Ebola Vaccines and Vaccination

Report of the SAGE Working Group on Ebola Vaccines and Vaccination with provisional recommendations for vaccination

September 30, 2015

SECTION A: INTRODUCTION, EPIDEMIOLOGY AND RISK FACTORS

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Background

In response to the ongoing widespread outbreak of Ebola Virus Disease (EVD) in west Africa, the World Health Organization (WHO) coordinated an effort to accelerate the development of vaccines against EVD for use in the current outbreak, as well as in response to future outbreaks.

In October 2014, the WHO Director General requested the Strategic Advisory Group of Experts (SAGE)[1] on Immunization to advise WHO on the use of the vaccine(s) for the control of EVD. In response to this request, the WHO SAGE secretariat established a Working Group with an urgent program of work to facilitate a SAGE review of the available and emerging evidence to inform the development of the recommendations for the use of Ebola vaccines.

The urgency of the task required that the SAGE Working Group process to review the available evidence and draft recommendations should proceed in parallel with the ongoing phase 1, phase 2 and phase 3 trials of candidate vaccines. Progress with the development and evaluation of vaccines has proceeded with an unprecedented speed. However, while there are several vaccine candidates undergoing clinical evaluation, none of them has as yet received regulatory authorization for use outside a study setting.

This report summarizes the available information on the epidemiology, risk factors and transmission patterns of EVD, with particular reference to the current epidemic in west Africa; the status of vaccine development, along with preliminary results from the evaluation of the most advanced vaccine candidates and the preparations for deployment of these vaccines; projections of the impact of vaccination under different epidemiological scenarios; and proposes provisional recommendations for the consideration of SAGE.

Epidemiology of Ebola Virus Disease

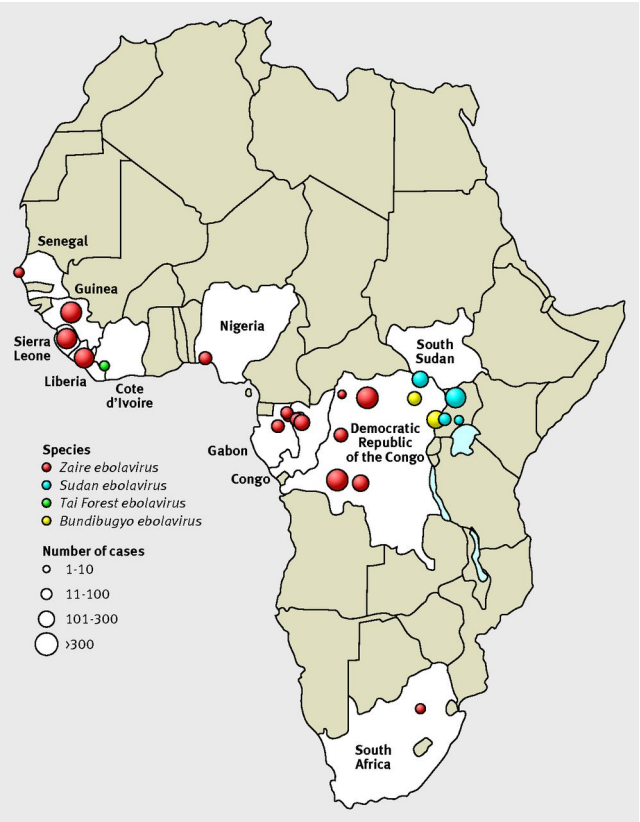
Ebola viruses and disease in humans: review of the published literature

Ebola viruses are members of the Filovirus family. Five species of *Ebolavirus* have been identified (*Zaire ebolavirus*, *Sudan ebolavirus*, *Bundibugyo ebolavirus*, *Tai Forest ebolavirus*, and *Reston ebolavirus*), of which the former three species have each caused multiple outbreaks of EVD; case fatality in these outbreaks has ranged from 40%-90%. Of note, while the current outbreak in West Africa is due to *Zaire ebolavirus*, approximately half of all previous outbreaks have been due to other species (*Sudan ebolavirus* or *Bundibugyo ebolavirus*). The geographic distribution of zoonotic spill-over events in previous EVD outbreaks roughly splits the continent of Africa, with all outbreaks due to *Zaire ebolavirus* occurring west of central Democratic Republic of Congo (DRC) and outbreaks due to *Sudan ebolavirus* and *Bundibugyo ebolavirus* occurring east of central DRC. Importantly, most of the current advanced vaccine prospects in clinical trials are monovalent vaccines containing the

[1] Strategic Advisory Group of Experts (SAGE) on Immunization- http://www.who.int/immunization/policy/sage/en/

Zaire ebolavirus glycoprotein and may have limited protection against other viral species. There is currently no efficacy data indicating cross-protection of *Zaire ebolavirus* glycoprotein in humans.

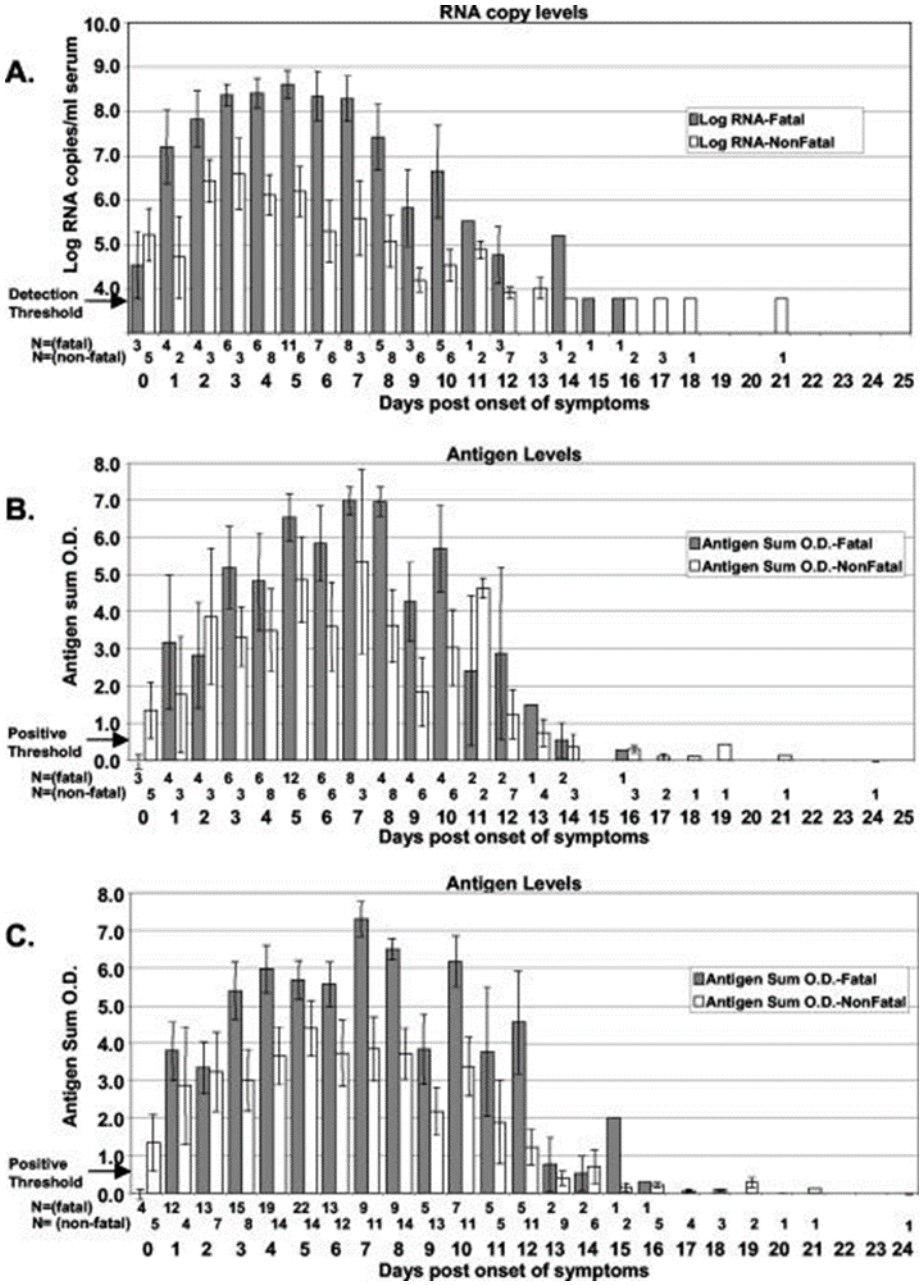
Figure 1: Geographic distribution of human EVD outbreaks (*Beeching et al., 2014*)



Ebola virus disease and transmission dynamics

The multiple species of the *Ebolavirus* genera are believed to be maintained in zoonotic reservoirs, however, once animal-human spill-over events occur, outbreaks are driven by person-to-person transmission. Ebola virus typically enters the body through penetration of the skin or by percutaneous exposure. The virus causes a disseminated infection, replicating in multiple organs, including the lymph nodes, liver, and kidneys, and eventually the endothelium (*Messaoudi et al, 2015*). Viraemia typically corresponds with the severity of the disease stage, with low titres early in disease, and increasingly higher titres during later, disseminated stages of disease, leading to eventual death or a decrease in titres corresponding with recovery and onset of adaptive immune response (*Ksiazek et al., 1999; Spengler et al., 2015; Towner et al., 2004*).

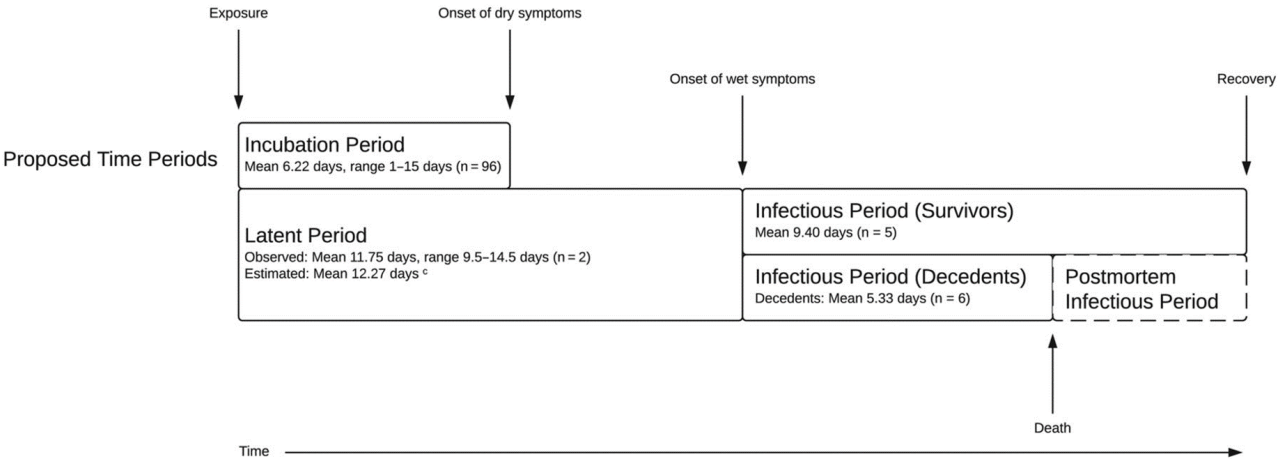
Figure 2: Kinetics of viraemia, relative to date of symptom onset, Gulu, Uganda (*Towner et al. 2004*)



The incubation period of Ebola virus in humans has been typically reported to be in the range of 2-21 days, with a mean of approximately a week. Early, non-specific signs and symptoms, including fever, chills, malaise, and myalgia mark the onset of disease. These are followed by late signs and symptoms, including general systemic signs and symptoms such as prostration, and organ system specific signs and symptoms involving the gastrointestinal (anorexia, nausea, vomiting, abdominal pain, diarrhoea), respiratory (chest pain, shortness of breath, cough, nasal discharge), vascular (conjunctival injection, postural hypotension, oedema), and neurological (headache, confusion, coma) systems. A subset of patients develops additional haemorrhagic symptoms including petechiae, ecchymosis, oozing from venepuncture sites, and mucosal haemorrhages (*Feldman and Geisbert, 2011*). In terms of risk of transmission, signs and symptoms can be classified as 'dry' (fever,

chills, myalgia, malaise etc.) and 'wet' (vomiting, diarrhoea, cough, petechiae, ecchymosis, oozing from venepuncture sites, and mucosal haemorrhages etc.). Wet symptoms and signs increase the risk of exposure to infectious body fluids and, therefore, the risk of transmission (*Velásquez et al. 2015*). A recent paper reviewed data from all known instances of EVD, associated with a known 1-day exposure, to characterize the disease development and risk of transmission on the basis of clinical signs and symptoms. Importantly, this review indicated the presence of distinct incubation and latent periods of disease, occuring a mean of 7 and 12 days post-exposure, respectively (*Velásquez et al. 2015*).

Figure 3 : Time line of Ebola virus disease (*adapted from Velásquez et al. 2015*)



Due to the high viral titres found in blood during viraemia, contact with blood of an actively infected patient represents a high-risk exposure for infection. In addition to blood, Ebola virus has been detected from a number of other clinical specimens from infected patients, including saliva, stool, semen, breast milk, tears, nasal blood, and skin swabs. However, there is limited ability to detect virus from environment samples of patient wards, suggesting a much higher risk of transmission from direct contact with bodily fluids than from contaminated surfaces (*Bausch et al., 2007*).

Consistent with the biological evidence that transmission is likely to be associated with contact with bodily fluids; studies from multiple outbreaks have provided similarly evidence. For instance, Dowell et al. (1999) evaluated risk factors for transmission in 27 households, in Kikwit, DRC, in 1995, which led to 28 secondary cases of EVD. In this investigation, all secondary cases had direct physical contact with a primary case and contact with bodily fluids conferred a high risk of transmission (RR=3.6; 1.9-6.8). Touching cadaver and exposure during the hospital phase were additionally noted as risk factors (*Dowell et al., 1999*). In a study by Francesconi et al., among 26 cases and 65 contacts in Gulu, Uganda, in 2001, contact with patient body fluid was the strongest risk factor for transmission (PRR=4.61; 1.73-12.29) (*Francesconi et al., 2003*).

Risk groups for transmission and infection with Ebolavirus and outcomes of disease

Based on epidemiologic data from multiple previous outbreaks, there are 3 risk groups that consistently have been at a high risk for acquiring EVD: household/close contacts of Ebola cases, healthcare workers, and individuals who attend funerals (*World Health Organization, 1978; Baron et*

al. 1983; Khan et al. 1999; Wamala et al., 2010; Borchert et al., 2011; Maganga et al., 2014). Importantly these risk groups are consistent with high risk of direct exposure to infected individuals or their bodily fluids.

Among household/close contacts, the primary risk factor identified for transmission of Ebola virus is direct contact with the infected patient. Osterholm et al. recently reviewed data involving household contact and Ebola virus transmission (*Osterholm et al., 2015*) and noted the strong association between direct physical contact and transmission, although they also noted that a small proportion of cases may be due to indirect or fomite spread (*Dowell et al., 1999; Baron et al., 1983; Francesconi P et al., 2003*).

Table 1: Summary data from Osterholm et al (*Osterholm et al., 2015*)

Study and contact status	Development of EVD		
	No. (%) who became ill	No. (%) who were not ill	Total
Dowell et al			
Direct contact	28 (100)	67 (46)	95
No direct contact	0 (0)	78 (54)	78
Total	28	145	173
Baron et al			
Direct contact	27 (93)	59 (57)	86
No direct contact	2* (7)	44 (43)	46
Total	29	103	132
Francesconi et al			
Direct contact	26 (96)	47 (80)	73
No direct contact	1** (4)	12 (20)	13
Total	27	59	86
Summation			
Direct contact	81 (96)	173 (56)	254
No direct contact	3 (4)	134 (44)	137
Total	84	307	391

* Contact status unknown

** The patient had probably fomite exposure, i.e. used a blanket that the primary case had used before death

The transmission of Ebola virus to healthcare workers has consistently been noted in numerous outbreaks, with healthcare workers sometimes accounting for a high proportion of the total number of cases in the outbreak. In general, nurses and physicians have had the highest incidence of disease among healthcare workers, however, transmission to other occupations, including laboratory workers and cleaners has been noted (*World Health Organization, 1978; Tomori O et al 1999; Muyembe-Tamfum et al, 1999; Centers for Disease Control 1995; Kerstiens et al. 1999; Borchert et al, 2011; Centers for Disease Control 2001; Wamala et al 2010; Bah et al, 2015; Kilmarx et al, 2014; Matanock et al, 2014*).

Across multiple outbreaks, the one consistent risk factor for fatal EVD is age, with the elderly tending to have higher risk of death. In contrast, gender typically has little impact in disease outcome. Higher viral loads have been reported among individuals with fatal outcomes, consistent with more severe infectious burden. While some studies have reported certain clinical signs and symptoms that are associated with fatal outcomes, there are no definitive high risk signs or symptoms and interpretation of data across multiple outbreaks, with varying degrees of clinical information

collected or coded, represents a significant challenge to interpretation of clinical data (*World Health Organization, 1978; Anonymous, 1978; Khan et al.; Ksiazek et al., 1999; Sadek et al., 1999; Rowe et al, 1999; Towner et al., 2004, ;MacNeil et al. 2010; Yan et al., 2015*) .

Potential for sexual transmission of Ebola virus

There are a number of lines of evidence that suggest potential for sexual transmission of Ebola virus from recovered individuals for a significant time period during convalescence. The potential for sexual transmission has been hypothesized for a number of years as a result of multiple studies identifying virus in semen of males, for months following recovery (*Rowe et al., 1999; Bausch et al., 2007*). A recent report has indicated the presumptive sexual transmission of Ebola virus, and re-introduction of the disease in Liberia, from a male patient who had recovered approximately 4 months prior to sexual contact with a partner who developed EVD (*Christie et al., 2015*). A presumptive explanation for the long-term presence of Ebola virus in semen is the persistence of virus within immune-privileged tissue sites within the body. Consistent with this hypothesis, recently, viable virus was detected in aqueous humor 9 weeks after clearance of viraemia from an EVD survivor with uveitis (*Varkey et al., 2015*).

Summary points

- Multiple species of Ebola virus are known to cause EVD, however, most currently advanced vaccine candidates contain only *Zaire ebolavirus* antigen
- Ebola virus infection results in a disseminated acute infection. Viraemia is highest at the severe stage of disease and the virus can be detected in numerous bodily fluids, indicating risk of infection is highest through direct contact with patients or their bodily fluids
- Common risk groups for infection in outbreaks include household/close contacts of cases, healthcare workers, and individuals attending funerals
- There is presumptive potential for sexual transmission of virus, from surviving patients, a number of months following recovery

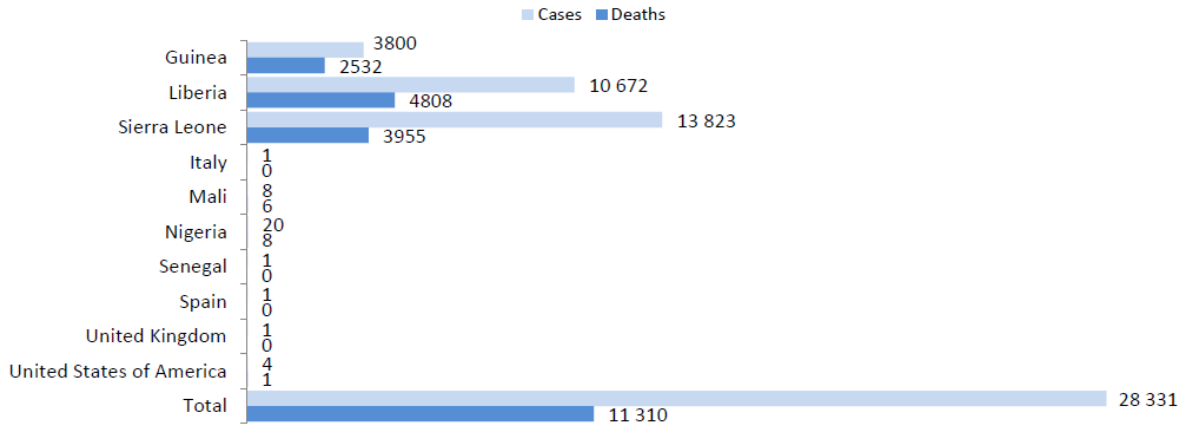
Epidemiology of the current epidemic of EVD in West Africa: analysis of reported data in the WHO viral haemorrhagic fever (VHF) database

Status of the current epidemic

(From the September 23 Ebola Situation Report. Latest situation report available at: http://apps.who.int/ebola/ebola-situation-reports)

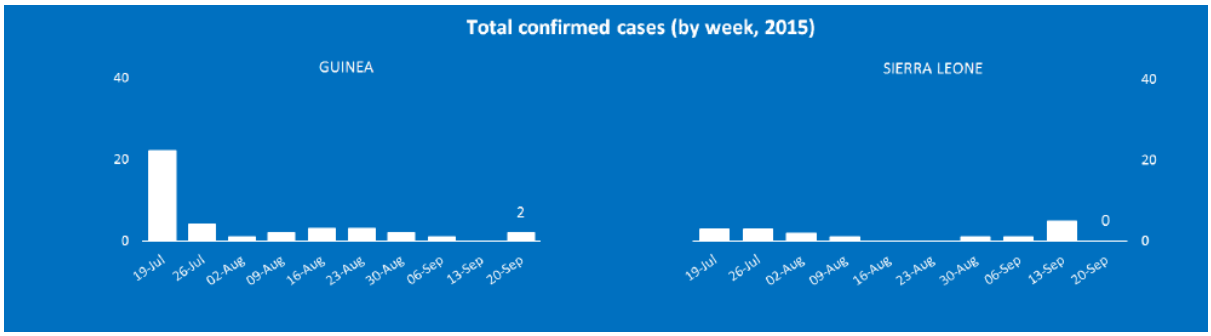
As of September 20, 2015, there were 28 331 cases of confirmed, probable and suspected cases of EVD related to the current outbreak in west Africa and 11 310 deaths (Figure 4).

Figure 4: Confirmed, probable and suspected EVD cases worldwide (data up to 20 September 2015)



There were 2 confirmed cases of EVD reported in the week of September 20, both of which were in Guinea. The number of cases has remained below 10 per week since the last week of July (Figure 5).

Figure 5: Total confirmed cases (by week), 2015



Over the same period of time, transmission of virus has been geographically confined to several small areas in western Guinea and Sierra Leone, marking a transition to a distinct third phase of the epidemic. Improvements to rapid and accurate case investigation and contact tracing, rapid isolation and treatment, and effective engagement with affected communities have all played a crucial role in reducing case incidence to its current low level. A refined phase 3 response[2] coordinated by the Interagency Collaboration on Ebola[3] will build on these existing measures to drive case incidence to zero and ensure a sustained end to Ebola virus transmission.

After recording 14 consecutive days with zero confirmed cases, two new confirmed cases were reported from Guinea during the week ending 20 September: a 10-year-old girl who died after moving from the Ratoma area of Conakry to Forecariah, and a 24-year-old woman who was identified as Ebola virus-positive in the Dixinn area of Conakry. Neither case was a registered contact, although both cases have a strong epidemiological link to a probable case thought to have died from EVD at the end of August. Investigations incorporating genetic sequencing of Ebola virus from both

[2] Ebola response phase 3: framework for achieving and sustaining a resilient zero: http://www.who.int/csr/resources/publications/ebola/ebola-response-phase3/en/

[3] Interagency Collaboration on Ebola: http://www.who.int/csr/resources/publications/ebola/ebola-response-phase3/en/

confirmed cases suggest they are part of the Ratoma chain of transmission—the only chain of transmission known to be currently active (past 21 days) in Guinea.

No new confirmed cases were reported from Sierra Leone in the week of 20 September. Over 700 contacts have been identified in association with the previous week's reported case from Bombali: a 16 year-old girl identified as EVD-positive after post-mortem testing. Investigations into the origin of her infection have not yet concluded, but preliminary findings suggest that a survivor may have been the source.

Robust surveillance measures are essential to ensure the rapid detection of any reintroduction or re-emergence of EVD in currently unaffected areas. Surveillance in the three countries will be enhanced in line with the phase-3 response framework.

Risk factors for Ebola Virus Disease in the general population

The analysis of data for the assessment of risk factors was limited to data from the current epidemic in Guinea, Liberia and Sierra Leone.

1. Risk of infection

The risk of infection in the general population was assessed by comparing the cumulative cases, attack rates and relative risk of EVD by age group and sex. The data are those presented to the WG as of August 12, 2015. While the number of cases has increased slightly since then, the general patterns and trends remain the same.

Table 2 shows the total numbers of cases reported to the VHF database, stratified by country, sex and age group as of 12 August, 2015.

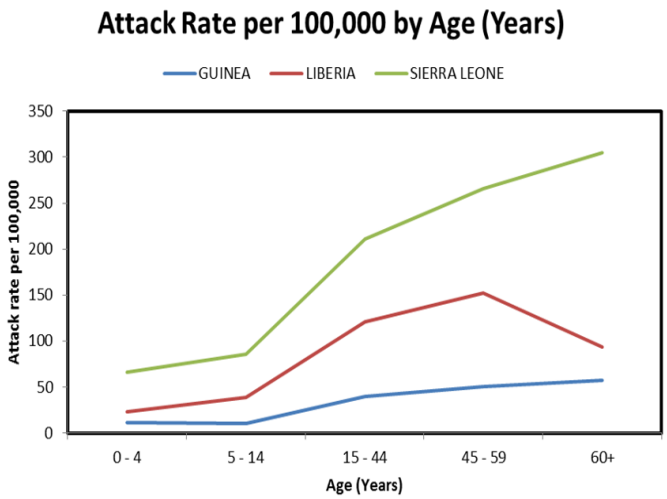
Table 2: Total Numbers of Cases by Age and Sex (12 August 2015)

	Number of cases				
	Cumulative				
	Confirmed				
	Male	Female	Both sexes		
Country	All ages (total)	All ages (total)	0-14	15-44	45+
Guinea	1589	1735	529	1894	857
Liberia	1911[i]	1838[i]	561[i]	2060[i]	703[i]
Sierra Leone	4792	5081	1978	5592	2129
All countries	8292[i]	8654[i]	3068[i]	9546[i]	3689[i]

The numbers of cases were similar in males and females in all three countries. The highest numbers of cases in each country, and in all three countries overall, was in the 15-44 year age group.

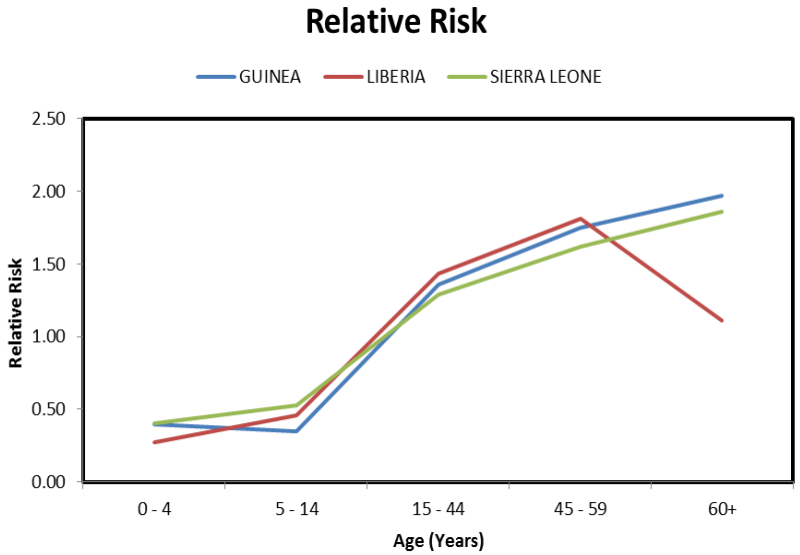
The attack rates and relative risk by age in each country are shown in Figures 6 and 7. Regardless of age, attack rate is highest in Sierra Leone followed by Liberia and Guinea. In general, the attack rates increase as age rises, the exception being a decrease in attack rates in those 60+ in Liberia, compared to those 45-59 of years.

Figure 6: Attack rates per 100,000 by age (years



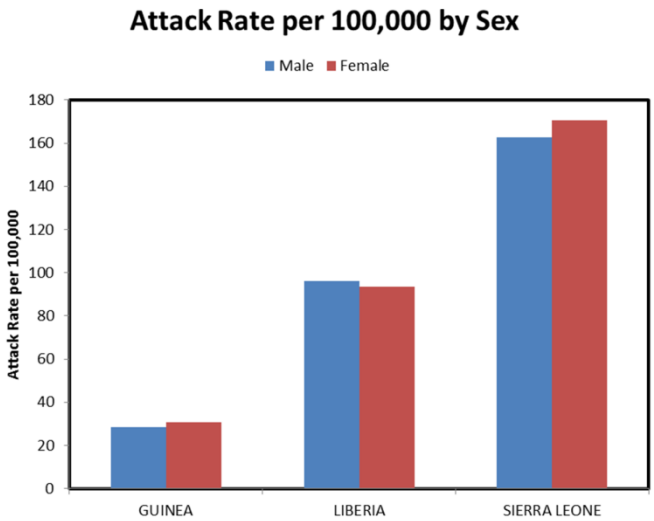
Source: VHF database; United Nations, Department of Economic and Social Affairs, Population Division (2013). World Population Prospects: The 2012 Revision.

Figure 7: Relative risk of disease by age



Source: VHF database; United Nations, Department of Economic and Social Affairs, Population Division (2013). World Population Prospects: The 2012 Revision.

Figure 8: Attack rates per 100,000 by sex



The calculations of the relative risks are based on the incidence of disease in the particular age group in reference to the overall incidence rate in the entire population in each of the three countries during the current epidemic, till the time of analysis.

Figure 8 shows the attack rates by sex in each of the three most affected countries. As stated earlier, the attack rate is highest in Sierra Leone, followed by Liberia and Guinea. However, there is no significant difference in attack rate between sexes in all the three countries.

2. Risk of death

Case Fatality Ratio (CFR) stratified by age and sex was used to evaluate the risk of death in the general population.

Figure 9: Case fatality ratio by age

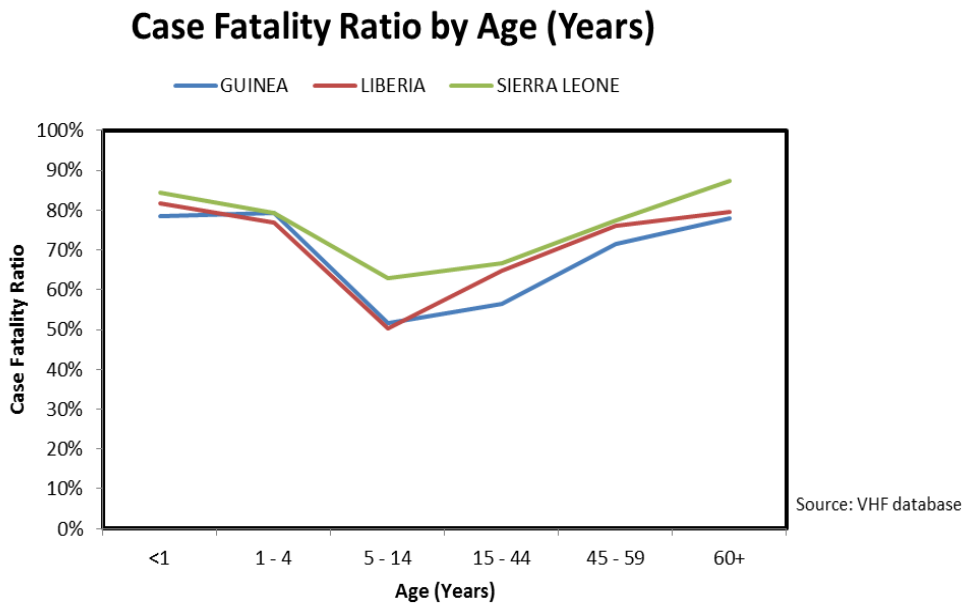
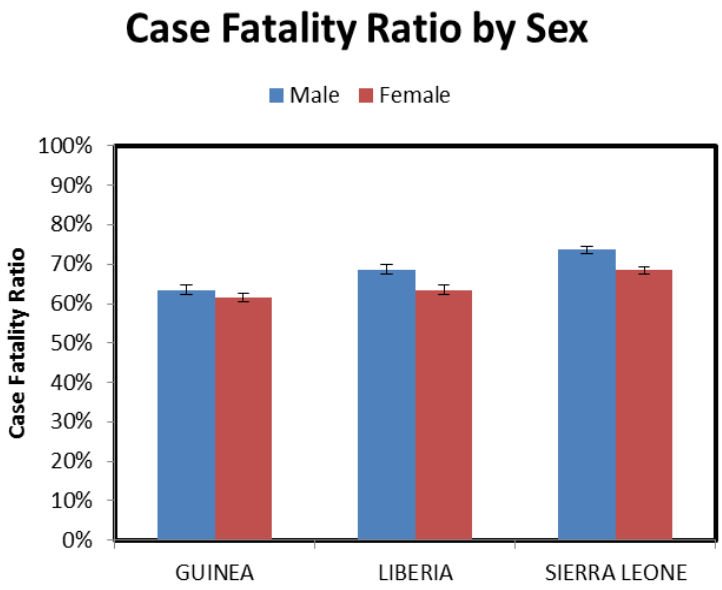


Figure 10: Case fatality ratio by sex



Figures 9 and 10 show the CFR by age and by sex, respectively. The curve lines for CFR by age in each of the countries were U-shaped, with highest CFR at the extremes of age and lower CFR in the 5 to 14 and 15- 44 year age groups.

The CFR was similar between males and females in all three countries.

Exposure patterns driving Ebola virus transmission in west Africa

Abstract from unpublished manuscript reviewed by the WG titled "Exposure patterns driving Ebola transmission in West Africa" from the WHO Ebola Response Team (corresponding authors: Christopher Dye (WHO, Geneva), Neil Ferguson, and Christophe Fraser (both Imperial College, UK))

To understand the drivers of the Ebola epidemic in west Africa, we investigated a unique dataset of nearly 10,000 exposures to potential source cases reported by more than 19,000 Ebola cases. We find transmission is highly variable, with evidence of super-spreading. Exposures have been concentrated within households and families, with exposure around death and at funerals playing a key role. Ebola Treatment Units provided more effective infection control than other health care facilities, and protection of health care workers improved over the course of the epidemic. We find that prompt hospitalization and reduced exposure from funerals predicts district-level epidemic intensity, suggesting that these measures contributed to epidemic control. Our findings contribute to the evidence-base for the control of Ebola.

Risk of disease and death in special populations

Most of the available data on risk of EVD are from health care and other front line workers. There are limited data on the risk of death and fetal and neonatal outcomes in pregnant women that indicate very high CFR among pregnant women and almost universal fetal loss or early neonatal death. A more detailed analysis of the available data from the current outbreak is being conducted by MSF, but was not available at the time of the WG review.

Health workers infections in Guinea, Liberia and Sierra Leone

Based on excerpts from "A preliminary report: Health worker Ebola infections in Guinea, Liberia and Sierra Leone" and additional analyses as requested.

See full "Preliminary report": **http://www.who.int/csr/resources/publications/ebola/health-worker-infections/en/**

Methods

- The Viral Haemorrhagic Fever (VHF) database, which was made available for these analyses by WHO headquarters, is comprised of the national VHF databases from Guinea, Liberia, and Sierra Leone. Ongoing efforts are underway to update and triangulate case information about cases from multiple sources. For these reasons, the number of health workers in this report is preliminary and may differ from the MOH Situation Reports
- The analyses in this study only include confirmed and probable EVD cases (suspected cases were excluded).
- Cumulative incidence was calculated using confirmed and probable cases from the beginning of the outbreak to March 31, 2015. The denominator data used to calculate the cumulative incidence rate is based on the most recent health workforce data obtained from the three

countries (Guinea: 2014[4], Sierra Leone: 2014[5], Liberia: 2015[6]). Workforce data from Liberia and Guinea were disaggregated by sex and age. Population figures for the cumulative incidence amongst the non-health worker population ≥ 15 years of age are based on estimates from the United Nations Department of Economic and Social Affairs, Population Division[7].

- Since the Human Resource databases of the countries are in the process of being updated, cumulative incidence rates were calculated only for selected registered professions where data were more complete.
- At the request of SAGE, analyses on additional types of health workers were performed with all associated limitations as described below.

Limitations

- First, under-reporting of health worker cases and conversely case duplications have been observed through special health workers studies. Therefore, it should be noted that these are preliminary data since the VHF databases of Liberia and Sierra Leone are currently being revised and updated. For this reason, our data might differ from those available in the countries. In addition, some health worker categories, particularly non-clinical health staff, such as hospital cleaners, ambulance drivers, burial team members, might not have been recorded as health workers. Finally, there is a significant number of suspected health worker infections for whom the final infection status remains unknown.
- Second, data were incomplete for some important variables for our analysis, such as health worker position.
- Third, the risk calculation is based on health workforce denominators which had its own limitations. Cumulative incidence rates were determined for selected health worker types where denominator data were likely to be most complete. Health worker denominators did not include the private sector and efforts are underway to improve the completeness and reliability of the Human Resource Information Systems. Future risk calculations will be able to utilize updated health worker denominator information for an expanded number of health worker types.

Results:

Health worker infection risk (**directly from Report**)

- The cumulative incidence was analyzed for "selected" health professions (medical doctors, registered nurses and laboratory technicians) for which the Human Resource databases may be more accurate and complete in the 3 countries. Depending on the health profession studied, the risk was between 21 to 32 times higher in health workers compared with non-health workers ≥ 15 years of age. While the risk of infection among those selected health workers is very high, it is however, much lower than the risk previously reported (Table 3).

[4] Guinea: Recensement biométrique des personnels de santé du Ministère de la Santé, République de Guinée, December 2014
[5] Sierra Leone: MOHS Human Resources for Health database, November 2014 (public sector only)
[6] Liberia: MOH Personnel Unit and MOH Office of Financial Management, February 2015 (public sector only)
[7] United Nations Department of Economic and Social Affairs, Population Division

Table 3: Cumulative EVD incidence rate for selected health worker types for the 3 countries combined, 1 Jan 2014 to 31 March 2015

	Cumulative incidence rate per 1000 (95% CI)	Rate ratio (95% CI)	p-value
Non-health workers ≥ 15 years	1.4 (1.4-1.4)	Reference	
Medical doctors	29.5 (22.6-36.4)	21.4 (17.0-27.1)	<0.01
Registered nurses	43.7 (37.5-49.9)	31.7 (27.5-36.6)	<0.01
Laboratory technicians	40.4 (26.2-54.6)	29.3 (20.7-41.7)	<0.01

Sources of health worker denominator data:

- *Guinea: Recensement biométrique des personnels de santé du Ministère de la Santé, République de Guinée, 2014*
- *Sierra Leone: MOH Human Resources for Health database, November 2014 (public sector only)*
- *Liberia: MOH Personnel Unit and MOH Office of Financial Management, February 2015 (public sector only)*
- *General population over 15 years of age are based on estimates from the Population Division, United Nations Department of Economic and Social Affairs.*

Additional analyses for SAGE-including all broad health worker categories:

Table 4: Cumulative EVD incidence rate and risk ratio by health worker categories for the 3 countries combined, 1 Jan 2014 to 31 March 2015

Health worker categories	Numerators	Denominators	Cumulative incidence rate per 1000	Risk Ratio (reference used: adult non-health workers)
Medical workers	**83**	**2854**	**29**	**21**
Registered nurses[1]	**183**	**4187**	**44**	**31**
Other nursing workers (include nurse assistants, aides and ATS but exclude MCHA[#])[1]	**163**	**9752**	**17**	**12**
Lab workers (includes lab techn and assistants)	**48**	**989**	**49**	**35**
Midwifery workers (registered midwife, midwife assistant, TBA**)+ MCHA (**maternal and child health aides)[#]	**50**	**3988**	**13**	**9**
Community health workers	**24**	**NA**	**NA**	**NA**
Pharmacy workers	**21**	**1335**		
Ambulance workers	**22**	**NA**	**NA**	**NA**
Trade and elementary workers (maintenance, cleaners, laundry, etc.)	**47**	**4110**	**11**	**8**
All others (surveillance, hygienists, counsellors, X-Ray, etc.)[2, 3]	**68**[3]	**1571**[3]	**43**	**31**
Health service management and admin	**9**	**3618**	**2.5**	**1.8**
Unknown positions	**97**	**NA**	**NA**	**NA**
All health workers (includes unknown positions)–upper level estimate	**815**	**32404**	**25**	**18**
All health workers excluding unknown positions-lower level estimate	**718**	**32404**	**22**	**16**
NON-HEALTH workers 15 years and older	**16231**	**11786439**	**1.4**	**reference**

1. Nursing workers were split in 2 categories since registered nurses had higher risk than other nursing workers which include nurse assistants, aides and ATS-agents techniques de santé (Guinea)
2. Include 1 burial team, 1 burial team/sprayer and 2 sprayers
3. Includes all other types of health workers for which the number of health care workers affected was less than 20 (except for Health service management and Admin used here to illustrate lowest risk among health workers). Includes also all types of health workers which could not be attributed to the other better defined categories because of limited info- therefore some of them may have been misclassified. Finally, denominator may not be accurate, hence, overestimating the risk.

Note: This differs from data reported in "A preliminary report" since MCHA were included under Nursing workers in the Report and are here included in Midwifery workers. In fact, their work is a blend of primary health and midwifery care (could likely be included in either one).

Based on the available data, with its limitations, three categories of risk were proposed to the WG, as shown in Table 5.

Table 5: Health worker categories by proposed level of risk among health workers

Higher risk level (direct contact with EVD patients or with infectious specimens)	Medium risk level (more limited or indirect contact with EVD patients)	Lower risk level among health workers (in principle, no contact with EVD patients)
Medical workers	All other health workers (excluding Health service management and admin)	Health service management and admin
Nursing workers (particularly registered nurses)		
Laboratory workers		

Note: unfortunately, the risk for burial workers, contact tracers, and community health workers could not be determined:

- first of all, because we do not have denominator data for these categories of health workers
- second, because there may have been under-reporting of, at least, burial workers and contact tracers as "health workers" since those positions were created in the context of the Ebola epidemic and may not have been considered and recorded as health workers.

Social Risk Factors for Ebola virus Transmission

The following draws together qualitative reports of the Ebola outbreak, and outlines some of the socio-cultural dimensions of Ebola virus transmission that should be taken account in prioritizing immunization efforts.

In general, anthropologists stress that behaviours in a situation of crisis are **highly dynamic** and many observations from the 2014-15 outbreak will be **context and time-specifi**c. There are, however, some general insights that are potentially relevant for prioritizing target groups for vaccination; or at the very least, in considering how best to approach deployment for future epidemics.

General Notes on population characteristics relevant for EVD risk

Ethnicity

- The affective region is home to a number of highly diverse cultural groups (e.g. Mende, Kissi, Kono, Krio, Temne, Fula, Mandingo/Malinké, and Toma/Loma) but share important commonalities of history and culture, and longstanding traditions of movement and mixing across national borders.

- The region has many religions, Christian, Muslim and 'traditional' beliefs, elements of which are often integrated into health and ritual practices. Depending on the locality, different community members will play a significant role in the care of the sick and preparation of the dead.

Social Geography

- National borders and identities will typically be of less relevance than local variations in practices—particularly true in rural areas, where many villages are highly self-reliant and there is a noticeable distrust of persons born outside the local community.
- Rural and 'interior' areas should not be considered to be separate or remote from urban areas, as people move frequently from village to town (and across national borders) for a wide array of social and economic reasons, including the search for health care.
- In crisis situations, people tend to return to family villages and avoid major conurbations.

Economy

- A long history of violence and resources extraction has entrenched population vulnerability and government distrust, exacerbated in rapidly expanding peri-urban settlements and isolated rural areas.

Gender

- Many people in the region belong to gender-specific initiation—or 'secret'—societies, which are central to the politics in the region and whose power has been reinforced by recent wars. These groups tend to be involved in funerary practices.
- Peripheral Health Units (PHUs) that offer primary care at the community level are often perceived as gendered facilities providing primarily maternal and child health care— a reflection of the substantial donor, government and NGO funds which have been channeled towards maternal and child health targets (most visible in the Free Health Care Initiative which offers free health care to pregnant women, nursing mothers and children under five).
- Since the outbreak, increasing gender-based violence has been reported and failure to observe safe-sex practices following recovery. Reports have focused on women; however, it is clear that men who have sex with men (MSM) are also at risk.

Key Points

1. Ethnic/religious differences are unlikely to map directly onto EVD risk.
2. Economic indicators are more relevant factors for EVD risk than cultural differences. Areas where there is limited access to basic infrastructure should be prioritized.
3. Engaging 'secret societies' can provide a critical foundation for community acceptance of a vaccine, it is equally important to approach these collectives with an appropriate local introduction to avoid suspicion and backlash.
4. The movement of populations across rural/urban areas and borders advises against prioritization of any one specific area and/or community over another.
5. As transmission rates drop, the likelihood of unpredictable flare-ups suggests that some special consideration should be given to local health providers in areas where services are scarce.

High Risk Socio-Cultural Domains

Reservoir Contact

- Bush meat consumption and trade are generally believed to precipitate EVD spill-over. A great deal of national and international policy attention and intervention has focused on bush meat sensitization and bans to varying success.
- Hunting of animals, which has continued fairly unabated in rural areas despite the ban, is generally carried out with dogs and machetes or traps designed and set by children. These varied practices, often occurring near the home rather than the 'bush', have raised some critical questions about other species as possible EVD vectors and other points and routes of spill-over.

Therapeutic Care

- In protecting 'Health Workers', attention should be given to the cohort of informal care-givers—traditional birth attendants, spiritual and private healers—who are usually the first to have contact with suspected cases.
- Where public services are weak and/or inaccessible, people tend to place trust in unofficial health providers for both everyday health needs and emergency care. These preferences often reflect a pragmatic response to a history of poor quality care rather than a deep-seated distrust of biomedicine.
- Belief in spiritual causes does not correlate to levels of education. People with secondary and tertiary education make sense of unfortunate events and circumstances in terms of spiritual causes.
- In times of panic, populations often tend to rely on more familiar styles of healthcare, traveling long distances to visit a traditional health practitioner with a good reputation.

Burials:

- Burials have been identified as key occasions for disease spread and amplification.
- Mortuary practices are generally orchestrated to enable the dead person to accede to the 'village of the ancestors,' where they might be reunited with their already-dead relatives and friends. A proper burial, performed in the deceased community of origin, is a key aspect of west African social life.
- There are several aspects of mortuary practices that may involving touching the bodies – e.g. the corpses is usually washed, oiled (often twice), wrapped in a fie cloth and re-clothed for burial.
- In general, men will prepare men and women, women. Corpse preparation and burial of leading members of the Secret Societies are matters for those societies and the procedures are secret.

Stigma/Marginalization

- Survivors face a number of challenges, from physical complications from the disease to social ostracisation and financial ruin. They face uncertainties about their risk of transmitting to others and also about potentially contracting the disease again.
- The risk of sexual transmission is a central concern for sex workers, both female and male.
- Drug users will also be at risk.

Key points

a. Children, who engage with animals in the context of play, may be the first points of contact but are often neglected in these campaigns.
b. Traditional or private healers, herbalists and birth attendants are often among the first to whom many infected with Ebola virus will turn. Health worker or frontline worker category must be expanded to include the diverse range of informal care providers
c. Burial practices are not standardized, have changed in response to the outbreak, and therefore, need to be discussed on a locality-by-locality basis. However, while practices differ, corpse preparation is often carried out by elders.
d. Pregnant women are at high risk and should be considered, also for program acceptability. If they must be excluded for safety reasons, alternatives and outreach programs should be devised.
e. Community members should be approached to ensure program acceptance.

Annex 1. Health worker categorization

Health workers categories	ISCO codes*	Examples of health worker positions entered in VHF database (English and French) – may include positions not usually included in the ISCO categories.
Medical workers	2211, 2212,	Doctor, MD, physician assistant, medical student, médecin, stagiaire en médicine
Nursing workers	2221, 3221	Nurse, nurse aide, nurse assistant, Maternal and Child Health (MCH) Aide, vaccinator, infirmier, Assistant Technique en santé (ATS, equivalent to nurse aide)
Midwifery workers	2222, 3222	Midwife, traditional birth attendant (TBA) , matronne, sage-femme
Ambulance Workers	3258	Ambulance worker, ambulancier, brancardier Note> ambulance drivers were included in this category but not the other drivers.
Laboratory workers	2312, 3141	Laboratory technician, laboratory aide
Pharmacy workers	2262, 3213	Pharmacist, dispenser, pharmacy technician, pharmacien,
Community Health care workers	3253	Community health worker, community health volunteer, community health assistant, CHO-community health officer, agent communautaire
Social work and counselling	2635	Social worker, mental health, HIV counsellor
Radiology workers	3211	Radiologist, X-ray technician, radiologie
Hygiene workers	No code	Burial team, sprayer, hygienist, hygiéniste, morgue
Trade and Elementary workers	No code	Maintenance, cleaner, janitor, housekeeper, laundry, driver, garcon de salle, agent d'entretien
Surveillance workers	No code	Surveillance officer, public health worker, contact tracer,
Health service management and administration	1342	Manager, hospital matron, Public health officer(PHO) Administrative, accountant, registrar, data clerk
Other	----	Security, volunteer, gardien, volontaire, etc.

*Codes from on the International Standard Classification of Occupations (ISCO, 2008 revision) used for broad categorization purpose only.

Annex 2: Background references for section on epidemiology (published literature)

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