104 outbreak in a company cafeterias	Frankfurt	2011
Measles outbreak after a school trip	Berlin	2011
Mumps outbreak at a school	Nueremberg	2011
<i>Salmonella</i> Senftenberg outbreak	Germany	2011
Increase of Hepatitis E cases	Germany	2011
<i>Salmonella</i> Typhimurium outbreak	Saxony-Anhalt	2011
EHEC/HUS outbreak	Northern Germany	2011
Cohort study on cluster of STEC O104:H4 cases	Göttingen	2011

Gastrointestinal outbreak in a teaching conference	Menorca, Spain	2011
ESBL- <i>Klebsiella</i> -outbreak on a neonatal care unit in Germany	Bremen	2011
EHEC/HUS-outbreak after a birthday celebration	Lower Saxony	2011
<i>Salmonella</i> Newport	German federal states	2011
HBV in a home for the elderly	Görlitz	2011
Measles outbreak	Baden-Wuerttemberg	2011
<i>Varicella</i> outbreak	Baden-Wuerttemberg	2011
Nosocomial MRSA outbreak in a neonatology ward	Berlin	2010
Nationwide outbreak of <i>Salmonella</i> Panama	Germany	2010
Measles outbreak at school	Berlin	2010
Anthrax outbreak in Europe, an active surveillance study	Aachen region	2010
Severe infections of <i>Salmonella</i> Enteritidis after BBQ	Rhineland Palatinate	2010
Outbreak of <i>Salmonella</i> Montevideo associated with a dietary food supplement flagged in the Rapid Alert System for Food and Feed (RASFF)	Western Germany	2010
<i>Varicella</i> in an asylum seeker home	Bavaria	2010
<i>Salmonella</i> Montevideo	German federal states	2010
Food-borne <i>Listeria monocytogenes</i> outbreak associated with a traditional herring product	Germany	2010
<i>Shigella sonnei</i> in two kindergartens and several families	Landau	2010
Norovirus outbreak	Bavaria	2010
Hepatitis B outbreak in a nursing home for elderly	Lower Saxony	2010
Measles outbreak in an asylum seeker shelter	Neumünster, Schleswig-Holstein	2010
Community <i>Legionella</i> outbreak	Ulm/Neu-Ulm	2010
Outbreak of <i>Salmonella</i> Enteritidis in a kindergarten	Bavaria	2010
Cluster of pertussis cases in schoolchildren	Bavaria	2010
<i>Varicella</i> outbreak in asylum seekers hostels	Bavaria	2010
Gastroenteritis outbreak in a holiday camp	Bavaria	2010
Outbreak of gastroenteritis after a wedding party,	Bavaria	2010
Adenovirus-Keratoconjunctivitis outbreak	Germany	2010
Case-control study of a large (~350 cases) outbreak of gastrointestinal disease amongst hill walkers frequenting an alpine hut	Oberallgäu, Bavaria	2009
Influenza A/H1N1 outbreak after a teenage party	Würzburg, Bavaria	2009
Tuberculosis in a school	Wilhellshaven, Lower Saxony	2009
<i>Salmonella</i> Enteritidis in a bakery	Bavaria	2009
Outbreak of <i>Salmonella</i> Enteritidis in a bakery	North-Rhine-	2009

	Westphalia	
Norovirus-gastroenteritis in a military barrack	Leipzig	2009
Preliminary case report of fatal anthrax in an injecting drug user	North-Rhine-Westphalia	2009
HUS outbreak due to sorbitol-fermenting EHEC O157:H-	Hamburg	2009
Pertussis in a physician's practice	Saxony-Anhalt	2009
<i>Salmonella</i> Infantis in a rehab centre	Calw, Baden-Wuerttemberg	2009
Nosocomial <i>Enterobacter</i>	Homburg, Saarland	2009
Legionellosis on a cruise ship	Dubai	2009
<i>Salmonella</i> Ohio	Germany	2009

4.2. Mission statement

The department's superior goal is

Prevention, Detection and Control of Infectious Diseases in Germany's Population

through

- Continuous surveillance and assessment of the epidemic situation
- Implementation and support of outbreak investigations
- Development and evaluation of strategies for prevention and intervention
- Research and method development in the field of infectious disease epidemiology
- Execution of legal duties in the field of infectious disease control
- Support and advice for other partners of the public health service and political decision makers
- Development of evidence-based recommendations for the public health service
- Information for the public
- Exchange with other national and international health authorities
- Qualification and further training in the field of public health with emphasis on infectious disease epidemiology

We pursue that objective with the following self-conception:

- We foster intensive scientific exchange and cooperation with partners within and outside the institute.
- We are a partner in the national and international public health service.
- Urgent threats to public health have high priority and we react quickly, flexibly and with high commitment.
- We conduct scientific projects according to good epidemiological practice and acknowledged ethical standards.
- Our recommendations and decisions are based on academic evidence.
- We assure for continuity in regards of content.
- We work scientifically independent.
- We communicate new findings quickly.
- We make our procedures and decisions transparent.
- We are a team.
- We appreciate our team's diversity and stand up for each other.
- Further qualification and personal development are important to us.
- We are able to make use of flexibility in work time and content.
- We use interdisciplinary approaches and take on responsibility.
- All technical and professional areas contribute equally to the success of our work.

4.3. Pathogens Prioritised for Surveillance and Epidemiological Research

From Balabanova Y et al. PLoS One 2011; 6(10):e25691

Table 3. List of pathogens in groups of priority (n = 127), Germany.

Highest priority group: scores between 76 and 100 (n = 26)	High priority group: scores between 51 and 76 (n = 39)	Medium priority group: scores between 26 and 50 (n = 45)	Low priority group: scores between 0 and 25 (n = 17)
<i>Campylobacter</i> spp	<i>Acinetobacter</i>	<i>Bacillus anthracis</i>	Actinomycosis
<i>Chlamydia trachomatis</i>	Adenovirus	<i>Bacillus cereus</i>	Astrovirus
<i>Clostridium difficile</i>	Arthropod-borne viral encephalitides	<i>Bartonella quintana</i>	<i>Chlamydia pneumoniae</i>
<i>Escherichia coli</i> , shiga toxin producing (STEC/HUS)	<i>Aspergillus</i> spp.	<i>Bordetella pertussis</i>	Coxsackievirus
<i>Escherichia coli</i> (non-gastro illnesses)	<i>Brucella</i> spp	<i>Borrelia burgdorferi</i>	<i>Cyclospora cayetanensis</i>
<i>Enterobacter</i> spp.	<i>Corynebacterium ulcerans</i> and <i>Corynebacterium pseudotuberculosis</i>	<i>Burkholderia cepacia</i>	<i>Entamoeba histolytica</i>
<i>Enterococcus</i> spp. (blood)	Prions causing Creutzfeldt Jakob Diseases	<i>Burkholderia pseudomallei</i> and <i>mallei</i>	Fungi (other)*
Hantavirus	Crimean-Congo hemorrhagic fever virus	<i>Candida</i> spp.	Helminths (flukes)**
<i>Helicobacter pylori</i>	<i>Cryptosporidium parvum/hominis</i>	<i>Chlamydia psittaci</i>	Helminths (nematodes)***
Hepatitis B virus	Dengue fever virus	<i>Citrobacter</i> spp.	Helminths (tapeworms)****
Hepatitis C virus	Early summer meningoencephalitis virus and other tick-borne meningoencephalitis viruses	<i>Clostridium botulinum</i>	HHV -6 and 7 (roseolovirus)
Human immunodeficiency virus (HIV)	Ebola and Marburg virus	<i>Clostridium perfringens</i>	<i>Histoplasma capsulatum</i>
Influenza virus	Enteroviruses spp. incl. echoviruses	<i>Clostridium tetani</i>	<i>Klebsiella granulomatis</i>
<i>Klebsiella</i> spp.	Epstein-Barr virus (HHV-4)	Coronaviruses	Molluscipoxvirus
<i>Legionella pneumophila</i>	<i>Giardia lamblia</i>	<i>Corynebacterium diphtheriae</i>	<i>Mycobacterium leprae</i>
Measles virus	<i>Haemophilus influenzae</i>	<i>Coxiella burnetii</i>	<i>Pneumocystis jiroveci</i>
<i>Mycobacterium tuberculosis</i>	Hepatitis A virus	Cryptococcosis	Unidentified agent causing Kawasaki syndrome
<i>Neisseria meningitidis</i>	Hepatitis D virus	Cytomegalovirus (HHV-5)	
<i>Pseudomonas</i> spp.	Hepatitis E virus	<i>Escherichia coli</i> , enteropathogenic (non STEC/HUS), enterotoxigenic strains, enteroinvasive, enteroaggregative and diffuse-adherence strains	
Respiratory syncytial virus (RSV)	Human papilloma virus (HPV)	<i>Francisella tularensis</i>	
<i>Salmonella</i> spp. (non-typhi and non-paratyphi)	Lassa fever virus	Herpes simplex virus (HSV)-1	
<i>Staphylococcus aureus</i> incl. methicillin resistant (MRSA) and <i>Staphylococcus aureus</i> , toxigenic	<i>Listeria monocytogenes</i>	Herpes simplex virus (HSV)-2	
<i>Staphylococcus epidermidis/Coagulase-negative staphylococci</i>	<i>Microspora and trichophyton</i>	HHV-8 (Kaposi's sarcoma associated)	
<i>Streptococcus pneumoniae</i>	Mumps virus	Human T-cell lymphotropic virus (HTLV)	
<i>Streptococcus</i> spp. other than <i>Streptococcus pneumoniae</i>	<i>Mycoplasma</i> spp.	<i>Leishmania</i> spp.	
Varicella zoster virus (VZV)	<i>Neisseria gonorrhoeae</i>	<i>Leptospira interrogans</i>	
	Norovirus	<i>Mycobacterium</i> , other (non-tuberculous)	
	Parainfluenza viruses	Parvovirus B 19	
	Pediculosis (head, body and pubic lice)	<i>Plasmodium</i> spp.	
	Polio virus	Rhinoviruses	
	Rabies virus	<i>Rickettsia prowazekii</i> , <i>typhi</i> and <i>Orientia tsutsugamushi</i>	
	Rotavirus	<i>Rickettsia</i> spp.	
	SARS coronavirus (SARS-CoV)	Rubella virus	
	<i>Toxoplasma gondii</i>	<i>Salmonella paratyphi</i> and <i>Salmonella typhi</i>	
	Variola virus	<i>Sarcoptes scabiei</i>	
	Viruses, others causing hemorrhagic fevers (Chikungunya, Rift Valley)	<i>Shigella</i> spp.	
	West Nile virus	<i>Stenotrophomonas (Pseudomonas) maltophilia</i>	
	Yellow fever virus	<i>Treponema pallidum</i>	
	<i>Yersinia enterocolitica</i> and <i>pseudotuberculosis</i>	<i>Trichinella spiralis</i>	
		<i>Trichomonas vaginalis</i>	
		<i>Trypanosoma brucei gambiensi</i> and <i>brucei rhodesiensi</i>	
		Vaccinia virus	
		<i>Vibrio cholera</i>	
		<i>Vibrios</i> (non-cholera): <i>V. parahaemolyticus</i> , <i>V. vulnificus</i> and <i>V. cholerae</i> (non O1 and O139)	
		<i>Yersinia pestis</i>	

*Fungi (other) group includes: Blastomyces, Fonsecaea, Phialophora, Cladosporium, Fonsecaea, Coccidioides immitis and posadasii, Actinomyces, Sporothrix, Paracoccidioides, Zygomycota.

**Helminths (flukes) group includes: Clonorchis sinensis, Opisthorchis felinus, Opisthorchis viverrini, Fasciolopsis buski, gigantica and hepatica, Paragonimus, Schistosoma.

***Helminths (nematodes) group includes: Ancylostoma braziliense and caninum, Angiostrongylus, Ascaris lumbricoides, Capillaria philippinensis, hepatica and aerophila, Dracunculus medietensis, Enterobius vermicularis, Filaria (Onchocerca volvulus, Loa loa, Wuchereria bancrofti, Brugia malayi and Brugia timori), hookworms (Ancylostoma duodenale and Necator americanus), Strongyloides stercoralis, Toxocara canis and cati, Trichuris trichiura. Trichinella spiralis was scored as a separate pathogen.

****Helminths (tapeworms) group includes: Diphyllobotrium latum, Echinococcus granulosus, Echinococcus multilocularis, Hymenolepis nana, Taenia saginata, Taenia solium.

4.4. Networks of National Reference Centres and Consiliary Laboratories (German Version)

Network for parasites, tropical and vectro transmitted diseases (spokesperson: B. Fleischer, Hamburg)

Regular members: NRC Tropical infectious agents, NRC Borreliosis, CL Ehrlichia, CL Echinococces, CL Filoviruses, CL Early Summer Meningo-Encephalitis

Additional members: CL *Cryptococcus neoformans*, *Pseudallescheria boydii*/ *Scedosporium* sp. and non-european systemic mycotic pathogens

Network for enteric infections (Spokesperson: A. Flieger, Wernigerode)

Regular members: NRC Salmonella and other bacterial enteric pathogens, CL Bacterial gastrointestinal infections, CL Haemolytic uremic syndrome (HUS), CL Listeria, CL Noroviruses, CL Rotaviruses, CL Hepatitis-A-Virus, Hepatitis-E-Virus, CL *Clostridium difficile*, CL Electron-microscopial diagnosis of pathogens, CL *Treponema*, CL Whipple-Bacterium

Additional members: NRC Tropical infectious agents, CL Adenoviruses

Network for invasive bacterial infections (spokesperson: M. Frosch/ U. Vogel, Würzburg)

Regular members: NRC Meningococci, NRC Streptococci, CL diphtheria, CL *Haemophilus influenzae*

Additional member: CL Anaerobic bacteria

Network for respiratory infections(spokesperson: B. Schweiger, Berlin)

Regular members: NRC Influenza, NRC Mycobacteria, CL Adenoviruses, CL Klebsiella, CL Legionella, CL *Bordetella pertussis*, CL Mykoplasm, CL Respiratory syncytial viruses Parainfluenzaviruses, Metapneumoviruses, CL Actinomyzes CL Chlamydia

Additional members: NRC Streptococci, CL Parvoviruses, CL *Cryptococcus neoformans*, *Pseudallescheria boydii*/ *Scedosporium* sp. and non-european systemic mycotic pathogens, CL *Aspergillus*, CL Mukoviszidosis-bacteriology

Network for mykoses (spokesperson: U. Groß, Göttingen)

Regular members: NRC Systemic mycoses, CL *Aspergillus*, CL *Cryptococcus neoformans*, *Pseudallescheria boydii*/ *Scedosporium* sp. and non-European systemic mycotic pathogens, CL dermatophytes

Additional member: CL Mukoviszidosisi bacteriology

Network for sexually or blood transmitted infections (spokesperson: H. Pfister, Köln)

Regular members: NRC Hepatitis-C-Virus, NRC Retroviruses, NRC Papilloma and Polyomaviruses, NRC Hepatitis-B-Virus und Hepatitis-D-Virus, CL *Treponema*, CL Gonococci

Additional members: CL Parvoviruses, CL Chlamydia

Network for infections during immune deficiency or pregnancy (spokesperson: T. Mertens, Ulm)

Regular members: NRC Measles, Mumps, Rubella , NRC Poliomyelitis and enteroviruses, CL Epstein-Barr-Virus, Human Herpes-Virus 6, 7, 8, CL *Herpes-simplex-Virus*, *Varizella-Zoster-Virus*, CL Humanes cytomegalivirus (HCMV), CL Congenital virus infections(HCMV), CL Parvoviruses, CL Toxoplasma

Additional members: NRC Streptococci, NRC Papilloma- and polyomaviruses, CL Adenoviruses, CL Listeria, CL *Treponema*

Network for antimicrobial resistence (spokesperson: G. Werner, Wernigerode)

Regular members: NRC Staphylococciand enterococci, NRC *Helicobacter pylori*, NRC Surveillance of nosocomial infections, NRC Gramnegative hospital pathogens, CL Anaerobic bacteria, CL

Mukoviszidosis bacteriology

Additional members: NRC Systemicmycoses, NRC Salmonella and other bacterial enteric pathogens, CL Klebsiella

Network for zoonoses (spokesperson: V. Kempf, Frankfurt/Main)

Regular members: CL Bartonella, CL Brucella, CL *Coxiella burnetii*, CL Hantavirus, CL Smallpox viruses, CL Rabies, CL Tularemia, CL *Yersinia pestis*, CL Leptospirosis, CL Elektron microscopic diagnosis of pathogens

Additional members: NRC Tropical pathogens, NRC Streptococci, NRC Salmonella and other bacterial enteric pathogens, CL Early summer meningo encephalitis, CL Chlamydia, CL Toxoplasmosis, CL Filoviruses

Network for infections of the central nervous system (spokesperson: I. Zerr, Göttingen)

Regular members: NRC Surveillance of transmissible spongiform encephalopathies, NRC Poliomyelitis und enteroviruses, CL Viral CNS infections

Additional members: CL *Cryptococcus neoformans*, *pseudallescheria boydii* *scedosporium* sp. and non-european systemic mycotic pathogens, CL Early summer meningo encephalitis, CL Toxoplasma, CL Treponema

Unit PAE: Training Programmes in Infectious Disease Epidemiology

Unit Head: Dr. Katharina Alpers

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1. General information - PAE

Postgraduate Training for Applied Epidemiology (PAE) and European Programme for Intervention Epidemiology Training (EPIET)

Head: **Dr. Katharina Alpers**

Deputy: **Dr. Manuel Dehnert**

2. Tasks and goals of the unit

2.1. Summary

The major goal of the unit “training programmes in infectious disease epidemiology” is competency based and service-oriented training of experts in infectious disease control and prevention in order to create a national and international network of experts who employ the appropriate resources and epidemiologic methods to identify the source of public health problems and to establish immediate and long term control and prevention measures.

The postgraduate training for applied epidemiology (PAE) is a 2- year fellowship programme which provides training in field epidemiology by supervised learning-by-doing.

The fellows in training and the alumni form a task force which responds to outbreaks and other public health challenges in a timely and competent manner.

2.2. Current status of the work and summary of relevant results

When the German Ministry of Health (MOH) initiated a number of measures to strengthen the capacity in the field of infectious disease epidemiology in the 1990s, training in infectious disease epidemiology was one of the central initiatives to provide the German public health service (ÖGD) with scientists who are skilled to use epidemiological methods for the prevention of infectious diseases.

The main pillar was the installation of a two-year national field epidemiology training programme (FETP) in 1996 following the successful model of the Epidemic Intelligence Service (EIS) at the United States’ Centers for Disease Control and Prevention (US CDC), which had been founded in 1951 by Alexander Langmuir. The German FETP is based at the department for Infectious Disease Epidemiology at the Robert Koch Institute. In 2009 the (PAE) PAE-unit (Postgraduate Training for Applied Epidemiology) was created reporting directly to the director of the department. In order to link with the European network for infectious disease control it has been organisationally closely linked to the 'European Programme for Intervention Epidemiology Training' (EPIET) as a so-called EPIET-associated programme since the very beginning.

The independent use of acquired techniques under close expert supervision is a central feature of both programmes and makes up 90% of the training period while only 10% are covered by classical academic forms of education (lectures, seminars and case studies). The programme focuses particularly on the investigation of outbreaks in cooperation with the respective authorities of the ÖGD, the analysis of infectious disease surveillance data, the evaluation of surveillance systems as well as the development and implementation of application-orientated epidemiological research projects. All aspects of the training are practice-oriented and aimed at finding and implementing appropriate action for the prevention of infectious diseases.

In addition to the practical training, theoretical knowledge is communicated through different training modules, most of which are offered in cooperation with EPIET and take place in the different member states of the European Union. In addition to the EPIET modules RKI is conducting a one-week introductory module and a laboratory module for PAE at the RKI laboratories (bacteriology and virology) as well as additional activities such as journal clubs and scientific seminars.

The PAE primarily targets individuals with fairly advanced training and work experience in a medical or related discipline and aims to attract young professionals from outside the public health service, with a scientific background to dedicate and strengthen their skills for public health epidemiology.

The programme started with two participants and - due to various kinds of additional government funding - has had up to nine participants per cohort. Meanwhile, the cohort size has been stabilised at 5 participants per year.

PAE fellows function as an essential resource for the investigation of outbreaks and the control of other infectious disease threats and they participate as duty officer in the RKI 24/7 hotline for public health emergencies.

Since 2006 PAE around two PAE fellows per cohort are seconded to state public health agencies and thus play an important role in the collaboration with the federal states. Up to now the state public health agencies of Baden Wuerttemberg, Bavaria, Hesse, Lower Saxony and Rhineland-Palatinate have been recognised as EPIET-training sites.

Since the winter term 2009/2010 a Master of Science programme in Applied Epidemiology (MSAE) was newly established in cooperation with the Charité in Berlin and the Berlin School of Public Health (BSPH). The two-year fulltime course of 120 ECTS credit points is integrated into the PAE and EPIET training programmes. So far, two cohorts of students have graduated with a master degree (9 in 2011 and 6 in 2012)

Of the 64 graduates of the programme 1996-2012, 55 (86%) have taken positions in public health after completion the programme, many of them in leading functions.

2.3. Major goals and contribution to the goals of the department

The fellows, supervisors and coordinators of the Training Programmes in Infectious Disease Epidemiology (PAE/EPIET) make a fundamental contribution to the major goal of the department.

They participate in the management of national crises (such as the pandemic influenza 2009 and the HUS/EHEC outbreak 2010) and perform outbreak investigations. Additionally, they conduct projects in the fields of surveillance and applied research and participate in routine activities dictated by the German Infection Prevention Act (IfSG). Through these projects they help to develop prevention strategies and give evidence-based recommendations for policy makers and the German public health service.

By working in the federal states and assisting local public health units they help to strengthen the network within the German national public health-system and they function as multipliers who help to teach the concepts of infectious disease epidemiology to a broader audience within the German public health system. Furthermore, through their involvement in the EPIET network they advance the exchange with other players in the European public health system.

PAE- and EPIET- fellows have participated in nearly all of the over 60 outbreak investigations in which the department was involved during the years 2009-2012 (for list see 4.1.9., AL3). A considerable proportion of these outbreak investigations were conducted by fellows based in the federal states.

PAE- and EPIET- fellows have conducted the following projects during the years 2009-2012:

- Report on actual situation of Lyme borelliosis in the new federal states of Germany, 2007-2008
- Implementation and Conduction of a timely limited hospital surveillance of cases with Pandemic Influenza A(H1N1)v infections and associated cases of death in Germany, 2009-2010
- Implementation and Conduction of a timely limited Rotavirus surveillance of cases with Rotavirus vaccination in children between 0-24 months living in Mecklenburg-West Pomerania (MV), 1. July 2010- 30. June 2011
- Hospitalisation and death rates of notified salmonellosis by serotype, age and federal state in Germany, 2004-2008
- Pilot study regarding the use of Nuclein acid-amplification tests to detect *Chlamydia* and *Gonococci* from pharyngeal and rectal swabs collected in STI screenings among MSM and FSW in German cities
- Surveillance project on severe cases by 2009 H1N1 influenza among children in Germany
- HCV Surveillance
- AIDS defining illnesses in the HIV-1 seroconverter cohort
- implementation of a lab-based *Chlamydia*-sentinel system accompanying the existent, opportunistic screening program in Germany
- Analysis of Pandemic influenza A H1N1 breakthrough infections and estimates for vaccine effectiveness
- Hepatitis E Surveillance

- Knowledge, acceptance and status of HPV-vaccination in students in 10th grade of school in Berlin
- Comparison of disease burden of infections with *Salmonella* Typhimurium DT 193 (monophasic *S. Typhimurium*) and other Lysotypes (in particular DT104) on the basis of hospital data of notified infections in Germany, January 2008-June 2010
- Implementation of an SARI surveillance system in 9 Berlin hospitals to monitor SARI and to depict Influenza activity
- BorderNETwork project at RKI
- Comparative analysis and characterisation of the IfSG surveillance data of noro- and rotavirus outbreaks
- Surveillance of bloody diarrhoea in emergency departments during the outbreak of bloody diarrhoea and haemolytic uraemic syndrome caused by Shiga toxin/verotoxin-producing *Escherichia coli* in Germany, 2011
- Clinical manifestations and risk factors in patients with A(H1N1) infection
- Evaluation of the influenza surveillance in Bavaria and investigation of the potential calculation of the population denominator for the influenza sentinel network in Bavaria
- Risk of acquisition of a Granulocytic Anaplasmosis in comparison to the risk of acquiring Lyme disease after tick exposure in Bavaria
- Trends in incidence of gastroenteric infections in refugees (asylum seekers) in Rhineland-Palatinate (TIGIR)
- Prospective assessment of *Clostridium difficile* incidence in hospital patients and staff (PACIPS)
- Novel Influenza prevalence in intensive care units of a community hospital in Rhineland-Palatinate (NIPI)
- Incidence of Pandemic and Seasonal Influenza in hospitalised children (IPSI)
- Factors associated with fatal outcome of 2009 pandemic influenza (H1N1) infections in Germany
- Screening for information of infection sources and evidence of secondary infections among patients in nephrology department during the large HUS-outbreak, 2011
- Social environment and infectious diseases in Berlin
- Descriptive analysis of SurvNet and laboratory data of Norovirus cases and clusters in Lower Saxony
- Intensified Hantavirus surveillance in Lower Saxony
- ARMIN (antibiotic drug resistance monitoring in Niedersachsen/Lower Saxony)
- MRSA prevalence study (EurSafety project) 23-27th May 2011
- Capture-recapture study on adverse events following immunisation in Lower Saxony, 2001-2010
- Optimising the analysis and reporting of the TB TOM in Germany (2010-2011)
- Evaluation of current achievement of *Rubella* elimination in Germany (2010-2012)
- STEC Sero-epidemiological study (2011)
- Study of Pandemrix effectiveness in preventing infection with influenza (2011)
- Underreporting of enteropathic *E. coli* (2011)
- Evaluation of the *E.-coli*-enteritis notifications (laboratory methods used, serogrouping, pathogenicity factors, etc.) in order to analyse completeness of reporting, and identify if the surveillance system is useful in its present state (2010-2012)
- Survey among AGI sentinel-doctors concerning praxis and information management during 2009 H1N1 Influenza Pandemic
- IfSG-Influenza-surveillance - mortality and hospitalisation, vaccine-effectiveness (2011)
- Influenza-Project: paper and pencil survey amongst all AGI sentinel-doctors concerning praxis and information management during 2009 H1N1 Pandemic
- Intensified surveillance of HEV with integrated case control study (2011-2012)
- Epidemiology of typhoid fever in Germany 1995-2010
- Implementation of an enhanced surveillance system for the Women's FIFA World Cup 2011 in Germany

- Development of a new mumps case definition as part of the newly introduced nationwide mandatory reporting (Infection Against Protection Act 2001)
- Mumps epidemiology in Germany 2001-2011
- Estimation of mumps incidence in Germany based on insurance data 2007-2010
- Household transmission of Shiga-toxin producing *E. coli* (STEC) (2011-2012)
- Further development of a web-based surveillance to monitor the flu status in Germany (Grippe-Web)
- Contact-tracing in international public transportation
- Descriptive analysis of extra pulmonary TB data from 2002-2009
- Serological survey of Schmallenberg virus antibodies in farmers from NRW, Germany
- Implementation of a surveillance system for nosocomial outbreaks in Germany
- Hantavirus & Q-fever Surveillance – control of notifiable cases in Bavaria
- Estimating the vaccine effectiveness of the pertussis vaccination in the five eastern German states.
- Analysis of mandatory notification data on Varicella infection in the German New Federal States
- Quality of TB treatment in Germany using Insight Health data
- Sexually transmitted infections among Female Sex Workers in Germany
- Measles vaccination coverage among 20-35 year old in Rhineland-Palatinate
- Determinants of vaccination coverage among preschool children in Germany: Results from three cross-sectional surveys

2.4. Additional work and methods for investigations

New training tools and evaluation tools are continuously being developed and implemented in cooperation with the EPIET coordination team. The EPIET team is presently undertaking a new quality assurance project based on the core competencies for public health officials developed by ECDC and the European member states.

At present, the MSAE is participating in the accreditation of all medical study courses of the Charité performed by the Accreditation Agency for Study Programmes in Health and Social Sciences (AHPGS).

The training course for public health officials organised by the department since 1995 is currently being evaluated in respect to its usefulness to improve the management of outbreaks at the local level. For this purpose the training programme team is participating in the evaluation of the course by conducting a survey among former participants to the course and planning focus group discussions among stakeholders. An expert in adult education is being consulted to assist in this process.

2.5. Scientific advice and consulting services

As an EPIET associated programme the PAE is regularly involved in the quality assurance and planning for the EPIET curriculum.

Scientists of the department of infectious disease epidemiology are regularly involved in the specialisation courses for public health physicians by planning and conducting training units at the academies for specialisation in public health in Southern Germany (Akademie für Gesundheit und Lebensmittelsicherheit, AGL) and Western Germany (Akademie für den Öffentlichen Gesundheitsdienst, AfÖG) as well as the newly established specialisation course at the Berlin School of Public Health (BSPH).

2.6 Training and teaching activities

The major goal of the unit “training programmes in infectious disease epidemiology” is service-oriented training of experts in infectious disease control and prevention. Members of the unit participate in the following training and teaching activities:

- Two year training programme postgraduate training for applied epidemiology (PAE) with integrated Master of Science in Applied Epidemiology (MSAE)
- Short courses for public health officials in Germany
- Teaching in university courses for public health and epidemiology
- Teaching at the German academies for specialisation of public health officials
- Participation in international training activities (e.g. ECDC train the trainer courses)

3. Cooperation with other scientists or research institutions

3.1. Internal (within RKI)

PAE fellows conduct their scientific projects under supervision from scientists in the units 32 to 37 at the department for infectious disease epidemiology, projects are also conducted in cooperation with various units in the RKI department 1, 2 and ZBS.

PAE/EPIET also closely cooperates with the fellows and supervisors of the European Programme for Public Health Microbiology Training (EUPHEM) based at ZBS and RKI department 1. An actual example is the project “A systematic overview of laboratory diagnosis of paediatric tuberculosis in the European Union”. This international study is conducted within the framework of the EUPHEM programme and under the supervision of the Department for Infectious Disease Epidemiology. The aim of the study is to attain a systematic overview of the range of diagnostic tests and their success in different specimens used to diagnose active tuberculosis in children across European Union (EU) countries. Primary scientific partner and the main project site is the Health Protection Agency National Mycobacterium Reference Laboratory (HPA NMRL), London, UK. Routinely collected laboratory data (within the period of 2007-2011) on conventional and molecular laboratory tests used in children are analysed across several other partner sites: German National Mycobacterium Reference Laboratory; Lithuanian National Tuberculosis Reference Laboratory; Latvian National Tuberculosis Reference Laboratory, Croatian National Reference Laboratory. Additionally 22 national tuberculosis reference laboratories in the EU took part in a complementary survey aiming to identify the commonalities and differences between the countries in the workload related to paediatric specimens, types of specimens obtained from children and diagnostic methods applied.

3.2. External / National

Since 2006, a proportion of each cohort of PAE-fellows is placed at some selected public health offices of the Federal States. Scientists from these institutions are involved in the design and supervision of their projects and contribute to the network of trainers.

Since 2009 in collaboration with the Berlin school of Public Health (BSPH) and the Charité Medical University in Berlin a Master of Science degree in Applied Epidemiology (MSAE) has been integrated in the PAE-programme. The study regulations have been published in the “Amtliches Mitteilungsblatt” Nr. 055 dated 16.11.2009 (www.charite.de/charite/presse/publikationen/amtliche_mitteilungsblaetter/?no_cache=1&cid=31353&did=23136&sechash=98f7bcf7)

Katharina Alpers is member of EPIET Alumni network (EAN)

3.3. External / International

As an EPIET associated programme the PAE is part of this important EU training network and regularly contributes to the organisation and further development of theoretical and practical aspects of the programme (Krause G et al., *Euro Surveill* 2009).

PAE is also member of the Training Programmes in Epidemiology and Public Health Interventions NETWORK (TEPHINET) which was founded in 1997 and aims to improve networking between the FETP in different countries (www.tephinet.org). Today 56 FETP world-wide are officially members of TEPHINET.

4. Appendix

4.1 Overview on achievements of the unit, 2009-2012

4.1.1. Scientific publications, 2009 – 2012

Number of peer-review publications co-authored by trainings programmes: 86

Impact factor (IF) according to JCR (of 2012 publications: according to 2011 IF)

2009: 59.0

2010: 45.0

2011: 192.4

2012: 70.1

Cumulative 2009-12: 366.5

A) Original research articles in peer-review journals

2012 (until Sept.)

Adlhoch C, Wadl M, Behnke M, Pena Diaz L A, Clausmeyer J, Eckmanns T: Pandemic influenza A(H1N1)pdm09 in hospitals and intensive care units - results from a new hospital surveillance, Germany 2009/2010. *Influenza Other Respi Viruses* 2012; 6(6):e162-e168

Adlhoch C, Hoehne M, Littmann M, Mas Marques A, Lerche A, **Dehnert M**, Eckmanns T, Wichmann O, Koch J. Rotavirus Vaccine Effectiveness and Case-Control Study on Risk Factors for Breakthrough Infections in Germany, 2010-2011. *Pediatr Infect Dis J* 2012,

Altmann M, Fiebig L, Buda S, von Kries R, **Dehnert M**, and Haas W: Unchanged severity of Influenza a(H1N1)pdm09 infection in children during first postpandemic season. *Emerg Infect Dis* 2012; 18:1755-1762.

Altmann M, an der Heiden M., Scheufele R., Hartmann K., Houareau C., Bartmeyer B., Hamouda O., for the German HIV-1 Seroconverter Cohort. The risk of AIDS-defining events is decreasing over time in the German HIV-1 Seroconverter Cohort. *BMC Infect Dis* 2012, 12:94.

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4.1.2. Selected relevant publications

Five important publications for the scientific community 2009–2012

1. Frank C, Werber D, Cramer JP, **Askar M**, Faber M, an der Heiden M, Bernard H, Fruth A, Prager R, Spode A, Wadl M, Zoufaly A, Jordan S, Kemper MJ, Follin P, Muller L, King LA, Rosner B, Buchholz U, Stark K, Krause G, HUS Investigation Team. Epidemic profile of Shiga-toxin-producing *Escherichia coli* O104:H4 outbreak in Germany. *N Eng J Med* 2011; 365(19): 1771-80.
2. Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D; **RKI Working Group Pandemic Influenza**, Krause G, Haas W. The first wave of pandemic influenza (H1N1) 2009 in Germany: from initiation to acceleration. *BMC Infect Dis* 2010, 10:155.
3. **Williams CJ**, Schweiger B, Diner G, Gerlach F, Haaman F, Krause G, Nienhaus A, Buchholz. Seasonal influenza risk in hospital healthcare workers is more strongly

associated with household than occupational exposures: results from a prospective cohort study in Berlin, Germany, 2006/07. *BMC Infect Dis* 2010, 10 (1): 8.

4. **Williams CJ**, Schenkel K, Eckmanns T, Altmann D, Krause G. FIFA World Cup 2006 in Germany: Enhanced surveillance improved time to detection. *Epidemiol Infect* 2009, 139 (4): 597-605.
5. Krause G, Aavitsland P, **Alpers K**, Barrasa A, Bremer V, Helynck B, Perra A. Differences and Commonalities of National Field Epidemiology Training Programmes in Europe. *Euro Surveill* 2009;14(43)

Five important publications for the public 2009–2012

1. Studienordnungen Weiterbildender Masterstudiengang „Applied Epidemiology“ der Charité - Universitätsmedizin Berlin, Amtliches Mitteilungsblatt der Charité Nr.55, vom 16.11.2009

4.1.3. Overview on collaborations in networks

- EPIET Scientific Coordination Team
- EPIET Training Site Forum
- TEPHINET (Training Programs in Epidemiology and Public Health Interventions Network)

4.1.4. Memberships and participation in Advisory Boards

Dr. Katharina Alpers

- Participation in TEPHINET Board (representative for the European Region)

4.1.5. List of completed dissertation or master theses in the unit, 2009 – 2012

Year	Title	Name	Degree	University/Supervisor RKI
since 2011	Statistical modelling of dynamic systems for infectious disease epidemiology	F. Weidemann	Dr. rer. nat.	PD Dr. M. Höhle (RKI), Dr. M. Dehnert (RKI)
2012	Beispiele für das Public Health Management von Infektionskrankheiten bei gefährdeten Personengruppen durch lokale, nationale und internationale Gesundheitsbehörden	E. Aichinger	M.Sc.	Dr. K. Alpers (RKI), Dr. G. Pfaff (Federal Health Authority Baden- Wuerttemberg)
2012	Die Identifizierung von Risikofaktoren als Grundlage für gezielte Präventionsmaßnahmen am Beispiel von lebensmittelassoziierten Erkrankungen	M. Askar	M.Sc.	Prof. K. Stark (RKI), Dr. Bettina Rosner (RKI)
2012	Das Landesgesundheitsamt als Schnittstelle zwischen Gesundheitsämtern und Robert Koch Institute im öffentlichen Gesundheitsdienst in Deutschland. Ausgewählte Aufgaben des niedersächsischen Landesgesundheitsamts (NLGA) am Beispiel von wissenschaftlichen Studien im Bereich der angewandten Epidemiologie	M. Diercke	M.Sc.	Prof. G. Krause (RKI), Dr. J. Dreesmann (Federal Health Authority Lower Saxony)
2012	Importance of data quality for surveillance, outbreak detection and epidemiological studies - a regional perspective on the	H. Englund	M.Sc.	Dr. I. Karagiannis (RKI), Dr. Wolfgang Hautmann (Federal Health Authority Bavaria)

German surveillance system for infectious diseases				
2012	Challenges in surveillance and importance of laboratory collaboration in intervention epidemiology - examples of tuberculosis, rubella, measles and EHEC	S. Lassen	M.Sc.	Dr. I. Karagiannis (RKI), Dr. B. Hauer (RKI)
2012	Die Bedeutung von Prävention und früher Intervention bei impfpräventablen Erkrankungen – am Beispiel von Projekten zu Mumps und Masern (The importance of prevention and early intervention in vaccine preventable diseases – projects on mumps and measles)	A. Takla	M.Sc.	K. Tolksdorf (RKI), Dr. J. Koch (RKI)
2011	Das Erkennen, Bekämpfen und Verhüten von Infektionskrankheiten	C. Adlhoch	M.Sc.	Prof. Dr. G. Krause (RKI), Dr. T. Eckmanns (RKI)
2011	Identifying risk factors and formulating public health recommendations using surveillance data	A. Altmann	M.Sc.	Dr. I. Karagiannis (RKI), Dr. O. Hamouda (RKI)
2011	Analysis and interpretation of surveillance and research data - four examples how to address public health relevant questions	S. Dudareva	M. Sc.	Dr. I. Karagiannis (RKI), Dr. C. Frank (RKI)
2011	Pandemische Influenza und Gastroenteritis-Ausbrüche – epidemiologische Studien im Rahmen des Masterstudiengangs „Applied Epidemiology“ (MSAE) der Charité - Universitätsmedizin Berlin	B. Greutelaers	M. Sc.	Dr. I. Karagiannis (RKI), Dr. Anette Siedler (RKI)
2011	Angewandte Infektions-epidemiologie - Prospektive Erfassung der Influenza-Inzidenz in einer sensitiven Subpopulation und Auswertung von Routinedaten des öffentlichen Gesundheitsdienstes	E. Mertens	M.Sc.	Dr. K. Alpers (RKI), Florian Burckhardt (Federal Health Authority Rhineland-Palatinate)
2011	Infektionsepidemiologische Synopsis aus den Erfahrungen mit SARI-Surveillance in Berlin, STI-Surveillance in vier europäischen Ländern, einem MRSA-Ausbruch sowie einer Meningokokken-Zeitreihenanalyse	M. Nachtnebel	M.Sc.	Dr. M. Dehnert (RKI), Dr. Sabine Reiter (RKI)
2011	Angewandte Infektionsepidemiologie - Praktische Datenerhebung und -analyse sowie public value ausgewählter Infektionsgeschehen als Baustein des Infektionsschutzes in Deutschland	P. Stöcker	M.Sc.	Dr. M. Dehnert (RKI), Dr. Y. Déleré (RKI)
2011	Analyse und Interpretation von Surveillance-Daten – Drei Beispiele zur Erkennung von Risikofaktoren und der Formulierung von Public-	H. Wilking	M.Sc.	Prof. K. Stark (RKI), Dr. T. Eckmanns (RKI)

Health-Empfehlungen				
2011	Toolbox of applied epidemiology in public health	B. v. Wissmann	M.Sc.	Dr. K. Alpers (RKI), Dr. Wolfgang Hautmann (Federal Health Authority Bavaria)
2010	Mathematische Modellierung der Auswirkung von Impfungen auf die Dynamik des Rotavirus	S. Werner	Dipl. Math.	PD Dr. G. Jetschke (Friedrich-Schiller-Universität Jena) / Dr. M. Dehnert (RKI)

4.1.6. Presentations as invited speaker, 2009 – 2012

Staff from the Unit PAE were invited to speak at 7 conferences.

4.1.7. Reports and written scientific advice to the Ministry of Health, 2009-2012

There were 3 reports and written scientific advice to the Ministry of Health between 2009 and 30.09.2012.

Unit 31: Data Management

Unit Head: Dr. Hermann Claus

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1. General information - Unit 31

Head: **Dr. Hermann Claus**

Deputy: **Dr. Göran Kirchner**

2. Tasks and goals of the unit

2.1. Summary

The Data Management unit is responsible for **design, development and management** of IT-projects within the Department for Infectious Disease Epidemiology at RKI and moreover provides scientific services and consultancies for other units at RKI as well as external partners and in the general public. The main project is the **national reporting system** for surveillance of notifiable infectious diseases (SurvNet@RKI) according to the infection protection act (IfSG). In the field of **surveillance applications** the most notables are those for Influenza ('Arbeitsgemeinschaft Influenza' -AGI), sexual transmitted diseases (in particular HIV) and antibiotic resistance. Other applications are laboratory information management programs for laboratories at RKI. Additionally there are a lot of smaller projects.

All these projects include the joint **conceptual design** with experts and potential users as well as the **development** of all required IT components (databases, Windows applications, Web applications). Furthermore the unit does the whole **management** and technical **support**, allocation of required tools to analyse the data, and the creation of official data for **publishing**. This includes the **statistical analysis** for users at RKI and external users (see 3.2., Unit 31). The aim is to use automated solutions for all data processing steps (routine import/export of data files and regular reports).

During the reporting period the unit realised a project on epidemiologic **modelling** of infectious diseases and co-initiated an EU-funded project to use **natural language processing** and other **data mining** methods to make web 2.0 contents usable for public health topics.

2.2. Current status of the work and summary of relevant results

2.2.1. National Reporting System for surveillance of notifiable infectious diseases

Since 2001, Germany has an electronic reporting system for communicable diseases. Cases are notified by medical practitioners, hospitals and laboratories via fax, mail or telephone to the local health authorities, where they are assessed and then electronically reported via the regional to the national level. Since then many local health departments and all regional ones use a tool developed by Unit 31 for data collection and analysis (SurvNet@RKI).

A complete **redesign** of this software for data collection and transport of case reports from local health departments via state health departments to RKI was done and SurvNet@RKI was rolled out during the reporting period. Besides RKI and all 16 state health departments over 100 of about 400 local health departments in Germany and the German armed forces use this software. Various training courses for the software SurvNet@RKI were held (see. 2.6., Unit 31).

To publish the data the unit operates the web application SurvStat@RKI (<http://www3.survstat.de>). Moreover, the notification data are also periodically **published** in several other formats, such as weekly in 'Epidemiologisches Bulletin', yearly in 'Infektionsepidemiologisches Jahrbuch', report on tuberculosis, and map of risk areas for tick-borne encephalitis, reports to ECDC according to the TESSy-system, to the Federal Statistical Office, and to health reporting of the states.

Using a special service-tool the unit 31 supports the external users with **installation and configuration** of the software. Definitions used in the software are provided to other software producers working on the same subject. So these companies can integrate a SurvNet@RKI compatible module into their products. The unit develops and applies several small applications and tools for running the reporting system and integration of additionally data.

2.2.2. Deutsches Elektronisches Meldesystems für Infektionsschutz (DEMIS)

After the pandemic 2009 and the HUS/EHEC outbreak 2011, an assessment is underway, to advice whether the German system for communicable diseases can be improved by introducing an electronic notification, in order to reduce delays and enhance data quality.

Part of this process is the development of secure and trustworthy infrastructure which can be used by medical practitioners, hospitals, laboratories as well as schools, kindergartens and residential care homes for the elderly, to **seamlessly integrate their systems into an electronic one**. The main goal is to avoid media interruptions as far as possible and allow a **flexible adaption of contents and distribution paths** to be well prepared for future challenges.

Modern instruments of sharing information will be used, e.g. apps, interactive data mining tools, personalised information etc. Many of the recommended changes would require a variation of the classical notification cascade from local over regional to national public health authorities. The suggested functionalities will be considered in the revision of the German notification system for communicable diseases. The role of unit 31 in this process is to contribute their experience in requirements engineering, technology and process knowledge and software architectural skills.

2.2.3. Working Group on Infectious Disease Control (AGI)

All existing applications for the surveillance of influenza and other respiratory diseases (since 2002) have been new designed and developed in the reporting period. During this process former tasks of 'Deutsches Grünes Kreuz' were adopted. For example the following projects were implemented: Digitalisation of fax reports (with commercial software 'Teleform') and data migration of the AGI file, migration of SEED-ARE data (automated import of attached files in email messages), migration of laboratory data from the national reference centre of influenza (unit 12 RKI) and some states, data presentation inclusively graphs and maps on RKI website (<http://influenza.rki.de>) with the opportunity to recall personal data for participating physicians, and a variety of tools for data analysis in RKI. Furthermore unit 31 supports unit 36 within the projects 'Shedding' and 'GrippeWeb' (<https://grippeweb.rki.de/>).

2.2.4. Projects for unit 34 (unit responsible for sexually transmitted diseases)

A new application for data collection according §7.3 IfSG (particularly HIV and syphilis) was designed. The aim of this application which is still under development is to simplify the data entry explicitly (yearly ca. 6000 reports each) as well as to structure the complex evaluation and analysis of the data. Another project ('ClinSurv') is also still in development; it is a system for physicians to report important information on HIV surveillance of their patients to RKI. Within another project, supported by the ministry of health ('applications with additional benefit of the electronic health insurance card') a special technique of electronic data transfer was designed. This technique was adapted to the project 'Chlamydia-Sentinel' and is already used by some laboratories to transmit data to RKI automatically. Furthermore a complex interface was developed to use the epidemiological HIV-database of unit 34 and the laboratory database of unit 18 for data exchange in joint projects.

2.2.5. Applications for laboratories within the RKI

Since 1996 laboratories at RKI have been supported by special laboratory information systems. Most of the currently used systems were developed and are supported by unit 31. Because of the very specific tasks of the laboratories this in-house-solution is well-proven. There are applications in unit 11, unit 12, unit 13, unit 15, unit 16, unit 17, and unit 18. In the reporting period unit 31 works on the following subjects: required extensions for accreditation of the laboratories were embedded, an interface to web services of Stanford-University to evaluate resistance of HIV-gene sequences automatically was established, and a tool to transmit diagnostic findings and reports was implemented. Unit 31 realises currently adaption of the applications because of frequently changing workflows and tasks in the laboratories. To support the activities in the laboratories interfaces to commercial software products like 'GelCompar' were established, and data exports to cooperation partners like WHO were realised.

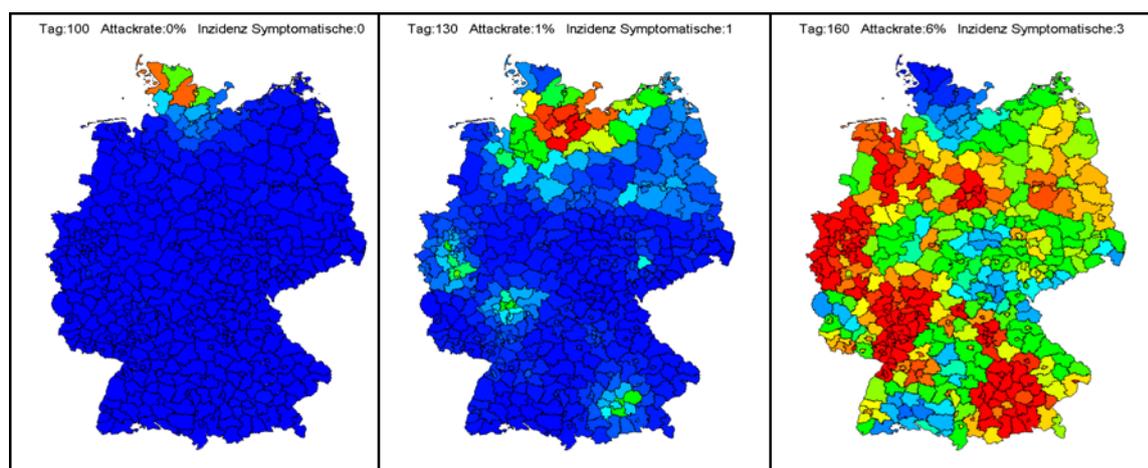
2.2.6. Antibiotic resistance

The basic activities of the IT-projects in this field are done by a member of unit 32 staff. Unit 31 gives support if it is needed. Detailed information on the project can be found in the report of unit 32. This applies to the administration of the sentinel data from the National Association of Statutory Health Insurance Physicians too. Within these projects data-mining techniques were used for the first time.

2.2.7. Mathematical modelling

The project '**Modelling of the spread of infectious diseases**' was funded by the Federal Ministry of Health and finished in June 2009. Within this project a mathematical model was developed that simulates the spatial spread of an infectious disease like influenza in Germany. The model allowed simulations stratified by county, age, and risk groups. It is a common SEIR-model based on ordinary differential equations and implemented in 'MatLab'. Several strategies of prevention like Immunisation, the use of antiviral drugs, and contact reduction by restraint of public transport or closing schools can be considered. Disease-specific parameters as well as information like population size, contact behaviour, and dynamic data were used in the model. In 2009 the model was used to find recommendations for optimal Immunisation strategies against pandemic influenza.

Figure 5: Spread of influenza in Germany according to SEIR model at days 100, 130, and 160 of an example epidemic



2.2.8. M-Eco – Using Web 2.0 resources for event detection

Unit 31 realised a substantial part in the architectural design and management of data and dataflow within the EU-funded project '**M-Eco**' (<http://www.meco-project.eu>). These results can be used to supplement the data of notifiable infectious diseases with data from the Web. An early warning system for potential disease outbreaks that uses **information from media and social networks** was prototyped and evaluated regarding the quality, timeliness, usability and usefulness. Many new insights in the handling of unstructured text through natural language technologies (computational linguistics) were gained.

2.2.9. Other projects

Unit 31 developed a special application to support the **study group varicella** (AGV) which contains the opportunity to adopt the data administration from German green cross.

With the transfer of the project **enterovirus-surveillance** from NLGA Hannover (Governmental Institute of Public Health of Lower Saxony) to unit 15 at RKI unit 31 takes care about data management of the project. A new application for collecting and processing the data and a website to publish these data was developed.

Unit 31 offers a special '**zip-code-tool**' (<http://tools.rki.de/plztool>) to support the reporting system of notifiable infectious diseases, currently with maintenance of the underlying data.

A special concept for data encryption was developed to secure confidentiality in the human resources management system at RKI. The implementation can start when the organisational requirements will be established. The invented methods can be used for other project with need to secure confidentiality like data transport via internet.

In several projects run in unit 31 we use special data from other firms (like 'Insight Health'), to use these information special preparation of the data is necessary.

Another task is the administration of web- and database servers and the IT support within Department for Infectious Disease Epidemiology.

2.3. Major goals and contribution to the goals of the department

The Data Management Unit is responsible for national reporting system for surveillance of notifiable infectious diseases (SurvNet@RKI) according to the infection protection act (IfSG). It is also responsible for the design, development and management of IT-projects within the Department. All details are listed in the chapter 2.2.

2.4. Additional work and methods for investigations

One main emphasis of unit 31 is the **maintenance** of applications for on-going projects, the adaption to new software methodologies, and to open up **new technologies**. During the reporting period the development platform for several projects has changed from Microsoft-Access to C#.Net (C#, XAML) under Visual-Studio (Microsoft) together with MS SQL Server technologies. We introduced Team-Foundation-Server (Microsoft) for project management and collaboration. The functionalities developed are made available through web services for reuse. Many processes were automatized. XSL-transformations are used to process huge amount of XML-formatted data.

The Analysis Services component of MS SQL Server is becoming the standard tool to analyse large amounts of data efficiently. In particular, using these technologies (Online Analytical Processing (OLAP)) for **data mining** and **multidimensional data processing**, the unit can support the users of all current projects by providing means to handle the data fast and easily even if the analysis is very complex. This requires an improved storage of **master data** to ensure the integrity of information and consistency of data across different applications. First steps in this direction have already been taken by using MS SQL Master Data Services.

2.5. Scientific advice and consulting services

Unit 31 provides support in generating special data files and **statistical analysis** for scientific projects within the Department for Infectious Disease Epidemiology. One important area of investigation is the improvement of **outbreak detection algorithms**. In joint work with other units of the department these algorithms were implemented and are subject to continuous further development.

As already mentioned above the field of **data mining** is the most active area of research. Nearly all the above mentioned projects either already have implemented or will implement new tools for the profound analysis of the vast amount of data collected within the department.

The knowledge gained during the **modelling** project provides the unit with elaborated means to understand the spread of diseases and to test conjectures for interventions thereof. Further improvements are expected through the collaboration with the newly established professorship of mathematical modelling at RKI, especially in the field of **complex networks**.

Part of the services developed within M-eco project mentioned above will be continued to improve the capabilities in **text mining** and to extend the resources to build epidemiologic knowledge through the assessment of raw and unstructured text. Here the field of **natural language processing** is touched.

A minor but still important area is the development of **domain specific languages** (DSL) to describe and conserve ideas, concepts and models within the domain of epidemiology. First steps were done during the redesign of SurvNet@RKI to generate (and thereby to automate the build) a good portion of the system. Further work will bridge the gap from special queries to completely free-form input. The long-term goal is to make epidemiologic knowledge computable and accessible.

Many of the above mentioned technologies are not developed separately. It is especially their interaction and skilful orchestration which helps to reduce the complexity of problems and to improve the knowledge acquired.

2.6. Training and teaching activities

- For the software SurvNet@RKI thirty training courses for staff members at local and state health departments were held. Additionally there were in-house-courses for the Department for Infectious Disease Epidemiology at RKI.
- Since 2005 in each year one or two apprentices started their 3-year apprenticeship as Computer Specialist for Applications Development ('Fachinformatiker für Anwendungsentwicklung') in unit 31. Five of them successfully completed their training and two more will finish it in 2013. Two of them gained a permanent position at RKI.

3. Cooperation with other scientists or research institutions

3.1. Internal (within RKI)

Data-driven applications developed and managed in Unit 31:

- AGI - Unit 36
- AGV - Unit 33
- BSD (Data management solution for blood donor data) - Unit 34
- Cdiff (Data management solution for *C. difficile* lab) - Unit 13
- EARSS (Data management solution for hospital-based data of the antimicrobial resistance project) - Unit 32
- Entero (Data management solution for *Enterococcus* lab) - Unit 11
- EVSurv (Data management solution for Enterovirus surveillance project) - Unit 15
- EVSurvWeb (Web site for Enterovirus surveillance project) - Unit 15
- FSME (Data management solution for FSME-virus lab) - ZBS₁
- Gastro (Data management solution for for Noro- and Rotavirus lab) - Unit 15
- Giardia (Data management solution for *Giardia* lab) - Unit 16
- GrippeWeb (Webapplication and data management for GrippeWeb-project) - Unit 36
- HCV (Data management solution for HCV lab) - Unit 15
- HIV (Data management solution for HIV lab) - Unit 18
- HIVInzidenz (Data management solution for HIV-incidence project) - Unit 34
- HIVReg (Data management solution for ClinSurv-project) - Unit 34
- Influenza (Data management solution for Influenza lab) - Unit 12
- MaMuRoe (Data management solution for Measles Mumps *Rubella* lab) - Unit 12
- MortSurv (Data management solution for mortality surveillance project) - Unit 32
- Myko (Data management solution for mycology lab) - Unit 16
- Pneumo (Data management solution for *Pneumococcus* surveillance) - Unit 33
- Polio (Data management solution for Polio- and Enterovirus lab) - Unit 15
- Problag (Management application for specimen storage) - Dept. 1, ZBS
- Salmo (Data management solution for *Salmonella* lab) - Unit 13
- Shedding (Data management solution for the shedding project) - Unit 36
- SpezErreger (Data management solution for biohazardious agents) - ZBS₁
- SurvNet@RKI (Reporting system for infectious diseases) - Dept. 3
- STD (Data management solution for sexually transmitted diseases project) - Unit 34
- WNV (Data management solution for West Nile virus lab) - ZBS₁
- Ticks (Data management solution for viral tick-borne diseases lab) - ZBS₁

3.2. External / National

- SurvNet@RKI
- Local and state health departments
- Bundeswehr
- Software vendors (easysoft GmbH Dresden, Computerzentrum Strausberg GmbH, software.house informationstechnik AG Kiel, mikroprojekt GmbH Kaiserslautern, UniSoft Gesellschaft für Software Engineering mbH Roth)

3.3. External / International

- ECDC Stockholm - TESSy

4. Appendix

4.1 Overview on achievements of the unit, 2009-2012

4.1.1. Scientific publications, 2009 – 2012

Number of peer-review publications co-authored by members of the unit: 21

Impact factor (IF) according to JCR (of 2012 publications: according to 2011 IF)

2009: 13.9

2010: 8.5

2011: 26.7

2012: 2.8

Cumulative 2009-2012: 51.9

A) Original research articles in peer-review journals

2011

Altmann M, Wadl M, **Altmann** D, Benzler J, Eckmanns T, Krause G, Spode A, an der Heiden M: Timeliness of Surveillance during Outbreak of Shiga Toxin–producing *Escherichia coli* Infection, Germany, 2011 *Emerg Infect Dis* 2011; 17(10):1906-1909.

Denecke K, **Kirchner** G, Dolog P, Smrz P, Linge J, Backfried G, Dreesman J: Event-driven Architecture for Health Event Detection from Multiple Sources. *In: Proceedings of the XXIII International Conference of the European Federation for Medical Informatics (MIE 2011), 28-31. August, 2011, Oslo, Norway.*

Hauri AM, Westbrock HJ, **Claus** H, Geis S, Giernat S, Forßbohm M, Uphoff H: Electronic outbreak surveillance in Germany: A first evaluation for nosocomial norovirus outbreaks *PLoS One* 2011

Mette A, Reuss A, **Feig** M, Kappelmayer L, Siedler A, Eckmanns T, Poggensee G: Under-reporting of measles - An evaluation based on data from North Rhine-Westphalia, [Untererfassung von Masern - Eine Evaluation basierend auf Daten aus Nordrhein-Westfalen]. *Dtsch Arztebl* 2011

Uphoff H, an der Heiden M, Schweiger B, Campe H, Beier D, Helmeke C, Littmann M, Haas W, Buda S, **Faensen** D, **Feig** M, **Altmann** D, Wichmann O, Eckmanns T, Buchholz U: Effectiveness of the AS03-Adjuvanted Vaccine against Pandemic Influenza Virus A/(H1N1) 2009 - A Comparison of Two Methods; Germany, 2009/10. *PLoS One* 2011; 6(7):1-9.

Wadl M, Rieck T, Nachtnebel M, Greutelaers B, an der Heiden M, **Altmann** D, Hellenbrand W, Faber M, Frank C, Schweickert B, Krause G, Benzler J, Eckmanns T: Enhanced surveillance during a large outbreak of bloody diarrhoea and haemolytic uraemic syndrome caused by Shiga toxin/verotoxin-producing *Escherichia coli* in Germany, May to June 2011 *Euro Surveill* 2011; 16(24):1-5.

2010

Buchholz U, Brockmann S, Duwe S, Schweiger B, an der Heiden M, **Reinhardt** B, Buda S: Household transmissibility and other characteristics of seasonal oseltamivir-resistant influenza a(H1N1) viruses, Germany, 2007-8. *Euro Surveill* 2010

Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, **Altmann** D, Krause G, Haas W: The first wave of pandemic influenza (H1N1) 2009 in Germany: From initiation to acceleration *BMC Infect Dis* 2010; 10(155): 1-12.

Reuss A, **Feig** M, Kappelmayer L, Eckmanns T, Poggensee G: Determination of vaccination coverage and disease incidence using statutory health insurance data , [Bestimmung von Impfquoten und Inzidenzen von Erkrankungen anhand von Daten der kassenärztlichen Vereinigungen] *Gesundheitswesen* 2010

Reuss AM, **Feig** M, Kappelmayer L, Siedler A, Eckmanns T, Poggensee G: Varicella vaccination coverage of children under two years of age in Germany. *BMC Public Health* 2010; 10:502.

Reuss AM, Walter D, **Feig** M, Kappelmayer L, Buchholz U, Eckmanns T, Poggensee G: Influenza vaccination coverage in the 2004/05, 2005/06, and 2006/07 seasons: A secondary data analysis based on billing data of the German associations of statutory health insurance physicians, [Influenzaimpfquoten der Saisons 2004/05, 2005/06 und 2006/07: Eine Sekundärdatenanalyse von Abrechnungsdaten der kassenärztlichen Vereinigungen]. *Dtsch Arztebl* 2010

Spackova M, **Altmann** D, Eckmanns,T, Koch J, Krause G: High Level of Gastrointestinal Nosocomial Infections in the German Surveillance System, 2002–2008. *Infect Control Hosp Epidemiol* 2010; 31 (12): 1273-1278.

Wichmann O, Stöcker P, Poggensee G, **Altmann** D, Walter D, Hellenbrand W, Krause G, Eckmanns T: Pandemic influenza A(H1N1) 2009 breakthrough infections and estimates of vaccine effectiveness in Germany 2009-2010 *Euro Surveill* 2010; 15(18):1-4

Wilking H., Buda S., von der Lippe E., **Altmann** D., Krause G., Eckmanns T., Haas W. Mortality of 2009 pandemic influenza A(H1N1) in Germany *Euro Surveill* 2010; 15(49):

2009

Alpers K, **Altmann** D, an der Heiden M, Bartels C, Bätzing-Feigenbaum J, Becker A, Behnke S, Bergholz A, Bernard H, Bielecke J, Biere B, Böhmer M: Description of the early stage of pandemic (H1N1) 2009 in Germany, 27 April-16 June 2009 *Euro Surveill* 2009; 14(31).

an der Heiden M, Buchholz U, Krause G, **Kirchner** G, Claus H, Haas W: Breaking the waves: Modelling the potential impact of public health measures to defer the epidemic peak of novel influenza A/H1N1. *PLoS One* 2009; 4(12):e8356.

Cuny C, Nathaus R, Layer F, Strommenger B, Witte W, **Altmann** D: Nasal Colonization of Humans with Methicillin-Resistant Staphylococcus aureus (MRSA) CC398 with and without Exposure to Pigs *PLoS One* 2009; 4(8): :e6800.

Dettmann M , Poggensee G, Buda S, Claus H, Krause G: Demographic characteristics of influenza A (H1N1) cases in Germany: From April to the end of August 2009. *MMW Fortschr Med* 2009; 151(40):35-37.

Reuss AM, Wiese-Posselt M, Weißmann B, Siedler A, Zuschneid I, an Der Heiden M, **Claus** H, von Kries R, Haas WH: Incidence rate of nontuberculous mycobacterial disease in immunocompetent children a prospective nationwide surveillance study in Germany *Pediatr Infect Dis J* 2009; 28(7):642-644.

Ritter S, Willand L, **Reinhardt** B, Hamouda O: Blutspenderpopulationen in Deutschland: Demographie und Spendeaktivität – Ergänzung zum Bericht des Robert Koch Institutes zu den Meldungen nach § 22 Transfusionsgesetz. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009;

Williams C J, Schenkel K, Eckmanns T, **Altmann** D, Krause G: FIFA World Cup 2006 in Germany: enhanced surveillance improved timeliness and detection *Epidem Infect* 2009; 137: 597-605.

4.1.2. List of reports and written scientific advice to the Ministry of Health, 2009-09/2012

There were 14 reports and written scientific advice to the Ministry of Health between 2009 and 30.09.2012.

Unit 32: Surveillance

Unit Head: Dr. Tim Eckmanns

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1. General information - Unit 32

Head: **Dr. Tim Eckmanns**

Deputy: **PD Dr. Gabriele Poggensee** (until 31 July 2010)

Dr. Justus Benzler (as of 1 August 2010 until 31 March 2012)

Dr. Muna Abu Sin (as of 1 April 2012)

2. Tasks and goals of the Unit

2.1. Summary

Unit 32 “Surveillance” was responsible for the infectious disease surveillance and co-ordinated the epidemiological and organisational aspects of the surveillance system within the framework of the Protection against Infection Act (IfSG). Since 2006 the unit was responsible for the surveillance of antimicrobial resistance and antibiotic consumption. The unit was characterised by an interdisciplinary approach with expertise in social and infectious disease epidemiology, veterinary medicine, information technology, medicine, microbiology, virology, infection control, and hospital epidemiology. The following description of the unit refers to the period till Sept 2012, before the reorganisation described in 2.3.1. and 2.3.3, AL3.

2.2. Current status of the work and summary of relevant results

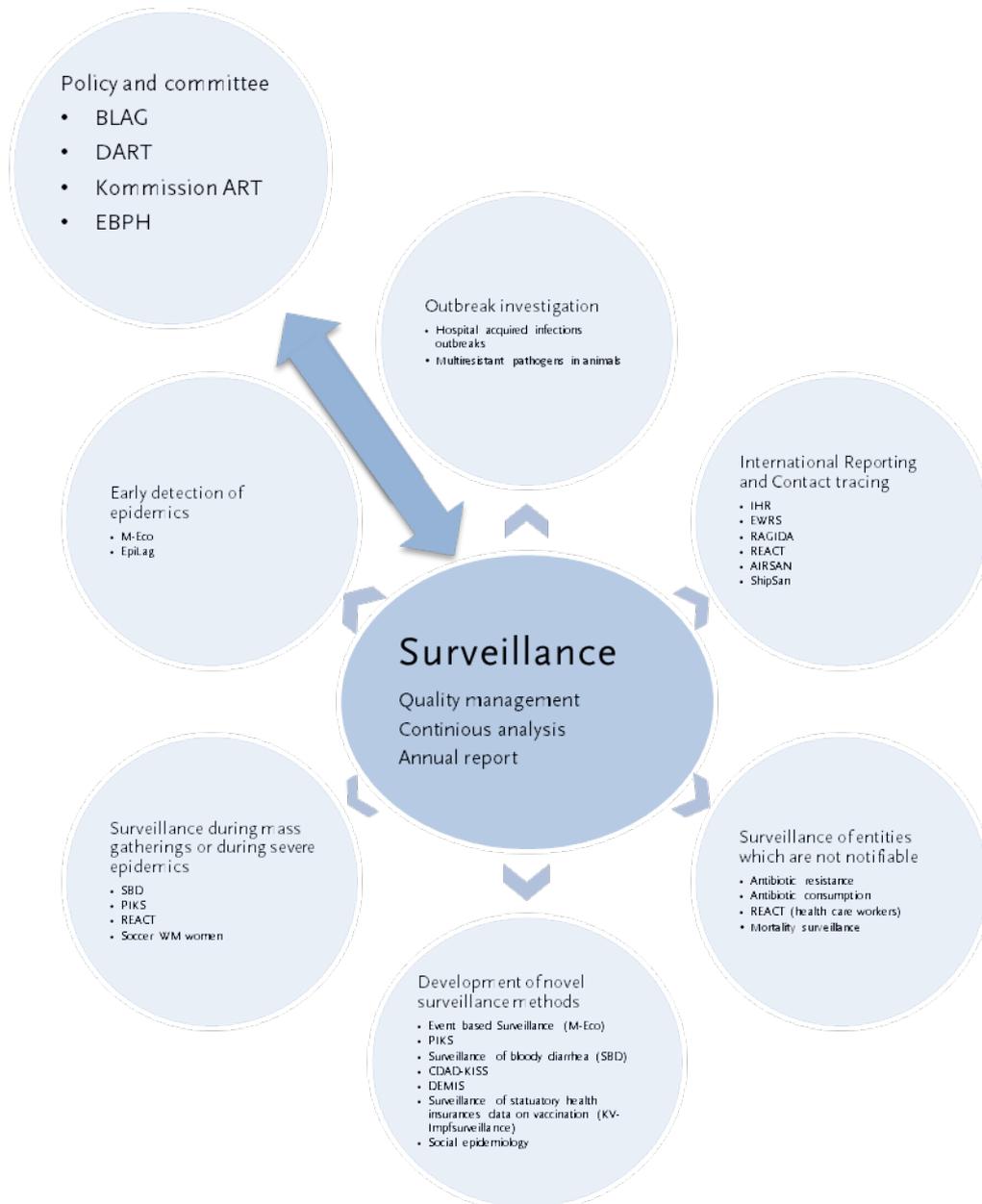
The character of the unit was generic. The unit supported the other more disease specific units in general questions of surveillance and international reporting. Important goals were improvement of early warning and early detection of outbreaks, as well as the development, implementation and evaluation of new surveillance systems especially during extraordinary events like mass gathering and severe epidemics (Takla A et al., *BMC Public Health* 2012, Adlhoch C et al. *Influenza Other Respi Viruses* 2012, Wadl M et al., *Euro Surveill* 2011, Williams C et al., *Epidemiol Infect* 2009). Also international reporting with a special focus in investigating the need for contact tracing (Mohr O et al., *Euro Surveill* 2012, Askar M et al., *Euro Surveill* 2012, Leitmeyer K, *Euro Surveill* 2011), close cooperation with public health authorities on the one side and hospitals and ambulatory medicine on the other side, and continuously improving surveillance of healthcare associated infections/outbreaks, antimicrobial resistance (Schweickert et al., *Eur J Clin Microbiol Infect Dis* 2012), and antibiotic consumption were further important goals. Surveillance of antimicrobial resistance and antibiotic consumption was a new area and was for the first time dealt with in a wider range in the department.

The main tasks are

- Continuous epidemiological analysis of notifiable diseases and entities/events in the framework of the IfSG
- Quality management of surveillance data
- Development of case definitions
- Development of recommendations on procedures for the surveillance of infectious diseases and events
- Early detection of epidemics and communicable diseases with the potential of threatening public health
- Development and implementation of the antibiotic resistance surveillance system (ARS), including an early warning system as a tool for data quality check for participating laboratories
- Development of a surveillance system for antibiotic consumption
- Development, implementation and evaluation of novel surveillance methods especially during extraordinary events
- Coordination of a working group comprised of health departments from government and the federal states on surveillance (“Bund-Länder-Arbeitsgruppe”) and the weekly epidemiological situation telephone conference “EpiLag” with federal states
- Support for investigating healthcare associated outbreaks and severe outbreaks/epidemics
- Implementation of targets of the German strategy to combat antibiotic resistance (DART)
- Establishment of a centre for the prevention and control of antibiotic resistance
- Hosting of the executive secretary of the German Committee on Antimicrobials Resistance and Therapy (ART)
- Implementation of the International Health Regulation (IHR)

- Reporting to the ECDC, WHO and to European Networks

Figure 6: Tasks of the Surveillance Unit



(BLAG: Bund Länder Arbeitsgruppe Surveillance, DART: Deutsche Antibiotikaresistenz Strategie, ART: Antiinfektiva Resistenz und Therapie, EBPH: Evidence Based Public Health, M-Eco: Medical Ecosystem, Epilag: epidemiologische Lagekonferenz, SBD: Surveillance Blutige Durchfälle, PIKS: Pandemische Influenza Krankenhaus Surveillance, REACT: Response to Emerging infectious disease: assessment and development of core Capacities and Tools, CDAD-KISS: Clostridium difficile associated infection Krankenhausinfektionen Surveillancessystem, DEMIS: Deutsches Elektronisches Meldesystem für Infektionsschutz, KV: Kassenärztliche Vereinigung, IHR: International Health Regulation, EWRS: Early Warning and Response System, RAGIDA: risk assessment guidelines for infectious diseases transmitted on aircraft, AIRSAN: Coordinated action in the aviation sector to control public health threats (granted in 2012, starting 2013))

2.2.1. Surveillance

The main task of the unit was surveillance with all the other tasks grouping around this subject (Figure 6). General tasks were quality management of surveillance of notifiable diseases and events

as imposed by the IfSG, continuous epidemiological analysis of the surveillance data, and further development of case definitions and criteria for transmission and interpretation. Additionally, recommendations on procedures for the surveillance of infectious diseases were prepared in cooperation with the disease specific units. From 2009 to 2012 18 informational briefs (“Infobriefe”) were developed and distributed to local health departments. In addition handling of § 7 (3) notifications (malaria, congenital toxoplasmosis and congenital rubella, and *Echinococci* infection) was part of the tasks of the unit. These data as well as all other diseases to be notified are published weekly in the weekly epidemiological bulletin (Epid Bull), SurvStat@RKI (a public useable interactive program), and the annual report of infectious diseases (“Jahrbuch Infektionsepidemiologie”), the epidemiological part of these publications was always organised in the unit. The annual report is written by the whole department. The editorial responsibility is in the Surveillance Unit. The first part of the reports is an actual description with recent amendments of the IfSG further the reports included a part with general information for each notifiable disease (regional distribution, sex distribution, outbreaks, hospitalisation), followed by a more extensive and detailed information for each notifiable disease (short description, actual data, comparison to former data).

2.2.2. Development of novel surveillance approaches and methods

An important task of the unit was to develop new surveillance methods.

One very important area in this field is event based surveillance (see 2.2.5., Unit 32).

In cooperation with all 17 Associations of Statutory Health Insurance Physicians (KVen) in Germany (covering approximately 85% of the German population, i.e. 70 Million people) insurance refund claim data are transmitted to RKI and analysed continuously for the epidemiological assessment of vaccine preventable diseases and estimation of vaccination coverage. The project was initiated, implemented and evaluated in Unit 32 (Siedler A et al., *Euro Surveill* 2012, Reuss A et al., *Gesundheitswesen* 2010, Reuss A et al., *BMC Public Health* 2010, Reuss A et al., *Dtsch Arztebl Int* 2010). In August 2012, it was transferred to the Immunisation Unit to be used as a routine tool for the monitoring of vaccination coverage especially in children before school entry and in adolescents.

Together with the national reference centre for surveillance of nosocomial infections, a hospital based surveillance system for hospital acquired *C. difficile* infections was developed (CDAD KISS, now situated at the NRZ) (Gastmeier P et al., *Int J Antimicrob Agents* 2009).

In the year the 2009 MRSA in bloodstream and liquor had become a pathogen to be notified. The unit developed together with unit 31 the reporting system (Schweickert B et al., *Eur J Clin Microbiol Infect Dis* 2012).

The unit is responsible for the surveillance of healthcare associated outbreaks. Since August 2011 health-care associated outbreaks are reported mandatory via the federal state public health authorities to the RKI. In the first year data were collected by faxed or e-mailed standardised questionnaires and line lists; currently an electronic version is developed together with unit 31 and will be fully implemented soon. For the first time systematic data of hospital acquired outbreaks are available.

Further, a working group engaged in social epidemiology within the unit has since 2009 examined health disparities as increased risk of acquiring infections and accordingly has developed methods for the surveillance of socio-behavioural factors of infectious disease. The aim of one study was to describe in an ecological analysis the impact of different social factors on the risk of acquiring infectious diseases in an urban setting (Wilking H et al., *Int J Health Geogr* 2012). The specific outcome of interest was the spatial distribution of hospitalised patients with Rotavirus infections in Berlin, which are a leading cause of acute gastroenteritis among infants and also a burden in the elderly in Germany. A spatial Bayesian Poisson regression model was used for the statistical analysis of incidences at neighbourhood level in relation to socio-demographic variables. The results may help to generate more specific hypothesis for infectious disease transmission in this urban area. The field of social epidemiology should gain more importance, and closing the gap should be a prioritised goal.

2.2.3. Surveillance during severe epidemics and during mass gathering

The development of surveillance systems in extraordinary situations is a challenge, and during epidemics the introduction of these systems must be very fast; even still, it must include the consideration of needs and expenditure assessments (especially during mass gathering).

In recent major outbreaks of community-acquired diseases (Pandemic Influenza 2009/2010 and the outbreak of entero-haemorrhagic *Escherichia coli* (EHEC) and haemolytic-uremic syndrome (HUS) in 2011), the Surveillance Unit complemented the existing reporting system with additional event-related surveillance systems in hospitals. The Pandemic Influenza A/H1N1 hospital surveillance (PIKS, Adlhoch C et al., *Influenza Other Respi Viruses* 2012) and the surveillance of bloody diarrhoea (SBD) were quickly implemented and able to capture data timely and effectively both to the severity and course of the pandemic influenza of 2009/2010 and the outbreak of EHEC and HUS in spring and summer of 2011. As the structures and especially contacts to German hospitals still exist, a hospital surveillance system can easily be set up and implemented again, in case of an occurring severe outbreak.

Mass gatherings often require a temporarily intensified surveillance. Unit 32 was responsible for national coordination of intensified surveillance measures during the 2011 FIFA Women's World Cup (Takla A et al., *BMC Public Health* 2012). Based on previous experience with intensified surveillance during the 2006 FIFA Men's World Cup (Williams C et al., *Epidemiol Infect* 2009), we conducted a needs assessment with the district health authorities in the 9 host cities in March 2011. Specific measures with majority consent were implemented. During the event, we surveyed the 9 district and their corresponding 7 state health authorities to evaluate the implemented measures. Implemented measures, including moving from weekly to daily (Monday - Friday) reporting within the routine infectious disease surveillance system, regular feedback on those notification reports and summaries of national and international World Cup-relevant epidemiological incidents, were rated as adequate. Involvement of the participating stakeholders early-on in the planning phase secured ownership of and guaranteed support for the chosen strategy. The enhanced surveillance for this event resulted as a low-level surveillance. However, we included mechanisms for rapid upscaling if the situation would require adaptations.

2.2.4. Surveillance of entities which are not notifiable

Furthermore the Surveillance Unit has established a timely monitoring of all-cause mortality in the state of Berlin to be able to identify an unusual increase in mortality and a possible underlying public health threat. The Surveillance Unit is an active partner of The European Mortality Monitoring Project and delivers weekly the mortality data of Berlin, which are published on the project's website (www.euromomo.eu). Efforts are underway to develop a timely German national mortality monitoring as it already exists in many other countries worldwide.

In October 2009 the third interdisciplinary expert workshop on Lyme borreliosis was organised by Unit 32. Main objective were to identify research deficits and to prioritise areas which need to be addressed. Among the research areas which have to be prioritised are the standardisation of diagnostic tests, the development of markers to detect an active infection, the improvement of the epidemiological data and the analysis of the burden of disease (Freitag M et al., *Int J Med Microbiol* 2009).

On the latter issue, initiatives have been taken to analyse the sera of children and adolescents for antibody seroprevalence of *Borrelia burgdorferi* in the nationwide and representative KiGGS-study herewith sound data on the distribution and on risk factors in Germany could have been obtained (Dehnert et al., *PLoS ONE* 2012).

The responsibility for Lyme borreliosis changed to Unit 35 in August 2011.

Typical hospital pathogens are not notifiable in Germany that means special surveillance systems have to be developed.

"Antibiotika-Resistenz-Surveillance in Deutschland (ARS)" is the National Antimicrobial Resistance Surveillance System. It is a major component of the German Strategy for Detection, Prevention and Control of Antimicrobial Resistance (DART) and its implementation was funded by the Ministry of Health from January 2007 to June 2010. ARS operates as a network of laboratories participating on

a voluntary basis submitting data from routine susceptibility testing of clinical samples from hospitals as well as from outpatient care settings in a standardised format via an electronic interface to the RKI for central processing. The main objective is to provide reference data for antimicrobial resistance of the most important pathogens in inpatient and outpatient care on national and regional level (Noll I et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012, Schweickert B et al., *Eur J Clin Microbiol Infect Dis* 2012, Wadl M et al., *Infection* 2010). These data are accessible through an interactive database on the ARS website (<https://ars.rki.de/>). Participating laboratories receive hospital reports as feedback as well as alerts in case of rare resistance events. ARS provides data on trends in resistance as well as for comparisons by region (yet limited) or by structural characteristics such as ward type or specialties thus allowing for identification of resistance problems that can be used for developing recommendations and strategies for the containment of antimicrobial resistance. ARS is part of the European Antimicrobial Resistance Surveillance Network (EARS-Net); by submitting resistance data according to the EARS-Net protocol as well as denominator data once a year it contributes to EARS-Net reports and publications. Running and developing the national antimicrobial resistance surveillance system needs good service for participating laboratories and recruitment of new participants to obtain a nationwide coverage. Maintenance of the ARS database and ARS website and further development of tools and algorithms for data analysis such as for multi-resistance and notifiable resistance phenotypes are major IT-requirements. In the field of resistance the unit paid special attention to multiresistant pathogens especially MRSA, VRE, ESBL and carbapenem-resistant gram negative pathogens, and *C. difficile*.

Another task is antibiotic consumption in the ambulatory sector. In Germany, antibiotics are only available on prescription and the surveillance of antibiotic consumption primarily relies on reimbursement data of the legal insurance systems, which cover around 85% of the German population. There are two institutions which bring together data on antibiotic consumption from the different associations of Statutory Health Insurance Physicians (Kassenärztlichen Vereinigungen): the Central Institution for statutory health care provision (Zentralinstitut für kassenärztliche Versorgung, ZI) and the Scientific Institution of the AOK, one of the statutory health insurance funds (Wissenschaftliches Institut der AOK, WiDO). The RKI took the initiative for collaboration with the ZI in order to acquire data on antibiotic consumption in the ambulatory sector and to cooperate in the field of data evaluation and the provision of feedback and advice to the medical practitioners. So far, a realisation of this project was not successful for technical reasons (an appropriate certification for the transfer of data according to current data protection rules can currently not be realised by the RKI). Currently, the WiDO provides data on antibiotic consumption in aggregated form to GERMAP (Report on antibiotic consumption and resistance in human and veterinary medicine) and, in collaboration with the RKI, provides data to the European Surveillance System of Antibiotic Consumption –Network (ESAC-Net).

The surveillance of antibiotic consumption in hospital care requires a different methodological approach. The sources of data for the acquisition of antibiotic consumption are pharmacies. Several years ago, a project for the monitoring of antibiotic consumption in hospitals was initiated and established by the University Hospital of Infectiology, Freiburg and the Society of German hospital pharmacists (Bundesverband deutscher Krankenhausapotheker, ADKA). This project has initially been funded by the BMBF and since 2010 is continued with the support of the RKI (financial and technical support) with the aim to extend the project over the regional borders in order to obtain nationally representative data and provide reference data. This surveillance system is conceived as a sentinel system and does currently not provide comprehensive coverage of all German hospitals. Awaiting the new “Deutsches Elektronisches Meldesystem für Infektionsschutz (DEMIS)”, the RKI has abstained from developing innovating IT-technical tools for the automated collection of antibiotic consumption data in hospitals.

In 2011, §23 of the IfSG has been supplemented by a new regulation, which obliges hospitals to monitor antibiotic consumption. In order to support the hospitals in the implementation of an appropriate surveillance system and in order to promote the connection of the results of other established surveillance systems with data on antibiotic consumption, the RKI, in cooperation with the NRZ of Nosocomial Infections, intends to initiate a new project: the establishment of a unit on antibiotic consumption that will be associated with the existing KISS-System. The technical and financial requirements have been determined according to the detailed project specifications.

Together with the UK HPA (Leader), the unit also developed a surveillance system for monitoring infectious disease outbreaks among Health Care Workers. This was part of the REACT project (see 2.2.7., Unit 32).

2.2.5. Early detection of epidemics

In 2010, the RKI joined a consortium of computer scientists to address novel methods for event-based and syndromic surveillance. The objective of the project - called the Medical Ecosystem (M-Eco), was to create an accessible technology for the early detection of public health incidents (potentially indicating outbreaks) that occur in news and social media. During the duration of the project, computer scientists developed detection mechanisms with the aim to continuously scan the Internet for these media types, based on the simple semantic (disease names and symptoms) and statistically relevant (varying search algorithms) epidemiological requirements deemed critical for the surveillance of different infectious diseases. Development of these functionalities resulted in a “search function” on a Web-based user interface that enables epidemiologists to monitor “mentions” of diseases and symptoms occurring in Twitter and news media (fed via a news aggregate technology) over time, and geo-located to enable comparison with other sources of epidemiological information, including standard governmental infectious disease surveillance and monitoring. The project was closed in 2012.

In January 2009, a weekly telephone conference with all competent authorities of the German federal states and the RKI was established to identify, discuss and respond to infectious disease events in real-time (Mohr O et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2010). The topics of the conferences focused on national events involving more than one federal state, on events at regional level, and on international events with potential relevance for Germany. In this sense, the teleconference is part of early warning. Further, these conferences are used for the exchange of scientific and organisational information and serve as a platform to provide IT support for the surveillance software SurvNet.

2.2.6. Outbreak investigation

A multidisciplinary team with expertise in clinical medicine, microbiology, infection control and epidemiology supports upon request from the responsible state authorities local public health authorities in investigating and managing healthcare associated outbreaks. Over the past years the unit was increasingly involved in several outbreak investigations in different hospital settings (alone 2012 official involvement in 5 outbreaks) (Hermes J et al., *Gesundheitswesen* 2011, Weiss B et al. *Infect Control Hosp Epidemiol* 2009. Strong collaboration with national reference laboratories and laboratories within the RKI is well established to combine epidemiological as well as microbiological and molecular typing and sequencing expertise to investigate healthcare associated outbreaks.

Multiresistant pathogens in animals and the potential transmission of these pathogens to human have large outbreak potential (Walther B et al. *PLoS ONE* 2012). In response, the MedVet-Staph research network including veterinarians, biologists, human physicians, epidemiologists, bioinformaticians and experts for risk assessment and simulation was established. In summary, the interdisciplinary network analyses the mechanisms facilitating the spread of *Staphylococcus aureus*/MRSA within one species and across species barriers. The project aims to provide robust data on transmission of livestock associated MRSA (LA-MRSA) to humans exposed to animals (farmers, veterinarians) and further transmission to their non-exposed contact persons. A cohort of MRSA-positive veterinarians (including their families) from all over Germany and a control group have been established in order to study dynamics, risk factors for and clinical significance of colonisation with MRSA.

In another project, *C. difficile* and potential transmission between human and domestic animals is investigated.

2.2.7. International reporting and contact tracing

Reporting to the WHO and to the European Networks especially the EWRS (Early Warning and Response System) and assessment of the necessity of contact tracing are important; however there are still many questions which need to be addressed systematically.

The unit started to work in a scientific way in this area with a tender of the ECDC (RAGIDA risk assessment guidelines for infectious diseases transmitted on aircraft, Mohr O et al., *Euro Surveill* 2012, Askar M et al., *Euro Surveill* 2012). The guiding principle behind RAGIDA was the development of algorithms to enable efficient disease control and prevention for a range of infectious diseases. For a total of 12 diseases, ranging from anthrax to SARS, the authors systematically reviewed and summarised the scientific literature and, if available, related air transportation guidelines. Then the evidence retrieved from the literature was combined with expert knowledge. The resulting paper provides a host of viable options for decision makers, particularly when faced with the decision whether to contact trace air travellers and crew that were exposed to infectious diseases during a flight.

The REACT (Response to Emerging infectious disease: assessment and development of core Capacities and Tools) project (EU financed, RKI scientific lead) was created to support an improved and better coordinated response to the outbreak of infectious diseases – especially newly emerging infections – within the European Union. The project was organised in subject-specific work packages: "Enhanced surveillance during international mass gatherings", "Surveillance of infectious disease outbreaks among Health Care Workers" "Tools for local implementation of the International Health Regulations (IHR)" and "International contact tracing after exposure to infectious diseases". The choice of the four areas of interest was inspired by the observation that in these areas little is known or done and that existing international regulations for surveillance urgently need reinforcement for effective implementation. The general objective of the project has been to provide evidence and tools towards a common European standard for the response to emerging public health threats. In order to use the available expertise in all areas of interest four European public health institutions from Poland, UK, Norway and Germany took over responsibility each for one area of response. In all four areas all planned products and tools – training modules, education and information material, guidelines and protocols - have been elaborated and tested. The React tools are now available for dissemination and application.

Another important point in this area was the implementation of the International Health Regulation (IHR). According to the Act on the International Health Regulations (2005) (IHR) of 23 May 2005, dated 20 July 2007 (Federal Law Gazette II, p. 930), the Robert Koch Institute is the responsible point of contact for the German IHR focal point in the field of prevention and control of communicable diseases. In the Robert Koch Institute, currently the department for infectious disease epidemiology is the responsible point of contact and also ensures the capacity to detect, assess, notify and report events in accordance with the IHR, as specified in Annex 1.

Furthermore, the Surveillance Unit was asked by the German Federal Ministry of Health to develop recommendations on the core capacities of German airports and ports that were designated in accordance with paragraph 1 of Article 20 of the IHR. The purpose of these already developed recommendations was to define the core capacity requirements according to Annex 1 B of the IHR in more detail, thus to create a manageable instrument to develop and maintain these core capacities at designated German airports and ports.

Within the scope of the implementation of the IHR (2005) the Surveillance Unit was recently awarded a grant by the EU (DG SANCO) in the framework of the "Second Programme of Community action in the field of health (2008-2013)". The project, named AIRSAN (Coordinated action in the aviation sector to control public health threats) aims to support European Member States in IHR implementation by creating a functioning Network of stakeholders in the aviation and public health sector across the EU and by reviewing existing and developing new SOPs, regulations and guidelines in the area of response to public health threats on aircraft. In addition the unit is involved in the SHIPSAN project which is the corresponding project for ports.

2.2.8. Policy and Committee

A further important task was the coordination of the working group of the government and federal states on the IfSG ("Bund-Länder-Arbeitsgruppe"). Three to four times per year, one- or two-day conferences with representatives of the competent authorities of the German federal states, the German armed forces and the RKI. During the conferences, developments of the surveillance system, planned and on-going studies on infectious diseases involving the participation of more than one federal state, and outstanding public-health events were presented and discussed. The most frequently discussed topics were developments of the electronic surveillance software

SurvNet, case definitions, reporting and transmission issues and outbreak investigations. Tuberculosis, influenza, and Norovirus infections were the most frequently discussed diseases.

A further task was the realisation of the German strategy to combat antibiotic resistance (DART, Noll I, Eckmanns T, *Hyg Med* 2011). Since 2008, the unit has initiated a number of different studies to investigate underlying socio-behavioural factors of influence for antibiotic prescribing and antibiotic resistance in Germany to get background information for DART (Velasco E et al. *BMJ Open* 2012, Velasco et al., *Infection* 2011, Faber et al., *Euro Surveill* 2010). The studies comprising this research area included a literature review, focus group discussions with medical professionals, a national representative cross-sectional study of physicians and a Web-based survey of the general population. Further components to realise DART were first steps to establish a centre for the prevention and control of antibiotic resistance, and the preparation of hosting the executive secretary of the German Standing Committee on Antimicrobials Resistance and Therapy (ART) in the unit (according to The German Protection against Infection Act (Infektionsschutzgesetz) (§23)). One of the main tasks of the Committee will be the development of state-of-the art guidelines for diagnostic and therapeutic principles in the context of multiresistant pathogens.

Principles of evidence based public health (EBPH) will hereby be applied. In this field strong cooperation with Unit 33 is planned. Experiences with the principals of EBPH were gathered in the RAGIDA and REACT projects. In both projects guideline development was one aim and systematic reviews on infectious disease transmission on airplanes and other vehicles were conducted.

In the PRECEPT (tender of ECDC lead by RKI) project the application of EBPH for guideline development will be investigated further with a focus on antimicrobial resistance.

2.3. Major goals and contribution to the goals of the department

International reporting was one of the major goals of the department. This was done in a regular and reliable manner by the unit and RKI is a confidential partner for the WHO and the EU / ECDC.

Implementation of the IHR was another important goal in the last years. RKI was not only successful in this task but in addition RKI is established as a leading research institute in this area in Europe. It started with the RAGIDA tender, followed by the REACT project and now continued by the AIRSAN project - all 3 projects were or are coordinated by RKI.

In the field of surveillance during severe epidemics and mass gathering the unit implemented and evaluated successfully surveillance systems as shown in several publications.

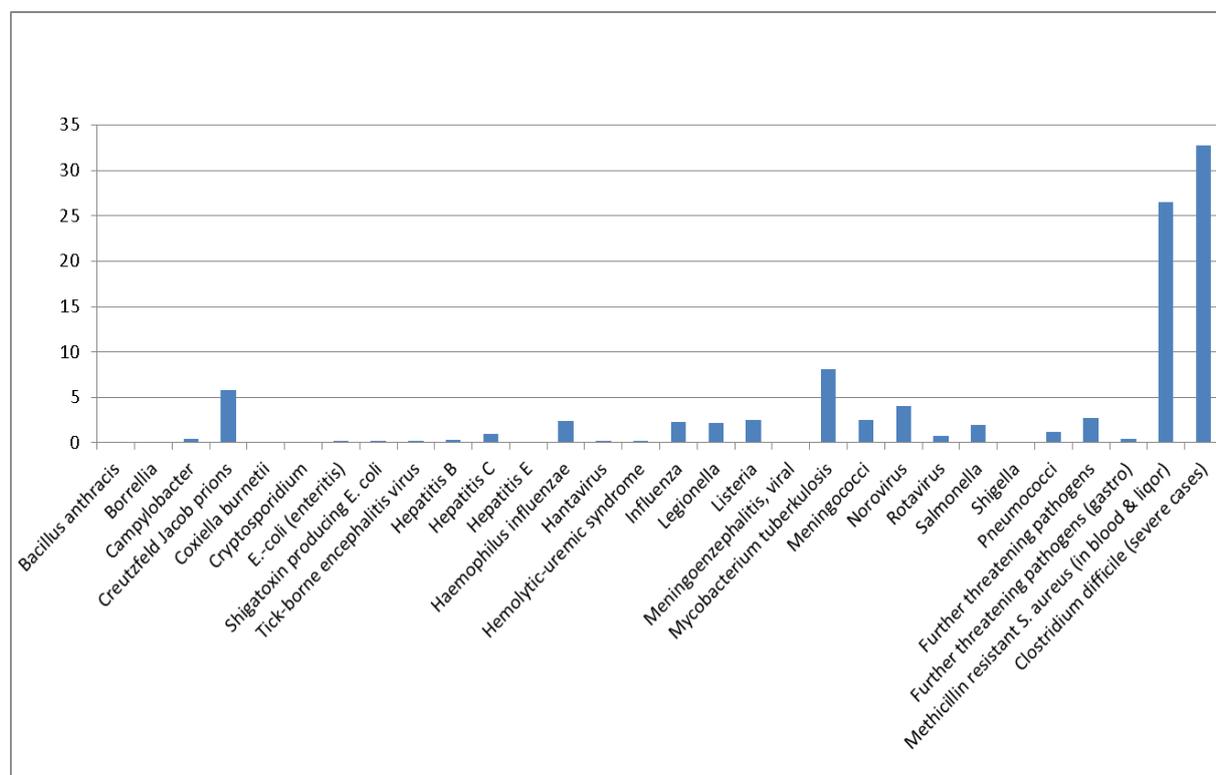
One goal of the unit was to integrate social epidemiology as part of infectious disease epidemiology. Nowadays no epidemiological studies should be conducted without considering social factors as risk factors and no measures should be implemented without investigation how the social gap is influenced as consequence of the introduced measures.

Especially in the area of healthcare associated infections, antibiotic resistance and antibiotic use public health and the clinical medicine are getting closer. In the revised German Protection against Infection Act the legal responsibilities for hospitals concerning healthcare associated infections and antibiotic resistance and use increase. With surveillance of infection control and hospital epidemiology issues like antibiotic resistance, antibiotic consumption, hospital acquired infections / outbreaks was for the first time dealt with in a wider range in the department. Only two (MRSA in blood culture and liquor and severe cases of *C. difficile*) of the typical hospital pathogens are notifiable. These two pathogens are responsible for more than 50 % of reports of death notification (Fig. 7). Analysis of reporting data of severe cases of *C. difficile* is complicated as compliance with notification is low, as it is a rather complicated notification algorithms which is not very known among physicians. More work has to be done on this pathogen and in the area of multi-resistant pathogens.

In future there will be a specific unit for this field established in the Department of Infectious Diseases Epidemiology. The reorganisation of the department will be a huge task for the units, the department, and the whole institute. Until recently surveillance of antibiotic resistance and antibiotic consumption was an integrated part of the Surveillance Unit. Now there are two new units and new strategies and goals have to be developed. For the area of antibiotic resistance,

antibiotic consumption, and healthcare associated infections reorganisation within the RKI will be necessary affecting not only the Department of Infectious Diseases Epidemiology.

Figure 7: Percentage of deceased (n = 1,115) of diseases to be notified (excluding IfSG §7.3 notifications) in the year 2012 (until 31st of October)



2.4. Additional work and methods for investigations

Evidence based public health

Event based surveillance (EpiLag, M-Eco)

Social epidemiology in infectious diseases

2.5. Scientific advice and consulting services

1) Scientific advice to the German MoH:

In 2009–2012, under the lead of the Surveillance Unit a total of reports have been written upon the request of the MoH. Details are listed in the appendix of the department report.

2) Scientific advice or guidance to healthcare professionals:

- Yearly workshop for laboratories participating in ARS, 20 to 30 participants, certified as a training course by the Chamber of Physicians;
- 1. and 2. Antibiotic Resistance Workshop at the RKI (in cooperation with the DGHM, DGI and EURSAFETY) 2010 and 2012, 2 days with ca. 90 participants (microbiologist, infection control physicians, public health physicians, clinicians), certified as a training course by the Chamber of Physicians
- Telephone support or email support for interpretation of The German Protection against Infection Act (about 800 calls per year)

3) Consulting service for state and local Public Health authorities on best practice for implementing and putting into practice of IHR and IfSG

4) Support of the local public health authorities concerning outbreak investigation especially healthcare associated outbreaks

5) 18 informational briefs (“Infobriefe”) were developed and distributed to local health departments.

2.6 Training and teaching activities

- Participation as facilitators in bi-annual 1-week courses on field epidemiology for public health workers in Germany hosted by the department.
- Project supervisors for fellows of the German Postgraduate program for Applied Epidemiology (PAE) and the European Intervention Epidemiology Training program (EPIET)
- Activities as lecturers and supervisors in the Masters Program in International Health (Charité University Medicine, Berlin), Masters Program in Public Health (Berlin School of Public Health), and the Masters Program in Applied Epidemiology (Robert Koch Institute), and within the programme of the International Research Training Group GRK1673 “Functional Molecular Infection Epidemiology”.
- Supervisors for dissertations and master theses (currently 2 master thesis projects).
- Participation as facilitators in teaching modules of the EPIET program
- Lecturer in the DGHM infection control course, in the training course for infection control link physicians, in the education of infection control nurses, and for medical students in infection control and hospital epidemiology (University, Charité)
- Lecturer in the trainings course for antibiotic stewardship (University, Freiburg)
- Trainings for the local health departments and the states in the international health regulation (IHR) and the IfSG
- Lecturer in the training course for medical officers (Akademie für öffentliches Gesundheitswesen, Düsseldorf)

3. Cooperation with other scientists or research institutions

3.1. Internal (within RKI)

Department 1 (Unit 13, NRC for *S. aureus*: G. Werner; Unit 11: A. Flieger, Unit 17: Schweiger)

- Abu Sin et al. 2012
- Dudareva et al.2011
- Wichmann et al.2010
- Jansen et al. 2010
- Kola et al. 2009

3.2. External / National

National Reference Laboratory for surveillance of nosocomial infections (P. Gastmeier)

- Adlhoch et al. 2012
- Schweickert et al.2011
- Kola et al. 2009
- Gastmeier et al. 2009

Institute of Microbiology and Epizootics, Veterinary Faculty, Freie Universität Berlin (L.H. Wieler)

- Walther et al. 2012

German state health departments

- Abu Sin et al. 2012, Wilking et al.2012, Uphoff et al. 2011, Adlhoch et al. 2010, Mohr et al. 2010

3.3. External / International

Health Protection Agency, London, UK (M. Catchpole)

- Aghaizu et al. 2011

4. Appendix

4.1 Overview on achievements of the Unit, 2009-2012

4.1.1. Scientific publications, 2009-2012

Number of peer-review publications co-authored by members of unit: 82

Impact factor (IF) according to JCR (for 2012 according to 2011)

2009: 25,3

2010: 42,0

2011: 226,7

2012: 58,8

Cumulative 2009-2012: 352,8

A) Original research articles in peer-review journals

2012 (until Sept.)

Abu Sin M, Takla A, Flieger A, Prager R, Fruth A, Tietze E, Fink E, Korte J, Schink S, Höhle M, **Eckmanns T**: Carrier prevalence, secondary household transmission and long-term shedding in two districts during the *Escherichia coli* O104:H4 outbreak in Germany, 2011. *J Infect Dis* 2012.

Adlhoch C, **Wadl M**, Behnke M, Pena Diaz L A, Clausmeyer J, **Eckmanns T**: Pandemic influenza A(H1)pdm09 in hospitals and intensive care units - results from a new hospital surveillance, Germany 2009/2010. *Influenza Other Respi Viruses* 2012; 6(6):e162-e168.

Adlhoch C, Kaiser M, Loewa A, Ulrich M, Forbrig C, Adjogoua E V, et al.: Diversity of Parvovirus 4-like Viruses in Humans, Chimpanzees, and Monkeys in Hunter-Prey Relationships. *Emerg Infect Dis* 2012; 18(5):859-862.

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Klein S, **Schöneberg I**, Krause G: Vom Zwang zur Pockenschutzimpfung zum Nationalen Impfplan - Die Entwicklung des Impfwesens vom Deutschen Kaiserreich bis heute [The historical development of immunization in Germany : From compulsory smallpox vaccination to a National Action Plan on Immunization]. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012, 55(11-12):1512-1523.

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Nachtnebel M, **Greutelaers B**, Falkenhorst G, Jorgensen P, Dehnert M, Schweiger B, Trader C, Buda S, **Eckmanns T**, Wichmann O, Hellenbrand W: Lessons from a one-year hospital-based surveillance of acute respiratory infections in Berlin- comparing case definitions to monitor influenza. *BMC Public Health* 2012; 12:245.

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Antimicrobial Resistance Surveillance (ARS)]. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012, 55 (11-12):1370-6.

Schweickert B, Noll I, Feig M, Claus H, Krause G, Velasco E, Eckmanns T: MRSA-surveillance in Germany: data from the Antibiotic Resistance Surveillance System (ARS) and the mandatory surveillance of MRSA in blood. *Eur J Clin Microbiol Infect Dis* 2012; 31(8):1855-1865.

Siedler A, **Rieck T**, Reuss A, Walter D, **Poggensee G**, Poethko-Muller C, et al.: Estimating vaccination coverage in the absence of immunisation registers - the German experience. *Euro Surveill* 2012; 17:pil=20152.

STEC Workshop Reporting Group: Experiences from the Shiga toxin-producing *Escherichia coli* O104:H4 outbreak in Germany and research needs in the field, Berlin, 28-29 November 2011. *Euro Surveill* 2012, 17(7):pil=20091.

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Aghaizu A, Elam G, Ncube F, Thomson G, Szilagyi E, **Eckmanns T**, et al.: Preventing the next 'SARS' - European healthcare workers' attitudes towards monitoring their health for the surveillance of newly emerging infections: qualitative study. *BMC Public Health* 2011; 11:541.

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Intensivierte Surveillance während eines großen EHEC-/HUS-Ausbruchs in Deutschland, Mai-Juni 2011. *Epid Bull* 2011;25:225-229.

Zur Entwicklung der Erkrankungszahlen im aktuellen EHEC/HUS-Ausbruch in Deutschland - Update. *Epid Bull* 2011;24:215-217.

Zum Weltgesundheitstag 2011: DART - gemeinsam Antibiotikaresistenzen verhüten und bekämpfen. *Epid Bull* 2011;13:97-99.

Deutsche Antibiotikaresistenzstrategie – eine Zwischenbilanz des RKI. *Epid Bull* 2011;13:98-99.

Bericht zum 1. Workshop "Antibiotikaresistenz". *Epid Bull* 2011;13:99-101.

Überarbeitete Falldefinitionen zur Übermittlung von Nachweisen von Denguevirus und Norovirus und Erkrankungs- oder Todesfällen an Denguefieber und an Norovirus-Gastroenteritis. *Epid Bull* 2010;49:494-495.

Evaluation des Infektionsepidemiologischen Jahrbuchs meldepflichtiger Krankheiten für 2009 - Eine Umfrage unter Lesern des Jahrbuchs. *Epid Bull* 2010;47:472-475.

Ratgeber *Clostridium difficile*; *Epid Bull* 24| 2010

Clostridium-difficile-Infektionen: Übermittlungen gemäß IfSG von 01/2008 bis 12/2009; *Epid Bull* 10/2010

Bundesweite Häufung von Erkrankungen durch S. Panama 2010. *Epid Bull* 2010;40:399-400.

Reiseassoziierte Infektionskrankheiten 2009. *Epid Bull* 2010;38:379-387.

Auswertung der bundesweit übermittelten Meldedaten zu Adenovirus-Konjunktividen. *Epid Bull* 2010;37:369-272.

Meldepflicht gemäß Infektionsschutzgesetz (IfSG): Hinweise zur Meldepflicht für Labore. *Epid Bull* 2010;29:275.

Creutzfeldt-Jakob-Erkrankungen in den Jahren 2008 und 2009. *Epid Bull* 2010;27:253-259.

Lyme-Borreliose: Analyse der gemeldeten Erkrankungsfälle der Jahre 2007 bis 2009 aus den sechs östlichen Bundesländern. *Epid Bull* 2010;12:101-07.

Pandemische Influenza A/H1N1 Krankenhaus-Surveillance (PIKS): Erste Ergebnisse. *Epid Bull* 2010;4:31-34.

Reiseassoziierte Infektionskrankheiten. *Epid Bull* 2009;39:385-393.

Krankheiten, für die gemäß LVO eine erweiterte Meldepflicht zusätzlich zum IfSG besteht (Stand 2009). *Epid Bull* 2009;5:33-49.

Falldefinitionen übertragbarer Krankheiten für den ÖGD: Krankheiten, für die gemäß LVO eine erweiterte Meldepflicht zusätzlich zum IfSG besteht (Stand 2009). *Epid Bull* 2009;5:33-49.

4.1.2. Appendix with selected relevant publications

Five important publications for the scientific community 2009–2012

1. **Abu Sin M**, Takla A, Flieger A, Prager R, Fruth A, Tietze E, Fink E, Korte J, Schink S, Höhle M, **Eckmanns T**: Carrier prevalence, secondary household transmission and long-term shedding in two districts during the *Escherichia coli* O104:H4 outbreak in Germany, 2011. *J Infect Dis* 2012. Published online 21 Nov 2012.
2. **Schweickert B**, **Noll I**, **Feig M**, Claus H, Krause G, **Velasco E**, **Eckmanns T**: MRSA-surveillance in Germany: data from the Antibiotic Resistance Surveillance System (ARS) and the mandatory surveillance of MRSA in blood. *Eur J Clin Microbiol Infect Dis* 2012; 31(8):1855-1865.
3. **Mohr O**, Askar M, **Schink S**, **Eckmanns T**, Krause G, **Poggensee G**: Evidence for airborne infectious disease transmission in public ground transport - a literature review. *Euro Surveill* 2012; 17:pii=20255.
4. Adlhoch C, **Wadl M**, Behnke M, Pena Diaz L A, Clausmeyer J, **Eckmanns T**: Pandemic influenza A(H1)pdm09 in hospitals and intensive care units - results from a new hospital surveillance, Germany 2009/2010. *Influenza Other Respi Viruses* 2012; 6(6):e162-e168.
5. **Weiss B**, Kleinkauf N, **Eckmanns T**, an der Heiden M, Neumann M, Michels H, Jansen A: Risk factors related to a hospital-associated cluster of *Clostridium difficile* PCR ribotype 027 infections in Germany During 2007. *Infect Control Hosp Epidemiol* 2009; 30(3):282-284.

Five important publications for the public 2009–2012

1. **Abu Sin M**, Takla A, Flieger A, Prager R, Fruth A, Tietze E, Fink E, Korte J, Schink S, Höhle M, **Eckmanns T**: Carrier prevalence, secondary household transmission and long-term shedding in two districts during the *Escherichia coli* O104:H4 outbreak in Germany, 2011. *J Infect Dis* 2012. Published online 21 Nov 2012.
2. Wilking H, Höhle M, **Velasco E**, Suckau M, **Eckmanns T**: Ecological analysis of social risk factors for Rotavirus infections in Berlin, Germany, 2007-2009. *Int J Health Geogr* 2012; 11(1):37.
3. **Velasco E**, Espelage W, Faber M, **Noll I**, Ziegelmann A, Krause G, **Eckmanns T**: A national cross-sectional study on socio-behavioural factors that influence physicians' decisions to begin antimicrobial therapy. *Infection* 2011; 39:289-297.
4. Adlhoch C, **Wadl M**, Behnke M, Pena Diaz L A, Clausmeyer J, **Eckmanns T**: Pandemic influenza A(H1)pdm09 in hospitals and intensive care units - results from a new hospital surveillance, Germany 2009/2010. *Influenza Other Respi Viruses* 2012; 6(6):e162-e168.
5. Faber MS, Heckenbach K, **Velasco E**, **Eckmanns T**: Antibiotics for the common cold: expectations of Germany's general population. *Euro Surveill* 2010; 15(35):pii=19655.

4.1.3. List of reports and written scientific advice to the Ministry of Health, 2009-2012

There were 138 reports and written scientific advice to the Ministry of Health between 2009 and 30.09.2012.

4.1.4. Overview on collaborations in networks

ECDC:

- National Epidemiology Contact Point for EARS-Net: Ines Noll

- National Epidemiology Contact Point for ESAC-Net: Britta Schweickert
- National Focal Point Surveillance: Tim Eckmanns

WHO

- IHR Expert Roster: Tim Eckmanns

4.1.5. Memberships and participation in Advisory Boards

Dr. Tim Eckmanns

- Member of „Ständige Arbeitsgemeinschaft Allgemeine und Krankenhaushygiene“ since 2009 (DGHM)
- Schriftführer „Fachgruppe Infektionsprävention und Antibiotikaresistenz in der Krankenhaushygiene“ since 2009 (DGHM)
- Member ECCMID 2006
- From 2006 to 2009 deputy of the “Working Group Infectious Disease Epidemiology of the DGEPI”
- Editor of “Krankenhaushygiene Prävention nosokomialer Infektionen update” since 2011

4.1.6. List of completed dissertation or master theses in the Unit, 2009 – 2012

Year	Title	Name	Title	University/ Supervisor RKI
2009	Epidemiological situation of Lyme borreliosis in Germany: Surveillance data from six Eastern German States, 2002 to 2006	Balazs Fülöp	Dr. med	Charité / G. Poggensee
2012	Bestimmung von Impfquoten und Inzidenzen impfpräventabler Erkrankungen anhand von Daten der Kassenärztlichen Vereinigungen	Annicka Reuß	Dr. rer. medic.	Charité / G. Poggensee
2012	Socio-behavioural determinants for antimicrobial prescribing and antimicrobial resistance in hospital and outpatient care practice in Germany	Edward Velasco	Dr. rer. medic.	Charité / G. Krause
2009	Bestimmung von Risikofaktoren für Antibiotikaresistenzen in <i>Escherichia coli</i> Auswertung eines laborgestützten Surveillance Systems in Deutschland	Kirsten Heckenbach	MSE	Charité / T. Eckmanns
2011	Systematic literature review on event-based public health surveillance	Tumacha Agheneza	MPH	Hamburg / T. Eckmanns
2012	Prävalenz bakterieller Erreger in Blutkulturen – Daten aus Antibiotika-Resistenz-Surveillance Eine retrospektive Analyse der Erreger von Bakteriämien der Jahre 2008 bis 2010	Franziska Krüger	M.A.	Bremen / T. Eckmanns
2012	Auswertung der an das Robert Koch Institute übermittelten Datensätze zu weiteren bedrohlichen Krankheiten, 2002-2011	Ralph Berger	Master of Science in Epidemiology (MSc)	Charité / B. Greutelaers

4.1.7. Presentations as invited speaker, 2009 - 2012

Staff from the Surveillance Unit were invited to speak at 54 conferences.

Unit 33: Immunisation

Unit Head: PD Dr. Ole Wichmann

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1. General information Unit 33

Head: PD Dr. Ole Wichmann

Deputy: Dr. Anette Siedler

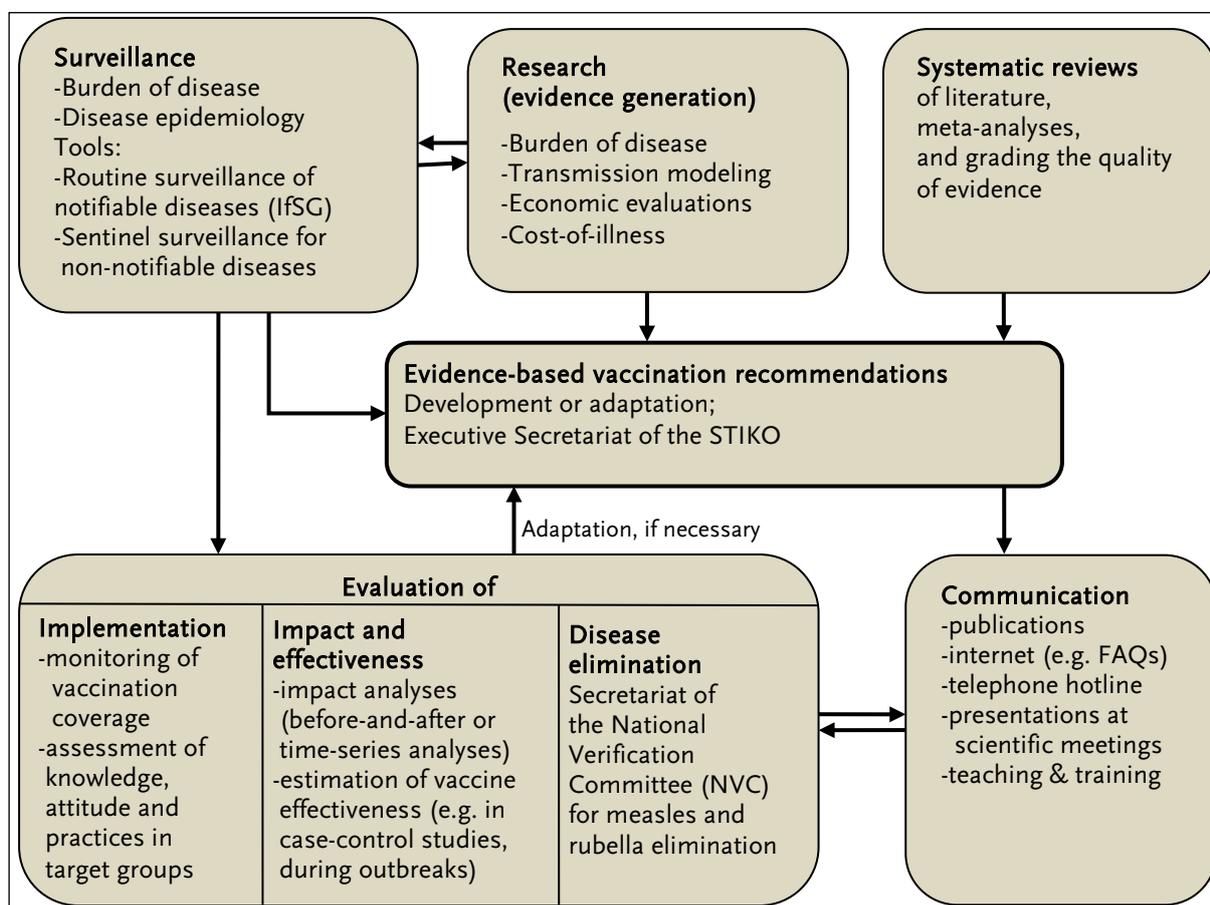
2. Tasks and goals of the Unit

2.1. Summary

The Immunisation Unit is responsible for a wide range of activities related to the development and evaluation of evidence-based vaccination recommendations (Figure 8). According to The German Protection against Infection Act (IfSG §20), the unit hosts the executive secretariat of the German Standing Committee on Vaccination (STIKO), which is responsible for developing national vaccination recommendations. These recommendations serve as a basis for the federal states' vaccination guidance, for the inclusion in the Immunisation guidelines of the Federal Joint Committee (which is linked to the reimbursement of vaccines: G-BA), and as a “best-practice” guidance to clinicians. Focus of the unit’s activities is therefore the generation of evidence and review of scientific literature, but also the communication of new recommendations as well as monitoring their implementation and impact (Figure 8).

As a tool for the estimation of baseline disease burden and assessment of vaccination impact, the unit monitors the epidemiology of vaccine-preventable diseases (VPD) in Germany. In addition to routine national disease surveillance, the unit currently operates enhanced sentinel surveillance systems for varicella/herpes zoster and for invasive pneumococcal diseases. The unit is also responsible for the collection, analysis, and publication of vaccination coverage data for Germany, and conducts research on the barriers and facilitating factors of vaccine uptake in specific target groups. The unit also conducts epidemiological research on disease burden, the effectiveness of vaccines in the post-licensure phase, and the impact of vaccination on a population level, as well as projects on disease transmission modelling, health economic evaluations of vaccines, and cost of illness studies. Since the end of 2012, the unit also hosts the executive secretariat of the National Verification Committee (NVC) for measles and rubella elimination.

Figure 8: Major activities / tasks of the Immunisation Unit



2.2. Current status of the work and summary of relevant results

2.2.1. Health economic evaluations and transmission modelling

Besides data on the efficacy and safety of vaccines (available from published literature) and local disease burden, transmission modelling and health economic evaluations provide important information to guide decisions whether to adopt a vaccination into the national Immunisation plan or not (Figure 9). Until recently, such models were not available or considered for vaccination decisions in Germany, mainly due to the lack of expertise in the RKI and in the STIKO.

Since 2010, projects on transmission modelling and health economic evaluations (e.g. cost-effectiveness analyses (CEA) or cost-utility analyses (CUA)) of vaccinations have been conducted by external research groups with funds provided by RKI and in close cooperation with the Immunisation Unit. The following evaluations have been completed or are currently in process: CEA, CUA and impact of HPV vaccination (completed in 2011, manuscripts submitted), CEA and CUA of rotavirus vaccination (completed in 2012, manuscript in preparation), CEA, CUA and transmission modelling of varicella vaccination (project started in 2012), and CEA and CUA of meningococcal B vaccination (project will start in 2013). Furthermore, the unit applied successfully for internal funding of two PhD-positions: A 3-year PhD-position for a health economic project (2011-13, CEA and CUA of herpes zoster vaccination) and a 3-year PhD-position for a transmission modelling project (2012-14, rotavirus transmission).

2.2.2. Communication

Healthcare professionals and local/state health authorities are the main target groups of the health-communication activities of the Unit, with the aim of improving knowledge and advising on appropriate procedures concerning vaccinations. The Immunisation Unit operates a telephone hotline twice a week, where healthcare professionals can obtain information on questions regarding the implementation of STIKO recommendations. This enables the Unit also to identify misperceptions in the healthcare community and requirements for further online information (two-way communication approach).

With the development of newly designed RKI web pages, the Immunisation Unit also updated and expanded its online information services, including FAQ that provide a broad overview on questions related to Immunisation and vaccines, also for the general public. A new link provides rapid access to this information: www.rki.de/impfen

To increase its visibility and the communication capacity, a separate web page was created for STIKO: www.stiko.de. With this easy-to-remember link, healthcare providers now have quicker access to all STIKO recommendations and the scientific background papers. STIKO-recommendations were translated into English in 2011 to support the international exchange with other Immunisation technical advisory groups and experts: www.stiko.de/en

Within a Ministry of Health (MoH) funded project on “Immunisation and migration” a new web module was created in 2012, available under www.rki.de/impfen. Here, the current 2012 national Immunisation plan and information sheets for measles, mumps, rubella and varicella vaccination are available in 15 languages.

2.2.3. Monitoring of vaccination coverage and barriers to vaccine uptake

One of the tasks of the Immunisation Unit is to collect, analyse and publish national vaccination coverage data that are routinely collected by local health authorities at school entry (age 5-6 years). In the absence of an Immunisation register in Germany, these data are the only representative national coverage data available on an annual basis. These data are also reported to the World Health Organization. However, no routine data are available for children below 5 years of age and for adolescents or adults. Therefore, only limited information exists in Germany e.g. on the uptake of HPV vaccines, of newly introduced vaccines in infants (e.g. against *pneumococci*) or of vaccines recommended for adults. To close some of these data gaps, the Immunisation Unit utilises two important data sources:

a) **Assessment of vaccination coverage through billing data:** Within a MoH-funded project in cooperation with all 17 Associations of Statutory Health Insurance Physicians in Germany (covering

approximately 85% of the German population, i.e. 70 Million people) insurance refund claim data are transmitted to RKI and analysed continuously for the epidemiological assessment of VPD and estimation of vaccination coverage. The project was initiated, implemented and evaluated by the surveillance unit (Unit 32), and was transferred to the Immunisation Unit in 2012 to be used as a routine tool for the monitoring of vaccination coverage especially in children before school entry and in adolescents. This tool also allows analysis of vaccination coverage at district level in Germany and for 24-months-old children, which is the standard age for vaccination coverage figures reported to the World Health Organization and the United Nations. If this project can be maintained, it will be used as a routine tool for the assessment of coverage data reported to these international authorities in the future.

b) **GEDA:** The Immunisation Unit has contributed to the development of questions on vaccinations in the “German Health Update” (GEDA) telephone survey, which is conducted annually by RKI Department 2. Based on the survey data, the Immunisation Unit in collaboration with Department 2 calculated coverage estimates for influenza, pertussis and tetanus vaccinations in adults and analysed socio-demographic determinants for vaccine uptake in adults living in Germany. Results were published in various papers (e.g. Böhmer et al., *BMC Public Health* 2012; Böhmer et al., *Vaccine* 2011; Böhmer et al. *Human vaccines* 2011).

2.2.4. Research on the impact and effectiveness of vaccines

a) **Varicella/Zoster sentinel surveillance:** Until 2010, RKI was the scientific coordinator of a public-private partnership project to monitor the impact of measles and varicella vaccination in a network of approximately 1,000 private physician offices (paediatricians and family doctors) (Siedler & Arndt, *Euro Surveill* 2010). In 2011 the project was transferred to the sole responsibility of the RKI Immunisation Unit, with funds provided by MoH (project planned for 2011-2014). Since measles incidence was decreasing in recent years and only rarely reported from this sentinel, the project’s focus is now on the surveillance of varicella disease, varicella breakthrough infections, and herpes zoster. Mathematical modelling suggests that a shift in the age-distribution of varicella cases or an increase in zoster incidence might occur in the decades following the implementation of routine varicella vaccination (in Germany since 2004). So far, no such epidemiological changes have been observed in the sentinel. Based on these sentinel data, the effectiveness of 1-dose varicella vaccination was estimated (Höhle et al., *Epidem Infect* 2011).

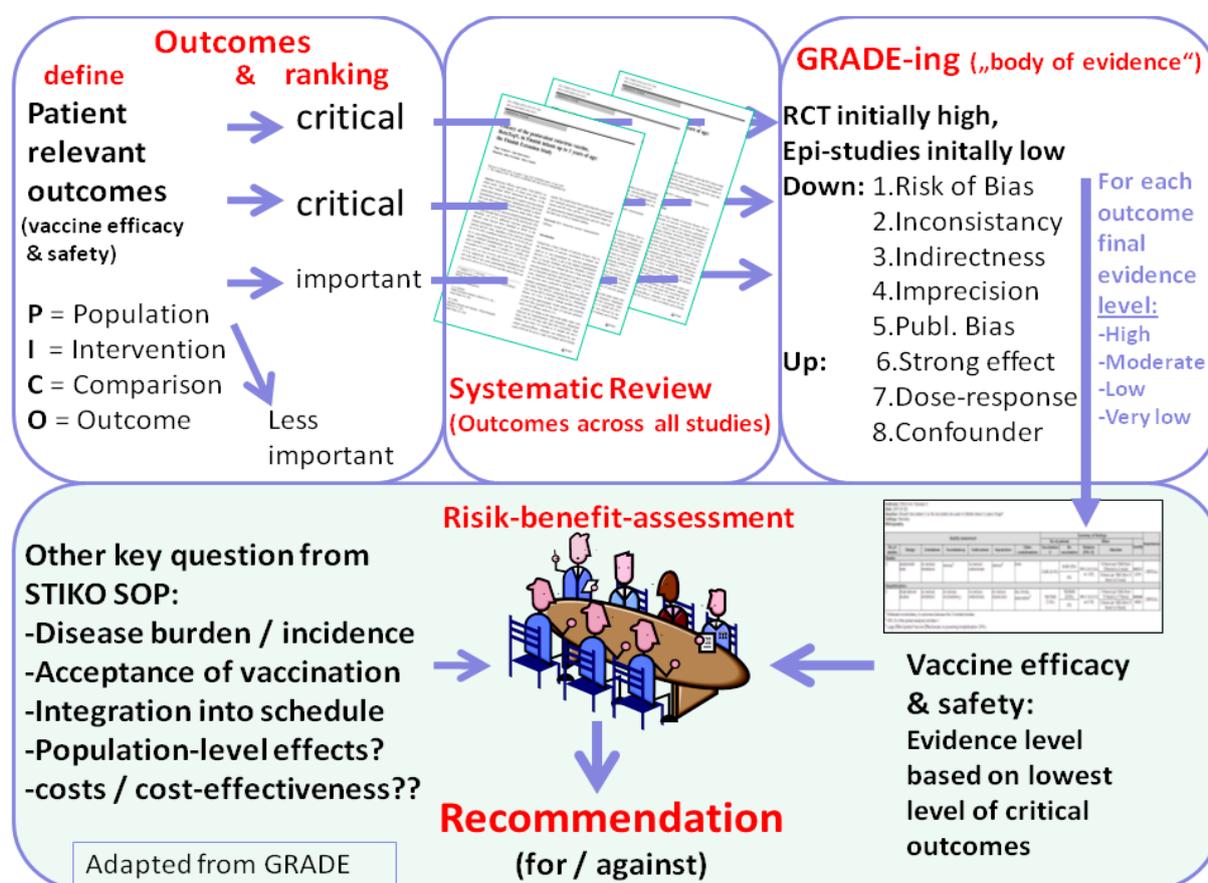
b) **Impact analyses:** Analyses to evaluate the impact of vaccination on the disease incidence at the population level were performed and published in collaboration with external partners. Before-and-after analyses, regression analyses, and time-series analyses were conducted and published for rotavirus, meningococcal and varicella disease (Dudareva-Vizule et al., *Human vaccines & immunother* 2012; Hellenbrand et al., *J infect* 2012; Höhle et al., *Epidem Infect* 2011).

c) **Assessment of vaccine effectiveness:** There are several study designs that can be applied to assess vaccine effectiveness. In contrast to vaccine efficacy, which is assessed in the pre-licensure phase in randomised-controlled trials by usually including only healthy participants and administering the vaccine according to a standard protocol, vaccine effectiveness is measured in the post-licensure phase after widespread use of the vaccine in the general population under “real-life” conditions. During the 2009/10 H1N1 influenza pandemic, the Immunisation Unit assessed H1N1 vaccine effectiveness against medically-attended laboratory-confirmed H1N1-influenza by applying the screening method, and against H1N1-associated hospitalisation by conducting a hospital-based case-control study in a network of 9 clinics in Berlin (in collaboration with the Vivantes Clinic Network) (Wichmann et al., *Euro Surveill* 2010; Hellenbrand et al., *BMC Infect Dis* 2012). In cooperation with the state health authority in Mecklenburg Western-Pomerania the effectiveness of rotavirus vaccination and risk factors for breakthrough infections were investigated in 2011 (Adlhoch et al., *Ped Infect Dis J* 2012, in press). In collaboration with federal/local health authorities, the effectiveness of vaccines against measles (in Berlin), mumps (in Bavaria), and varicella (in seven day-care centres) was assessed during outbreaks in 2009-12 (Spackova et al., *Vaccine* 2010; additional papers submitted or in preparation). Results from such studies can confirm the effectiveness of these vaccines (excellent for measles, less effective for mumps), demonstrate differences between vaccine products (varicella), and suggest waning of vaccine-induced immunity (rotavirus).

2.2.5. Methods for the development of evidence-based vaccination recommendations

In 2010 and 2011, the Immunisation Unit organised two international workshops on procedures for the development of evidence-based vaccination recommendations in Berlin, which were funded by the German Ministry of Health (MoH). Members of national and international Immunisation technical advisory groups or their executive secretariats (e.g. from the US and Canada, other European countries, and the World Health Organization's SAGE) as well as experts from ECDC and the GRADE working group participated in these meetings. The main results of the first meeting were published in an international journal (Matysiak-Klose *et al.* Vaccine 2012). Based on this exchange and following intensive discussions within the "STIKO Methods working-group", a new Standard Operating Procedure (SOP) for the development of vaccination recommendations was developed and endorsed by STIKO in 2011 (www.stiko.de/en). The framework of this new methodology is presented in Figure 9.

Figure 9: Current framework of the STIKO / executive secretariat in Unit 33 for the development of evidence-based vaccination recommendation (based on GRADE)



2.3. Major goals and contribution to the goals of the department

2.3.1. Short-term goals

- Support the implementation and conduct communication activities after the parliament's decision to make **mumps, postnatal rubella, pertussis, and varicella notifiable** in Germany. A parliament decision for the commensurate amendment of the German Protection against Infection Act (IfSG) is expected by the end of 2012 or beginning of 2013. The Immunisation Unit has already developed and finalised case definitions for these four diseases, in collaboration with Unit 31/Unit 32 and by formal consultations of the federal states.
- According to a request of the World Health Organization Regional Office for Europe to establish a National Verification Committee for measles and rubella elimination (NVC), the German MoH asked the RKI Immunisation Unit in 2012 to host the **executive secretariat**

of the NVC. With the constitutive meeting of the NVC, which is expected to take place in the beginning of 2013, the secretariat will start its work with the preparation of the first NVC report and will support the development of a national action plan.

- c. Publication of the **rotavirus vaccination recommendation** and the scientific background paper, the first STIKO recommendation developed according to the new SOP, by mid-2013.
- d. Release an **interim report on varicella vaccination**: In 2009, STIKO committed to evaluating the recommendation to vaccinate all children against varicella with 2 vaccine doses. A publication of preliminary results on the impact of the varicella vaccination and on open questions for further research is planned for 2013.
- e. **Continue** the systematic review, grading of evidence, and preparation of background papers required for **STIKO's** decisions on vaccination recommendations related to **high priority topics** (i.e. vaccination against meningococcal B disease, update of the hepatitis B vaccination recommendation, and adult pneumococcal conjugate vaccination) in 2013/14.
- f. **Start** preparations for **STIKO's** decisions on vaccination recommendations related to the **medium priority topics** (i.e. reassessment of the influenza vaccination recommendation, HPV vaccination for boys, and infant vaccination schedule 2+1 vs. 3+1).

2.3.2. Medium- to long-term goals

- a) Continue the process of implementation and evaluation of the new STIKO **methodology for the development of evidence-based vaccination recommendations** (Figure 9). This process will be supported by a continued exchange with other national and international Immunisation technical advisory groups and by an ECDC-funded project on methods for evidence-based public health.
- b) Develop a standard **methodology for the conduct of health economic evaluations** of vaccines/vaccinations in Germany and the integration of the results of such analyses into the decision-making process of STIKO and other relevant stakeholders. Resources need to be identified to build on this recently developed expertise in the Immunisation Unit and to continue this important process in close cooperation with other relevant stakeholders in Germany.
- c) **Increase the capacity and expertise in the unit to conduct systematic reviews.** The new methodology for the development of evidence-based vaccination recommendation has led to a dramatic increase in work load. However, the resources of the executive secretariat have not grown accordingly. Therefore, STIKO was compelled to undertake a prioritisation of current relevant topics. This means that certain tasks like the re-evaluation of current STIKO recommendations had to be postponed and new STIKO recommendations may be delayed in the future.
- d) **Increase research capacity and expertise in the unit** related to the evaluation of vaccination recommendations and vaccination strategies. This includes the conduct of data analyses and epidemiological studies for the assessment of vaccine effectiveness and impact of vaccination after introduction in the population.
- e) Integrate continuous **vaccination coverage assessment through health insurance refund claim data** into the routine tasks of the Unit. Currently, this is a MoH-funded research project. Funding will end in 2013 and resources will be required to continue this important activity.
- f) Expand and improve information resources on vaccines and on the benefit/risk of vaccinations on the webpages of RKI and STIKO. Foster the collaboration with the German Federal Centre for Health Education (BZgA) to improve two-way **communication activities** with the professional community and the general public, including the utilisation of new media and new technologies.
- g) **Create an understanding among stakeholders/policymakers** that the introduction of new vaccines requires a well-functioning system. Such a system includes the systematic review of evidence as a basis for national vaccination recommendations, implementation of vaccinations supported by two-way communication activities, the monitoring of vaccine uptake in all target groups, and the systematic evaluation of the risks and benefits of vaccination after introduction in the population.
Such a system helps
 - i) to identify the most efficient use of vaccines and to avoid the waste of public resources,
 - ii) to identify effects of vaccinations in a timely manner and adapt recommendations if

needed, and
 iii) to better inform the public about the benefits/risks of vaccinations to counteract increasing vaccination scepticism in the population and support equal access to the benefits of vaccination.

2.3.3. Contributions to the goals of the department

- a) One of the main goals of the department is the protection of the population from infectious disease. The unit contributes substantially to this goal through:
 - a. the continuous surveillance and evaluation of the epidemiologic situation of vaccine preventable diseases (VPD);
 - b. targeted research activities on the impact of widespread vaccination on the epidemiology of specific VPDs in the German population and on vaccine effectiveness;
 - c. the development of scientific background papers, the publication of STIKO recommendations, and the communication of vaccination-related issues to healthcare professionals (Figure 9);
 - d. scientific advice and guidance of public health authorities on state and local level in implementing prevention and containment strategies and decisions with regard to VPD, including support in VPD outbreaks and publication of best practice;
 - e. constant dialogue with vaccinating health care professionals and local public health authorities through a telephone hotline twice a week.
 - f. Exchange of experiences gained in the development and implementation of methods for evidence-based public health decisions.
- b) Support of other RKI-units during large outbreaks and in public health crises.

2.4. Additional work and methodologies for investigations

2.4.1. Surveillance activities

- a) Routine surveillance of notifiable VPD in close co-operation with Unit 31 and Unit 32 as well as with national reference laboratories and with the state public health institutes: Analysis of serotype distribution, outbreak detection, trend analysis etc.
- b) Sentinel surveillance for VPD, which are not notifiable:
 - PneumoWeb: laboratory-based sentinel reporting system on invasive pneumococcal disease (IPD) to evaluate the impact of infant vaccination with pneumococcal conjugate vaccines on IPD-incidence and serotype distribution in children and adults (herd protection)
 - Varicella/zoster sentinel: see 2.2.4, Unit 33
- c) Supportive research projects if no routine population-based or sentinel surveillance systems are available: For HPV, a population-based representative cross-sectional study with cervical self-sampling was conducted in 2011/12 among unvaccinated women aged 20-25 years to assess a baseline HPV genotype prevalence (shortly after vaccine introduction). Results of the pilot phase have been published (Deleré et al. *J Clin Microbiol* 2011), an interim analysis was presented at EUROGIN 2012, and a paper with the results of the cross-sectional study is in preparation. Such a cross-sectional study should be repeated in 4-8 years.
- d) Identification of TBE risk areas in Germany in cooperation with unit 31 based on district incidences. Results are published annually together with a TBE surveillance summary.

2.4.2. Methods for evidence-based public health

In an ECDC-funded project, a comprehensive methodology will be developed for the appraisal of evidence in the field of public health, with a particular focus on infectious disease epidemiology,

prevention and control. Within a consortium (led by the RKI Immunisation Unit) between European public health agencies, academic institutions and the GRADE working group, the framework will cover interventional as well as non-interventional study designs.

2.4.3. Workshops organised by the Immunisation unit

Between 2009 and 2012, the Immunisation unit has organised a number of scientific workshops to support the exchange with national and international experts.

- a) Workshop on methods for the assessment of vaccination coverage. National workshop with the federal states and other experts in the field in 2012 (responsible: S. Reiter, D. Walter);
- b) Workshop on methods for defining TBE risk areas. National workshop with federal states and other experts in the field in 2011 (responsible: W. Hellenbrand);
- c) International workshops on methods for the development of evidence-based vaccination recommendations. Two MoH-funded workshops in 2010 & 2011 (see also 2.2.1, Unit 33) (responsible: D. Matysiak-Klose). The agenda, presentations, and meeting reports of the two workshops are published on the RKI web pages: www.stiko.de/en/methods
- d) Challenges after introduction of HPV vaccines – Experiences and results from HPV post-licensure monitoring in industrial countries. Satellite Symposium to the 27th International Papillomavirus Conference in 2011 (responsible: Y. Deleré);
- e) Workshop on vaccination and migration. National workshop with experts in the field in 2011 (responsible: K. Atzpodien). A meeting report was published in the *Epid Bull* 48/2011;
- f) Workshop with experts in the field of Immunisation, public health or health communication on “Challenges in a complex media environment” in 2011 (responsible: S. Reiter, D. Walter)
- g) Workshop on rotavirus vaccination. National workshop with experts in the field in 2010 (responsible: J. Koch).

2.5. Scientific advice and consulting services

- a) Scientific advice to the German MoH. In 2009–2012, the Immunisation Unit wrote a total of 192 ad-hoc reports requested by the MoH.
- b) Scientific advice or guidance to healthcare professionals:
 - Publication of STIKO-recommendations which include beside the routine vaccinations (Figure 10) also recommendations for specific indications like health status or occupation (see www.stiko.de/en).
 - Development and publications of FAQ and other information resources on vaccination-related issues online. From January to October 2012, there were a total **2.37 million clicks** on the webpages of STIKO and www.rki.de/impfen;
 - Response to written inquiries (email, fax or letters). In 2009–2012, there were a total **3,802 written inquiries** (as of 30. October 2012);
 - Answering inquiries by telephone. In 2009–2012, an estimated total **8,000 telephone requests** were answered (as of 30 October 2012);
 - Contributions to the “epidemiological year book” of the department and the “guide for physicians” (“Ratgeber für Ärzte”);
 - Preparation of detailed surveillance reports for publication in the *Epidemiologisches Bulletin* at regular intervals.
- c) Participation in scientific advisory boards (see 4.1.5., Unit 33).
- d) Scientific advice for state (and on special demand for local) public health authorities on best practice for VPD control and supplemental vaccination activities, i.e. in case of vaccination campaigns or outbreaks of VPD, or for the development of the National Vaccine Plan (published by the federal states in 2012).

Figure 10: Routine vaccination calendar according to current STIKO recommendations

VACCINATION	Infants (in months)			Toddlers		Children (in years)			Adolescents		Adults	
	2	3	4	11–14	15–23	2–4	5–6	7–8	9–11	12–17	from 18	from 60
		U4		U6	U7	U7/A8	U9			J1		
Tetanus	G1	G2	G3	G4	N		A1	N		A2	A (every 10 years, N if required)	
Diphtheria	G1	G2	G3	G4	N		A1	N		A2	A (every 10 years, N if required)	
Whooping cough Pertussis	G1	G2	G3	G4	N		A1	N		A2	A (N if required) ^e	
Polio Poliomyelitis	G1	G2 ^d	G3	G4	N					A1	N (if required)	
Hepatitis B	G1	G2 ^d	G3	G4	N							
Hib Haemophilus influenzae type b	G1	G2 ^d	G3	G4	N ^f							
Pneumococcal disease	G1	G2	G3	G4	N ^f						S ^b	
Meningococcal disease Serogroup C				G1 (from 12 months)			N					
Measles Mumps Rubella				G1	G2		N				S ^c	
Chicken pox Varicella				G1	G2		N					
Flu Influenza											S (annually)	
HPV Human papillomavirus										G1–G3 ^d		

EXPLANATORY NOTES

- C** PRIMARY IMMUNISATION (up to 4 doses of vaccine G1–G4)
- S** STANDARD VACCINATION
- A** BOOSTER VACCINATION
- N** CATCH-UP VACCINATION (primary immunisation of persons not yet vaccinated or completion of an incomplete vaccination series)
- U** Well-child visit
- J** Well-adolescent visit (J1 aged 12–14 years)

- ^a This dose is not required if a monovalent vaccine is administered.
- ^b Single dose vaccination, booster vaccination only recommended for specific indications.
- ^c Single dose vaccination against measles for all individuals born after 1970 ≥ 18 years with an unclear vaccination status, who have not been vaccinated or only received one vaccination as a child. Preferably with an MMR vaccine.
- ^d Standard vaccination for girls and young women.
- ^e One-time booster vaccination, if possible simultaneously with the next vaccination against tetanus/diphtheria/if required, poliomyelitis.
- ^f The number of required vaccine doses depends on the age group.

2.6. Training and teaching activities

- Participation as facilitators in biannual 1-week courses on field epidemiology for public health workers in Germany hosted by the department.
- Project supervision and hosting of fellows attending the German Postgraduate Program for Applied Epidemiology (PAE) and the European Intervention Epidemiology Training Program (EPIET): 9 fellows were trained within the Immunisation Unit from 2009-2012.
- Activities as lecturers and supervisors in the Masters Program in International Health (Charité University Medicine, Berlin), Masters Program in Public Health (Berlin School of Public Health), and the Masters Program in Applied Epidemiology (Robert Koch Institute).
- Supervisors for PhD/dissertations and master theses (currently 5 PhD/dissertation projects in the unit and 2 master thesis projects).
- Participation as facilitators in teaching modules of the EPIET program.
- Supervisors of international guests of the unit (like Fulbright scholars) working on scientific questions concerning vaccinations
- Lecturer in the RKI-coordinated teaching module "Infectious Diseases Epidemiology" at the Charité University Medicine, Berlin.
- Teaching at midwives colleges (Charité University Medicine, Berlin).

3. Cooperation with other scientists or research institutions

3.1. Internal (within RKI)

Department 1, FG12 (NRC for Measles/Mumps/Rubella: A. Mankertz)

- Siedler A et al., *J Infect Dis* 2011
- Bätzing-Feigenbaum J et al., *Euro Surveill* 2010
- Wichmann O et al., *Bulletin of the World Health Organisation* 2009

Department 1, FG15 (National Certification Committee Poliomyelitis: S. Dietrich; and German consultant laboratory for rotavirus: A. Mas Marques)

- Participation in the meetings of the National Certification Committee (NCC) Poliomyelitis and provision of poliomyelitis vaccination coverage data for the NCC report to the World Health Organization.
- Adlhoch C et al., *Ped Infect Dis J* 2012

Department 1, FG17 (NRC for influenza: B. Schweiger)

- Nachtnebel M et al., *BMC Pub Health* 2012
- Hellenbrand WJ et al., *BMC Infect Dis* 2012

Department 2, FG23 (M. Schlaud)

- Siedler A et al., *Euro Surveill* 2012
- Schmitz R et al., *Dtsch Arztebl Int* 2011
- Jorgensen P et al., *Epidem Infect* 2010

Department 2, FG25 (C. Lange)

- Böhmer MM et al., *BMC Pub Health* 2012
- Böhmer MM et al., *Vaccine* 2011
- Böhmer MM et al., *Human Vaccines* 2011

3.2. External / National

National Reference Laboratory for Meningococci, Würzburg (M. Frosch)

- Hellenbrand W et al., *J Infect* 2012. Epub ahead of print Oct 5
- Vogel U et al., *Kinderarztl Prax* 2010

National Reference Laboratory for Pneumococci, Aachen (M. van der Linden)

- van der Linden M et al., *Vaccine* 2012
- Rückinger S et al., *Klin Padiatr* 2011
- Rückinger S et al., *Pediatr Infect Dis J* 2009
- Rückinger S et al., *Vaccine* 2009

National Consultation Laboratory for Rabies, Essen (R.S. Ross) and National and OIE Reference Laboratory for Rabies, WHO Collaborating Centre for Rabies Surveillance and Research, Wusterhausen/Dosse (C.M. Freuling, T. Müller)

- Ross RS et al., *Berl Munch Tierarztl Wochenschr* 2012

Vivantes Clinic Network, Berlin (C. Träder)

- Nachtnebel M et al., *BMC Public Health* 2012
- Hellenbrand WJ et al., *BMC Infect Dis* 2012

Clinic for Gynecology, Charité University Medicine Berlin (A. Kaufmann)

- Deleré Y et al., *J Clin Microbiol* 2011

Institute for Social Medicine, Epidemiology and Health Economic, Charité University Medicine Berlin (T. Reinhold)

- Ultsch B et al., *BMC Infect Dis* 2011

Paul-Ehrlich-Institute, PEI (B. Keller-Stanislawski)

- Dudareva-Vizule S et al., *Hum Vaccin Immunother* 2012

Federal Centre for Health Education, BZgA (S. Wortberg)

- Wortberg S et al., *Dtsch Med Wochenschr* 2010
- Wortberg S et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2009

Institute of Social Pediatrics and Adolescent Medicine, University of Munich (R. v. Kries)

- von Kries R et al., *PLoS One* 2011
- Höhle M et al., *Epidemiol Infect* 2011

University of Bielefeld (W. Greiner/O. Damm) and Helmholtzzentrum für Infektiologie Braunschweig (R. Mikolajczyk)

- Publication submitted on HPV vaccination impact and cost effectiveness.
- Project on varicella transmission modeling and cost-effectiveness ongoing

University of Cologne and Düsseldorf (I. Schubert and A. Icks)

- Publication submitted on herpes zoster cost-of-illness

3.3. External / International

VENICE network (see also 4.2.5):

- Haverkate MDA et al., *Euro Surveill* 2012
- Dorleans F et al., *Euro Surveill* 2010

Dutch National Institute for Public Health and the Environment, RIVM (M. Kretzschmar)

- Bonacic-Marinovic AAS et al., *Emerg Infect Dis* 2012
- van Boven M et al., *J R Soc Interface* 2010

National Institute of Public Health, Warsaw, Poland (P. Stefanoff)

- Stefanoff P et al., *Zoonoses Public Health* 2012
- Hellenbrand W et al., *Epidemiol Infect* 2011

4. Appendix

4.1. Overview on output achievements of the unit 2009-2012

4.1.1. Scientific publications 2009–2012

Number of peer-review publications co-authored by members of the unit: 81

Impact factor (IF) according to JCR (for 2012 according to 2011)

2009: **62.9**

2010: **26.3**

2011: **207.1**

2012: **72.5**

Cumulative 2009-12: **368.8**

A) Original research articles in peer-review journals

2012

Adlhoch C, Hoehne M, Littmann M, Mas Marques A, Lerche A, Dehnert M, Eckmanns T, **Wichmann O, Koch J**. Rotavirus Vaccine Effectiveness and Case-Control Study on Risk Factors for Breakthrough Infections in Germany, 2010-2011. *Pediatr Infect Dis J* 2012, epub ahead of print.

Böhmer MM, Walter D, Falkenhorst G, Müters S, Krause G, Wichmann O: Barriers to pandemic influenza vaccination and uptake of seasonal influenza vaccine in the post-pandemic season in Germany. *BMC Public Health* 2012, 12(1):938.

Bonacic-Marinovic AAS, Swaan C, **Wichmann O**, van Steenbergen J, Kretzschmar M. Effectiveness and Timing of Vaccination during School Measles Outbreak. *Emerg Infect Dis* 2012; 18(9):1405-1413.

Cramer JPM, Mac T, Hogan B, Stauga S, Eberhardt S, **Wichmann O**, Mertens T, Burchard GD. Influenza A(H1N1)pdm09 antibodies after pandemic and trivalent seasonal influenza vaccination as well as natural infection in November 2010 in Hamburg, Germany. *Euro Surveill* 2012; 17: pii=20052.

Dudareva-Vizule S, **Koch J**, An der Heiden M, Oberle D, Keller-Stanislawski B, **Wichmann O**. Impact of rotavirus vaccination in regions with low and moderate vaccine uptake in Germany. *Hum Vaccin Immunother* 2012; 8(10): 1407-15.

Haverkate MDA, D'Ancona F, Giambi C, Johansen K, Lopalco P, Cozza V, Appelgren E, VENICE project gatekeepers and contact points (including **Reiter S**). Mandatory and recommended vaccination in the EU, Iceland and Norway: results of the VENICE 2010 survey on the ways of implementing national vaccination programmes. *Euro Surveill* 2012; 17: pii=20183.

Hellenbrand W, Jorgensen P, Schweiger B, **Falkenhorst G**, Nachtnebel M, Greutelaers B, Traeder C, **Wichmann O**. Prospective hospital-based case-control study to assess the effectiveness of pandemic influenza A(H1N1)pdm09 vaccination and risk factors for hospitalization in 2009- 2010 using matched hospital and test-negative controls. *BMC Infect Dis* 2012; 12:doi:10.1186/1471-2334-12-127.

Hellenbrand W, Elias J, **Wichmann O**, Dehnert M, Frosch M, Vogel U. Epidemiology of invasive meningococcal disease in Germany, 2002-2010, and impact of vaccination with meningococcal c conjugate vaccine. *J Infect* 2012; Oct 5: pii: S0163-4453(12)00259-9.

Kurkela S, Pebody R, Kafatos G, Andrews N, Barbara C, Bruzzone B, Butur D, Caplinskas S, Davidkin I, Hatzakis A, **Hellenbrand W**, Hesketh LM, Nardone A, Nemecek V, Pistol A, Sobotova Z, Vranckx R, Anastassopoulou CG. Comparative hepatitis A seroepidemiology in 10 European countries. *Epidemiol Infect* 2012; 140(12): 2172-81.

- Mereckiene JC, Cotter S, Weber JT, Nicoll A, D'Ancona F, Lopalco PL, Johansen K, Wasley AM, Jorgensen P, Lévy-Bruhl D, Glambi C, Stefanoff P, Dematte L, O'Flanagan D, VENICE project gatekeepers group (including **Reiter S**). Influenza A(H1N1)pdm09 vaccination policies and coverage in Europe. *Euro Surveill* 2012; 17: pii=20064.
- Muscat M, Zimmerman L, Bacci S, Bang H, Glismann S, Mølbak K, Reef S; EUVAC.NET group (including **Siedler A**). Toward rubella elimination in Europe: an epidemiological assessment. *Vaccine* 2012; 30:1999-2007.
- Nachtnebel M, Greutelaers B, **Falkenhorst G**, Jorgensen P, Dehnert M, Schweiger B, Traeder C, Buda S, Eckmanns T, **Wichmann O**, **Hellenbrand W**. Lessons from a one-year hospital-based surveillance of acute respiratory infections in Berlin- comparing case definitions to monitor influenza. *BMC Public Health* 2012; 12: 245.
- Ross RS, Freuling CM, **Deleré Y**, Thomas Müller T. Assessment of the human medical significance of the rabies zoonosis in Germany – analysis of available data and desiderata. *Berl Munch Tierarztl Wochenschr* 2012; 125: 272–277.
- Siedler A**, **Rieck T**, Reuss A, **Walter D**, Poggensee G, Poethko-Müller C, **Reiter S**. Estimating vaccination coverage in the absence of immunisation registers – the German experience. *Euro Surveill* 2012; 17:pii=20152.
- Stefanoff P, Pfeffer M, **Hellenbrand W**, et al. Virus Detection in Questing Ticks is not a Sensitive Indicator for Risk Assessment of Tick-Borne Encephalitis in Humans. *Zoonoses Public Health* 2012. epub ahead of print
- Stöcker P, Dehnert M, Schuster M, **Wichmann O**, **Deleré Y**. Human papillomavirus vaccine uptake, knowledge and attitude among 10th grade students in Berlin, Germany, 2010. *Hum Vaccin Immunother* 2012; 9, epub ahead of print.
- Takla A**, Barth A, **Siedler A**, Stocker P, **Wichmann O**, **Deleré Y**. Measles outbreak in an asylum-seekers' shelter in Germany: comparison of the implemented with a hypothetical containment strategy. *Epidemiol Infect* 2012; 140(9):1589-98.
- van der Linden M, Weiss S, **Falkenhorst G**, **Siedler A**, Imohl M, von Kries R. Four years of universal pneumococcal conjugate infant vaccination in Germany: Impact on incidence of invasive pneumococcal disease and serotype distribution in children. *Vaccine* 2012; 30: 5880-5.
- Vong S, Goyet S, Ly S, Ngan C, Huy R, Duong V, **Wichmann O**, Letson GW, Margolis HS, Buchy P. Under-recognition and reporting of dengue in Cambodia: a capture-recapture analysis of the National Dengue Surveillance System. *Epidemiol Infect* 2012; 140(3): 491-9.
- Walter D**, **Böhmer MM**, **Reiter S**, Krause G, **Wichmann O**. Risk perception and information-seeking behaviour during the 2009/10 influenza A(H1N1)pdm09 pandemic in Germany. *Euro Surveill* 2012; 17:pii=20131.

2011

- Bätzing-Feigenbaum J, Kollan C, Kühne A, **Matysiak-Klose D**, Gunsenheimer-Bartmeyer B, Hamouda O. Cohort profile: the German ClinSurv HIV project – a multicentre open clinical cohort study supplementing national HIV surveillance. *HIV Med* 2011; 12: 269-78.
- Balabanova Y, Gilsdorf A, Buda S, Burger R, Eckmanns T, Gartner B, Gross U, Haas W, Hamouda O, Hubner J, Janisch T, Kist M, Kramer MH, Ledig T, Mielke M, Pulz M, Stark K, Suttorp N, Ulbrich U, **Wichmann O**, Krause G. Communicable Diseases Prioritized for Surveillance and Epidemiological Research: Results of a Standardized Prioritization Procedure in Germany, 2011. *PLoS One* 2011; 6(10): e25691.
- Böhmer MM**, **Walter D**, Krause G, Muters S, Gosswald A, **Wichmann O**. Determinants of tetanus and seasonal influenza vaccine uptake in adults living in Germany. *Hum Vaccin* 2011; 7: 1317-25.
- Böhmer MM**, **Walter D**, Muters S, Krause G, **Wichmann O**. Seasonal influenza vaccine uptake in Germany 2007/2008 and 2008/2009: Results from a national health update survey. *Vaccine* 2011; 29: 4492-8.

- Buchholz U, Bernard H, Werber D, **Böhmer MM**, **Remschmidt C**, Wilking H, **Deleré Y**, et al. German outbreak of *Escherichia coli* O104:H4 associated with sprouts. *N Eng J Med* 2011; 365(19): 1763-70.
- Deleré Y**, Schuster M, Vartazarowa E, Hansel T, Hagemann I, Borchardt S, Perlitz H, Schneider A, **Reiter S**, Kaufmann Am. Cervicovaginal self-sampling is a reliable method for determination of prevalence of human papillomavirus genotypes in women aged 20 to 30 years. *J Clin Microbiol* 2011; 49(10): 3519-22.
- Domingo C, Niedrig M, Gascon J, Palacios G, Reyes N, Malo MJ, **Wichmann O**, et al. Molecular Surveillance of Circulating Dengue Genotypes Through European Travelers. *J Travel Med* 2011; 18(3): 183-90.
- Fluegge K, Wons J, Spellerberg B, Swoboda S, **Siedler A**, Hufnagel M, Berner R. Genetic differences between invasive and noninvasive neonatal group B streptococcal isolates. *Pediatr Infect Dis J* 2011; 30(12): 1027-31.
- Frank C, Werber D, Cramer JP, Askar M, Faber M, an der Heiden M, Bernard H, Fruth A, Prager R, Spode A, Wadl M, Zoufaly A, Jordan S, Kemper MJ, Follin P, Muller L, King LA, Rosner B, Buchholz U, Stark K, Krause G, HUS Investigation Team (incl. **Reiter S**, **Böhmer MM**, **Deleré Y**, **Falkenhorst G**, **Hellenbrand W**, **Koch J**, Schuster M, **Ultsch B**, Wlater D). Epidemic profile of Shiga-toxin-producing *Escherichia coli* O104:H4 outbreak in Germany. *N Eng J Med* 2011; 365(19): 1771-80.
- Frank C, Faber MS, Askar M, Bernard H, Fruth A, Gilsdorf A, Hohle M, Karch H, Krause G, Prager R, Spode A, Stark K, Werber D; HUS investigation team (incl. **Atzpodien K**, **Böhmer MM**, **Ultsch B**). Large and ongoing outbreak of haemolytic uraemic syndrome, Germany, May 2011. *Euro Surveill* 2011; 16.
- Höhle M, **Siedler A**, Bader HM, et al. Assessment of varicella vaccine effectiveness in Germany: a time-series approach. *Epidemiol Infect* 2011; 139: 1710-9.
- Koch J**, **Wiese-Posselt M**. Epidemiology of Rotavirus Infection in Children Less Than 5 Years of Age: Germany, 2001-2008. *Pediatr Infect Dis J* 2011; 30: 112-117.
- Mette A, Reuss AM, Feig M, Kappelmayer L, **Siedler A**, Eckmanns T, Poggensee G. Under-reporting of measles: an evaluation based on data from north rhine-westphalia. *Dtsch Arztebl Int* 2011; 108(12): 191-6.
- Rückinger S, van der Linden M, **Siedler A**, von Kries R. Potential Benefits From Currently Available Three Pneumococcal Vaccines for Children - Population-Based Evaluation. *Klin Padiatr* 2011; 223: 61-4.
- Schmitz R, Poethko-Müller C, **Reiter S**, Schlaud M. Vaccination status and health in children and adolescents: findings of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS). *Dtsch Arztebl Int* 2011; 108(7): 99-104.
- Ultsch B**, **Siedler A**, Rieck T, Reinhold T, Krause G, **Wichmann O**. Herpes zoster in Germany: Quantifying the burden of disease. *BMC Infect Dis* 2011; 11: 173.
- Uphoff H, an der HM, Schweiger B, Campe H, Beier D, Helmeke, C, Littmann, M, Haas W, Buda S, Faensen D, Feig M, Altmann D, **Wichmann O**, et al. Effectiveness of the AS03-adjuvanted vaccine against pandemic influenza virus A/(H1N1) 2009- a comparison of two methods; Germany, 2009/10. *PLoS One* 2011; 6: e19932.
- von Kries R, Weiss S, **Falkenhorst G**, et al. Post-Pandemic Seroprevalence of Pandemic Influenza A (H1N1) 2009 Infection (Swine Flu) among Children <18 Years in Germany. *PLoS One* 2011; 6: e23955.
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- Wadl M, Rieck T, Nachtnebel M, et al. Enhanced surveillance during a large outbreak of bloody diarrhoea and haemolytic uraemic syndrome caused by Shiga toxin/verotoxin-producing *Escherichia coli* in Germany, May to June 2011. *Euro Surveill* 2011; 16: pii=19893.

Walter D, Böhmer MM, Heiden M, Reiter S, Krause G, Wichmann O. Monitoring pandemic influenza A(H1N1) vaccination coverage in Germany 2009/10 - results from thirteen consecutive cross-sectional surveys. *Vaccine* 2011; 29: 4008-12.

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Amarasinghe A, **Wichmann O**, Margolis HS, Mahoney RT. Forecasting dengue vaccine demand in disease endemic and non-endemic countries. *Human Vaccines* 2010; 6(9): 745-53.

Bätzing-Feigenbaum J, Pruckner U, Beyer A, Sinn G, Dinter A, Mankertz A, **Siedler A**, Suckau M. Spotlight on measles 2010: Preliminary report of an ongoing measles outbreak in a subpopulation with low vaccination coverage in Berlin, Germany, January-March 2010. *Euro Surveill* 2010; 15(13): pii=19527.

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Abu Sin M, Zenke R, Rönckendorf R, Littmann M, Jorgensen P, **Hellenbrand W**. Pertussis outbreak in primary and secondary schools in Ludwigslust, Germany – the role of waning immunity. *Pediatr Infect Dis J* 2009; 28(3): 242-4.

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B) Overview articles or systematic reviews in peer-review journals

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- Zur Situation bei ausgewählten Infektionskrankheiten in Deutschland. Invasive Meningokokken-Erkrankungen, 2009 – 2011. *Epid Bull* 2012: 39, 389-97.
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- RKI-Ratgeber Infektionskrankheiten - Merkblätter für Ärzte. Tollwut. *Epid Bull* 2009: 15, 135-8.
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- Invasive Meningokokken-Erkrankungen: Retrospektive Erhebung von Verdachtsmeldungen nach § 6 Abs. 1 IfSG. Deutschland, 2001–2007. *Epid Bull* 2009: 8, 69-75.

4.1.2. Selected relevant publications

A) Five important publications for the scientific community 2009–2012

1. Adlhoch C, Hoehne M, Littmann M, Mas Marques A, Lerche A, Dehnert M, Eckmanns T, **Wichmann O, Koch J**. Rotavirus Vaccine Effectiveness and Case-Control Study on Risk Factors for Breakthrough Infections in Germany, 2010-2011. *Pediatr Infect Dis J* 2012, epub ahead of print
2. **Deleré Y**, Schuster M, Vartazarowa E, Hansel T, Hagemann I, Borchardt S, Perlitz H, Schneider A, **Reiter S**, Kaufmann AM. Cervicovaginal self-sampling is a reliable method for determination of prevalence of human papillomavirus genotypes in women aged 20 to 30 years. *J Clin Microbiol* 2011; 49(10): 3519-22.
3. **Wichmann O**, Stöcker P, Poggensee G, Altmann D, **Walter D, Hellenbrand W**, Krause G, Eckmanns T. Pandemic influenza A(H1N1) 2009 breakthrough infections and estimates of vaccine effectiveness in Germany 2009-2010. *Euro Surveill* 2010; 15(18): pii=19561.
4. Spackova M, **Wiese-Posselt M**, Dehnert M, **Matysiak-Klose D**, Heininger U, **Siedler A**. Comparative varicella vaccine effectiveness during outbreaks in day-care centres. *Vaccine* 2010; 28(3): 686-91. Koch
5. Muscat M, Bang H, Wohlfahrt J, Glismann S, Molbak K, EUVAC.Net Group (for Germany **Siedler A**). Measles in Europe: an epidemiological assessment. *Lancet* 2009; 373(9661): 383-9.

B) Five important publications for the public 2009–2012

1. Annual STIKO recommendations
2. Webpage of the STIKO and the RKI Immunisation Unit: www.stiko.de and www.rki.de/impfen
3. Vaccination - 20 objections and responses (In German: „Schutzimpfungen – 20 Einwände und Antworten des Robert Koch Institutes und des Paul-Ehrlich-Instituts“). Available online at www.rki.de/impfen
4. Annual publication of geographic areas at risk for tick-borne encephalitis in Germany
5. Annual publications of vaccination coverage data

4.1.3. Awards and honours, 2009–2012

- Detlef Petzoldt-Award 2012 (German Society for Sexually-Transmitted Diseases) in recognition of the study/publication on cervico-vaginal self-sampling as a method to determine HPV genotype prevalence in Women: Yvonne Deleré

4.1.4. Overview on collaborations in networks

a) ECDC: National Epidemiology Contact Point for vaccine-preventable diseases

- Measles: Dorothea Matysiak-Klose
- Mumps: Judith Koch
- Varicella: Anette Siedler
- Pertussis: Wiebke Hellenbrand
- Meningococcal Disease: Wiebke Hellenbrand
- Haemophilus influenzae b: Yvonne Deleré

b) VENICE: ECDC-funded project “Vaccine European New Integrated Collaboration Effort” (VENICE). In the network all 27 EU member states and two EEA/EFTA countries (Iceland and Norway) participate with the aim to collect and share information on the national vaccination programs through a network of professionals and to build up a knowledge base endeavoring to

improve the overall performance of the Immunisation systems.
National Gatekeeper: Until 2012 Sabine Reiter; since end of 2012 Ole Wichmann.

c) PRECEPT: ECDC-funded “project on a Framework for Rating Evidence in Public Health”. Consortium partners are the Health Protection Agency Scotland, NICE, SIGN, University of Rotterdam, Liverpool School of Tropical Medicine, Dutch Tropical Institute, GRADE working group, University of Munich, and German Cochrane Center Freiburg.

Project Coordinator: Thomas Harder

4.1.5. Memberships and participation in Advisory Boards

Ole Wichmann

- Member of the Advisory Board of the German Surveillance System for Rare Pediatric Diseases (ESPED)
- Member of the Expert Committee “Influenza” of the German Association for the Control of Viral Diseases (DVV)
- Member of the Advisory Board for the “Study on the association of pH1N1-vaccination and Guillain-Barré Syndrome in Germany” conducted by the Paul Ehrlich Institute 2009/10:

Wiebke Hellenbrand

- Member of the Advisory Board for the “Study on the association of pH1N1-vaccination and Guillain-Barré Syndrome in Germany” conducted by the Paul Ehrlich Institute 2009/10
- Member of the Extended Board of the European Meningococcal Disease Society (EMGM)

4.1.6. List of completed dissertation or master theses in the Unit, 2009 – 2012

Year	Title	Name	Title of thesis	University / RKI Supervisor
2012	MSc Applied Epidemiology	Anja Takla	The importance of prevention and early intervention in vaccine preventable diseases – projects on mumps and measles	J. Koch and K. Alpers
2011	MSc Applied Epidemiology	Petra Stöcker	Angewandte Infektionsepidemiologie – praktische Datenerhebung und –Analyse sowie public value ausgewählter Infektionsgeschehen als Baustein des Infektionsschutzes in Deutschland	Y. Deléré and K. Alpers
2011	Master in Public Health (MPH)	Jonas Erhardt	Attitude and practice of private physicians related to seasonal and pandemic influenza vaccination in Germany: Analysis of a telephone survey conducted in 2010	Hannover / M. Böhmer, D. Walter
2011	Dr. med.	Thomas Hänsel	Assessment of HPV prevalence in women aged 20-30 years by using a self-sampling device	Y. Deléré and G. Krause
2010	MSc Public Health	Julia Fricke	Communication of preventive measures during measles outbreak in populations with inadequate vaccination coverage	A. Siedler and G. Krause

4.1.7. Presentations as invited speaker, 2009 - 2012

Staff from the Immunisation Unit were invited to speak at 66 conferences.

4.1.8. Reports and written scientific advice to the Ministry of Health, 2009 - 2012

There were 192 reports and written scientific advice to the Ministry of Health between 2009 and 30.9.2012. Total number under the responsibility of the Immunisation Unit: 185

Unit 34: HIV/AIDS, STI and other Blood-borne Infections

Unit Head: Osamah Hamouda

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1. General information - Unit 34

Head: **Dr. Osamah Hamouda**

Deputy: **Dr. Viviane Bremer**

2. Tasks and goals of the Unit

2.1. Summary

The unit for HIV/AIDS, STI and Bloodborne Infections (unit 34) is in charge of the control of HIV/AIDS, sexually transmitted infections (STI), blood-borne infections such as hepatitis B and C, Creutzfeldt-Jakob disease as well as the safety of blood donations. Unit 34 staff collects reports of infection with HIV and syphilis that are directly reported anonymously to the RKI. Furthermore, the unit is responsible for the laboratory notifications of viral hepatitis B and C and Creutzfeldt-Jakob disease. Staff members collect data on blood donations and the number of infections detected in blood donors through for the blood donor surveillance.

Unit 34 maintains additional surveillance systems: The voluntary AIDS registry, the “HIV 1-Serokonverter” study for HIV-patients with known date of HIV-seroconversion, “InzSurvHIV”, to measure the proportion of recent HIV diagnoses, “ClinSurv HIV” cohort study to follow up the clinical course of HIV patients. Also, data on HIV resistance data is routinely collected. A laboratory sentinel system for the detection of chlamydia has been set up to monitor chlamydia screening programme. Chlamydia prevalence has been measured using material from the national survey in children (KIGGS) and adults (DEGS).

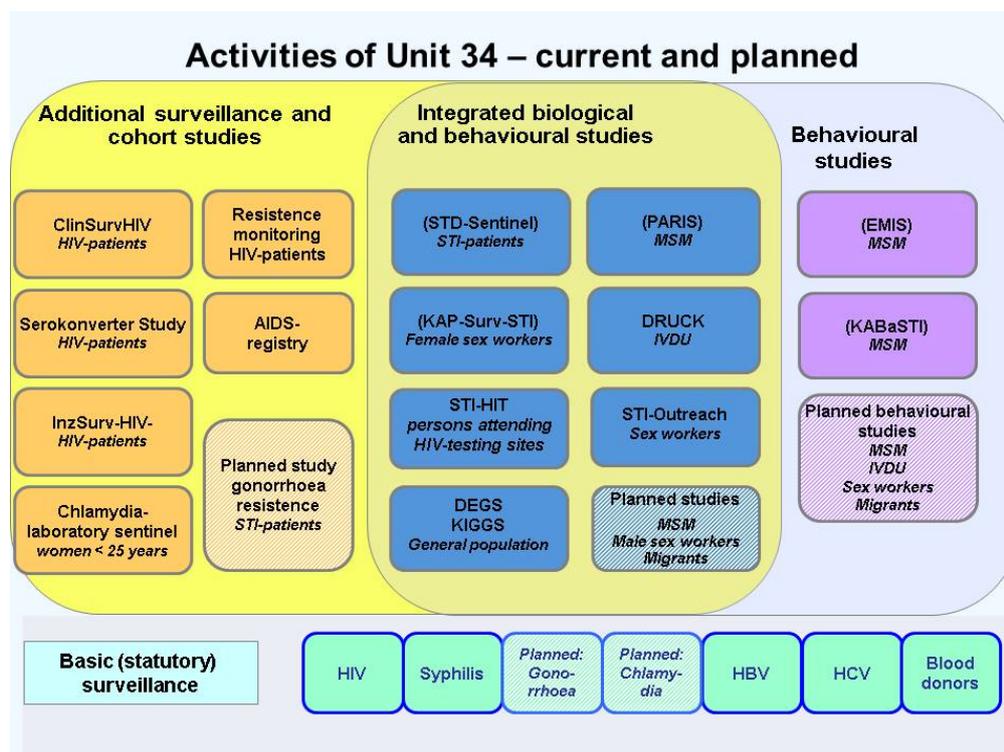
Unit 34 has carried out integrated behavioural and biological surveillance in targeted populations, such as men who have sex with men, sex workers and i.v. drug users.

Unit 34 is in charge of the investigation of outbreaks of STI and hepatitis B and C. The unit participates in the design and the realisation of national, European and international surveillance and research networks. The unit participates in the further development of prevention concepts for HIV, STI and hepatitis B and C in close cooperation with the Federal Centre for Health Education (Bundeszentrale für gesundheitliche Aufklärung), expert societies and non-governmental organisations (e.g. Deutsche AIDS-Hilfe). Unit staff is involved in setting up guidelines both for treatment and for prophylaxis of HIV, STI and Blood-borne infections.

2.2. Current status of the work and summary of relevant results

The activities of Unit 34 are divided in basic (statutory) surveillance, additional surveillance and cohort studies, integrated behavioural and biological studies and behavioural studies. An overview is given in Figure 11.

Figure 11: Overview over current and planned activities of Unit 34: Basic surveillance, additional surveillance and cohort studies, integrated biological and behavioural surveillance and behavioural studies



2.2.1. Statutory surveillance systems

Unit 34 staff collects reports of infection with **HIV and syphilis** that are directly reported anonymously to the RKI according to §7.3 of the Infection Protection Act. Laboratory reports are completed by physician's information on symptoms and possible way of transmission. In 2011, 2911 newly diagnosed HIV-infections were reported, most of them in MSM. The number of syphilis diagnoses has increased by 22% from 2010 to 2011 to 3698 cases. Of these, 94% have been reported in men.

Unit 34 is responsible for the laboratory notifications of viral **hepatitis B, C and D and Creutzfeldt-Jakob disease**. Hepatitis B and C are reported through physicians and laboratories to the local health units. These reports are forwarded anonymously to the RKI via the state-level health authorities. Trends for notified cases of acute hepatitis B with clinical symptoms and laboratory confirmation show a decrease since 2001 and have stabilised at a level of 800 cases per year since 2008. Incidence of newly diagnosed acute or chronic hepatitis C cases is decreasing continuously since 2004 from 9,000 cases to 5,000 cases in 2011. New diagnoses are mainly reported in persons who inject drugs. Laboratory confirmed hepatitis D cases as super infection or simultaneous infection with hepatitis B are rare in Germany. Annual notifications of cases are in the range of 7 to 21 cases.

All sites in Germany collecting blood or blood products are requested to report on a quarterly base aggregated data on blood donations and the number of infections by HIV, hepatitis B, hepatitis C and syphilis detected in blood donors through for the **blood donor surveillance** according to the Transfusion Act. Since 2001 the prevalence and incidence of HBV and HCV among blood has declined whereas incident HIV-infections reached a peak in 2008 and 2010 and show an increasing trend. Also, the proportion of syphilis infections among first time donors was highest in 2010. From 2008 to 2010, the prevalence for HIV ranged from 6.6 to 7.0/100.000, for HCV from 68.9 to 81.6/100.000, for HBV from 116.2 to 136.6/100.000 and for syphilis from 31.0 to 42.1/100,000 donations. The proportion of incident infections/100,000 donations ranged from 0,8-0,9 for HIV, 0,8-1,0 for HCV, 0,3-0,5 for HBV and 1,4-1,6 for syphilis.

Surveillance data are regularly analysed and fed back to national and regional stakeholders through yearly reports and presentations at national and international conferences.

2.2.2. Additional surveillance systems and cohort studies

The voluntary **AIDS registry** collects data on AIDS cases and deaths since 1982. These data provide information on the HIV/AIDS epidemic, demographic characteristics of AIDS patients and AIDS-related opportunistic infections, medical care and treatment. Completeness of the system has decreased from 85% in the mid-90ies to 50%.

The **HIV 1-Serokonverter Study** aims to collect epidemiological and laboratory information on newly infected HIV-patients with known date of HIV-seroconversion. These data are used to estimate the time between HIV seroconversion and Aids or other important clinical endpoints, to monitor the spread of HIV subtypes and the dynamic of HIV resistance in Germany in order to optimise treatment. Overall prevalence of transmitted drug resistance is stable at 11% in this study population. NRTI resistance was observed most frequently (6%), followed by NNRTI associated resistance (2.4%) and PI resistance (2%). HIV subtype B is predominantly reported in the study cohort (subtype B: 92% vs. non B-subtype 8%). Currently samples of patients co-infected with HIV and hepatitis B and C viruses were analysed serologically as well as bio-molecularly by using phylogenetic analysis. To investigate influences by host on the HIV disease progression genome wide association studies are performed by exome sequencing in patients with rapid disease progression as well as in elite controllers to identify host polymorphisms influencing the course of the HIV disease.

The **German Incidence Study** (2008-2010) aimed to monitor recent HIV infections in a representative study sample in Germany for the first time. A nationwide cross-sectional study was initiated to estimate the proportions of recent infections (RIs) among newly diagnosed HIV cases in Germany. The overall proportion of RI in the study sample was 29.2%. Men were found to be recently infected in 30.8% (793/2575), whereas the proportion of RI in women was 21.4% (107/499) (OR=1.6; 95%CI [1.3;2.1]). In order to detect trends the “Study for Surveillance of recent HIV infections in Germany (InzSurvHIV)” was launched in December of 2010.

The “**InzSurvHIV**” (2010-2013) aims to measure the proportion of recent HIV diagnoses among reported HIV diagnoses in Germany and to identify populations at risk, time trends and regional differences among patients with recent HIV infections. The study also explores whether incidence testing can be implemented into routine HIV surveillance. In 2011 the proportion of recent infections overall was 26%. Highest proportions were found in MSM, indicating frequent testing and on-going HIV transmission in that group. Proportion of RI among migrants, especially from sub-Saharan Africa are lower (<15%) which might be attributed to limited access to HIV testing. The implementation of HIV-incidence testing into routine HIV-surveillance seems to be possible and practicable and is planned for 2014.

The “**ClinSurvHIV**” multicentre cohort study has been established in 1999 to follow up the clinical course of HIV patients. Data on demographics, HIV-associated and Aids-defining diseases as well as detailed information on antiretroviral treatment are regularly collected from centres specialised in HIV-care. The Clinical Surveillance of HIV Disease in Germany (ClinSurv HIV) was initiated in 1999 as collaboration between major HIV treatment centres and the Robert Koch Institute (RKI). The ClinSurv Cohort is a national multi centre prospective observational open cohort. The study design allows assessing the associations between demographic and clinical characteristics, different treatment regimens and trends of disease progression over time under routine clinical care conditions. The cohort represents the clinical reality of HIV treatment and care for a large proportion of HIV-infected patients in Germany (21% of all patients under care in Germany). Currently 16,751 patients were enrolled into the cohort (113.825 person years of observation; 31.12.2011). Follow-up of clinical care of patients infected with HIV in Germany requires additional surveillance systems. Thus the study design of the ClinSurv HIV study complements the cross sectional mandatory HIV surveillance in Germany. Antiretroviral treatment success in the study population is high (more than 80% under the viral detection limit <50 copies/ml). Time on treatment interruption declined in this study collective during the period of observation to currently 2%.

Following the establishment of a national chlamydia screening programme offered to women less than 25 years of age, a **chlamydia laboratory sentinel system** for the detection of chlamydia has been set up. The aim of the sentinel system is to monitor the proportion of positive chlamydia tests. Current data set provides information on approximately 19% (433.622) of all Chlamydia tests

performed in Germany in years 2008 to 2012 (August). Among all tests performed in women 20% were screening tests for women less than 25 years of age, 38% screening for pregnant women, and 33% were diagnostic tests. Positivity rates were 5.5%, 2.5% and 3.7%, respectively.

2.2.3. Integrated behavioural and biological studies

Chlamydia prevalence studies (2007-10): Prevalence of *Chlamydia trachomatis* has been measured using urines from the representative national survey in children and teenagers (KIGGS) and adults (DEGS). Prevalence among 1925 teenagers was highest in 17-year old girls with 3.3%. Risk factors for chlamydia infection were smoking, marijuana and alcohol consumption and low social status. Prevalence among 6800 tested adults was 0.7%. Highest prevalence among women was in the group aged 18-20 year (4.5%) and among men in the group aged 25-30 years (4.9%). Risk factors were smoking and social status.

STD-Sentinel surveillance (2003-2009) was a multicentre sentinel system to collect data on STI diagnoses in different clinical settings. STI patients were also asked to fill in a questionnaire on their sexual behaviour and social status. Chlamydia trachomatis was the most frequently diagnosed STI. The sentinel system was not able to provide representative data on STI trends nor prevalences.

Pharyngeal and Rectal Infection Screening Study (PARIS) (2009-10): A total of 2247 MSM was screened for gonorrhoea and chlamydia using urethral, rectal and pharyngeal swabs. Laboratory results were combined with information on sexual behaviour, sexual practices and medical history. The aim was to measure gonorrhoea and chlamydia prevalence and co-infection in different sites and to describe factors associated with the infection in order to better understand the need for a routine screening. PARIS has been the first multicentre study in Germany measuring the infection burden of rectal and pharyngeal infections with gonococci and chlamydia in MSM. In addition, most Chlamydia-positive samples have been subtyped to determine the proportion of L-subtypes (causing LGV) among Chlamydia-positive MSM in Germany. Chlamydia prevalence was 1.5% in pharyngeal, 8.0% in rectal, and 3.3% in urethral specimen. Gonorrhoea prevalence was 5.5% in pharyngeal, 4.6% in rectal, and 1.9% in urethral specimens. Rectal and pharyngeal infection was significantly more likely in men reporting multiple partners and men diagnosed with HIV. Rectal infection was more likely in men practising receptive anal intercourse without condom. In a subsample of Chlamydia positive specimens LGV prevalence was 16.5% in rectal and 15.4% in pharyngeal specimens. Two publications have been submitted to peer review journals and are currently under review.

STI Prevalence and Behaviour in female sex workers (KAP-Surv-STI) (2010-11): Information on STI diagnoses, sexual behaviour and social status were collected from female sex workers attending STI testing sites. Among 1425 recruited sex workers, 3% were diagnosed with an STI. Three quarters of sex workers were of non-German origin and 44% had a valid health insurance. Risk factors for STI were young age, street work, lack of German language skills and unprotected sex.

KABP-survey as part of the German HIV-Incidence Study (2008-2010): Clinical and socio-demographic data and dried blood spots (DBS) of 348 persons newly diagnosed with HIV and 320 HIV negative controls, matched for age, gender, and HIV-transmission route were collected by physicians in six sentinel regions in Germany. Cases and controls completed a KABP-questionnaire. To distinguish recent (<5 months) from longstanding (>5 months) infection, the BED IgG-capture EIA was performed from DBS. Reported risk behaviour of cases with recent infection was compared with controls. Among MSM controls were more often in a relationship of >6 months. Controls also more often used condoms with acquaintances, with partners met online and with partners of unknown serostatus, whereas cases more often had unprotected anal sex with partners of unknown serostatus. Having a conversation about serostatus was protective.

Serobehavioural survey in injecting drug users (DRUCK study) (2012-15): This survey aims to determine HIV, hepatitis C and hepatitis B prevalence and risk profiles among injecting drug users in selected German cities to improve prevention of HIV and Hepatitis among this population in Germany. Blood samples and behavioural data are collected of 2,000 IDUs recruited via respondent driven sampling. Results of a pilot study in 2011 showed high prevalence for antibodies against hepatitis C (in Berlin (n=337) 52.5%, in Essen (n=197) 79.7% and hepatitis C RNA (Berlin: 36.9%; Essen: 58.0%). HIV prevalence was 3.9% in Berlin and 3% in Essen. In the coming years six others cities in Germany will be explored.

2.2.4. Behavioural studies

European MSM Internet Survey (EMIS) (2009-11): EMIS was an EU-funded study coordinated by Unit 34. The aim of the survey was to harmonise indicators to measure sexual health in MSM and contribute to set up an European HIV/STI-second generation surveillance among MSM. Data on sexual health, sexual behaviour, HIV- and STI-testing patterns and potential prevention factors were collected online. Over 55,000 participants were recruited from Germany. EMIS was the first European-wide MSM survey, and is so far the largest scientific behaviour survey among MSM worldwide with more than 180,000 participants. A final report of the project will be published by the European Centre for Disease Control and Prevention (ECDC) in the first quarter of 2013. Several publications in international peer review journals are currently in preparation. EMIS collected comparable data for MSM to be used for Global AIDS Response Progress (GARP – WHO/UNAIDS) and Dublin Declaration Monitoring (EU) Reporting.

HIV-Surveillance with migrants from sub-Saharan Africa (2012): Using a participatory research approach this project aims to develop a study design and recruitment strategy with community members and other partners (e.g. NGOs) in order to gain understanding of the HIV prevention needs in African communities in Germany.

2.2.5 Other studies

Estimation of the HIV prevalence and incidence: We established a unified back calculation model based on the AIDS case register and the HIV diagnoses from the national mandatory surveillance system. Recent estimates show that 78.000 people are living with HIV (PLWH) in Germany in 2012 and 3.400 new HIV infections must be expected for the same year. The estimated number of PLWH who are on antiretroviral treatment has increased to 50.000 or 85% of those diagnosed with HIV, but at the same time the number of undiagnosed HIV infections has risen to 14.000 in 2012.

Demographic studies on blood donors: The demographic characteristics of blood donors were analysed to estimate whether aging of the general population would lead to a lack of blood donors in future years. Although the general population eligible to donate blood is on the decline since 2003, with a loss of 2 % between 2006 and 2010, this has not led to a decrease in number of blood donors and donations. Instead, the number of new and repeat whole blood donors increased by 8 % and 7 %, respectively. At the same time, the number of new plasma donors grew by 23 %, that of repeat plasma donors by 41 %. In 2010, more than 4.3 % of the population aged 18 to 68 years were active as repeat whole blood donors; 0.4% repeatedly donated plasma or platelets. Since 2006 the percentage of donors among the general population increased significantly, especially among the youngest age group (18 to 24 years).

2.3. Major goals and contribution to the goals of the department

The unit has a complementary approach to cover its broad public health mission in the field of HIV and other STI, Hepatitis and other blood born infections and therewith of the department for infectious disease epidemiology. By maintaining the statutory surveillance systems for HIV, Syphilis, Hepatitis B, C and D, for infection markers in blood donors and for Creutzfeld-Jacob disease, it takes part in one of the main tasks of the department, the collection analysis and interpretation of data communicated to the RKI as a result of the Protection against Infection Act (Infektionsschutzgesetz, IfSG).

As an important complement, the unit conducts numerous and partly extensive additional surveillance systems and cohort studies to improve the health status of the German population in the fields of interest of the unit.

On basis of two large cohort studies in the scope of HIV research (ClinSurv und HIV 1-Seroconverter study), Unit 34 analyses real-life factors influencing the spread and course of HIV infection, dynamics of and influencing factors for HIV therapy resistance in Germany, and outcomes of antiviral therapy. Therewith, the unit compiles data for evidence based prevention approaches and therapy optimisation.

The additional surveillance systems in the field of HIV/AIDS, the voluntary AIDS registry and the InzSurv-HIV study, collect data important to monitor and evaluate the dynamics of the disease

complementing the statutory surveillance and allowing for giving in-depth information and advice to the MoH and the public health authorities on federal and communal level as a main task of the department. Regarding research on the dynamics of other STI, this is supplemented by the laboratory based Chlamydia sentinel, and by collaborating with other departments of the RKI in the scope of the general national health surveys in children (KIGGS) and adults (DEGS) regarding STI prevalence.

As another methodological complement to specify the knowledge regarding the infections covered by the unit, several large surveys on knowledge, attitude and behaviour (KAB) as well as integrated behavioural and biological surveillance studies (IBBS) in main groups at risk such as men who have sex with men (MSM), injecting drug users (IDU), and sex workers were or are conducted. In collaboration with national, federal and communal partners in Germany, these studies are used as the basis to tailor prevention strategies targeting specifically these groups.

The unit was concerned with several outbreak investigations (e.g. a hepatitis B outbreak in a nursing home in Thüringen in 2011, and an outbreak of anthrax among injecting drug users in several federal states of Germany and other European countries in 2009, 2010 and 2012).

Through its cooperation in networks on scientific level and with public health authorities on international, national, federal and communal level, the unit supports another important public health task of the department. The unit collaborates and gives its advice in setting up guidelines, in compiling public health approaches, in conducting outbreak investigations etc. On methodological level, the unit takes part in improving methods, such as for estimating HIV incidences and prevalence on country and federal state level. Existing surveillance instruments are improved constantly in terms of second generation surveillance approaches, to ameliorate quality and validity of epidemiological data. Concerning all these issues, the unit represents the department in numerous national and international political and scientific committees (, Unit 34)

As part of the communication tasks of the department and in addition to numerous workshops of the particular projects of the unit, the unit invented a bi-annual meeting of the epidemiological HIV/STI-projects of the RKI. On October 28th and 29th 2011, nineteen lectures on RKI-projects were held; the auditorium consisted of about 200 participants from partnering research institutions, public health authorities, physicians and the interested public.

2.4. Additional work and methods for investigations

Statistical methods

- Survival analysis (e.g. to describe the risk of AIDS-defining events over time in the German HIV-1 Seroconverter Cohort., to analyse the association of cumulative viremia and AIDS-related lymphoma in the ClinSurv cohort)
- Back calculation methods (to estimate HIV-prevalence and –incidence in different risk groups)
- Time series analysis (to analyse time trends of syphilis and HSV-2 co-infection among men who have sex with men in the German HIV-1 seroconverter cohort from 1996-2007)
- Multiple imputation for missing values (e.g. to estimate the HIV-prevalence and –incidence, to analyse late presentation for HIV diagnosis and care in Germany)

Respondent driven sampling

Since 2011, unit 34 has been implementing respondent-driven sampling (RDS) as part of the integrated behavioural and biological study (“DRUCK-study”) among people who inject drugs. RDS is a method of data collection based on peer-to-peer recruitment (similar to snowball-sampling) as well as a statistical method (“RDS inference”) to adjust for biases in the recruitment. In 2012, staff of unit 34 participated in the RDS training organised by the “Respondent WHO Collaborating Centre for HIV Surveillance” (Zagreb, Croatia).

2.5. Scientific advice and consulting services

Unit 34 is directly involved in advising the MOH in issues regarding epidemiology, prevention and provision of health services in the field of HIV/AIDS, STI and blood borne infections. The head of the unit represents the RKI in the National AIDS Board (Nationaler AIDS Beirat) as well as the Joint Bund-Länder Coordination Board for AIDS prevention (Bund-Länder Koordinierungsgremium AIDS). Advice in the above mentioned field is also provided for the supreme health authorities (Landesgesundheitsämter) of the 16 German federal states as well as the numerous local health offices (Gesundheitsämter). Consulting services are made available for health care providers as well as the scientific expert audience providing up-to-date information on issues like post exposure prophylaxis or antiretroviral treatment guidelines within the 24/7 on call duty and beyond. On request of the supreme health authorities of the federal states we advise and support local health authorities in conducting outbreak investigations or other epidemiological research. In addition unit 34 staff participates in the work of several medical associations developing guidelines (e.g. Recommendations for HIV positive health care providers, STI-treatment guidelines, antiretroviral treatment guidelines, Revision of the vaccination guidelines for hepatitis B).

Within the department statistical advice is provided for other units:

- Multivariable Analysis (e.g. in household studies to investigate risk factors for influenza transmission – Unit 36)
- Estimation of secular trends (e.g. to describe the impact of rotavirus vaccination – Unit 33)
- Capture-recapture methods (e.g. to estimate the incidence rate of nontuberculous mycobacterial disease in immunocompetent children – Unit 36, to estimate the total number of cases of human alveolar echinococcosis in Germany from 2003 through 2005, Unit 32)
- Estimation of excess consultations to estimate the number of consultations due to influenza – Unit 36
- Now-casting during outbreaks (e.g. during the big EHEC outbreak in Germany 2011 – Unit 35)
- Imputation of missing values (e.g. for data from emergency units during the STEC outbreak in Germany 2011, Unit 32) (see also list of publications)

2.6. Training and teaching activities

- Participation as facilitators in biannual 1-week courses on field epidemiology for public health workers in Germany hosted by the department (an der Heiden, Scheufele, Jansen, Dudareva-Vizule).
- Project supervision and hosting of fellows attending the German Postgraduate Program for Applied Epidemiology (PAE) and the European Intervention Epidemiology Training Program (EPIET): 6 fellows were trained in projects within Unit 34 from 2009-2012.
- Activities as lecturers and supervisors in the Master's Program in Public Health (Berlin School of Public Health), and the Master's Program in Applied Epidemiology (Robert Koch Institute) (Hamouda, Nielsen).
- Supervisors for PhD/dissertations and master theses (currently 2 master thesis projects).
- Participation as facilitators in teaching modules of the EPIET program: Computer Tools in Outbreak Investigations, multivariable Analysis, Time Series Analysis (an der Heiden, Bremer)
- Supervisors of international guests of the unit working on scientific questions concerning HIV and STI
- Lecturer in the RKI-coordinated teaching module "Infectious Diseases Epidemiology" at the Charité University Medicine, Berlin.
- Training of physicians applying for a board certification in transfusion medicine (Offergeld)

3. Cooperation with other scientists or research institutions

3.1. Internal (within RKI)

FG15 Molecular Epidemiology of Viral Pathogens

1. DRUCK study: validation of hepatitis B (HBV) and C (HCV) serology and molecular biology from filter-dried capillary blood spots in 2012, since October 2012 testing for HBV and HCV of the DRUCK study samples (ongoing)
2. HIV 1-Seroconverter study: HBV- and HCV-genom associated studies, e.g. resistance patterns and phylogenetic studies

FG18 Centre of HIV and other Retroviruses and Unit 34

1. Surveillance of transmitted drug resistance in patients recently infected with HIV (HIV 1-Seroconverter study)
2. Genome wide association studies within HIV-1 seroconverters (HIV 1-Seroconverter study)
3. Surveillance of incident HIV infections: Validation of resistance testing and subtype determination from dried plasma spots
4. DRUCK study: validation of HIV serology and molecular biology from filter-dried capillary blood spots in 2012, since October 2012 testing for HIV of the DRUCK study samples (ongoing)
 - Bartmeyer B et al., *PLoS One* 2010
 - Bätzing-Feigenbaum J et al., *HIV Med* 2009
 - Bätzing-Feigenbaum J, Loschen S, Gohlke-Micknis S, Zimmermann R, Kücherer C; Hamouda O: Piloting second generation HIV surveillance in Berlin, Germany, 2005 - 2007: Risk profile of recently acquired HIV infections in MSM. *J AIDS HIV Res* 2009

Unit 26 Central Epidemiological Laboratory

Longitudinal serological screening for HBV, HCV and syphilis of samples of HIV1 seroconverters (HIV 1-Serokonverter study)

Unit 36 respiratory diseases/tuberculosis and Unit 34 ClinSurv HIV

Tuberculosis as AIDS-defining disease in Germany: occurrence, case characteristics, course of disease and treatment

- Fiebig L et al, *PLoS One* 2012

Department 2 Epidemiology and Health Reporting

1. Prevalence of *Chlamydia trachomatis* among youth (KIGGS) in Germany
2. Prevalence of *Chlamydia trachomatis* among in adult population in Germany
3. Hepatitis B immunogenicity and hepatitis B seroprevalence in children and teenagers
4. HIV-denominator study: Together with unit 24 an online survey was launched that was sent to all HIV-diagnostic laboratories in Germany to gain understanding of the number of HIV-tests conducted in 2011.
 - Desai S et al., *Sex Health* 2011
 - Haar K et al., *J US-China Med Sci* 2011
 - Jorgensen P et al., *Epidemiol Infect* 2010
 - Cai W et al., *Pediatr Infect Dis J* 2011

Department 1, (ZBS), Unit 35 and Unit 34:

Collaboration concerning the Anthrax outbreak among injecting drug users in Germany and Europe in 2009/10 and 2012

- Radun D et al., *Euro Surveill* 2010

Department 3

Unit 34 staff was intensely involved in supporting the department wide effort to manage the large EHEC outbreak (2011) as well as the Influenza2009 pandemic. This included lead management of the situation room, participation of on-site outbreak investigations, data management and statistical analyses.

3.2 External / National

Unit 34 and the ClinSurv HIV Study Group

The ClinSurv-study is part of the German centre for Infection research (DZIF). Collaborating clinical centres are: Berlin: PD Dr K. Arastéh, D. Hampf: Auguste-Viktoria-Klinikum; Dr. F. Bergmann, M. Warncke: Charité Campus Virchow; Bonn: Prof. Dr. J. Rockstroh, Dr. J. Wasmuth, S. Hass: Universitätsklinikum Bonn; Düsseldorf: PD Dr. S. Reuter, L. Rollmann: Universitätsklinik Düsseldorf; Essen: Dr. S. Esser, P. Schenk-Westkamp: Universitätsklinikum Essen; Hamburg: Prof. Dr. A. Plettenberg, T. Lorenzen, I. Walther: ifi; Drs. A. Adam/ L. Weitner/ K. Schewe, H. Goey, Drs. S. Fenske/ T. Buhk/ HJ. Stellbrink, PD Dr. C. Hoffmann: IPM Studycenter; PD. Dr. J. van Lunzen, K. Wassmus; Universitätsklinikum Eppendorf; Hannover: Prof. Dr. M. Stoll, S. Gerschmann: Medizinische Hochschule Hannover; Frankfurt: Dr. A. Haberl, Dr. P. Kaikhin, Universitätsklinikum der Johann Wolfgang-Goethe-Universität Frankfurt Kiel: Prof. Dr. H. Horst, S. Trautmann: Universitätsklinikum Schleswig Holstein W Campus Kiel; Köln: Prof. Dr. G. Fätkenheuer, T. Kümmerle, D. Gillor: Universitätsklinik Köln; München: Prof. Dr. J. Bogner, B. Sonntag: Universitätsklinikum München; Regensburg: Prof. Dr. B. Salzberger: Universitätsklinik Regensburg; Rostock: Dr. C. Fritzsche: Universitätsklinik Rostock

- Bätzing-Feigenbaum J et al., *HIV Med* 2011
- Brunner J et al., *Dtsch Med Wochenschr* 2010
- Kastenbauer U et al., *Eur J Med Res* 2009
- Stoll M et al., *PLoS One* 2011
- Zoufaly A et al., *J Infect Dis* 2009
- Zoufaly A et al., *HIV Med* 2012
- Zoufaly A et al., *J Infect Dis* 2011

Unit 34 and the HIV-1 Seroconverter study group

The HIV 1-Serokonverterstudie collaborates with the RESINA study network and with the (former) national reference centre for HIV in Erlangen as well as with the Institute for Microbiology of the Charité, Berlin. Collaborating clinical centres are: Aachen: Dres. Habets and Knechten; Augsburg: Dr. Hammond (Klinikum Augsburg); Berlin: Dres. Mayr, Schmidt, Speidel, and Strohbach (Medizinisches Versorgungszentrum, Ärzteforum Seestraße), PD Dr. Arastéh (Auguste-Viktoria-Krankenhaus/Vivantes), Dres. Bieniek and Cordes, Dr. Claus, Dres. Baumgarten, Carganico, and Dupke, Dres. Freiwald and Rausch, Dres. Gölz, Klausen, Moll, and Schleeauf, Dr. Hintsche, Dres. Jessen and Jessen, Dres. Köppe and Krauthausen, Dr. Reuter; Bielefeld: Dr. Pfaff (Krankenhaus MARA II); Bochum: Prof. Dr. Brockmeyer (St. Joseph-Hospital); Bonn: Prof. Dr. Rockstroh (Universitätsklinik Bonn); Dortmund: Prof. Dr. Gehring and Dr. Schmalöer and Dr. Hower (Klinikum Dortmund, ID27 Ambulanz); Dresden: Prof. Dr. Spornraft-Ragaller (Universitätsklinikum Dresden); Duisburg: Dr. Becker-Boost, Dr. Kwirant; Düsseldorf: Prof. Dr. Häussinger and PD Dr. Reuter (Universitätsklinik Düsseldorf); Frankfurt/Main: Prof. Dr. Helm (Universitätsklinik Johann-Wolfgang-Goethe-Universität); Frankfurt/Oder: Dr. Markus; Halle/Saale: Dr. Kreft (Universitätsklinik Martin-Luther-Universität); Hamburg: Prof. Dr. Plettenberg, Dr. Stoehr, Dr. Graefe, and Dr. Lorenzen (Institut für Infektionsmedizin, ifi, Allgemeines Krankenhaus St. Georg); Dres. Adam, Schewe, and Weitner, Dr. Fenske, DrHansen, Prof. Dr. Stellbrink

(Infektionsmedizinisches Zentrum Hamburg, ICH); Hannover: Prof. Dr. Schmidt (Medizinische Hochschule Hannover), Dres. Buck and Leugner; Koblenz: Prof. Dr. Eisenhauer and Dr. Rieke (Krankenhaus Kemperhof); Köln: Dr. Bihari, Dr. Ferdinand, Prof. Dr. Fätkenheuer (Universitätsklinik Köln); Prof. Dr. Oette, Krankenhaus der Augustinerinnen, Köln; Leipzig: Dr. Pfeil (Universitätsklinik Leipzig); Magdeburg: Prof. Dr. Malfertheiner and Dr. Wolle (Universitätsklinik Otto-v.-Guericke-Universität); Mainz: Prof. Dr. Galle (Klinikum der Joh.-Gutenberg-Universität); München: Dres. Jäger and Jägel-Guedes, Dr. Malm, Dr. Rieger, Städtisches Krankenhaus 12 München-Schwabing, Prof. Dr. Fröschl (Technische Universität München); Münster: Prof. Dr. Rahn, (Universitätsklinik Münster); Norderstedt: Dr. Soldan; Nürnberg: Dr. Brockhaus (Klinikum Nürnberg); Osnabrück: Dr. Mutz (Städtische Klinik Natruper Holz); Regensburg: Prof. Dr. Salzberger, Prof. Dr. Schölmerich, and Dr. Schneidewind (Universitätsklinik Regensburg); Remscheid: Dr. Steege; Rostock: Dr. Kreft, Prof. Dr. Ziegler and Prof. Dr. Reisinger (Universitätsklinik Rostock); Stuttgart: Dres. Ißler, Schaffert, Schnaitmann, and Trein, Dres. Frietsch, Müller, and Ulmer; Dr. Wagner-Wiening (Landesgesundheitsamt Stuttgart); Ulm: Prof. Dr. Kern and Prof. Dr. Dr. Kreidler (Universitätsklinik Ulm); Viernheim: Dr. van Treek; Wiesbaden: Dr. Starke.

- Oh DY et al., *AIDS* 2009
- Bartmeyer B et al., *PLoS One* 2010
- Spielmann N et al., *Sex Transm Infect* 2010
- Altmann M et al., *BMC Infect Dis* 2012

InzSurv-HIV

Cooperation partners of this study are HIV-diagnostic laboratories that send dried plasma or serum spots of newly diagnosed and reported HIV-cases. Abteilung Mikrobiologie, Krankenhaushygiene, Infektionsschutz, Infektionsepidemiologie, Hannover; Landesgesundheitsamt Baden-Württemberg, Stuttgart; Institut für Medizinische Virologie, Frankfurt (Main); Institut für Laboratoriumsmedizin Hygiene-Institut des Ruhrgebiets, Gelsenkirchen; Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit, Oberschleißheim; Institut für Medizinische Mikrobiologie, Virologie und Hygiene, Hamburg; Labor Prof. Gisela Enders & Partner, Stuttgart; Landeslabor Berlin-Brandenburg, Fb-III-4 Infektionsdiagnostik, Berlin; Institut für Virologie, Universitätsklinikum Heinrich-Heine-Universität, Düsseldorf; Institut für Virologie, Klinikum der Universität zu Köln; Institut für Virologie - Klinische und Molekulare Virologie, Universitätsklinikum Erlangen; MVZ für Labordiagnostik Köln GbR, Synlab Köln; Medizinisch-Diagnostisches Labor Kempten; Labor Dr. Limbach & Kollegen, Abteilung für Immunologie, Infektionsserologie und Genetik, Heidelberg; Abteilung für medizinische Mikrobiologie, Institut für Hygiene und Umwelt, Hamburg; Medizinisches Versorgungszentrum Dortmund ; Dr. Eberhard & Partner, Medizinisches Versorgungszentrum ; Laboratoriumsmedizin & Mikrobiologie Kassel; Gemeinschaftspraxis für Laboratoriumsmedizin, Mikrobiologie und Humangenetik Dr. Stein & Kollegen, Mönchengladbach; Gemeinschaftspraxis für Laboratoriumsmedizin, Mikrobiologie und Infektionsepidemiologie, Medizinische Laborien Düsseldorf; Medizinisches Labor Prof. Seelig und Kollegen, Karlsruhe; Labor Ingelheim mit Zentrum für Humangenetik, Bioscientia Institut für Medizinische Diagnostik GmbH, Ingelheim am Rhein ; Institut f. Transfusions- und Laboratoriumsmedizin, Rhön-Klinikum, Klinikum Pforzheim; Laboratoriumsmedizin Köln, Dres. med. Wisplinghoff & Kollegen, Köln; Labor Krone, Bad Salzufen; Laborärztliche Gemeinschaftspraxis Lübeck; Hygiene-Institut, Abt. Virologie, Universitätsklinikum Heidelberg; Labor Becker, Olgemöller & Kollegen, München; Labor Schottdorf MVZ GmbH, Augsburg; Labormedizinisches Versorgungszentrum, LADR GmbH, Geesthacht; Labor-Zentralinstitut Springe, DRK Blutspendedienst NSTOB, Springe; Labor Dr. A.v. Froreich und Kollegen GmbH, Hamburg; Laborärzte Sindelfingen; MVZ Wagnerstibbe für med. Mikrobiologie, Göttingen; Institut für Laboratoriumsmedizin Berlin (IFLB), Berlin; Medizinisches Versorgungszentrum für Laboratoriumsmedizin und Mikrobiologie, Synlab München, Dachau; Institut für Laboratoriumsmedizin, Klinik am Eichert, Kliniken des Landkreises Göppingen gGmbH; Abt. Med. Mikrobiologie und Hygiene, Landesuntersuchungsanstalt für das Gesundheits- und Veterinärwesen Sachsen, Dresden ; Gemeinschaftspraxis Labor 28, Berlin ; Landesamt für Verbraucherschutz des Landes Sachsen-Anhalt, Fachbereich 2 – Hygiene, Magdeburg; IMD - Institut für Medizinische Diagnostik, Gemeinschaftspraxis für Labormedizin, Mikrobiologie, Transfusionsmedizin, Berlin; Labor Lademannbogen, Hamburg; Institut für Medizinische Mikrobiologie & Hygiene, Universität Regensburg; Gemeinschaftspraxis für Laboratoriumsmedizin

Köln; MVZ für Laboratoriumsdiagnostik GbR, Synlab Augsburg; MVZ für Laboratoriumsmedizin Koblenz-Mittelrhein, Labor Koblenz; Centrum für Laboratoriumsmedizin, Universitätsklinikum Münster; Institut für Transfusionsmedizin, Universitätsklinikum Schleswig-Holstein, Lübeck; Institut Lütjensee, DRK-Blutspendedienst Nord gGmbH, Lütjensee; Zentrallabor Hagen, DRK-Blutspendedienst West, Hagen; Medizinisches Labor Dres. Brunner-Zillikens & Kommerell, Konstanz; Institut für medizinische Mikrobiologie, Otto-von-Guericke-Universität Magdeburg; Institut für Transfusionsmedizin Cottbus, DRK-Blutspendedienst Ost GmbH, Cottbus; Medizinisches Labor Dr. Berg, Berlin; Institut für Laboratoriumsmedizin & Mikrobiologie, Evangelisches Krankenhaus Oberhausen; Institut für Transfusionsmedizin Suhl gGmbH, Suhl; Laborarztpraxis Dres. med. Jochem, Walther und Kollegen, Bad Homburg; Institut für Transfusionsmedizin, Universitätsklinikum Münster; Universitätsklinikum Essen Institut für Virologie, Essen; Institut für Infektionsmedizin mit Medizinaluntersuchungsamt, Universitätsklinikum Schleswig-Holstein, Kiel; Justus-Liebig-Universität Gießen, Institut für Medizinische Virologie, Gießen; Universität Tübingen, Hygiene-Institut / Abt. Virologie, Tübingen; Institut für Virologie und Immunologie, der Universität Würzburg; Max-von-Pettenkofer-Institut, Virologie, München ; Katharinenhospital, Zentralinstitut für klin. Chemie und Laboratoriumsmedizin, Stuttgart; Klinikum der LMU, Dermatologische Klinik, Serologisches Labor, München; Medizinische Hochschule, Abt.Virologie u. Seuchenhygiene, Hannover; Institut für Klinische Chemie, Laboratoriumsmed. & Transfusionsmed., Klinikum Nürnberg – Zentrallaboratorium, Nürnberg; Staatliches Untersuchungsamt Hessen, Standort Dillenburg; Universitätsklinikum Homburg, Institut f. Med. Mikrobiologie u. Hygiene, Homburg (Saar); Landesuntersuchungsamt Koblenz, Institut für Hygiene und Infektionsschutz, Koblenz; Universitätsklinikum Charité, Inst. für Mediz. Virologie, Berlin; Arztpraxis für med. Mikrobiologie und Labordiagnostik, Dessau; Medizinisch-Diagnostische Institute, Berlin; Fachärzte für Laboratoriumsmedizin, Dr. Hermann & Dr. Holzer, Würzburg; Laborpraxis in Kooperatin mit Bioscientia, Dres. Lorenz und Kollegen, Berlin; CSL Plasma GmbH, Labor Göttingen; Medizinisches Versorgungszentrum, AescuLabor - Karlsruhe GmbH; Labor Dr. Latza und Partner, St. Ingbert/Rohrbach; MEDILYS Institut für Labormedizin, Mikrobiologie und Krankenhaushygiene, Zentrallabor c/o Asklepios Klinik Altona, Hamburg; Klinikum Dortmund gGmbH, Institut für Transfusionsmedizin, Laboratoriumsmedizin und medizinische Mikrobiologie, Dortmund

Unit 34 STI-HIT and STI-Outreach

Cooperation partners of these ongoing prevalence studies of STI in persons asking for anonymous HIV tests and sex workers in North Rhine-Westphalia are Dres Münstermann, Tiemann, Lucht (Labor Krone), and public health authorities of Aachen, Bielefeld, Bonn, Bochum, Disburg, Düsseldorf, Essen, Euskirchen, Hochsauerlandkreis, Grevenbroich, Gütersloh, Köln, Leverkusen, Wesel/Moers, Münster, Recklinghausen, Siegen-Wittgenstein, Soest, Warendorf, Wuppertal. The study is ongoing.

DRUCK-pilot study (Unit 34) and National reference Centre for Hepatitis C (Department of Virology, University of Essen; Prof. Stefan Ross):

Validation of HIV, HBC and HCV serology and molecular biology from filter-dried capillary blood spots in 2010/11, testing for HIV, HBV and HCV including genotyping of HCV of 534 specimens of the DRUCK pilot study in 2011

- Ross RS et al., *Virology* (submitted for publication)

DRUCK-pilot study (Unit 34) and co-operating partners (2011):

Fixpunkt e.V. Berlin (Kerstin Dettmer, Astrid Leicht), Suchthilfe direkt Essen (Bärbel Marrziniak, Johannes Bombeck), Local Health Department of Essen (Brigitte Menze) and Department of Psychiatrics, University hospital Essen (Prof. Norbert Scherbaum); Deutsche AIDS Hilfe (Dirk Schaeffer)

Euro-GASP

Cooperation partner consiliary laboratory for gonococci and ECDC.

- Annual epidemiological report 2011 - Reporting on 2009 surveillance data and 2010 epidemic intelligence data.
http://www.ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DisForm.aspx?ID=767

Unit 34 Blutspendersurveillance

Bundesärztekammer (Federführung G. Bein)/Paul-Ehrlich-Institut (M. Heiden, R. Seitz): gemeinsamen Arbeitsgruppe „Blutspendeausschluss von Personen mit sexuellem Risikoverhalten (RKI: R. Offergeld, R. Burger, Gast: O. Hamouda).

- blood donor management' at
http://www.edqm.eu/medias/fichiers/paphts_11_28_2r_european_committee_partial_agreement.pdf

3.3. External / International

Annecy Group

The Annecy Group was founded in 1996 as a network of leading epidemiologist in the field of HIV from Canada, the US, Australia, UK, France, Italy, Spain and Germany to discuss state of the art HIV surveillance in industrialised countries. Recent topics cover surveillance of HIV incidence, modeling of HIV incidence and prevalence for national estimates, HIV/STI co-infection

- Sullivan PS et al., *Ann Epidemiol* 2009

CHAIN

ClinSurv collaborates with EU funded project “Collaboration on HIV and anti-HIV drug resistance network, CHAIN.

EUROCOORD-COHERE

ClinSurv Cohort takes part in the Collaboration of Observational HIV Epidemiological Research in Europe (EUROCOORD-COHERE).

EUROCOORD-CASCADE

The **HIV 1-Seroconverter study** is member of the Concerted Action on SeroConversion to AIDS and Death in Europe (EUROCOORD-CASCADE).

- van der Helm JJ et al., *AIDS* 2011
- Zugna D et al., *Antivir Ther* 2012
- Jarrin I et al., *Clin Infect Dis* 2012
- Pantazis N et al., *PLoS One* 2012
- Madec Y et al., *AIDS* submitted

ESAR

The **HIV 1-Seroconverter study** is member of the European Society for antiviral resistance (ESAR).

- Theys K et al., *Retrovirology*. 2012

BEST HOPE

On basis of the **HIV 1-Seroconverter** study, the unit is project coordinator for the project Bio-Molecular and Epidemiological Surveillance of HIV Transmitted Drug Resistance, Hepatitis Co-Infections and Ongoing Transmission Patterns in Europe (BEST HOPE), collaborating with partners in Portugal (Instituto de Higiene e Medicina Tropical (IHMT), Universidade Nova de Lisboa; Lisbon) and Romania (National Institute for Infectious Diseases “Prof. Dr. Matei Bals” (NIID), Bucharest) in the time frame 7/2012-6/2015.

EMIS

The EMIS Network consists of Associated Researchers: Rigmor A. Berg (Norwegian Knowledge Centre for the Health Services, Oslo); Michele Breveglieri (Regione del Veneto, Verona); Laia Ferrer (CEEISCat, Barcelona); Percy Fernández-Davila (CEEISCat, Barcelona); Cinta Folch (CEEISCat, Barcelona); Martina Furegato (Regione del Veneto, Verona); Ford Hickson (Sigma Research, London); Harm J. Hospers (University College Maastricht); Ulrich Marcus (Robert Koch Institute, Berlin); David Reid (Sigma Research, London); Axel J. Schmidt (Robert Koch Institute, Berlin); Todd Sekuler (Robert Koch Institute, Berlin); Peter Weatherburn (Sigma Research, London).

National collaborating partners of the EMIS Network: AIDS-Hilfe Wien (Austria); Facultés Universitaires Saint-Louis, Institute of Tropical Medicine, Ex Aequo, Sensoa, Arc-en-ciel (Belgium); Vstrecha (Belarus); National Centre of Infectious and Parasitic Diseases, Queer Bulgaria Foundation (Bulgaria); Charles University, Institute of Sexology (Czech Republic); Research Unit in Behaviour & Social Issues (Cyprus); University of Zagreb, Faculty of Humanities and Social Sciences (Croatia); Statens Serum Institut, Department of Epidemiology, stopaids (Denmark); National Institute for Health Development (Estonia); University of Tampere, Department of Nursing Science, Finnish AIDS council (Finland); Institut de veille sanitaire (InVS), AIDeS, Act UP Paris, Sida Info Service, Le kiosque, The Warning (France); Berlin Social Science Research Center (WZB), Deutsche AIDS-Hilfe (DAH), Federal Centre for Health Education, Cologne (BZgA) (Germany); Positive Voice (Greece); Hungarian Civil Liberties Union, Háttér (Hungary); Gay Men's Health Service, Health Services Executive (Ireland); University of Bologna, Italian Lesbian and Gay Association (Arcigay), Istituto Superiore di Sanità (National AIDS Unit) (Italy); The Infectiology Center of Latvia, Mozaika (Latvia); Center for Communicable Diseases and AIDS (Lithuania); GenderDoc-M (Moldova); schorer (Netherlands); Norwegian Knowledge Centre for the Health Services, The Norwegian Institute of Public Health (Norway); National AIDS Centre, Lamda Warszawa (Poland); GAT Portugal, University of Porto, Medical School, Inst. of Hygiene and Tropical Med. (Portugal); PSI Romania (Romania); PSI Russia (Russia); Safe Pulse of Youth (Serbia); OZ Odysseus (Slovakia); National Institute of Public Health, SKUC-Magnus, Legebitra, DIH (Slovenia); National Centre of Epidemiology, stopsida, Ministerio de Sanidad, Política Social e Igualdad (Spain); Malmö University, Health and Society, RFSL, National Board of Health and Welfare (Sweden); Institut universitaire de médecine sociale et préventive, AIDS-Hilfe Schweiz (Switzerland); Turkish Public Health Association, Siyah Pembe Üçgen İzmir, KAOS-GL, Istanbul-LGBT (Turkey); Gay Alliance, Nash Mir, LiGA, Nikolaev (Ukraine); City University London, Department for Public Health, Terrence Higgins Trust and the CHAPS partners including GMFA, The Eddystone Trust, Healthy Gay Life, The Lesbian and Gay Foundation, The Metro Centre London, NAM, Trade Sexual Health, Yorkshire, MESMAC (United Kingdom).

European Collaborating Partners: International Gay and Lesbian Organization (ILGA); European AIDS Treatment Group (EATG); PlanetRomeo.com; Manhunt and Manhunt Cares

- Marcus U et al., *BMC Public Health* 2012

SIALON II

The unit takes part in the SIALON II study, collaborating with the following partners: Institute of Tropical Medicine (Antwerp, Belgium); NCIPD, National Reference Laboratory of HIV (Bulgaria); Azienda Universitaria Ospedaliera Integrata (Regione Veneto, Verona, Italy); Istituto Superiore di Sanità (Rome, Italy); Istituto Nazionale Malattie Infettive (Italy); Centre for Communicable Diseases and AIDS (Lithuania); National Institute of Public Health – National Institute of Hygiene (Poland); Instituto Higiene e Medicina Tropical (Lisbon, Portugal); National Institute of Infectious Diseases “M. Bals” (Bucharest, Romania); Slovak Medical University (Bratislava, Slovak Republic); National Institute of Public Health (Ljubljana, Slovenia); Centre d'Estudis Epidemiològics sobre la Sida de Catalunya (CEEISCAT) (Barcelona, Spain); Swedish Institute for Communicable Disease Control (Sweden); Centre for Health Research, University of Brighton (UK).

Unit 34 Blutspendersurveillance

European Directorate for the Quality in Medicines and healthcare (EDQM). Working group TS057 “Sexual risk behavior having an impact on blood donor management”. Chair: Rut Norda (Sweden)

Vice Chair M. Heiden (Germany). Publication of the Technical memorandum at http://www.edqm.eu/medias/fichiers/paphts_11_28_2r_european_committee_partial_agreeme.pdf

Bordernetwork

Budget Holder: SPI-Forschung Berlin

Austria: Coordinator: Aids-Hilfe Wien.

SMZ Süd/Kaiser Franz Josef Spital, 4. Med. Abt. (Infektiologie u. Tropenmedizin) Vienna; Allgemeines Krankenhaus der Stadt Wien, Univ.Klinik f. Dermatologie; STD-Ambulanz, Vienna; KA Rudolfstiftung, Abt. für Allgemeine Dermatologie, Vienna; STD-Ambulatorium der Stadt Wien (MA15) Vienna; Pilzambulatorium Floridsdorf; Pilzambulatorium Schlüsselgasse GmbH, Vienna; Pilzambulatorium Hietzing GmbH, Vienna; Praxisgemeinschaft Wieng (GP specialised in HIV-care), Vienna; Aids Hilfe Wien, Vienna; Dr. Bernd Gmeinhardt (dermatologist, GP), Vienna; Medizinische Universität Graz, Klin. Abt. f. Umweltdermatologie u. Venerologie, Graz; Aids Hilfe Steiermark, Graz; Aids Hilfe Oberösterreich, Linz.

Bulgaria: Coordinator: HESED (Health and Social Development Foundation)

District Dispensary for Dermato-Venereal Diseases, Plovdiv; Department of Dermatology and Venereology, Medical University, Plovdiv; Multiprofile Hospital for Active Treatment "St. Ana " Unit 203 Dermato-Venerology, Varna; District Dispensary for Dermato- Venereal Diseases, Sofia; Department of Dermatology and Venereology, Medical University, Sofia.

Romania: Coordinator: ARAS (Romanian Association against Aids)

Dermato-Venerological Unit, Clinical Hospital "Prof.Dr. Scarlat Longhin", Bucharest; Dermato-Venerological Clinic in Hospital Constanta, Constanta; Baylor Marea Neagra Foundation, Constanta; ARAS – Titan drop-in clinic, Bucharest; ARAS Bucuresti – ARENA drop-in clinic and mobile unit, Bucharest; Public Health Department Brasov, Brasov; Hospital of Infectious Diseases "Str. Memorandului, Brasov; ARAS - VCT Community Centre Brasov; ARAS, Constanta; ARAS, Timisoara; VCT Community Centre ARAS, Neamt; ARAS, Iasi; 2nd Dermatological Clinic "Carol Davila" University of Medicine and Pharmacy Colentina Clinical Hospital Sos., Bucharest.

Slovakia: Coordinator: PRIMA (

Miloš Mokráš, Infectologist, Bratislava; Slovak Medical University, Bratislava; Klin. Žen. Chorob, Bratislava; Nestatna kozna ambulancia, Bratislava; FNŠP Ružinov Urol.Klinika, Bratislava; FN Kožná Klinika, Bratislava; Slovenskej zdravotnickej univerzity (narodne referencne centrum), Bratislava; Mária Belovičová, Hepatologist, Interná amb. Bard.Kúpele s.r.o., Bard. Kúpele; FILACERM s.r.o., Bratislava.

- Interim Report. BORDERNETwork Sentinel-Surveillance. June 2011. http://www.bordernet.eu/cms/media/uploads//Uploads/Interim_Report_Sentinel-Surveillance.pdf
- Bridging research on HIV/STI prevalence and risks to evidence-based effective practice. Final Report: HIV/STI Sentinel-Surveillance.

4. Appendix

4.1 Overview on achievements of the unit, 2009-2012

4.1.1. Scientific publications, 2009 – 2012

Number of peer-review publications co-authored by members of the unit: 67

Impact factor (IF) according to JCR (for 2012 according to 2011)

2009: 52,6

2010: 32,0

2011: 138,6

2012: 62,8

Cumulative 2009-12: 286,0

A) Original research articles in peer-review journals

2012 (until Sept.)

Altmann M, an der Heiden M, Scheufele R, Hartmann K, Houareau C, Bartmeyer B, Hamouda O, for the German HIV-1 Seroconverter Cohort. The risk of AIDS-defining events is decreasing over time in the German HIV-1 Seroconverter Cohort. *BMC Infect Dis* 2012; 12:94.

Altmann M, Fiebig L, Buda S, von Kries R, Dehnert M, Haas W. Unchanged severity of influenza A(H1N1)pdm09 infection in children during first postpandemic season. *Emerg Infect Dis* 2012 <http://dx.doi.org/10.3201/eid1811.120719>

Bremer V, Marcus U, Hamouda O. Syphilis on the rise again in Germany - results from surveillance data for 2011. *Euro Surveill* 2012; 17(29). pii: 20222.

Dudareva-Vizule S, Koch J, **an der Heiden M**, Oberle D, Keller-Stanislawski B, Wichmann O.: Impact of rotavirus vaccination in regions with low and moderate vaccine uptake in Germany. *Hum Vaccin Immunother* 2012; 8(10).

Fiebig L, Kollan C, Hauer B, **Gunsenheimer-Bartmeyer B, an der Heiden M, Hamouda O**, Haas W. HIV-prevalence in tuberculosis patients in Germany, 2002-2009: an estimation based on HIV and tuberculosis surveillance data". *PLoS One* 2012; 7(11):e49111.

Holzmann T, Frangoulidis D, Simon M, Noll P, Schmoltd S, Hanczaruk M, Grass G, Pregler M, Sing A, Hörmansdorfer S, Bernard H, Grunow R, **Zimmermann R**, Schneider-Brachert W, Gessner A, Reischl U (2012): Fatal anthrax infection in a heroin user from southern Germany, June 2012. *Euro Surveill*; 17(26): pii=20204.

Jarrin I, Pantazis N, Gill MJ, Geskus R, Perez-Hoyos S, Meyer L, Prins M, Touloumi G, Johnson A, **Hamouda O**, de Olalla PG, Porter K, del Amo J; CASCADE Collaboration in EuroCoord. Uptake of combination antiretroviral therapy and HIV disease progression according to geographical origin in seroconverters in Europe, Canada, and Australia. *Clin Infect Dis* 2012; 54(1):111-118.

Marcus U, Hickson F, Weatherburn P, **Schmidt AJ**: Prevalence of HIV among MSM in Europe: Comparison of self-reported diagnoses from a large scale internet survey and existing national estimates. *BMC Public Health* 2012; 12:978.

Offergeld R, Ritter S, Hamouda O: HIV-, HCV-, HBV- und Syphilissurveillance unter Blutspendern in Deutschland 2008-2010. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012; 55; S-907-913.

Pantazis N, Morrison C, Amornkul PN, Lewden C, Salata RA, Minga A, Chipato T, Jaffe H, Lak S, Karita E, Porter K, Meyer L, Touloumi G; CASCADE Collaboration in EuroCoord and ANRS 1220 Primo-CI Study Group (**Hamouda O, Bartmeyer B** for Germany). Differences in HIV

natural history among African and non-African seroconverters in Europe and seroconverters in sub-Saharan Africa. *PLoS One* 2012; 7(3):e32369.

Remschmidt C, Stöcker P, **an der Heiden M**, Suess T, Luchtenberg M, Schink SB, Schweiger B, Haas W, Buchholz U.: Preventable and non-preventable risk factors for influenza transmission and hygiene behavior in German influenza households, pandemic season (H1N1) 2009/2010. *Influenza Other Respi Viruses* 2012 Jul 16. doi: 10.1111/j.1750-2659.2012.00407.x. [Epub ahead of print]

Ritter S, Hamouda O, Offergeld R: Demografie und Spendeaktivität von Blut- und Plasmaspendern in Deutschland. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012; 55: S-914-922.

Santos-Hövenner C, von Unger H (2012): Kultursensible HIV/STI-Prävention bei Sexarbeiterinnen mit Migrationshintergrund. [Culturally sensitive HIV/STI prevention with migrant sex workers]. *Prä. Gesundheitsf* 2012; *Epub Mar 25*. DOI: 10.1007/s11553-012-0336-3.

Zoufaly A, **an der Heiden M, Marcus U**, Hoffmann C, Stellbrink HJ, **Voß L**, Van Lunzen J, **Hamouda O**: Late presentation for HIV diagnosis and care in Germany. *HIV Med* 2012; 13(3):172-181.

Zugna D, Geskus RB, De Stavola B, Rosinska M, **Bartmeyer B**, Boufassa F, Chaix ML, Babiker A, Porter K; the CASCADE Collaboration in EuroCoord: Time to virological failure, treatment change and interruption for individuals treated within 12 months of HIV seroconversion and in chronic infection. *Antivir Ther* 2012; 17(6):1039-1048.

2011

Altmann M, Spode A, Altmann D, Wadl M, Benzler J, Eckmanns T, Krause G, **an der Heiden M**: Timeliness of surveillance during outbreak of Shiga Toxin-producing *Escherichia coli* infection, Germany, 2011. *Emerg Infect Dis* 2011; 17(10):1906-1909.

Bätzing-Feigenbaum J, Kollan C, Kühne A, Matysiak-Klose D, **Gunsenheimer-Bartmeyer B, Hamouda O**. ClinSurv HIV Study Group. Cohort profile: the German ClinSurv HIV project-a multicentre open clinical cohort study supplementing national HIV surveillance. *HIV Med* 2011; 12 (5):269-278.

Buchholz U, Bernard H, Werber D, Böhmer MM, Remschmidt C, Wilking H, Deleré Y, **an der Heiden M**, Adlhoch C, Dreesman J, Ehlers J, Ethelberg S, Faber M, Frank C, Fricke G, Greiner M, Höhle M, Ivarsson S, Jark U, Kirchner M, Koch J, Krause G, Lubert P, Rosner B, Stark K, Kühne M.: German outbreak of *Escherichia coli* O104:H4 associated with sprouts. *N Engl J Med* 2011; 365(19):1763-1770.

Frank C, Werber D, Cramer JP, Askar M, Faber M, **an der Heiden M**, Bernard H, Fruth A, Prager R, Spode A, Wadl M, Zoufaly A, Jordan S, Kemper MJ, Follin P, Müller L, King LA, Rosner B, Buchholz U, Stark K, Krause G; HUS Investigation Team: Epidemic profile of Shiga-toxin-producing *Escherichia coli* O104:H4 outbreak in Germany. *N Engl J Med* 2011; 365(19):1771-1780.

Haar K, Meyer T, Desai S, Thamm M, **an der Heiden M, Bremer V, Hamouda O**. Low sensitivity of pooled Chlamydia testing in a sample of the young German general population. *US-China Med Sci* 2011; 8(10): 577-580.

Jaffe HW, De Stavola BL, Carpenter LM, Porter K, Cox DR; CASCADE Collaboration (**Hamouda O, Bartmeyer B** for Germany). Immune reconstitution and risk of Kaposi sarcoma and non-Hodgkin lymphoma in HIV-infected adults. *AIDS* 2011; 25(11):1395-1403.

Mall S, Buchholz U, Tibussek D, Jurke A, **an der Heiden M**, Diedrich S, Schweiger B, Alpers K. A large outbreak of influenza B-associated benign acute childhood myositis in Germany, 2007/2008. *Pediatr Infect Dis J* 2011; 30(8):e142-6.

Marcus U, Schmidt AJ, Hamouda O (2011): HIV serosorting among HIV-positive men who have sex with men is associated with increased self-reported incidence of bacterial sexually transmissible infections. *Sexual Health* 2011, 8: 184-193.

Roth WK, Busch M, Schuller A, Ismay S, Cheng A, Seed CR, Jungbauer , Minsk PM, Sondag-Thull D, Wendel S, Levi JE, Fearon F, Delage G, Xie Y, Jukic I, Turek P, Ullum H, Tefanova H, Tilk M, Reimal M, Castren J, Naukkarinen M, Assal A, Jork C, Hourfar MK, Michel P, **Offergeld R**, Pichl L, Schmidt M, Schottstedt V, Seifried E, Wagner F, Weber-Schehl F, Politis C, Lin C, O’Riordan J, Gottreich A, Shinar E, Yahalom V, Velati C, Satake M, Sanad N, Sisene I, Bon AH, Koppelman M, Flanagan P, Flesland O, Brojer E, Łętowska M, Nascimento F, Zhiburt E, Chua SS, Teo D, Levicnik Stezinar S, Vermeulen M, Reddy R, Park Q, Castro E, Eiras A, Gonzales Fraile I, Torres P, Ekeremo B, Niederhauser C, Chen H, Oota S, Brant LJ, Eglin R, Jarvis L, Mohabir L, Brodsky J, Foster G, Jennings C, Notari E, Stramer S, Kessler D, Hillyer C, Kamel H, Katz L, Taylor C, Panzer , Reesink WH. International survey on NAT testing of blood donations: expanding implementation and yield from 1999 to 2009. *Vox Sang* 2011. doi: 10.1111/j.1423-0410.2011.01506.x.

Schmidt AJ, Marcus U: Self-reported history of sexually transmissible infections (STIs) and STI-related utilization of the German health care system by men who have sex with men: data from a large convenience sample. *BMC Infect Dis* 2011; 11:132.

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2012

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Marcus U: HIV-Infektionen und AIDS-Erkrankungen - Bericht zur Entwicklung im Jahr 2009 aus dem Robert Koch Institute. *HIV&more* 2/2010: 44-48.

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Offergeld R, Burger R. Die Rolle des Robert Koch Institutes im *Transfus Med Hemother* 2010; 14:74-78

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2009

Arbeitskreis Blut, Untergruppe „Bewertung Blutassoziierter Krankheitserreger“. Arboprotozoae (für das FG 34 **Offergeld R**). *Transfus Med Hemother* 2009;36:8-31

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2011

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2010

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Marcus U: Medizinische und strukturelle Prävention von HIV-Infektionen und Aids-Erkrankungen. In Strukturelle Prävention, AIDS-Forum DAH, 2010, S. 170-183

Offergeld R, Burger R: The role of the Robert Koch Institute in Transfusion Medicine. Transfusion medicine in Germany: Current Status and Perspectives, Frankfurt, :22-25

E) Articles in the Epidemiological Bulletin

Erneuter Anstieg der Syphilis-Meldungen in 2011. *Epid Bull* 2012; 24: 221-223.

HIV bei Migranten in Deutschland. *Epid Bull* 2012; 3: 19-21.

DRUCK-Studie – Drogen und chronische Infektionskrankheiten in Deutschland. *Epid Bull* 2012; 33: 335-339.

Virushepatitis B, C und D im Jahr 2011. *Epid Bull* 2012; 38: 371-385 .

Zur Situation bei wichtigen Infektionskrankheiten in Deutschland. Virushepatitis B, C und D im Jahr 2010. *Epid Bull* 2011; 29: 261-271.

Gonorrhö: Erster Cefixim-resistenter Stamm führt in Österreich zu Therapieversagen; Situation in Deutschland (für das FG 34 **Haar K**). *Epid Bull* 2011 (47):429-30

Sechs Jahre STD-Sentinel-Surveillance in Deutschland – Zahlen und Fakten (für das FG 34 **Haar K**). *Epid Bull* 2010 (3), 20-27

Zur Situation bei wichtigen Infektionskrankheiten in Deutschland. Virushepatitis B, C und D im Jahr 2009. *Epid Bull* 2010; 20: 177-187

Webbasierte Erhebung zur HIV-Diagnostik in Deutschland 2009. *Epid Bull* 2010; 39: 391-395

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Zur Situation bei wichtigen Infektionskrankheiten in Deutschland Virushepatitis B, C und D im Jahr 2008. *Epid Bull* 2009 (20), 189-199

4.1.2. Selected relevant publications

Five important publications for the scientific community 2009–2012

1. Zoufaly A, Stellbrink HJ, **an der Heiden M**, **Kollan C**, Hoffmann C, van Lunzen J, **Hamouda O**; ClinSurv Study Group. Cumulative HIV viremia during highly active antiretroviral therapy is a strong predictor of AIDS-related lymphoma. *J Infect Dis* 2009; 200(1):79-87.

2. **Schmidt AJ**, Rockstroh JK, Vogel M, **an der Heiden M**, Baillot A, Krznicar I, **Radun D**. Trouble with bleeding: risk factors for acute hepatitis C among HIV-positive gay men from Germany--a case-control study. *PLoS One* 2011; 6(3):e17781.
3. **Marcus U, Schmidt AJ, Hamouda O** (2011): HIV serosorting among HIV-positive men who have sex with men is associated with increased self-reported incidence of bacterial sexually transmissible infections. *Sexual Health* 2011, 8: 184–193.
4. **Bartmeyer B**, Kuecherer C, **Houareau C**, Werning J, Keeren K, Somogyi S, **Kollan C**, Jessen H, Dupke S, **Hamouda O**, on behalf of the German HIV-1: Prevalence of Transmitted Drug Resistance and Impact of Transmitted Resistance on Treatment Success in the German HIV-1 Seroconverter Cohort. *PLoS One* 2010; 5(10): e12718.
5. **Desai S**, Meyer T, Thamm M, **Hamouda O**, **Bremer V**. Prevalence of Chlamydia trachomatis among young German adolescents, 2005-06. *Sexual Health* 2011; 8(1):120-122.

Five important publications for the public 2009–2012

1. Rabenau HF, Gottschalk R, Gürtler L, Haberl AE, **Hamouda O**, et al: Prävention der nosokomialen Übertragung von humanem Immunschwächevirus (HIV) durch HIV-positive Mitarbeiterinnen und Mitarbeiter im Gesundheitswesen. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2012, (55):937-943.
2. Stoll M, **Kollan C**, Bergmann F, Bogner J, Faetkenheuer G, Fritzsche C, Hoepfer K, Horst H.-A, van Lunzen J, Plettenberg A, Reuter S, Rockstroh J, Stellbrink H.-J., **Hamouda O**, **Bartmeyer B**: Calculation of direct antiretroviral treatment costs and potential cost savings by using generics in the German HIV ClinSurv Cohort, *PLoS One*, 2011; 6(9).
3. **Bremer V**, Brockmeyer N, Hagedorn H, Knoell A, **Marcus U**, Meyer T, Nitschke H, Nick S, Ross, Straube E: Gemeinsame Stellungnahme des RKI, PEI und der DSTIG: Schnelltests in der Diagnostik sexuell übertragbarer Infektionen. *Epid Bull* 2012 (5): 38-41
4. **Haar K, Marcus U**, Ehrhard I, Nielsen S, **Jansen K, Hamouda O**, Kohl P: Therapieversagen durch Cefixim-Resistenz von Neisseria gonorrhoeae in Österreich, Situation in Deutschland. *HIV & More* 2011; 4.
5. **Bremer V, Marcus U, Hamouda O**: Syphilis on the rise again in Germany - results from surveillance data for 2011. *Euro Surveill* 2012; 17(2).

4.1.3. Awards and honours, 2009 – 2012

2010

Dr. Barbara Gunsenheimer-Bartmeyer, Dr. Osamah Hamouda: Deutsche Medizinische Wochenschrift Walter Siegenthaler Preis 2010: Langfristig wirksame Zweit Therapie der HIV Infektion bei Klassenwechsel nach virologischem Versagen unter Protease Inhibitoren: Brunner J., Seybold U., Gunsenheimer-Bartmeyer B., Hamouda O., Bogner J. *DMW* 2010; 135

2012

Dr. Karin Haar: Detlef-Petzold Award of the DSTIG (Deutsche STI-Gesellschaft - German STI-Society) for the original scientific work "Low Sensitivity of Chlamydia Testing in a Pooled Sample of the Young German General Population"

4.1.4. Overview on collaborations in networks

Dr. Bartmeyer

HIV

EUROCoord HIV, EuroCoord-CASCADE Network European network of HIV/AIDS cohort studies to coordinate at European and International level clinical research on HIV/AIDS

CHAIN Network CHAIN is a large scale integrating project aimed to effectively and durably combat new and existing anti-HIV drug resistance in clinical settings, with a special emphasis on Eastern Europe and in heavily affected resource-poor regions in Africa.

CJD

National expert of surveillance of transmissible spongiforme encephalitis infections in the European network

Dr. Zimmermann

National expert for the indicator “drug related infectious diseases” at the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)

Member of Deutsche Gesellschaft für Suchtmedizin (DGS)

C. Santos-Hövenner

Working Group HIV Prevention and Migration: LABAS Berlin (Statewide Association Berlin of organisations working in the field of Hepatitis, HIV and STIs)

K. Jansen

Member for „Methodology & Standards“ of Steering Committee of the German Competence Network for HIV/AIDS

Member of the Section Sexual Health of the German STI Society

4.1.5. Memberships and participation in Advisory Boards

Dr. Hamouda

- Representative of the RKI in the National AIDS Board (Nationaler AIDS Beirat)
- Representative of the RKI in the Joint Bund-Länder Coordination Board for AIDS prevention (Bund-Länder Koordinierungsgremium AIDS)
- Chairman of the ECDC Coordination Group for HIV/AIDS surveillance
- Chairman of the ECDC Coordination Group for STI surveillance
- Member of the ECDC Coordination Group for Hepatitis B and -C surveillance
- Member of the Board and Council of the European Society for Antiviral Resistance (ESAR)

Dr. Bremer

- Member of the Executive Board of the German STI Society (treasurer)
- Spokeswoman of the Section Sexual Health of the German STI Society

Dr. Offergeld

- Managing director of the National Advisory Committee “Blood” (Arbeitskreis Blut)
- Member of the epidemiology group of the European Medicines Agency (EMA)
- Expert, EDQM, TS 057
- Member of the German Society of Transfusion Medicine and Immunhaematology (DGTI)

Dr. Marcus

- Member of the Northern Dimension Partnership in Public Health and Social Wellbeing (NDPHS) Expert Group on HIV/AIDS and Associated Infections

4.1.6. List of completed dissertation or master theses in the Unit, 2009 – 2012

Year	Title	Name	Titel	University/Supervisor RKI
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2012	Untersuchung infektionsepidemiologischer Meldedaten von Anti-HBc-positiven und HBsAg-negativen Blutspendern in Deutschland von 2006-2009	Margareta Kang	MSc Epi	Berlin School of Public Health / G. Krause, O. Hamouda
2012	HIV-Surveillance among sub-Saharan African migrants in Germany. How could this be improved?	Tanja Charles	MSc Publ Health	Berlin School of Public Health/C. Santos-Hövenner
2012	Die Capture-Recapture Methode zur Bestimmung verborgener Populationsgrößen – Im Rahmen des Sero- und Verhaltenssurvey bei injizierenden Drogengebern des Robert Koch Institutes	Benjamin Wenz	MSc Public Health	Charité Berlin / U. Marcus
2012	Prävalenz von urogenitalen Chlamydia trachomatis- Infektionen bei Teilnehmern des bundesweiten Kinder- und Jugendgesundheits-surveys (KiGGS)	Karin Haar	MSc Public Health	Berlin School of Public Health/ O. Hamouda
2012	Risikoprofil von injizierenden Drogen- gebrauchernInnen im Rahmen der DRUCK - Studie (Drogen und chronische Infektionskrankheiten in Essen)	Judith Stumm	MSc Public Health	Hochschule Fulda/ R. Zimmermann/ O. Hamouda
2012	Erhebung der regionalen Abdeckung der Chlamydia trachomatis Diagnostik in Deutschland sowie Begutachtung bisher angewendeter diagnostischer Nachweisverfahren	Daniel Schmidt	MSc Public Health	Beuth Hochschule für Technik Berlin Haar/Hamouda
2012	Prävalenz übertragener HIV-Resistenz und Einfluss übertragener HIV-Resistenz auf den Therapieerfolg der First-Line-Therapie in der HIV-1 Serokonverter Kohorte in Deutschland	Fabia zu Knyphausen	MPH	Berlin School of Public Health Gunsenheimer-Bartmeyer/Hamouda
2012	Risk factors for Chlamydia, Gonorrhoea, and Trichomonas infections for sex workers in Germany	Martyna Gassowski	MSc Epidemiology	Radboud Universiteit Nijmegen Nielsen, Stine
2011	Prävalenz von urogenitalen <i>Chlamydia trachomatis</i> -Infektionen bei Teilnehmern des bundesweiten Kinder- und Jugendgesundheits-surveys (KiGGS)	Karin Haar	MPH	Charité - Berlin School of Public Health/ Dr. Osamah Hamouda
2011	Identifying risk factors and formulating public health recommendations using surveillance data	Mathias Altmann	MPH	Charité - Berlin School of Public Health/ Dr. Osamah Hamouda
2009	Wer testet was und wen in Köln? – Versorgungssituation von HIV- und STD-Testungen am Beispiel Köln	Alexandra Hofmann	MPH	Freie Universität Berlin Prof. Dieter Kleiber Dr. Osamah Hamouda

4.1.7. Presentations as invited speaker, 2009 - 2012

Staff from the HIV/AIDS, STI and other Blood-borne Infections Unit were invited to speak at 67 conferences.

4.1.8. List of reports and written scientific advice to the Ministry of Health, 2009-2012

There were 173 reports and written scientific advice to the Ministry of Health between 2009 and 30.09.2012.

Unit 35: Gastrointestinal Infections, Zoonoses and Tropical Infections

Unit Head: Prof. Dr. Klaus Stark

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1. General information - unit 35

Head: Prof. Dr. Klaus Stark

Deputy: Christina Frank, PhD

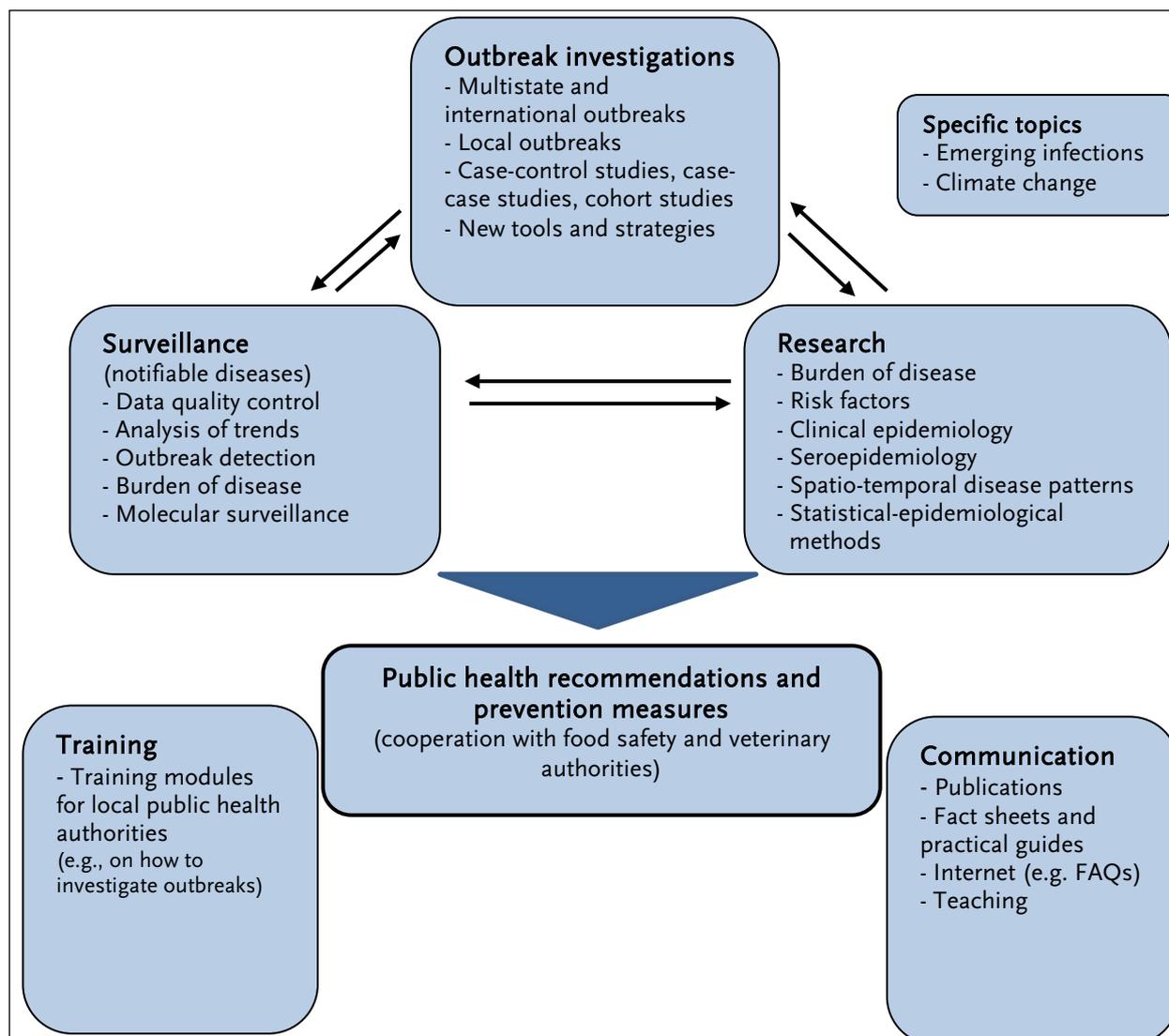
2. Tasks and goals of the unit

2.1. Summary

The unit is responsible for infections with a wide range of gastrointestinal and zoonotic pathogens - about two thirds of all pathogens notifiable in Germany. The spectrum includes the classical gastrointestinal and food-borne pathogens such as salmonellae, campylobacter, Shiga toxin-producing *E. coli*, listeria, Norovirus, hepatitis A virus, other zoonotic agents such as hepatitis E virus, hantavirus, leptospirosis, and vector-borne pathogens (e.g., *Borrelia burgdorferi*, Plasmodium species, Dengue virus, West Nile virus). One major focus is placed on outbreak investigations. Since 2009 Unit 35 has coordinated and managed various large outbreak investigations. It also has supported public health authorities in many local and regional outbreaks.

Additional important work areas are disease surveillance and research (especially epidemiological studies regarding burden of disease, risk factors for infection, importance of emerging pathogens for human health in Germany), development of epidemiological and statistical methods, training of German public health service staff (especially in how to investigate food borne outbreaks), and the formulation of preventive schemes and public health recommendations based on epidemiological findings. Aside from food borne, vector-borne and zoonotic infections, the unit focuses on the topics of climate change and infectious diseases, emerging infections, and molecular epidemiology.

Figure 12: Major activities / tasks of Unit 35



2.2. Current status of the work and summary of relevant results

2.2.1. Outbreak investigations

Outbreak investigations are a major work focus. In recent years they concerned food-borne outbreaks as well as outbreaks due to zoonotic pathogens transmitted via other routes (e.g. hantavirus, leptospirosis, or anthrax among injecting drug users).

In large multistate or international outbreaks the unit is prepared to assume a leading role in coordination and investigations into the scope and dynamics of the outbreak and to identify the vehicle of infection. Since 2009 the unit has participated in or coordinated many outbreak investigations. Prime examples are the large outbreak of STEC O104:H4 caused by sprouts in 2011, generating the largest number of HUS cases in an outbreak worldwide (Figure 13), the Norovirus outbreak of more than 10,000 cases caused by frozen strawberries in 2012, and an outbreak caused by *S. Newport* in 2011, again associated with sprouts. The unit's work was pivotal for identifying the vehicles of infection in these outbreaks.

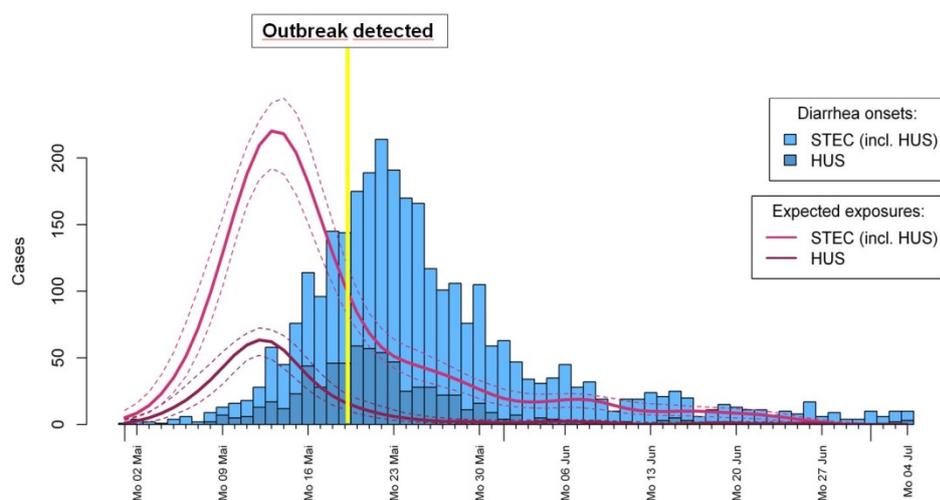
Unit 35 leads the communication and cooperation with the federal food safety authorities (Bundesinstitut für Risikobewertung, Bundesamt für Verbraucherschutz und Lebensmittelsicherheit), and with the state health departments. In such outbreaks the unit has also a major role in the communication of the epidemiological findings and management issues to the scientific and medical community and the public.

In international outbreaks where the German population is affected (but not the centre of the outbreak), we collaborate intensively with partner institutions abroad, e.g., within the framework of ECDC's Food and water borne diseases network.

In local or regional outbreaks (involving only one federal state), Unit 35 assists responsible public health authorities. The assistance activities range from telephone consultations regarding strategy and study design, supply of data collection tools (e.g., specific questionnaires, templates for analytic studies) and supporting staff, to coordinating the local outbreak investigation on behalf of the local health department.

Cooperating with our partners, the local and state health and food safety authorities, laboratories and hospitals, outbreaks frequently could be "solved" (identification of the vehicle/source of infection). Results are routinely published in international scientific journals (see publication list). In addition, outbreak reports are produced and made accessible to the scientific and the general population via the RKI website and the Epidemiological Bulletin.

Figure 13: Outbreak of HUS and STEC gastroenteritis caused by STEC O104:H4 in Germany, 2011 – Epidemiologic curve and back projection of the exposure phase



2.2.2. Surveillance

Surveillance data (infections notifiable by law) are analysed weekly in order to detect changing trends or disease clusters (outbreak algorithms). These activities form the basis for outbreak detection and for scientific in-depth analyses of spatio-temporal trends of relevant pathogens. Timely detection of multistate food-borne outbreak is challenging. Molecular subtyping surveillance is a useful tool for this purpose, but currently subtyping is not routinely conducted in Germany. Therefore, a concept for a systematic subtyping surveillance of selected food-borne enteric pathogens (e.g., EHEC, *Listeria monocytogenes*, non-typhoidal *Salmonella* serotypes) is being developed in collaboration with the Department for Infectious Diseases (Dept. 1).

Germany has experienced several outbreaks of infection with a rare sorbitol-fermenting clone of EHEC O157. Outbreaks are characterised by a predominance of paediatric patients with HUS, a life-threatening post infectious sequelae of EHEC infection, and only very few cases of diarrhoea-only cases. Consequently, we have established active surveillance for paediatric “enteropathic” (i.e., diarrhoea-associated) HUS in collaboration with the German Society of paediatric nephrology.

If we notice conspicuous changes in the incidence or distribution of notified infections, we assess the reasons for such trends (e.g., changes in epidemiologic patterns and risk factors, or changes in diagnostic procedures). This may trigger in-depth epidemiological studies (e.g., hepatitis E, *Giardia lamblia*).

We routinely assess the surveillance data (notifiable infections) regarding their validity and completeness. Since 2004, for example, every death marked on a notified infectious disease report falling into the responsibility of Unit 35, is subject to quality control. An email is sent to the local health department with the purpose of verifying the death notice and the assessment of a (co-)causal contribution of the infectious disease. The data are compared with the cause-of-death census statistic in irregular intervals to assess completeness of the passive surveillance system and to more accurately assess the burden these pathogens cause.

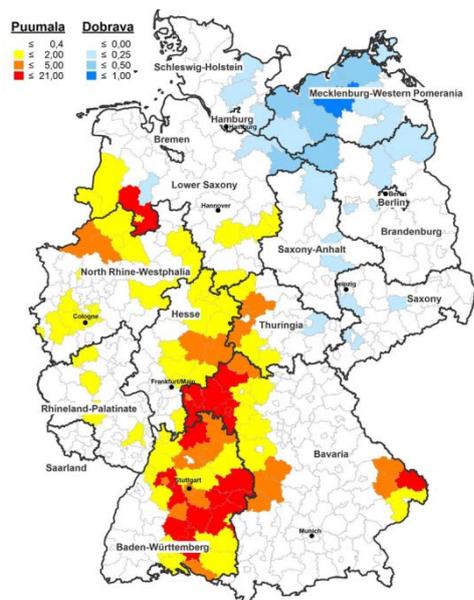
2.2.3. Research

Studies are being conducted in the following fields:

Burden of disease, frequency and trends in gastroenteric and zoonotic diseases

These include telephone surveys on the frequency of acute gastroenteritis in a representative population subsample (n=22,000), as well as analyses on burden of disease (case-fatality, years-of-life-lost) based on surveillance data of important gastrointestinal infections. The survey showed that acute gastroenteritis is very common (incidence 0.9 per person-year) and is associated with variables such as body mass index or diabetes. Time series analyses provide important findings regarding temporal trends, geographic and demographic distribution of infectious diseases. We have performed and published such analyses for yersiniosis, salmonellosis, Norovirus enteritis, and leptospirosis providing important clues for prevention and further epidemiological investigations. Serosurveys on markers of infection in representative population subsamples (Lyme borreliosis and hepatitis E) and in special-risk populations (*Coxiella burnetii* in veterinarians) were also conducted. Surprisingly high seroprevalences were found. About 20% of the adult population showed antibodies against HEV. *Borrelia burgdorferi* seroprevalence was 6% among children and increased significantly with age. In the veterinarians, the seroprevalence of *Coxiella burnetii* was about 40% and associated with cattle obstetrics. Another topic of interest is the spatio-temporal variation of hantavirus infection and its determinants. In an externally funded project, burden of disease of non-cholera vibrio infections in Germany (diarrheal disease, wound infections) is being studied (Figure 14).

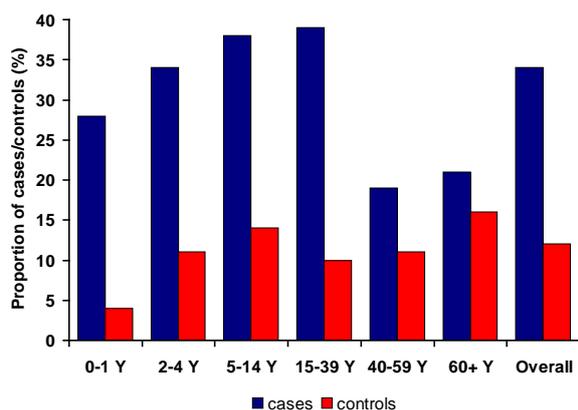
Figure 14: Mean annual incidence of notified hantavirus infections by place of infection (county) and serotype (Puumala or Dobrava), Germany 2004-10 (n=4412)



Risk factor studies are essential for targeted public health measures

They supply new scientific knowledge which leads to new or improved public health recommendations. In this context we conducted a large multi-state case-control study on risk factors for sporadic *Yersinia enterocolitica* infection in conjunction with the public health service, yielding the somewhat surprising finding that even in (very young) children, consumption of raw ground pork is the main risk factor for infection. In other case-control studies, risk factors for sporadic infection with hantaviruses and *Giardia lamblia* were studied. Currently we are conducting large nation-wide or multi-state case-control studies on sporadic campylobacteriosis, listeriosis and on specific risk factors for hepatitis E virus infections.

Figure 15: Case control study on the risk factors for yersiniosis in Germany: Consumption of raw minced pork by age group in cases and controls

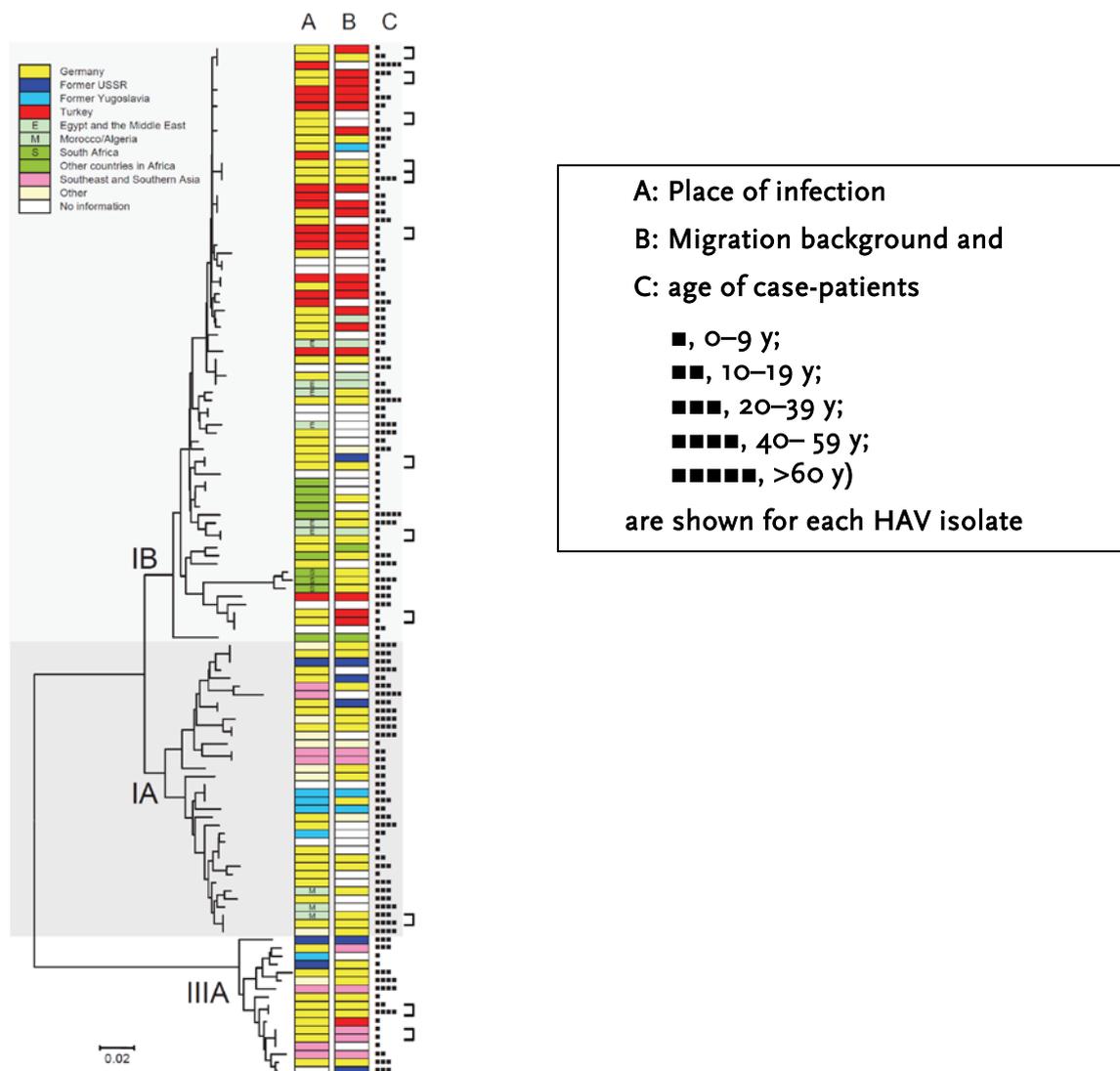


Molecular Epidemiology

There is growing awareness of the importance of molecular epidemiology at the cross roads between classic infectious disease epidemiology and microbiology/virology. Linkage of epidemiological and molecular data (regarding human, food, and environmental samples) allows dynamic monitoring of specific pathogens (and their subtypes) in various populations, as well as a better quantification of the importance of various source and vehicles of infection in Germany. For example, the unit conducted and published studies regarding hepatitis A and E in collaboration jointly with the respective expert laboratories (Dr. Schreier/Dr. Höhne, RKI and Prof. Jilg, Regensburg). A current study on the molecular epidemiology of campylobacterioses is being

conducted in cooperation with Prof. Suerbaum, Hannover (Medical School, Institute of Medical Microbiology and Hospital Hygiene). The study results should enable us to quantify the impact of different groups of food items on the campylobacter incidence in Germany, the most common bacterial gastrointestinal infection (annually 70,000 notified cases).

Figure 16: Molecular epidemiology of hepatitis A in Germany: Neighbor-joining phylogenetic tree of a 348-bp section of the viral capsid protein 1/2A junction region of hepatitis A virus (HAV)



Emerging and re-emerging infectious diseases/zoonoses

In recent years Lyme borreliosis has been a focus of attention. Notification data available only from 5 eastern German states are of variable quality and thus allow very limited conclusions on the epidemiology of the disease in Germany as a whole. Consequently population-based studies on antibody seroprevalence are paramount and are being done in collaboration with Department 2 on sera collected for the national “Kids and youths” (KiGGS) and the “Adult health” surveys (DEGS) (see above). For pathogens newly emerging in Germany, it is important to determine possible threats for humans. A good example is Schmallenberg virus (SBV), discovered in November 2011 by the Friedrich-Loeffler-Institut (federal institute for veterinary health) in sick dairy cows in North Rhine-Westphalia. In view of the German and international public health interest (this was also recommended by ECDC), it had to be quickly determined whether these animal infections posed a risk for human health. In conjunction with our colleagues in the laboratory (ZBS1), Unit 35 assessed

the risks based on quickly developed laboratory assays and a rapidly organised epidemiological study among exposed shepherds. We were able to conclude and publish in a timely manner, that the human health risk of SBV is negligible. Unit 35 has the appropriate expertise and cooperation links to replicate such rapid risk assessments in similar situations in the future.

Imported infections

Surveillance data on imported mosquito borne diseases (malaria, dengue fever, chikungunya fever) are constantly monitored and analysed for trends. This enables the unit to issue pertinent information for travel medicine experts and the public. Based on mathematical modelling, potential autochthonous transmission of relevant pathogens is addressed. Unit 35 collaborates closely with the Bernhard-Nocht-Institut for Tropical Medicine. To promote entomological monitoring, Unit 35 has initiated an external project (funded by RKI) on the systematic monitoring of potential mosquito vectors in Germany and is curating the project, which is carried out by the Friedrich-Loeffler-Institut.

Climate Change

The risk of changes in the occurrence of climate sensitive infections during times of climate change are being assessed (publication in *Bundesgesundheitsbl-Bundesgesundheitsforsch-Bundesgesundheitschutz*, Climate Assessment Report). Studies are being conducted, e.g., on the importance of ecological and climatic factors on the incidence of hantavirus infections in Germany, on scenarios for potential autochthonous transmission of dengue virus in South West Germany, on the impact of extreme weather events like rain storms on outbreaks of climate sensitive pathogens, and on the correlation of very warm summers with the incidence of wound infections with marine non-cholera vibrio.

Statistical-epidemiological Methods

The unit (with its full-time biostatistician) is also involved in interdisciplinary research on the boundary between biostatistical methods and infectious disease epidemiology. This ranges from statistical consulting within the unit and department to interfacing with statistical research environments at universities. As a consequence, state-of-the art methods are readily applied in the unit's projects or, where necessary, extended to address RKI specific needs. Examples are: real-time tracking of epidemic curves during outbreaks, exposure estimation using back-projection methods in foodborne outbreaks, outbreak detection algorithms and model selection for case-control and cohort studies in light of missing data and exposure misclassification. Furthermore, when combining notification data with additional geo-referenced information (e.g., variables on demographics, socio-economics, climate or land use) spatial and spatio-temporal ecological regression is performed. Open-source software is provided whenever possible, which contains an implementation of the methodological extensions.

2.2.4. Training

Training of staff in public health institutions is another major area of work. In various federal states, we carried out training workshops for public health service staff on how to investigate food-borne outbreaks epidemiologically. To this end, we developed a simple tool based on Excel, which can be efficiently used by (local) public health authorities in outbreak investigations to timely record relevant epidemiological data (demographics, exposures) from patients and control persons. The tool is programmed to automatically calculate bivariable measures of association (e.g., odds ratios, relative risks).

2.3. Major goals and contribution to the goals of the department

The major goals for the coming years are:

- To timely detect outbreaks, particularly multistate outbreaks. Improved statistical algorithms are being developed, as well as concepts for systematically integrating subtyping information for specific pathogens (e.g., STEC, Listeria, non-typhoidal *Salmonella* serotypes) (in collaboration with the Department for Infectious Diseases, Abt. 1).

- To further develop and refine methods and tools to identify more timely and more frequently the vehicles and sources of infection in food-borne outbreaks.
- To carry out research into the burden of disease of the major gastrointestinal infectious and vector-borne diseases.
- To investigate the distribution, risk factors and the clinical outcome of relevant gastrointestinal and zoonotic pathogens in Germany in large multistate epidemiological studies. When appropriate, classical epidemiological and molecular methods (molecular epidemiology) are being combined.
- To assess the effectiveness of intervention measures for relevant gastrointestinal and zoonotic infections.
- To investigate the impact of travel-associated infections and to assess the potential of autochthonous transmission of selected pathogens in Germany.
- To analyse the effects of climate patterns on the occurrence and distribution of climate-sensitive infectious diseases.
- To intensify the work on statistical-methodological methods (e.g., outbreak detection, spatio-temporal models).
- To provide tools, training and practical support for public health authorities to investigate outbreaks.
- To provide sound scientific evidence for consumer advice and public health recommendations.

2.4. Additional work and methods for investigations

In addition to the scientific and training activities, which are described in the respective chapters, we regularly inform the public and the scientific community not only by peer-reviewed publications but also by a substantial number of reports written for the Epidemiological Bulletin of the RKI and we produce the Fact Sheets (Ratgeber) for Physicians on selected gastrointestinal and zoonotic pathogens. We have also coordinated the interim and final reports on the large food-borne outbreaks in 2011 (STEC O104:H4) and 2012 (Norovirus due to contaminated frozen strawberries), and we contributed to Assessment Reports (e.g., on Climate Change and Health). We published (in collaboration with other authorities and institutes such as the Friedrich-Loeffler-Institut and National Reference Laboratories) recommendations on prevention of selected gastrointestinal and zoonotic pathogens (e.g., hantavirus) or contributed to consumers' advice (e.g., by the Federal Institute of Risk Assessment on consumption of raw minced pork or sprouts).

We are developing innovative methods especially in the field of statistical-epidemiological methods (See 2.2, Unit 35).

2.5. Scientific advice and consulting services

Unit 35 provides (scientific) advice to a range of national and international authorities and bodies:

Federal Ministry of Health

Advice on trends in food-borne and zoonotic infections (e.g., emerging and re-emerging pathogens), on climate change and infectious diseases, and on priority setting. Assessment of risk to the general population in foodborne or other outbreak situations.

Public Health and Food Safety authorities

Advice concerning strategies and tools (e.g., questionnaires) in outbreak investigations, hygienic measures in the context of food-borne and zoonotic outbreaks.

Advice concerning interpretation of case definitions, surveillance data, epidemiologic findings etc.

Federal Environment Agency, and Federal Ministry for the Environment, Nature Conservation and Nuclear Safety

Advice on vector-borne pathogens and on climate change and infectious diseases.

Clinicians, scientists from other institutes etc.

Advice on interpretation of surveillance data and epidemiological findings. Provision of data, figures, presentations, etc.

Advice on epidemiological methods (study design, data collection, data analysis).

Public

Telephone and written advice regarding risks from food-borne and zoonotic pathogens (routes of transmission etc.).

Berlin School of Public Health

Advice and collaboration concerning training in infectious disease epidemiology and on PhD programme (epidemiology).

European Food Safety Authority (EFSA)

- Working Group on Food-borne outbreak reporting, 2008/10 (D. Werber)
- Working Group on Epidemiological Criteria on Meat Inspection 2010/11 (C. Frank)

European Center for Disease Prevention and Control (ECDC)

Advice on surveillance, epidemiology and control of food-borne, zoonotic, and travel-associated infections in Germany (and cross-border).

Advice and collaboration concerning molecular typing for public health surveillance (K. Stark).

2.6. Training and teaching activities

- Coordination of the module Infectious Diseases Epidemiology within the master programmes (Public Health, Epidemiology) at the Berlin School of Public Health (BSPH), Charité Medical School, Berlin
- Mentoring of fellows of the training Programme Applied Epidemiology (PAE) and the European Programme for Intervention Epidemiology Training (EPIET)
- Contribution to EPIET training modules
- Lectures at the Charité for medical students, in the Master Programme International Health (Module Epidemiology), and at the University of Bonn (Medical Geography)
- Teaching on “Statistical Methods for Infectious Diseases” in various Biostatistics programmes (University of Munich, University of Zurich) or as short courses
- Supervision of master’s and doctoral theses

3. Cooperation with other scientists or research institutions

3.1. Internal (within RKI)

Department of Infectious Diseases (Dept. 1), Division 11 Bacterial Infections

- Outbreak investigations, epidemiological studies (STEC, salmonellae, listeria), molecular surveillance
- Frank C et al., *Euro Surveill* 2011
- Frank C et al., *N Eng J Med* 2011
- Stöcker P et al., *Euro Surveill* 2011
- Koch J et al., *Foodborne Pathog Dis* 2010
- Nielsen S et al., *Zoonoses public health* 2011
- Weiss B et al., *Vector Borne Zoonotic Dis* 2011

Department of Infectious Diseases (Dept. 1), Division 15 Molecular Epidemiology of Viral Pathogens

- Molecular epidemiological studies (hepatitis A, norovirus).
- Faber MS et al., *Emerg Infect Dis* 2009
- Wadl M et al., *BMC Infect Dis* 2010

Department of Epidemiology and Health Reporting (Dept. 2), Divisions 21, 22, 23, 24, 25, 26

- Studies on seroprevalence of various pathogens in the general population in Germany. Case-control studies (control populations).
- Faber MS et al., *Emerg Infect Dis* 2012
- Dehnert M et al., *PLoS One* 2012

Centre for Biological Security, ZBS1 Highly Pathogenic Viruses

- Studies on emerging viruses.
- Ducomble T et al., *Emerg Infect Dis* 2012

Centre for Biological Security, ZBS2 Highly Pathogenic Microorganisms

- Studies on emerging bacteria.
- Holzmann T, et al. *Euro Surveill* 2012.

3.2. External / National

University of Regensburg, Institute of Microbiology, Dept. of Virology (Prof. Jilg)

- Hepatitis E (Studies on seroprevalence in the general population, risk factors, molecular epidemiology)
- Faber MS, et al. *Emerg Infect Dis* 2012 (see also under Internal Cooperation)

University hospitals, clinical departments of other hospitals

- Frank C et al., *N Eng J Med* 2011
- Holzmann T et al., *Euro Surveill* 2012

Consiliar Laboratory for *Coxiella burnetii*, Stuttgart (Landesgesundheitsamt, Dr. Wagner-Wiening)

- Bernard H et al., *Vector Borne Zoonotic Dis* 2012

Consiliar Laboratory for Hantavirus, Berlin (Charité, Institute of Virology, Prof. Krüger)

- Faber MS et al., *Euro Surveill* 2010

Consiliar Laboratory for Leptospirae, Berlin (Federal Institute for Risk Assessment, Dr. Nöckler)

- Desai S et al., *Clin Infect Dis* 2009

National Reference Centre for *Borrelia burgdorferi*, München (Landesamt für Gesundheit und Lebensmittel, Dr. Fingerle)

- Dehnert M et al., *PLoS One* 2012

Consiliar Laboratory for Haemolytic-Uraemic Syndrome, Münster (University Münster, Institute of Hygiene, Prof. Karch), and Research Network Food-borne zoonotic bacterial infections (FBI-Zoo)

- Werber D et al., *Lancet* 2011
- Frank C et al., *Euro Surveill* 2011
- Mellmann A et al., *Emerg Infect Dis* 2009
- Alpers K et al., *Epidemiol Inf* 2009

German Society of pediatric nephrology

- Active Surveillance of Pediatric HUS

Hannover Medical School, Institute for Medical Microbiology and Hospital Hygiene (Prof. Suerbaum)

- Vonberg R et al., *Clin Infect Dis*; in press.

National and Federal State Food Safety Authorities (e.g., Federal Institute of Risk Assessment, Federal Authority for Consumer Protection and Food)

- Buchholz U et al., *N Eng J Med* 2011
- Kamga Wambo GO et al., *Euro Surveill* 2011
- Frank C et al., *Euro Surveill* 2009
- Pires SM et al., *Foodborne Pathog Dis* 2009

Friedrich-Loeffler-Institute for Veterinary Health, Riems

- Faber MS et al., *Euro Surveill* 2010

VibrioNet (BfR, Alfred-Wegener-Institut, FU Berlin, LAVES, TU Dresden, Q-Bioanalytic)

- Alter T et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2011

Bernhard-Nocht-Institute for Tropical Medicine, Hamburg

- Schmidt-Chanasit J et al., *Infection* 2012
- Schmidt-Chanasit J et al., *Euro Surveill* 2010

Federal State Authorities for Infectious Disease Epidemiology

- Bernard H et al., *Vector Borne Zoonotic Dis* 2012
- Holzmann T et al., *Euro Surveill* 2012
- Kamga Wambo GO et al., *Euro Surveill* 2011
- Brockmann S et al., *BMC Infect Dis* 2010
- Faber MS et al., *Euro Surveill* 2010
- Alpers K et al., *Epidemiol Inf* 2009

- Schroeter M et al., *Epidemiol Inf* 2009
- Winter CH et al., *Epidemiol Inf* 2009

District Public Health Authorities (various)

- Wilking H et al., *Emerg Infect Dis* 2012
- Frank C et al., *N Eng J Med* 2011

Institute of Tropical Medicine, Berlin

- Zoller T et al., *Malaria J* 2009

Ludwig-Maximilians-Universität München (Institute of Statistics)

- Meyer S et al., *Biometrics* 2012

German Armed Forces/Bundeswehr (Institute for Microbiology, Medical Service Kiel, and other units)

- Holzmann T et al., *Euro Surveill* 2012
- Wadl M et al., *BMC Infect Dis* 2010

3.3. External / International

European Centre for Disease Prevention and Control

- Contributions to various rapid risk assessments

National Institute for Public Health and the Environment (RIVM), The Netherlands

- Haagsma JA et al., *Epidemiol Infect* 2012
- Verhoef L et al., *Epidemiol and Infect* 2012:1-11.
- Verhoef L et al., *Emerg Infect Dis* 2011
- Pires SM et al., *Foodborne Pathog Dis* 2009

Statens Serum Institut, Denmark

- Kuhn K et al., *Euro Surveill* 2011
- Buchholz U et al., *N Eng J Med* 2011

Smittskyddsinstitutet (Swedish Institute for Communicable Disease Control), Sweden

- Buchholz U et al. *N Eng J Med* 2011

Austrian Agency for Health and Food Safety (AGES), Austria

- Fretz R et al., *Euro Surveill* 2010

National Public Health Institutes in Poland, Romania and Slovakia

- Desai S et al., *Clin Infect Dis* 2009

WHO-Europe, Health Authorities Montenegro and United Kingdom (HPA)

- Werber D et al., *Epidemiol Infect* 2009

4. Appendix

4.1 Overview on achievements of the unit, 2009-2012

4.1.1. Scientific publications, 2009 – 2012

Number of peer-review publications co-authored by members of the unit: 76

Impact factor (IF) according to JCR (for 2012 according to 2011)

2009: **62.2**

2010: **43.9**

2011: **235.7**

2012: **71.5**

Cumulative 2009-2012: **413.4**

Original research articles in peer-review journals

2012 (until Sept.)

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2012

Aktuelle West Nil-Fieber Situation in Europa und den USA. *Epid Bull* 35: 351.

Autochthone Dengue-Fälle auf Madeira. *Epid Bull* 43: 440.

Autochthone Malaria-Erkrankungen durch Plasmodium vivax in Griechenland. *Epid Bull* 35: 351.

Dritter Milzbrandfall bei Heroinkonsumenten, Berlin *Epid Bull* 27: 254.

Ergebnisse der Post-Ausbruchs-Surveillance nach dem erklärten Ende des Ausbruchs im Sommer 2011. *Epid Bull* 36: 355-360.

Ergebnisse des Workshops: "Experiences from the STEC O104:H4 outbreak in Germany and research needs for STEC". *Epid Bull* 9: 71-74.

Erneuter Milzbrandfall bei einem injizierenden Drogenkonsumenten. *Epid Bull* 24: 226.

Erneuter Milzbrandfall bei einer bayerischen Heroinkonsumentin. *Epid Bull* 25: 238.

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Hantavirus-Erkrankungen: Hinweise auf Anstieg der Fallzahlen in 2012. *Epid Bull* 10: 79-81.

Kein Hinweis auf Infektionen mit dem sogenannten Schmallenberg-Virus bei stark exponierten Schäfern in Nordrhein-Westfalen. *Epid Bull* 14: 120.

Molekulare Unterscheidbarkeit der zirkulierenden Hantavirus-Stämme in den verschiedenen Ausbruchsregionen Deutschlands. *Epid Bull* 25: 228-231.

Reiseassoziierte Infektionskrankheiten 2011. *Epid Bull* 43: 429-437.

Salmonella Newport-Ausbruch in Deutschland und den Niederlanden. Mungbohnenprossen wahrscheinliches Infektionsvehikel. *Epid Bull* 20: 177-184.

Seroprävalenz der Lyme-Borreliose bei Kindern und Jugendlichen. in Deutschland. *Epid Bull* 10. April 2012 / Nr. 14

Vierter Milzbrandfall bei Heroinkonsument in Deutschland. *Epid Bull* 38: 388.

Yersiniose - Risikofaktoren in Deutschland. *Epid Bull* 6: 47-51.

Zum Auftreten eines großen lebensmittelbedingten Gastroenteritis-Ausbruchs in fünf ostdeutschen Bundesländern. *Epid Bull* 40: 405.

Zwei Bundesweite Ausbrüche durch Salmonella Newport seit Oktober 2011. Mungbohnenprossen und Wassermelonen stehen in Verdacht. *Epid Bull* 5: 41-42.

2011

Ergebnisse der bayerischen FSME-Studie 2007 - Hohe diagnostische Sicherheit bei gemeldeten Fällen, aber zusätzliche Untersuchungen notwendig bei Patienten mit früherer FSME-Impfung. *Epid Bull*. 17: 142-145

Erkrankungsfälle von Sarkozystose bei Reiserückkehrern aus Malaysia. *Epid Bull* 44/11.

Ausbruch von Infektionen mit Katzenleberegel durch Verzehr von rohem Fisch, Mittelitalien. *Epid Bull* 35: 334.

Autochthone Malaria-Erkrankungen durch Plasmodium vivax in Griechenland. *Epid Bull* 33: 324.

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Informationen zum EHEC-/HUS-Ausbruchsgeschehen von Mai bis Juli 2011 in Deutschland - Ende des Ausbruchs. *Epid Bull* 31: 295-296.

Intensivierte Surveillance während eines großen EHEC-/HUS-Ausbruchs in Deutschland, Mai-Juni 2011. *Epid Bull* 25: 225-229.

Merkblätter für Ärzte. Gelbfieber. *Epid Bull* 1: 1-4.

Reiseassoziierte Infektionskrankheiten 2010. *Epid Bull* 41: 371-378.

RKI-Ratgeber für Ärzte - Hantataaviren. *Epid Bull* 24: 217-221.

RKI-Ratgeber für Ärzte Lassa-Fieber. *Epid Bull* 43: 389-393.

Zum EHEC- und HUS-Ausbruch 2011 (Datenstand 27.6. 2011). *Epid Bull* 26: 244.

Zur aktuellen Häufung von EHEC-Infektionen und HUS-Fällen in Deutschland, Supplement zum Epidemiologischen Bulletin 21/2011.

Zur Entwicklung der Erkrankungszahlen im aktuellen EHEC/HUS-Ausbruch in Deutschland - Update. *Epid Bull* 23: Seite 207- 209.

Zur Entwicklung der Erkrankungszahlen im aktuellen EHEC/HUS-Ausbruch in Deutschland. *Epid Bull* 22: Seite 199-201.

Zur Entwicklung der Erkrankungszahlen im aktuellen EHEC/HUS-Ausbruch in Deutschland-Update. *Epid Bull* 24: 215-217.

2010

Ein dritter Fall von Anthrax bei einem i. v. Heroinkonsumenten in Deutschland. *Epid Bull* 49: 492-493.

Aktuelle Zunahme der Hepatitis-E-Meldezahlen in Deutschland. *Epid Bull* 34/10.

Aus Kroatien importierte Denguevirus-Infektion. *Epid Bull* 40: 404.

Ausbruch von Listeriose-Erkrankungen in Deutschland und Österreich. *Epid Bull* 7: 68.

Autochthones Dengue-Fieber in Südfrankreich. 38

Bundesweite Häufung von Erkrankungen durch S. Panama 2010. *Epid Bull* 40: Seite 399-400.

Cholera-Fälle in der Dominikanischen Republik und Florida, importiert aus Haiti. *Epid Bull* 46: 462.

Fallbericht: Aus Südafrika importierte Infektion mit Riftal-Fieber-Virus. 17

Hantavirus-Erkrankungen: Hinweise auf eine starke Saison 2010. *Epid Bull* 07/10.

Hepatitis A, Anstieg importierter Fälle mit Infektionsland Afghanistan. *Epid Bull* 41: 410.

Importierte Cholera aus Pakistan. *Epid Bull* 39: 398.

Kutaner Milzbrand nach intravenösem Heroinabusus. *Epid Bull* 2: 15.

Listerien-Infektionen in Baden-Württemberg. *Epid Bull* 46: 462.

Listeriose 2001 bis 2009. *Epid Bull* 34: Seite 341-346.

Listeriose- Ausbruch in Deutschland und Österreich - Update. *Epid Bull* 8: 78.

Neues Cluster von Listeriose-Erkrankungen. *Epid Bull* 15: 136.

Reiseassoziierte Infektionskrankheiten 2009. *Epid Bull* 38: Seite 379-387.

RKI-Ratgeber Infektionskrankheiten - Merkblätter für Ärzte: Listeriose.. *Epid Bull* 24: Seite 229-233.

Starke Zunahme der Denguevirus-Infektionen, vor allem nach Thailand-Reisen. *Epid Bull* 42: 416.

Überarbeitete Falldefinitionen zur Übermittlung von Nachweisen von Denguevirus und Norovirus und Erkrankungs- oder Todesfällen an Denguefieber und an Norovirus-Gastroenteritis. *Epid Bull* 49: 494-495

Update zu Arbovirosen in Europa. *Epid Bull* 39: 398.

Zum Auftreten von West-Nil-Fieber in Europa und im Mittelmeerraum (Sommer 2010). *Epid Bull* 37: Seite 373-374.

Zweiter Fall von Milzbrand bei Heroinkonsument aus der Städtereion Aachen. *Epid Bull* 14: 124.

2009

Auch 2009 wieder gehäuft Meldungen von Paratyphus-B-Infektionen nach Türkeiufenthalten. *Epid Bull* 37: 376.

Aus Indien importierte Koinfektion mit dem Dengue- und Chikungunya-Virus - Informationen zum Erkrankungsrisiko. *Epid Bull* 23: Seite 227-228.

Chikungunya-Fieber nach Malediven-Aufenthalt. *Epid Bull* 38: Seite 384.

Chikungunya-Infektionen in Südostasien. *Epid Bull* 28: Seite 269.

Dengue-Fieber: Aktuelle Inzidenzdaten für Thailand. *Epid Bull* 2009; 9:79-80.

Deutschland erlebt im dritten Jahr in Folge eine Norovirus-Winterepidemie. *Epid Bull* 2009; 4: 26-29

Kuhpocken: Zu einer Häufung von Infektionen nach Kontakt zu „Schmuseratten“ im Großraum München. *Epid Bull* 6

Reiseassoziierte Infektionskrankheiten 2008. *Epid Bull* 39: 385-393.

RKI-Ratgeber Infektionskrankheiten – Merkblätter für Ärzte: Salmonellose (Salmonellen-Gastroenteritis). *Epid Bull* 13

Tollwutexposition durch Import von Tieren aus Endemiegebieten. Erfahrungsbericht aus dem Landkreis Lörrach *Epid Bull* 15: Seite 139.

Untersuchung eines Ausbruchs durch Lebensmittelvergiftung in drei Kindergärten in Berlin. *Epid Bull* 2009; 3: 17-21.

Zwei Erkrankungen an nicht-autochthonen Krim-Kongo hämorrhagischem Fieber diagnostiziert. *Epid Bull* 40: 397-398.

4.1.2. Selected relevant publications

Five important publications for the scientific community 2009–2012

1. **Ducomble T, Wilking H, Stark K, Takla A, Askar M, Schaade L, Nitsche A, Kurth A.** Lack of evidence for Schmallenberg virus infection in highly exposed persons, Germany, 2012. *Emerg Infect Dis* 2012;18(8):1333-5.
2. **Faber MS, Wenzel JJ, Jilg W, Thamm M, Höhle M, Stark K.** Hepatitis E Virus Seroprevalence among Adults, Germany. *Emerg Infect Dis* 2012;18(10):1654-7.
3. **Frank C, Werber D, Cramer JP, Askar M, Faber MS, Heiden MA, Bernard H, Fruth A, Prager R, Spode A, Wadl M, Zoufaly A, Jordan S, Kemper MJ, Follin P, Muller L, King LA, Rosner BM, Buchholz U, Stark K, Krause G, the HUS investigation team.** Epidemic Profile of Shiga-Toxin-Producing *Escherichia coli* O104:H4 Outbreak in Germany. *N Eng J Med* 2011;365(19):1771-80.
4. Buchholz U, **Bernard H, Werber D, Bohmer MM, Remschmidt C, Wilking H, Delere Y, Heiden MA, Adlhoch C, Dreesman J, Ehlers J, Ethelberg S, Faber MS, Frank C, Fricke G, Greiner M, Höhle M, Ivarsson S, Jark U, Kirchner M, Koch J, Krause G, Lubber P, Rosner BM, Stark K, Kuhne M, the HUS investigation team.** German Outbreak of *Escherichia coli* O104:H4 Associated with Sprouts. *N Eng J Med* 2011;365(19):1763-70.
5. **Faber MS, Stark K, Behnke SC, Schreier E, Frank C.** Epidemiology of hepatitis a virus infections, Germany, 2007-2008. *Emerg Infect Dis* 2009;15(11):1760-8.

Five important publications for the public 2009–2012

1. Final Report on the epidemiology of the Norovirus outbreak due to frozen strawberries, Germany 2012 (in German, Abschlussbericht) (Also see Report in the Epidemiological Bulletin 41/2012)
2. Yersiniosis – Risk factors in Germany. Epidemiological Bulletin 6/2012 (German) (based on **Rosner BM, et al.** *Epidemiol Infect* 2012;140(10):1738-47.)
3. Final presentation and evaluation of epidemiological findings in the EHEC O104:H4 outbreak, Germany 2011 (Abschlussbericht, in German and English)
4. Merkblatt: Informationen zur Vermeidung von Hantavirus-Infektionen (joint information sheet by RKI, Consiliar Laboratory for Hantaviruses, Friedrich-Loeffler-Institut, Bernhard-Nocht-Institut für Tropenmedizin)
5. Eis D, Helm D, Laußmann D, **Stark K.** Klimawandel und Gesundheit – Ein Sachstandsbericht. Robert Koch Institute, Berlin, 2010 (244 Seiten).

4.1.3. Awards and honours, 2009 - 2012

2010

Michael Höhle, 2nd Gustav-Adolf-Lienert-Preis 2010, German Region of the International Biometric Society (IBS), for his habilitation thesis "Statistical Modeling and Monitoring of Infectious Diseases".

4.1.4. Overview on collaborations in networks

Food-Borne Zoonotic Infections (Research Network FBI-Zoo, Germany):

Interdisciplinary research on the microbiology, clinical aspects and the epidemiology of food-borne bacterial zoonotic infections in humans and animals in Germany (*Campylobacter*, *Salmonella*, STEC, *Yersinia enterocolitica*).

VibrioNet

The research network VibrioNet connects different disciplines of human and veterinary medicine, ecology, molecular biology and epidemiology to evaluate the risk of climate change and the emergence of seafood- and waterborne infections with non-cholera-vibrio in Germany.

Food- and Waterborne Diseases Network (European Network, ECDC)

European network on surveillance, outbreak investigations, epidemiological research and control of food- and waterborne infections.

Network Rodent-Borne Pathogens (Germany)

Network (coordinated by Friedrich-Loeffler-Institut, Dr. Ulrich) on microbiology/virology, epidemiology and control of rodent-borne infections in Germany.

Food-borne viruses in Europe (coordinated by RIVM, The Netherlands)

European network on surveillance, outbreak investigations, epidemiological research and control of food- and waterborne infections.

Med-Vet-Net (European Network on Zoonoses Research, 2006-2010)

Interdisciplinary network involving institutes of veterinary health, public health institutes and university departments from many European countries (microbiology, virology, parasitology, epidemiological and clinical aspects, prevention and control).

4.1.5. Memberships and participation in Advisory Boards

Prof. Dr. Klaus Stark

- German Society of Epidemiology
(also: Member of the commission for the certificate in epidemiology)
- German Society of Medical Informatics, Biometrics and Epidemiology

Christina Frank, PhD

- ECDC: Member of FWD (Food- and Waterborne Diseases) Coordination Group

Dr. Bettina Rosner

- German Society of Epidemiology (DGEpi)
- Association for General and Applied Microbiology - VAAM

Dr. Helen Bernard

- EPIET Alumni Network (EAN) – Treasurer from 2009-2012

4.1.6. List of completed habilitation, dissertation or master theses in the Unit, 2009 - 2012

2012

Habilitation: PD Dirk Werber, Charité, Berlin School of Public Health

Year	Titel / Degree	Name	Title of thesis	University / Supervisor RKI
2010	MSc Epi	Katja Hille	"Years of life lost" ausgewählter Infektionskrankheiten anhand der Meldedaten nach Infektionsschutzgesetz	Charité / BSPH PD Dr. D. Werber
2010	BSc	Franca Kirchberg	Die Backcalculation-Methode und deren Anwendung zur Schätzung der HIV-Infektionsrate	Department of Statistics, University of Munich PD Dr. M. Höhle
2010	Diplom	Juliane Manitz	Automated detection of infectious disease outbreaks	Department of Statistics, University of Munich PD Dr. M. Höhle
2011	MSAE	Sandra Dudareva	Analysis and interpretation of surveillance and research data - four examples how to address public health relevant questions	Charité / BSPH C. Frank, PhD
2011	Diplom	Annika Witt	Count data time series modelling of diseases covered by the German Infection Protection Act	Department of Statistics, University of Munich PD Dr. M. Höhle
2011	Diplom	Mirjam Rehr	Statistische Methoden zur räumlichen und zeitlich-räumlichen Clusterdetektion	Department of Statistics, University of Munich PD Dr. M. Höhle
2011 ongoing	Ph.D.	Felix Weidemann	Statistical Modelling of Dynamic Systems for Infectious Disease Epidemiology	Department of Statistics, University of Munich PD Dr. M. Höhle
2012	MSc Epi	Karina Preußel	Vergleich der Virulenz gastrointestinaler Infektionserreger in Deutschland	Charité / BSPH PD Dr. D. Werber
2012	MSc Epi	Katrin Neubauer	Polio eradication - analysis of the Enterovirus surveillance in Germany	Charité / BSPH Prof. Dr. K. Stark
2012	MSAE	Mona Askar	Die Identifizierung von Risikofaktoren als Grundlage für gezielte Präventionsmaßnahmen am Beispiel von lebensmittelassoziierten Erkrankungen	Charité / BSPH Dr. B. Rosner
2012 ongoing	MSc	Michael Laimighofer	Stochastic differential equations and their parameter inference for the susceptible-infected-recovered model	Department of Statistics, University of Munich PD Dr. M. Höhle
2012 ongoing	PhD	Maëlle Salmon	Modern algorithms for the automatic detection of outbreaks	Enrolment ongoing PD Dr. M. Höhle

4.1.7. Presentations as invited speaker, 2009 – 2012

Staff from the Gastrointestinal Infections, Zoonoses and Tropical Infection Unit were invited to speak at 79 conferences.

4.1.8. Reports and written scientific advice to the Ministry of Health, 2009-2012

There were 188 reports and written scientific advice to the Ministry of Health between 2009 and 30.09.2012.

Unit 36: Respiratory Infections

Unit Head: PD Dr. Walter Haas

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1. Unit 36: Respiratory Infections

Head: PD Dr. Walter Haas

Deputy: Dr. Silke Buda

2. Tasks and goals of the Unit

Respiratory infections are the leading cause of death among infectious diseases and pneumonia is the leading single cause of death in children younger than five years of age - killing every year about 1.2 million children and accounting for approximately 18% of mortality in this age group worldwide (<http://www.who.int/mediacentre/factsheets/fs331/en/index.html>). In Germany, it is estimated that approximately 400,000-600,000 outpatient visits and 230,000 hospital admissions per year are caused by community-acquired pneumonia alone with 13% of these dying in the hospital (<http://www.sgg.de/ergebnisse/leistungsbereiche/ambulant-erworbene-pneumonie.html>).

In 2002, within the Centre for Infectious Disease Epidemiology at the Robert Koch Institute (RKI), a team was formed to work on the epidemiology of respiratory infections. With the establishment of the Department for Infectious Disease Epidemiology in 2003, this work was assigned to the Unit for Respiratory transmitted Diseases and Vaccine Prevention. With the recognition of the huge burden of respiratory infections, the need to prepare for the pandemic threat of influenza, and the opportunity to reorganise the Department with resources provided by RKI 2010 the Respiratory Infections Unit was established, in 2006.

2.1. Summary

Assessing the epidemiology of respiratory infections in the German population, the development and evaluation of strategies to reduce disease burden represent the main tasks of the Unit of Respiratory Infections. For this purpose the systematic analyses of data from the notification system, from the virological and syndromic sentinel surveillance is complemented by surveillance in collaboration with specific networks (e.g. paediatric hospitals, ICUs), outbreak investigations, and clinical epidemiological studies. A special focus is put on diseases with high priority for public health: Influenza, tuberculosis, and legionellosis. The results are regularly reported to the medical community and the public. Specific studies address the burden of Influenza (and other acute respiratory diseases), the risk of infection, factors facilitating transmission, and the efficacy of vaccination and nonpharmaceutical interventions. Since 2003 the Unit is in charge for scientific advice on pandemic influenza preparedness and the Influenza Task Force at RKI. Following in the tracks of Robert Koch, the unit is responsible for surveillance, epidemiology, and control of tuberculosis. A stagnating trend in case numbers and increasing incidence in children demonstrate the need of scientifically based strategies to prevent a resurgence of tuberculosis. In this context, we work to introduce new indicators for rapid assessment of the epidemiological situation and longer-term trends, as well as molecular epidemiological tools for the detection of clusters and the interruption of chains of infections. Vulnerable groups such as children, the elderly, migrants, prisoners, and people living with HIV/AIDS that suffer from active TB are addressed by different projects in collaboration with national and international partners. Only recently, we could extend our work to include travel associated cases of legionellosis within the European network.

2.2. Current status of the work and summary of relevant results

2.2.1 Surveillance of influenza and other acute respiratory infections

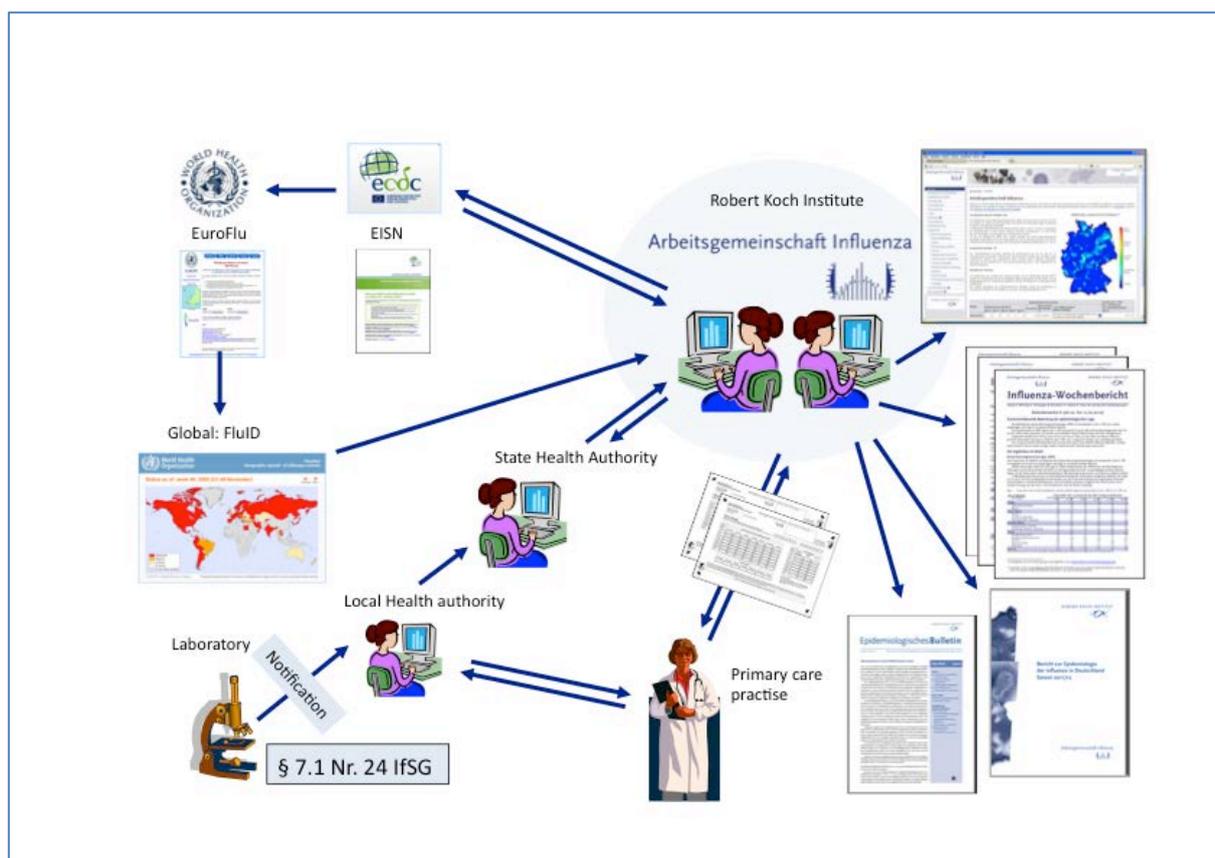
Syndromic surveillance of acute respiratory infections

The Working Group Influenza is a physician-based sentinel surveillance system of acute respiratory infections (ARI) with special focus on influenza that has been fully implemented by Unit 36 in 2009. It consists of two complementary systems, the syndromic and the virological surveillance. The syndromic surveillance system relies on voluntarily participating physicians in primary care (general practitioners, internists in primary care and paediatricians) who report on consultations because of ARI among their patients (Buda et al., Bericht zur Epidemiologie der Influenza in Deutschland Saison 2011/12). Virological surveillance is done with a subsample of about twenty per cent of AGI physicians who were instructed to take samples of the upper respiratory tract, e.g. nasal swabs, of a weekly number of 3-5 patients with influenza-like illness (ILI) and send them to the National Reference Center for Influenza (NRCI).

The surveillance is carried-out year-round and we have developed a modelling approach to allow estimation of the burden of influenza that is attended to by the primary care sector.

Surveillance results are reported online and in a weekly (April to September monthly) bulletin that also includes notification data from the mandatory reporting of laboratory confirmed influenza, virological data by state reference laboratories of Baden-Württemberg, Bavaria, Mecklenburg-Western Pomerania, Saxony, Saxony-Anhalt and Thuringia, and a summary of the international situation based on reports published by the World Health Organization (WHO) and the European Centre for Disease Prevention and Control (ECDC). In Addition, the assessment of the epidemiological situation is transmitted to ECDC, WHO, and the Pandemic Influenza Working Group (PIWG) at the Global Health Security Action Group (GHSAG) thus contributing to their international reports.

Figure 17: Working Group on Influenza (AGI): Schematic flow of work and information



ICD10-based electronic surveillance

A new surveillance system easy to use for the physicians and affording automatic fast data processing has been developed by Unit 36, based on a pilot project in cooperation with Hessisches Landesprüfungs- und Untersuchungsamt im Gesundheitswesen starting in 2007. SEED^{ARE} is a surveillance instrument to monitor burden of acute respiratory diseases – especially of influenza – in the German population based on electronic patient records in physician information systems for primary care providers. At this time approximately one hundred primary care practices including general practitioners, paediatricians, and internists are taking an active part in the sentinel. The software interface was developed at the RKI and a corresponding software tool was integrated in five physician information systems which are in widespread use in Germany (approx. 25% of primary care practices). The software tool captures case based anonymized data such as consultation date, age, gender, ICD-10 codes of patients with acute respiratory diseases (defined by ICD-10 codes out of following blocks: J00-J06, J09-J18, J20-J22 and additionally, J44.0 and B34.9) for each patient consultation as well as aggregated data such as the number of all patients visiting the doctor(s) in the sentinel practice per day (stratified by 7 age groups). The physicians send an encrypted data file to the RKI once a week, where the data are automatically imported in a RKI database and analysed with validity and plausibility checks. First results of detailed data analyses

were published in annual reports of AGI for the influenza seasons 2009/10, 2010/11, and 2011/12. Beginning with the winter season 2012/13 the data of SEED^{ARE} are included in the weekly reports of AGI to strengthen the AGI surveillance system. In principle, the approach developed by our group can be extended to as surveillance instrument for monitoring of other diseases and interventions in primary care.

Web-based surveillance of ARI at the population level

As recently as 2011, with third-party research funding, an online surveillance system has been developed by Unit 36 to estimate the disease burden in the general population (i.e. independent of physician visits). This system, named GrippeWeb, is an online tool that enables RKI to "communicate" directly with the public. It allows the monitoring of the incidence of acute respiratory illnesses, including influenza-like illness. It was designed with the successful Dutch example in mind (De Grote Griepmeting) which has motivated also other countries to set up a similar system. Registered participants receive an e-mail once a week with the weblink to the results of the surveillance, which are published online, and a reminder to report symptoms of acute respiratory illness. The system is now running since 1.5 years and has attracted more than 4000 participants. It has generated interesting data, for example the frequency of consulting a physician in case of an acute respiratory illness in general (approx. 15-25%) or an influenza-like illness (40-50%) or the frequency of an acute respiratory illness throughout the year (children: 3-4 times/year, adults: (1-)2 times per year). It is envisaged to co-operate with the Helmholtz Zentrum für Infektiologie to stimulate participants to self-collect samples for virological validation of the syndromic results. So far, this system is unique in Germany and has also the potential to be extended to monitor other infectious disease syndromes.

Monitoring of published human cases of highly pathogenic avian influenza A(H5N1)

In addition, given the threat of avian influenza (AI) viruses to humans in Europe, a routine monitoring instrument was established in 2005 by Unit 36, condensing information on all human AI and other zoonotic influenza cases worldwide reported from the WHO and other sources into a single line list. This line list was maintained until March 2011 and made available online (http://www.rki.de/Prevention/Avian_Influenza/Avian_Influenza_node_en.html).

An epidemiological evaluation of the instrument (09/2006 to 08/2010) showed that these data from the public domain yield important epidemiological information on the global AI situation, which was not evident from single case reports. E.g., a longer delay from symptom onset to hospital admission and belonging to older age groups were associated with higher mortality in AI patients. There were independent country-specific effects such as a rather low CFR in Egypt which were not explained by the patients' young age and early hospital admission. Given these advantages, the placing of a publicly accessible line list of anonymised human AI cases, e.g. directly by WHO, was suggested (Fiebig et al., Euro Surveill 2011).

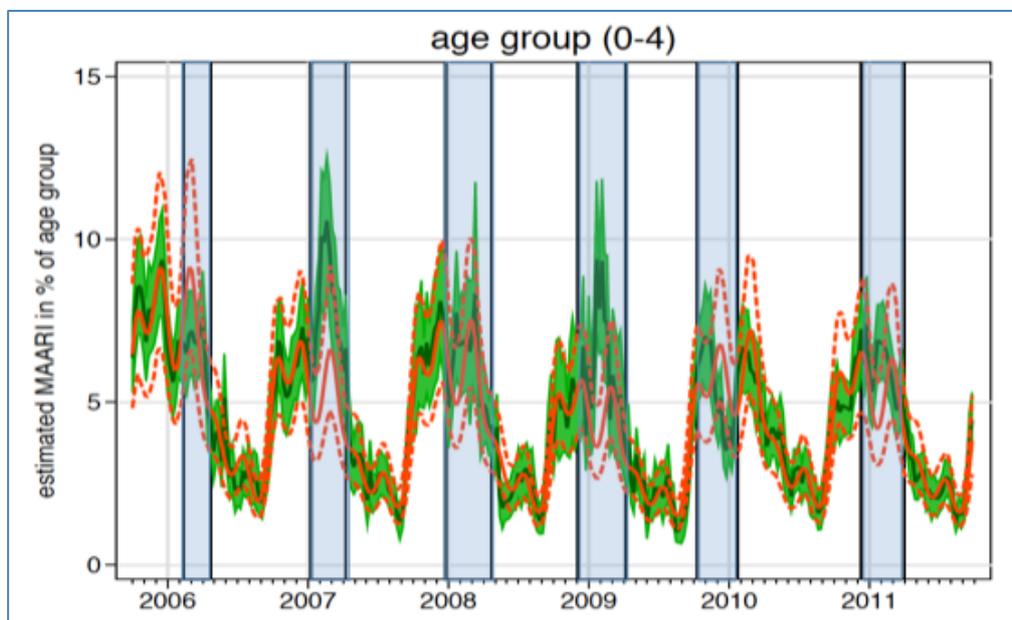
2.2.2 Burden of disease caused by influenza and other acute respiratory infections

Modelling the excess burden of influenza at the level of primary care

In the context of the course of the influenza pandemic (H1N1) 2009 it became clear, that the availability of estimates of the burden of disease in the population and the severity are of paramount importance. The number of patients seeking health care is a central indicator: (1) as a proxy for the impact on the burden of the primary care system; (2) as a starting point to estimate the number of persons ill with influenza (number seeking health care divided by the proportion of diseased seeking health care = total ill); (3) as the denominator data for the calculation of case fatality rate and the proportion hospitalised (severity indicators); (4) for economic calculations. Using data of the syndromic surveillance system, we developed a statistical model to estimate the excess of outpatient visits caused by ARI (manuscript submitted). For estimating the number of outpatient visits we used a regression model for counts and for the baseline a cyclic regression model. Using this approach, we estimated the highest ARI burden within the last 10 years for the influenza season 2004/05 with an excess of 7.5 mill outpatient visits (CI_{95%} 6.8-8.0). In contrast, the pandemic wave 2009 accounted for one third of this burden with an excess of 2.4 mill (CI_{95%} 1.9-2.8); we could show that during the pandemic school children in the age group 5-14 years were most affected with 9.6% (95%-CI 7.4%-12.0%), whereas in most years the age group of infants (0-4

years) was most frequently seen by a primary care physician. In addition to age specific analysis, the developed method allows separate estimates for 4 different geographic regions in Germany. Estimates can be produced also real time during the influenza waves, piloted for the first time for the 2012/13 influenza season.

Figure 18: Observed excess outpatient visits for acute respiratory infections (green) during periods of influenza virus circulation (light blue) influenza seasons 2006/07 to 2011/12 for the age group 0-4 years; modelled baseline and confidence intervals (dotted line) in red. (an der Heiden et al., submitted)



Modelling excess mortality associated with influenza

Modelling of excess mortality due to influenza is the standard method to calculate the magnitude of the most severe outcome of influenza in populations. Different methods exist, however, and methods can only use the data that are available. Recently, detailed historic mortality data (from 1999-2009) have become available which require to develop a new model and re-estimation of influenza-attributed mortality in those years (co-operation with statisticians in the department). Unit 36 also co-operates with two WHO supported teams on the global mortality of the pandemic A(H1N1)pdm09 virus. Both teams have presented estimates on the global mortality of pandemic influenza 2009 (partially published), already.

2.2.3 Transmission and risk of infection with influenza

Clinical epidemiological studies in households during seasonal and pandemic influenza

Over 4 seasons between 2007/08 and 2010/2011, spanning the pandemic wave 2009, our unit carried-out clinical epidemiological household studies on the virus shedding and transmission (and its prevention) of influenza. Primary care practices collaborating in these studies recruited index cases with laboratory confirmed influenza. For one week after onset of symptoms, the index case and members of the household were systematically monitored for symptoms and daily samples of nasal secretion were taken. In the seasons 2009/10 and 2010/11 a cluster-randomised intervention study was embedded in the investigation (ClinicalTrials.gov Identifier: NCT00833885). Households with an identified index case of influenza were randomised into one of three intervention arms: 1. group, where the household received general information about transmission of influenza virus and means to prevent it (Controls); 2. group, which received surgical masks and was asked to wear them whenever they are in close contact with the index case or other persons of the household that became ill during the observation period; 3. group, which was given and asked to wear surgical masks as well as to execute intensified hand hygiene. In addition to assessing the secondary attack rate as primary outcome measure, the compliance to those interventions was evaluated by questionnaires (Süss et al., *BMC Infect Dis* 2012).

Results of the intervention study demonstrated tolerability of wearing surgical facemasks also for (sick) children, which is most important for policy decisions concerning the choice of interventions. In addition, the non-pharmaceutical interventions tested most likely are effective to prevent transmission of the virus; the odds of developing influenza were reduced by 86% (adjusted OR=0,16, 95%KI=0,03-0,92), if the measures were implemented within 36 hours after the onset of symptoms in the index case or by 70% (adjusted OR=0,30, 95%KI=0,10-0,94), if they were applied stringently.

Analysis of virus shedding showed similar patterns for seasonal influenza and the pandemic virus that correlated well with the severity and course of symptoms. In symptomatic patients virus shedding started in 30% before onset of symptoms and was influenced little by antiviral treatment.

Serological surveillance

Due to the highly variable manifestation of clinical disease caused by acute viral infections, the serological measurement remains the standard approach to measure infections rates and transmission. With the 2009 pandemic, a revival of the need for population based studies on influenza infection was identified. In order to collect information on potential pre-existing immunity to the new virus and to measure age specific infection rates of the influenza A (H1N1) 2009 pandemic in Germany, we conducted a seroprevalence study based on samples from an on-going representative nationwide interview and examination survey for adults that had started 6 months prior to the first registered case of influenza A (H1N1)pdm09 in Germany (Dudareva et al, Plos One 2011). The highest proportions of cross-reactive antibodies at titre ≥ 40 before the pandemic were observed among 18–29 year olds, 12.5% (95% CI 7.3–19.5%). Despite this finding, the same age group showed also the highest increase in seroprevalence between pre- and post-pandemic of 29.9% (95% CI 16.7–43.2%).

Risk factors and complications of influenza and pneumonia

In 2011 a third-party funded project started to identify risk, concomitant, and secondary diseases of influenza and community-acquired pneumonia in Germany. The advantage of SEED^{ARE} technology for collecting anonymised patient data including ICD-10 diagnosis codes on a computerised basis should be exploited in this project. Therefore, based on the experience with the software interface of SEED^{ARE} the requirements for a new interface were developed at RKI suitable to collect over several months surrounding the event of acute illness the pertinent data from electronic patient records of physician information systems in 200 primary care practices for this study. A public tender was published Germany-wide in July 2012 for external programming of the new interface. The pilot phase will start in November 2012 and it is planned to roll-out the software to the 200 practices before start of the seasonal influenza wave 2012/13. Currently an extensive review of literature on complications of viral seasonal and the 2009 pandemic influenza is carried-out and a systematic literature-review is being prepared to prepare and guide the analysis of the data retrieved in the course of the project.

2.2.4 Outbreak investigations and interventions to prevent infection and severe disease

Information on nosocomial spread from SARI surveillance in paediatric hospitals

The potential of outbreaks of respiratory infections, especially in institutional settings (e.g. elderly homes, hospitals) is frequently underestimated. In collaboration with the paediatric network for rare diseases (ESPED) We conducted a nationwide hospital-based prospective study in Germany of influenza A(H1N1)pdm09 cases among children <15 years of age. Children admitted to paediatric intensive care units and related deaths during the 2009–10 pandemic and the 2010–11 post pandemic influenza seasons were included into the study. One striking result was, that 14% of these most severe cases represented hospital-acquired infections (Altmann et al, EID 2011; Altmann et al, EID 2012).

RSV-outbreak investigation in a haematology unit

In January 2012 RKI was invited to assist in the investigation of a large nosocomial RSV outbreak among adult haematology patients in a university hospital. It became clear that the outbreak was

the largest ever recorded in the literature among haematology patients and had started already in November 2011 (three months before the RSV wave in the community) and lasted until the end of January 2012. The outbreak was detected late because RSV (and other respiratory agents) was not tested for. Our analytic studies revealed that (mostly unrecognised) RSV patients had been placed in one room together with a susceptible, other patient; furthermore, patients who socialised more seemed to be at higher risk for infection. Due to the intervention-measures taken by the end of January a second wave of hospitalised cases admitted to the hospital with community acquired infections in February 2012 from the community did not lead to another nosocomial outbreak. The investigation was carried-out in collaboration with the University Hospital Heidelberg, the local health and state health authorities. A report agreed upon with all stakeholders has been finalised and currently a manuscript is being written up.

Monitoring of influenza vaccine effectiveness using surveillance data

Influenza viruses evolve constantly, therefore the influenza vaccine antigen composition needs to be adapted every year. The vaccine strains (containing one antigen of an A(H1N1), one of an A(H3N2) and one of a B reference strain) are recommended each year by the WHO. The protection of the vaccine against disease needs to be assessed through observational studies during the season. However, estimates of influenza vaccine effectiveness from previous years cannot be simply carried over to the next year. During the pandemic wave 2009 Unit 36 applied a test-negative case-control-study using national influenza data ($n=2.002$) of the Arbeitsgemeinschaft Influenza (AGI) to estimate vaccine effectiveness and established this approach for routine monitoring the seasonal vaccine effectiveness against influenza A (H3N2) during the season 2011/12. The influenza vaccine effectiveness adjusted for age group and week of disease onset was 49% (95% KI: 17 – 69 %). Point estimates of the influenza vaccine effectiveness were higher in younger age groups than in older age groups. Using this method, influenza vaccine effectiveness can be monitored during subsequent seasons. Results for the season 2011/12 are published in *Epid Bull* 41/2012.

Evaluation of the use of antivirals during the 2009 pandemic

The 2009 influenza pandemic provided a unique opportunity to investigate factors associated with severe clinical disease and the impact of pharmaceutical interventions. International and national guidelines recommend early antiviral treatment for patients with severe influenza or those at increased risk of severe illness. However, little was known about the use of antivirals in Germany. Using national notification data ($n=170,856$) we determined that the proportion of cases with laboratory confirmed A(H1N1)pdm09 infection that had been treated with antivirals during the pandemic in Germany was 21%. Multivariable analysis showed that the chance for being treated with antivirals was between one half to two thirds for children in comparison to adults, independent of underlying medical conditions and severity of disease. The underlying reasons leading to the observed differences in patient management of children remain to be investigated. The results were presented at 4. German Influenzakongress 2012 (Erfurt) and the 4. ESWI Influenza Conference 2011 (Malta). The publication is in progress

2.2.5 Pandemic influenza preparedness

In Germany, a National Pandemic Preparedness Plan was written by the Federal level and the Federal States level in 2005 and updated in 2007. During the recent H1N1-pandemic Unit 36 served as a think tank for the Institute and led the field-investigations of the first outbreaks in Germany, in Spring 2009. Within the first 13 weeks of the pandemic, 16 outbreak investigations were carried-out to investigate virus transmission and clinical presentation of the initial cases. These studies had been prepared and tested by our unit in the preceding two years.

Evaluation of the response to the 2009 pandemic

Immediately following the pandemic, evaluations of Germany's pandemic preparedness and response were carried-out by different institutions in the public health sector at the national, regional and local level. In March 2010, a national evaluation workshop was organised by RKI with representatives from different professions involved in the pandemic response. Furthermore, Unit 36 reviewed international and national reports and articles regarding the evaluation of national

pandemic preparedness activities and the response to the pandemic (H1N1) 2009 in Germany in order to identify key lessons.

Key findings of the evaluations were: optimise concepts for vaccine logistics, distribution and cost coverage, define a clearer role of medical and public health professionals in immunisation and aim for more flexible contracts. Influenza surveillance could benefit from strengthening the instruments for timely monitoring of severe disease (hospital and mortality surveillance) and of vaccination coverage. Risk and crisis communication have been identified as important areas for the planning process. These results were presented at 4. German Influenzакongress 2012 (Erfurt) and the 4. ESWI Influenza Conference 2011 (Malta).

Updating of pandemic preparedness plans

Unit 36 coordinates the update of the scientific part of the national pandemic preparedness plan. During this process, a new expert committee is being established (Expertenbeirat Influenza) consisting of public health experts of Federal institutes and of professional medical societies. These experts will support RKI. Furthermore, RKI advises the Federal States in which epidemiological situations during a pandemic which measures are appropriate.

RKI has an internal plan where the main tasks and responsibilities of the institute in case of a pandemic are described. Unit 36 coordinates the work of the RKI Task Force Influenza and the update of the influenza module in the crisis plan of the institute. In 2012, a meeting with all persons responsible for pandemic preparedness planning and general crisis planning took place. Focus of the discussions was the differentiation between general and disease specific planning.

2.2.6 Tuberculosis surveillance and control

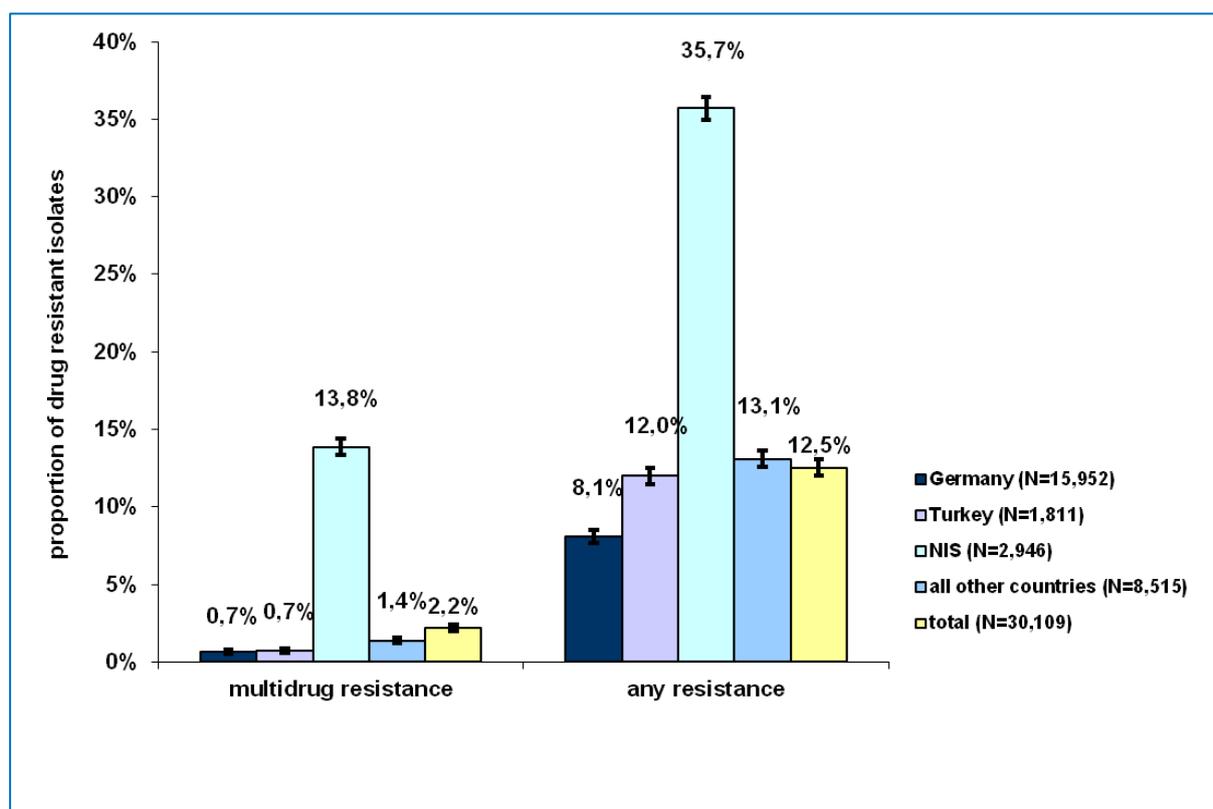
Monitoring progress of TB control in Germany

130 years after the first demonstration of the tubercle bacillus by Robert Koch in March 24th 1882 tuberculosis (TB) remains at the top of public health priorities among communicable diseases identified by RKI, shared only by HIV (Balabanova et al., Plos One 2011). The Berlin Declaration on Tuberculosis signed by the Ministers of Member States of the WHO European Region at a meeting with the WHO Regional Director for Europe and high-level partners at the WHO European Ministerial Forum on Tuberculosis "All against Tuberculosis", held in Berlin on 22nd October 2007, shows that the importance of TB control has also been recognised at the political level.

Member States also committed themselves to closely monitor and evaluate the implementation of the actions and commitments outlined in this Declaration. For this purpose, the M&E (Monitoring and Evaluation) Framework was developed by WHO Euro. Unit 36 participated in the development of this framework and tested this approach by selecting a set of indicators from the surveillance point of view, demonstrating that there were no specific gaps in Germany's TB surveillance and control. Furthermore, to assess trends, epidemiological indicators of the follow-up to the Framework TB Action Plan by ECDC were applied to Germany. All but one indicator fulfilled the defined targets. This suggests an overall decreasing TB trend and thus rather successful TB control in Germany. However, a potential increase in notification rates in children stresses the need for a close monitoring of childhood TB – including its possible determinants – and to implement countermeasures at best.

Multi and extensively drug resistant TB (M/XDR-TB), recognised as a major public health threat to the WHO Europe an region, has been recently addressed by WHO Euro with the "Roadmap to prevent and combat drug-resistant tuberculosis", where Unit 36 participated as a member of the steering group as well as member of the task force for the development of a respective M&E framework.

Figure 19: Proportions of any and multidrug-resistant tuberculosis by country of birth, Germany 2002-2009 (pooled data)



Surveillance of tuberculosis in Germany

Case-based electronic notification of tuberculosis has been introduced in Germany with the Communicable Disease Law Reform Act in 2001. The TB surveillance system was updated in agreement with international standards. The data allow detailed analysis of the TB epidemiology. Results of this analysis are compiled in a comprehensive yearly report that is presented to the public at World TB day in March each year, usually in the context of a scientific TB conference in Berlin. In addition, data are reported to the European level and to WHO Euro as requested.

A major benefit of the surveillance system implemented in 2001 has been the inclusion of information about drug resistance against first line anti-TB drugs. Effective treatment of drug resistant TB is crucial to avoid relapse or further development of drug resistance. A stratified analysis (covering 2002-2004) of drug resistance patterns observed in tuberculosis patients notified in Germany showed that only four drug resistance patterns contribute $\frac{3}{4}$ of resistant TB cases (>60% to Isoniazid/Streptomycin). MDR-TB equals resistance to at least four drugs in $\frac{2}{3}$ of cases. An on-going study builds upon the previous findings extending the data set on the recent notification years. This study is expected to highly contribute to improve the clinical management of TB patients in Germany by informing on the optimal initial treatment regimen of TB patients suspected of having drug resistant TB.

Assessing and improving treatment outcome of TB

A major achievement of the introduction of the new notification system is the availability of treatment outcome results as indicator for successful TB control and case management. However, definitions of treatment outcome differ between WHO, ECDC and the national level in Germany. Therefore a study evaluating what matters in tuberculosis treatment outcome monitoring was set-up using German 2002-2008 notification data.

Differences in case inclusion for treatment success rate (TSR) calculations were found to highly impact TSR: 80.6% were found for the RKI approach, statistically significantly ($P < 0.001$) higher than applying WHO (75.7%) or ECDC (76.6%) case inclusions, however still not reaching the European TSR target of 85%. In multivariable models, factors associated with treatment success

were investigated. Irrespective of ECDC, WHO and RKI case inclusion criteria, being male, of older age, having multi-drug resistance and living in an Eastern Federal State of Germany were negatively associated with treatment success. A third-party follow-up and extension of this study on a European level is planned for 2013.

Although up-to-date national guidance documents on TB treatment are available, little is known about adherence to recommendations and the overall quality of TB treatment (to note: all TB guidance documents are developed by the German Central Committee against Tuberculosis [DZK] in close collaboration with Unit 36). We currently perform an evaluation of TB therapy quality in Germany based on TB drug prescription data provided by Insight Health® for the years 2006-2009.

Surveillance of extrapulmonary TB

Gaps have also been identified for the surveillance of different TB forms. As TB surveillance commonly focuses on the main organ affected, which by definition is pulmonary whenever lungs are involved, we suspected an underestimation of extrapulmonary TB (EPTB) forms in routine analyses. We thus conducted a study to estimate the frequency of all individual EPTB forms (classified as main or secondary site), describe demographic and clinical characteristics of patients affected by specific extrapulmonary sites of disease, and identify factors associated with meningitis TB in order to illustrate the real EPTB burden.

We found that analysing solely the main site of disease ignored one third of extrapulmonary manifestations reported as the secondary site. Using of all available information, meningitis TB – involving a 25% case fatality ratio – accounted for 0.9% of TB patients. It was more likely among children younger than 10 years old, female patients and individuals born in the South-East Asia and the Eastern Mediterranean WHO regions. We concluded that EPTB manifestations were indeed more widespread in Germany than previously shown. A manuscript with these findings has been published (Ducombe T et al., Eurosurveillance 2013).

Molecular surveillance of TB

Molecular typing of TB strains has contributed significantly to a better understanding of transmission and populations at risk. However, the public health impact of molecular surveillance embedded in routine TB surveillance and control needs still to be determined. In collaboration with the public health offices (PHO) in Baden-Wuerttemberg and the National Reference Laboratory for mycobacteria in Borstel, Unit 36 has initiated a pilot project investigating the linkage of molecular typing and TB notification data (2008-2010). Among 860 notified TB patients from Baden-Wuerttemberg with available molecular typing information, 208 (24%) were cluster-associated (80 clusters). About 60% of these cluster involved two or more PHOs. About 52% of clusters, especially those involving two or more PHOs, were not confirmed by epidemiological links identified through conventional contact investigation. Molecular typing may thus complement classical contact tracing in uncovering transmission chains. The practical and public health relevance of molecular typing for the investigative work of PHOs remains to be further explored. In-depth analyses and interpretation of results are on-going.

2.2.7 Tuberculosis among vulnerable groups

Additional studies are carried-out based on the collected notification data to describe the epidemiology in specific groups at risk for TB or specific disease manifestations.

Improved diagnostics and surveillance of TB in children

Only recently, children have been internationally recognised as a neglected group for TB control and case management. Specific studies to enhance diagnostics and surveillance of childhood TB are specifically addressed by an investigation of diagnostic (PCR, culture) findings by use of gastric aspirate, embedded in a European study in the context of the EUPHEM fellowship program. At this, in collaboration with European NRLs a survey is performed to gain a systematic overview of laboratory diagnosis of paediatric TB in the EU/EEA member states; 20/30 member States participated in the survey; 4 provided 5-year raw data sets. The analysis is on-going. In addition Unit 36 contributes actively in the development of national and international recommendations for diagnostic and treatment of TB in children.

TB in the elderly

To address the impact and challenges in TB control for an aging population, demographic, clinical and bacteriological characteristics between elderly and younger adult TB patients among all TB cases notified in Germany between 2002 and 2006 were compared and published (Hauer et al., *Eur Respir J* 2011). The study identified several specific epidemiological features of TB in the elderly, such as a high proportion of genitourinary TB (predominantly among males), a considerable fraction of culture-confirmed TB cases, a relatively small contribution of active case finding, comparatively low drug-resistance rates except for pyrazinamide, low treatment success and high mortality rates. The study provided substantial new evidence that elderly adults present a vulnerable group for TB in Germany.

TB in big cities

In low incidence countries TB control increasingly focuses on populations at risk, with urban risk groups being one of the most relevant targets. Unit 36 initiated a survey on the TB situation in European Big Cities in 2008, which prompted the establishment of a Wolfheze European Consensus working group including members from Unit 36, the Health Protection Agency/UK, KNCV Tuberculosis Foundation/The Netherlands, ECDC, and other members from EU Member States. A Workshop was held at the RKI to work on a consensus document in 2011. The group is in the state of drafting several manuscripts in regard to TB control recommendations and the epidemiological situation in EU Big Cities.

TB in prisons

One specific population at risk is the prison population, although little is known in low incidence high resource settings. In collaboration with the prison hospital (Justizvollzugskrankenhause) Berlin in the context of a BSPH master thesis we performed a retrospective case series of tuberculosis patients in prisons in Berlin from 2007 to 2010, hereby following up on an investigation covering 1996-1998.

It was shown, that the case detection rate (CDR) for definite pulmonary TB based on X-ray entry screening had nearly halved between the two study periods in the Berlin prison system (208 in 1996-1998 vs 111 cases/100,000 X-ray examinations in 2007-2010). CDRs were particularly high among patients older than 60 years and those originating from the Former Soviet Union countries (estimate of 3,396 cases/100,000 population) .

The series of 62 TB cases documented from 2007-2010 was characterised by high proportions of male (94%) and foreign citizens (61%), as well as high levels of MDR-Tb (12%, N=34). It revealed Hepatitis B or C/TB and HIV/TB co-infections (18% vs 3%) at systematic screening. Entry screening remains hence important to avoid (potentially MDR)-TB transmission in prison. Approaches targeted to specific subpopulations and infection screening remains to be evaluated. Together with the German Committee to fight against Tuberculosis a best practices workshop bringing together local health authorities and physicians in charge of the health in prisons is planned for 2013.

TB in migrants and the population with migration background

Many Western European countries observe a significant impact on their epidemiological situation by TB occurring in persons originating from high TB prevalence countries or with other migration background. In an in depth 2002-2009 surveillance data analysis we found that declines in the incidence were higher in German than in foreign nationals (43.3% vs. 35.2%). In 2009, TB incidence in foreign nationals was 5.5-times higher than in Germans. The majority of patients born outside Germany originated from a Newly Independent State (NIS) of the former Soviet Union with 18.9% (362/1,918), followed by Turkey. The proportion of drug resistant TB was higher in foreign borns – particularly in patients from the NIS, but not from Turkey. Foreign born patients showed an almost two-times higher proportion of treatment interruption or defaulting.

In conclusion, in Germany TB increasingly concentrates in specific populations with migration background that differ according to proportions of drug resistance and treatment success. To assure effective TB-control and case management more detailed knowledge on different migration groups and their specific risks is necessary.

To investigate of the TB risk of second generation migrants, Unit 36 is performing a prospective cross-sectional study in Berlin in collaboration with Charité, the Tuberculosis Centre at the Local Health, Office Berlin-Lichtenberg, and DZK. Of 182 patients, 98 (54%) were first generation migrants, 20 (11%) were second generation migrants with the remainder being native residents. TB notification rates per 100,000 people were 4.1 for native residents, 28.8 for first generation (relative risk (RR): 7.0) and 13.1 for second generation migrants (RR: 3.2). These preliminary data suggest that two-thirds of all TB cases in Berlin occur among individuals with migration background. Both, first and second generation migrants are at increased risk of TB compared to native residents and should be considered for preventive measures.

2.2.8 HIV/TB comorbidity in Germany

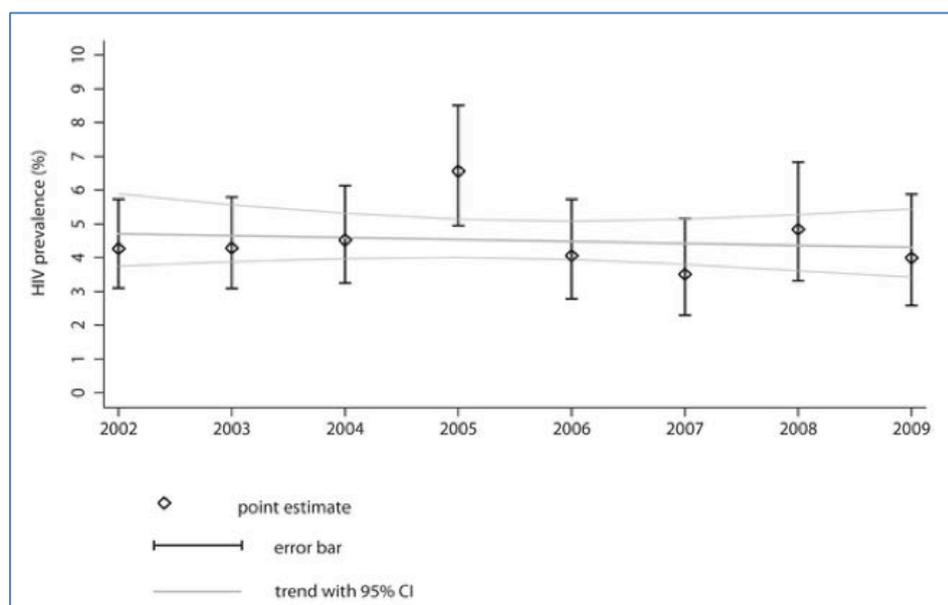
Tuberculosis (TB) and HIV comorbidity is, together with M/XDR-TB, considered a leading cause impairing success in TB control: TB as an AIDS-defining disease is a major cause of morbidity and mortality in people living with HIV; HIV-positive individuals infected with *M. tuberculosis* complex bacteria are placed at a 20 to 30 times greater risk of developing active TB.

However, the HIV/TB burden is difficult to assess in Germany (and other European countries) as data confidentiality precludes notifying the HIV status of TB patients in the national surveillance system. To still address this issue, we investigated the long-term observational open multicentre cohort ClinSurv HIV, which systematically captures TB diagnoses. Our aim was to first estimate the HIV-prevalence in TB patients, and second, to determine the occurrence of TB as AIDS-defining disease in Germany.

On average, the estimated HIV-prevalence in TB patients average was 4.5% from 2002-2009, without significant trend. This level approximates available surveillance data from neighbouring countries and indicates a non-negligible HIV/TB burden in Germany. Our estimation approach is valuable for epidemiological monitoring of HIV/TB within the current legal frameworks.

As to the occurrence of TB as AIDS-defining disease, we found that 2.7% (252/9,437) of the individuals enrolled in ClinSurv HIV from 2002-2011 were diagnosed with active TB. These HIV/TB patients were predominantly male, aged between 30-39 years and originating from Sub-Sahara Africa. The TB incidence density rate was 0.8 cases per 100 person-years (PY) overall. Highest rates were observed among female and male patients originating from Sub-Sahara Africa (2.2 vs. 3.4 per 100PY, respectively). These results help to target prevention and control strategies on risk groups and to consider them in HIV/TB monitoring.

Figure 20: Estimated HIV-prevalence in TB patients in Germany, 2002 to 2009. (Fiebig et al., *Plos One* 2012)



2.2.9 Disease caused by non-tuberculous Mycobacteria

Several industrialised countries have reported an increase of non-tuberculous mycobacterial (NTM) diseases in children. Worldwide, information on the therapeutic management and treatment outcomes in children are scarce. In a prospective nationwide study including all paediatric hospitals in Germany between October 2002 and September 2005, 102 immune-competent children with incident NTM disease had been identified and the epidemiology of NTM disease described. A follow-up study in 2011 on the long term course of disease, treatment regimens and outcomes in these children showed that children with NTM lymphadenitis are not treated in line with international and national guidelines in Germany and the cure rate was not satisfying. The Publication of the results is in progress.

In order to investigate treatment strategies and outcomes in-depth, a prospective nationwide study including all paediatric hospitals in Germany is carried out 2011 to 2013. During the course of the study, physicians fill in a questionnaire when children with new NTM diagnosis are admitted to hospital and a second questionnaire after six months of treatment.

2.2.10 Legionnaire's disease (LD)

Risk of LD and cut off values of the Drinking Water Ordinance (TrinkwV) and LD

The network for community-acquired pneumonia disease estimates that there are 20,000 cases per year in Germany (www.capnetz.de/). Although much is known about Legionella and the illness they cause, the relationship between their concentration in water and the risk of infection remains unclear. A workshop was held in 2009 co-organised by and supported by epidemiological data from Unit 36. This workshop brought together a comprehensive body of evidence and experience showing that the growth of Legionella in heated water distribution systems can be effectively controlled by following the preventive measures described in the generally acknowledged codes of practice. As orientation to trigger action, a technical action level of 100 colony-forming units in 100 ml water has been found

As a result of the scientific exchange facilitated by RKI and Unit 36 research questions were defined (Schäfer et al., *Bundesgesundheitsbl-Gesundheitsforsch Gesundheitschutz*. For the future, further research concerning the reported source of infection and exposition is planned based on the collected notification data. The epidemiology of legionnaires' disease (LD) in specific settings (especially nosocomial and travel associated LD) will be analysed in more detail. For this reason a number new algorithms have been created and a special dataset will be constructed by our Unit in cooperation with Unit 31.

Travel associated LD – international surveillance by EWGLI/ELDSNet

In April 2010, the European Surveillance Scheme for Travel Associated Legionnaires' Disease (EWGLINET) located at the UK's Health Protection Agency (HPA) in London was transferred to ECDC being continued as ELDSNet (European Legionnaires' Disease Surveillance Network). The aim of the network is the early detection of clusters of travel-associated Legionnaires' disease (TALD) in Europe in order to identify and eliminate the source of infection.

Until September 2012 Germany did not participate in these networks because of uncertainties concerning the legal situation especially regarding the publication of accommodations for which a cluster of legionnaires' disease has been reported. Based on a report from ECDC in September 2011 Unit 36 together with the legal office at RKI reassessed the possibility of participation in ELDSNet and Germany will now fully participate in the network.

Currently in cooperation with Unit 31 the technical requirements will be implemented in the German electronic surveillance system in order to include the necessary travel details (e.g. hotel Name, address, travel dates etc.) and report them weekly via the European Surveillance System (TESSy) to ELDSNet.

2.3. Major goals and contribution to the goals of the department

The major goals for the coming years are:

- Expanding the work on burden of acute respiratory infections to other viral and bacterial pathogens
- Development of systems and analytical tools to rapidly assess the severity of (new) respiratory infections
- Serological and immunological studies for estimating cross-protection against new influenza viruses and age-specific infection rates in the population (e.g. Influenza A(H3N2)v)
- Enhanced capacity for outbreak investigations of respiratory infections
- Investigation of epidemiology of community acquired pneumonia and its complications
- Population-based studies on the respiratory infections and the role of concomitant pathogens using self-sampling
- Establishing and evaluation of molecular surveillance of tuberculosis at the national level and development of indicators to estimate probability of true clusters
- Building an evidence-base for management and control of tuberculosis in vulnerable groups
- Cohort studies on latent tuberculosis infection (LTBI) in the German population (Helmholtz Cohort). To embark on the work on LTBI, a Knowledge-Attitude-Practice study is being prepared together with the Pediatric Pneumology Unit of Hannover Medical University

Surveillance of respiratory infections, the assessment of the burden of disease in the population and the identification of groups at risk for severe disease and complications by Unit 36 provide a clear picture of the epidemiology of respiratory infections in Germany. This is crucial for setting priorities in public health, devise and evaluate prevention strategies, early recognise changing disease trends and emergence of new diseases – all of which are central aims of the department. In a prioritisation exercise in 2011, respiratory infections, namely tuberculosis, influenza, RSV, and Legionellosis, were all in the group with the highest priority for public health (Balabanova et al., PLoS One 2011).

Our unit has developed and provides unique expertise for the department in syndromic surveillance, ICD10-based as well as web-based surveillance, and in the use of molecular tools for epidemiologic purposes. Specifically, the development of clinical epidemiological studies has been an important asset for early analysis of the risk of transmission in the 2009 influenza pandemic. Work on influenza mortality is carried-out in close collaboration with Unit 32 (surveillance unit) and has been instrumental in establishing the setting-up of modelling tools for excess mortality by infectious diseases and the effect of interventions on the spread of disease. Naturally, a close collaboration exists with Unit 33 (vaccine prevention) by providing disease-specific expertise and data for development of recommendations for vaccination.

Through the work on pandemic influenza preparedness, Unit 36 has gained important experience in planning for critical situations for the health of the population. In recent years, our unit developed or participated in several large national and international exercises on pandemic influenza. This has resulted in very practical expertise on organisation and setting-up a crisis centre, that has also been used in other situations, such as the EHEC outbreak 2011. The investigation on protective measures in the outbreak of influenza A(H5N1) and work on monitoring of human cases has led to additional attributes in the notification software and to a closer linkage of the Department with the Friedrich-Löffler-Institute on animal health.

2.4. Additional work and methods for investigations

One key element of tuberculosis control is treatment quality and adherence. To address this issue, we currently work on the development of methods to estimate the number of treatment courses for tuberculosis by using prescription data. Additional applications of this approach are the investigation of co-treatment for underlying chronic diseases, e.g. diabetes, or other infectious

diseases such as hepatitis C or B and HIV. This work is also expanded to other respiratory infections.

In 2011 a pilot study was started to investigate the feasibility of noninvasive diagnostics of pneumococcal pneumonia in children from stools. This proof of principle study was carried out in collaboration with the Junior Group on Novel Zoonoses at RKI and the Department of Pediatric Pneumology at Charité, Berlin. The approach was based on the field studies of the Junior Group to detect severe pneumococcal disease in great apes in Africa. A joint research proposal is under consideration.

Starting in 2010 a new lecture series on “Infectious Disease Epidemiology” has been developed by members of Unit 36 in collaboration with other units. The lectures function as an introduction into the topic to familiarise students with the wide area of infectious disease epidemiology.

Methodological issues and practical issues of designing a study protocol are also included. The series serves as obligatory teaching module for the ZIBI Graduate School Berlin and the Graduate School “Functional Molecular Infection Epidemiology” at the Free University Berlin. It has also been well received by students of the RKI PhD-Programme.

2.5. Scientific advice and consulting services

Unit 36 is directly involved in advising the Ministries of Health at the national and state level on all questions concerning respiratory transmitted diseases and their prevention. An important counterpart at the state level is the Working Group on Protection against Infection (Arbeitsgemeinschaft Infektionsschutz). A specific area of expertise is the scientific basis of influenza pandemic preparedness. Unit 36 is in charge of working out and updating the scientific part of the National Influenza Pandemic Preparedness Plan.

The Unit supports and advises local health authorities in regard to tuberculosis contact investigations and identification of sources of legionellosis outbreaks.

A seasonal recurring task is the advice to the public on individual as well as on generic strategies to prevent influenza infection and transmission.

In addition to active media work, including giving interviews for print media, radio as well as regional and national TV, our Unit continuously updates the disease-specific institutional internet pages. Areas covered are influenza (seasonal, pandemic, human cases of avian and swine influenza), tuberculosis, legionellosis, and RSV, but also rare or emerging pathogens, such as SARS or novel Coronavirus (hCoV-ECM). Hereby, the medical community as well as the public is addressed, providing comprehensive information on the epidemiologic situation in Germany, diagnostics, prevention, management and control, including response to frequently asked questions. Online access statistics reveal a highly frequent utilisation of these pages: e.g. the influenza pages are accessed more than 6 million per year, with more than 2 million per month during the season, and also the tuberculosis sites are very often accessed, and documents have been downloaded between April and September 2012 about 10.000 times.

Members of our Unit serve as scientific advisors for various scientific or professional associations, e.g. the Pediatric Infectious Disease Society, the German Central Committee against Tuberculosis, the Tuberculosis Working Group of the Protection of Infection Committee of the Federal Association of Public Health Service Physicians, or the Committee for Biological Agents. They are invited to participate in scientific Programme Committees of national scientific conferences, e.g. the 5th National Influenza Kongress in Erfurt 2012 or the TB symposia of the Koch.Metschnikow-Forum

At the international level, Unit 36 members serve as national epidemiological contact points, and are invited to participate in or facilitate international Workshops and Meetings at the European or WHO level. Recent examples are the WHO consultation on public health measures during the influenza A(H1N1)2009 pandemic (26–28 October 2010, Gammarth, Tunisia), the meeting of the WHO STOP TB childhood subgroup, which was co-organised in December 2011 at the RKI, a Workshop of the Consensus Group on TB control in Big Cities and urban risk groups in the EU in November 2011 hosted by RKI, and the tuberculosis Wolfheze Workshop in The Hague in May 2011. Unit 36 participated also on the WHO Technical Consultation on Global Tools and Manual

for Influenza Surveillance (WHO HQ) and the Working group to review regional guidance for influenza surveillance (WHO Euro)

Members of Unit 36 are frequently asked for scientific advice (sometimes ‘behind the scene’) on ECDC risk assessments, to participate in expert panels for the development of scientific guidance documents, e.g. the ECDC IGRA guidance 2011, to peer review recommendations and action plans, or to contribute to the future development of the work. Two current examples are the peer review of the second edition of the WHO Guidance for national tuberculosis programmes on the management of tuberculosis in children and the request for input and annotations in the WHO Childhood Tuberculosis Roadmap (both to be published in spring 2013).

Advice is further provided as peer reviewers for several national and international scientific journals and the head of the unit serves also as Assistant Editor of *BMC Public Health*

2.6. Training and teaching activities

In addition to the supervision and mentoring of fellows of the PAE- and EPIET- programme and of postgraduate Master students of the Berlin School of Public Health, members of Unit 36 are involved in regular teaching activities, represented in the following list of short term and continuous teaching activities:

- Lecture on Tuberculosis and Gender, Module 6 Health and Society: Gender and Diversity Studies, BSPH, Charité, Medical University Berlin
- Bed-side Teaching of clinical skills in paediatric respiratory infections, Department of Pediatric Pneumology, Charité, Medical University Berlin
- Training for German public health professionals (ÖGD-Kurs), one week course, organised by RKI (2x/ year)
- Lectures on control of infectious diseases within the module Infectious Disease Epidemiology at Charité, Medical University Berlin
- Excursion “Tuberculosis epidemiology and analysis of notification data”, Institute of Social Medicine, Epidemiology and Health Economics, Medical University Berlin
- Presentation on influenza epidemiology during a two-day seminar for continuing education for medical professionals (Fortbildung des Berufsverbands der Ärzte für Mikrobiologie, Virologie und Infektionsepidemiologie e. V. (BÄMI))
- Two-day seminar on basic principles of epidemiology at Apollon, University of Applied Sciences Health Economics (Apollon Hochschule der Gesundheitswirtschaft)
- EPIET/PAE-Module Computer tools in outbreak analysis, one week course (1x/year)
- Lecture within the Master in Epidemiology program at the Swiss Tropical and Public Health Institute (SwissTPH)
- Lecture Series on “Infectious Disease Epidemiology”. ZIBI Graduate School Berlin and the Graduate School “Functional Molecular Infection Epidemiology” at the Free University Berlin.

3. Cooperation with other scientists or research institutions

3.1. Internal (within RKI)

Department 1, FG14 (M. Mielke, N. Wischnewski)

- Schaefer B et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2011¹
- Ziegler R et al., *Gesundheitswesen* 2012

Department 1, FG17 (NRC for Influenza: B. Schweiger)

- Working Group Influenza (AGI): AGI-Homepage, Seasonal reports, weekly reports <http://influenza.rki.de/>
- Haas W et al., *Dtsch Arztebl* 2009
- Buchholz U et al., *Euro Surveill* 2010
- Buda S et al., *Epid Bull* 2011
- Dudareva S et al.; *PLoS One* 2011
- Uphoff H et al., *PLoS One* 2011

Department 2, FG26 (M. Thamm)

- Dudareva S et al., *PLoS One* 2011

Centre for Biological Security (L. Schaade, R. Grunow)

- Suess T et al., *Am J Epidem* 2010
- Schaade L et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2010

3.2. External / National

Friedrich-Loeffler-Institute (Federal Research Institute for Animal Health: T Harder, National reference laboratory for avian influenza and reference laboratory of the World Organisation for Animal Health (O.I.E.) for avian influenza)

- Harder, Reuß, Buda: Seasonal influenza report 2011/12, Chap. 9: Influenza a zoonosis (Kap. 9: Influenza als Zoonose, Bericht zur Epidemiologie der Influenza in Deutschland, Saison 2011/12). <http://influenza.rki.de/Saisonberichte/2011.pdf>
- Humane Fälle mit Infektion durch Schweineinfluenzaviren. *Epid Bull* 2011

Public health authorities of Federal States

- Mecklenburg-Western Pomerania:
Cai W et al., *BMC Infect Dis* 2009
- Lower Saxony:
Humane Fälle mit Infektion durch Schweineinfluenzaviren. *Epid Bull* 2011

State laboratories of Baden-Württemberg, Bavaria, Mecklenburg-Western Pomerania, Saxonia, Saxony-Anhalt and Thuringia (Partner of the Working Group Influenza)

- Uphoff H et al., *PLoS One* 2011
- Wirksamkeit der Influenza-Impfung gegen saisonale Influenza A(H3N2) in der Saison 2011/2012. *Epid Bull* 2012

¹ For full reference see Appendix 4.1.1

Ludwig-Maximilians-Universität, Munich/ESPED (Rüdiger von Kries)

- Altmann M et al., *Emerg Infect Dis* 2011
- Altmann M et al., *Emerg Infect Dis* 2012
- Reuss A et al., *Pediatr Infect Dis J* 2009

German Central Committee against Tuberculosis (DZK)

- Hauer et al. Tuberculosis in the elderly in Germany. *Eur Respir J* 2011
- Castell S et al., *Pneumologie* 2011
- Diel R et al., *Pneumologie* 2011.
- Ziegler R et al., *Pneumologie* 2012 und *Gesundheitswesen* 2012
- Schaberg T et al., *Pneumologie* 2012

National Reference Center for Mycobacteria (S. Rüsç-Gerdes; Linkage of Molecular Typing data and Epidemiological data)

- Devaux I et al., *Euro Surveill* 2010
- Ziegler R et al., *Pneumologie* 2012

German Society for Pneumology and Respiration Medicine (DGP, T. Schaberg)

- Schaberg T et al., *Pneumologie* 2012.

Tuberculosis working group of the Protection of Infection Committee of the Federal Association of Public Health Service Physicians (Arbeitsgruppe Tuberkulose beim Fachausschuss Infektionsschutz des BVÖGD)

- Arbeitskreis Tuberkulose im Fachausschuss Infektionsschutz des Berufsverbandes der Ärztinnen und Ärzte des ÖGD. *Epid Bull* 2012

Federal Environmental Agency (Umweltbundesamt) (B. Schaefer)

- Schaefer B et al., *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2011

Paul-Ehrlich-Society for Chemotherapy (GERMAP)

- Brodhun BH et al.: *Mycobacterium tuberculosis*. In: (BVL) BfVuL, editor. Germap 2010, Antibiotika-Resistenz und -Verbrauch 2011

German Society for Paediatric Infectious Diseases

- Bialek R et al.: Tuberkulose und nicht tuberkulöse mykobakterielle Krankheiten. In: DPGI Handbuch Infektionen bei Kindern und Jugendlichen 2009
- Johannes F et al.: Influenza (nicht aviär). In: (DPGI Handbuch Infektionen bei Kindern und Jugendlichen. Stuttgart 2009

German Social Accident Insurance Institution for the health and welfare services (Berufsgenossenschaft für Gesundheitsdienst und Wohlfahrtspflege, A. Nienhaus)

- Hauer B et al.: Die Tuberkulose als Berufskrankheit- ein historischer Abriss. In: Tuberkulose als Berufskrankheit, Ein Leitfaden zur Begutachtung und Vorsorge 2012
- Brodhun B et al.: Die Bedeutung der Tuberkulose-Aktuelle Trends und Entwicklung. B et al.: Die Tuberkulose als Berufskrankheit- ein historischer Abriss. In: Tuberkulose als Berufskrankheit, Ein Leitfaden zur Begutachtung und Vorsorge 2012
- Haas W: Tuberkulose-Meldeverfahren nach Einführung des Infektionsschutzgesetzes (IfSG). B et al.: Die Tuberkulose als Berufskrankheit- ein historischer Abriss. In: Tuberkulose als Berufskrankheit, Ein Leitfaden zur Begutachtung und Vorsorge 2012

University of Heidelberg (Department of Infectious Diseases, Virology and Department of Internal Medicine V)

- Geis S et al., *J Clin Microbiol* 2012

3.3. External / International

ECDC

- European Influenza Surveillance Network (EISN): Devaux I et al., *Euro Surveill* 2010
- Ciancio BC et al., *Euro Surveill* 2009
- European Tuberculosis Surveillance Network: Devaux I et al., *Euro Surveill* 2010

WHO-EURO

- EuroFlu (Brown, CS, Jorgensen): Martirosyan L et al., *BMC Infect Dis* 2012
- WHO Euro: Recommendations for good practice in pandemic preparedness: identified through evaluation of the response to pandemic (H1N1) 2009); Key changes to pandemic plans by Member States of the WHO European Region based on lessons learnt from the 2009 pandemic.
- WHO Europe: Roadmap to prevent and combat drug resistant tuberculosis. The Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant Tuberculosis in the WHO European Region, 2011-2015. WHO 2012 ISBN 978 92 890 0246 2

WHO Head Quarter, Geneva

- Hollmeyer HG et al., *Vaccine* 2009
- Van Kerkhove MD et al., *PLoS Med* 2011
- Hollmeyer H et al., *Influenza Other Respi Viruses* 2012
- WHO GLaMOR project: estimation of the global pandemic (H1N1)pdm09 mortality; publication pending.

Centers for Disease Control and Prevention, USA (Widdowson MA)

- Dawood FS et al., *Lancet Infect Dis* 2012

L'Istituto cantonale di microbiologia, Bellinzona, Schweiz

- Gandolfi-Decristophoris et al., *Am J Infect Control* 2011

4. Appendix

4.1 Overview on achievements of the Unit, 2009-2012

4.1.1. Scientific publications, 2009 – 2012

Number of peer-review publications co-authored by members of the unit: 67

Impact factor (IF) according to JCR (of 2012 publications: according to 2011 IF)

2009: 26,3

2010: 34,8

2011: 188,0

2012: 42,1

Cumulative 2009-12: 291,2

A) Original research articles in peer-review journals

2012 (until Sept.)

Altmann M, **Fiebig L**, **Buda S**, von Kries R, Dehnert M, **Haas W**. Unchanged severity of influenza A(H1N1)pdm09 infection in children during first postpandemic season. *Emerg Infect Dis* 2012; 18(11).

Fiebig L, Kollan C, **Hauer B**, Gunsenheimer-Bartmeyer B, An der Heiden M, Hamouda O, **Haas W**. HIV-Prevalence in Tuberculosis Patients in Germany, 2002-2009: An Estimation Based on HIV and Tuberculosis Surveillance Data. *PLoS One* 2012; 7(11):e49111.

Geis S, Prifert C, Weissbrich B, Lehnert N, Egerer G, Eisenbach C, **Buchholz U**, Aichinger E, Dreger P, Neben K, Burkhardt U, Ho AD, Krausslich HG, Heeg K, Schnitzler P. Molecular Characterization of a Respiratory Syncytial Virus (RSV) Outbreak in a Hematology Unit, Heidelberg, Germany. *J Clin Microbiol* 2012. Epub 2012/10/27.

Hollmeyer H, Hayden F, Mounts A, **Buchholz U**. Review: interventions to increase influenza vaccination among healthcare workers in hospitals. *Influenza Other Respi Viruses* 2012.

Martirosyan L, Paget WJ, Jorgensen P, Brown CS, Meerhoff TJ, Pereyaslov D, Mott JA, EuroFlu group (for Germany: **Buda S**, Schweiger B) The community impact of the 2009 influenza pandemic in the WHO European region: a comparison with historical seasonal data from 28 countries. *BMC Infect Dis* 2012; 12:36.

Nachtnebel M, Greutelaers B, Falkenhorst G, Jorgensen P, Dehnert M, Schweiger B, Trader C, **Buda S**, Eckmanns T, Wichmann O, Hellenbrand W. Lessons from a one-year hospital-based surveillance of acute respiratory infections in Berlin- comparing case definitions to monitor influenza. *BMC Public Health* 2012; 12:245.

Remschmidt C, Stocker P, An der Heiden M, **Suess T**, **Luchtenberg M**, **Schink S**, Schweiger B, **Haas W**, **Buchholz U**. Preventable and non-preventable risk factors for influenza transmission and hygiene behavior in German influenza households, pandemic season (H1N1) 2009/2010. *Influenza Other Respi Viruses* 2012.

Siedler A, Rieck T, **Reuss A**, Walter D, Poggensee G, Poethko-Muller C, Reiter S. Estimating vaccination coverage in the absence of immunisation registers--the German experience. *Euro Surveill* 2012; 17(17).

Suess T, **Remschmidt C**, **Schink S**, Schweiger B, Heider A, Milde J, Nitsche A, Schroeder K, Doellinger J, Braun C, **Haas W**, Krause G, **Buchholz U**. Comparison of shedding characteristics of seasonal influenza virus (sub)types and influenza A(H1N1)pdm09; Germany, 2007-2011. *PLoS One* 2012.

Suess T, Remschmidt C, Schink S, Schweiger B, Nitsche A, Schroeder K, Doellinger J, Milde J, **Haas W,** Koehler I, Krause G, **Buchholz U.** The role of facemasks and hand hygiene in the prevention of influenza transmission in households: results from a cluster randomised trial; Berlin, Germany, 2009-2011. *BMC Infect Dis* 2012; 12(1):26.

2011

Altmann M, **Fiebig L,** Soyka J, von Kries R, Dehnert M, **Haas W.** Severe cases of pandemic (H1N1) 2009 in children, Germany. *Emerg Infect Dis* 2011;17(2):186-192.

Balabanova Y, Gilsdorf A, **Buda S,** Burger R, Eckmanns T, Gartner B, Gross U, **Haas W,** Hamouda O, Hubner J, Janisch T, Kist M, Kramer MH, Ledig T, Mielke M, Pulz M, Stark K, Suttorp N, Ulbrich U, Wichmann O, Krause G. Communicable diseases prioritized for surveillance and epidemiological research: results of a standardized prioritization procedure in Germany, 2011. *PLoS One* 2011; 6(10):e25691.

Brodhun B, Buchholz U. Epidemiologie der Legionärskrankheit in Deutschland [Epidemiology of Legionnaires' disease in Germany]. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2011;54(6):680-687.

Buchholz U, Bernard H, Werber D, Böhmer MM, **Remschmidt C,** Wilking H, Deléré Y, an der Heiden M, Adlhoeh C, Dreesman J, Ehlers J, Ethelberg S, Faber M, Frank C, Fricke G, Greiner M, Höhle M, Ivarsson S, Jark U, Kirchner M, Koch J, Krause G, Lubber P, Rosner B, Stark K, Kühne M. German Outbreak of *Escherichia coli* O104:H4 Associated with Sprouts. *N Engl J Med* 2011;365(19):1763-1770.

Castell S, **Hauer B, Brodhun B, Haas W.** Epidemiology of tuberculosis: The current situation in Germany and worldwide [Epidemiologie der Tuberkulose: Aktuelle Situation in Deutschland und weltweit]. *Pneumologie.* 2011;8(1):9-16.

Dudareva S, Schweiger B, Thamm M, Hohle M, Stark K, Krause G, **Buda S, Haas W.** Prevalence of antibodies to 2009 pandemic influenza A (H1N1) virus in German adult population in pre- and post-pandemic period. *PLoS One* 2011;6(6):e21340.

Fiebig L, Soyka J, **Buda S, Buchholz U,** Dehnert M, **Haas W.** Avian influenza A(H5N1) in humans: new insights from a line list of World Health Organization confirmed cases, September 2006 to August 2010. *Euro Surveill* 2011;16(32).

Frank C, Faber MS, Askar M, Bernard H, Fruth A, Gilsdorf A, Hohle M, Karch H, Krause G, Prager R, Spode A, Stark K, Werber D, **team HUSI.** Large and ongoing outbreak of haemolytic uraemic syndrome, Germany, May 2011. *Euro Surveill* 2011;16(21).

Frank C, Werber D, Cramer JP, Askar M, Faber M, an der Heiden M, Bernard H, Fruth A, Prager R, Spode A, Wadl M, Zoufaly A, Jordan S, Kemper MJ, Follin P, Muller L, King LA, Rosner B, **Buchholz U,** Stark K, Krause G, **Team HUSI.** Epidemic profile of Shiga-toxin-producing *Escherichia coli* O104:H4 outbreak in Germany. *N Eng J Med* 2011; 365(19):1771-1780.

Gandolfi-Decristophoris P, De Benedetti A, Petignat C, Attinger M, Guillaume J, **Fiebig L,** Hattendorf J, Cernela N, Regula G, Petrini O, Zinsstag J, Schelling E. Evaluation of pet contact as a risk factor for carriage of multidrug-resistant staphylococci in nursing home residents. *Am J Infect Control* 2011(0).

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Hermes J, Bernard H, **Buchholz U,** Spackova M, Low J, Loytved G, **Suess T,** Hautmann W, Werber D. Lack of evidence for pre-symptomatic transmission of pandemic influenza virus A(H1N1) 2009 in an outbreak among teenagers; Germany, 2009. *Influenza Other Respi Viruses* 2011; 5(6):e499-503.

Houben RMGJ, Crampin AC, Ndhlovu R, Sonnenberg P, Godfrey-Faussett P, **Haas W,** Engelmann G, Lombard CJ, Wilkinson D, Bruchfeld J, Lockman S, Tappero J, Glynn JR. Human

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Mall S, **Buchholz U**, Tibussek D, Jurke A, An der Heiden M, Diedrich S, Schweiger B, Alpers K. A Large Outbreak of Influenza B-associated Benign Acute Childhood Myositis in Germany, 2007/2008. *Pediatr Infect Dis J* 2011;30(oxj, 8701858):e142-e6.

Mette A, **Reuss A**, Feig M, Kappelmayer L, Siedler A, Eckmanns T, Poggensee G. Under-Reporting of Measles—An Evaluation Based on Data From North Rhine–Westphalia *Dtsch Arztebl Int* 2011.

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Schaefer B, **Brodhun B**, Wischnewski N, Chorus L. Legionellen im Trinkwasserbereich: Ergebnisse eines Fachgespraches zur Pravention trinkwasserbedingter Legionellosen [Legionella in drinking water: outcomes of an exchange of ideas on the prevention of waterborne legionellosis]. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2011 ;54(6):671-679.

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M, Bousfiha AA, Baghdadi JE, Ozbek N, Aksu G, Keser M, Somer A, Hatipoglu N, Aydogmus C, Asilsoy S, Camcioglu Y, Gulle S, Ozgur TT, Ozen M, Oleastro M, Bernasconi A, Mamishi S, Parvaneh N, Rosenzweig S, Barbouche R, Pedraza S, Lau YL, Ehlayel MS, Fieschi C, Abel L, Sanal O, Casanova JL. Revisiting human IL-12Rbeta1 deficiency: a survey of 141 patients from 30 countries. *Medicine (Baltimore)* 2010;89(6):381-402.

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2009

Influenza. Prävention, Diagnostik, Therapie und öffentliche Gesundheit. **Haas W**, editor: Elsevier, Urban & Fischer; 2009.

E) Book chapters

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Hauer B, Kropp R, Nienhaus A. Die Tuberkulose als Berufskrankheit-ein historischer Abriss. In: Nienhaus A, Brandenburg S, Teschler H, editors. Tuberkulose als Berufskrankheit, Ein Leitfaden zur Begutachtung und Vorsorge. 3. aktualisierte Auflage ed. Heidelberg, München, Landsberg, Frechen, Hamburg: ecomed Medizin; 2012. p. 23-40.

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Haas W. Pandemieplanung. In: Haas W, editor. Influenza Prävention, Diagnostik, Therapie und öffentliche Gesundheit. München: Elsevier, Urban und Fischer; 2009. p. 209-30.

4.1.2. Appendix with selected relevant publications**A) Five important publications for the scientific community 2009–2012**

1. **Suess T, Remschmidt C, Schink S**, Schweiger B, Nitsche A, Schroeder K, Doellinger J, Milde J, **Haas W**, Koehler I, Krause G, **Buchholz U**. The role of facemasks and hand hygiene in the prevention of influenza transmission in households: results from a cluster randomised trial; Berlin, Germany, 2009-2011. *BMC Infect Dis* 2012;12(1):26.
2. Altmann M, **Fiebig L, Buda S**, von Kries R, Dehnert M, **Haas W**. Unchanged severity of influenza A(H1N1)pdm09 infection in children during first postpandemic season. *Emerg Infect Dis* 2012;18(11).
3. **Fiebig L**, Kollan C, **Hauer B**, Gunsenheimer-Bartmeyer B, An der Heiden M, Hamouda O, **Haas W**. HIV-Prevalence in Tuberculosis Patients in Germany, 2002-2009: An Estimation Based on HIV and Tuberculosis Surveillance Data. *PLoS One* 2012;7(11):e49111.
4. Dudareva S, Schweiger B, Thamm M, Hohle M, Stark K, Krause G, **Buda S, Haas W**. Prevalence of antibodies to 2009 pandemic influenza A (H1N1) virus in German adult population in pre- and post-pandemic period. *PLoS One* 2011;6(6):e21340.
5. An der Heiden M, **Buchholz U**, Krause G, Kirchner G, Claus H, **Haas W**. Breaking the waves: modelling the potential impact of public health measures to defer the epidemic peak of novel influenza A/H1N1. *PLoS One* 2009;4(12):e8356.

B) Five important publications for the public 2009–2012

1. Homepage of the Working Group Influenza (Arbeitsgemeinschaft Influenza): <http://influenza.rki.de/>
2. Wirksamkeit der Influenza-Impfung gegen saisonale Influenza A(H3N2) in der Saison 2011/2012. *Epid Bull* 2012(41).
3. Syndromische Surveillance akuter Atemwegserkrankungen unter direkter Mitarbeit der Allgemeinbevölkerung (Ein Bericht zum ersten Jahr des Bestehens von GrippeWeb). *Epid Bull* 2012(40).
GrippeWeb-Homepage <https://grippeweb.rki.de/>
4. Welttuberkulosestag 2012 – Tuberkulose im Fokus. *Epid Bull* 2012(11).
5. Studie zur Effektivität nichtpharmakologischer Interventionen zur Prävention von Influenza-Übertragungen in Haushalten. *Epid Bull* 2011(50).

4.1.3. Awards and honours, 2009 - 2012**2011**

Dr. Lena Fiebig, Best poster award in the “General category” at the HPA Health Protection conference for the poster entitled “Diagnostic findings for childhood tuberculosis by use of gastric aspirate, Germany, 2002 to 2009“

4.1.4. Overview on collaborations in networks

ECDC, WHO:

- Joint ECDC/WHO TB surveillance network
- European Influenza surveillance Network (EISN)
- EuroFlu (WHO Euro)
- National Contact Point for
 - Legionnaire's disease (ELDSNet): Bonita Brodhun (+ NTP-Manager)
 - Influenza: Silke Buda (EISN)
 - Tuberculosis: Walter Haas (+ NTP-Manager)
- Member of Programm Committee of Wolfheze Tuberculosis-Workshop

Stop TB Partnership:

Childhood TB subgroup of WHO Dots Expansion Working Group

- RKI as NTP-Manager and TB National Contact Point:
 - Walter Haas
 - Barbara Hauer

Union (former IUATLD):

- Member of Childhood TB Training Tools Working Group

WHO Euro:

- Member of steering group for the development of the WHO M/XDR-TB Actionplan (MAP)
- Member of Task Forces for the development of Monitoring and Evaluation Frameworks for MAP and the Berlin Declaration
- Member of Programm Committee of Wolfheze-Workshop
- Member of the Regional Interagency Coordinating Committee on Tuberculosis Control and Care (RICC-TB)
- Observer of WHO Europe Technical advisory group on Tuberculosis control (TAG-TB)

KNCV/Wolfheze:

- Member of the Wolfheze Workshop Programm Committee
- Member of the Consensus Group on TB control in Big Cities and urban risk groups in the EU (including Health Protection Agency, EU Member State representatives for TB from e.g. Belgium, France)
- Member of the consensus working group on TB contact investigation in low prevalence countries

Tuberculosis Surveillance Research Unit (TSRU)

- Representative for Germany (in collaboration with DZK)

BIPS (Institute for epidemiology and prevention research, Bremen):

- BMBF-supported program "Epi goes gender"

4.1.5. Memberships and participation in Advisory Boards

PD Dr. Walter Haas

- ECDC Expert Panel:
ECDC Guidance: Use of interferon-gamma release assays in support of tuberculosis diagnosis. ECDC 2011 ISBN 978-92-9193-240-5

- Member of the Pandemic Influenza Working Group (*PIWG*) of the Global Health Security Action Group (*GHSAG*)
- DGPI: Scientific adviser, Coordinator for recommendations on tuberculosis and influenza
- German Central Committee against Tuberculosis (DZK): Scientific adviser

Reviews:

- International Journal for Tuberculosis and Lung Diseases, Pediatric Infectious Disease Journal, Emerging Infectious Diseases, Eurosurveillance, BMC Infectious Diseases; Assistant Editor BMC Public Health

Dr. Barbara Hauer

- Observer of WHO Europe Technical Advisory Group on Tuberculosis Control (TAG-TB)
- Member of the Regional Interagency Coordinating Committee on Tuberculosis Control and Care (RICC-TB)
- Member of the Steering Group during the development process of the WHO M/XDR-TB Actionplan
- Scientific advisor for the scientific Koch Metschnikov Forum Symposium (yearly on March 24, World TB day)
- Scientific advisor of the Working group „Frequently asked questions tuberculosis“Subgroup 1 of the Committee for Occupational Medicine

Reviews:

- for European Respiratory Journal (ERJ), International Journal for Tuberculosis and Lung Diseases (IJTLD), Public Health Action, Pneumologie

Dr. Bonita Brodhun

- Member of the Steering committee of EWGLINet until 2009 (now: ELDSNet)

Dr. Udo Buchholz

- EISN: Member of the CNRL-Management team

Dr. Silke Buda

- Member of the EISN Coordination Group

4.1.6. List of completed habilitation, dissertation or master theses in the Unit, 2009 – 2012

Year	Title	Name	Title of thesis	University / RKI Supervisor
2012	Master in Public Health (MPH)	Basel Karo	Tuberculosis as AIDS-defining disease in Germany: occurrence, case characteristics and treatment	BSPH / W. Haas and L. Fiebig
2011	Master in Public Health (MPH)	Lena Bös	Die Tuberkulosesituation im Berliner Justizvollzug 2007-2010	BSPH / W. Haas
2011	Master of Science (M.Sc.)	Irina Köhler	Auswertungsroutinen für eine cluster-randomisierte Studie zur Wirksamkeit nicht-pharmakologischer Präventionsmaßnahmen gegen Influenza	BHT Berlin / U. Buchholz
2009	Master in Public Health (MPH)	Levke Quabeck	Epidemiologie und Kontrolle der Tuberkulose in Metropolen europäischer Niederrinzidenz-Länder	BSPH / W. Haas

4.1.7. Presentations as invited speaker, 2009 – 2012

Staff from the Respiratory Infections Unit were invited to speak at 75 conferences.

4.1.8. Reports and written scientific advice to the Ministry of Health, 2009-2012

There were 188 reports and written scientific advice to the Ministry of Health between 2009 and 30.09.2012.