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The tail of the epidemic and the challenge of tracing the very last Ebola case

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One year ago, on 23 March 2014, the World Health Organization (WHO) announced that it had been notified 'of a rapidly evolving outbreak of Ebola virus disease (EVD) in forested areas of south-eastern Guinea'. At that time, 49 cases, including 29 deaths had been reported. In the following months and weeks, the outbreak spread to the two neighbouring countries Sierra Leone and Liberia and peaked six months later, in October 2014, with up to 1,500 cases reported on a weekly basis. It was then when several scientific publications presented forecasts for the coming months that ranged from 60,000 EVD cases for the most conservative estimates, up to several hundred thousands of EVD cases [1-4] for the more forthcoming ones. As of 22 March 2015, the toll of the epidemic has been 24,907 reported cases including 10,326 deaths [5]. Despite these far too high numbers, the even higher forecasts were fortunately not attained. This can be partly attributed to the unprecedented mobilisation of resources generated by these high estimates.

In the past eight weeks, the number of new confirmed, probable and suspected EVD cases has been stabilising at around 365 notifications per week [6,7]. However, this trend results from the combination of heterogeneous patterns: while Liberia has almost interrupted human-to-human transmission, and the 'historical' epicentre of the epidemic in the forested area at the border of Sierra Leone and Guinea reports few new cases, there has been a shift of the epidemic towards the capital cities of Freetown and Conakry and their surrounding districts where there is sustained and even increasing transmission [8].

The elimination of human-to-human transmission of the Ebola virus in the affected countries is achievable. Liberia has shown that strict and comprehensive implementation of control measures are effective to interrupt this form of transmission [9]. This can be achieved since sufficient Ebola treatment units and laboratory capacity are currently available in the region [10]. It should also be feasible because the mobilisation of field epidemiologists trained in the various field-training programmes around the world has dramatically increased in recent months.

Upon entering what seems to be the tail of the epidemic and, as in any such moment, the 'Ebola endgame' strategy requires adaptation to the heterogeneity of the epidemiological situation. The tools for EVD control need to be fine-tuned and the commitment from the teams supporting local authorities in affected countries needs to be sustained. While the pressure on clinical and laboratory expertise gradually decreases, the demand shifts towards field epidemiologists to assist local public health experts and support community workers to engage in active surveillance and to monitor remaining transmission chains in affected communities. The priority at this stage of the epidemic is the early detection of possible re-emergence of transmission, in relation with importation of cases from areas still experiencing active transmission. Other contributing factors to re-emergence of transmission could be delayed secondary transmission, as suspected recently through sexual contact in Liberia and Macenta, Guinea or new primary zoonotic transmission from the animal reservoir given the long duration of the present outbreak [11,12]. However, no conclusive evidence is available for sexual transmission of the disease by convalescent EVD-negative individuals [13]. Moreover, no new primary zoonotic transmission has been documented in the affected countries.

A paper by Rexroth et al. in this issue of *Eurosurveillance*, presents results from a survey of European infectious disease epidemiologists and microbiologists about their decisions to apply for Ebola response missions in West Africa [14]. It sheds light on the motivation and concerns of experts with regards to apply for deployment in affected countries. The need to deploy larger number of international experts to support the local outbreak response became evident when the epidemic went out of control in West Africa during the autumn of 2014. At the same time, limited secondary transmission occurred from an imported case in the United States and a medically evacuated case in Spain [15,16]. This

gave rise to fear of the possibility that more imported cases and secondary transmission could occur, anywhere in our globally connected world [17]. Along with the dramatic forecasts, this led to concerns about the evolution of the epidemic and its potential spread, and an increase in deployed resources to the affected region.

The main concern for deployment of experts enrolled in the study was the concerns of their family and the lack of support from their employers. The study covers the period from 19 November to 7 December 2014. From March 2014 until 7 December, the European Centre for Disease Prevention and Control (ECDC) had facilitated the mobilisation of 13 experts to the affected countries through the WHO Global Outbreak And Response Network (GOARN) mechanism, all but three from the various field epidemiological training programmes in the European Union. In the three and half months since the study end, an additional 33 staff were mobilised. Currently, 19 experts mobilised through ECDC are deployed to West Africa: 14 in Guinea and five in Sierra Leone.

The paper by Walker et al. on a point-of-care blood test for identification of EVD, highlights the fact that the availability of a rapid diagnostic bedside test would be of great value in isolation facilities, especially when the proportion of patients infected with Ebola virus among suspected cases will have decreased as the epidemic is fading out [18]. The study shows that a 100% predictive negative value can probably be achieved with the presented rapid test, which would greatly reduce the amount of PCR tests necessitating considerable laboratory infrastructure and personnel. As discussed in the paper, applying the rapid test to safely discard suspected patients not infected with Ebola virus would dramatically reduce the burden on isolation unit beds and the need for confirmatory diagnostic PCR tests. For example, of 100 suspected EVD patients that would have to be tested and among which only 10 would be infected with Ebola virus, the rapid test, using a CT score of 6 as a threshold, would safely identify 87 persons as non-EVD patients and only require 13 diagnostic PCR tests to correctly identify these 10 EVD patients. Furthermore, as the epidemic continued to fade out, and if there would be only one Ebola virus infected patient among the 100 tested, the rapid test would identify 96 of the non-EVD patients and the PCR test would only need to be applied to the four remaining ones to identify the single case of EVD.

Complementing the considerations on the need for affordable and sustained field epidemiology and laboratory support, the paper by Fähnrich et al. reminds us that after one year into the epidemic, most affected areas still have no access to an appropriate information system to document the extent of the epidemic and to support the control. An information system able to monitor the epidemiological situation and the performance of the control measures is however, crucial for efficient outbreak response and should be implemented as early as possible. While such systems are still desirable at the current stage of the outbreak, they should eventually cover other epidemic-prone diseases also. Interestingly, the unavailability of computers in the field to register data can be effectively overcome by an approach relying on smart phone technology and cloud platforms [19].

The backbone of good surveillance is the timely provision of quality data to those who need it to steer interventions. Information systems such as the one presented will certainly improve processes involved in data acquisition. However, much still needs to be done to ensure the correct application of case definitions, the appropriate investigation of cases, and the exhaustiveness of reporting across affected districts and countries, in order to improve the ability to effectively depict the epidemiological situation and fully assess the progress and performance of the control programmes.

The paper by Alqahtani et al. on the perception of the risk and protective means regarding EVD among pilgrims from Australia to the Hajj, reports that one in six pilgrims thinks that Ebola transmits by air, one in five that they are at high risk of acquiring EVD during the Hajj, one in two that the use of masks would protect them [20]. These results remind us that misconception affecting pilgrims to the Hajj is certainly also true for members of EVD affected communities. While health advice to travellers should be strengthened in the context of epidemics, the mobilisation of anthropologists should support the surveillance and response teams in the affected communities and contribute to alleviate the fears of the community members towards the required control measures.

Finally, the article by Goodfellow et al. in this issue highlights the importance of the legacy of the international support to respond to the epidemic [21]. The authors stress that most of the laboratory technology now used in the affected countries may not be set up in a sustainable way and thus new strategies are required to ensure that in the aftermath of the epidemic there will be enough capacity to recognise and handle a future probable resurgence of EVD early. The paper calls for an extension of laboratory activities to cover essential clinical and microbiology services. The support activities should be extended beyond laboratory activities in the tail of the epidemic. They should ensure that EVD targeted activities are maintained until the last case of the last chain of transmission is controlled, while ensuring that surveillance and control of other epidemic-prone diseases are reactivated. This is particularly important during the rainy season that may lead to a dramatic increase in diseases such as measles, infectious diarrhoea, malaria, yellow fever or Lassa fever. Considering the low immunisation coverage overall, prior to the EVD epidemic [22], and the interruption of immunisation programmes during the

epidemic, all those involved in the control of the EVD outbreak should work hard to ensure that no devastating outbreak of a vaccine-preventable disease, such as measles, will be part of the legacy of the international support to the response to the Ebola outbreak. risk of leptospirosis exposure among these groups.

Conflict of interest

None declared.

Authors' contributions

Denis Coulombier has drafted the editorial, Kaja Kaasik-Aaslav provided epidemiological background.

References

1. Lewnard JA, Ndeffo Mbah ML, Alfaro-Murillo JA, Altice FL, Bawo L, Nyenswah TG, et al. Dynamics and control of Ebola virus transmission in Montserrado, Liberia: a mathematical modelling analysis. Lancet Infect Dis. 2014;14(12):1189-95. http://dx.doi.org/10.1016/S1473-3099(14)70995-8 PMID:25455986
2. Althaus CL. Estimating the reproduction number of Ebola Virus (EBOV) during the 2014 outbreak in West Africa. PLoS Curr. 2014;6: pii: ecurrents.outbreaks.91afb5e0f279e7f29e7056095255b288. PMID:25642364
3. Nishiura H, Chowell G. Early transmission dynamics of Ebola virus disease (EVD), West Africa, March to August 2014. Euro Surveill. 2014;19(36):20894. http://dx.doi.org/10.2807/1560-7917.ES2014.19.36.20894 PMID:25232919
4. Fisman D, Khoo E, Tuite A. Early Epidemic Dynamics of the West African 2014 Ebola Outbreak: Estimates Derived with a Simple Two-Parameter Model. PLOS Curr. 2014;6. pii: ecurrents.outbreaks.89c0d3783f36958d96ebbae97348d571. http://dx.doi.org/10.1371/currents.outbreaks.89c0d3783f36958d96ebbae97348d571 PMID:25642358
5. World Health Organization (WHO). Situation summary. Data published on 24 March 2015. Geneva: WHO; 2015. Available from: http://apps.who.int/gho/data/view.ebola-sitrep.ebola-summary-20150324?lang=en
6. World Health Organization (WHO). Ebola Situation Report - 18 March 2015. Geneva: WHO; 2015. Available from: http://apps.who.int/ebola/current-situation/ebola-situation-report-18-march-2015
7. World Health Organization (WHO). Ebola Situation Report 21 January 2015. Geneva: WHO; 2015. Available from: http://apps.who.int/iris/bitstream/10665/149314/1/roadmapsitrep_21Jan2015_eng.pdf?ua=1&ua=1
8. World Health Organization (WHO). Ebola Situation Report 25 March 2015. Geneva: WHO; 2015. Available from: http://apps.who.int/ebola/current-situation/ebola-situation-report-25-march-2015
9. Sharma A, Heijenberg N, Peter C, Bolongei J, Reeder B, Alpha T, et al.; Centers for Disease Control and Prevention (CDC). Evidence for a decrease in transmission of Ebola virus--Lofa County, Liberia, June 8-November 1, 2014. MMWR Morb Mortal Wkly Rep. 2014;63(46):1067-71. PMID:25412065
10. European Commission (EC). Emergency response coordination centre (ERCC) – ECHO daily map 19/03/2015. West Africa - Ebola virus disease (EVD) outbreak. Brussels: EC; 2015. Available from: http://erccportal.jrc.ec.europa.eu/getdailymap/docId/1102
11. Schnirring L. Ebola cases drop as progress shown in Guinea, Sierra Leone. Minneapolis: Center for Infectious Disease Research and Policy; 2015. Available from: http://www.cidrap.umn.edu/news-perspective/2015/03/ebola-cases-drop-progress-shown-guinea-sierra-leone
12. Government of Liberia. Liberia gets first confirmed Ebola case after counting 28 days. Monrovia: Government of Liberia. [Accessed 25 Mar 2015]. Available from: http://www.micatliberia.com/index.php/blog/latest-news/3090-breaking-news-liberia-gets-first-confirmed-ebola-case-after-counting-28-days.html
13. World Health Organization (WHO). Sexual transmission of the Ebola virus: evidence and knowledge gaps. Geneva: WHO; 2015. Available from: http://www.who.int/reproductivehealth/topics/rtis/ebola-virus-semen/en/
14. Rexroth U, Diercke M, Peron E, Winter C, an der Heiden MAG. Ebola response missions: To go or not to go? Cross-sectional study on the motivation of European public health experts, December 2014. Euro Surveill. 2015;20(12):21070.
15. López MA, Amela C, Ordobas M, Domínguez-Berjón MF, Álvarez C, Martínez M, et al. First secondary case of Ebola outside Africa: epidemiological characteristics and contact monitoring, Spain, September to November 2014. Euro Surveill. 2015;20(1):21003.
16. Texas Department of State Health Services. Second health care worker tests positive for Ebola. News release. Dallas: Texas Department of State Health Services; 2014. Available from: http://www.dshs.state.tx.us/news/releases/20141015.aspx
17. Fung IC, Tse ZT, Cheung CN, Miu AS, Fu KW. Ebola and the social media. Lancet. 2014;384(9961):2207. http://dx.doi.org/10.1016/S0140-6736(14)62418-1 PMID:25625391
18. Walker NF, Brown CS, Youkee D, Baker P, Williams N, Kalawa A, et al. Evaluation of a point-of-care blood test for identification of Ebola virus disease at Ebola holding units, Western Area, Sierra Leone, January to February 2015. Euro Surveill. 2015;20(12):21073.
19. Fähnrich C, Denecke K, Adeoye OO, Benzler J, Claus H, Kirchner G, et al. Surveillance and Outbreak Response Management System (SORMAS) to support the control of the Ebola virus disease outbreak in West Africa. Euro Surveill. 2015;20(12):21071.
20. Alqahtani AS, Wiley KE, Willaby HW, BinDhim NF, Tashani M, Heywood AE, et al. Australian Hajj pilgrims' knowledge, attitude and perception about Ebola, November 2014 to February 2015. Euro Surveill. 2015;20(12):21072.
21. Goodfellow I, Reusken CMK. Laboratory support during and after the Ebola virus endgame: towards a sustained laboratory infrastructure. Euro Surveill. 2015;20(12):21074.
22. Takahashi S, Metcalf CJ, Ferrari MJ, Moss WJ, Truelove SA, Tatem AJ, et al. Reduced vaccination and the risk of measles and other childhood infections post-Ebola. Science. 2015;347(6227):1240-2. http://dx.doi.org/10.1126/science.aaa3438 PMID:25766232

Ebola response missions: To go or not to go? Cross-sectional study on the motivation of European public health experts, December 2014

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We surveyed European infectious disease epidemiologists and microbiologists about their decisions to apply for Ebola response missions. Of 368 respondents, 49 (15%) had applied. Applicants did not differ from non-applicants in terms of age, sex or profession but had more training in field epidemiology and more international experience. Common concerns included lack of support from families and employers. Clearer terms of reference and support from employers could motivate application and support outbreak response in West Africa.

Background

In 2014–15, Guinea, Liberia and Sierra Leone suffered from the largest ever recorded Ebola virus disease (EVD) outbreak [1]. In any response to infectious disease outbreaks, epidemiologists and microbiologists are crucial: they trace contacts, analyse epidemiological data and support laboratory testing [2,3]. The World Health Organizations' (WHO) Global Outbreak Alert and Response Network (GOARN), Médecins Sans Frontières (MSF), the United Nations (UN) and other organisations have been involved in the outbreak response and recruited experts for field missions to West Africa, but the lack of or limited number of volunteers restricted scaling up efforts [4].

Within the last 20 years, the European Union (EU)/ European Economic Area (EEA) countries and – since its foundation in 2005 – the European Centre for Disease Prevention and Control (ECDC) have trained ca 400 epidemiologists and microbiologists in outbreak response through the European Programme for Intervention Epidemiology Training (EPIET), the European Programme for Public Health Microbiology Training (EUPHEM) and associated Field Epidemiology Training Programmes (FETP -e.g. in Germany, Norway, the United Kingdom). The EPIET Alumni Network (EAN) incorporates alumni from these FETPs [5,6].

Between 19 November and 7 December 2014, we surveyed European public health professionals in order to identify motivations and obstacles regarding their involvement in the local response to the Ebola outbreak. The knowledge gained from our study might help deploying organisations to adapt their recruitment strategies and thus strengthen the international response to large-scale outbreaks and other international public health emergencies.

Data collection and analysis

We collected information regarding applications for Ebola response missions, personal and professional background, and views on statements concerning qualification, motivation, fears and concerns related to those missions using a specifically developed online questionnaire.

The questionnaire included 85 questions. It was piloted among experts during the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE, 5–7 November 2014) and programmed in LimeSurvey software, hosted on a server located in the Netherlands [7].

We recruited participants via respondent-driven sampling. First, we sent the online questionnaire to current EAN-members and other members of European public health institutes using informal networks. Second, we invited respondents to further distribute the link to the questionnaire into their professional networks.

We only analysed filled-in questionnaires of participants who had given informed consent. The data protection officer at the Robert Koch Institute approved this anonymous study.

In the analysis, we compared respondents who applied with those who did not apply for Ebola field missions in terms of various characteristics. Additionally, for

each statement we compared agreeing and disagreeing respondents by frequency of applications to Ebola field missions, in order to measure the impact of the statement on the motivation to apply for missions. We calculated prevalence ratios (PR), 95% confidence intervals (95% CI) and p values (chi-square test and t-test) in STATA/SE 12.0 and considered a point estimate $p \leq 0.05$ as statistically significant.

Characteristics of respondents

A total of 368 respondents gave informed consent. Their median age was 38 years (range 21–66 years) and 69% were female. Fifty-one percent (173/342) had children; the median age of the youngest child was 5 years (range 0–37 years). Respondents resided in 32 different countries; 25 of these countries were part of the European Union (represented by 95%; 321/337 respondents); respondents from other countries such as Barbados, Mozambique, Norway, Switzerland, Turkey and the United States were also included.

Of all respondents, 249 (68%) were epidemiologists, 43 (12%) were microbiologists and 98 (27%) specified other professional backgrounds, including statistics, anthropology, biology, and veterinary medicine. Fifty-two percent (138/264) were medical doctors (multiple answers were possible). The median professional experience was six years (range 0-35 years). Most respondents worked in the public sector (97%; 316/327), had a permanent position (64%; 211/330), and had completed (or were currently enrolled in) an FETP (58%; 189/327). Forty-six percent (151/330) were involved in Ebola-related activities at the time of the survey. Twenty-eight percent (93/329) mentioned previous experience in international outbreak response, partly in sub-Saharan Africa (n = 52) or other developing countries (n = 21).

Fifteen percent (49/329) had applied for recent Ebola missions to West Africa. Deploying organisations included WHO (n = 34), MSF (n = 14) and others (n = 16). Eighteen of the 49 applicants had already completed a mission, including 13 deployed by WHO and two deployed by MSF (average duration of missions 28 days; range 4–60 days).

The vast majority of respondents was fluent in English (89%; 290/327), generally interested in missions (80%; 249/312) and felt physically and psychologically fit (81%; 248/308 and 74%; 229/310, respectively; Figure 1). Less than half considered themselves to be fluent in French (41%; 132/323).

Respondents' views and attitudes on Ebola missions

Seventy five percent of respondents thought they could be of help (245/328), 63% considered themselves qualified (205/328), 67% felt they were sufficiently trained about Ebola (217/325) and 71% had sufficient knowledge about self-protection from Ebola virus infection (229/322). Answers were more diverse concerning having the required vaccinations (52%; 160/308) and support of their supervisors (46%; 146/314). A minority had previous socio-cultural experience in the affected region (31%; 100/323) or time to go (27%; 82/305). Only 82 of 300 respondents (27%) had been asked directly to join one of the missions.

Factors increasing the motivation to apply for missions

Many respondents pointed to elements that would increase their motivation to apply, including a clear job description (88%; 248/283), meaningful tasks (84%; 233/277), guaranteed medical evacuation (83%; 232/281), a better match with own skills (82%; 230/279) and better preparation (78%; 220/281). Additionally, encouragement by the employer (74%; 205/276), personal recommendation by colleagues (59%; 157/266), or confidence that someone else would take care of their routine work (61%; 163/267) could motivate many experts. The prospects to conduct research studies (35%; 96/271), write publications (32%; 86/272) and better payment (33%; 90/272) were less important in motivating applications (Figure 2).

Factors that may hinder applications

Most respondents stated that their families were concerned about their well-being (87%; 265/303), or that their families did not want them to go (62%; 187/302). Sixty-two percent (196/315) agreed that they were essential at their current job. Fewer considered other issues more important than Ebola (27%; 77/283) or regarded missions as too long (24%; 70/290), or not well enough paid (12%; 34/281). The need to use personal protective equipment (PPE) (16%; 47/297), possibility of quarantine (17%; 49/293) or stigmatisation after return (11% 33/309) did not seem to be a major concern.

Comparison between applicants and non-applicants to Ebola response missions

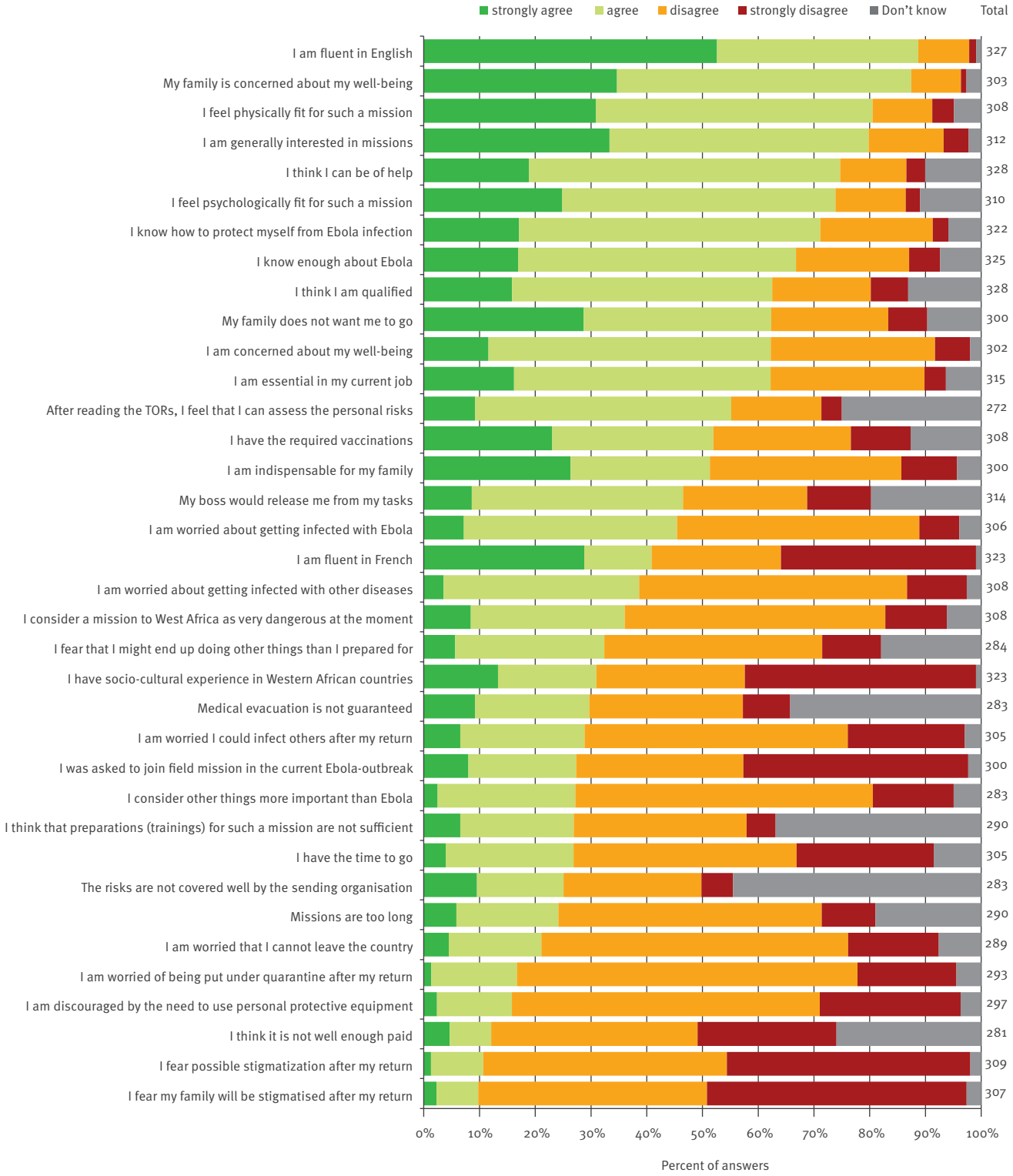
Applicants differed from non-applicants neither in terms of age, sex, professional background, years of experience, nor in the age of their youngest child. However, they less often considered a mission to West Africa as very dangerous (11%; 5/44 vs 43%; 103/239; $p < 0.001$) and less often worried about an Ebola infection (23%; 10/44 vs 52%; 126/244; $p < 0.001$).

Applicants were more often trained in an FETP (76%; 37/49 vs 54%; 145/268, $p = 0.005$) and experienced in international outbreak response missions (59%; 29/49 vs 23%; 62/273; $p < 0.001$), especially in sub-Saharan Africa (46%; 22/48 vs 10% 28/270; $p < 0.001$).

Applicants were significantly more often directly asked to join an outbreak response mission (58%; 22/38 vs 23%; 58/250; $p < 0.001$), had the time to go (59%; 22/37 vs 24%; 58/238; $p < 0.001$), had previous socio-cultural experience in West Africa (59%; 27/46 vs 26%; 69/268; $p < 0.001$), and had the required vaccinations

Figure 1

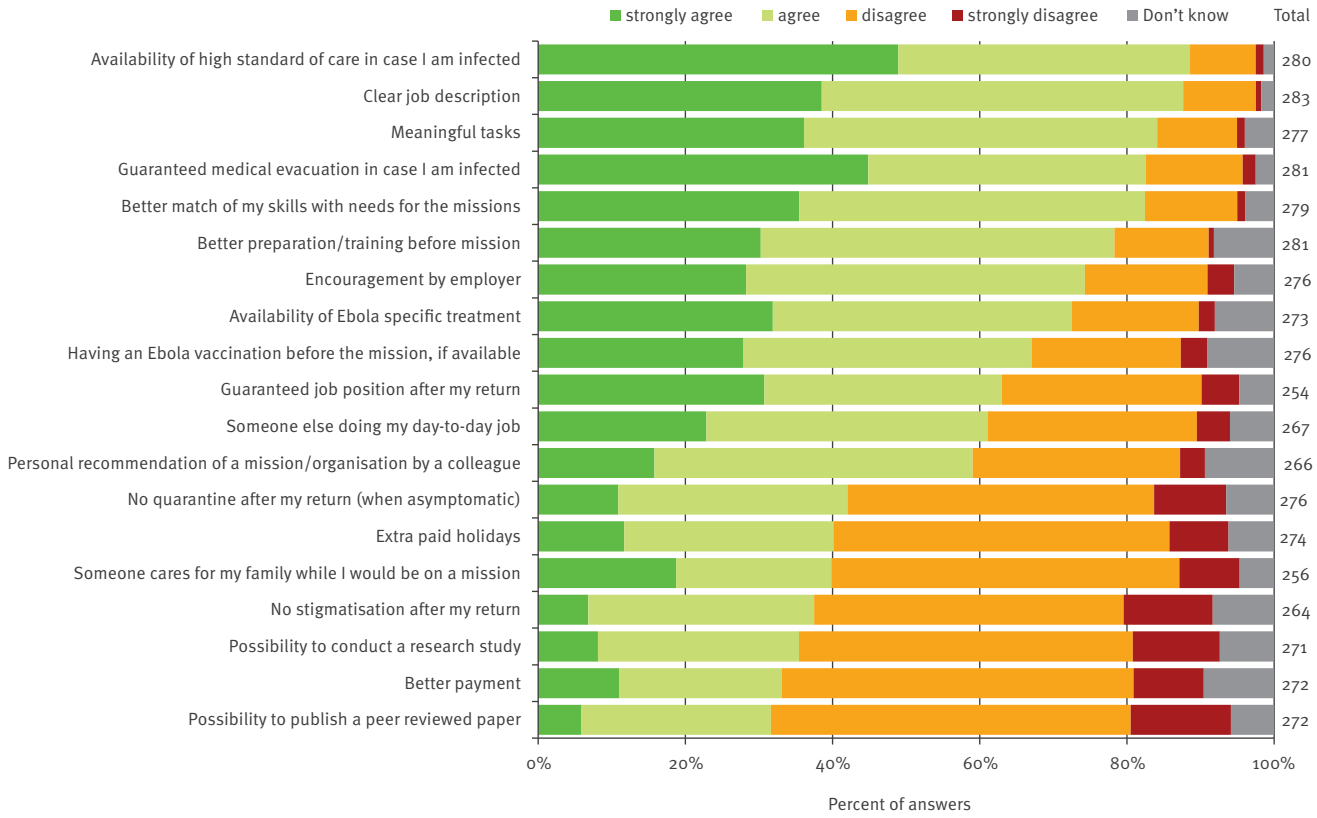
Statements concerning Ebola response mission by level of agreement of European public health professionals, December 2014



TOR: Terms of reference.

Figure 2

Motivations for European public health professionals to apply for an Ebola response mission, December 2014



(90%; 37/41 vs 54%; 122/225; p<0.001). Applicants also had more confidence in their knowledge on Ebola (91%; 42/46 vs 69%; 170/248, p=0.002), considered themselves as sufficiently qualified (90%; 43/48 vs 68%; 158/232, p=0.003) and knew how to protect themselves from Ebola (94%; 45/48 vs 72%; 182/252, p=0.001).

Comparison between experts who agree and those who disagree with statements

The table displays the frequency of applications depending on the views and attitudes of respondents (Table).

Nobody applied to an Ebola response mission if not generally interested in such missions, physically fit or convinced to be of help. The proportion of applicants was highest among those who were directly asked to join a mission, had the time to go and had previous socio-cultural experience in West Africa (28%; 22/80 each). Few applicants were found among respondents who were worried about an Ebola infection (8%; 10/136) or considered a mission to West Africa as very dangerous (5%; 5/108).

Experts who had returned from missions

Among the 18 respondents, who had already completed their deployment by the time of the survey, no one regarded a mission to West Africa currently as very dangerous. However, compared with the applicants who were still ahead of their deployment (n=26), they were less often convinced that reading the terms of references of a mission revealed the associated risks (8/12 vs 17/18). They agreed more often that medical evacuation was not guaranteed (7/12 vs 6/15), that risks were not covered well enough by sending organisations (5/12 vs 4/12), and that the preparation and trainings for such a mission were insufficient (5/12 vs 3/17). In general, they were more concerned about infections with other diseases than Ebola virus disease (7/15 vs 8/25). None of these differences were significant.

Discussion

International efforts to support the local response to the Ebola outbreak in West Africa encounter various difficulties and there may be questions regarding the mandate of deploying organisations, international treaties, and bilateral agreements. However, even if these were resolved, a considerable number of volunteering experts would be needed for a concerted and sustained response. Moreover, the individual decision to go or not to go on an Ebola response mission to West Africa will of course depend on careful personal considerations.

Table

Frequency of applications to Ebola response mission among respondents agreeing or not with various statements, European experts, December 2014

Statement[a]	Frequency of applications				Prevalence Ratio[b]	[95%CI]	P value
	Among agreeing respondents		Among disagreeing respondents				
	% (n/N)		% (n/N)				
I am generally interested in missions	18	(45/244)	0	(0/55)	NA	NA	0.001
I think I can be of help	20	(48/240)	0	(0/49)	NA	NA	0.001
I feel physically fit for such a mission	18	(45/244)	0	(0/44)	NA	NA	0.002
I feel psychologically fit for such a mission	19	(42/226)	2	(1/46)	8.55	1.21–60.55	0.005
I have the required vaccinations	23	(37/159)	4	(4/107)	6.22	2.29–16.96	<0.001
I know how to protect myself from Ebola infection	20	(45/227)	4	(3/73)	4.82	1.54–15.06	0.001
I know enough about Ebola	20	(42/212)	4	(4/82)	4.06	1.50–10.97	0.002
I was asked to join field mission in the current Ebola outbreak	28	(22/80)	8	(16/208)	3.58	1.98–6.45	<0.001
I have the time to go	28	(22/80)	8	(15/195)	3.58	1.96–6.53	<0.001
I think I am qualified	21	(43/201)	6	(5/79)	3.38	1.39–8.22	0.003
I have socio-cultural experience in Western African countries	28	(27/96)	9	(19/218)	3.23	1.89–5.51	<0.001
My boss would release me from my tasks	21	(30/145)	11	(11/104)	1.96	1.03–3.72	0.034
I am concerned about my well-being	11	(20/185)	23	(24/106)	0.48	0.28–0.82	0.007
I am worried I could infect others after my return	8	(7/84)	18	(37/207)	0.47	0.22–1.00	0.040
I am indispensable for my family	8	(12/152)	21	(28/132)	0.37	0.20–0.70	0.001
I am worried about getting infected with Ebola	7	(10/136)	22	(34/152)	0.33	0.17–0.64	<0.001
I consider a mission to West Africa as very dangerous at the moment	5	(5/108)	22	(39/175)	0.21	0.08–0.51	<0.001

CI: confidence interval; NA: not applicable.

[a] Only statements with significant differences are shown.

[b] Prevalence ratios are the proportions of applicants in agreeing over proportions of applicants in disagreeing respondents.

Our study may be limited by the convenience sampling, the possibility of information bias - i.e. respondents may have changed their decision and applied afterwards or withdrawn their application, which would result in misclassification - and the influence of social desirability bias. Nevertheless, it clearly showed that many European public health professionals felt sufficiently qualified and were willing to support the Ebola outbreak response in West Africa. Criteria that pertained to most respondents, including all those who applied for a response mission, were general interest in participating in such missions, thinking to be of help and physical fitness. Some respondents had applied for Ebola outbreak response missions despite concerns about their well-being, lack of support by their families, having small children and not having previous experience in international outbreak response missions. FETP training, international experience and confidence in own qualifications encouraged application, indicating the importance of investing into applied epidemiology and public health microbiology trainings.

A variety of obstacles hindered individual engagement though, including family constraints, uncertainty about the involved risks and work-related obstacles. Recently published articles on obstacles for volunteering health care workers in the United States and the United Kingdom also reported a lack of employers' support [8-10].

The engagement of more than 150 respondents in Ebola-related activities at the time of the survey indicated intensive resource investments of non-affected countries in their own Ebola preparedness efforts. The focus on improving own preparedness in non-affected countries is understandable. However, it might be worth reviewing how this impacts the availability of international experts for the support of affected countries.

Although stigmatisation after return, uncertainties regarding insurance coverage and medical evacuation were not considered to be a major concern, the number of applications for Ebola response missions might increase if deploying organisations took these issues into account in the planning of missions. Our survey showed that clear job descriptions, meaningful tasks, and improved preparation and training efforts would enhance the willingness of experts to apply for Ebola response missions. These understandable and realistic expectations towards the deploying organisations were also supported by the views of returning experts.

Finally, European public health organisations, deploying organisations and policy makers should further improve the required general conditions to enable the deployment of experts to international missions. This includes sustained investment in developing competencies and broadening international experience of experts e.g. through FETPs, and encouraging employers to support their employees if they volunteer for missions. These efforts should strengthen the response to the present Ebola outbreak, as well as improve and secure international response to future crises.

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Conflict of interest

None declared.

Authors' contributions

UR and MD drafted the questionnaire, conducted the analysis, wrote the manuscript; EP, CW, MadH and AG contributed to the questionnaire and revised the draft manuscript.

References

1. World Health Organization (WHO). Ebola Situation reports. Geneva: WHO. [Accessed 27 February 2015]. Available from: http://www.who.int/csr/disease/ebola/situation-reports/en/
2. Ebola: time to act. Nature. 2014;513(7517):143-4. http://dx.doi.org/10.1038/513143b PMID:25209760
3. Tambo E, Ugwu EC, Ngogang JY. Need of surveillance response systems to combat Ebola outbreaks and other emerging infectious diseases in African countries. Infect Dis Poverty. 2014;3:29. doi: 10.1186/2049-9957-3-29. eCollection 2014.
4. Gulland A. More health staff are needed to contain Ebola outbreak, warns WHO. BMJ. 2014;349(sep04 8):g5485. http://dx.doi.org/10.1136/bmj.g5485 PMID:25193934
5. Krause G, Aavitsland P, Alpers K, Barrasa A, Bremer V, Helynck B, Perra A. Differences and commonalities of national field epidemiology training programmes in Europe. Euro Surveill. 2009;14(43). PMID:19883560
6. Pezzoli L, Keramarou M, Ladbury G, Jaramillo-Gutierrez G, Williams CJ, LE Menach A. Time, place, and people: composition of the EPIET Alumni Network and its contribution to the European public health resource in 2013. Epidemiol Infect. 2014;1-8. http://dx.doi.org/10.1017/S0950268814003392 PMID:25521307
7. LimeSurvey Project Team / Carsten Schmitz. (2012). / LimeSurvey: An Open Source survey tool /LimeSurvey Project Hamburg, Germany. Available from: http://www.limesurvey.org
8. Rosenbaum L. License to serve--U.S. trainees and the Ebola epidemic. N Engl J Med. 2015;372(6):504-6. http://dx.doi.org/10.1056/NEJMp1415192 PMID:25517575
9. Mello MM, Merritt MW, Halpern SD. Supporting those who go to fight ebola. PLoS Med. 2015;12(1):e1001781. http://dx.doi.org/10.1371/journal.pmed.1001781 PMID:25622033
10. Turtle L, McGill F, Bettridge J, Matata C, Christley R, Solomon T. A Survey of UK Healthcare Workers' Attitudes on Volunteering to Help with the Ebola Outbreak in West Africa. PLoS ONE 2015;10(3):e0120013. http://dx.doi.org/10.1371/journal.pone.0120013 PMID:25760763

Australian Hajj pilgrims' knowledge, attitude and perception about Ebola, November 2014 to February 2015

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Upon return from Hajj 2014, 150 Australian pilgrims were interviewed about their understanding of the Ebola epidemic. Most (89%, 134/150) knew of the epidemic before travelling and 60% (80/134) of those knew Ebola transmits through body fluids. Pilgrims who received pre-travel health advice were more conscious of Ebola (69% vs 31%, p=0.01) and adhered better to hand hygiene after touching an ill person (68% vs 31%, p<0.01). Mass media was the main information source (78%).

As the largest known, the 2014 Ebola outbreak has affected more than 24,700 people in the three most affected West African countries, claiming ca 10,200 (41%) lives [1,2]. With ca 100,000 pilgrims from those affected countries attending Hajj each year, the possible introduction of Ebola to a Hajj event could be catastrophic. To minimise the risk, the Saudi Arabian authorities suspended Hajj visas for pilgrims from the affected countries and at the time of publication of this report, no Hajj-associated Ebola case has been reported [3]. Without an effective vaccine, public awareness of the need to avoid exposure through minimising contact with patients and body fluids, using personal protective measures, and cancelling non-emergency travel to affected countries remain the mainstays of prevention [4]. However, travellers' awareness about Ebola has not been assessed. We conducted a short survey among Australian pilgrims returning from Hajj 2014 to assess their knowledge about Ebola, its mode of transmission, and their compliance to preventive measures during Hajj.

Survey

Between November 2014 and February 2015, an anonymous cross-sectional survey was conducted among Australian pilgrims returning home from Hajj in October 2014. Participants were recruited by two methods: pilgrims attending post-Hajj seminars or social gatherings in New South Wales were invited to participate in person; other Australian pilgrims were invited to participate by telephone. The latter group were randomly chosen from a list of participants who took part in an ongoing cluster randomised trial during the Hajj 2014 which has been described elsewhere [5].

The questionnaire collected data on socio-demographic characteristics, travel itinerary, pre-travel health advice, pilgrims' knowledge on Ebola, and compliance to protective measures such as hand hygiene and use of face masks. Pilgrims' knowledge and attitude about Ebola were assessed through five questions: (i) whether the pilgrims had heard about Ebola before their travel; (ii) their knowledge on Ebola transmission; (iii) how serious they thought Ebola was; (iv) how concerned they were about contracting Ebola during Hajj; and (v) their perceived risk of Ebola at Hajj.

Participants' voluntary completion of the questionnaire was implicitly considered as consent and the survey was anonymous. This study was approved by the Human Research Ethics Committee (HREC) at the University of Sydney (Project no: 2014/599).

Knowledge, attitude and perception regarding Ebola among Hajj pilgrims

A total of 150 pilgrims participated. They were between 18 and 72 years old (median: 41 years), and 46% (69/150) were male. Half (75/150) had a university degree and about two thirds (96/150) were employed. One third (49/150) of the participants had pre-existing chronic medical conditions (Table 1). Seventy-nine per cent (119/150) of respondents performed Hajj for the first time, 7% (10/150) for the second time and 16% (24/150) had attended Hajj more than twice.

Table 1

Demographic characteristic and knowledge about Ebola of survey participants, Hajj pilgrims, New South Wales, Australia, November 2014–February 2015 (n = 150)

	n (%)	Had knowledge about Ebola
Age (years)		
18–30	28 (19)	25 (89)
31–45	75 (50)	72 (96)
46–65	39 (26)	33 (85)
>65	8 (5)	3 (38)
Sex		
Male	69 (46)	66 (96)
Female	76 (51)	66 (87)
Co-morbidities		
Diabetes	5 (3)	3 (60)
Asthma	9 (6)	8 (89)
Lung diseases	3 (2)	3 (100)
Heart diseases	1 (1)	1 (100)
Cancer	3 (2)	3 (100)
Education level		
None	5 (3)	3 (60)
School certificate (year 10 equivalent)	11 (7)	11 (100)
High school (year 12 equivalent)	22 (15)	19 (86)
Certificate/diploma	32 (21)	28 (88)
University degree	47 (31)	43 (91)
University postgraduate degree	28 (19)	28 (100)
Occupational status		
No	49 (33)	41 (84)
Yes	96 (64)	91 (95)
Occupational type		
Self-employed	17 (11)	17 (100)
Full time	61 (41)	57 (93)
Casual	4 (3)	4 (100)
Part time	14 (9)	13 (93)

Sixty-six per cent (99/150) reported receiving general health advice before Hajj; 20% (n = 30) from travel agents, 16% (n = 24) from general practitioners, 6% (n = 9) from the Internet, 6% (n = 9) from friends and family members, 4% (n = 6) from the *smarttraveller* website (http://www.smartraveller.gov.au), 3% (n = 4) from professional travel health services and the remaining 11% (n = 17) from other sources.

Eighty-nine per cent (134/150) of participants had been aware of the current Ebola outbreak before travelling. Of these, 78% (105/134) reported the mass media as their main source of information, followed by the Internet (9%; n = 12), general practitioners (GPs) (6%; n = 8), friends and family members (5%; n = 6) and travel agents (1%; n = 2).

Respondents aged 45 years and younger were more aware of the epidemic than older respondents (94% vs 76%; p < 0.01), and those with a university education were more aware of Ebola than those with less education (54% vs 46%; p = 0.05). Pilgrims who sought health advice before travelling were more conscious of Ebola than those who did not seek such advice (69% vs 31%; p = 0.01).

Of those who had heard of Ebola, 60% (80/134) stated that the virus transmits through contact with infected body fluids, 17% (n = 23) said it spreads through air, 1% (n = 1) believed it transmits through contaminated food, whereas 22% (n = 30) did not know how it transmits.

Eighty-six per cent (115/134) of participants thought that Ebola is a serious and life-threatening disease, 4% (n = 6) thought it is serious but not life-threatening, 1% (n = 1) said it is minor infection and 7% (n = 10) did not know if it is serious.

Twenty-two per cent (29/134) of those who were aware of Ebola believed there was no risk of contracting it during Hajj, 38% (n = 51) thought the risk was low, 19% (n = 26) considered it a moderate risk and 21% (n = 28) believed the risk was high. Nevertheless, 45% (60/134) were not concerned of contracting Ebola during Hajj, while 29% (n = 39) were slightly concerned, 8% (n = 11) were moderately concerned and 18% (n = 24) were very concerned.

Regarding preventive measures during their tent stay in Mina, Saudi Arabia, about half of the participants reported using face masks, most reported washing hands with plain water and two thirds reported using soap (Table 2). More than half (55%) reported washing their hands after touching an ill person. Those who sought health advice before travelling were more likely to practice hand washing (97% vs 88%, p = 0.03), especially after touching an ill person (68% vs 31%, p < 0.01).

Of those who observed hand hygiene, 66% (98/148) believed it to be an effective method of preventing infections and 36% (53/148) considered it easy to implement. Of those who used face masks 61% (50/82) did so to protect themselves from disease, and 33% (27/82) to protect themselves from air pollution.

Discussion

This survey indicates that most Hajj pilgrims were aware of the Ebola outbreak. Pilgrims who received travel advice were more informed than those who did not; however, 40% of pilgrims had no accurate knowledge of Ebola transmission. Almost all respondents adhered to hand washing several times a day, but less than half complied with hand hygiene after touching an ill person.

This study shows that 40% of the respondents saw a risk of Ebola at Hajj, but 45% pilgrims had no fear of contracting Ebola during Hajj. Those who were younger and/or had higher levels of education were more aware of Ebola. A survey from the United States showed that

Table 2

Respondents' compliance with preventative health measures during Hajj 2014, New South Wales, Australia, November 2014–February 2015 (n = 134)

Preventative measures	Uptake n (%)	Pilgrims' perception about the effectiveness of these measures n (%)			
		Very effective	Moderately effective	A little effective	Not effective
Face mask use	83 (55)	52 (35)	58 (39)	19 (13)	21 (14)
Hand hygiene	148 (99)	107 (71)	29 (20)	10 (7)	4 (3)
Use of soap-based hand disinfectant	111 (74)	56 (37)	45 (30)	16 (11)	33 (22)
Alcoholic hand disinfectant	75 (50)	74 (49)	43 (29)	23 (15)	10 (7)
Avoiding contact with ill people	65 (43)	67 (45)	56 (37)	18 (12)	9 (6)

less educated respondents were more concerned about Ebola than those with better education [6].

Pilgrims who sought pre-travel health advice were more likely to be aware of Ebola and to practise hygienic measures than those who did not seek advice. A large Geo Sentinel study has confirmed that travellers who received pre-travel health advice were less likely to contract infectious diseases [7]. This survey shows that two thirds of pilgrims received some form of pre-travel advice and only one sixth received formal pre-travel advice despite the fact that all pilgrims routinely need to contact healthcare for mandatory vaccinations. This may indicate that although pilgrims visit GPs for vaccinations, formal pre-travel advice or sufficiently long interaction between the healthcare providers and travellers is rare. A previous survey by our team demonstrated that tour operators play an important role in providing Hajj pilgrims with advice on vaccination [8]. A study in the United Kingdom showed that community leaders (e.g. Imams) are important motivators of health promotion measures [9]. Direct engagement with the tour operators and community leaders could help reach the pilgrims with better pre-travel advice.

Adherence of hand hygiene among participants with just water was high (99%), however fewer participants (74%) reported using soap, and compliance with hand washing after touching an ill person was low (55%). The difference between soap use and plain water could reflect Muslims' daily practice of washing their hands, faces and nostrils five times a day before ritual prayer [10]. According to the European Centre for Disease Prevention and Control (ECDC), hand hygiene is strongly recommended for travellers who travel to or in countries affected by Ebola outbreak [11]. Compliance with the use of face mask was also low (55%). These findings are in agreement with a review by Benkouiten et al. who found that compliance of Hajj pilgrims was high for hand hygiene but not for use of face masks [12].

A large proportion of pilgrims reported that mass media was their main source of Ebola knowledge. It has been demonstrated that social media activity increases during an outbreak and the main influencers of the activity were news media outlets (e.g. CNN, Yahoo, Reuters) [13]. However, social media (e.g. twitter) were also found to be the dominant source of misinformation on Ebola [14]. Therefore, public health authorities should be encouraged to influence social media feeds through integration of correct health education with mass media. Studies involving pilgrims from other countries have shown that pilgrims' exposure to health messages can improve their engagement in protective measures [15] and direct health education for pilgrims is another effective way of improving their knowledge on preventive measures [16].

Although the findings from this survey cannot be generalised for all travellers, they provide important information about the knowledge about Ebola and hygiene practices of participants of one of the world's largest annual mass gatherings. Also, it should be noted that, at the moment, the risk of Ebola at Hajj is only theoretical and there are many other common infections that are preventable (e.g. by vaccination) but often take a heavy toll [17]. More importantly, the risk of Middle East Respiratory Syndrome coronavirus (MERS-CoV) remains a concern, while, according to a survey conducted early last year, only 35% of the Australian Hajj pilgrims were aware of the MERS-CoV epidemic in Saudi Arabia [18]. Public health authorities, media and GPs should encourage the travellers to seek formal travel health advice to prevent those infections. Further studies are needed to analyse this and formulate strategies to keep the travellers informed about infectious diseases.

Conflict of interest

Professor Robert Booy has received funding from vaccine manufacturers; the other authors have declared no conflict of interest in relation to this work.

Authors' contributions

Amani S Alqahtani: designing the study, data collection, analysing data and drafting the manuscript. Harunor Rashid: designing the study, supervising data analysis and revising all versions of the manuscript. Kerrie E. Wiley, Harold W. Willaby, Nasser F. BinDhim, Mohamed Tashani, Anita E. Heywood and Robert Booy: substantial contribution to study design, and drafting and editing the manuscript.

References

1. Tosh PK, Sampathkumar P. What clinicians should know about the 2014 Ebola outbreak. Mayo Clin Proc. 2014;89(12):1710-7. http://dx.doi.org/10.1016/j.mayocp.2014.10.010 PMID:25467644
2. World Health Organization (WHO). Ebola situation report - 18 March 2015. Geneva: WHO. [Accessed 20 Mar 2015]. Available from: http://apps.who.int/ebola/current-situation/ebola-situation-report-18-march-2015
3. Memish ZA, Al-Tawfiq JA. The Hajj in the time of an Ebola outbreak in West Africa. Travel Med Infect Dis. 2014;12(5):415-7. http://dx.doi.org/10.1016/j.tmaid.2014.09.003 PMID:25257580
4. Tseng CP, Chan YJ. Overview of Ebola virus disease in 2014. J Chin Med Assoc. 2015;78(1):51-5. http://dx.doi.org/10.1016/j.jcma.2014.11.007 PMID:25547820
5. Wang M, Barasheed O, Rashid H, Booy R, El Bashir H, Haworth E, et al. A cluster-randomised controlled trial to test the efficacy of facemasks in preventing respiratory viral infection among Hajj pilgrims. J Epidemiol Glob Health. 2015. Forthcoming. http://dx.doi.org/10.1016/j.jegh.2014.08.002
6. McCarthy M. Four in 10 US people fear large outbreak of Ebola. BMJ. 2014;349:g5321. http://dx.doi.org/10.1136/bmj.g5321 PMID:25163929
7. Schlagenhauf P, Weld L, Goorhuis A, Gautret P, Weber R, von Sonnenburg F, et al.; EuroTravNet. Travel-associated infection presenting in Europe (2008-12): an analysis of EuroTravNet longitudinal, surveillance data, and evaluation of the effect of the pre-travel consultation. Lancet Infect Dis. 2015;15(1):55-64. http://dx.doi.org/10.1016/S1473-3099(14)71000-X PMID:25477022
8. Barasheed O, Rashid H, Heron L, Ridda I, Haworth E, Nguyen-Van-Tam J, et al.; Hajj Research Team. Influenza vaccination among Australian Hajj pilgrims: uptake, attitudes, and barriers. J Travel Med. 2014;21(6):384-90. http://dx.doi.org/10.1111/jtm.12146 PMID:25145836
9. Ahmed F, King R. Development and testing of a smoke-free homes intervention with Muslim faith leader in Leeds, UK. Lancet. 2012; 380:S22.
10. Allegranzi B, Memish ZA, Donaldson L, Pittet D, World Health Organization Global Patient Safety Challenge Task Force on Religious and Cultural Aspects of Hand HygieneWorld Alliance for Patient Safety. Religion and culture: potential undercurrents influencing hand hygiene promotion in health care. Am J Infect Control. 2009;37(1):28-34. http://dx.doi.org/10.1016/j.ajic.2008.01.014 PMID:18834738
11. European Centre for Disease Prevention and Control (ECDC). Rapid risk assessment: Outbreak of Ebola virus disease in West Africa, Ninth update, 30 January 2015. Stockholm: ECDC; August 2014. Available from: http://ecdc.europa.eu/en/publications/publications/rra-ebola-feb-2014.pdf
12. Benkouiten S, Brouqui P, Gautret P. Non-pharmaceutical interventions for the prevention of respiratory tract infections during Hajj pilgrimage. Travel Med Infect Dis. 2014;12(5):429-42. http://dx.doi.org/10.1016/j.tmaid.2014.06.005 PMID:24999278
13. Househ M. Communicating Ebola through social media and electronic news media outlets: A cross-sectional study. Health Informatics J. 2015;pii=1460458214568037. [Epub ahead of print]. PMID:25656678
14. Oyeyemi SO, Gabarron E, Wynn R. Ebola, Twitter, and misinformation: a dangerous combination? BMJ. 2014;349:g6178. http://dx.doi.org/10.1136/bmj.g6178 PMID:25315514
15. Balaban V, Stauffer WM, Hammad A, Afgarshe M, Abd-Alla M, Ahmed Q, et al. Protective practices and respiratory illness among US travelers to the 2009 Hajj. J Travel Med. 2012; 19: 163-8.
16. Turkestani A, Balahmar M, Ibrahem A, Moqbel E, Memish ZA. Using health educators to improve knowledge of healthy behaviour among Hajj 1432 (2011) pilgrims. East Mediterr Health J. 2013;19(Suppl 2):S9-12. PMID:24673092
17. Charrel RN. Hajj, Umrah, and other mass gatherings: which pathogens do you expect? Beware of the tree that hides the forest! Travel Med Infect Dis. 2014;12(5):418-9. http://dx.doi.org/10.1016/j.tmaid.2014.09.002 PMID:25241204
18. Tashani M, Alfelali M, Barasheed O, Fatema FN, Alqahtani A, Rashid H, et al. Australian Hajj pilgrims' knowledge about MERS-CoV and other respiratory infections. Virol Sin. 2014;29(5):318-20.

Evaluation of a point-of-care blood test for identification of Ebola virus disease at Ebola holding units, Western Area, Sierra Leone, January to February 2015

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Current Ebola virus disease (EVD) diagnosis relies on reverse transcription-PCR (RT-PCR) technology, requiring skilled laboratory personnel and technical infrastructure. Lack of laboratory diagnostic capacity has led to diagnostic delays in the current West African EVD outbreak of 2014 and 2015, compromising outbreak control. We evaluated the diagnostic accuracy of the EVD bedside rapid diagnostic antigen test (RDT) developed by the United Kingdom's Defence Science and Technology Laboratory, compared with Ebola virus RT-PCR, in an operational setting for EVD diagnosis of suspected cases admitted to Ebola holding units in the Western Area of Sierra Leone. From 22 January to 16 February 2015, 138 participants were enrolled. EVD prevalence was 11.5%. All EVD cases were identified by a positive RDT with a test line score of 6 or more, giving a sensitivity of 100% (95% confidence interval (CI): 78.2–100). The corresponding specificity was high (96.6%, 95% CI: 91.3–99.1). The positive and negative predictive values for the population prevalence were 79.0% (95% CI: 54.4–93.8) and 100% (95% CI: 96.7–100), respectively. These results, if confirmed in a larger study, suggest that this RDT could be used as a 'rule-out' screening test for EVD to improve rapid case identification and resource allocation.

Introduction

than one year after the first human-to-human transmission, the largest Ebola virus disease (EVD) outbreak continues in West Africa, with an estimated 24,701 cases reported and 10,194 deaths by 15 March 2015 [1]. To date, Sierra Leone is the most severely affected country.

Case identification is essential for effective EVD control and rapid case detection is critical for rationalisation of resources and implementation of early treatment interventions [2]. A locally adapted EVD clinical case definition allows suspected cases to be identified and isolated in Ebola holding units (EHU), but this alone is inadequate to reliably differentiate EVD cases from patients with other conditions that mimic EVD presentation [3]. A confirmed EVD diagnosis is a prerequisite for transfer of a patient to an EVD treatment centre (ETC) to access EVD-specific care. All patients meeting the suspected case definition require isolation, laboratory sampling and diagnostic testing. For such patients, a negative EVD result is required before admission into general healthcare.

Current EVD diagnosis relies on reverse transcription-PCR (RT-PCR) technology [4]. This test is highly sensitive and specific but requires skilled laboratory personnel and technical infrastructure [5]. In the early months of the current West African outbreak, these personnel and infrastructure were largely absent locally. As the EVD response has grown, laboratory infrastructure in the region has improved, but this may not be sustainable in the long term or available at the onset of future outbreaks. In addition, the current EVD diagnostic pathway has cost, resource and safety implications relating to venous blood sampling inside the EHU, timely transport of samples to the EVD diagnostic laboratory, potential for labelling error, and rapid relay of results [6].

One immunofiltration antigen-based assay developed in the mid-2000s has been tested on field specimens from 2003, but is not yet available in routine clinical practice and requires a photometer for analysis [7].

A rapid diagnostic test for EVD, performed at the bedside in EHUs or other isolation facilities would be of great benefit [8]. The Defence Science and Technology Laboratory (DSTL) in the United Kingdom (UK) has developed a rapid antigen diagnostic test (RDT) for EVD diagnosis. The DSTL EVD RDT is a bedside lateral flow assay using capillary blood rather than venous blood to detect presence of an undisclosed Ebola virus antigen. The test can be conducted and interpreted with minimal training and the result is obtained within 20 min. A semi-quantitative result is obtained by scoring a test line on colour intensity.

In this study, we evaluate the diagnostic accuracy of the DSTL EVD RDT compared with the gold standard Ebola virus (EBOV) RT-PCR in an operational setting for EVD diagnosis of suspected EVD cases admitted to EHUs in the Western Area of Sierra Leone.

Methods

The study was conducted at four EHUs in the Western Area of Sierra Leone that routinely isolated suspected EVD cases and collected diagnostic blood samples for EVD testing: Connaught Government Hospital (the national adult referral hospital), Macauley Street Government Hospital, Rokupa Government Hospital, and Newton Health Centre. These sites belong to a network of holding units supported by King's Sierra Leone Partnership (KSLP) and managed by the Ministry of Health and Sanitation (MOHS) and use a screening tool based on the national case definition for suspected EVD cases, combining exposure risk evaluation and a symptom checklist for identification of suspected EVD cases. Each centre had trained phlebotomists and local healthcare workers who routinely provided patient care. Clinical staff were invited to training in the use of the RDT and study protocol which was undertaken in three one-hour sessions.

Staff who completed the training were approved to enrol patients and perform the RDT. Trained clinical staff obtained verbal informed consent from consecutive patients newly admitted to the EHU during the study period, wearing appropriate personal protective equipment [9]. Patients who could not give informed consent (e.g. due to young age, cognitive impairment or confusion) and patients who withheld consent were not enrolled.

Enrolment occurred on the day of admission or on the following day when patients were admitted during the night. In all cases, enrolment occurred before the results of routine EVD diagnostic testing were available, i.e. only suspected cases were enrolled. The RDT was performed at the bedside. All equipment for the RDT was provided in individually packaged test kits. Capillary blood for the RDT was obtained using a sterile lancet to prick a finger. Blood was applied to the well of the lateral flow device with a small pipette, followed by three drops of buffer. After 20 min, the RDTs were read in designated areas with good lighting and scores were obtained with the aid of a scorecard. RDTs were scored C when a single control (C) line was visible and CT when the C line and the test (T) line were visible. If visible, the T line was scored [2-10] on colour intensity by matching the T line to samples on the scorecard. Clinical staff performing RDTs were blind to RDT score interpretation.

Venepuncture for routine EVD diagnostic testing was performed as per routine clinical care, usually on the same day as the RDT. Venous blood samples were transported to the Public Health England (PHE) laboratory at Port Loko for EVD RT-PCR testing with the Altona RealStar Filovirus screen kit for real-time PCR (Altona Diagnostics Gmbh, Germany). Extraction was performed using a manual method with the Qiagen QIAamp Viral RNA kit (Qiagen). Altona quote a detection limit of 1.39 copies/µL of eluate (range: 0.69 to 5.32) for Zaire EBOV and 100% specificity against a range of viruses. In a small number of cases, routine EVD diagnostic testing by RT-PCR on venous blood was performed at other local diagnostic laboratories. Laboratory personnel were blind to the RDT result. The Altona assay has been selected by the World Health Organization (WHO) as the reference standard for this outbreak.

Study enrolment and results were recorded in a password protected spreadsheet and matched to EVD RT-PCR results for analysis by the study coordinator (NFW). Analysis was performed in Excel (Microsoft Corporation), Prism 6 (GraphPad Software, Inc), and Medcalc version 15.2.2 (Medcalc Software, Ostend Belgium). As the DSTL EVD RDT provides a quantitative result, analysis was performed to establish the diagnostic accuracy of the test for the range of CT scores, in comparison with the gold standard result. Results were anonymised before dissemination. Reporting of results follows the STARD (Standards for Reporting Diagnostic Accuracy Studies) statement [10].

The study was approved by the Sierra Leone Ethics and Scientific Review Committee (SLESRC, 16/01/2015).

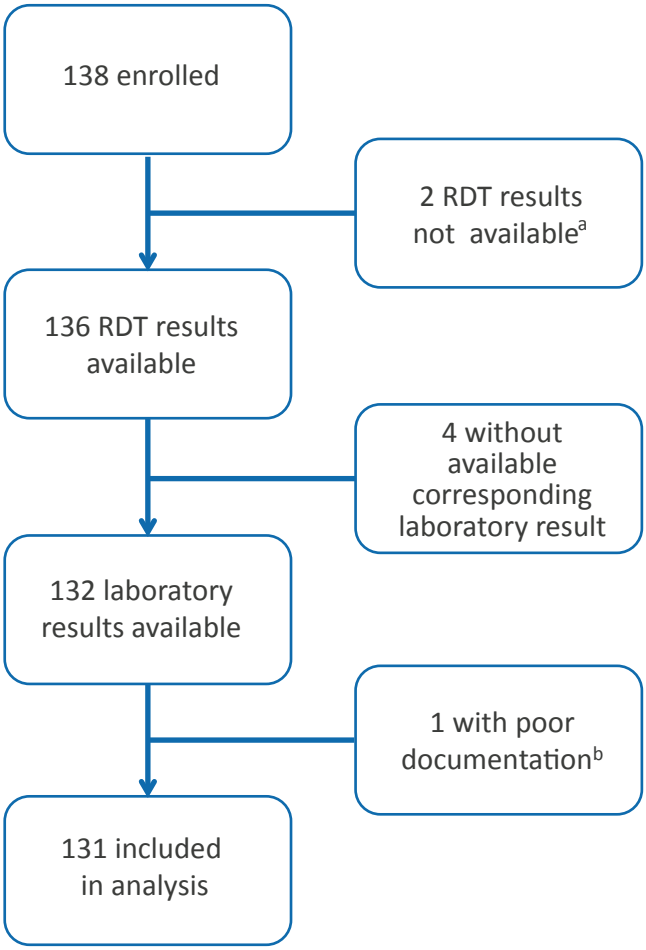
Results

Participants and enrolment

Participants were recruited consecutively at study sites, from 22 January to 16 February 2015. A total of 138 participants were enrolled. At Connaught Hospital, 112 patients were enrolled. This constituted 83% of 135 total admissions at Connaught Hospital EHU during the study period. Seven enrolled participants were excluded at the analysis stage because insufficient information was available (Figure 1). Of these patients, four had RDT tests performed but did not have corresponding EVD RT-PCR results available. The RDT result

Figure 1

DSTL rapid diagnostic antigen test for Ebola virus disease, study enrolment and inclusion, Sierra Leone, January–February 2015 (n = 138)



DSTL: Defence Science and Technology Laboratory; RDT: rapid diagnostic antigen test.

[a] In one case the RDT attempt failed as an extremely small volume of blood was collected after the pinprick, in a second case no RDT result was documented.

[b] Possible double entry of a patient with discordant RDT results

was negative in each of these cases. One patient had a negative EVD RT-PCR result but did not have an RDT result recorded. One patient had neither RDT nor EVD RT-PCR result available. One patient with a negative RDT had no corresponding EVD RT-PCR result available but similar clinical details to a subsequent participant, suggesting that this was an error in documentation and possibly a double entry. Finally, 131 participants were included in the analysis. Of those, 90 (68.7%) were male, and the median age was 32 years (interquartile range (IQR): 24–47 years).

Ebola virus disease diagnosis

Fifteen of 131 patients tested positive for EVD by EVD RT-PCR, giving a study EVD prevalence of 11.5% (Figure 2). Data on duration of symptoms before presentation for EVD-positive patients was available for seven of 15 (47%) cases. In these patients, median symptom duration before date of EVD diagnostic testing was four days (IQR: 3–5 days). The PHE Port Loko laboratory processed 125 of the laboratory samples (95%). Three samples were processed at the PHE Kerry Town laboratory using the same diagnostic assay and standard operating procedure as PHE Port Loko, and three samples were processed at other laboratories.

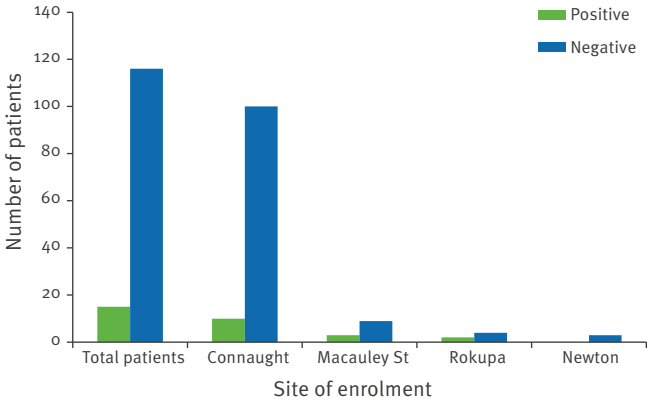
Performance of the rapid diagnostic antigen test

Twenty-four patients had RDT results with both C and T line visible (CT). In 15 of these patients, an EVD diagnosis was made by positive EVD RT-PCR and in nine cases, EVD RT-PCR results were negative (Table 1). In all confirmed cases of EVD, a T line was present on the RDT (Table 1 and Figure 3). Higher CT scores were found in patients with EVD than those without EVD (Table 1 and Figure 3).

Table 2 details the sensitivity and specificity of the RDT with increasing CT score. If any test with a visible T line (corresponding to CT score of CT2 and above) was classified as positive, the RDT had a sensitivity of 100% (95% confidence interval (CI): 78.2–100) and a specificity of 92% (95% CI: 85.8–96.4) compared with the gold standard RT-PCR. If any test with a T line score above 4 (corresponding to a CT score of CT6 and above) was classified as positive, the RDT remained 100% sensitive (95% CI: 78.2–100), but had a higher specificity of 97% (95% CI: 91.4–99.1). The specificity of the test increased with higher CT score threshold for a positive result, but the corresponding sensitivity was reduced

Figure 2

Diagnosis by gold standard (Ebola virus PCR) in study participants for the DSTL rapid diagnostic antigen test for Ebola virus disease, Sierra Leone, January–February 2015 (n = 131)*



DSTL: Defence Science and Technology Laboratory.

Table 1

Results of DSTL rapid diagnostic antigen test for Ebola virus disease, Sierra Leone, January–February 2015 (n = 131)

	RDT result		RDT test (T) line score				
	C	CT	CT2	CT4	CT6	CT8	CT10
EVD PCR-positive (n)	0	15	0	0	4	5	6
EVD PCR-negative (n)	107	9	1	4	2	1	1

DSTL: Defence Science and Technology Laboratory; EVD: Ebola virus disease; RDT: rapid diagnostic antigen test.

for a CT score of 8 or above. A specificity of 99% (95% CI: 95.3–100.0) was achievable if an RDT score above CT8 was

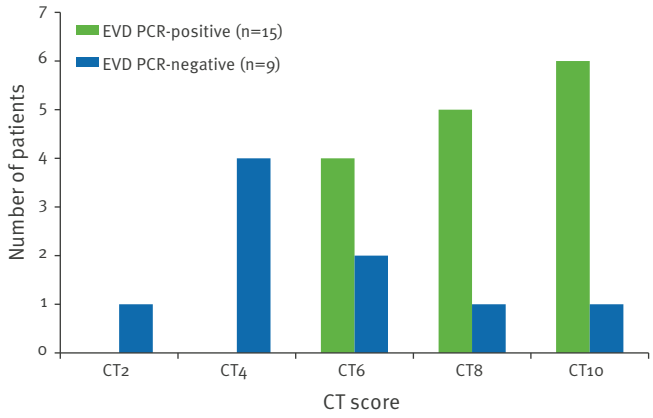
The positive predictive value (PPV) of the DSTL EVD RDT, for the study population EVD prevalence of 11.5%, was 79.0% (95% CI: 54.4–93.8) for a CT score of 6 and above and increased at higher CT score thresholds for a positive result (Table 3). A negative predictive value of 100% was achievable if a CT score 2 and above, a CT score 4 and above, or a CT score 6 and above, were classified as a positive result.

Discussion

Our data suggest that the DSTL EVD RDT is highly sensitive, specific and performs well in an operational setting. A high sensitivity is critical to EVD diagnostic test acceptability. A highly sensitive screening test such as this would allow high-risk suspected EVD cases to be prioritised for isolation and confirmatory diagnostic testing with RT-PCR, reducing non-EVD admissions in EHUs. If the sensitivity was lower, EVD-positive cases could be inappropriately discharged to inpatient wards, with risks of onward nosocomial transmission.

Figure 3

CT scores for the DSTL rapid diagnostic antigen test for Ebola virus disease, Sierra Leone, January–February 2015 (n = 24)



DSTL: Defence Science and Technology Laboratory; EVD: Ebola virus disease.

Although the specificity was high, a small number of non-EVD patients tested positive with the RDT at all T Line scores. Using the DSTL EVD RDT as a 'rule-in' test for EVD would result in some EVD-negative patients being inappropriately referred to ETCs and exposed to nosocomial risk, unless confirmatory testing by RT-PCR was undertaken.

Therefore the RDT may be best used as a 'rule-out' screening test. If the high sensitivity of the RDT is confirmed by further evaluation, this would allow RDT-negative patients to be discharged, reducing pressure on isolation unit beds and diagnostic laboratories. It would allow safe and rapid referral of sick, RDT-negative patients to general wards to receive appropriate healthcare, or for patients with milder illness to be discharged. In addition, emergency surgical procedures and obstetric deliveries could be performed without EVD transmission risk, following a negative RDT. This would allow healthcare workers to confidently and safely treat non-EVD conditions without being exposed to potentially infectious patients and may allow normal healthcare services to be maintained in future epidemics. This has been a significant challenge during the current epidemic [11]. Those with a positive RDT should be considered high-probability suspected EVD cases, prioritised for isolation in the appropriate risk-stratified area of the EHU, with confirmatory diagnostic testing performed by RT-PCR.

Our results, particularly if confirmed by larger studies on stored samples, support the use of this test for screening purposes.

Limitations

The number of admissions in the study period was lower than expected and the EVD prevalence lower than that observed in late 2014, reducing the power of the study. In addition, it was intended that all consecutive EHU admissions should be recruited at study sites. This was not always possible as a limited number of trained staff were available to enter the EHUs to enrol patients and some patients were unable to give informed consent. However, at Connaught Hospital EHU, the main site of enrolment, the majority (83%) of admissions were enrolled. The wide confidence intervals around sensitivity will need further confirmatory work before routine clinical use.

Table 2

Diagnostic accuracy of DSTL rapid diagnostic antigen test for Ebola virus disease compared with gold standard PCR, by CT score, Sierra Leone, January–February 2015 (n = 131)

CT score	Sensitivity %	95% CI	Specificity %	95% CI
≥2	**100.0**	78.2–100.0	**92.2**	85.8–96.4
≥4	**100.0**	78.2–100.0	**93.1**	86.9–97.0
≥6	**100.0**	78.2–100.0	**96.6**	91.4–99.1
≥8	**73.3**	44.9–92.2	**98.3**	93.9–99.8
10	**40.0**	16.3–67.7	**99.1**	95.3–100.0

CI: confidence interval; DSTL: Defence Science and Technology Laboratory.

The prevalence of EVD was low in our study compared with earlier in the outbreak, when up to 75% of admissions to the Connaught Hospital EHU were EVD-positive. This has resulted in a relatively low PPV for the RDT. As the PPV only applies for a particular population prevalence, the performance of the test should be confirmed at a higher population prevalence. It is likely that the PPV would be higher at a higher EVD prevalence.

We compared the RDT result to gold-standard EVD diagnosis with RT-PCR. The WHO recommends repeat testing of symptomatic patients who test negative for EVD by RT-PCR less than three days after the onset of their illness, as the sensitivity of EVD RT-PCR may be lower early in the clinical course of EVD [4]. Our routine practice complied with this policy. However, it remains possible that we have classified some patients as false-positive RDTs who were infected with Ebola virus but had RT-PCR results below the assay detection limits. If this was the case, our study underestimates the diagnostic accuracy of the DSTL EVD RDT. PHE has now moved to an alternative in-house assay which his more sensitive than the Altona RT-PCR and may verify the DSTL test results in any future work. Further study is required to assess the performance of the RDT early in the clinical course of EVD and in the EVD incubation period.

Table 3

Positive and negative predictive values of DSTL rapid diagnostic antigen test for an Ebola virus disease prevalence of 11.5%, by CT score, Sierra Leone, January–February 2015 (n = 131)

CT score	PPV %	95% CI	NPV %	95% CI
≥2	**62.5**	40.6–81.2	**100.0**	96.6–100.0
≥4	**65.2**	42.7–85.6	**100.0**	96.6–100.0
≥6	**79.0**	54.4–93.8	**100.0**	96.7–100.0
≥8	**84.6**	54.5–97.6	**96.6**	91.5–99.1
10	**85.7**	42.2–97.6	**92.7**	86.7–96.6

CI: confidence interval; DSTL: Defence Science and Technology Laboratory; NPV: negative predictive value; PPV: positive predictive value.

Relationship to other studies

The WHO approved the first RDT for use as a screening test for EVD (ReEBOV Antigen Rapid Test) on the basis of a reported sensitivity of 91.8% (95% CI: 84.5–96.8) and a specificity of 84.6% (95% CI: 78.8–89.4). This RDT was evaluated on 147 fresh venous blood and 146 frozen plasma samples in a laboratory setting in Sierra Leone [12]. Performance of this test in an operational setting has not been reported. Our findings suggest that the DSTL EVD RDT performs well against this benchmark, exceeding these reported findings in an operational setting.

Conclusion

The performance of the DSTL EVD RDT in this study strongly supports its use as a 'rule-out' screening test for EVD. Further laboratory and operational data are required to improve confidence and inform further on sensitivity and specificity in a broader setting.

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Conflict of interest

None declared.

Authors' contributions

NF Walker, CS Brown, D Youkee, K Russell, N Bentley, T Boyles, A Simpson, T Brooks, A Kamara, TB Kamara, M Lado, O Johnson designed the research; NF Walker, P Baker, D Youkee, N Williams, A Kalawa, B Healey and the RDT study team performed the research; AF Samba, F Koroma, MB King, BE Parker, M Thompson, B Kargbo, D Bash-Taqi, TB Kamara, A Kamara contributed vital technical support; NF Walker, CS Brown, P Baker analysed the data; NF Walker, CS Brown, P Baker, T Boyles wrote the draft manuscript; all authors have seen and approved the final manuscript.

*Erratum: On 12 June 2015, the x axis label in Figure 2 was corrected to read 'Site of enrolment'.

References

1. World Health Organization (WHO). Ebola situation report - 18th March 2015. Geneva: WHO; 2015. Available from: http://apps.who.int/ebola/current-situation/ebola-situation-report-18-march-2015
2. WHO Ebola Response Team. Ebola virus disease in West Africa--the first 9 months of the epidemic and forward projections. N Engl J Med. 2014;371(16):1481-95. http://dx.doi.org/10.1056/NEJMoa1411100 PMID:25244186
3. Youkee D, Johnson O, Amardeep K, Hall A, Lado M. King's Sierra Leone Partnership Ebola holding units standard operating procedure. Freetown: KSLP; 2014.
4. World Health Organization (WHO). Laboratory diagnosis of Ebola virus disease. Geneva: WHO; 2014. Available from: http://apps.who.int/iris/bitstream/10665/134009/1/WHO_EVD_GUIDANCE_LAB_14.1_eng.pdf
5. Towner JS, Rollin PE, Bausch DG, Sanchez A, Crary SM, Vincent M, et al. Rapid diagnosis of Ebola hemorrhagic fever by reverse transcription-PCR in an outbreak setting and assessment of patient viral load as a predictor of outcome. J Virol. 2004;78(8):4330-41. http://dx.doi.org/10.1128/JVI.78.8.4330-4341.2004 PMID:15047846
6. Pathmanathan I, O'Connor KA, Adams ML, Rao CY, Kilmarx PH, Park BJ, et al.; Centers for Disease Control and Prevention (CDC). Rapid assessment of Ebola infection prevention and control needs--six districts, Sierra Leone, October 2014. MMWR Morb Mortal Wkly Rep. 2014;63(49):1172-4. PMID:25503922
7. Lucht A, Formenty P, Feldmann H, Gotz M, Leroy E, Bataboukila P, et al. Development of an immunofiltration-based antigen-detection assay for rapid diagnosis of Ebola virus infection. J Infect Dis. 2007;196(s2) Suppl 2;S184-92. http://dx.doi.org/10.1086/520593 PMID:17940948
8. World Health Organization (WHO). Urgently needed: rapid, sensitive, safe and simple Ebola diagnostic tests. Geneva: WHO; 2014. Available from: http://www.who.int/mediacentre/news/ebola/18-november-2014-diagnostics/en/
9. World Health Organization (WHO). Clinical management of patients in the Ebola Treatment Centres and other care centres in Sierra Leone. December 2014. Interim emergency guidelines. Geveva: WHO; 2014. Available from: https://extranet.who.int/ebolafmt/content/clinical-management-patients-ebola-treatment-centres-and-other-care-centres-sierra-leone
10. University of Amsterdam (UOA). STARD Statement. Standards for the reporting of diagnostic accuracy studies. Amsterdam: UOA. [Accessed: 24 Feb 2015]. Available from: http://www.stard-statement.org/
11. Jain V, Brown CS, Johnson O. Sierra Leone: the forgotten mortality. Glob Health Action. 2015;8(0):26757. http://dx.doi.org/10.3402/gha.v8.26757 PMID:25669239
12. World Health Organization (WHO). WHO emergency use assessment and listing for Ebola virus disease IVDs. Public report. Product: ReEBOV™ Antigen Rapid Test Kit EUAL Number: EA 0011-011-00. Geneva: WHO; 2015. Available from: http://www.who.int/diagnostics_laboratory/procurement/150219_reebov_antigen_rapid_test_public_report.pdf

Wild bird surveillance around outbreaks of highly pathogenic avian influenza A(H5N8) virus in the Netherlands, 2014, within the context of global flyways

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Highly pathogenic avian influenza (HPAI) A(H5N8) viruses that emerged in poultry in east Asia since 2010 spread to Europe and North America by late 2014. Despite detections in migrating birds, the role of free-living wild birds in the global dispersal of H5N8 virus is unclear. Here, wild bird sampling activities in response to the H5N8 virus outbreaks in poultry in the Netherlands are summarised along with a review on ring recoveries. HPAI H5N8 virus was detected exclusively in two samples from ducks of the Eurasian wigeon species, among 4,018 birds sampled within a three months period from mid-November 2014. The H5N8 viruses isolated from wild birds in the Netherlands were genetically closely related to and had the same gene constellation as H5N8 viruses detected elsewhere in Europe, in Asia and in North America, suggesting a common origin. Ring recoveries of migratory duck species from which H5N8 viruses have been isolated overall provide evidence for indirect migratory connections between East Asia and Western Europe and between East Asia and North America. This study is useful for better understanding the role of wild birds in the global epidemiology of H5N8 viruses. The need for sampling large numbers of wild birds for the detection of H5N8 virus and H5N8-virus-specific antibodies in a variety of species globally is highlighted, with specific emphasis in north-eastern Europe, Russia and northern China.

Introduction

Wild aquatic birds are the natural reservoir for low pathogenic avian influenza A (LPAI) viruses, which are classified based on their surface proteins haemagglutinin (HA, H1–H16) and neuraminidase (NA, N1–N9) [1,2]. These viruses can be carried over long distances along migratory flyways [3-5]. LPAI viruses of the H5 and H7 subtype can evolve into highly pathogenic avian influenza (HPAI) viruses upon introduction into poultry. HPAI H5N8 viruses, such as A/duck/Jiangsu/k1203/2010, were first detected in birds on live bird markets in China in 2010 [6]. These H5N8 viruses contain genes derived from HPAI H5N1 viruses of the so-called A/Goose/Guangdong/1/1996 (GsGd) lineage [7] that have caused outbreaks in numerous countries of the eastern hemisphere since 1997.

In January 2014, HPAI H5N8 viruses were detected in South Korea, where they infected birds of 161 poultry farms and resulted in the culling of 14 million poultry by September 2014 [8]. In April 2014, HPAI H5N8 virus was detected on a chicken farm in Japan. Over the summer of 2014, no new cases were reported outside South Korea. In September, HPAI H5N8 virus was detected in China in a domestic duck and an environmental sample. During the same month, H5N8 virus was also detected in north-eastern Russia in a Eurasian wigeon (*Anas penelope*). From November 2014 to February 2015, HPAI H5N8 virus has been found in poultry and/or free-living wild birds in Asia (Japan and Taiwan), Europe (Germany, Hungary, Italy, the Netherlands and the United Kingdom (UK)), and North America (US) [9,10]. HPAI H5N8 virus was also detected in captive wild birds: dead gyrfalcons (*Falco rusticolus*) in the north west of the United States (US) and white storks (*Ciconia ciconia*) in a zoo in Germany (Table 1) [11]. The HA of HPAI H5N8 viruses detected in domestic and wild birds in Asia, Europe and North America belonged to the GsGd H5 clade 2.3.4.4 [12]. Genetic closely related H5N8 viruses belonging to the same GsGd H5 clade 2.3.4.4 were detected in China since 2010.

So far, HPAI H5N8 virus has been isolated from free-living wild birds of the orders *Accipitriformes*, *Anseriformes*, *Charadriiformes*, *Falconiformes* and *Gruiformes* in several countries including Germany, Japan, Russia, South Korea, Taiwan, the Netherlands,

Table 1

Global detection of highly pathogenic avian influenza A(H5N8) virus and other viruses belonging to the H5 clade 2.3.4.4 in wild birds and poultry, 2014

Host type	Order	Family	Poultry type or bird species	AIV subtype	Geographical area
Captive	*Anseriformes*	Ducks	Domestic duck	H5N2; H5N3; H5N8	Canada (H5N2); China (H5N8; H5N2); Hungary (H5N8); Netherlands (H5N8); South Korea (H5N8); Taiwan (H5N2, H5N3, H5N8); UK (H5N8); US (H5N2, H5N8)
		Geese	Domestic Goose	H5N2; H5N3; H5N8	Canada (H5N2); South Korea (H5N8); Taiwan (H5N2, H5N3, H5N8); US (H5N2, H5N8)
	Galliformes	Chickens	Chicken	H5N1; H5N2; H5N3; H5N8	Canada (H5N1, H5N2); China (H5N2); Japan (H5N8); Netherlands (H5N8); South Korea (H5N8); Taiwan (H5N2, H5N3, H5N8); US (H5N2, H5N8)
		Turkeys	Domestic turkey	H5N2; H5N3; H5N8	Canada (H5N2); Germany (H5N8); Italy (H5N8); Taiwan (H5N2, H5N8); US (H5N2, H5N8)
	Ciconiiformes	Storks	White stork (*Ciconia ciconia*)	H5N8	Germany
	Falconiformes	Falcons	Gyrfalcon (*Falco rusticolus*)	H5N8	US
			Peregrine falcon (*Falco peregrinus*)	H5N2	US
	Strigiformes	Owls	Great horned owl (*Bubo virginianus*)	H5N2	US
Wild	*Accipitriformes*	Eagles	Bald eagle (*Haliaeetus leucocephalus*)	H5N8	US
		Hawks	Cooper's hawk (*Accipiter cooperii*)	H5N2	US
			Red-tailed hawk (*Buteo jamaicensis*)	H5N2	US
	Anseriformes	Ducks	Baikal teal (*Anas formosa*)	H5N8	South Korea
			Mallard (*Anas platyrhynchos*)	H5N2; H5N8	Germany (H5N8); Japan (H5N8); South Korea (H5N8); US (H5N2, H5N8)
			Common teal (*Anas crecca*)	H5N8	Germany; South Korea
			Green-winged teal (*Anas carolinensis*)	H5N1; H5N8	US
			Spot-billed duck (*Anas poecilorhyncha*)	H5N8	South Korea
			Eurasian wigeon (*Anas penelope*)	H5N8	Netherlands; Russia
			Northern pintail (*Anas acuta*)	H5N2	US
			Mandarin duck (*Aix galericulata*)	H5N8	Japan
			Gadwall (*Anas strepera*)	H5N8	US
			American wigeon (*Anas americana*)	H5N8	US
			Wood duck (*Aix sponsa*)	H5N2	US
			Northern shoveler (*Anas clypeata*)	H5N2	US
		Geese	Bean goose (*Anser fabalis*)	H5N8	South Korea
			White-fronted goose (*Anser albifrons*)	H5N8	South Korea
		Swans	Bewick's swan (*Cygnus columbianus bewickii*)	H5N8	Japan; South Korea
	Charadriiformes	Gulls	Great black-backed gull (*Larus marinus*)	H5N8	Germany
	Falconiformes	Falcons	Peregrine falcon (*Falco peregrinus*)	H5N8	US
	Gruiformes	Cranes	White-naped crane (*Grus vipio*)	H5N8	Japan
			Hooded crane (*Grus monacha*)	H5N8	Japan
		Coots	Common coot (*Fulica atra*)	H5N8	South Korea
	Passeriformes	Bulbuls	Light-vented bulbul (*Pycnonotus sinensis*)	H5N3	Taiwan
	Pelecaniformes	Herons	Black-crowned night-heron (*Nycticorax nycticorax*)	H5N2	Taiwan

AIV: avian influenza virus; UK: United Kingdom; US: United States.
Data from [8,9].

and the US (Table 1). In live wild birds, H5N8 virus detections were limited to ducks (order: *Anseriformes*) of the species common teal (*Anas crecca*), mallard (*Anas platyrhynchos*), spot-billed duck (*Anas poecilorhyncha*), Eurasian wigeon, American wigeon (*Anas americana*) and gadwall (*Anas strepera*) [8,9] (Table 1). In addition, H5N8-virus-specific antibodies were detected in 10 to 53% of ducks of the species Baikal teal (*Anas formosa*), common teal, mallard, Eurasian wigeon and spot-billed duck in South Korea [8], suggesting that this virus had been circulating in these species for some time and that these individual birds had survived infection and thus may have played a role in the dispersal of H5N8. Wild ducks of some species (e.g. *Anas* spp.) may be less likely to exhibit clinical signs when infected with HPAI H5N8 than e.g. geese, swans and cranes; alternatively, ducks are more intensively hunted and sampled, potentially explaining a higher detection rate of H5N8 in live wild ducks than in other wild bird species. Despite H5N8 virus detections in a range of wild bird species globally, it is unknown to what extent these viruses circulate in wild bird populations in Europe.

This study presents data on wild bird surveillance activities in the Netherlands that were intensified in the country, in response to the HPAI H5N8 virus outbreaks on poultry farms at the end of 2014. We present our findings in the perspective of the distribution and migratory flyways of H5N8-virus-positive bird species.

Methods

Sampling wild birds

After detection of HPAI H5N8 virus on a chicken farm in the Netherlands on 14 November 2014, sampling of live wild birds of various species was intensified in the country in an attempt to detect H5N8 virus. Birds were captured using duck decoys, clap nets, mist nets, noose or by hand. Capturing of wild birds was approved by the Dutch Ministry of Economic Affairs based on the Flora and Fauna Act (permit number FF/75A/2009/067 and FF/75A/2014/054). Handling and sampling of wild birds were approved by the Animal Experiment Committee of the Erasmus MC (permit number 122–11–31). Sampling activities targeted long-distance migratory bird species and/or bird species that had been found infected with HPAI H5N8 virus earlier in 2014, e.g. Bewick's swan (*Cygnus columbianus bewickii*) in Japan. Sample locations were both within and outside a 10 km radius of Dutch poultry farms where H5N8-virus-infections had been detected and varied in function of the distribution of wild bird species of interest combined with capture opportunities. Disposable gloves and disinfectants for boots and equipment (Virkon S) were used. Birds were sampled for virus detection by collecting samples from cloaca, from both cloaca and oropharynx, or from fresh faeces as described by Munster et al. [13]. For cloaca and oropharynx samples, the number of tested birds depended on the bird species, capture method and capture success. For fresh faeces, swab samples were collected from flocks of single species. The number of faeces droppings sampled per flock was on average less than 40% of the total number of birds in the flock with at least one metre in between each dropping (to limit sampling the same individual twice).

Virus detection, isolation and characterisation

Samples for virus detection were analysed for presence of H5N8 virus using a matrix-specific and H5-specific polymerase chain reaction (PCR) followed by H5 sequencing. Samples that tested positive in matrix-specific PCR were used for virus isolation in embryonated chicken eggs as described previously [13].

Virus sequencing and phylogeny

Of the HPAI H5N8 viruses isolated within this study, the sequences of the complete genome were obtained and deposited in a public database (http://www.gisaid.com). Sequencing was performed using specific primers as described previously [14]. Nucleotide (nt) sequences were supplemented with sequences of HPAI H5 viruses of clade 2.3.4.4 detected globally in 2014 and with sequences of HPAI H5N8 viruses detected in China before 2014. These additional sequences were obtained from public databases as of 3 March 2015, which included the Global Initiative on Sharing Avian Influenza Data database (http://www.gisaid.com) (Table 2) and Genbank (www.ncbi.nlm.nih.gov). Sequences retrieved from GenBank had the following accession numbers: AJE30335; AJE30344; AJE30360; AJM70554; AJE30333; AJM70565; AJM70567; AJM70576; AJM70578; AJM70587; AJM70598; AJM70609. Maximum Likelihood (ML) phylogenetic trees were constructed based on the HA gene of 1,545 nt in length (position: 108–1,652) and the NA gene of 1,377 nt in length (position: 1–1,377). ML trees were generated using the PhyML package version 3.1 using the general time-reversible model with the proportion of invariant sites (GTR+I model) of nt substitution, performing a full heuristic search and subtree pruning and regrafting (SPR) searches. The best-fit model of nt substitution was determined with jModelTest [15]. The reliability of the phylogenetic grouping was assessed with 1,000 bootstrap replicates. Trees were visualised using Figtree version 1.4.0 (http://tree.bio.ed.ac.uk/software/figtree).

Results

Wild bird surveillance activities to detect H5N8 virus in the Netherlands: newly acquired and historical data

Surveillance of avian influenza virus in wild birds in the Netherlands has been in place in the country since 1998. After the first HPAI H5N8 detection in poultry on 14 November 2014, activities to detect the virus were increased and a total of 4,018 wild birds of 25 different species belonging to five orders were sampled (Table 3). Of those, 623 birds (16%) were sampled within 10 km of farms previously affected by HPAI H5N8-virus. In the six months before the first detection of HPAI H5N8 in poultry, a total of 2,745 wild birds of nine different

Table 2A

Information on influenza A virus sequences obtained from the Global Initiative on Sharing Avian Influenza Data used for the study

Segment ID	Segment	Country	Collection date	Isolate name	Originating laboratory	Submitting laboratory	Authors
EPI552760	HA	NL	2014-Nov-24	A/eurasian wigeon/Netherlands/emc-1/2014 (H5N8)	Erasmus MC	Erasmus MC	Fouchier et al.
EPI552762	NA	NL	2014-Nov-24	A/eurasian wigeon/Netherlands/emc-1/2014 (H5N8)	Erasmus MC	Erasmus MC	Fouchier et al.
EPI552768	HA	NL	2014-Nov-24	A/eurasian wigeon/Netherlands/emc-2/2014 (H5N8)	Erasmus MC	Erasmus MC	Fouchier et al.
EPI552770	NA	NL	2014-Nov-24	A/eurasian wigeon/Netherlands/emc-2/2014 (H5N8)	Erasmus MC	Erasmus MC	Fouchier et al.
EPI552776	HA	NL	2014-Nov-21	A/chicken/Netherlands/emc-3/2014 (H5N8)	Erasmus MC	Erasmus MC	Fouchier et al.
EPI552778	NA	NL	2014-Nov-21	A/chicken/Netherlands/emc-3/2014 (H5N8)	Erasmus MC	Erasmus MC	Fouchier et al.
EPI547678	HA	NL	2014-Nov-14	A/Chicken/Netherlands/14015526/2014 (H5N8)	Central Veterinary Institute	Central Veterinary Institute	Heutink et al.
EPI547683	NA	NL	2014-Nov-14	A/Chicken/Netherlands/14015526/2014 (H5N8)	Central Veterinary Institute	Central Veterinary Institute	Heutink et al.
EPI548623	HA	NL	2014-Nov-15	A/chicken/Netherlands/14015531/2014 (H5N8)	Central Veterinary Institute	Central Veterinary Institute	Heutink et al.
EPI548626	NA	NL	2014-Nov-15	A/chicken/Netherlands/14015531/2014 (H5N8)	Central Veterinary Institute	Central Veterinary Institute	Heutink et al.
EPI544756	HA	DE	2014-Nov-04	A/turkey/Germany-MV/R2472/2014 (H5N8)	Friedrich-Loeffler-Institut	Friedrich-Loeffler-Institut	NA
EPI544759	NA	DE	2014-Nov-04	A/turkey/Germany-MV/R2472/2014 (H5N8)	Friedrich-Loeffler-Institut	Friedrich-Loeffler-Institut	NA
EPI552746	HA	DE	2014-Nov-04	A/turkey/Germany/R2474-Lo0899/2014 (H5N8)	Friedrich-Loeffler-Institut	Friedrich-Loeffler-Institut	NA
EPI552748	NA	DE	2014-Nov-04	A/turkey/Germany/R2474-Lo0899/2014 (H5N8)	Friedrich-Loeffler-Institut	Friedrich-Loeffler-Institut	NA
EPI547673	HA	UK	2014-Nov-14	A/duck/England/36254/14 (H5N8)	Animal and Plant Health Agency (APHA)	Animal and Plant Health Agency (APHA)	Hanna et al.
EPI547675	NA	UK	2014-Nov-14	A/duck/England/36254/14 (H5N8)	Animal and Plant Health Agency (APHA)	Animal and Plant Health Agency (APHA)	Hanna et al.
EPI553144	HA	IT	2014-Dec-15	A/turkey/Italy/14VIR7898-10/2014 (H5N8)	Istituto Zooprofilattico Sperimentale Delle Venezie	Istituto Zooprofilattico Sperimentale Delle Venezie	Luca et al.
EPI555068	NA	IT	2014-Dec-15	A/turkey/Italy/14VIR7898-10/2014 (H5N8)	Istituto Zooprofilattico Sperimentale Delle Venezie	Istituto Zooprofilattico Sperimentale Delle Venezie	Luca et al.
EPI553349	HA	RU	2014-Sep-25	A/wigeon/Sakha/1/2014 (H5N8)	State Research Center of Virology and Biotechnology Vector	State Research Center of Virology and Biotechnology Vector	Susloparov et al.
EPI553350	NA	RU	2014-Sep-25	A/wigeon/Sakha/1/2014 (H5N8)	State Research Center of Virology and Biotechnology Vector	State Research Center of Virology and Biotechnology Vector	Susloparov et al.
EPI548485	HA	JP	2014-Nov-18	A/duck/Chiba/26-372-48/2014 (H5N8)	National Institute of Animal Health	National Institute of Animal Health	NA
EPI548487	NA	JP	2014-Nov-18	A/duck/Chiba/26-372-48/2014 (H5N8)	National Institute of Animal Health	National Institute of Animal Health	NA
EPI548493	HA	JP	2014-Nov-18	A/duck/Chiba/26-372-61/2014 (H5N8)	National Institute of Animal Health	National Institute of Animal Health	NA
EPI548495	NA	JP	2014-Nov-18	A/duck/Chiba/26-372-61/2014 (H5N8)	National Institute of Animal Health	National Institute of Animal Health	NA
EPI553208	HA	JP	2014-Nov-23	A/crane/Kagoshima/KU1/2014 (H5N8)	Kagoshima University	Kagoshima University	NA
EPI553210	NA	JP	2014-Nov-23	A/crane/Kagoshima/KU1/2014 (H5N8)	Kagoshima University	Kagoshima University	NA
EPI553343	HA	JP	2014-Dec-16	A/chicken/Miyazaki/7/2014 (H5N8)	National Institute of Animal Health	National Institute of Animal Health	NA
EPI553345	NA	JP	2014-Dec-16	A/chicken/Miyazaki/7/2014 (H5N8)	National Institute of Animal Health	National Institute of Animal Health	NA
EPI553362	HA	JP	2014-Dec-01	A/environment/Kagoshima/KU-ngr-H/2014 (H5N8)	Kagoshima University	Kagoshima University	NA
EPI553364	NA	JP	2014-Dec-01	A/environment/Kagoshima/KU-ngr-H/2014 (H5N8)	Kagoshima University	Kagoshima University	NA
KJ476669	HA	CN	2013-Nov-14	A/duck/Zhejiang/W24/2013 (H5N8)	NA	Other database import	Wu et al.

CA: Canada; CN: China; DE: Germany; IT: Italy; JP: Japan; KR: South Korea; NL: Netherlands; RU: Russia; UK: United Kingdom.

Table 2B

Information on influenza A virus sequences obtained from the Global Initiative on Sharing Avian Influenza Data used for the study

Segment ID	Segment	Country	Collection date	Isolate name	Originating laboratory	Submitting laboratory	Authors
KJ476673	NA	CN	2013-Nov-14	A/duck/Zhejiang/W24/2013 (H5N8)	NA	Other database import	Wu et al.
EPI507673	HA	CN	2013-Nov-18	A/mallard_duck/Shanghai/SH-9/2013 (H5N8)	Institute of Military Veterinary, Academy of Military Medical Sciences	Institute of Laboratory Animal Sciences, Chinese Academy	Fan et al.
EPI507675	NA	CN	2013-Nov-18	A/mallard_duck/Shanghai/SH-9/2013 (H5N8)	Institute of Military Veterinary, Academy of Military Medical Sciences	Institute of Laboratory Animal Sciences, Chinese Academy	Fan et al.
JQ973694	HA	CN	2010-Dec-05	A/duck/Jiangsu/k1203/2010 (H5N8)	NA	Other database import	Zhao et al.
JQ973696	NA	CN	2010-Dec-05	A/duck/Jiangsu/k1203/2010 (H5N8)	NA	Other database import	Zhao et al.
KJ413842	HA	KR	2014-Jan-17	A/broiler_duck/Korea/Buan2/2014 (H5N8)	NA	Other database import	Lee et al.
KJ413844	NA	KR	2014-Jan-17	A/broiler_duck/Korea/Buan2/2014 (H5N8)	NA	Other database import	Lee et al.
KJ413850	HA	KR	2014-Jan-17	A/baikal_teal/Korea/Donglim3/2014 (H5N8)	NA	Other database import	Lee et al.
KJ413852	NA	KR	2014-Jan-17	A/baikal_teal/Korea/Donglim3/2014 (H5N8)	NA	Other database import	Lee et al.
KJ746111	HA	KR	2014-Feb-05	A/mallard/Korea/W452/2014 (H5N8)	NA	Other database import	Choi et al.
KJ746113	NA	KR	2014-Feb-05	A/mallard/Korea/W452/2014 (H5N8)	NA	Other database import	Choi et al.

CA: Canada; CN: China; DE: Germany; IT: Italy; JP: Japan; KR: South Korea; NL: Netherlands; RU: Russia; UK: United Kingdom.

species belonging to three orders had also been sampled for HPAI H5 virus detection (Table 3). Results of the surveillance before and after mid-November 2014 are presented, covering a period from 14 May 2014 to 20 February 2015.

Taking into consideration the whole sampling period (May 2014 to February 2015), most avian influenza viruses were detected in ducks (719 of 4,495; 16%), swans (23 of 183; 13%) and gulls (254 of 1,185; 21%). Avian influenza viruses of the H5 subtype were detected in common teal, Eurasian wigeon and mallard, whereby most H5 viruses were LPAI viruses (27 of 29; 93%). On 24 November 2014, HPAI H5N8 virus was isolated from two of 52 faecal samples collected from 150 Eurasian wigeons foraging on grassland between Kamerik and Kockengen (52 °08'35.5"N, 4°55'22.7"E). The birds were located ca 15 to 28 km away from three of five H5N8-virus-infected poultry farms; the remaining two H5N8-virus-infected farms were located ca 80 km away. In the Netherlands, the affected poultry farms were located in wild-bird-rich areas where water is abundant and with low to medium poultry densities. The distribution in time of sampled birds is shown per age, location, sample type and species in Figure 1.

Genetic analyses of H5N8 viruses

Genetic analyses of the HA and NA gene showed that H5N8 viruses from Europe and Russia were genetically most closely related to H5N8 viruses detected in Japan in November and December of 2014 followed by viruses detected in South Korea in 2014 (Figure 2). Also, genetic analyses of the HA gene showed that H5N8 viruses from North America were genetically most closely related to HPAI H5N2 and H5N1 viruses detected in North America followed by H5N8 virus detected in South Korea and Japan. The NA of North American H5N8 viruses was genetically most closely related to H5N8 viruses from South Korea and Japan (i.e. A/crane/Kagoshima/KU1/2014, Figure 2).

Genetic analyses of all gene segments showed that the gene constellation of H5N8 viruses from domestic and wild birds in Europe and from birds in North America was very similar to H5N8 viruses from domestic and wild birds in South Korea and Japan (data not shown). Of these viruses, four of eight gene segments (i.e. basic polymerase 2 (PB2), HA, nucleoprotein (NP) and NA) were derived from viruses similar to A/Duck/Jiangsu/k1203/2010 (H5N8). Of those, PB2 and HA genes were derived from viruses of the HPAI H5 GsGd lineage. The remaining four gene segments (i.e. basic polymerase 1 (PB1), acidic polymerase (PA), matrix protein (MP) and non-structural protein (NS)) were derived from common LPAI viruses [6,7]. Nucleotide sequence identity per segment between European, North American and the genetically closest Asian relatives was high (i.e. 99 to 100% identical). Two genetic lineages (A and B) of H5N8 virus were identified in both domestic and wild birds from South Korea in January 2014, of which lineage A was more frequently detected in both domestic

Table 3A

Wild bird species sampled for highly pathogenic avian influenza (HPAI) H5N8 virus before and after the first detection of HPAI H5N8 virus in poultry on 14 November 2014, the Netherlands, May 2014–February 2015 (n=6,763)

Order	Family	Species[a]	Sampling period							
			14 May–13 November 2014				14 November 2014–20 February 2015			
			No. birds sampled	No. birds AIV positive	No. birds H5 positive	Pathotype	No. birds sampled	No. birds AIV positive	No. birds H5 positive	Pathotype
Anseriformes	Ducks	**Duck species**	**2,071**	**455**	**19**	**LPAI**	**2,424**	**264**	**10**	**2 HPAI; 8 LPAI**
		Common teal (*Anas crecca*)	19	3	1	LPAI	85	19	1	LPAI
		Egyptian goose (*Alopochen aegyptiaca*)	0	0	0	–	40	0	0	–
		Eurasian wigeon (*Anas penelope*)	140	26	8	LPAI	1,185	33	2	HPAI
		Gadwall (*Anas strepera*)	18	2	0	–	127	1	0	–
		Mallard (*Anas platyrhynchos*)	1,876	422	10	LPAI	979	208	7	LPAI
		Northern pintail (*Anas acuta*)	2	0	0	–	0	0	0	–
		Northern shoveler (*Anas clypeata*)	16	2	0	–	4	2	0	–
		Red-breasted merganser (*Mergus serrator*)	0	0	0	–	1	1	0	–
		Tufted duck (*Aythya fuligula*)	0	0	0	–	3	0	0	–
	Geese	**Goose species**	**0**	**0**	**0**	**0**	**340**	**3**	**0**	**–**
		Barnacle goose (*Branta leucopsis*)	0	0	0	–	38	2	0	–
		Brent goose (*Branta bernicla*)	0	0	0	–	39	1	0	–
		Greylag goose (*Anser anser*)	0	0	0	–	17	0	0	–
		White-fronted goose (*Anser albifrons*)	0	0	0	–	246	0	0	–
	Swans	**Swan species**	**0**	**0**	**0**	**–**	**183**	**23**	**0**	**–**
		Bewick's swan (*Cygnus columbianus bewickii*)	0	0	0	–	72	4	0	–
		Mute swan (*Cygnus olor*)	0	0	0	–	109	18	0	–
		Whooper swan (*Cygnus cygnus*)	0	0	0	–	2	1	0	–
Charadriiformes	Gulls	**Gull species**	**434**	**219**	**0**	**–**	**751**	**35**	**0**	**–**
		Black-headed gull (*Chroicocephalus ridibundus*)	434	219	0	–	611	22	0	–
		Caspian gull (*Larus cachinnans*)	0	0	0	–	3	0	0	–
		Common gull (*Larus canus*)	0	0	0	–	35	2	0	–
		Great black-backed gull (*Larus marinus*)	0	0	0	–	10	0	0	–
		Herring gull (*Larus argentatus*)	0	0	0	–	85	10	0	–
		Lesser black-backed gull (*Larus fuscus*)	0	0	0	–	7	1	0	–
	Terns	**Tern species**	**240**	**1**	**0**	**–**	**0**	**0**	**0**	**–**
		Black tern (*Chlidonias niger*)	176	1	0	–	0	0	0	–
		Common tern (*Sterna hirundo*)	64	0	0	–	0	0	0	–

AIV: avian influenza virus; HPAI: highly pathogenic avian influenza; LPAI: low pathogenic avian influenza; No: number.

[a] Unless otherwise specified.

Table 3B

Wild bird species sampled for highly pathogenic avian influenza (HPAI) H5N8 virus before and after the first detection of HPAI H5N8 virus in poultry on 14 November 2014, the Netherlands, May 2014–February 2015 (n=6,763)

Order	Family	Species[a]	Sampling period							
			14 May–13 November 2014				14 November 2014–20 February 2015			
			No. birds sampled	No. birds AIV positive	No. birds H5 positive	Pathotype	No. birds sampled	No. birds AIV positive	No. birds H5 positive	Pathotype
Gruiformes	Coots	**Coot species**	**0**	**0**	**0**	–	**289**	**9**	**0**	–
		Common coot (*Fulica atra*)	0	0	0	–	289	9	0	–
	Rails	**Rail species**	**0**	**0**	**0**	–	**20**	**0**	**0**	–
		Common moorhen (*Gallinula chloropus*)	0	0	0	–	20	0	0	–
Passeriformes	Crows	**Crow species**	**0**	**0**	**0**	–	**1**	**0**	**0**	–
		Carrion crow (*Corvus corone*)	0	0	0	–	1	0	0	–
Strigiformes	Owls	**Owl species**	**0**	**0**	**0**	–	**1**	**0**	**0**	–
		Barn owl (*Tyto alba*)	0	0	0	–	1	0	0	–
Total	–	–	**2,745**	**675**	**19**	–	**4,018**	**334**	**10**	–

AIV: avian influenza virus; HPAI: highly pathogenic avian influenza; LPAI: low pathogenic avian influenza; No: number.

[a] Unless otherwise specified.

and wild birds [7,8,16]. H5N8 viruses detected in Europe (Germany, Italy, the Netherlands, and the UK), Russia and in North America belonged to lineage A based on analyses of the HA gene [8]. The close genetic relationship between European, Asian and North American isolates suggested that these H5N8 viruses have a common origin.

Distribution and migratory flyways of H5N8-virus-positive bird species

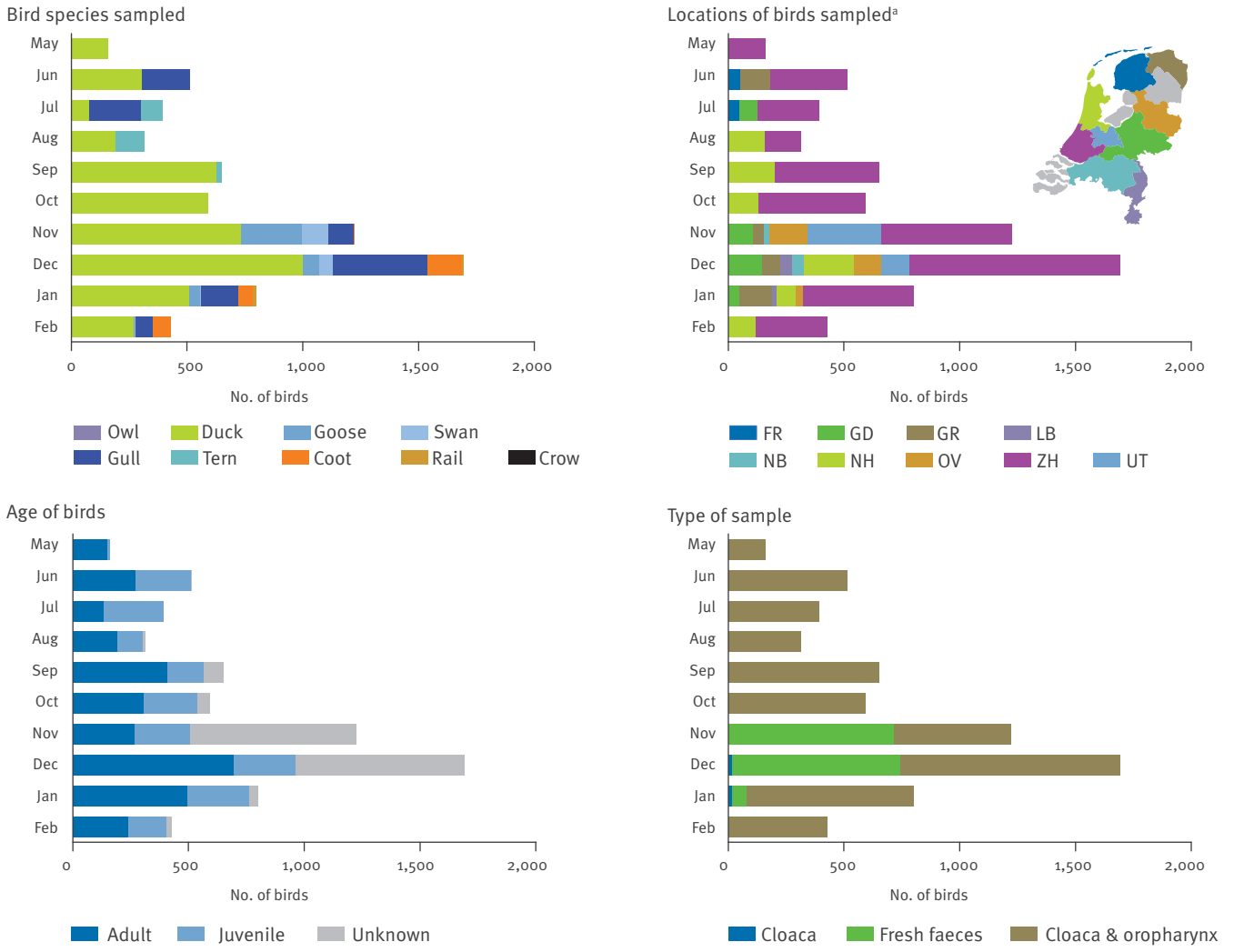
Migrating birds from which H5N8 viruses have been isolated (Table 1) and that have circumpolar breeding grounds (e.g. northern pintail, *Anas acuta*) or that cover multiple major migratory flyways (e.g. Eurasian wigeon) are of specific interest with respect to global H5N8 virus epidemiology (Figure 3). Most of those species can be divided into distinct populations based on their geographically separate wintering areas. However, less is known about the degree of mixing among these populations in their breeding areas in Russia, and to which degree birds are loyal to their wintering areas.

Ring recoveries suggest that some waterfowl species (including ducks and geese) with populations wintering in East Asia and populations wintering in western Europe may have overlapping breeding grounds. For instance, ring recoveries of Eurasian wigeon and northern pintail ringed in Japan indicate that they migrate mostly north to north-east to the Russian Far East during spring migration, but a minority strays more north-west, some as far as the Western Siberian Lowlands [17] (Figure 3A and 3B). Here, ring recoveries indicate that some conspecifics originating from western Europe also may be found [18] (Figure 3A and 3B). Hence, although the probability of an actual meeting between east and west seems low, ring recoveries suggest it is not impossible. Furthermore, ring recoveries of Eurasian wigeon and northern pintail indicated a direct migratory connection between north Russia and north India (Figure 3A and 3B). Baikal teal and spot-billed duck, from which H5N8 viruses have also been isolated, have more restricted ranges, but could be involved in transport of virus from wintering grounds to breeding grounds in north-eastern Russia (Figure 3C and 3D). Mallards and teals have extensive ranges, and potentially can also be involved in transport of virus, but ring-recovery data from Russia were not available (Figure 3E and 3F).

Ring recoveries and satellite tracking have shown various waterfowl species from East Asia to be in indirect and sometimes even direct migratory connection with North America. Satellite tracking and colour banding of various waterfowl species, including emperor goose (*Chen canagica*) [19], black brant (*Branta bernicla nigricans*) [20], lesser snow goose (*Chen caerulescens caerulescens*) [21] and northern pintail have shown them to cross the Bering Strait [22]. Ring recoveries of northern pintail in particular show that the connection between East Asia and North America is quite strong, albeit most likely still indirect with contact zones in the

Figure 1

Monthly sampling of wild birds for H5N8 virus detection, by species, location, age, and sample type, the Netherlands, 14 May 2014–20 February 2015 (n=6,763)



FR: Friesland; GD: Gelderland; GR: Groningen; LB: Limburg; NB: Noord-Brabant; NH: Noord-Holland; OV: Overijssel; UT: Utrecht; ZH: Zuid-Holland.

[a] Locations were categorised according to Dutch provinces.

Russian Far East and Wrangel Island [17,23]. The same is true for some other species than waterfowl, which have not been identified as H5N8 virus hosts, but may play a role in the epidemiology of influenza, such as waders [24,25].

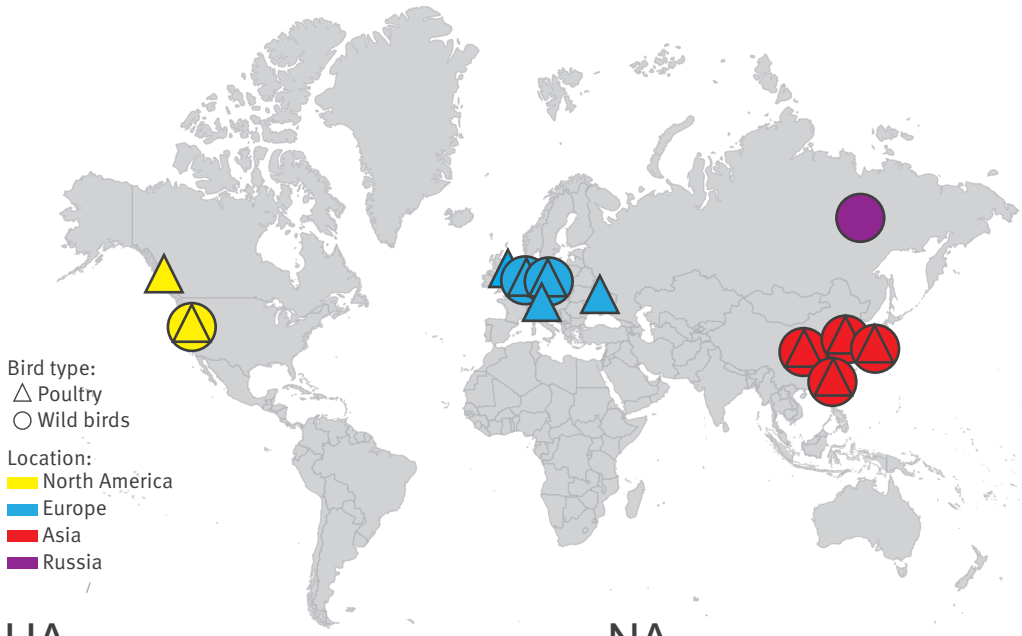
Discussion

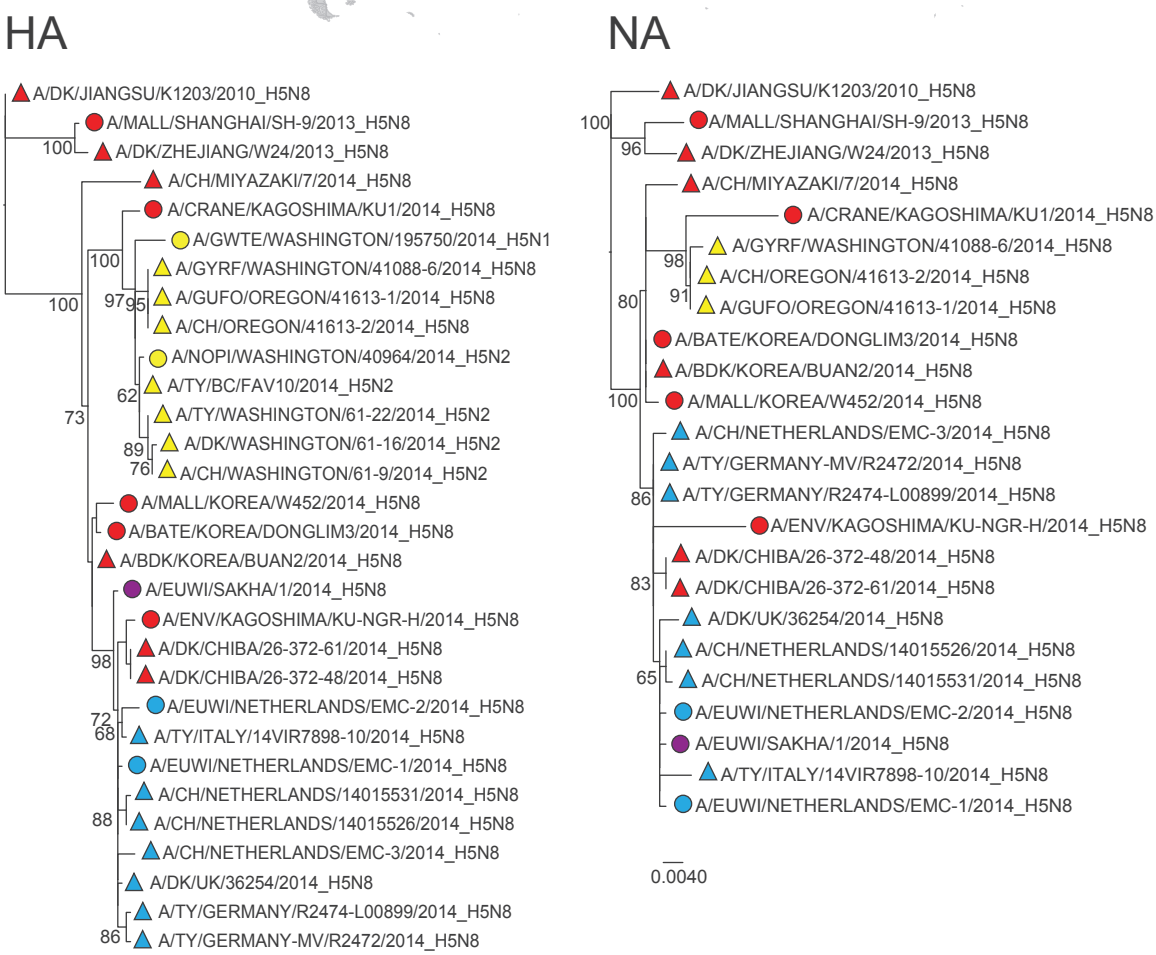
The detection of the newly emerging HPAI H5N8 virus in at least 17 migratory bird species in Asia, Europe and North America, emphasises the need to study the role of migratory birds in the epidemiology of these H5N8 viruses. After the first detection of H5N8 virus in poultry in the Netherlands, wild bird sampling activities were intensified and HPAI H5N8 virus was detected in samples from two of 4,018 birds sampled within a three months period. The virus was isolated from Eurasian wigeons exclusively, whereas other bird species like mallards, white-fronted geese (*Anser albifrons*), black-headed gulls (*Chroicocephalus ridibundus*) and common coots (*Fulica atra*) also had been sampled intensively. The Eurasian wigeon is a long-distance migrant in which species H5N8-virus-specific antibodies had been detected in South Korea in 2014 [8]. As HPAI H5N8 virus, like other avian influenza viruses, causes an infection of short duration in birds [26], the chance of detection is low and large sample sizes are needed to determine its presence in the population. The chance of detection of H5N8-virus-specific antibodies in wild bird sera is much higher, and serology can be used as a tool to target surveillance and determine past exposure to H5N8 virus, as H5 viruses of the HPAI GsGd lineage differ antigenically from common LPAI H5 viruses [27].

The H5N8 viruses isolated from wild birds in the Netherlands were genetically closely related to and had

Figure 2

Phylogenetic analysis of haemagglutinin (HA) and neuraminidase (NA) genes from highly pathogenic avian influenza (HPAI) H5N8 viruses recovered in China in 2010–2013 together with respective HA and NA genes from HPAI H5N8 and other HPAI viruses belonging to the H5 clade 2.3.4.4, detected in poultry and wild birds in Asia, Europe, Russia and North America in 2014



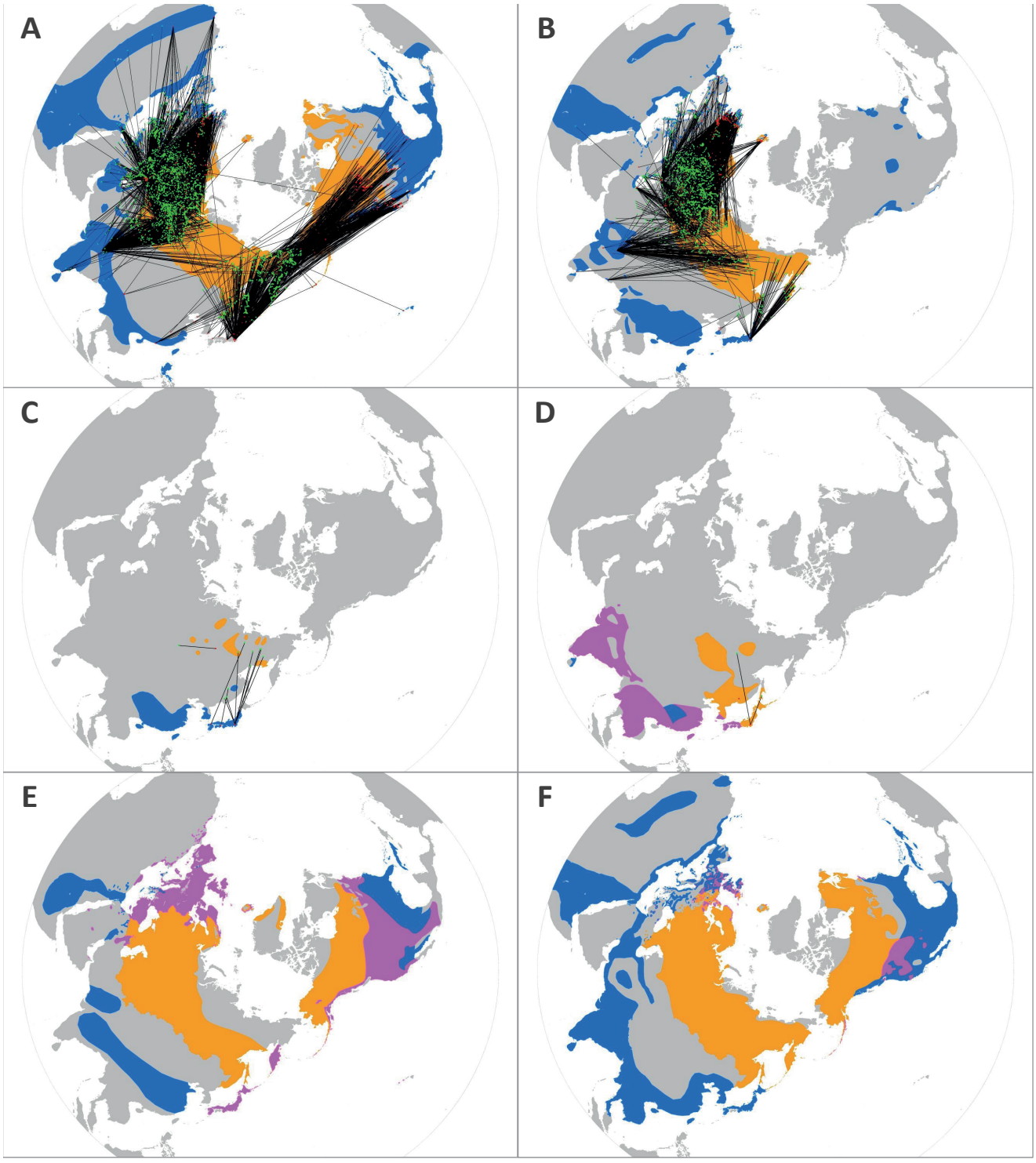


BATE: Baikal teal; BDK: broiler duck; CH: chicken; DK: duck; ENV: environment; EUWI: Eurasian wigeon; GUFO: guinea fowl; GWTE: green-winged teal; GYRF=gyrfalcon; HPAI: highly pathogenic avian influenza; MALL: mallard; NOPI: northern pintail; TY: turkey.

Maximum likelihood trees were based on the haemagglutinin gene (HA; 1,545 nucleotides) and neuraminidase gene (NA; 1,377 nucleotides). Bootstrap values are shown if >60%.

Figure 3

Breeding and wintering range and ring recoveries from 1940–2010[a] of wild duck species from which highly pathogenic avian influenza (HPAI) H5N8 viruses have been isolated



Top: wide range, long-distance migratory species northern pintail (*Anas acuta*) (A) and Eurasian wigeon (*Anas penelope*) (B); **Middle:** restricted range, short-distance migratory or resident species Baikal teal (*Anas formosa*) (C) and spot-billed duck (*Anas poecilorhyncha*) (D); **Bottom:** wide-range, long-distance migratory or resident species mallard (*Anas platyrhynchos*) (E), and teal (*Anas crecca / carolinensis*) (F).

Orange: summer (breeding) range, blue: wintering range, purple: all-year (resident) range. Lines in maps A, B, C and D connect ringing locations (red dots) and recovery locations (green dots).

[a] The majority of ring recoveries were conducted during 1960–1990.

Data source: Lines in maps A, B, C and D are based on ring-recovery data from the database of the Russian ringing scheme and are reprinted with permission from the Waterfowl Migration Atlas from the Bird Ringing Centre of Russia database and OMPO. Breeding and wintering ranges are reproduced from [30]. Breeding ranges of Baikal teal and spot-billed duck have been updated from [31].

the same gene constellation as H5N8 viruses detected elsewhere in Europe, in Asia and in North America, suggesting a common origin. In wild and domestic birds in North America, HPAI reassortant viruses of the subtypes H5N2 and H5N1 have been detected. These viruses contain genes originating from both HPAI H5N8 and LPAI viruses. Reassortant viruses of the subtypes H5N2 and H5N3 have been detected in domestic birds in Taiwan. In Europe, no reassortant viruses with HPAI H5N8 genes have been detected so far. Monitoring wild birds to detect H5N8 virus and derived reassortants is warranted given their potential to cause severe disease and mortality in poultry and some species of wild birds (e.g. eagles and hawks).

Ring recoveries of migratory duck species from which H5N8 viruses have been isolated provide evidence for indirect migratory connections between East Asia and western Europe and between East Asia and North America. In addition, ring recoveries of northern pintails and Eurasian wigeons demonstrated a direct migratory connection between north India and north Russia and between north India and Europe. If these species are involved in the global spread of H5N8 virus, we hypothesise that H5N8 viruses may also spread to north India as occurred previously with HPAI H5N1 virus of clade 2.2 [28]. During large-scale surveillance activities in north India from 2009 to 2011, no avian influenza viruses had been detected in 3,522 wild bird samples [29]. To which extent migrating bird populations of different flyways come in direct or indirect contact (e.g. using the same water source during stop over) with each other needs further study. To understand the role of wild birds in the epidemiology of H5N8 virus, sampling activities need to aim at detection of both the virus and specific antibodies with an emphasis on migrating birds in north-east Europe, Russia, and north China.

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Conflict of interest

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Authors' contributions

JH: compiling the data, drafting the manuscript; HJ: initiation of study, providing data, critical review the manuscript; BN: providing data, drafting the manuscript, critical review the manuscript; RS: initiation of study, providing data, critical review the manuscript; SK: providing data Russian ring recoveries; PV: collecting field data, working on figure; OV: analysing samples; FM: collecting field data; TK: collecting field data, critical review the manuscript; RF: initiation of study, providing data, critical review the manuscript.

References

1. Webster RG, Bean WJ, Gorman OT, Chambers TM, Kawaoka Y. Evolution and ecology of influenza A viruses. Microbiol Rev. 1992;56(1):152-79. PMID:1579108
2. Olsen B, Munster VJ, Wallensten A, Waldenström J, Osterhaus AD, Fouchier RA. Global patterns of influenza a virus in wild birds. Science. 2006;312(5772):384-8. http://dx.doi.org/10.1126/science.1122438 PMID:16627734
3. Koehler AV, Pearce JM, Flint PL, Franson JC, Ip HS. Genetic evidence of intercontinental movement of avian influenza in a migratory bird: the northern pintail (Anas acuta). Mol Ecol. 2008;17(21):4754-62. http://dx.doi.org/10.1111/j.1365-294X.2008.03953.x PMID:19140989
4. Dusek RJ, Hallgrimsson GT, Ip HS, Jónsson JE, Sreevatsan S, Nashold SW, et al. North Atlantic migratory bird flyways provide routes for intercontinental movement of avian influenza viruses. PLoS ONE. 2014;9(3):e92075. http://dx.doi.org/10.1371/journal.pone.0092075 PMID:24647410
5. Hill NJ, Takekawa JY, Ackerman JT, Hobson KA, Herring G, Cardona CJ, et al. Migration strategy affects avian influenza dynamics in mallards (Anas platyrhynchos). Mol Ecol. 2012;21(24):5986-99. http://dx.doi.org/10.1111/j.1365-294X.2012.05735.x PMID:22971007
6. Zhao K, Gu M, Zhong L, Duan Z, Zhang Y, Zhu Y, et al. Characterization of three H5N5 and one H5N8 highly pathogenic avian influenza viruses in China. Vet Microbiol. 2013;163(3-4):351-7. http://dx.doi.org/10.1016/j.vetmic.2012.12.025 PMID:23375651
7. Kim Y, Pascua PNQ, Kwon HI, Lim GJ, Kim EH, Yoon SW, et al. Pathobiological features of a novel, highly pathogenic avian influenza A(H5N8) virus. Emerging Microbes and Infections. 2014.
8. Jeong J, Kang HM, Lee EK, Song BM, Kwon YK, Kim HR, et al. Highly pathogenic avian influenza virus (H5N8) in domestic poultry and its relationship with migratory birds in South Korea during 2014. Vet Microbiol. 2014;173(3-4):249-57. http://dx.doi.org/10.1016/j.vetmic.2014.08.002 PMID:25192767
9. World organization for animal health (OIE). Update on highly pathogenic avian influenza in animals (type h5 and h7). Paris: OIE; 2014. Accessed [06 Mar 2015]. Available from: http://www.oie.int/animal-health-in-the-world/update-on-avian-influenza/2014/
10. Adlhoch C, Gossner C, Koch G, Brown I, Bouwstra R, Verdonck F, et al. Comparing introduction to Europe of highly pathogenic avian influenza viruses A(H5N8) in 2014 and A(H5N1) in 2005. Euro Surveill. 2014;19(50):20996. http://dx.doi.org/10.2807/1560-7917.ES2014.19.50.20996 PMID:25597538
11. ProMED-mail. Avian influenza. Archive number 20150202. 02 Feb 2015. Available from: http://www.promedmail.org/‹/eref›
12. Shepard SS, Davis CT, Bahl J, Rivailler P, York IA, Donis RO. LABEL: fast and accurate lineage assignment with assessment of H5N1 and H9N2 influenza A hemagglutinins. PLoS ONE. 2014;9(1):e86921. http://dx.doi.org/10.1371/journal.pone.0086921 PMID:24466291
13. Munster VJ, Baas C, Lexmond P, Bestebroer TM, Guldemeester J, Beyer WE, et al. Practical considerations for high-throughput influenza A virus surveillance studies of wild birds by use of molecular diagnostic tests. J Clin Microbiol. 2009;47(3):666-73. http://dx.doi.org/10.1128/JCM.01625-08 PMID:19109483
14. Hoffmann E, Stech J, Guan Y, Webster RG, Perez DR. Universal primer set for the full-length amplification of all influenza A viruses. Arch Virol. 2001;146(12):2275-89. http://dx.doi.org/10.1007/s007050170002 PMID:11811679

15. Posada D. jModelTest: phylogenetic model averaging. Mol Biol Evol. 2008;25(7):1253-6. http://dx.doi.org/10.1093/molbev/msn083 PMID:18397919
16. Lee YJ, Kang HM, Lee EK, Song BM, Jeong J, Kwon YK, et al. Novel reassortant influenza A(H5N8) viruses, South Korea, 2014. Emerg Infect Dis. 2014;20(6):1087-9. http://dx.doi.org/10.3201/eid2006.140233 PMID:24856098
17. Dobrynina DV, Kharitonov SP. The Russian waterbird migration atlas: temporal variation in migration routes. In: Boere GC, Galbraith CA, Stroud DA, editors. Waterbirds around the world. Edinbrugh: The Stationary Office; 2006. p. 582-9
18. Atkinson PW, Robinson RA, Clark JA, Miyar T, Downie IS, du Feu CR, et al. Migratory movements of waterfowl: a web-based mapping tool. EURING report to the EU Commission. BTO, 2007.
19. Hupp JW, Schmutz JA, Ely CR, Syroechkovskiy JEE Jr, Kondratyev AV, Eldridge WD, et al. Moult migration of emperor geese Chen canagica between Alaska and Russia. J Avian Biol. 2007;38(4):462-70. http://dx.doi.org/10.1111/j.0908-8857.2007.03969.x
20. Derksen DV, Bollinger KS, Ward DH, Sedinger JS, Miyabayashi Y. Black Brant from Alaska staging and wintering in Japan. Condor. 1996;98(3):653-7. http://dx.doi.org/10.2307/1369583
21. Ely CR, Takekawa JY, Wege ML. Distribution, abundance and age ratios of Wrangel Island Lesser Snow Geese Anser caerulescens during autumn migration on the Yukon-Kuskokwim Delta, Alaska. Wildfowl. 1993;44:24-32.
22. Miller MR, Takekawa JY, Fleskes JP, Orthmeyer DL, Casazza ML, Perry WM. Spring migration of Northern Pintails from California's Central Valley wintering area tracked with satellite telemetry: routes, timing, and destinations. Can J Zool. 2005;83(10):1314-32. http://dx.doi.org/10.1139/z05-125
23. Flint PL, Ozaki K, Pearce JM, Guzzetti B, Higuchi H, Fleskes JP, et al. Breeding-season sympatry facilitates genetic exchange among allopatric wintering populations of northern pintails in Japan and California. Condor. 2009;111(4):591-8. http://dx.doi.org/10.1525/cond.2009.090100
24. Van Gils J, Wiersma P. Baird's Sandpiper (Calidris bairdii). In: del Hoyo J, Elliott A, Sargatal J, Christie DA, de Juana E, editors. Handbook of the Birds of the World Alive. Barcelona: Lynx Edicions; 1996.
25. Van Gils J, Wiersma P, Bonan A. Buff-breasted Sandpiper (Calidris subruficollis). In: del Hoyo J, Elliott A, Sargatal J, Christie DA, de Juana E, editors. Handbook of the Birds of the World Alive. Barcelona: Lynx Edicions; 2013.
26. Kaewcharoen J, van Riel D, van Amerongen G, Bestebroer T, Beyer WE, van Lavieren R, et al. Wild ducks as long-distance vectors of highly pathogenic avian influenza virus (H5N1). Emerg Infect Dis. 2008;14(4):600-7. doi: 10.3201/eid1404.071016.
27. Gilbert M, Koel BF, Bestebroer TM, Lewis NS, Smith DJ, Fouchier RA. Serological Evidence for Non-Lethal Exposures of Mongolian Wild Birds to Highly Pathogenic Avian Influenza H5N1 Virus. PLoS ONE. 2014;9(12):e113569. http://dx.doi.org/10.1371/journal.pone.0113569 PMID:25502318
28. Pandit PS, Bunn DA, Pande SA, Aly SS. Modeling highly pathogenic avian influenza transmission in wild birds and poultry in West Bengal, India. Sci Rep. 2013;3:2175. http://dx.doi.org/10.1038/srep02175 PMID:23846233
29. Pawar SD, Kale SD, Rawankar AS, Koratkar SS, Raut CG, Pande SA, et al. Avian influenza surveillance reveals presence of low pathogenic avian influenza viruses in poultry during 2009-2011 in the West Bengal State, India. Virol J. 2012;9:151. http://dx.doi.org/10.1186/1743-422X-9-151 PMID:22867041
30. BirdLife International. Nature Serve. Bird species distribution maps of the world. Cambridge, UK/Arlington, USA: BirdLife International; 2014.
31. Syroechkovsky EE. Field Guide for Anseriformes of Russia. Moscow: Goose, Swan and Duck Study Group of the Northern Eurasia; 2011.

Laboratory support during and after the Ebola virus endgame: towards a sustained laboratory infrastructure

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The Ebola virus epidemic in West Africa is on the brink of entering a second phase in which the (inter)national efforts to slow down virus transmission will be engaged to end the epidemic. The response community must consider the longevity of their current laboratory support, as it is essential that diagnostic capacity in the affected countries be supported beyond the end of the epidemic. The emergency laboratory response should be used to support building structural diagnostic and outbreak surveillance capacity.

As of 18 March 2015, the Ebola epidemic in West Africa has resulted in more than 10,194 deaths and more than 24,701 cases, however the most recent situation reports from the World Health Organization (WHO) [1] suggest that the weekly number of new cases in the first months of 2015 has been the lowest since June 2014. All indications therefore suggest that the epidemic has entered a second phase, making the end of the epidemic a real possibility. Importantly however, the feasibility of eradication of Ebola virus disease (EVD) in the human population in West Africa remains completely dependent on the sustained commitment of everyone involved in the response until all cases have been identified and transmission chains have stopped. This is illustrated by the slight increase in cases in Sierra Leone and Guinea reported in the first weeks of February [1].

One of the pillars of the response to this outbreak has been the provision of laboratory support that has facilitated the rapid testing of suspected cases [2,3]. The lack of laboratory capacity during the early stages of the epidemic will undoubtedly have been a contributing factor to the rapid expansion of the epidemic. With the aid of the international community, in-country laboratory capacity is no longer a significant limiting factor with respect to testing of patient samples and the turnaround time for samples in most areas is less than 24 hours, rather than several days as during the early days of the epidemic [4]. Given that the end of the epidemic is now a real possibility, we feel it is essential to begin active discussions with national agencies, the WHO and potential sponsors, regarding a 'post-Ebola legacy' of laboratory support. Several countries have been involved in the deployment of in total 27 laboratories to provide rapid in-country testing for Ebola virus (EBOV) [1,4]. The laboratories deployed in the region are equipped to do molecular diagnostic testing, which has become the standard of care in clinical microbiology in other parts of the world. Therefore, the basic laboratory set-up currently provided in the EBOV response could be in the future extended to develop essential clinical and public health microbiology services also for other diseases.

With the decreasing number of patients in the EVD holding and treatment centres, the number of laboratory requests are falling rapidly, to the point that the conditions for laboratory testing need to be redefined. With the transition to the second phase of the EVD outbreak, a transition from acute testing for clinical triage to surveillance testing is needed, in which the threshold for the case definition should be lower, to demonstrate the absence of EBOV in the local population. In addition, it is widely accepted that the epidemic has had an impact way beyond the individuals infected with EBOV, the consequences of which will only become apparent long after the epidemic is over [5-7]. This impact is evident at many levels, including healthcare services and laboratory support for the detection of other circulating pathogens. Minor modifications of the procedures currently in use in the affected countries would make it possible to establish PCR-based diagnostic tests for a selected number of endemically circulating pathogens and could, as we enter the second phase of the epidemic, provide interim laboratory support to reduce the overall impact of the epidemic on public health by timely detection of endemic diseases enabling treatment and guiding control measures. If planned strategically, this could be a first step on the road to a sustained local laboratory infrastructure that will provide access to up-to-date facilities. Local laboratory experts took care of such activities with very limited resources before the start of the EVD outbreak; in the transition phase, it is therefore crucial to engage with these partners in order to discuss the way forward.

The international community must consider the longevity of their support, as it is essential that diagnostic capacity in the affected countries is supported beyond the end of the EVD epidemic. So far, the laboratories have largely been operated by teams of volunteers, flown in on a rotation of four to six weeks from research and public health laboratories around the world. With the outbreak ending, some laboratories will be closed in the coming months. We foresee an all too familiar pattern: equipment is left unused after an outbreak or even removed from the country because local staff lack the necessary training and affordable reagents and equipment are not available [8-10]. By building on the expertise in country and using the infrastructure currently present, the network of diagnostic and public health laboratories could be strengthened, strategically placed to facilitate reliable logistics as well as population coverage. Such a network should be capable of both routine and response modes and could be supported through telemedicine programmes, training programmes outside and within the country and international reference laboratories to provide improved access to additional laboratory services.

Rather than copying the workflows used in the United States and Europe, it is essential that fit-for-purpose diagnostic algorithms are developed, such as a combined laboratory package to diagnose sickle cell anaemia, infection with human immunodeficiency virus and hepatitis B virus, coupled with essential haematology and clinical chemistry as well as the ability to rule out EVD and Lassa fever in maternity clinics. A large advantage of the molecular era is that the division between clinical and public health work becomes blurred, creating an opportunity to kill two birds with one stone. It is time to step away from the 'one pathogen-one laboratory network' approach, which raises costs tremendously but is the standard set by international reference centres [11-15]. This is by no means an easy task, as it requires collaborative and out-of-the-box thinking. It also requires novel research to provide low-cost solutions and alternatives for the expensive assays that are currently available. The most commonly used EBOV laboratory test costs ca EUR 45 per patient (for diagnosis and pre-discharge testing). We invite suppliers and manufacturers of key laboratory equipment and reagents to suggest more affordable solutions that take into consideration the limited local cold chain capacity and to provide adequate regional technical support. Innovative solutions such as open source laboratory equipment may be one possibility to make equipment accessible.

The current epidemic and previous serological surveys [16] indicate that EBOV and other highly virulent pathogens are circulating in West Africa and will continue to do so beyond the end of the current epidemic. The reality is that EVD is likely to remain a problem in West Africa and this will not be the last epidemic we see in this area. The establishment of an integrated network of support laboratories would strengthen epidemic preparedness and response capabilities for the inevitable introductions of highly pathogenic zoonotic pathogens in the local human population.

Conflict of interest

None declared.

Authors' contributions

All authors: design and writing of manuscript.

References

1. World Health Organization (WHO). Ebola data and statistics. Situation summary. Data published on 18 March 2015. Geneva: WHO; 19 Mar 2015. Available from: http://apps.who.int/ebola/current-situation/ebola-situation-report-18-march-2015
2. Chowell D, Castillo-Chavez C, Krishna S, Qiu X, Anderson KS. Modelling the effect of early detection of Ebola. Lancet Infect Dis. 2015;15(2):148-9. http://dx.doi.org/10.1016/S1473-3099(14)71084-9 PMID:25749063
3. Dhillon RS, Srikrishna D, Garry RF, Chowell G. Ebola control: rapid diagnostic testing. Lancet Infect Dis. 2015;15(2):147-8. http://dx.doi.org/10.1016/S1473-3099(14)71035-7‹/jrn›
4. World Health Organization (WHO). Ebola data and statistics. Situation summary. Data published on 21 January 2015. Geneva: WHO; 19 Mar 2015. Available from: http://apps.who.int/ebola/en/status-outbreak/situation-reports/ebola-situation-report-21-january-2015
5. Check Hayden E. Ebola outbreak shuts down malaria-control efforts. Nature. 2014;514(7520):15-6. http://dx.doi.org/10.1038/514015a PMID:25279895
6. Edelstein M, Angelides P, Heymann DL. Ebola: the challenging road to recovery. Lancet. 2015 Feb 9. pii: S0140-6736(15)60203-3. [Epub ahead of print]. http://dx.doi.org/10.1016/S0140-6736(15)60203-3
7. Takahashi S, Metcalf CJ, Ferrari MJ, Moss WJ, Truelove SA, Tatem AJ, et al. Reduced vaccination and the risk of measles and other childhood infections post-Ebola. Science. 2015;347(6227):1240-2. http://dx.doi.org/10.1126/science.aaa3438 PMID:25766232
8. Petti CA, Polage CR, Quinn TC, Ronald AR, Sande MA. Laboratory medicine in Africa: a barrier to effective health care. Clin Infect Dis. 2006;42(3):377-82. http://dx.doi.org/10.1086/499363 PMID:16392084
9. Bates I, Maitland K. Are laboratory services coming of age in sub-Saharan Africa? Clin Infect Dis. 2006;42(3):383-4. http://dx.doi.org/10.1086/499368 PMID:16392085
10. Ndihokubwayo JB, Kasolo FN, Yahaya AA, Mwenda J. Strengthening Public Health Laboratories in the WHO African Region: A Critical Need for Disease Control. Report World Health Organization Regional Office for Africa.; 23 March 2015. Available from: https://www.aho.afro.who.int/sites/default/files/ahm/reports/20/ahm12pages47to52.pdf
11. World Health Organization (WHO). Rotavirus Laboratory network. Geneva: WHO; 2015. . [Accessed: 23 Mar 2015] Available from: http://www.who.int/immunization/monitoring_surveillance/burden/laboratory/Rotavirus/en/
12. World Health Organization (WHO). WHO HPV Laboratory Network. Geneva: WHO. [Accessed: 23 Mar 2015]. Available from: http://www.who.int/biologicals/vaccines/hpv/en/
13. World Health Organization (WHO). Laboratory network. Geneva: WHO. [Accessed: 23 Mar 2015]. Available from: http://www.who.int/hiv/topics/drugresistance/laboratory/en/
14. World Health Organization (WHO). The Global Polio Laboratory Network (GPLN) Geneva: WHO. [Accessed: 23 Mar 2015]. Available from: http://www.polioeradication.org/Dataandmonitoring/Surveillance/GlobalPolioLaboratoryNetwork.aspx
15. World Health Organization (WHO). Measles and rubella laboratory network. Geneva: WHO. [Accessed: 23 Mar 2015]. Available from: http://www.wpro.who.int/immunization/laboratory/measles_rubella/en/
16. Schoepp RJ, Rossi CA, Khan SH, Goba A, Fair JN. Undiagnosed acute viral febrile illnesses, Sierra Leone. Emerg Infect Dis. 2014;20(7):1176-82. http://dx.doi.org/10.3201/eid2007.131265 PMID:24959946

Surveillance and Outbreak Response Management System (SORMAS) to support the control of the Ebola virus disease outbreak in West Africa

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In the context of controlling the current outbreak of Ebola virus disease (EVD), the World Health Organization claimed that 'critical determinant of epidemic size appears to be the speed of implementation of rigorous control measures', i.e. immediate follow-up of contact persons during 21 days after exposure, isolation and treatment of cases, decontamination, and safe burials. We developed the Surveillance and Outbreak Response Management System (SORMAS) to improve efficiency and timeliness of these measures. We used the Design Thinking methodology to systematically analyse experiences from field workers and the Ebola Emergency Operations Centre (EOC) after successful control of the EVD outbreak in Nigeria. We developed a process model with seven personas representing the procedures of EVD outbreak control. The SORMAS system architecture combines latest In-Memory Database (IMDB) technology via SAP HANA (in-memory, relational database management system), enabling interactive data analyses, and established SAP cloud tools, such as SAP Afaria (a mobile device management software). The user interface consists of specific front-ends for smartphones and tablet devices, which are independent from physical configurations. SORMAS allows real-time, bidirectional information exchange between field workers and the EOC, ensures supervision of contact follow-up, automated status reports, and GPS tracking. SORMAS may become a platform for outbreak management and improved routine surveillance of any infectious disease. Furthermore, the SORMAS process model may serve as framework for EVD outbreak modelling.

Introduction

The spread of the current outbreak of Ebola virus disease (EVD) in West Africa has slowed down in most affected areas, but daily case numbers are still high as of 11 March 2015 [1]. Even enhanced awareness and increasing international support did not prevent contacts of known cases from travelling to unaffected areas causing further spread. As a consequence, although the rise of new EVD cases slowed down, the number of foci has increased, causing new operational challenges for health officials and field epidemiologists [1]. The interruption of person-to-person transmission includes proactive case finding i.e., supervision of timely isolation, diagnosis and treatment, as well as identification and prospective monitoring of contact persons [2]. High population mobility, stigmatisation of persons considered infectious and fears of persons who had been in contact with them, require a large number of staff to reach out and maintain contact to patients and contact persons. At the same time, a large amount of rumours entering the public health service through a variety of channels and formats need to be validated. Existing surveillance systems are usually not built to address such challenges. In addition, uncertainty and delay of surveillance data due to different information sources and infrastructural hurdles such as irregular availability of communication or transportation services in the affected countries have led to limited reliability of epidemiological analyses. This was exemplified by the fact that the World Health Organization (WHO) needed to retrospectively correct the official outbreak reports in week 45/2014, resulting in 299 fewer cases than previously reported [3].

Table 1

User and system requirements for management systems to support the Ebola virus disease outbreak response

Priority system requirements
Authorised persons should be able to immediately report on suspected EVD cases.
Reporting of case status including results from laboratory tests should be supported.
Monitoring of contacts and management of contact tracing activities should be supported.
Monitoring of infection prevention measures (e.g. decontamination, safe burials) should be enabled.
User requirements
Information on suspected EVD cases needs to reach simultaneously the health authorities in charge at district, state and national level and the Ebola Outbreak Emergency Operations Centre.
Changes in case status and changes from contact status to a suspected case need to be administered without generating new datasets.
Incoming information on suspected cases including unstructured information and unverified rumours and the respective decisions of further follow up need to be documented.
Status reports on cases, contacts and their respective classifications and follow up status need to be generated by the system automatically.
Reports should be compatible with reporting requirements of the International Health Regulations of the WHO [28], but should also allow for higher resolution epidemiological analyses via mapping, histograms etc. as exemplified by the current WHO and national situation reports on the EVD outbreak.
Variables included in existing standard forms on haemorrhagic fever as well as in the module for viral haemorrhagic fevers of EpiInfo [29] need to be reflected in the system.
The system needs to support supervisors in assuring that all contact persons are identified, documented and that their respective fever monitoring is executed without interruption.
The system needs to support supervisors in assuring that infection control measures and social mobilisation in affected districts have been carried out.
Technical requirements
Data exchange with existing surveillance systems is necessary, at least through a standardised output format to enable integration with the Integrated Disease Surveillance and Response System.
The system should be available as mobile application without a need for special configuration or installation.
Desktop applications for supervisors are required.
The system should be runnable on Android mobile devices (Jelly Bean Android OS, large touch screen interfaces or QWERTY keys).
Efficient network providers for mobile devices and tablets are required.
GPS tracking software for locating stolen devices is necessary.

EVD: Ebola virus disease; GPS: global positioning system; WHO: World Health Organization.

The first case of EVD was imported to Nigeria in August 2014 resulting in 19 additional secondary infections. Tremendous intensity, rigour, and timely control measures together with beneficial circumstances around the case identification led to the control of the outbreak and allowed WHO to declare the end of the Ebola outbreak for this country by 20 October 2014 [4].

Systematic analyses and review of the experiences of Shuaib et al. [5] revealed that a comprehensive management system needs to be in place already to ensure successful containment of similar emergencies even if they occur under less beneficial circumstances. At the time of the outbreak, the Ebola reporting tool, called Open Data Kit (ODK) [6] was established to document visits of contact persons, but it did not address case finding, bidirectional information flow and other aspects of outbreak response.

To address this need, a consortium of Nigerian and German public health and research institutions and a global software company have developed the Surveillance and Outbreak Response Management System (SORMAS). The objective of SORMAS is to ensure availability of validated real-time surveillance data and to manage the verification of cases as well as tracing and monitoring of their contacts as it is typically needed during an EVD and other disease outbreaks. This report describes the generic requirements, process models, and technical infrastructure of SORMAS.

Development of SORMAS

We identified the user requirements in Design Thinking [7] workshops and by reviewing the reports of Shuaib et al. [5]. Additionally, we took into account requirements identified in reviews and analyses on contact tracing, outbreak management and electronic surveillance systems for other diseases also, not only EVD [8-12]. The identified requirements to be addressed by an outbreak management system are listed in Table 1.

Specification of personas

By reviewing the processes of the EVD outbreak management in Nigeria, we identified the different SORMAS user types, i.e. personas, involved in the process. Regular staff or volunteers of different hierarchical levels and with different job descriptions may be summarised within one persona, if their respective role and interaction with SORMAS are the same [13]. We defined the role, the needs with respect to the system, the interaction with other personas and the required artefacts (e.g. checklists and forms) for each persona. We consider an artefact a specification of a physical piece of information that is used or produced by a software development process, or by deployment and operation of a system. By systematically analysing the processes and roles, we were able to condense the number of originally 15 personas to seven personas. Some of these represent officers with different professions and training background. The process of defining the personas and their system expectations allowed us to design SORMAS according to users' needs.

Table 2 depicts the identified and defined seven personas that are directly interacting with SORMAS. Additionally, there is the persona case officer who is involved in the process, but will not directly interact with SORMAS since they wear protective clothes and are thus unable to use a mobile device for entering

Table 2

Persona of SORMAS with their respective activities, artefacts and interactions

Persona	Activities	Artefacts	Interaction
Informant	Looks for disease rumours in the population Collects information on death or sickness among healthcare workers	• Checklist on standard operating procedures • Rumour information (demographics, travel, contact)	Reports to surveillance officer
Rumour officer	Conducts initial triage on all incoming rumours on possible cases	• Checklist with required information on rumour • Rumour information	Reports to the surveillance supervisor
Surveillance officer	Reports notifiable diseases to state epidemiologist, receives rumours on cases and forwards them to surveillance supervisor to decide on further investigation Conducts investigation to verify status of case, e.g. suspect or confirmed and is responsible for active case finding	• EVD active surveillance form • Checklist on rumour triage • Contact list of healthcare facilities • Rumour information	Reports to surveillance supervisor Supervises informant
Surveillance supervisor	Coordinates the input from rumour officers and surveillance officers Supports rumour officer in deciding on the investigation on a new rumour	• Alert investigation form • Checklist for incoming rumours	Reports to the heads of the unit (Epidemiology/Surveillance and Case Management) who are in turn reporting to the incident manager Supervises surveillance officer
Case supervisor	Coordinates all necessary steps of handling cases, e.g. triage, transport, laboratory tests, decontamination Forwards information about a suspected case to the contact and surveillance supervisor	• Checklist with tasks for case handling • Case investigation form / case report (available in folder artefacts) • Task list for case officers	Reports to the heads of the unit (Epidemiology/Surveillance and Case Management) who are in turn reporting to the Incident manager. Supervises case officer
Contact officer	Conducts contact tracing within a particular district	• Contact list for the day / week • Daily report for contact supervisor • Case report relevant for currently followed contact • Suspected case information • Contact tracing form • Interview guide for contact interview • Meeting calendar • Contact list of new potential contacts to be traced	Reports to contact supervisor
Contact supervisor	Coordinates the work of the contact officers Informs the case supervisor about suspected cases	• Information on traced contacts • List of contacts to trace and their details • List of contact officers • Task list for each contact officer • Meeting protocol from daily meeting with all contact officers • Daily reports from each contact officer • Information on suspected case	Reports to case supervisor Supervises contact officers

EVD: Ebola virus disease; SORMAS: Surveillance and Outbreak Response Management System.

data. The complete listing of needs of the respective personas as well as the detailed process model is available at http://www.helmholtz-hzi.de/sormas.

Information flow and interactions between personas

Figure 1 indicates the interactions between the personas, the information flow and interactions in more detail, reflecting the information from the process model.

The informant can be a volunteer functioning as community informant, an Ebola focal person in a private healthcare facility, or a community healthcare worker. Therefore, the educational level and institutional affiliation may differ widely. The rumour officer is part of the EOC team and collects all rumours on possible cases that come in through different channels, e.g. phone, mail, media reports etc. from citizen, healthcare workers, or indirectly via the hotline.

The surveillance supervisor may be a disease surveillance and notification officer (DSNO). They decide if and what kind of verification action is to be taken upon incoming rumours or notifications and direct this task to the surveillance officer in the field. They apply the criteria of the case definition and takes decision of the respective case classification based on available clinical epidemiological and laboratory data. Once a suspected case is identified by a rumour officer, the

surveillance supervisor informs the case supervisor to initiate isolation and treatment, laboratory confirmation and decontamination. Besides receiving hints on potential cases, the surveillance officer also reaches out to hospitals to assure zero reporting and may verify on site whether criteria of case definitions apply for a possible case.

The contact officer reports contacts as 'suspected cases' to the contact supervisor, as soon as the contact develops symptoms. Contacts or relatives of contacts who have issues with stigmatisation, rejection or are difficult to deal with are also referred to the case supervisor. The contact officers are often DSNOs, staff members from the Ministry of Health, graduates and residents from the Nigeria Field Epidemiology and Laboratory Training Programme, Red Cross Volunteers, or surveillance officers from WHO.

The case supervisor coordinates the activities of several case officers by assigning tasks such as clinical management of cases at the isolation facility, decontamination of residences and facilities, safe burial of corpses, psychosocial support of cases, contacts and relatives.

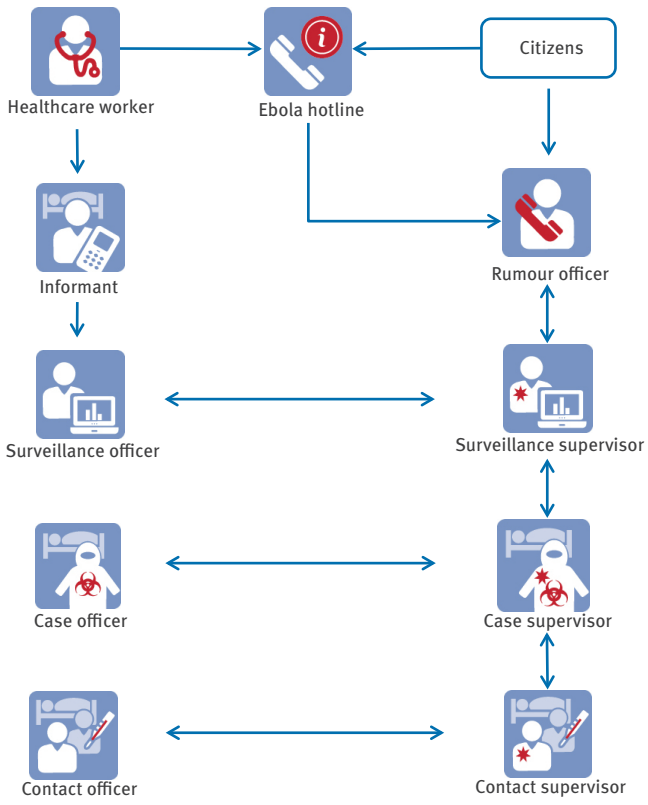
Technical infrastructure

We specified the technical infrastructure addressing the needs and tasks of the personas. We decided to focus on applications for mobile devices for the front end since the cellular network has become the first choice for Internet access in West Africa [14]. We further chose a scalable, cloud-based software architecture to allow non-dedicated computing resources on-site and to leave required maintenance to the cloud service provider.

The back end of the system is based on a cloud-based SAP HANA applying In-Memory Database (IMDB) technology [15]. A selected IMDB building block is the columnar database layout in order to enable real-time processing of analytical queries and lightweight data compression techniques. With the insert-only or append-only paradigm, IMDBs store the complete history of data changes to reconstruct the database state for any given point in time. Figure 2 depicts the software system architecture modelled as Fundamental Modelling Concepts block diagram [16]. Field workers use mobile devices to document acquired information directly in the cloud system. Available devices are registered in the cloud-based device management software SAP Afaria. The local cellular phone network provider provides data transfer to the Internet. All data exchange is encrypted using latest web standards, e.g. HTTPS protocol. All applications are configured by the cloud service provider and incorporate latest IMDB technology which allows storing all data in an encrypted format [17]. In case the mobile devices are to be used at times or in areas without mobile phone connectivity, the data entered will be automatically uploaded to the system as soon as connectivity is available again. As a back-up option, data can also be downloaded from the encrypted SIM card.

Figure 1

Interactions between SORMAS users involved in the Ebola virus disease containment process



SORMAS: Surveillance and Outbreak Response Management System.

Arrows between personas represent the information flow.

User interface

The user interface was designed to fulfill all data collection and information needs of the seven personas, i.e. the artefacts have been implemented through corresponding screens. Bootstrap, a set of software tools for creating web applications based on HyperText Markup Language (HTML), Cascading Style Sheets (CSS), and JavaScript [18-20], has been used for this purpose. Some examples of screen shots for mobile devices are shown in Figure 3. The design of the icons, depicting the different personas and functions, went through six modifications to assure universally applicable, immediately understandable, and culturally sensitive design.

Comparison with other systems

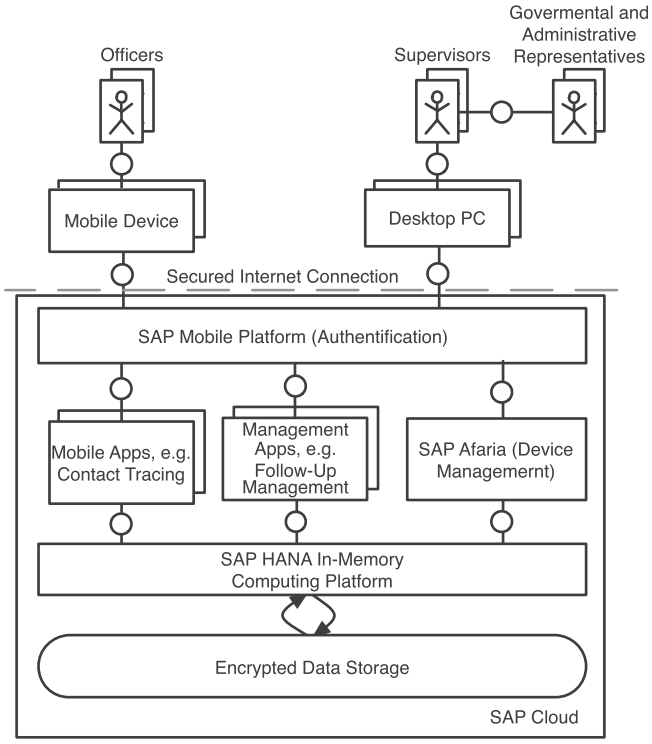
The four main characteristics of SORMAS presented here are (i) its focus on the multilevel management functionality designed on the basis of systematic and in-depth analyses of the actual processes and personas involved in the successful EVD control in Nigeria,

(ii) its concept to ensure real-time synchronisation with surveillance systems already existing in many African countries such as IDSR and transfer interfaces to other EVD related database systems such as the EpiInfo Viral Haemorrhagic Fever application, (iii) its centralised back-end IT architecture using established software and database components with big data capacity, in combination with (iv) its mobile interface for bi-directional information exchange for staff in the field applicable on standard smart phones without any further configuration.

Through the combination of those four characteristics, SORMAS is distinct from various other tools aiming to support the control of the EVD and other outbreaks by means of mobile phone based applications. Detailed technical information on the existing systems is still available only to a limited extent. However, the existing tools do not support bidirectional information exchange and a task management as designed for SORMAS. For example, during the outbreak in Nigeria in August / September 2014, an Ebola reporting tool, called Open Data Kit (ODK) [6] was established running on Android phones. It allows reporting suspected cases, and sending of GPS data of cases/contacts, and integrated laboratory results with feedback to field workers. The ODK mainly digitised the data collection forms. ODK concentrated on contact tracing and follow-up. Only the contact officers had access to the system.

Figure 2

SORMAS software architecture



SORMAS: Surveillance and Outbreak Response Management System; VM: virtual machine.

In contrast, SORMAS will be made available to several relevant personas, is more detailed and focuses on active case finding and surveillance.

The Centers for Disease Control and Prevention (CDC) developed a VHF module based on EpiInfo for contact tracing [21]. It provides support in case management, analysis, and reporting during outbreaks of EVD, Marburg virus, Lassa virus, Rift Valley Fever, and Crimean-Congo haemorrhagic fever. This module allows users to link cases with contacts and track those contacts continually over a 14- or 21-day follow-up window and to set up databases of patient information including names, sex, ages, locations, status, e.g. such as dead or alive, and case classification, for suspected case, confirmed case or no case. In contrast to SORMAS, the EpiInfo VHF module is not designed for bidirectional information exchange and does not address the challenge of information exchange.

The Ebola Care App supports contact tracing, patient data collection by ambulance teams, and Ebola education as well as observation and evaluation of children under quarantine [14]. Basing upon cloud data storage, it further gives decision makers real-time access to data from the field. It is currently tested by the Liberian government. CommCare is an open source mobile platform that supports a range of Ebola management needs. It has been developed and pilot tested to assist community healthcare workers [22,23]. CommCare operates through the use of Java-enabled phones or high-end Android smartphones. The system intends to provide a range of functions (some of them are still under development): household visit tracking, data collection, record keeping, day planning, and data exploration. Additionally, systems were developed that try to stimulate reporting by citizens or to provide citizens with information on prevention measures. EbolaTracks is an automated SMS system designed for monitoring persons potentially exposed to EVD, including travellers returning from Ebola-affected countries [24]. It enables monitoring of EVD contacts by SMS to inquire about development of symptoms.

SORMAS, as well as most of the above mentioned IT-based tools to support the EVD outbreak control, makes use of the mobility and widespread availability of mobile phones in West Africa. This allows independence from variable wire-based IT and telecommunication infrastructure. In contrast to some of these approaches, SORMAS does not require any special configuration on the mobile devices which has proven to be a major obstacle when the ODK was used during the outbreak in Nigeria in August 2014. The use of SAP Afaria enables remote management of devices including their automated update as well as track and wipe of lost devices to ensure a high level of data security [25]. Using a cloud service provider also eliminates the need for local IT management. Data are uploaded to the cloud when an Internet connection is available. Otherwise SORMAS works in an offline mode where

Figure 3

Screenshots of the mobile SORMAS user interface

SORMAS: Surveillance and Outbreak Response Management System.
The name of the person is fictitious.

data are stored locally until an Internet connection is available.

Discussion and conclusion

An advantage of SORMAS is the usage of the IMBD technology that was applied successfully in the analysis of big enterprise data and medical data,, e.g. in supporting the identification of similar patient cases and the protection of markets from injecting pharmaceutical counterfeits [26,27]. We consider IMDB technology as a toolbox of IT building blocks enabling real-time analysis of big datasets [15]. IMDB technology also provides combined processing of structured data, e.g. relational database tables, and unstructured data, e.g. text documents. Furthermore, IMDB technology integrates statistical tools, such as clustering and machine learning algorithms. These functionalities would at a later stage allow development of complementary functionalities into SORMAS such as identification of social media messages and their linkage to reported cases.

Using such advanced IT technology might be perceived as a risk to acceptability and sustainability in countries in which computer systems may not work reliably due to lack of qualified maintenance or technical infrastructure. However, the use of a high performance architecture built with established components reduces the risk of break-down due to overload, allows flexible adaptation to country-specific needs and ensures a high level of data protection.

The process model has different dimensions:

1. centralised vs. field-based activities, carried out by respective personas who would in turn also use mobile devices vs desktop PC for their work.
2. the differentiation between
   - intake of information (in form of rumours, notifications and reports of suspect cases),
   - case verification,
   - isolation management of the case, and
   - identification and follow up of contacts of that case,
   - monitoring of infection control measures (decontamination, safe burial) and social mobilisation.

SORMAS supports realising these control measures by providing reminders and check-lists to the user and confirming completed tasks. Standard operating procedures are thus automatised as much as possible. This will hopefully help reduce the time for action-taking and provide accountability. Another dimension of the process is the distinction between supervision and decision making (as represented by surveillance supervisor, case supervisor and contact supervisor) and the execution of these tasks by the respective personas.

Since the process model was based on the practical experience in the field it might serve as basis for epidemiological models on the impact of different intervention strategies.

One limitation is that SORMAS has not been used in the field yet. It remains to be seen until the foreseen pilot phase whether SORMAS can truly improve the control of EVD or other outbreaks. A table top prototype test based on two simulated scenarios was performed in February 2015 to evaluate the functionality of the system. A four-week pilot phase in Nigeria is planned for May 2015 to systematically evaluate SORMAS under field conditions. In order to allow proper piloting in the absence of EVD, we have identified alternative notifiable diseases and developed respective process models so that SORMAS will soon also contain functionalities

for surveillance and case management of additional epidemic prone diseases. In the Nigerian context, this would encompass measles, cerebrospinal meningitis, cholera, Lassa fever, rabies, acute flaccid paralysis, bloody diarrhoea/shigellosis, and Dengue fever. In order to realise this, the process model and data structures need to be redesigned taking existing public health guidelines and the respective surveillance processes into account.

Since SORMAS is designed to export information for integration in the IDSR forms, it may help to improve quality and efficiency of routine disease surveillance and control even in the absence of large epidemics. Possibly, SORMAS will only become available for implementation after the current EVD outbreak in West Africa has diminished in size. However, SORMAS is likely to be a very useful instrument to enhance routine surveillance of epidemic prone diseases as well as inhibiting the speed with which the disease is spreading. Currently we concentrate our work on adapting the system to surveillance tasks associated with other diseases such as measles and avian influenza A(H5N1). Beyond the actual system development, our work resulted in a better in-depth understanding of the processes and personas involved in the case management and surveillance tasks of EVD.

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Conflicts of interest

RR is employed by SAP, the provider of the platform used in this study. All other authors declare that there are no conflicts of interest.

Authors' contributions

Cindy Fähnrich, Kerstin Denecke and Gérard Krause drafted the manuscript. Cindy Fähnrich developed the process model and user interface, with contributions of Kerstin Denecke, Justus Benzler, Hermann Claus and Göran Kirchner, Olawunmi Olubunmi Adeoye, Sabine Mall, Daniel Tom-Aba, Gabriele Poggensee and Norbert Schwarz. Matthieu-P. Schapranow reviewed the process model. Cindy Fähnrich defined and specified the persona with contributions and discussions with Daniel Tom-Aba, Kerstin Denecke, Justus Benzler, Hermann Claus and Göran Kirchner, Olawunmi Olubunmi Adeoye, Sabine Mall, Gabriele Poggensee and Norbert Schwarz. Justus Benzler, Hermann Claus, Göran Kirchner and Kerstin Denecke developed the data model with contributions from Daniel Tom-Aba and Gabriele Poggensee. Ralph Richter, Matthieu-P. Schapranow and Matthias Uflacker designed the technical infrastructure. Kerstin Denecke discussed the results in comparison to related work. Gabriele Poggensee and Daniel Tom-Aba analysed the SORMAS requirements. Gérard Krause supervised the project and contributed to all developments. All authors commented on the manuscript at all stages.

References

1. World Health Organization (WHO). Ebola Situation Report. Ebola Situation Report - 11 March 2015. Geneva: WHO. Date. Available from: http://apps.who.int/ebola/current-situation/ebola-situation-report-11-march-2015
2. Khan AS, Tshioko FK, Heymann DL, Le Guenno B, Nabeth P, Kerstiëns B, et al. The reemergence of Ebola hemorrhagic fever, Democratic Republic of the Congo, 1995. Commission de Lutte contre les Epidémies à Kikwit. J Infect Dis. 1999;179(s1) Suppl 1;S76-86. http://dx.doi.org/10.1086/514306 PMID:9988168
3. European Centre for Disease Prevention and Control (ECDC). Epidemiological Update: outbreak of Ebola virus disease in West Africa. 14 November 2014. Stockholm: ECDC. Available from: http://ecdc.europa.eu/en/press/news/_layouts/forms/News_DispForm.aspx?List=8db7286c-fe2d-476c-9133-18ff4cb1b568&ID=1113
4. World Health Organization (WHO). Nigeria is now free of Ebola virus transmission. Geneva: WHO. 20 Oct 2014. Available from: http://who.int/mediacentre/news/ebola/20-october-2014/en/
5. Shuaib F, Gunnala R, Musa EO, Mahoney FJ, Oguntimehin O, Nguku PM, et al. Ebola virus disease outbreak - Nigeria, July-September 2014. MMWR Morb Mortal Wkly Rep. 2014;63(39):867-72. PMID:25275332
6. Ibukun Y. Nigeria Uses Android App with Facebook to fight Ebola. Bloomberg. [Accessed 27 Dec 2014]. Available from: http://www.bloomberg.com/news/2014-10-07/nigeria-uses-android-app-with-facebook-to-beat-ebola.html
7. Plattner H, Meinel C, Leifer L, editors. Design Thinking Research. Building Innovators. Series: Understanding Innovation. Springer International Publishing. 2015.
8. Benzler J, Kirchner G, Diercke M, Gilsdorf A. Das Projekt DEMIS - Konzeptionelle und technische Vorarbeiten für ein elektronisches Meldesystem für den Infektionsschutz. [The DEMIS Project - Conceptual and Technical Preparations for an Electronic Notification System for Infection Control]. Der Hygieneinspektor. Feb 2014. German. Available from: http://www.bundesverband-hygieneinspektoren.de/wp-content/uploads/2015/01/Der-Hygieneinspektor-02-14-Das-Projekt-DEMIS.pdf
9. Krause G, Altmann D, Faensen D, Porten K, Benzler J, Pfoch T, et al. SurvNet electronic surveillance system for infectious disease outbreaks, Germany. Emerg Infect Dis. 2007;13(10):1548-55. http://dx.doi.org/10.3201/eid1310.070253 PMID:18258005
10. Mohr O, Hermes J, Schink SB, Askar M, Menucci D, Swaan C, et al. Development of a risk assessment tool for contact tracing people after contact with infectious patients while travelling by bus or other public ground transport: a Delphi consensus approach. BMJ Open. 2013;3(10):e002939. http://dx.doi.org/10.1136/bmjopen-2013-002939 PMID:24157815
11. Krause G, Frank C, Gilsdorf A, Mielke M, Schaade L, Stark K, et al. [The 2011 HUS epidemic in Germany. Challenges for disease control: what should be improved?]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2013;56(1):56-66. German. http://dx.doi.org/10.1007/s00103-012-1585-1 PMID:23275957
12. Schaade L, Reuss A, Haas W, Krause G. [Pandemic preparedness planning. What did we learn from the influenza pandemic (H1N1) 2009?]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2010;53(12):1277-82. German. http://dx.doi.org/10.1007/s00103-010-1162-4 PMID:21161478
13. Lidwell W, Holden K, Butler K. Universal Principles of Design. Massachusetts: Rockport Publishers, 2010: 182.
14. Ebola Care. EbolaCareApp. [Accessed 11 Dec 2014]. Available from: http://www.appsagainstebola.org/
15. Plattner H. A Course in In-Memory Data Management: The Inner Mechanics of In-Memory Databases. 2nd Edition. Springer, 2014.
16. Knöpfel A, Grone B, Tabeling P. Fundamental Modeling Concepts: Effective Communication of IT Systems. John Wiley & Sons, 2006.
17. SAP SE. SAP HANA Cloud Platform. [Accessed 3 Dec 2014]. Available from: https://account.hana.ondemand.com/
18. Bootstrap Front-End Framework. [Accessed 7 Jan 2015]. Available from: http://getbootstrap.com/
19. Cascading Style Sheets (CSS) Specification. [Accessed 7 Jan 2015]. Available from: http://www.w3.org/TR/CSS2/
20. Flanagan D. JavaScript: The Definitive Guide. O'Reilly Media, Inc., 2006.
21. The Epi Info Viral Hemorrhagic Fever Application. [Accessed 11 Dec 2014]. Available from: http://epiinfovhf.codeplex.com/
22. Millennium Villages. CommCare. [Accessed 11 Dec 2014]. Available from: http://millenniumvillages.org/videos/commcare-as-a-mobile-health-solution/

23. World Health Organization (WHO). mHealth Alliance. Assisting community health workers in India. Dimagi's CommCare. Geneva: WHO. 2013. Available from: http://apps.who.int/iris/bitstream/10665/92802/1/WHO_RHR_13.18_eng.pdf
24. Tracey LE, Regan AK, Armstrong PK, Dowse GK, Effler PV. EbolaTracks: an automated SMS system for monitoring persons potentially exposed to Ebola virus disease. Euro Surveill. 2015;20(1):20999. http://dx.doi.org/10.2807/1560-7917.ES2015.20.1.20999. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20999 PMID:25613652
25. SAP SE. SAP Afaria White Paper. [Accessed 3 Dec 2014]. Available from: http://www.sap.com/bin/sapcom/en_us/downloadasset.2013-09-sep-05-11.Protect%20Your%20Enterprise%20by%20Securing%20All%20Entry%20and%20Exit%20Points-pdf.html
26. Plattner H, Schapranow MP. High-Performance In-Memory Genome Data Analysis: How In-Memory Database Technology Accelerates Personalized Medicine, In-Memory Data Management Research. Springer. 2014.
27. Schapranow MP. Real-Time Security Extensions for EPCglobal Networks: Case Study for the Pharmaceutical Industry. Springer. 2013.
28. World Health Organization (WHO). International Health Regulations. Geneva: WHO. Available from: http://www.who.int/ihr/en/
29. Dhillon RS, Srikrishna D, Sachs J. Controlling Ebola: next steps. Lancet. 2014;384(9952):1409-11. http://dx.doi.org/10.1016/S0140-6736(14)61696-2 PMID:25308287