Eurosurveillance

Volume 14, Issue 43 - 29 October 2009

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Building capacity in field epidemiology: lessons learned from the experience in Europe

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This article was published on 29 October 2009.
Citation style for this article: Walke HT, Simone PM. Building capacity in field epidemiology: lessons learned from the experience in Europe. Euro Surveill. 2009;14(43):pii=19376. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19376

This issue of *Eurosurveillance* is devoted to training of field epidemiologists within diverse public health systems and highlights the contributions these programmes are making in Europe. The articles describe national field epidemiology training programmes (FETPs) [1], the European Programme for Interventional Epidemiology Training (EPIET) [2] and its transition to the European Centre for Disease Prevention and Control (ECDC) [3], how ECDC through its training activities is contributing towards building capacity in surveillance and response in communicable diseases, as well as the strengths and challenges of the various models of applied epidemiology training [4].

FETPs are two-year training programmes in applied epidemiology, based on a model of 'learning by doing'. They build public health capacity infrastructure by strengthening the public health workforce and surveillance systems. Key elements of these programmes enable their success and sustainability (Box) [5,6].

FETPs fill an important gap by increasing the number of competent field epidemiologists, but the programmes go beyond training: the fellows also provide services needed by the host country, such as outbreak detection and response. Furthermore, and perhaps most importantly, the programmes contribute to the strengthening of the public health system as a whole. The majority of graduates stay within the public health system, and many take on positions of leadership, changing the culture to one of using data for decision making [6-8].

EPIET, the national FETPs, and the EPIET-associated programmes (where fellows from national programmes participate in the classroom training with the EPIET fellows) described here are part of a larger community of FETPs, linked together in a global network, the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET). Currently within TEPHINET there are 32 registered programmes (www.tephinet.org). Through partnerships with the host countries, the European Union (EU), the World Health Organization (WHO), TEPHINET, the United States Centers for Disease Control and Prevention (US CDC), multiple donors as well as private organisations, the number of FETPs continues to grow. The US CDC engage with 18 of these programmes outside Europe, providing a range of support from short-term technical assistance to placing a resident advisor from the US CDC within the ministry of health of the host government.

Within Europe, these applied epidemiology programmes are vigorously involved in public health surveillance and response activities, especially outbreak investigations. Bosman *et al.* report that EPIET and EPIET-associated programmes produced 340 publications in peer-reviewed journals over 12 years, all derived from fellowship projects [2]. Measuring FETPs' successes must take into account their intent to both train the next generation of public health leaders in epidemiology and to provide service and strengthen the health systems of their host governments. Success indicators such as number of graduates, field investigations, publications, and international missions are easier to obtain, while tracking career choices after graduation, number of graduates in leadership positions in public health, and their impact on policy decisions and public health systems are much harder to quantify.

Although the various programmes are linked in their approach to train epidemiologists, they use different models based on the respective country's needs and the programme's objectives. Krause *et al.* provide an overview of five national FETPs and compares them to EPIET [1]. The authors address a number of challenges related to retention and sustainability. For example, teaching in the native language in national FETPs assures that more of the most qualified and appropriate candidates can participate and may improve retention of the graduates in the country, but lack of English proficiency often limits the ability of the fellows to participate in activities in the international scientific community. Recruiting into the programmes from within the public health service may also improve retention, but may limit the ability to attract new, young scientists. Providing a university degree upon completion of the programme may enhance recruitment, retention, and opportunities for promotion in some countries, but may jeopardise the quantity and quality of field work if rigid university requirements reduce the availability of fellows for field activities. Sustainability relies

Box

Key elements of field epidemiology training programmes

1. Competency-based curriculum
2. Mentorship by a senior field epidemiologist
3. Majority of participant's time spent in field and in service to host government priorities
4. Recruitment and training of graduates as mentors as the programme expands
5. Translation of data for evidence-based decision making
6. Programme initiates sustainability planning at an early stage

heavily on the ability to retain graduates, as the programmes cannot be sustained or expanded unless fellows serve as mentors and supervisors after their graduation. Finally, the need to train more field epidemiologists is constantly threatened by funding and administrative issues.

It requires substantial resources to start and maintain an applied epidemiology training programme. Bosman *et al.* estimate that the EPIET programme costs between EUR 2.3 and 3.2 million per year for cohorts 8 through 11 [2]. Bremer *et al.* report that since the transition of EPIET to the ECDC in 2007, 84% of the participants' salaries are funded by ECDC [3]. In the national FETPs, the country usually covers the costs of the participant's salary, since the participants are performing services for the government during their training. The majority of the costs are related to personnel required to supervise the participants and to supporting the introductory course and intermittent modular trainings.

Despite the relatively high costs, a demand for more qualified epidemiologists in Europe remains. Several articles appeal for the number of EPIET fellows to be increased, for strategies to facilitate return of these fellows to their country of origin, and creation of more FETP-like national programmes [3,4]. Krause *et al.* [4] suggest seconding an EU senior epidemiologist to new FETPs, much like the seconding of US CDC experts to the German and Italian FETPs. In some cases a regional approach might make sense. The cost of a national FETP in Europe is not presented, but the average cost of supporting a FETP by the US CDC is about USD 1 million per year, in the case where CDC remains fully engaged over a period of approximately five years. The costs decrease when the CDC resident advisor departs and the country takes over full responsibility for the programme.

Expanding the scale of FETPs within countries is another way of addressing the need for skilled epidemiologists. FETPs typically train 10 to 15 professionals in each cohort per year at the national level. Even with unlimited resources, there is an operational limit in the number of participants due to size of classrooms, number of supervisors and mentors, office space, etc. Having multiple FETPs within a country is an option, with each catering to different audiences. State-based FETP-like programmes exist in the US [9], and provincial FETPs are established in China. These programmes work together; for example, the national FETP in China sends fellows to the provinces for field experiences and the provinces ask the national FETP to assist with modular trainings. An annual scientific conference provides another opportunity for the provincial and national programmes to interact and learn from each other.

A key question is how many epidemiologists are needed. The Council of State and Territorial Epidemiologists (CSTE) in the US has recommended that the number of epidemiologists working in a state in the US be proportional to population size at the rate of at least one per 100,000 [10]. Based on this recommendation, the US currently has 30% fewer epidemiologists than recommended, even though the Epidemic Intelligence Service (EIS) programme has produced more than 3,000 graduates since 1951, with an additional 161 officers currently enrolled in the programme. Certainly not all epidemiologists working within a country need to go through FETP training. At different levels of the public health system, epidemiologists will need different skill sets. The Central America Regional FETP is an example of a comprehensive approach to training epidemiologists at multiple levels [8]. The curriculum is divided into a three-tiered training pyramid that corresponds to the needs at the local, district and central levels of the health system.

The articles in this special edition of Eurosurveillance disclose a vibrant network of applied epidemiology training programmes and epidemiology training activities, which are building public health workforce capacity in Europe. The health workforce is one of the six fundamental building blocks in the WHO health system framework [11], yet one of the greatest challenges to building effective public health systems globally continues to be the critical shortage of skilled public health workers [12]. Building sustainable health systems with a strong public health workforce and well-functioning surveillance and response systems will require commitment and support from all parts of the global public health community, based on the principles of the "Paris Declaration on Aid Effectiveness" calling for greater harmonisation of development resources [13]. By investing more strategically, donors and partner countries can not only achieve immediate impact through disease-specific programmes, but also contribute to the strengthening and the long-term sustainability of the health system. Within the global epidemiology community, we have a responsibility to address the critical needs through strengthening international and regional networks, evaluating programmes, piloting innovative approaches, sharing experiences and lessons learned, and determining the most effective approaches to support further investment.

Graduates from applied epidemiology training programmes, such as the ones described in this special edition, will play leading roles in defining and addressing crucial health problems in their countries and the international community.

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The European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) - selected papers from the conference 2008

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This article was published on 29 October 2009.
Citation style for this article: The ESCAIDE Scientific Committee. The European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) - selected papers from the conference 2008. Euro Surveill. 2009;14(43):pii=19377. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19377

This issue of Eurosurveillance has two focuses: a special issue on capacity building and training for applied field epidemiology in Europe [1] and a focus on the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) by featuring two papers based on presentations made at ESCAIDE 2008. The authors of these papers were invited by the Eurosurveillance editors to submit an article for peer-review after the abstract selection had taken place, because of their overall quality and the focus on information for action. In their contribution from Thailand, Pawun et al. report on a field-investigation of a nosocomial outbreak of bullous impetigo in newborns, caused by *Staphyloccoccus aureus*, in a hospital in northern Thailand [2]. The results from this investigation lead to the implementation of immediate measures that stopped the outbreak. Moreover, the awareness raised of the problems identified during the investigation triggered the implementation of measures to prevent similar outbreaks in the future. The second paper by Girardi *et al*. reports on the diagnosis of latent tuberculosis infection, an issue of considerable debate [3]. The authors compare sensitivity and specificity of interferon-gamma assays for latent tuberculosis infection by assessing the association of test results with tuberculosis occupational exposure in 115 health care workers by using latent class analysis. They found that the estimated specificity of in vitro assays was higher than that of Tuberculin skin tests (TST) also among individuals who were not BCG-vaccinated and from their data the authors conclude that when applied in healthcare workers, in vitro assays may provide a significant increase of specificity for tuberculosis infection compared to TST, even among non- vaccinated individuals, at the cost of some sensitivity.

The two papers presented serve as good examples for some of the unique features of ESCAIDE; the conference's focus not only on applied science and epidemiology (including field investigations), but on the direct, concrete application of study results for public health action. ESCAIDE is supported by European Centre for Disease Control and Prevention (ECDC) and jointly organised by ECDC, the European Programme for Intervention Epidemiology Training (EPIET), the EPIET Alumni Network (EAN) and the Training Programs in Epidemiology and Public Health Intervention NETwork (TEPHINET EUROPE). Besides sharing scientific knowledge, ESCAIDE provides an excellent opportunity for experts with a wide range of various backgrounds who are involved in epidemiology and infectious disease control and prevention to strengthen and expand networks and share experiences. The first ESCAIDE took place in October 2007 in Stockholm and was followed by a conference in Berlin in October 2008. At the time of publication of this editorial, the third ESCAIDE in Stockholm has just come to its end. From start, ESCAIDE has been a success with constantly well over 600 visitors and an annual increase of submitted abstracts of around 10 percent. Even if the focus of the conference is Europe, its' reach is global; in 2009, besides from Europe, participants came from Australia, Brazil, Canada, China, Hong Kong, New Zealand, Pakistan, the Philippines, Thailand, the Unites States and Vietnam. Pandemic H1N1 influenza has understandably been given some focus during the 2009 conference. However, as in previous years, many other topics were covered in the various sessions. Topics covered by plenary sessions ranged from ageing and infectious diseases to influenza vaccination and to new methods for analysing outbreaks. A new and special focus on this year's ESCAIDE meeting was the viewpoint from the laboratory and its role in public health, with a plenary session on what genotyping has to offer epidemiologists. More specific information on the conference can be found on a dedicated website (www.escaide.eu/) [4].

Given that ESCAIDE is both a forum for exchanging scientific knowledge and good practice as well as for networking and personal professional development, the two focuses of this Eurosurveillance issue stand well side-by-side: ESCAIDE and capacity building and training for applied field epidemiology in Europe.

Members of the ESCAIDE scientific committee are: Andrea Ammon, ECDC, Arnold Bosman, ECDC, Viviane Bremer, ECDC/EPIET, Johan Giesecke, ECDC (chair), Gérard Krause, ECDC Advisory Forum, Marion Koopmans, European Society for Clinical Virology , Davide Manissero, ECDC, Barbara Schimmer, EPIET Alumni Network, Ines Steffens, ECDC, Howard Needham, ECDC, Panayotis Tassios, European Society of Clinical Microbiology and Infectious Diseases..

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Differences and Commonalities of National Field Epidemiology Training Programmes in Europe

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This article was published on 29 October 2009.
Citation style for this article: 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):pii=19378. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19378

From 1994 to 2009, national field epidemiology training programmes (FETP) have been installed in Spain, Germany, Italy, France and Norway. During their two year duration, different components of the FETP are devised as follows: 63-79 weeks are spent on projects in hosting institutes, 2-26 weeks in outside projects, 9-30 weeks in courses and modules, and 1-2 weeks in scientific conferences. A considerable proportion of the Spanish FETP has is provided conventional 'class room training'. The content of the modules is very similar for all programmes. Except from the Italian programme, all focus on infectious disease epidemiology. The German and Norwegian programmes are so called EPIET-associated programmesas their participants are integrated in the modules and the supervision offered by EPIET, but salaries, facilitators, and training sites are provided by the national programme. These EPIET-associated programmes require strong communications skills in English. Alumni of all five FETP are generally working within the public health work force in their respective countries or at international level, many of them in leading functions. Although three new FETP have been installed since the last published 'Euroroundup' in Eurosurveillance on European FETP in 2001, the progress with respect to the establishment of national FETP or EPIET-associated programmes has been slow. Member States should be aware of how much support EPIET can offer for the establishment of national FETP or EPIET-associated programmes. However, they also need to be ready to provide the necessary resources, the administrative environment and long-term dedication to make field epidemiology training work.

Introduction

In March 2001, a special issue of Eurosurveillance presented reports on different field epidemiology training programmes (FETP) in Europe and the United States [1,2]. At that time, in Europe, national FETP were in place in France, Germany and Spain. These three programmes now look back on more than 10 years of experience and Norway and Italy have created additional national FETP since. This 'Euroroundup' aims to provide an overview of the existing five national FETP. It focuses on their respective history, their objectives and organisational details and discusses differences and commonalities with reference to the European Programme for Intervention Epidemiology Training (EPIET) as it is a multinational field epidemiology training programme in Europe. Furthermore, the analysis intends to provide a basis for further discussions of the strengths of FETPS for capacity building in Europe and the remaining challenges.

France

Since the late 1990s, changes occurred in the French public health arena: in 1998 the Institute of Public Health Surveillance (InVS) and its regional offices were created to reinforce the surveillance of and response to alerts and threats to public health and in 2002, in the context of bioterrorist threats, the French Field Epidemiology Training Programme PROFET (Programme de formation à l'épidémiologie de terrain) was launched. The programme was run in cooperation between the InVS and the National School of Public Health (EHESP) and built on a three-week intervention epidemiology course (IDEA) which had been ongoing since 1984 [3,4]. PROFET was set up with the aim to build capacity for preparedness and response in the field of public health, and in the development of public health surveillance. It intended to provide qualified professionals primarily to the national institute and its regional offices.

As most FETP, PROFET is based on the principle of 'learning by doing', fellows may carry out projects in the field of communicable diseases and environmental health, but also in occupational health, chronic diseases and injuries. They are expected to publish in the French national epidemiologic bulletin or in other national or international journals, and to give an oral presentation at an epidemiologic conference. During their two year training, the fellows attend six one-week training modules with specific topics: computer tools for outbreak investigation, risk assessment in environmental health, logistic regression, sampling, scientific writing, surveillance. The training is conducted in French by InVS epidemiologists and set up specifically for the fellows. However, some modules are open for external participants as well. At the end of the training, an assessment is made of the outcomes of the fellows but no formal diploma is awarded upon completion.

PROFET targets young public health professionals who are willing to get involved in field epidemiology in the French public health system. Candidates must have a master degree in the field

of public health, or equivalent. The programme is run jointly by two scientific coordinators from InVS and EHESP (respectively 0.7 and 0.3 fulltime equivalents [FTE]). Fellows are employed and paid by InVS with a specific trainee salary. The cost of the programme is mainly made up of salaries (90%) and of travel costs for training and conferences (9%). Costs directly related to the daily activities are included in the training site's budget. Since 2002, seven cohorts have been enrolled, amounting to 40 fellows (five cohorts of six fellows each and the two last cohorts of five fellows each). Trainees were mainly public health graduates (master in public health, or epidemiology), public health engineers, biostatisticians, pharmacists, public health nurses and veterinarians. Only one physician entered PROFET because medical students who want to specialise in field epidemiology generally apply for a residency at InVS during their public health medicine training. All 30 fellows of the five completed cohorts have successfully terminated the programme and all, except one, have been recruited in the public health network after this: 19 at InVS (11 at the national headquarters, 8 in regional offices) and 10 work for other public health partners in France.

After eighteen years of successful experiences with the IDEA course, the start of PROFET was intended to accompany the development and the regionalisation of the surveillance and response capacities in the French public health system. The cost of such training activities are usually seen as a challenge in setting up and maintaining programmes but an evaluation of PROFET carried out in 2008 showed that the training sites highly value the input of fellows, not only as a 'workforce' but also because of their organisational and methodological skills. The next challenge for PROFET will be to become part of the European network of training programmes. The collaboration of InVS with the European Centre for Disease Prevention and Control (ECDC) and its involvement in the European Programme for Intervention Epidemiology Training (EPIET) as well as the European focus of the EHESP are opportunities for PROFET to be addressed in the future.

Germany

In the 1990s the German Ministry of Health (MOH) initiated a number of measures to strengthen the federal capacity in the field of infectious disease epidemiology. One of these measures was the installation of a national FETP in 1996 [5]. The idea was that participants would upon completion of their training either join the Robert Koch Institute (RKI) or return to the peripheral health departments, from where most of them were initially recruited. The programme started with two participants and - due to various kinds of additional government funding - has in the meanwhile had up to six participants per cohort. In 2006 the programme was named Postgraduate Training for Applied Epidemiology (PAE).

From start, the PAE was organised as an EPIET-associated programme, which means that the PAE fellows participate in all EPIET modules and benefit from facilitation by EPIET coordinators. However, salaries for fellows, the German facilitators and coordinators within the EPIET programme and the training sites are provided by the RKI. This EPIET-associated FETP requires strong communication skills in English. 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. In addition to the requirements for EPIET fellows [6,11], PAE fellows are expected to write at least one publication in the national weekly epidemiological bulletin, one chapter in the annual national epidemiological report and are involved in the regular quality control procedures of the national surveillance system. Usually PAE fellows also enrol as duty officer in the RKI 24/7 hotline for public health emergencies.

The PAE primarily targets individuals with fairly advanced training and work experience in a medical or related discipline. Besides a university degree, eligibility criteria include knowledge in public health or epidemiological methods, at least one year programme-related work experience and fluency in English and German. RKI closely cooperates with EPIET. The institute provides facilitators, locations and sometimes funding for some of the EPIET modules. For cohort 13/14 (2006-2009) RKI is training site for six PAE and two EPIET fellows. In addition four PAE fellows are currently being trained at the respective state public health agencies of Hesse, Lower Saxony, North Rhine-Westphalia and Baden Wuerttemberg. In 2009, two of the state agencies have also become EPIET training sites and one is now hosting an EPIET fellow.

Of the 42 fellows who entered the programme between 1996-2008, 36 had a medical degree, thee a university degree in veterinary medicine, one a degree in biology, one in traditional Chinese medicine and one in public health. Most participants had worked outside the public health service upon entry to the programme, seven had completed a master degree in a public health-related field before starting the training, four obtained a master degree after termination of the PAE. Most fellows (38) had applied from outside RKI but within Germany, two applicants came from a neighbouring European country, two had no European citizenship. Forty of the 42 fellows admitted have successfully completed their training, two dropped out before completion of the programme (one because of another job offer, one for personal reasons).

Retrospectively, the main challenge in setting up the programme was to reach an acknowledgement at ministerial level that such a training programme is a necessary and fruitful investment. The PAE has undergone a remarkable expansion and stabilisation in the past years [7]. To have some of the PAE fellows trained in state public health agencies is maybe one of the most important achievements given the difficulties for such collaboration in a federal setting. As a result of close collaboration between RKI and the Charité Medical University in Berlin, the cohort starting 2009, will upon successful completion of the PAE also obtain a Master of Science degree in Applied Epidemiology (MScAE).

Italy

At the end of the 1980s, after several exchanges of experiences and health professionals with the US Centers for Disease Control and Prevention (CDC), Atlanta, the Istituto Superiore di Sanità (ISS, National Institute of Health) set up an experimental training programme to train some health professionals from the different regions in order to improve the preparedness to intervene essentially on outbreaks and to carry out epidemiological surveillance of infectious diseases. In 2000, the training programme for applied epidemiology PROgramma di Formazione in Epidemioloiga Applicata (PROFEA) was created. At present, most of the curriculum focuses on prevention for chronic diseases, even if a section of the training is devoted to infectious disease surveillance and outbreak investigation.

The curriculum contains 10 different modules followed by a field training assignment of one or two months. Each trainee has to achieve some formative objectives using exclusively data and information from his/her reality and is required to devote 1,500 hours during two years PROFEA, approximately 50% of the working time of a health professional employed by the National Health System. The training is held in Italian, even if the curriculum requires an article for a scientific journal and that all participants are invited write their article in English. In 2002, PROFEA became a post-graduate Master course, through collaboration with the 'Tor Vergata' University in Rome.

In the past mostly medical doctors, veterinarians, biologists and statisticians have applied for PROFEA directly via the university. A particular condition to be eligible for PROFEA is a letter from the region or local health administration (LAH) of the applicant in which it confirms to financially support courses, workshops and fieldworks and assures that the candidate will be able to dedicate 50% of his/her working time to the training programme. Organised by the National Centre of Epidemiology (CNESPS), of the ISS, the training programme is carried out by teachers and tutors from CNESPS. So far, secured permanent funding has come from the Italian CDC (CCM from the Ministry of Health). All participants are already employed by regions or LHA and their employers cover financial costs of courses, travels, hotel and other costs generated from training or fieldwork activities.

Since 2001, six cohorts have enrolled the programme. Fifty participants now work in public health in Italy, many of whom were promoted to posts of greater responsibility, while others are involved in national and regional committees.

At the moment, PROFEA and the CNESPS face many challenges. Italy is becoming a federal republic and the national level is only entitled to establish essential levels of care for citizens, except in cases when emergencies or for health issues implicate several regions, but the strategies to achieve them are decided and implemented at regional level. For the new 'National Plan of Prevention', the CNESPS will be adapting PROFEA training modules to assure that health professionals acquire the skills and competencies necessary for these new tasks. In the future selection of candidates will be possibly carried out by the regions and the number PROFEA trainees could rise to 20 per cohort. The funds for the programme could come directly from the interested regions and not from the national level (Ministry of Health).

Norway

The Norwegian Field Epidemiology Training Programme (Nor-FETP) started in 2001 with the objective 'to strengthen Norway's capacity to prevent and control communicable diseases by training highly qualified physicians, veterinarians and public health nurses in surveillance, outbreak investigations, applied research, communication, and support for decision making'. The focus of the programme is infectious disease prevention and control. It has from the start benefited immensely from a close collaboration with EPIET and as such adopted the EPIET associated-programme model.

During the two-year training period, fellows are actively involved in field investigations, surveillance and related research activities, and get acquainted with laboratory methods relevant to epidemiological investigations. If feasible they also take part in the Nordic summer school of infectious disease epidemiology (two weeks), go on a site visit to another European department of infectious disease surveillance, to the ECDC or the World Health Organisation (WHO) for at least one week and attend an international scientific conference. The objectives of the Nor-FETP are the same as those of EPIET plus some additional Nor-FETP objectives, such as: becoming acquainted with the Norwegian Surveillance System for Communicable Diseases, the EpiNorth collaboration [8] and with one ECDC/EU network for surveillance of infectious diseases [9].

The main working language is Norwegian but most reports, presentations and publications are in English, depending on the target audience. The three most recent fellows to join the programme are in parallel involved in training for the medical specialty in public health medicine. Their Nor-FETP training will count towards this specialisation. Normally, one fellowship is awarded per year. Nor-FETP uses the same criteria for selection as EPIET plus: fluency in a Scandinavian language; the intention to work in public health in Norway and international experience, e.g. in research or NGO work.

The Nor-FETP is managed by the Norwegian Institute of Public Health. The daily administration is in the Department of Infectious Disease Epidemiology, where the fellows are trained. To fulfil the training objective of training other professionals, the Nor-FETP programme collaborates with the EpiNorth project, the International School of Public Health in Arkhangelsk, Russia and the Nordic School of Public Health.

Since its inception, four fellows have completed training while three are in the programme now and one has been selected for the upcoming cohort and there was no drop-out. Among these eight, four are physicians, one is a veterinarian with a PhD and three are registered nurses with a master degree in public health when entering the programme.

The main challenge when setting up Nor-FETP was to organise training modules for so few people. The collaboration with EPIET solved this and is crucial for the programme and which is expected to continue in its current form.

Spain

The Spanish Applied Field Epidemiology Training Programme (PEAC) was launched in 1994 by the Ministry of Health supported by the US CDC, Atlanta [10]. The programme is hosted by the National Centre for Epidemiology in close collaboration with the National School of Public Health, both at the Instituto de Salud Carlos III (ISCIII, National Public Health Institute). The mission of ISCIII is to provide and offer scientific and technical support, as well as high quality research and training, to the national health system and the society. Within this framework, the objective of the PEAC is to strengthen the capacity of response of the national surveillance system to epidemics and other health emergencies.

PEAC starts with a three-month introductory course together with the Spanish Master of Public Health course at the national public health institute. Additional modules include: data management and data analysis, outbreak investigation (general and special aspects), communication, infectious disease epidemiology, environmental epidemiology, occupational epidemiology, analysis of health situation and application of systems dynamics. Participation is obligatory for all modules which are all held in Spanish. The

Table

Structural and conceptual characteristics of five existing national Field Epidemiology Training Programmes (FETP) in Europe compared to the European Programme for Intervention Epidemiology Training (EPIET)

Country	Europe	France	Germany	Italy	Norway	Spain
Population	**505 million**	**64 million**	**82 million**	**60 million**	**5 million**	**47 million**
History and objectives						
Programme acronym	EPIET	PROFET	PAE	PROFEA	Nor-FETP	PEAC
Institution(s) in charge of the programme	National and regional public health institutes, European Centre for Disease Prevention and Control (ECDC)	French Institute for Public Health Surveillance (InVS) and National School of Public Health (EHESP)	Robert Koch Institute (RKI, Federal Public Health Agency)	National Centre of Epidemiology (CNESPS) Tor Vergata University, Rome	Norwegian Institute of Public Health (NIPH)	Instituto de Salud Carlos III (ISCIII); National Centre for Epidemiology
Exists since	1995	2002	1996	2001	2001	1994
Subject focus	Mainly infectious diseases	Mainly infectious diseases and environmental health	Infectious diseases	Chronic diseases	Infectious diseases	Infectious diseases
Competencies to be acquired (explicitly stated)						
Run/evaluate surveillance system	Yes	Yes	Yes	Yes	Yes	Yes
Investigate outbreaks	Yes	Yes	Yes	Yes	Yes	Yes
Design study protocol/ perform applied research	Yes	Yes	Yes	Yes	Yes	Yes
Communicate results	Yes	Yes	Yes	Yes	Yes	Yes
Teach epidemiology	Yes	Yes	Yes	Yes	Yes	Yes
Risk assessment	No	Yes	No	No	No	No
Conduct survey	No	Yes	No	Yes	No	No
Manage data	No	Yes	Yes	Yes	Yes	Yes
Conduct public health intervention	No	No	No	Yes	No	No
Curriculum						
Duration (years)	2	2	2	2	2	2
Weeks spent on projects in hosting institute	79	79	76	58	75	63
Weeks spent on project outside hosting institute	6	7	7	26	7	2
Weeks in courses	10	9	12	12	13	30
Weeks in conferences	2	2	2	1	2	2
National FETP/ EPIET-associated programme		National	EPIET-associated programme	National	EPIET-associated programme	National
Three week introductory course	Yes	Yes	Yes	Yes (2 weeks)	Yes	No

Obligatory modules	Computer tools, multivariate analysis, vaccinology, project review	Computer tools, multivariate analysis, risk assessment in environmental health; sampling, scientific writing, surveillance	Same as EPIET plus laboratory module	N/A	Same as EPIET	Same as EPIET, plus data management, outbreak investigation, communication, infectious disease epidemiology, environmental epidemiology, occupational epidemiology, analysis of health situation, application of systems dynamics to epidemiological analysis
Facultative modules	Two of the four following: time series analysis, communication and scientific writing, rapid assessment, laboratory essentials for epidemiology	None	Two of the three following: time series analysis, communication, rapid assessment	None	Same as EPIET	None
Teaching languages of modules	English	French	English, German	Italian	English	Spanish
Training sites (e.g. national, district, county level)	Mostly national level	National or regional level	National and state level	County level	National level	National level
Application requirements						
Long-term contract in public health system Required upon admission	No	No	No	Required	Required	No
Motivation to work in public health in the future	Yes	Yes	Yes	Yes	Yes	Yes
Specific nationality	EU-citizenship	No	No	No	No	No
University degree	Yes	Yes	Yes	Yes	Yes	Yes
Academic degree upon completion	No	No	Incoming cohort 2009 will complete with MSc in applied epidemiology	MSc in applied epidemiology	No	MSc in applied epidemiology
Language skills	English + 1 other EU language	French	German + English	Italian	Scandinavian + English	Spanish
Infrastructure						
FTE of supervisors dedicated uniquely to the training programme	4.4 FTE coordinators minimum 1 local supervisor per fellow	1 FTE	2 FTE	3 FTE	0.25 FTE	5 FTE
Number of project-supervisors involved in FETP projects	At least 40	At least 15	Approx. 20	2	6	3-6
Outcome						
Number of yearly admissions (min/ actual/max)	6/19/19	5/5/6	2/8/8	8-20	1	5-10
The three most common degrees upon admission	Physicians, veterinarians, biologists	MPH/Epidemiology, public health engineer, pharmacists	Physicians, veterinarians, biologists	See above	Physicians, nurses with MPH, veterinarians	Physicians, veterinarians, biologists

Age of applicants upon admission min/ median/max	24/33/49	23/26/33	29/33.5/50	31/46/50	25/ - /35	
Percent women	64%	82.5%	52%	79%	88%	
Work place of fellows after training						
No work experience, no position, unemployed	0%	3%	0%	0%	0%	0%
Local / state / district public health	12%	51%	17%	86%	25%	82%
National public health service	43%	43%	38%	6%	75%	6%
International public health institution	33%	3%	31%	8%	0%	6%
Hospital / medical practice	3%	0%	7%	0%	0%	4%
Academia	3%	0%	0%	0%	0%	0%
Pharmaceutical company	2%	0%	0%	0%	0%	0%
Other/unknown	4%	0%	7%	0%	0%	2%

EPIET: European Programme for Intervention Epidemiology Training; FETP: field epidemiology training programme; FTE: fulltime equivalents; MPH: Master of Public Health; PAE: Postgraduate Training for Applied Epidemiology; PEAC: Programa de Epidemiología Aplicada de Campo; PROFEA: PROgramma di Formazione in Epidemiologia Applicata; PROFEI: Programme de formation à l'épidémiologie de terrain.

programme mainly focuses on infections diseases. During the two-year programme, trainees have to evaluate or implement a surveillance system, develop an epidemiologic study and conduct an outbreak investigation and study at least one outbreak. At the end of the training, fellows obtain a master degree.

Application requirements for PEAC include a university degree in a health-related field, and professional experience of at least two years in public health. Every year the ISCIII offers at least five fellowships, complemented by at least one additional fellowship from the Spanish International Cooperation Agency for applicants from Latin America or Africa, and one fellowship from the Ministry of Defense for a member of the army. The cohort can also be completed with professionals currently working at the Autonomous Regions' health administrations. The PEAC coordination team consists of one academic director and two full time scientific coordinators. Scientific coordinators follow the development of the trainees' objectives, review all the draft projects and lead some of them. For some specific projects, senior epidemiologists from national and regional level are involved in the supervision and contribute to training modules.

PEAC is currently running cohorts 14 and 15 with seven and nine fellows respectively. Up to now 109 professionals have been trained, 4 to 10 fellows per cohort. Fellows are mainly physicians (78) followed by biologists (9) and veterinarians (9). The Spanish programme is also hosting normally one EPIET fellow per year. The programme has trained 10 professionals from Latin-América (Argentina, Colombia, Cuba, Haití, Nicaragua, Uruguay and Venezuela) and Africa (Mozambique and Cape Verde). Ninety-five percent of the PEAC graduates currently work in epidemiological surveillance, alert and response units or surveillance of non-communicable diseases. Over half of the PEAC graduates are working in leading positions in epidemiological surveillance in public health administration at local, regional, or central level in Spain and in other countries. Some are collaborating actively in training field epidemiologists in their administrations.

The PEAC was created in an institution belonging to the Ministry of Health, and it was oriented to cover the shortage of professionals trained in applied epidemiology at central and regional levels. The first trainees were professionals from within the public health administration and the curriculum was based on short courses with very specific goals tailored to their specific needs. Meanwhile, applicants have often less work experience in the public health service and use the programme as a way to enter the public health work force. In response to this change PEAC is now including core courses on general public health. In 2009, the programme was moved to the Ministry of Science and Innovation which has improved the facilitation of original research but has diminished collaboration with the autonomous regions and thus lessened the fellows' opportunities to participate in outbreak investigations. The challenge is now to intensify the cooperation with the autonomous regions again.

Conclusion

Our overview shows that the existing five national FETP in Europe are differently organised in the various countries, and it is not evident whether the methodological differences reflect a difference in training needs or rather are the result of historic opportunities and training traditions in the respective countries. However, we demonstrate that all national programmes fulfil one of their main objectives which is to strengthen the national capacity

in applied field epidemiology, in such that most people do work in public health in their countries after completion the programme, many of them in leading functions. These findings are in line with those published in the paper by Bosman *et al*. in the same issue of this journal.

As concerns the particularities of the various programmes, the Italian FETP is very much a close system, while the German PAE seems to have been able to attract young professionals from outside the public health service, with a scientific background to dedicate and strengthen their skills for public health epidemiology. This may of course not be a result of the training programmes themselves but more a result of the overall flexibility of the staffing activities and penetration possibilities in the respective public health service, which in turn may become the most important determinant on how the public health work force in European countries will develop.

Looking back at the situation of FETP in 2001, some impressive improvements are visible. Three more programmes, the Italian, French and Norwegian FETP were created, the German FETP has become stronger and new EPIET-associated programmes were installed. In the editorial to the above mentioned overview in Eurosurveillance in 2001, Reingold has predicted Europe to face a bright future with respect to FETP [1]. Given the time that has elapsed since that statement, the indisputable progress with respect to the establishment of national FETP or EPIET-associated programmes is admittedly slow. Member States should be aware of how much support EPIET can offer for the establishment of national FETP or EPIET-associated programmes. However, they also need to be ready to provide the necessary resources, the administrative environment and long-term dedication to make field epidemiology training work.

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Contribution of EPIET to public health workforce in the EU, 1995-2008

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This article was published on 29 October 2009.
Citation style for this article: Bosman A, Schimmer B, Coulombier D. Contribution of EPIET to public health workforce in the EU, 1995-2008. Euro Surveill. 2009;14(43):pii=19381. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19381

We analyse activities and outputs of fellows of the European Programme for Intervention Epidemiology Training (EPIET) between 1995 and 2008 and describe the employment history of graduates after the training to demonstrate the contribution of this programme and of national EPIET-associated programmes to the public health workforce in the European Union and Norway. Up to 2008, some 161 fellows entered the training: 121 in EPIET and 40 in EPIET-associated programmes. Of these 149 were awarded a diploma. Fellows engaged in projects in all areas of surveillance, in outbreaks and field investigations and produced 340 publications in peer-reviewed journals. Seventy fellows were sent to 98 individual assignments on 65 international missions. The vast majority of graduates (90%) take up a position and remain employed in applied public health, either on regional, national or international level. Several (27) are working outside the EU, all in public health, including 13 working in Switzerland for international organisations. Only three of the 12 EU Member States that joined the EU since 2004, employ EPIET graduates. A major challenge for training the public health workforce is the retention of professionals in countries with limited job opportunities or wages significantly below the EU average.

Introduction

In order to increase the capacity to respond to emerging and ongoing threats from communicable diseases the European Commission launched a call for proposals for a two-year training programme for intervention epidemiologists in the European Union in 1994. Responding to this, experts from several national institutes for Public Health came together and the 2-year European Programme for Intervention Epidemiology Training (EPIET) was set up, starting in 1995, taking the Epidemic Intelligence Service (EIS) training programme of the United States' Centers for Disease Control and Prevention (US CDC) as an example [1,2]. The EPIET curriculum is set up to deliver independent, mid level epidemiologists with skills in the areas of surveillance, outbreak investigations, field-based epidemiological studies, scientific communication and teaching. The programme was integrated into the European Centre for Disease Control and Prevention (ECDC) in 2007. The set up and specific training objectives are described elsewhere in this journal [3].

The first cohort of EPIET fellows started in September 1995 and soon after, in January 1996, the German National Field Epidemiology Training Programme (FETP) at the Robert Koch Institute (RKI) in Berlin was established as a national training programme associated with EPIET [4,5]. From the start of the German FETP (currently renamed into German Postgraduate training for Applied Epidemiology, PAE), there has been a strong interaction with EPIET, since the association includes sharing scientific coordinators and core teaching modules [4,5]. After this, other countries: Norway, Austria, Finland, Slovenia, followed linking national training activities to the EPIET programme which are referred to as EPIET-associated programmes [3]. These programmes are required to employ fellows in an acknowledged EPIET training site and to use selection criteria and daily working activities that are similar to the EPIET.

In December 2008 the European Commission published a Green Paper on the European Workforce for Health highlighting the problem of shortages in health professions, including public health, now and in the near future [6]. The strengthening of public health capacity through training has been defined by the ECDC as a strategic target in the multi-annual programme 2007-2013 [7].

In order to demonstrate the contribution of the EPIET and EPIET-associated programmes to the public health workforce in the EU Member States and Norway, we analyse activities and outputs of fellows from cohorts 1 to 12 (October 1995- September 2008), and describe the employment history of graduates after the training. Since there are strong links in programme content, philosophy and scientific review between EPIET and EPIET-associated programmes, we chose to analyse these programmes together.

Material and methods

We used the EPIET programme office archives to compare the curriculum of the programme, including training objectives and composition of short training modules. throughout the cohorts. The concept of 'site' also needed defining. A site is considered acknowledged by EPIET when it employs at least one senior epidemiologist that participated in training-of-trainer activities, including facilitation at the three week introductory course for new fellows. Information on training-of-trainers and the number of external participants to EPIET training activities was extracted from the database described below.

The contribution of the EPIET and EPIET- associated programmes was defined and measured in terms of the number of people trained, the number of peer-reviewed publications published on work performed during the training, the number of participations

in international missions and the type of employment taken up after training. The output of all fellows has been registered in a 'pedagogical database', including publications (in the categories peer reviewed journals, bulletins, reports, abstracts and other), attendance to modules and projects, participation in international field missions, graduation results and abstracts presented at conferences. Information regarding publications was reported by the fellows using the quarterly reports or incremental progress reports. This information was complemented with a PubMed® search for publications of work performed during the fellowship. Data on publications were stored in EndNote® version X.0.2.

To track current employment, we used data on employment after graduation as registered in a database by the EPIET Alumni Network (EAN). These data were provided by alumni themselves using a structured form in MS Excel. Missing employment information was collected using web-based social networks such as LinkedIn® and FaceBook® and using affiliation information from publications retrieved through Medline®.

We also analysed the costs of the EPIET programme, using budget data from the 2002-2005 financial reports sent by the budget holder to the European Commission. Finally we used information from the ECDC budget for training 2006-2009 to calculate the costs to train one person during a one-week course. Data were analysed using MS Excel and MS Access.

TABLE 1

Training modules developed within the EPIET curriculum

Name of the module	Currently in use
Communication and dealing with the press	
Communication and scientific writing	**x**
Computer tools in outbreak investigations	**x**
Data management	
Geographical information systems (GIS)	
Logistic regression	
Time series and logistic regression	
Multivariable analysis	**x**
Rapid assessment and deliberate release threats	
Rapid assessment in complex emergencies	**x**
Time series analysis	**x**
Training-of-trainers	
Vaccinations	**x**

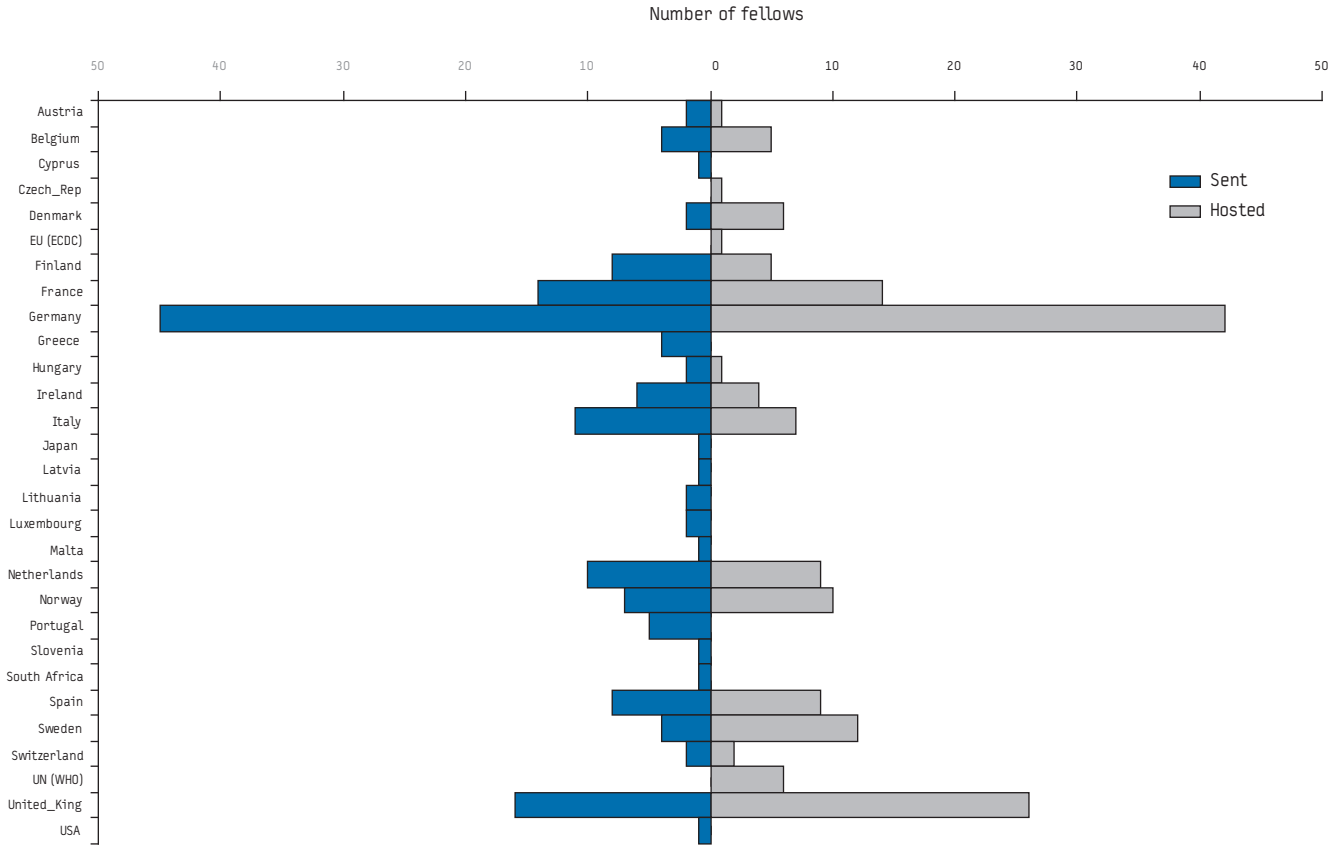
Results

EPIET curriculum through the years

The ratio of theoretical teaching versus supervised training has remained unchanged throughout the years; a maximum of 10 weeks

FIGURE 1

Number of fellows sent and hosted in EPIET and EPIET-associated programmes, by country, cohorts 1-12, 1995-2008 (n=161)



of teaching in modules and courses versus 22 months of supervised work at the training site or during field missions.

In total 13 short training modules, of which six are currently included in the curriculum, were developed for the EPIET between 1995 – 2008 (cohort 1-12) (Table 1). All training materials and training module curricula developed within the EPIET network are available to FETP-like training programmes. Since the migration of EPIET to ECDC, these modules have served as templates to develop short courses for EU Member States [8].

EPIET training sites and trainers

In 2008, twenty-four training sites in 16 different countries were acknowledged by EPIET: Austria, Belgium, the Czech Republic, Denmark, Finland, France (3 sites), Germany (3 sites), Hungary, Ireland, Italy, the Netherlands, Norway, Spain, Sweden, Switzerland and the United Kingdom (5 sites). Recently however, the sites in the Czech Republic and Hungary were inactivated as supervisors moved to other employment.

During the first 12 cohorts 268 professionals from 66 different organisations participated as facilitator in EPIET modules and courses. On average, a facilitator returned twice to teach. Most facilitators (189) were employed at public health institutes at national, regional or local level in the EU who participated without requiring teaching fees. A minority of facilitators were private consultants (23) hired to teach highly specific technical topics. The remaining facilitators (56) were employed by public health institutes outside the EU, universities, NGO's or the ECDC and also donated their time and expertise for free. Approximately one third of the trainers in EPIET started teaching through a 'training of trainers' activity such as the preparation week of the introductory course, or through supervised teaching by more senior trainers in specific modules.

Cohorts 1-12, 1995-2008

Fellows, projects and publications

In cohorts 1-12, a total of 161 fellows entered the training: 121 in EPIET and 40 in EPIET-associated programmes. Of 27 EU countries plus Norway, 22 have sent fellows to the programmes and 15 have hosted fellows in acknowledged EPIET training sites. In addition, fellows have been trained at EPIET sites in Switzerland, at the ECDC, at the World Health Organization (WHO) Lyon office and at the WHO Headquarters Geneva (Figure 1). The EPIET diploma was awarded to 149 fellows. Reasons for not receiving the diploma included failure to achieve the EPIET training objectives and terminating the training prematurely.

The European Commission (DG SANCO) funded 61 of the 121 EPIET salaries, nine were funded by ECDC, four by the WHO and one by Switzerland. The remaining 46 salaries were funded by Member States.

Fellows engaged in projects in all areas of surveillance, in outbreaks and field investigations have produced 340 publications in 71 different peer-reviewed, Medline-listed journals (Figure 2). These publications appeared in Eurosurveillance (114), Epidemiology and Infection (47), Emerging Infectious Diseases (22) and the Lancet (11). A number were published in general infectious diseases journals (35) and in national journals (23). Eleven articles were published in journals in the domain of microbiology.

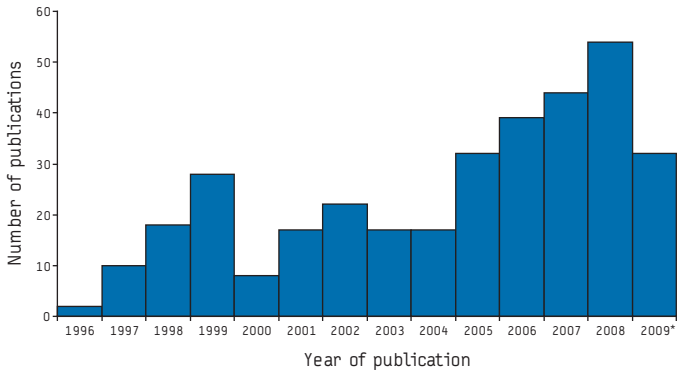
The top 10 topics of the 340 publications include mainly food- and waterborne diseases and vaccine preventable diseases (Table 2).

International missions

Fellows were requested to participate in missions by various international organisations: WHO (regional office Europe [EURO], Geneva Headquarters and Regional Office for the

Figure 2

Publications in Medline from EPIET and EPIET-associated programme fellows from fellowship projects, January 1996-April 2009 (n=340)



*Publications until 10 April

Table 2

Top-10 topics in peer -reviewed publications from EPIET and EPIET-associated programme fellows from fellowship projects, 1996-2009 (as of 10 April)

Topic of the study	Number of publications
Salmonellosis	33
Measles	16
Norovirus / Norwalk-like agent	13
Hepatitis A virus infections	12
Campylobacteriosis	11
Meningococcal disease	11
Influenza	10
Shigellosis	9
E.coli O157	7
Mumps	7

Table 3

Level of employment of EPIET and EPIET-associated programme graduates, in first and current employment, cohort 1-12, 1996-2008

Level of employment	First job (N=140)	Current job (N=139)
International public health	29%	33%
National public health	46%	44%
Regional public health	14%	13%
Private sector	4%	5%
Other	6%	5%

Eastern Mediterranean [EMRO], Caribbean Epidemiology Center [CAREC]), the ECDC, Epicentre, the Nordic Council, US CDC and the Norwegian National Institute for Public Health (FHI). To date, 70 fellows have been sent to 98 individual assignments 65 missions on behalf of the EU. Assignments included 32 outbreak investigations, one risk assessment, 17 surveillance projects, nine epidemiological surveys, four teaching and two other types of missions in 45 different countries, seven EU and EEA/EFTA, seven other European, 17 African, 10 Asian and four in South America. The pedagogical coordination of these missions was managed by the team of EPIET Scientific Coordinators, on occasion jointly with programme directors of the national field epidemiology training programmes in Canada, Germany and Spain.

Career track after graduation

We retrieved information on the first employment after graduation for 140 of the 149 graduates from cohorts 1-12 who received an EPIET diploma. For 139 alumni we were also able to retrieve the current employment. The vast majority of graduates (90%) take up a position and remain employed in applied public health, either on regional, national or international level (Table 3). Jobs in the private sector include consultancy and working with epidemiology in pharmaceutical companies. The category 'other' jobs include teaching.

Overall, 65% of the graduates currently have the same employer as immediately after their graduation. Of the 139 EPIET graduates where information on current employment is available, 27 are working in the public health sector outside the EU, including 13 working in Switzerland for international organisations (such as WHO, the United Nations High Commissioner for Refugees [UNCHR] and Médecins Sans Frontières [MSF])(Table 4). In terms of organisational position, one graduate is director of an international public health organisation, two coordinate EU disease specific networks, six are scientific coordinators of various FETP's and six are heads of unit.

Costs of EPIET

The costs per cohort of EPIET based on analysis of four cohorts (8-11, 2002-2005), ranged from 2.3 (cohort 8) to 3.2 million EUR (cohort 11), totalling 10.8 million EUR. These costs included 4.96 million EUR contributed by EU Member States in the form of salary costs for facilitators and supervisors and by hosting EPIET modules and courses. These contributions of the Member States were not

Table 4

Geographical location (country/continent) of current employment of EPIET graduates and EPIET-associated programme graduates, cohort 1-12, 1996 -2008

Country of employment	Public health			Private industry	Other	Total	Number of sent fellows
	International	National	Regional				
Austria		1				1	2
Belgium				1		1	4
Denmark	3	3				6	2
Finland		4				4	8
France	5	7	2	3		17	13
Germany	2	12	5		2	21	42
Greece		3				3	3
Hungary		1				1	2
Ireland		1	2			3	6
Italy	1	2				3	11
Lithuania		1				1	2
Luxembourg	1					1	1
Malta		1				1	1
Netherlands	1	3	1			5	10
Norway		5				5	5
Portugal	1	2	1			4	4
Spain		1			1	2	7
Sweden	11	1	1	1	1	15	4
United Kingdom	2	4	6	2	3	17	16
Subtotal EU	**27**	**52**	**18**	**7**	**7**	**111**	**143**
Africa	1	2				3	
Asia	4	4				8	
Caribbean		1				1	
Europe	13					13	
North America		2				2	
South America		1				1	
Subtotal non-EU	**18**	**10**				**28**	

reimbursed from the EPIET budget, yet they were a condition in the grant agreements on EPIET with the European Commission: Member States were expected to contribute approximately 40% of the total costs for EPIET.

From cohorts 8-11, 62 EPIET fellows were trained and external participants joined for 226 person-weeks in EPIET modules and courses. The average cost per year to train an EPIET fellow therefore is 88,300 EUR. This amount includes the total salary costs, which are on average 60,000 EUR per year, including all additional costs for the employer such as taxes, social security fees and insurance. This means that the annual costs exclusively attributed to the training of one EPIET fellow, when excluding salary, is 28,300 Euro. This includes participation to modules and courses (travel, accommodation, per diem, calculated salaries of the facilitators), costs of the salaries for EPIET scientific coordinators, EPIET Programme office and the salary of the supervisors on site.

In comparison, the average cost to train a participant during a one-week ECDC course is approximately 2,700 EUR, including trainer fees, flights, accommodation, meals and per diem.

Discussion

We present the result of an objective exploitation of available data to describe the contribution of EPIET to public health workforce. A thorough impact analysis of the programme will be provided in the near future through an external evaluation of EPIET, which will focus on elements of the programme such as quality, appropriateness, required capacity to train, costs, administration and organisation.

The curriculum of EPIET has remained focussed on structured, supervised skills development (learning by doing). The knowledge-based teaching (modules and courses) has evolved through the years with the development of specific teaching modules, which possibly reflects the ability of the programme to adapt to changes in the competence requirements of intervention epidemiologists.

The high proportion of graduates working in public health in the EU reflects the successful achievement of the programme's objectives. EPIET contributes to the key objective of the Green Paper on Workforce for Health [6] to 'achieve self sufficiency at EU level' and to 'promote circular movement of staff moving to another country for training and returning with additional experience and skills'.

Our data show that the top-five countries benefitting from employment of the highest numbers of EPIET graduates are Germany, France, United Kingdom, Sweden and Denmark. This most likely reflects a mix of factors such as nationality of those who entered the programme ('fellows sent'), availability and number of EPIET training sites and job opportunities. Germany heads the list, probably because of the national PAE, which is included in this analysis. In addition, the United Kingdom, Germany and France have the highest number of EPIET training sites within in the country, which may also be an indicator of employment opportunities after graduation. Three countries employ less than one third of the number of EPIET fellows they have sent to cohorts 1 to 12: Belgium, Italy and Spain. There is no obvious explanation for this observation, though this may also be linked to relatively fewer employment opportunities for EPIET graduates as compared to other EU Member States. So far, only three of the 12 EU Member States that joined the EU since 2004 employ EPIET graduates. Since cohort 12 (2006), an additional two 'new' EU Member States opened EPIET acknowledged training sites, but two operating sites were inactivated since cohort 12 due to trained supervisors taking up other employment. Even though the current cohorts in training include fellows from nine of the 'new' Member States, it will still take a while before job opportunities for EPIET graduates will be at the level of 'old' Member States.

One of the major challenges for training the public health workforce is the retention of professionals in countries with limited job opportunities or wages significantly below the EU average. Strategies to fill this gap may include development of more EPIET-associated programmes in new Member States and increased efforts to identify new supervisors to join the EPIET training-of-trainers programme. The number of fellows that needed to be trained each year to address the needs of public health in the EU will be addressed in the external evaluation of EPIET. At this stage we observe that the size of the latest EPIET cohort, cohort 15 consisting of 29 fellows including fellows from EPIET-associated programmes, is less than half the number of EIS officers recruited yearly in the US programme, while the EU population is significantly larger.

The increase of scientific output of the EPIET fellowship keeps the pace of the increase in size of the cohorts, with the areas of food- and waterborne diseases, vaccine preventable diseases, influenza and meningococcal disease among the most frequently published topics. The majority of articles were published in the 'Eurosurveillance' and 'Epidemiology and Infection' journals. We are aware that scientific publications provide a very limited indicator of a programme's performance, however this was the most convenient and complete set of data available for analysis. For future analysis it would be useful to look into citation indices and impact factors of the journals. In addition, it could be considered by the programme to create an indicator of public health actions that were the consequence of the work performed by fellows.

The costs to train one EPIET fellow should be seen in the light of the programme approach, which is learning by doing. The fellow works at an institute at least at the level of a junior scientist and is available for 90% of the working time when corrected for absence for modules and conferences. Therefore, the salary costs of an EPIET fellow should not be considered as costs for training but as similar to the cost for employing a public health professional.

In addition to the measurable outcomes of the EPIET training as mentioned in the results, the side benefits of the EPIET training are to be found in the training-of-trainers approach of the programme towards new facilitators and supervisors and the opportunity for external participants to training modules and courses when spare seats are available. For each fellow, at least three external participants were accepted in EPIET modules without charge and the fact that 24 training sites cooperate with the scientific coordinators to deliver consistency in methods of applied epidemiology, thus achieving 'one professional language' and tangible professional bonds between institutes. This 'professional bonding' is considered an important outcome of the programme, which is difficult to measure [9].

In conclusion, we believe that the EPIET programme is successful in achieving the programme objectives by developing a European Network of Intervention Epidemiologists practicing uniform methods, by developing a capacity to respond to public

health crisis in and beyond Europe and by strengthening the workforce in communicable disease surveillance and control in EU Member States.

Though many countries around the world have national FETP, the character of EPIET is rather unique in the sense that it is shared by 27 Member States as a joint effort for capacity building through training. After the two-year training, graduates are able to apply the relevant competencies in cross-border activities, addressing the specific challenges that communicable disease control poses at the European level. The fact that such a network of epidemiologists has been trained in one language (both professionally as linguistic) offers a great advantage in the joint response to disease control in Europe.

Acknowledgements

German, Finnish, Norwegian and Austrian FETP's for making data available on alumni from the fellows linked to EPIET. Ana-Belen Escriva for her advice on the analysis of publications, Viviane Bremer, Carmen Varela Santos, Vladimir Prikazsky for their critical review of the drafts of this article.

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New perspectives after the transition of EPIET to ECDC – the future of the programme

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This article was published on 29 October 2009.
Citation style for this article: Bremer V, Bosman A, Coulombier D. New perspectives after the transition of EPIET to ECDC – the future of the programme. Euro Surveill. 2009;14(43):pii=19374. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19374

Strengthening capacity in intervention epidemiology is key to the overall goal of responding to the challenge to detect and counter threats posed by outbreaks of infectious diseases in the European Union (EU). Since its founding in 1995, the European Programme for Intervention Epidemiology Training (EPIET) has become a core resource in training in intervention epidemiology in the EU. EPIET was integrated into the European Centre for Disease Prevention and Control (ECDC) on 1 November 2007 and this has resulted in an increased sustainability of the programme, allowing for long-term planning. Also, a new training programme, the European public health microbiology training (EUPHEM), was set up in 2008 to increase the response capacity for microbiology. Collaboration with EU Member States and other training programmes has been further intensified. Merging EPIET and other training activities in the ECDC training section has created the opportunity to develop an integrated multilevel approach to training in applied field epidemiology. An integrated approach to training activities on EU level, and increasing the number of EPIET and EPIET-associated fellows are essential to respond to the training needs of EU Member States, particularly new Member States. An external evaluation of EPIET in 2009 will provide guidance for a future strategy for the programme. This article examines the achievements of the EPIET programme after its transition to ECDC and provides an outlook on its future.

Introduction

The European Programme for Intervention Epidemiology Training (EPIET) was created in 1995 [1, 2]. The aims of EPIET are to develop a European network of intervention epidemiologists using commonly agreed methods, to build a response capacity inside and beyond the European Union (EU) and to strengthen communicable disease surveillance and control in EU Member States and at Community level. The programme is aimed at EU health professionals with previous experience in public health and a strong interest in epidemiology. The purpose of the programme is for EPIET fellows to gain practical experience in intervention epidemiology [1].

The programme lasts two years and is competency-based [3] with a 'learning by doing' approach. It starts with a three-week introductory course in infectious disease epidemiology. Following the introductory course, fellows spend 23 months at a training site at a national or regional centre for surveillance and control of communicable diseases in an EU Member State or Norway [4, 5], different from the country of origin of the fellow. Ten percent of the time of the programme is used for formal training courses and the remainder for supervised activities at a training site, where fellows are considered as a part of the public health workforce and are required to perform outbreak investigations as well as to carry out projects in the area of surveillance and do research on relevant public health issues. In addition, they are expected to present the results of their work to the scientific community during the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) and publish in peer-reviewed journals.

EPIET was integrated into the European Centre for Disease Prevention and Control (ECDC) on 1 November 2007 [6]. Prior to its integration, the European Commission and EU Member States were funding the programme and the salaries of the fellows on a project basis. The Swedish Institute for Infectious Disease Control administrated the budget and hosted the EPIET programme office responsible for all logistical and administrative issues between 2002 and 2007. Representatives of the training sites provided guidance on the programme strategy through the annual meeting of the EPIET Steering Committee. This article examines the changes within the EPIET programme after the transition to ECDC and provides an outlook on the future of the programme.

Evolution of EPIET after transition to ECDC

Administration

Since November 2007, EPIET is part of the section for Epidemiological Training of ECDC's Preparedness and Response Unit (PRU) and has a secured budget since its integration into ECDC. The EPIET programme office at ECDC continues to handle logistical and administrative issues of the fellows. The EPIET chief coordinator is also based at ECDC in Stockholm in the Section for Epidemiological Training. A framework partnership agreement between ECDC and four European national institutes for public health (Robert Koch-Institute, Institut de Veille Sanitaire, Health Protection Agency, Instituto Carlos III) has allowed the placement of the other EPIET scientific coordinators in Germany, France, the UK and Spain, also after the transition to ECDC. The fellows' contracts, salaries, removals and travel arrangements are handled by ECDC's Administrative Service Unit.

One year before the transition, starting in October 2006, ECDC took over the funding of EPIET fellows previously paid by the EU Commission. ECDC recruited fellows of the cohorts 12 to 14 and placed them in the training sites. Salaries offered by Member States were used to fund additional fellows. Since 2009, all salaries were transformed into individual grants. The former EPIET steering committee was replaced by the EPIET Training Site Forum to allow continued input from the Member States after the

transition to ECDC. All national training sites, a representative for the fellows currently in training and the EPIET alumni association are represented in the EPIET Training Site Forum. The Forum provides feedback on the functioning of the curriculum and current programme, identifies training needs for trainers, and participates in the recruitment of fellows and facilitators.

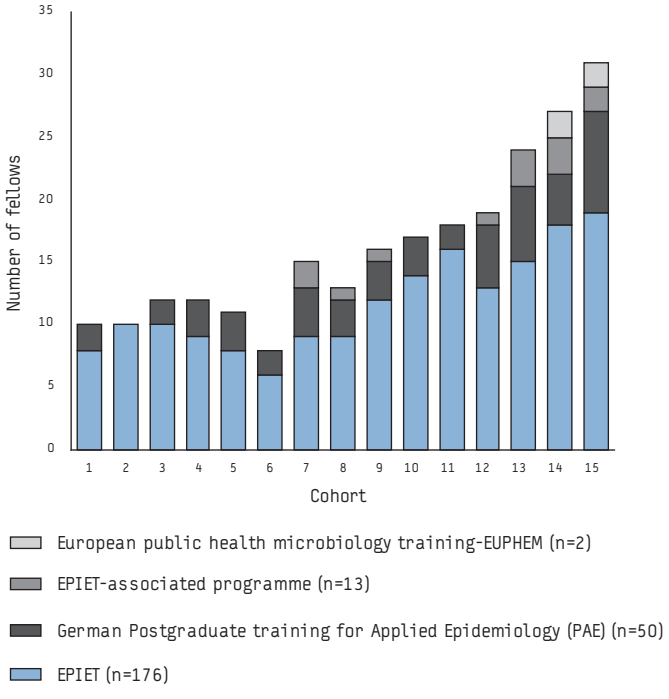
Growth of EPIET

The number of salaries provided for trainees increased from nine in 2002 to 19 in 2009. Before the transition, the number of salaries funded by Member States needed to equal at least those funded from the EU budget. This condition has been removed and in 2008 most salaries (84%) were funded by the ECDC. In addition to the increase of fellows funded by ECDC and Member States, a rising number of Member States started training fellows at national EPIET training sites. These fellows participate at EPIET modules and EPIET scientific coordinators review their progress, using the same appraisal criteria as for EPIET fellows. After successful completion of the training, these fellows also receive the EPIET diploma. This type of training is referred to as an "EPIET-associated programme". In 2008, four fellows recruited by Germany for the Postgraduate training for Applied Epidemiology (PAE) and one fellow recruited by Finland, Slovenia and Norway, respectively, were included into EPIET [6]. Thus, a total of 26 fellows have been included in the 14th EPIET cohort which started in September 2008 (Figure).

Compared to 2002 (cohort 7/8), the number of fellows currently in training (cohort 13/14) has increased from 28 to 47, corresponding to an increase of 68%.

Figure

Number of EPIET, German Postgraduate training for Applied Epidemiology (PAE), EPIET-associated and EUPHEM fellows, 1995-2009 (n=141)



Following the growth of the number of fellows, the number of EPIET scientific coordinators has increased from four to six, which corresponds to an increase of 2.8 to currently 4.4 full time equivalents.

Public Health Microbiology training programme

A laboratory component has been introduced by some field epidemiology training programmes in recent years [7]. In 2008 two EPIET salaries were used for the first time to recruit two fellows for the newly created European public health microbiology training (EUPHEM). The aim of this two-year pilot training is to develop a European network of public health microbiologists, a response capacity for microbiology inside and beyond the EU and to strengthen communicable disease surveillance and control through an integrated laboratory-field epidemiology network for outbreak detection, investigation and response EUPHEM fellows are placed in national public health laboratories and carry out outbreak investigations, surveillance and research activities in close collaboration with epidemiologists. Another aim of the placement is to develop skills in laboratory techniques and understand the specific methods, challenges and requirements for public health laboratories. EUPHEM fellows follow some of the modules of the EPIET programmes and are currently monitored by EPIET scientific coordinators.

International collaboration

Since the start of EPIET, the programme has relied strongly on the contribution from Member States. Fellows are currently hosted and trained in 21 training sites in the EU Member States and Norway. Estimating an average of four hours of supervision per week, these training sites contributed a total of 8,000 hours in 2008. EPIET continues to recruit facilitators for its modules from the pool of senior epidemiologists and EPIET alumni working in national or regional public health institutes. In 2008, they contributed a total of 37 weeks of facilitation to EPIET modules and a large proportion of these was provided by the Member States hosting EPIET-associated fellows.

EPIET aims to intensify its collaboration with the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET), which is a professional alliance of field epidemiology training programmes (FETPs), located in thirty-two countries around the world linking all existing field epidemiology training programmes [8]. Among other activities, EPIET/ECDC exchanged trainers and organised joint events with other independent FETPs, for example with the French and Spanish programmes, PROFET and PEAC as well as the Canadian Field Epidemiology Program.

Conclusions and recommendations

Integration of EPIET into ECDC

The transition of EPIET from an EU funded project to ECDC has resulted in increased sustainability of the programme. This opens the possibility for long-term planning of training in field epidemiology in the EU. In addition, merging EPIET and other training activities in the ECDC training section has created the opportunity to develop an integrated multilevel approach to training in applied epidemiology. An integrated approach to all training activities is essential to address training needs of EU Member States at national and regional level and should be pursued further.

Future growth of EPIET

Training more EPIET fellows is necessary in order to respond to the need for public health epidemiologists in Member States.

Strengthening capacity in intervention epidemiology is key to the overall goal of responding to the challenge to detect and counter threats posed by outbreaks of infectious diseases in the EU. Even though the number of fellows increased substantially over the past six years, it is still insufficient to fulfil the needs in all 27 Member States. Large Member States need to recruit a large number of fully trained epidemiologists at local, regional or national level. The majority of the twelve new Member States do not yet have any EPIET alumni who have returned to work in their country of origin. Finally, two thirds of EPIET alumni currently work in Member States at either national or regional level, while the remainder started working at international level, in the private sector or outside Europe [10].

Therefore the number of EPIET fellows needs to be increased further to respond to the needs of Member States. Especially training of fellows from new Member States is of outmost importance. In addition, ECDC and Member States need to consider developing strategies to facilitate the return of EPIET alumni to their countries of origin. The creation of more FETP or EPIET-associated programmes might contribute to build local capacities, as fellows trained in their own country are more likely to remain there after graduation and contribute to intervention epidemiology [10].

EUPHEM will contribute to create a network of professionals who will be able to collaborate with epidemiologists in the field of surveillance, outbreak investigation and applied research and this increased cross-sectoral cooperation will strengthen the capacity of outbreak investigation. Similarly to EPIET, EUPHEM requires a network of trainers available for supervision and coordination of the programme.

International collaboration

EPIET will continue to rely on the existing excellent collaboration with training sites in the Member States which are identified through a structured appraisal process by the EPIET scientific coordinators. Up to now, only few training sites are located in new Member States. With a growing number of fellows, there is a strong need for new training sites with experienced training site supervisors, teachers and facilitators. The number of experienced trainers available to teach highly specialised topics in intervention epidemiology is limited. Therefore, the training of future trainers is of high importance to ensure the quality of the EPIET programme. ECDC has started to address this issue by coordinating four workshops organised by the EPIET alumni association, TEPHINET, the Canadian Field Epidemiology Training Programme and the Robert Koch Institute. These workshops were specifically aimed at trainers and arranged around ESCAIDE. These efforts need to be continued to assure that a sufficient number of experienced trainers will be available.

Most of the EPIET scientific coordinators work at Member States' level and this has helped to maintain strong links with Member States. EPIET has reinforced the links to national institutes which host EPIET-associated programmes by increasing the number of facilitators originating from them. This collaboration, as well as maintaining strong links between EPIET and independent FETPs such as the French Programme de formation à l'épidémiologie de terrain (PROFET) and Spanish Programa de Epidemiología Aplicada de Campo (PEAC), is extremely useful to facilitate the sharing of resources and the development of joint training materials. TEPHINET has the potential to become the platform for these exchanges. EPIET should therefore take a more active role in TEPHINET, especially on the European level.

In addition to the collaboration with the Member States, ECDC's technical units for Preparedness and Response, Surveillance, Scientific Advise and Health Communication are increasingly offering activities corresponding to the EPIET objectives [11, 12, 13]. Therefore, EPIET will promote the involvement of its fellows in projects carried out by ECDC.

Challenges

After the integration into ECDC, the EPIET has developed into the most important source of training in intervention epidemiology in the EU. In the past it has played central role in building a public health capacity in surveillance, outbreak investigation and applied research in the EU and it will continue to do so in the future. Whether linking the successful completion of EPIET to an academic title would help to increase the programme's visibility and reputation has been discussed repeatedly. For example, the PEAC is tied to a master degree [14]. Similarly, the German PAE cohort starting in 2009 will be awarded a Master of Science in Applied Epidemiology at the end of their training. EPIET modules will count as an integral part of their theoretical training [15].

An external evaluation of the programme has been commissioned that will take place in 2009. It will provide strategic advice and guidance for the future development of EPIET and address the future role of EPIET-associated programmes.

Acknowledgements

We thank the EPIET scientific coordinators Alicia Barrasa, Marion Muehlen, Brigitte Helynck, Doris Radun, Marie-Anne Botrel and the coordinator of the German PAE programme Katharina Alpers for their comments of the manuscript.

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Applied epidemiology training in Europe: quite a success - but more to be done

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This article was published on 29 October 2009.
Citation style for this article: Krause G, Stefanoff P, Moren A. Applied epidemiology training in Europe: quite a success - but more to be done. Euro Surveill. 2009;14(43):pii=19375. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19375

This article describes the development of training in applied epidemiology in Europe and outlines the current situation in Europe with a view of how the system can be improved to meet future challenges.

Applied epidemiology training is often being referred to as training in field or intervention epidemiology. Field epidemiology has been characterised as "quick and appropriate" meaning that it addresses important public health problems in the community in a timely manner and employs the appropriate resources and epidemiologic methods to probe causality to the degree sufficient to identify the source or aetiology of the problem and to establish immediate and long term control and prevention accordingly [1].

The origin of training in field epidemiology

The first structured programme deliberately focussing on applied epidemiology training was the Unites States Centers for Disease Control and Prevention (US CDC) Epidemic Intelligence Service (EIS). It was founded in 1951 by Alexander Langmuir as a two-year on-the-job training at the CDC. [2]. Although the scope of topics to be covered and some of the methods have further developed since, the hallmark of the EIS remains the combination of a three-week introductory course followed by a two-year public health assignment interrupted only by a few specialised training modules. Due to increasing demand from foreign applicants and also in order to stimulate a common international methodological and conceptual training approach, the CDC started supporting the creation of "Field Epidemiology Training Programmes" (FETP) in many other countries [3-5]. In that context CDC seconded staff as long term consultants, temporary supervisors or course facilitators to other countries and provided training material. The Training Programmes in Epidemiology and Public Health Interventions NETwork (TEPHINET) was founded in 1997 and aims to improve networking between the FETP [6]. Today some 42 FETP are officially members of TEPHINET. Others exist independently from TEPHINET.

The development of field epidemiology training in Europe

The European Programme for Intervention Epidemiology Training (EPIET) was founded in 1995. It is a special form of FETP as it was set up from the very beginning to have a collaborative, multinational approach [7]. It has been a principle of EPIET that participants coming from one country of the European Union (EU) be assigned to a training site of another EU country, so as to increase networking on the European level.

National FETP also exist in the EU. They generally assign national participants exclusively to training sites within the country, and training is done in the national language. A variation of this are the EPIET-associated programmes in which fellows are assigned to a training site inside their country of origin but attend the modules and receive supervision organised by EPIET. In the following discussion, the FETP, the EPIET and the EPIET-associated programmes will be referred to collectively as the Applied Epidemiology Training Programmes (AETP).

The AETP in Europe generally have similar training objectives. They aim at enabling participants to apply epidemiological tools in the practical public health context. Outbreak investigations, surveillance activities and epidemiologic research represent the core approaches to rapid infectious disease control and are the main focus of the projects to be completed during the programme. European AETP have a lot in common with the EIS as most of the architects of EPIET and heads of the departments hosting the French, the Italian and the German FETP, as well as various facilitators and supervisors, are EIS alumni.

Country-specific aspects of AETP in the EU

The existing European FETP have different approaches [7]. The Italian programme has a very strong focus on non-communicable diseases and highlights the programmatic and preventive aspects of public health instead of the surveillance and intervention aspects in infectious diseases which largely characterise the other national FETP.

The European FETP also have different strategies for capacity building. The Italian FETP places emphasis on "in house capacity building" where public health workers who already have permanent positions in peripheral health departments are recruited to strengthen their skills in their established functions. The German FETP on the other hand attempts to "attract and specialise external workforce" placing elevated application requirements with respect to prior academic degrees, work experience and language skills in order to attract young scientists from various academic disciplines into the public health workforce. The French and Norwegian programmes are somewhere in between those approaches and the

Spanish FETP is currently moving from the "in-house capacity building" strategy towards "attracting external workforce".

The Italian, French and Spanish programmes are purely national in that all modules and training activities are carried out within the country without direct interaction with the EPIET or the other FETP. The advantages of offering modules and courses in the national language are that applicants selected for training do not have to be proficient in English. This in turn may attract applicants who are more likely to remain working in the national public health workforce instead of moving on to (possibly more attractive) positions in other countries. On the other hand, for the time being, English remains the lingua franca in medical science: a literature review, foundation of any epidemiological study, requires reasonable English reading skills at least; and sharing epidemiologic findings within the scientific community will in many instances be most effective if done in international scientific networks, journals and conferences. Given the new International Health Regulations and multiple networks within the EU, the ability to communicate in English has become a daily necessity on national level. This will inevitably and increasingly hold true also for local public health officers. One very important and successful characteristic of EPIET is to require proficiency in English and at least one other European language. During the EPIET fellows have to learn the language of their hosting country. This sometimes represents a tremendous challenge. However this challenge has many benefits. Being exposed to other languages and cultures, EPIET fellows become better equipped to negotiating and networking at the European level. Because of these very reasons it would therefore be desirable that English language proficiency also be required and developed in national FETP, so that fellows and alumni of national FETP can also be active members of the European epidemiologists network as EPIET and EPIET-associated programmes' fellows already are.

Academic recognition and accreditation

Applied epidemiology training differs from university-based training such as the Master in Public Health (MPH) or Master of Science in Epidemiology programmes. Master studies are usually characterised by a typical "class room" kind of curriculum. Applied epidemiology training is typically organised as a two-year full time programme in which over 80% of the time is filled with supervised on-the-job training. Lectures, seminars, case studies and other training formats common in academic training only make up for less than 20% of the time [8].

The Spanish FETP (PEAC) has a strong "class room" approach requiring fellows to attend a three-month introductory course at the national local school of public health (Escuela Nacional de Sanidad, ENS). The French, German and Italian FETP also cooperate with universities to varying degrees but without it affecting the on-the-job training approach.

Graduates of the Italian and Spanish FETP receive a MPH. Similarly the German FETP is now providing a Master of Science in Applied Epidemiology upon completion. Those formal titles have immediate implications on career chances and salaries in many European countries. Other AETP such as EPIET or the French FETP do not result in academic diplomas. The fellows that attend those programmes can however individually use the teaching modules and practical work conducted during their training to gain academic credits with specific European universities. Many alumni believe that, given the quality of the AETP, it should be appropriate that successful completion of the two-year programmes be acknowledged accordingly. Others recognise that pursuing an MPH and an AETP at the same time could jeopardise the quality of both.

It should be noted that the EIS, in over 50 years of its existence in the United States (US), never needed to be recognised with an academic degree. The visibility of the EIS programme and the career boost that it represents relies mainly on the quality of the work performed during the two-year training. Most EIS alumni complement their practical training with an MPH or a PhD degree obtained before or after the EIS programme.

In Europe academic diplomas do not automatically imply professional accreditation or board certification in public health medicine or epidemiology. Such accreditation is lacking in many countries and at the European level. However it must be recognised that the combination of an MPH and an AETP with an EU professional accreditation would provide a good basis for a career in field epidemiology. Applied epidemiology training is therefore not redundant to public health or preventive medicine training but should rather be seen as complementary.

Role of AETP in epidemiology training capacity in the EU

FETP and EPIET have been commended for the high level of training quality and the successful integration of alumni in the European public health workforce [9]. In the last 15 years EPIET and FETP fellows have participated in most of the major outbreak investigations conducted at the national and EU level as well as in the response to major international outbreaks [10]. They constitute a force of intervention within Europe and to some extend beyond it although the involvement of the European Centre for Disease Prevention and Control (ECDC) in activities outside EU is limited.

While EIS officers and most FETP fellows are regular staff members of the respective institutions, EPIET fellows are currently funded through a scholarship, in order to overcome specific administrative obstacles within the EU regulations. This scholarship status however runs the risk that EPIET participants are seen and see themselves as students, without the privileges and duties of regular staff members. EPIET and especially the respective training sites must therefore take care that EPIET fellows be visible as full members of the European workforce in intervention epidemiology.

While the expansion of EPIET in the recent years is impressive, the needs in terms of human resources are not met. The European training capacity lags behind the US EIS as far as the number of trained experts is concerned [11]. In the US with a population of around 305 million people the EIS has currently around 80 EIS officers per cohort, that is to say it is training about one expert per 3.8 million inhabitants [12]. In comparison, in the EU and EFTA countries with a population of about 505 million people, EPIET and all FETP taken together have around 50 fellows per cohort which would result in one expert per 10.1 million inhabitants. Furthermore this very rough comparison does not take into account three additional factors: first, the need for field epidemiologists is not only determined by the size of the population but also by the number and complexity of administrative levels; second, the long existence of EIS has already generated a solid basis of a field epidemiologist workforce; and third, a number of states in the US have their own complementary field epidemiology training programmes which have not been included in the calculation above.

For all these reasons it seems save to say that the European training capacity for applied epidemiology should be increased.

AETP are very resource-intensive. They usually operate on the borderline of the mandates of ministry of health and ministry of research and education and generate conflicts regarding their funding by national, regional or local governments. This mixture leads to a situation in which the need of such programmes is easily agreed upon yet the organisational and financial responsibilities are often being disputed between various entities. Most of the five existing FETP in Europe have undergone critical phases when the source of funding was uncertain and other administrative problems impeded their functioning. For many years Poland and Hungary have tried to initiate FETP. Yet the lack of logistic capacities, especially in terms of human resources, made it impossible so far.

Role of AETP in European integration

Most countries that accessed the EU after 2004 have large, centralised public health systems, which have undergone several reforms, and different models of public health training have been in place. The main obstacle in capacity building in the new Member States - although not necessarily limited to these countries - is the poor availability of experienced epidemiologists, mostly due to still limited university training. Especially the local public health departments lack professionals who can apply epidemiological methods, perform epidemiological studies, publish their results, and generally use a "language" common with their Western colleagues.

Well-trained epidemiologists from the new Member States often choose a carrier in Western Europe, the US or in international organisations, due to much higher salaries and an environment more suitable to their professional development. This situation creates barriers for the development of FETP programmes in these countries since the few epidemiologists working there are not available as supervisors. The role of EPIET in this matter is also limited as only few EPIET alumni from the "new" EU countries have returned to their home countries to help in capacity building.

Future perspectives of applied epidemiology training in Europe

The capacity building in applied epidemiology in Europe is likely to be more successful if new FETP and EPIET-associated programmes are created and integrated in a European Network of national FETP rather than increasing the size of EPIET alone. According to Article 9 of the founding regulation of ECDC it is one of its tasks to "assist Member States to have sufficient numbers of trained specialists, in particular in epidemiological surveillance and field investigations, and to have a capability to define health measures to control disease outbreaks" [13]. Therefore it seems it should be a priority for ECDC not only to run EPIET and offer training courses (which it is already doing) but also to assist Member States in creating FETP and to support the concept of EPIET-associated programmes.

It should be acknowledged that the Spanish, German and Italian FETP benefitted from the secondment of US CDC experts to those countries [3]. Following this example, seconding EU senior epidemiologists to European countries willing to develop an FETP is a practice that needs to be further developed and accepted by Member States. With ECDC hosting a stable and ever increasing EPIET, the conditions have never been as good and the steps to be taken never as clear to actually foster cooperation between existing FETP and to create new ones in Europe.

National ministries of health need to assume responsibility in generating and assuring an internationally compatible workforce in applied epidemiology, including the creation of national applied epidemiology training programmes while EPIET should function as a breeding ground for these programmes.

Acknowledgements

In July 2008 current and former coordinators of EPIET and the five existing FETP as well as representatives of two national public health institutes planning to initiate an FETP met in Berlin to discuss the future of field epidemiology training programmes and their interaction with EPIET. We would like to thank the participants of this workshop for contributing their perspectives and thoughts which laid the foundation to this manuscript: P. Aavitsland, K. Alpers, A. Barrasa, N. Binkin, A. Bosman, V. Bremer, I. Czumbel, B. Helynck and D. Herrera.

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An outbreak of hospital-acquired Staphylococcus aureus skin infection among newborns, Nan Province, Thailand, January 2008

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This article was published on 29 October 2009.
Citation style for this article: Pawun V, Jiraphongsa C, Puttamasute S, Putta R, Wongnai A, Jaima T, Tithsayatikom P, Wattanasri S. An outbreak of hospital-acquired Staphylococcus aureus skin infection among newborns, Nan Province, Thailand, January 2008. Euro Surveill. 2009;14(43):pii=19372. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19372

In January 2008, we investigated a cluster of neonates with bullous impetigo in a hospital of northern Thailand in order to control the outbreak and identify a potential source of the infection. We reviewed medical records and working timetables of healthcare workers (HCWs) and conducted a case-control study. We performed an environmental study and took bacteriological samples from HCWs and equipments. According to our case definitions, we identified 16 confirmed cases and 14 probable cases. The attack rate was 42%. Most cases had skin blisters (28 cases) followed by pustules (five cases) and exfoliation (three cases). The location of the lesion was the trunk (17 cases), neck (14 cases) or armpits (nine cases). Nineteen cases had symptoms onset after discharge from hospital. Median age at onset was 4 days. The strain isolated from an infected newborn shared the same phage type as the contaminated equipment. Insufficient hand hygiene was an observed risk behaviour of HCWs and visitors. Exposure to a nasal carrier of *Staphylococcus aureus* (adjusted OR: 80.3, 95% CI: 4.8 – 1350.3) and ward sharing with a symptomatic case (adjusted OR: 35.6, 95% CI: 1.9 – 654.7) increased the risk of acquiring the infection. The outbreak ended abruptly after implementation of hand hygiene practices and equipment cleaning.

Introduction

Bullous impetigo is a superficial bacterial skin infection, mainly affecting infants and small children, usually caused by *Staphylococcus aureus* which can lead to severe illness in the form of staphylococcal scalded skin syndrome (SSSS), septicaemia, or pneumonia [1,2]. Newborn infants are prone to skin infection due to the vulnerability of their skin [3]. Healthy carriers of *S. aureus* such as healthcare workers (HCWs) [4,5] can transmit the bacteria to others [6,7]. Thai Ministry of Public Health included nosocomial infections in mandatory reporting in 1982 [8]. The prevalence of nosocomial infections in Thailand was 11.7% in 1988, it diminished to 7.4% in 1992, to 6.4% in 2001 and slightly increased to 6.5% in 2006 [9]. Most hospitals in Thailand have targeted surveillance systems in place for high risk population such as intensive care patients, post-surgery patients and patients with invasive devices. However, staff shortage and high workload are the main problems in tackling nosocomial infections in Thailand [10-12].

Hospital A is a district hospital with 90 beds and 50-60 births take place here on average, every month. This hospital takes care of seemingly uncomplicated pregnancies. If the woman is considered at high risk, she is transferred to the provincial hospital, which offers better facilities for critical care.

A pregnant woman close to delivery stays in the pre-delivery room until delivery is imminent, when she is transferred to the delivery room. If caesarean section becomes necessary, she is transferred to the operating room. After delivery, mother and newborn stay in the same room and bed at the postpartum ward. There are two postpartum wards, ward A and ward B. Ward A is the first priority for hospital stay after the delivery because it is located in the same building with the delivery room. Ward B is usually empty and the room is used as the alternative ward if ward A is full. Newborns delivered by caesarean section stay in the nursery for approximately one hour for close observation of vital functions. If their condition is stable, they are sent to the postpartum ward immediately. After uncomplicated deliveries, mother and child may be discharged from hospital even after 48 hours.

Methods

On 25 January 2008, a medical officer at hospital A notified the Bureau of Epidemiology, Department of Disease Control in the capital, of an increasing number of neonates with bullous impetigo and requested assistance for an outbreak investigation. In this report we describe an outbreak of the staphylococcal bullous impetigo occurring in a district hospital in northern Thailand between 11 and 27 January 2008. Our objectives were to control the outbreak, to identify potential sources of infection and to investigate risk factors for illness.

During the outbreak, hospital A had 34 HCWs of whom 19 were exposed to newborns (eight nurses, five student nurses, four nurses' aids and two doctors). These 19 HCWs worked in all the units of maternal and newborn care. Following the rules and policies of Hospital Accreditation, there was one infection control nurse (ICN) responsible for hospital infection control activities which included surveillance for hospital-acquired infections, supervision of infection control practices for healthcare workers, and evaluation of medical products that could increase the risk for infection. Due

to shortage of staff, this nurse was also involved in direct patient care.

Descriptive epidemiology

We started our study by reviewing medical records of the cases occurring in hospital to identify the first case of the cluster. We determined the investigation period by counting backward ten days from the onset of the first case [13]; thus the observation period began on 1 January 2008. A probable case was defined as a newborn infant (age ≤30 days) with skin pustule, blister or exfoliation on any part the body who was born between 1 January and 25 January 2008. A confirmed case had in addition methicillin-sensitive *Staphylococcus aureus* isolated from the skin lesion. We contacted the parents of all 71 neonates who were born during 1-25 January 2008. Sixty of them responded. The paediatrician was asked to collect date of onset of each case and to describe the skin lesion by anatomical location. In addition, all parents of cases were interviewed about potential community infection risk factors.

Environmental and laboratory investigation

We interviewed eight HCWs who worked in the delivery room and post partum wards and observed their routine neonatal care practice. We inspected the delivery room, the neonates' room and the disinfection unit where we observed the adherence to standard infection control procedures. We enquired about schedules for room cleaning and requested disinfection protocols from the ward's chief nurse. A laboratory technician collected samples from the most frequently used neonatal care equipments, such as radiant warmer, weight scale, baby-crib and stethoscopes. Environmental samples, 37 specimens, from the bathing counter, soap and washing water for instance were also collected for bacterial culture. Hand swab and nasal swab samples were collected from all HCWs. We took swabs on the first web space between the thumb and index finger and in the right nostril. In order to confirm the epidemiological links between positive culture samples from cases and environmental samples, we performed limited phage typing.

Analytic epidemiology

We conducted a case-control study by comparing 16 laboratory-confirmed cases with 30 healthy neonates (no skin lesion) that were born in the same hospital during the same period. Type of birth, room location for neonates, exposure to neonatal equipment and exposure to each HCW were tested for statistical association with case status by calculating odds ratio (OR) and 95% confidence interval (CI). We used the working timetable of each HCW as a proxy of newborn exposure by matching their schedule to the first 24 hours after birth of each neonate. We used multiple logistic regression technique to diminish the effect of possible confounding factors. The variables with significant p-value, less than 0.05, from the univariate analysis were put in the model. We used Excel 2003 and STATA 10.0 programmes for data analysis.

Results

Descriptive results

The onset date of the index case was on 11 January 2008. Sixty (84.5%) out of 71 neonates were physically examined again from 25 January to 27 January 2008, of which we identified a total of 30 cases (attack rate = 42%): 16 confirmed and 14 probable cases. Skin blister was the most common symptom (28 cases), followed by skin pustule (five cases) and skin exfoliation (three cases). Skin lesions were located at the trunk (17 cases), neck (14 cases), armpits (9 cases), groins (seven cases), upper extremities (seven cases) and lower extremities (five cases).

No serious case or complication has been recorded during this outbreak. The age of illness onset ranged from 1 to 12 days; median age was 4 days. Eleven of the 30 cases had symptoms during hospitalisation and 19 showed symptoms only after discharge from hospital. From the interviews with the parents, we found out that no other family members had skin infections during that time. The sex specific attack rate was 46% (16/35) for male and 56% (14/25) for females. The attack rate by room location was highest in ward A (61%) followed by the nursery (44%) and zero in ward B.

The epidemic curve (Figure) illustrated a gradually increasing number of cases at the beginning of the outbreak, a sharp increase

Table 1

Phage typing from one case, from neonatal care equipment and from carriers among healthcare workers, hospital A, Nan Province, Thailand, January 2008

Sample	Result
Case 1	MSSA- phage type 29/52/80/3C/55/95/81/94/96
Radiant warmer in the delivery room	MSSA- phage type 29/52/80/3C/55/95/81/94/96
Weighting scale in the delivery room	MSSA- phage type 29/52/80/3C/55/95/81/94/96
Baby crib in ward A	MSSA- phage type 29/52/80/3C/55/95/81/94/96
Bathing counter in ward A	MSSA- phage type 29/52/80/3C/55/95/81/94/96
Nurses' aid A4 (nasal swab)	MSSA- phage type 29/52/80/3A/3C/55/6/47/53/54/75/77/83A/94/96
Nurse R5 (hand swab)	MSSA- phage type 29/52/52A/80/3A/71
Student nurse S5 (nasal swab)	Non-typable

Table 2

Univariate analysis of potential exposures of neonates with bullous impetigo, hospital A, Nan Province, Thailand, January 2008 (n=46)

Exposures	Crude OR (95% confidence interval)	p-value
Admission in ward A	11.3 (1.3 – 512.2)	0.011
Ward sharing with symptomatic cases	5.4 (0.9 – 54.9)	0.034
Exposure to nurses' aid A4 (carrier)	12.1 (2.0 – 122.0)	0.001
Exposure student nurse S2 (non carrier)	7.0 (1.5 – 36.6)	0.004
Exposure student nurse S4 (non carrier)	4.6 (1.1 – 20.5)	0.018

Table 3

The association between neonates with bullous impetigo and five exposures, significant p-value (p<0.05) from univariate analysis, by multiple logistic regression, hospital A, Nan Province, Thailand, January 2008 (n=44)

Exposures	Adjusted OR (95% confidence interval)	p-value
Admission in ward A	14.5 (0.4 – 578.2)	0.156
Ward sharing with symptomatic cases	35.6 (1.9 – 654.7)	0.016
Exposure to nurses' aid A4 (carrier)	80.3 (4.8 – 1350.3)	0.002
Exposure to student nurse S2 (non carrier)	0.8 (0.08 – 7.9)	0.860
Exposure to student nurse S4 (non carrier)	6.2 (0.6 – 60.5)	0.116

in the second week, and a peak on 25 January. The outbreak ended rapidly after ward closure for two days during 26 and 27 January. A week before the outbreak started, five student nurses had arrived at the maternal and neonatal care unit for nursing practice and they left in February 2008. When an increasing number of bullous impetigo cases was noticed, the ward nurses began to strengthen hand washing. However, they did not report the cases to the hospital infection control nurse until 25 January, because previously, newborn skin infections had not been included in the hospital infection surveillance protocol.

Environmental investigation and laboratory results

Our investigation revealed that the delivery room was cleaned with household detergent three times per week. We found that some equipment such as radiant warmers and the weight scale were cleaned only on superficial surfaces after utilisation. Postpartum wards, where the newborns stayed, were usually crowded with many visitors, who could easily touch and play with newborns without having properly washed hands.

Laboratory results

Methicillin-sensitive *Staphylococcus aureus* (MSSA) from all 16 confirmed cases had the same antibiotic sensitivity pattern and all were resistant to penicillin. Only one isolate was phage typed because the other isolates had already been discarded. Among 37 samples from neonatal care equipments, four specimens were positive for *S. aureus*. Two positive items, a radiant warmer and a weight scale, were found in the delivery room and three, a bathing counter, a baby-crib and a bed sheet of a case, were found in ward A. Three out of 34 healthy HCWs had positive cultures for *S. aureus*. Nurses' aid A4 and student nurse S5 had nasal carriage of *S. aureus* and nurse R5's hand swab was positive for *S. aureus*. None of the three carriers had a skin lesion.

MSSA phage type 29/52/80/3C/55/95/81/94/96 was identified from all four samples of contaminated neonatal care equipment. In addition, we identified phage type 29/52/52A/80/3A/71 and 29/52/80/3A/3C/55/6/47/53/54/75/77/83A/94/96 from nurse R5 and nurses' aid A4 respectively while phage type of Student nurse S5 was non-typable due to the limitations of laboratory technique (Table 1). The phage type of the newborn case was 29/52/80/3C/55/95/81/94/96, the same as the contaminated equipments and shared the same group as the carriers.

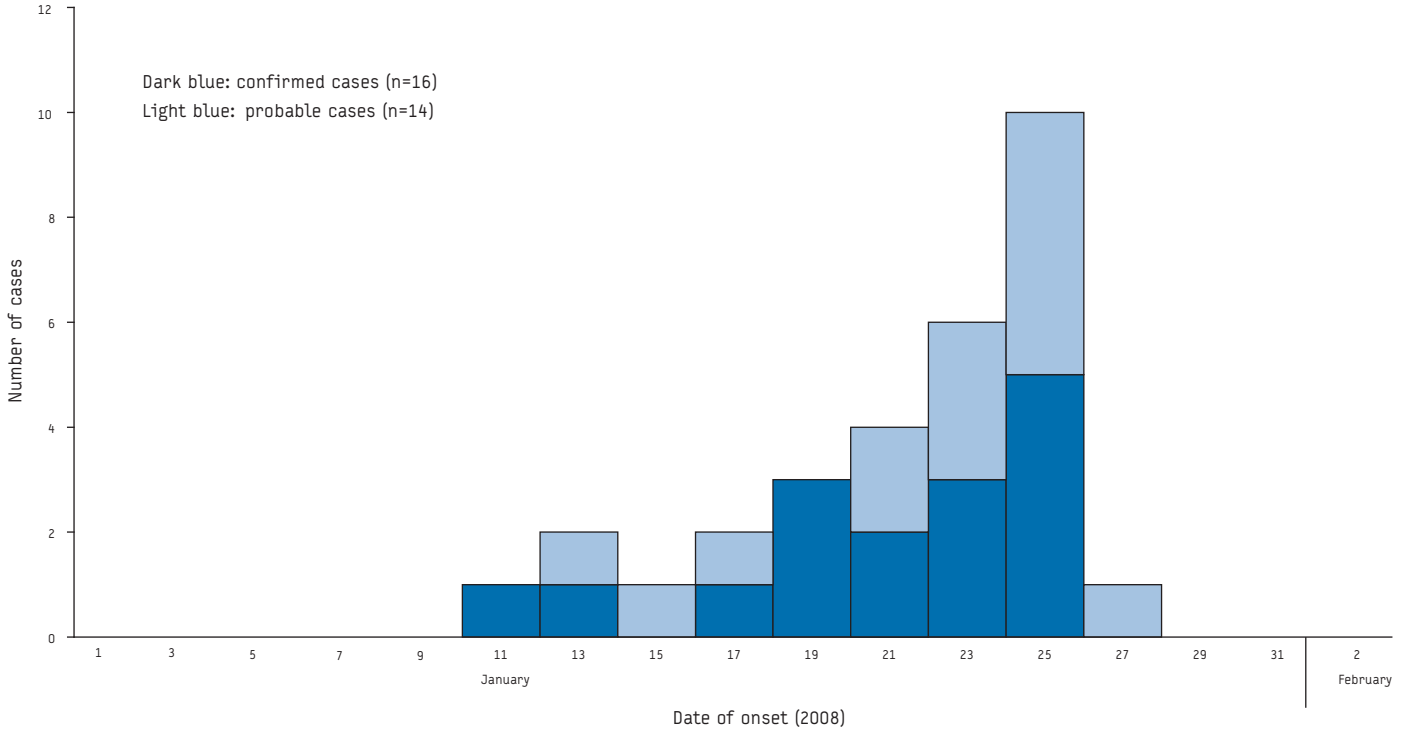
Analytic results

In the case-control study, neonates exposed to nurses' aid A4, who was a nasal carrier of *S. aureus*, had the highest risk of illness [crude OR: 12.1 (95% CI: 2.0 – 122.0), p=0.001]. In the analytic study, 36 potential exposures were tested for association; among these, only five variables as displayed in Table 2 had p value less than 0.05.Univariate analysis (Table 2) also indicated an association between illness and four other variables: staying in ward A [crude OR: 11.3 (95% CI: 1.3 – 512.2), p=0.011], exposure to non-carrier student nurse S2 [crude OR: 7.0 (95% CI: 1.5 - 36.6), p=0.004], sharing ward with the symptomatic case during hospitalisation [crude OR: 5.4 (95% CI: 0.9 - 54.9), p=0.034] and exposure to non-carrier student nurse S4 [crude OR: 4.6 (95% CI: 1.1 - 20.5), p=0.018].

In the multiple logistic regression model shown in Table 3, we found that both exposure to nurses' aid A4 and sharing ward with a symptomatic case remained significantly associated with illness

Figure

Epidemic curve of staphylococcal bullous impetigo cases by date of onset in a district hospital, Nan Province, Thailand, January 2008 (n=30)



in our model with adjusted OR equal to 80.3 [(95% CI: 4.8 – 1350.3), p=0.002] and 35.6 [(95% CI: 1.9 – 654.7), p=0.016] respectively.

Control action and outbreak response

After confirmation of the outbreak, the following measures were taken:

- Cases were treated and isolated in ward B;
- Delivery room and ward A were closed between 26-27 January 2008 for cleaning and disinfection;
- Medical devices such as the radiant warmer and newborn weight scale were cleaned with detergent and disinfected with 70% alcohol;
- HCWs carriers of *S. aureus* were treated with the topical antibiotic Muropicin, and required to abstain from nursing until nasal swabs were negative, i.e. seven days;
- Adherence to infection control measures was enforced such as hand hygiene, wearing masks and hair caps during routine nursing care;
- Alcohol hand rub was provided at each bed in postpartum wards.

Furthermore, we also recommended strengthening the hospital infection surveillance system with competency building for ward nurses to detect outbreaks and early report them to the hospital infection control practitioners.

On the last day of our investigation we joined the hospital meeting, presented the investigation results and discussed the infection control breaches such as insufficient hand hygiene and personal protective equipment. This meeting led to cleaning of the delivery room on a daily basis and cleaning neonatal care equipments after every use with detergent and 70% alcohol. Moreover, the chief ward nurse decided to implement new strategies such as limiting the number of visitors permitted to stay in the postpartum wards. Surveillance of newborns' skin infection was included in the infection control policy.

Discussion and conclusion

This outbreak of staphylococcal skin infections in newborns was detected late because most of the cases developed symptoms only after discharge. We implicated the environmental equipment as possible source of infection because it had the same phage type as the one from a case. Contact with a HCW who was a staphylococcal carrier was an important risk factor in our study, as has been seen in previous studies (7,14,15). With our limited resources it was impossible to determine if, and if so, which HCW could have been the source of the outbreak, although two of them were suspected. The high attack rate may be due to the circumstance that all newborns were exposed to the same equipment, such as the radiant warmer, weight scale and baby crib.

In a review by Williams [4] nose was the most frequent body site yielding staphylococci (40 to 44%) and the carrier rate among nurses in hospital ranged between 21 to 70%. Our study suggested a low prevalence (9%) of carrier status. However, our carrier rate may be underestimated because of a different technique of specimen collection and the limited laboratory capacity in a Thai district hospital.

Our investigation demonstrates that deficient infection control procedures may lead to outbreaks of staphylococcal infections among newborns. However, implementation of recommended infection control methods, such as proper hand washing and thorough cleaning of equipment, can quickly control an epidemic outbreak as demonstrated in this case and other similar cases [14,15]. The insufficient budget allocation for infection control is however a major problem in Thai medical system.

Acknowledgements

We would like to thank Dr. Kittisak Kasetsinsombat, director of Hospital A, all of Thai FETP staff, Dr.Potjaman Siriarayapon, Dr. Sopon Iamsirithaworn, Dr.Charung Muangchana, Dr. Siwaporn Kumthong, Dr. Michael Orilly, Dr. Alden Henderson, Dr. Michael Bell and Dr. Elissa Meites from DHQP, US-CDC, and Dr. Hjordis M Foy from the University of Washington.

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Estimating diagnostic accuracy of tests for latent tuberculosis infection without a gold standard among healthcare workers

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This article was published on 29 October 2009.
Citation style for this article: Girardi E, Angeletti C, Puro V, Sorrentino R, Magnavita N, Vincenti D, Carrara S, Butera O, Ciufoli AM, Squarcione S, Ippolito G, Goletti D. Estimating diagnostic accuracy of tests for latent tuberculosis infection without a gold standard among healthcare workers. Euro Surveill. 2009;14(43):pii=19373. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19373

The evaluation of diagnostic accuracy of new *in vitro* diagnostic assays for tuberculosis infection has been hampered by the lack of a standard reference test. The aim of this study was to compare sensitivity and specificity of interferon gamma assays for latent tuberculosis infection by assessing the association of test results with tuberculosis occupational exposure and by using latent class analysis. We analysed data from 115 healthcare workers on whom tuberculin skin test (TST) and the following *in vitro* tests were performed: in-house ELISPOT for RD1 proteins, T.SPOT-TB and Quantiferon-TB Gold. Results of all tests were associated with increased occupational risk of exposure to *Mycobacterium tuberculosis*, but only TST was associated with *Bacillus* Calmette-Guérin (BCG) vaccination. Sensitivity/specificity (95% confidence intervals) estimated by a latent class model were: 99.9%/64.2% (53.0-74.1) for TST, 95.3% (61.8-99.6)/87.5% (78.0-93.2) for in-house ELISPOT, 96.7% (69.3-99.7)/85.6% (75.3-92.0) for T.SPOT-TB, and 76.3% (55.9-89.1)/93.6% (85.4-97.3) for Quantiferon. The estimated specificity of *in vitro* assays was higher than that of TST also among individuals who were not BCG-vaccinated. In conclusion, when used in healthcare workers, *in vitro* assays may provide a significant increase of specificity for tuberculosis infection compared to TST, even among non vaccinated individuals, at the cost of some sensitivity.

Introduction

Identification and treatment of individuals with latent tuberculosis infection is an important component of tuberculosis elimination strategies in low incidence countries, and may contribute to the global tuberculosis control efforts [1-4]. In this context, healthcare workers represent an important target population for latent tuberculosis infection screening programmes [5]. The effectiveness of these programmes, however, has been limited by the fact that the standard tool used to diagnose latent tuberculosis infection, the tuberculin skin test (TST), has a limited diagnostic accuracy, mainly because it relies on the use of protein purified derivative (PPD), which is a mixture of antigens shared by many pathogenic and non-pathogenic mycobacteria, including *Bacillus* Calmette-Guérin (BCG) strains used for vaccination [6].

Recently, new immunologic tests have been introduced for diagnosing tuberculosis infection [7,8]. These tests, often referred to as interferon gamma release assays (IGRAs) are based on the detection of *in vitro* response to proteins encoded by genes located within the region of difference 1 (RD1) of *M. tuberculosis* genome, the early secreted antigenic target 6 protein (ESAT-6) and the culture filtrate protein 10 (CFP-10), that are not shared with BCG strains or most environmental mycobacteria [9,10]. Two of these tests have been made commercially available. Both measure interferon gamma released *in vitro* in response to RD1-encoded antigens, although they use different antigen preparations (overlapping peptides spanning the entire length of these proteins) and different assay formats (ELISA and ELISPOT) [11,12]. Recent guidelines recommend that these tests be used instead of [1,2] or in addition to [13] TST.

A number of studies have evaluated IGRA, in comparison to TST, as a tool for screening latent tuberculosis infection among healthcare workers [14-19]. To our knowledge, however, no study has compared different IGRAs in this population group.

The lack of a gold standard for the diagnosis of latent tuberculosis infection has hampered the assessment of the diagnostic accuracy of IGRAs. Different strategies have been used so far to address this issue, including the evaluation of the proportion of positive tests among individuals with active tuberculosis (as a proxy for sensitivity), and of the proportion of negative tests among individuals at low risk for tuberculosis infection (as a proxy for specificity) [1,2,7]. Another approach that has been proposed for the validation of IGRAs is based on the assessment of the association of test results with risk factors for tuberculosis infection

[11,20]. Finally, latent class analysis, a statistical method which has been proposed for the assessment of diagnostic tests in the absence of a gold standard, could be used in this context [21]. In the frequentist statistical approach used in the present study, this analysis requires availability of results from at least three different diagnostic tests on the same individual, and it is based on the concept that different tests for the same disease are influenced by a common latent variable, the disease status, which cannot be measured directly [21-23].

Healthcare workers remain at risk for tuberculosis infection also in countries with low tuberculosis incidence [24]. However, especially in countries such as Italy where until recently BCG vaccination has been widely used in healthcare workers, surveillance of tuberculosis infection has been hampered by the low specificity of TST. In the present paper, we analysed data on healthcare workers in Italy who were tested by TST and by three *in vitro* interferon gamma tests, an in-house ELISPOT assay based on RD1 proteins [25], a commercial ELISPOT assay and a commercial whole blood ELISA using RD1 peptides. To validate the use of these tests in this population group, we assessed their association with occupational tuberculosis risk and estimated their sensitivity and specificity by using a latent class analysis.

Methods

Study design and participants

We conducted a cross-sectional study in 2004-2005 at two tertiary care hospitals in Rome, Italy, which include wards that routinely treat pulmonary tuberculosis patients. Healthcare workers at these institutions who had had a routine periodic health check in 2004 or 2005 were considered for inclusion, if they had a positive TST result in the 12 months, or a negative TST result in the three months before we did the *in vitro* tests. There was no formal calculation of the sample size prior to the study. No incentive was offered for participation. The study was approved by the ethics committees at participating institutions and study participants gave written informed consent.

For each individual enrolled in the study, the following data were abstracted from personal charts: age, sex, place of birth, job category, ward or service of present and past employment, BCG vaccination, household tuberculosis contacts. Ward or service of employment were classified either as high risk if more than one patient with tuberculosis was cared for per year, or as low risk if that was not the case.

Diagnostic assays

The TST was administered by trained nurses at participating institutions by the Mantoux procedure using 5 IU of PPD (Chiron). Results were read after 48 to 72 hours. For the purpose of the present analysis an induration of at least 10 mm was scored as a positive response [1,2].

The in-house ELISPOT assay based on ESAT-6 and CFP-10 proteins (Lionex) was performed as previously described [25], and results were scored positive if the average number of spot-forming cells (SFCs) in cultures stimulated with these antigens was at least three-fold higher than the average number of SFCs in the control. Interferon gamma values are presented as number of SFCs per million PBMC, after subtraction of the appropriate control according to the described criteria.

The commercial ELISPOT assay used was the T-SPOT.TB (Oxford Immunotec) and it was performed as previously described [11]. Responses were scored positive if the test wells contained a mean of at least six spot-forming cells more than the mean of the negative control wells, and if this number was at least twice the mean of the negative control wells.

The commercial ELISA assay was the enhanced 'in-tube' version of QuantiFERON-TB Gold (QFT-G, Cellestis Limited).This assay is based on peptides spanning the entire sequences of ESAT-6 and CFP-10 as well as another peptide representing a portion of the TB7.7 antigen [12]. It involves two stages: incubation of whole blood with the antigens, and measurement of interferon gamma production in harvested plasma by ELISA. As recommended by the manufacturer, the cut-off value for a positive test was 0.35 interferon gamma IU/ml.

All blood test were performed on the same blood sample. For 47 individuals (45.3%), the blood sample was taken on the day the TST was performed, while for the remaining individuals, it was taken eight to 365 days after the TST. ELISA and ELISpot were performed at the study site, and all assays met quality control standards.

Statistical methods

Standard univariable methods were used to describe the association between participant characteristics and results of diagnostic assays.

The association of test results with risk factors for tuberculosis infection was studied by fitting four multivariable logistic regression models, one for each diagnostic test, with the same covariates, and results were shown as odds ratios (OR) with the associated 95% confidence intervals (CI). Risk factors introduced in the models were age (as a continuous variable), sex and all variables that were significant in the univariable anlaysis for at least one diagnostic test. Whether the association with each risk factor varied by type of diagnostic assay was assessed by testing the hypothesis of homogeneity of the relative odds ratios. The test was performed using seemingly unrelated regression that takes into account the correlation between diagnostic test results of the same participant.

To estimate sensitivity and specificity of different diagnostic tests we performed a latent class analysis [21-23,26] a family of statistical models based on the concept of 'latent variable', that can simply be thought as an unobservable random variables. LCA is appropriate to study situations in which categorical responses are observed on n subjects and these responses are dependent by a categorical unobservable characteristic of the subject. Briefly, parameters of interest were estimated by modelling the relations between an unobservable (latent) and observable variables. In this respect, the observed results of the diagnostic tests are considered as a measure, prone to error, of an unobservable dichotomous latent variable, the true disease status. From these imperfect measures we can estimate a 'consensus' gold standard used, in turn, to evaluate sensitivity and specificity of the tests as well as the prevalence of the disease [22].

Let us assume that D represents the unknown disease status for each subject (1 for diseased and 0 for not diseased) and θ_d (d=0,1) its probability. Moreover let t_j be the observed result of our jth test (j=0,…,p) that can take on the values 0, negative,

or 1, positive. If we denote with π_{jd} the conditional probability of a positive response at the jth test given D=d, the parameters of interest for our study, i.e. the sensitivity and specificity of each test, are π_{j1} and $1-\pi_{j0}$, respectively. Each subject i (i=1,.....,n) will have a vector of observed responses, $T_i=(t_1,\ldots,t_p)$, and the marginal probability of T_i that follows a multivariate Bernoulli distribution is given by

$$Pr(\mathbf{T}_i) = \sum_{d=0}^{1} \theta_d Pr(T_i \mid D = d) \quad (1).$$

Assuming for each subject the independence between responses to the p tests, given the true disease status, equation (1) can be written as:

$$Pr(\mathbf{T}_i) = \sum_{d=0}^{1} \theta_d \prod_{j=1}^{p} \pi_{jd}^{t_j}(1-\pi_{jd})^{1-t_j} \quad (2).$$

Both θ_d and π_{jd} were modelled on a log odds, or logit, scale and we could also account for the effect of covariates using the usual approach of logistic model. The equations describing prevalence and conditional probabilities of positive response were as follows:

$$Logit(\theta_d \mid \mathbf{v}) = \alpha \quad (3) \text{ and}$$

$$Logit(\pi_{jd} \mid \mathbf{x}) = \gamma_j + \lambda_j \eta_d + \mathbf{x}'\boldsymbol{\beta} \quad (4),$$

where:

1. x was a vector of covariates for the ith subject, with their relatives vectors of parameters β;
2. η_d was the (random) effect, common for all tests, exerted by the unknown true disease status;
3. λ_j were the factor loadings that allow the effect of ηd to differ between tests and
4. γ_j represented the (fixed) effect of each test on conditional probability [22,26].

In order to make a latent class model estimable, the number p of diagnostic tests used on the same study sample must provide at least as many degrees of freedom as the number of parameters to be estimated, in other words the condition $(2^p-1)\geq(2p+1)$ has to be satisfied and this imply that at least three tests are requested for our study. Prevalence as well as sensitivity and specificity were modeled as logit (log odds). We included BCG as a covariate in the model for sensitivity and specificity. The fit of the model without covariates was assessed by using the Pearson's chi-squared statistic (the sum of squared difference between observed and expected frequencies over the expected). Nested models were compared using the log-likelihood ratio (LR) test [27-29].

The significance of the difference in accuracy between pairs of diagnostic assays was evaluated by using Wald test for fixed coefficients of the latent class model.

In traditional latent class analysis, it is assumed that the results of each individual for a given disease status are independent (the so-called conditional independence) or, in other words, that the observed associations between tests are explained only by the latent variable. In our study this condition could not be satisfied, regarding the similarities in technological characteristics of assays. To verify whether a lack of conditional independence between tests could have influenced our estimates, we introduced in the equation (4) an additional subject-specific random variable z with Gaussian distribution to take into account the correlation between the assays that was not due to the disease status [27,29]. The results from the traditional latent class analysis were then compared with those from the model with random effect using the Akaike Information Criterion (AIC) and Pearson's statistic.

Statistical analyses were performed with Stata, Release 9 (Stata Corp). The programme "gllamm" in Stata [30] and "randomLCA" package for R [31] were used to fit latent class analysis models.

Results

Study population

Included in the present analysis were 115 healthcare workers. Of these, 39 (33.9%) were currently employed in wards in which the risk of being exposed to tuberculosis was high (such as wards for infectious diseases and respiratory diseases), and 76 (66.1%) were employed in hospital services in which the risk of exposure to tuberculosis was low (such as paediatrics, internal medicine and hospital epidemiology). Of those currently employed in low-risk services, seven had worked in services with high exposure risk in the past. The median age of the participants was 41 years and the majority were female. BCG vaccination was documented for 43 participants (37.4%).

Association of results in the four diagnostic assays with participants characteristics

Overall 61 individuals (53.0%) were TST-positive, 40 (38.4%) were positive by in-house ELISPOT, 42 (36,5%) by T-SPOT.TB and 29 (25,2%) by QFT-G . The results of the different diagnostic assays by participant characteristics are shown in Table 1. A higher proportion of positive tests was observed among those who had at one point been employed in high-risk services, compared to those employed only in other hospital services. This difference was statistically significant for all tests except for the QFT-G test. In addition, older study participants were more likely to be positive in all tests. A positive result in the TST only was associated with a previous BCG vaccination. Physicians had the lowest prevalence of positive results in all tests, but this difference was significant for QFT-G only. Surprisingly, the prevalence of positive results in the three *in vitro* assays was not elevated among those reporting household tuberculosis contact, and differences were not statistically significant.

As shown in Table 2, 40 individuals (34.8%) were negative in all the four tests, while 75 (65.2%) individuals were positive in at least one test. Of those 75, 22 (19.1%) were positive in all the four tests. Nineteen individuals (16.5%) were positive only in the TST.

In a multivariable analysis (Table 3), having worked in high-risk tuberculosis services increased the probability of a positive result for all diagnostic tests (homogeneity test: p=0.52), although the effect was significant only for the T-SPOT.TB and the in-house ELISPOT. Sex was not significantly associated with the probability of a positive result and the odds ratios were not significantly different among diagnostic tests (p=0.41). Older individuals, however, had a significantly higher probability of a positive result for all tests. The effect of BCG vaccination was not homogeneous among diagnostic tests (p=0.001) and significant only for the TST, with a higher odds ratio for a positive result for BCG-vaccinated compared to not vaccinated subjects. Physicians were at a lower risk of a positive result compared to nurse assistants; this result was significant for TST and QFT-G.

Table 1

Results of diagnostic tests for tuberculosis infection by characteristics of healthcare workers in Rome, Italy (n=115)

Characteristic (no.)	Tuberculin skin test no. of positives (%)	In-house RD1 ELISPOT no. of positives (%)	T-SPOT.TB no. of positives (%)	QuantiFERON TB Gold no. of positives (%)
Ward/service				
Low TB risk (69)	30 (44)	17 (25)	18 (26)	16 (23)
High TB risk* (46)	31 (67) †	23 (50) †	24 (52) †	13 (28)
Sex				
Male (48)	22 (46)	17 (35)	19 (40)	11 (29)
Female(67)	35 (52)	23 (34)	23 (34)	18 (27)
Place of birth				
EU (110)	57 (53)	38 (35)	40 (37)	26 (24)
Non-EU (5)	3 (60)	1 (20)	1 (20)	2 (40)
BCG vaccination				
No (72)	30 (42)	26 (36)	24 (33)	22 (31)
Yes (43)	31 (72) †	14 (32)	18 (42)	7 (16)
Household TB contact				
No (102)	53 (52)	37 (36)	40 (39)	27 (27)
Yes (13)	8 (62)	3 (23)	2 (15)	2 (15)
Job category				
Physician (18)	6 (33)	4 (22)	6(33)	1 (5.6)
Nurses (67)	40 (60)	24 (36)	23 (34)	16 (24)
Nurse assistant (30)	15 (50)	12 (40)	13 (43)	12 (40) †
Age (years)				
≤41 (59)	41 (36)	11 (19)	12 (20)	8 (14)
>41 (56)	40 (71) †	29 (52) †	30 (54) †	21 (38) †

BCG: Bacillus Calmette-Guérin; EU: European Union; TB: tuberculosis.
* currently or in the past
† p<0,05

Table 2

Response patterns to four different diagnostic tests for tuberculosis infection observed among healthcare workers in Rome, Italy, and predicted by a latent class analysis model with and without a random effect (n=115)

Response pattern				Observed		Predicted LCA	Predicted LCA with random effect
Tuberculin Skin test	In-house RD1 ELISPOT	T-SPOT.TB	QuantiFERON TB Gold	No.	%	No.	No.
-	-	-	-	40	34.8	37.8	39.9
+	+	+	+	22	19.1	21.8	21.9
+	-	-	-	19	16.5	21.1	19.4
+	+	+	-	7	6.1	7.3	7.1
+	-	+	-	7	6.1	3.9	4.7
-	+	-	-	5	4.3	5.4	4.6
-	-	-	+	4	3.5	2.6	2.1
+	+	-	-	3	2.6	3.2	3.9
-	-	+	-	3	2.6	6.4	5.3
-	+	+	-	2	1.7	0.9	1.0
+	+	-	+	1	0.9	1.0	0.9
+	-	+	+	1	0.9	1.3	1.3
+	-	-	+	1	0.9	1.5	1.8
-	+	+	+	0	0.0	0.1	0.2
-	+	-	+	0	0.0	0.4	0.3
-	-	+	+	0	0.0	0.4	0.5

LCA: latent class analysis.

Estimation of the accuracy of the assays by latent class analysis

The tuberculosis infection prevalence in the population estimated in the latent class analysis model was 26.9% (95% CI: 18.1% to 35.7%). The predicted frequencies for the patterns of response to the four tests (Table 2) showed a good fit with the observed data (Pearson's statistic p-value=0.25).

In the latent class analysis (Table 4), TST had the highest estimated sensitivity but a very low specificity. The two ELISPOT-based tests, the in-house ELISPOT and the T-SPOT.TB, both had a sensitivity close to that of the TST, while their estimated specificity was still high. QFT-G had a very high estimated specificity, although its sensitivity was lower than that of the other three tests. When

Table 3

Multivariable odds ratios (95% confidence intervals) of a positive result for selected risk factors by diagnostic test among healthcare workers in Rome, Italy (n=115)

	Diagnostic test assumed as outcome variable				
	Tuberculin Skin test	In-house RD1 ELISPOT	T-SPOT.TB	QuantiFERON TB Gold	
	MOR# (95% CI)	MOR# (95% CI)	MOR# (95% CI)	MOR# (95% CI)	p*
Ward/service					
Low TB risk	1.00	1.00	1.00	1.00	
High TB risk	2.48 (0.97-6.35)	3.88 (1.52-9.91)	3.10 (1.28-7.48)	1.68 (0.63-4.49)	0.519
p**		0.472	0.681	0.491	
BCG Vaccination					
No	1.00	1.00	1.00	1.00	
Yes	4.32 (1.56-11.95)	0.62 (0.23-1.67)	1.49 (0.58-3.81)	0.41 (0.14-1.23)	0.001
p**		0.001	0.060	<0.001	
Gender					
Male	1.00	1.00	1.00	1.00	
Female	2.13 (0.73-6.21)	1.23 (0.46-3.26)	1.28 (0.50-3.26)	0.82 (0.29-2.31)	0.413
p**		0.449	0.401	0.107	
Age (per five years increase)	1.86 (1.39-2.48)	1.69 (1.29-2.22)	1.56 (1.21-2.02)	1.50 (1.16-1.95)	0.485
p**		0.599	0.231	0.215	
Job category					
Physician	0.20 (0.04-0.92)	0.25 (0.05-1.23)	0.39 (0.09-1.63)	0.07 (0.01-0.70)	0.480
p**		0.758	0.393	0.377	
Nurses	1.64 (0.49-5.51)	1.21 (0.38-3.87)	0.67 (0.22-2.04)	0.63 (0.21-1.91)	0.211
p**		0.721	0.159	0.156	
Nurse assistant	1.00	1.00	1.00	1.00	

BCG: Bacillus Calmette-Guérin; CI: Confidence Interval; MOR: multivariable odds ratio. TB: tuberculosis.
Adjusted for all the variables in the table by fitting a logistic regression model.
* p-value for the hypothesis of no difference among OR, obtained by fitting a seemingly unrelated regression model.
**p-value for the hypothesis of no difference to the OR for tuberculin skin test, obtained by fitting a seemingly unrelated regression model.

Table 4

Specificity and sensitivity of four diagnostic assays for tuberculosis infection estimated among 115 healthcare workers in Rome, Italy by a latent class analysis model

	Specificity [%]			Sensitivity [%]		
	Estimate	95% confidence interval		Estimate	95% confidence interval	
Tuberculin skin test	64.2	53.0	74.1	99.9	NC	NC
In-house RD1 ELISPOT	87.5	78.0	93.2	95.3	61.8	99.6
T-SPOT.TB	85.6	75.3	92.0	96.7	69.3	99.7
QuantiFERON TB Gold	93.6	85.4	97.3	76.3	55.9	89.1

NC: not computable.

the tests were compared in pairs to evaluate differences in their diagnostic accuracy, statistically significant differences were recorded for the comparison between TST and the other three tests (p=0.003, p=0.005 and p<0.001, respectively, for the comparison with in-house ELISPOT, T-SPOT.TB and QFT-G), while the difference between the T-SPOT.TB and QFT-G was of borderline statistical significance (p=0.057).

To explore the impact of BCG vaccination on the diagnostic accuracy of the TST, we also fitted a latent class analysis models solely for those subjects who had not been vaccinated against BCG. In this analysis, the estimated prevalence of tuberculosis infection was 26.3%. As shown in Table 5, the sensitivity of the TST was similar to that estimated for the entire population. In contrast, an increased specificity was estimated for TST among not BCG-vaccinated subjects (79.1%), although it remained lower than that estimated for the *in vitro* assays. The estimated accuracy of IGRAs did not vary markedly in this analysis, except for QFT-G sensitivity which increased from 76.3 to 94.8.

Finally, we compared the traditional latent class analysis model to a model with a subject-specific random effect in order to assess whether the removal of conditional independence assumption among tests had an impact on the results. The estimate of tuberculosis infection prevalence in the latter model was 25.0%, and the predicted frequencies for the patterns of response to the four tests were similar to the former model with a slight worsening of the AIC (476.97 and 477.77 in the latent class analysis and the model with subject-specific random effect, respectively), and an equally slight improvement in Pearson's statistic (p=0.267). The estimates of diagnostic accuracy were remarkably similar in the two models (Table 6).

Discussion

We compared the results obtained in the TST and three *in vitro* assays for tuberculosis infection in healthcare workers. We found that positive results in all four assays were associated with increased occupational risk of exposure to *M. tuberculosis*, but only the TST was correlated with BCG vaccination. Taking advantage of the fact that the results of four different assays for tuberculosis infection were available for the same groups of individuals, we provided an estimate of the diagnostic accuracy of these assays by using a latent class analysis model. In this analysis, the *in vitro* tests were found to be more specific for tuberculosis infection than the TST, even among non-vaccinated individuals, at the cost of some sensitivity. Moreover, our data suggest that ELISPOT-based tests may differ in accuracy from the ELISA-based test.

Previous studies conducted among healthcare workers in countries with low and high tuberculosis incidence [14-17] have shown an association between QFT-G results and occupational exposure to patients with active tuberculosis. Our results are consistent with these findings and show an even stronger association with occupational exposure for ELISPOT-based assays, although no statistically significant differences were recorded when association coefficients for the four different tests were compared. Moreover, as in previous studies [32,33], we found that TST results were associated with previous vaccination, while this was not the case for *in vitro* assays.

We also used latent class analysis to estimate and compare the sensitivity and specificity of different tests for tuberculosis infection. Latent class analysis allows addressing a major issue in the evaluation of diagnostic tests, i.e. the estimation of diagnostic accuracy when a gold standard test is not available, and for this reason it has been used in different infectious conditions in which a

Table 5

Comparison of specificity and sensitivity of four diagnostic assays for tuberculosis infection estimated among 72 not BCG-vaccinated healthcare workers by a latent class analysis model

	Specificity %			Sensitivity %		
	Estimate	95% confidence interval		Estimate	95% confidence interval	
Tuberculin skin test	79.1	65.9	88.1	100.0	N.C.	N.C.
In-house RD1 ELISPOT	84.6	72.2	92.1	94.4	65.8	99.3
T-SPOT.TB	90.4	78.4	96.1	100.0	N.C.	N.C.
QuantiFERON TB Gold	92.3	81.3	97.1	94.8	63.1	99.5

NC: not computable.

Table 6

Comparison of specificity and sensitivity of four diagnostic assays for tuberculosis infection estimated among 115 healthcare workers by a latent class analysis model with and without a subject-specific random effect

	Specificity %		Sensitivity %	
	LCA	LCA with random effect	LCA	LCA with random effect
Tuberculin skin test	64.2	64.4	99.9	100.0
In-house RD1 ELISPOT	87.5	88.5	95.3	97.5
T-SPOT.TB	85.6	86.9	96.7	98.8
QuantiFERON TB Gold	93.6	94.3	76.3	81.4

LCA: latent class analysis.

definitive demonstration of the infecting organism was not feasible [22].

As reported in a recently published systematic review, the sensitivity of IGRAs for tuberculosis infection has previously been estimated in a number of studies by calculating the proportion of positive patients among those diagnosed with culture-proven tuberculosis [32]. The sensitivity in these studies ranged from 55% to 93% for QFT-G with a pooled estimate of 78% for the first version of the QFT-G or 70% for the in tube version of this assay, and from 83 to 100% for T-Spot.TB with a pooled estimate of 90%. In the studies in which both IGRAs were performed on the same group of patients, the positivity rate tended to be higher for the ELISPOT assay. Our estimates of the sensitivity of interferon gamma tests for latent infection, obtained by latent class analysis, were above 95% for ELISPOT-based assays and 76.3% for the ELISA assay, thus consistent with those obtained from patients with active tuberculosis. Nevertheless, the TST had the highest estimated sensitivity (99.9%) in our study, which is in contrast to the results of studies on patients with active tuberculosis, most of which reported a higher sensitivity for interferon gamma assays compared to the TST [34]. However, there is evidence that estimates of sensitivity of TST for active infection may differ from that for latent infection: On average 10 to 25% of patients with active TB do not respond to the TST, and reactivity may be restored after initiation of treatment in most of the patients who were initially negative [35]. In contrast, sensitivity estimates derived from studies on healthy individuals may exceed 95% [36]. Moreover, some studies conducted to assess the accuracy of diagnosis of latent tuberculosis infection suggest that the sensitivity of interferon gamma tests may indeed be somewhat lower than or equal to that of the TST [33,37,38]. On the other hand, in a recent study carried out among healthcare workers in India, in which a Bayesian latent class analysis was used to compare accuracy of QFT-G and TST, Pai *et al.* estimated that the QFT-G had an higher sensitivity than the TST (89.9% and 79.5 %, respectively) [39]. The results reported by Pai *et al*. are not directly comparable to those of the present study since a different statistical approach was used to construct the latent class model and results from only two different tests were available for each subject. Moreover, the subjects in the two studies were enrolled in countries with very different tuberculosis incidence.

In this study, specificity was estimated to be consistently higher for IGRAs compared to the TST. This finding was not unexpected since these *in vitro* assays are based on antigens that, differently from the PPD antigens used in the TST, are present almost exclusively in bacteria of the *M. tuberculosis* complex. Previous studies included in the aforementioned systematic review [34] have shown that, among individuals at low risk for tuberculosis infection, QFT-G is negative in 92-98% of cases (estimated pooled specificity 99% and 96% in BCG-vaccinated and non-vaccinated individuals, respectively), and T-SPOT.TB in 85-100% of cases (estimated pooled specificity 93%). These figures are consistent with specificity values estimated for IGRAs in our study. Moreover, there is indirect evidence that these tests have higher specificity for latent tuberculosis infection than the TST. It has in fact been shown that, when used in contact tracing studies, these tests yield a better correlation to the degree of exposure to tuberculosis cases than the TST, and that their results are not influenced by the BCG vaccination status [32,33,37]. The specificity of the TST estimated in our study was quite low. It has been shown that large variations in the specificity of the TST can be observed when the test is applied to different populations [38], and in our study, the high prevalence of previous BCG vaccination among healthcare workers may be one cause of low specificity. However, TST specificity was estimated to be low also among non-vaccinated healthcare workers. A similar finding has been reported for healthcare workers in the United States, and it has been attributed to infection with non-tuberculous mycobacteria [40]. In contrast, a higher value for the specificity of the TST (87.4%) resulted from the application of a Bayesian latent class model in spite of the fact that 71% of subjects were BCG-vaccinated [39].

The statistical model we used also allowed an overall comparison of diagnostic accuracy of the tests analysed. We found that the diagnostic accuracy of the TST was significantly different from that of blood tests. This finding is not surprising if it is considered, in addition to the higher specificity of the antigens used, that the *in vitro* tests avoid a series of operational problems that may affect the accuracy of the TST, including variability in the intradermal injection of the antigen and in the reading of the response [8].

When the three *in vitro* tests were compared, we found a difference of borderline significance between QFT-G and T-SPOT.TB. The reasons for this difference are unclear. One may speculate that the ELISPOT technique, thanks to the ability to detect single cells that secrete interferon gamma in response to specific stimuli, may provide a higher sensitivity at the cost of some specificity. The cut-off value used to define positivity could also account for differences in sensitivity and specificity, at least in part. In fact, a study in which the commercial T-SPOT.TB and ELISA were used, has shown that the differences in diagnostic accuracy between the two tests become negligible when new cut-off points are used that have been optimised on the same population [41].

Before drawing firm conclusions, it is important to appreciate the limitations of the statistical method we used [21,22]. Latent class analysis assumes the existence of a 'true disease status' which influences the results of diagnostic tests, and this mathematically defined entity does not necessarily have a clear clinical or biological sense. There is consistent evidence that the TST predicts the development of active tuberculosis [6]. Thus the presence of latent tuberculosis infection, as identified by a positive TST, is associated with an increased risk of active disease. It remains to be determined if the same meaning could be attributed to the random variable identified as 'latent tuberculosis infection' in the present analysis.

Another drawback of the traditional version of latent class analysis is the assumption of conditional independence, i.e. the absence of correlation among test results given the disease status. This is often unrealistic in practice due to similarities among tests. However, following the approach proposed by Qu *et al.* [27] to relax this assumption, we used an additional random effect, with which it is possible to model all the non-observable factors at the subject level that could introduce correlation between test results. The estimates of diagnostic accuracy for the model with subject-specific random effect were very similar to those obtained in the traditional latent class analysis, and the measures of goodness of fit were comparable in the two models as well.

Other limitations of the present study need to be mentioned. First, all the individuals included were healthy adults, and thus our results should not be generalised for different populations, in particular for children or immunocompromised individuals in whom a significant proportion of indeterminate results may be observed,

in particular when using ELISA-based assays [40]. Similarly, the diagnostic accuracy estimated for latent tuberculosis infection is not necessarily similar to that obtained when using these tests to diagnose active tuberculosis infection. Second, tuberculin skin tests have been administered and read by different trained nurses, and thus inter-reader variability in interpreting the results should be expected. Third, the confidence intervals around our estimates of association coefficients and of sensitivity and specificity were rather wide because of the limited size of the population studied. Nevertheless, we were able to demonstrate statistically significant differences in the diagnostic accuracy of the different tests used.

Longitudinal studies comparing the ability of the TST to predict the risk of active tuberculosis with that of interferon gamma assays would be needed to establish the usefulness of the new tests for tuberculosis infection. Preliminary data suggest that positive IGRAs results may indeed be associated with the risk of active tuberculosis [42]. However, these studies will be difficult to perform in populations such as healthcare workers. In this context, the present study provides further evidence on the advantages in terms of specificity, and on the potential loss of sensitivity for latent tuberculosis infection of blood tests in comparison to the TST. Moreover, it provides comparative estimates of diagnostic accuracy of different blood tests and thus may contribute to choosing the strategies for diagnosing tuberculosis infection among heath careworkers. In particular, our results may suggest the use of IGRAs, either alone or as confirmatory tests in TST-positive individuals, in a population with a high prevalence of previous BCG vaccination. These choices, however, will also need to take other considerations into account, including the economical and operational aspect, and the stability of test results over time [43].

Acknowledgements

The authors thanks S Carrara and F Bizzoni for their help with laboratory tests, L Pischedda, S Lodi, S Console, A Moretti, M Paparatti and M Sorcelli for their help with participants' data collection, and C Nisii for editing the manuscript.

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