NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

COMMUNICABLE DISEASES SURVEILLANCE BULLETIN

VOLUME 12. NO 4 NOVEMBER 2014

FOREWORD

The 2014 Ebola epidemic in West Africa has fast become an international public health emergency, yet there have been 23 Ebola virus outbreaks prior to the 2014 epidemic, most of which occurred in very secluded rural parts of equatorial Africa. A summary of Ebola disease outbreaks to date, with special emphasis on the 2014 epidemic, including possible reasons why it is so severe compared to previous outbreaks, is given in this issue.

Closer to home, South Africa's HIV epidemic marches on, yet monitoring HIV-related mortality in South Africa has proved to be particularly challenging. In this issue, the national reporting system and estimator models of HIV-mortality are critically reviewed, and recommendations to improve the accuracy of the data are given. The topic of HIV is further explored in the broader context of sexually transmitted infections (STIs) which facilitate the transmission and acquisition of HIV. Surveillance data on STIs in Johannesburg are given for the 2013/2014 period and emphasise the high rate of HIV co-infection in STI patients.

The 2014/2015 malaria season in South Africa has begun, and the malaria control programmes in Limpopo, Mpumalanga and KwaZulu-Natal provinces are just completing their annual insecticide spraying rounds. In order to make malaria control more efficient, new or better insecticide formulations are currently being developed, and this issue includes a recent evaluation of a new long-lasting insecticide formulation for controlling malaria vector mosquitoes.

Surveillance reports in this issue detail the 2013 rotavirus and severe acute respiratory illness (SARI) incidences and trends in South Africa. Importantly, the 2013 rotavirus season may signify a biennial "high" season, and the SARI surveillance programme has enabled descriptions of the prevalence of additional respiratory pathogens in patients with different clinical presentations at enhanced surveillance sites.

This is the final issue for 2014 and we wish all our readers and contributors a safe and joyous holiday season.

Basil Brooke, Editor

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EBOLA VIRUS DISEASE OUTBREAKS IN AFRICA AND THE 2014 EPIDEMIC

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Background

Ebola virus disease (EVD) has transgressed from a curious tropical disease of Africa to an international health emergency threat worldwide in 2014. The first occurrence of EVD was reported in 1976 in the Democratic Republic of Congo (then Zaire) during a highly fatal outbreak of haemorrhagic fever.[1] Since 1976 and before 2014, a total of 23 outbreaks of EVD has been reported in Africa (figure 1). During these outbreaks, 2,345 laboratory confirmed cases cumulatively were reported of which 1,541 were fatal.

The history of EVD has been characterized by unpredictable outbreaks in mostly secluded and very rural settings of equatorial Africa. The first outbreaks in 1976-1979 were followed by a period of apparent quiescence up to and including 1993 (figure 2). Since 1994, outbreaks of EVD have been recorded regularly in east and central Africa, but the 2014 EVD epidemic in West Africa is the first on record in this region and the largest in the history of outbreaks of this disease. At time of writing, the EVD situation in Guinea, Liberia and Sierra Leone continues to deteriorate with widespread and persistent transmission.

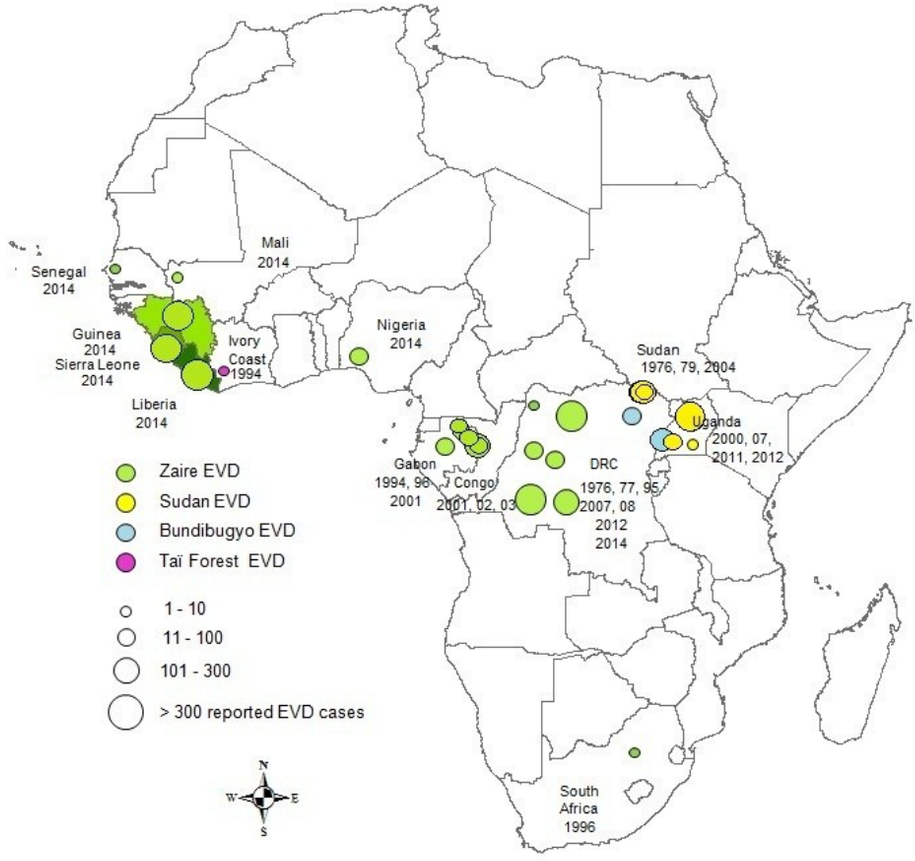
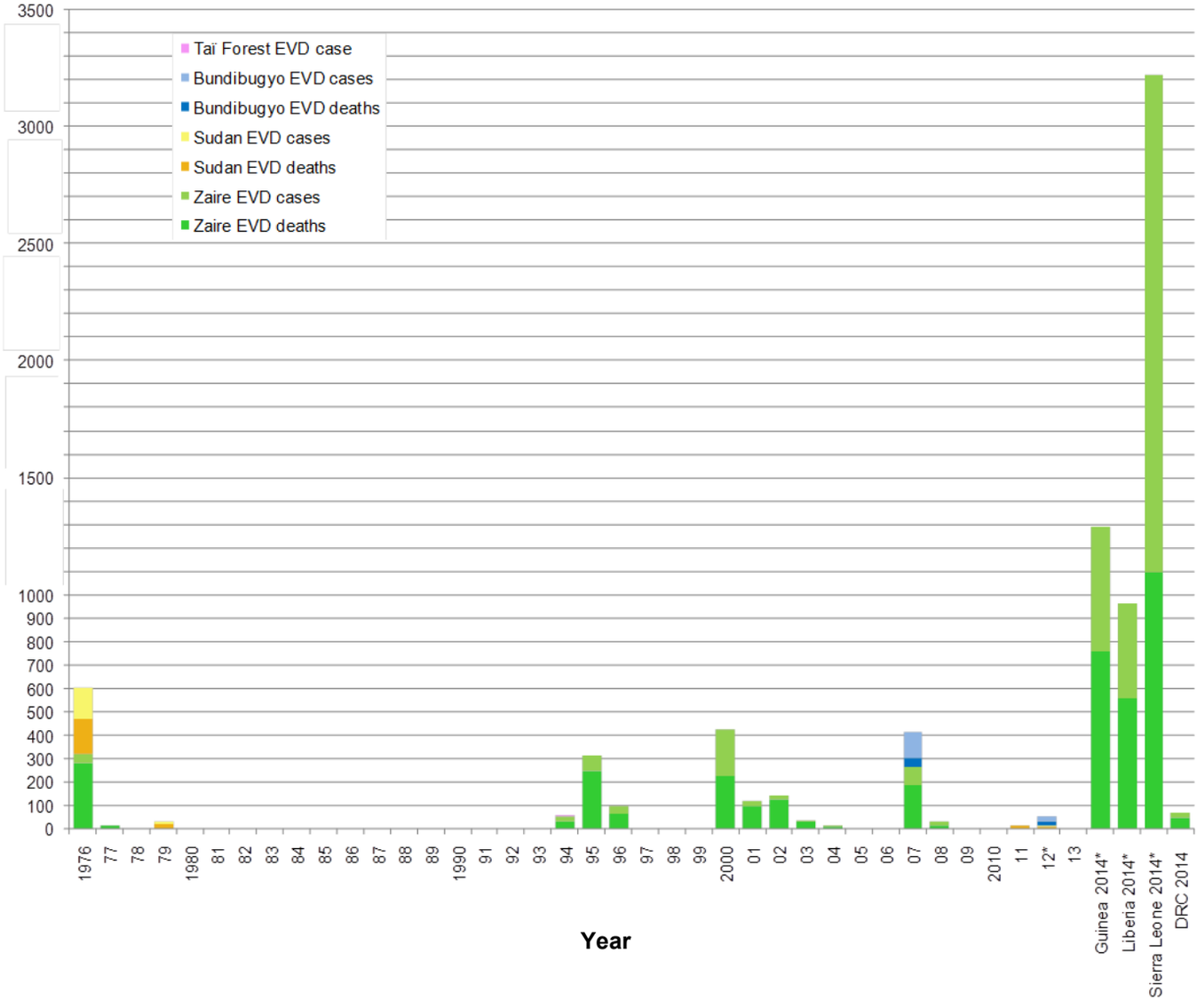


Figure 1: Geographical distribution of Ebola virus disease (EVD) outbreaks in Africa to date. Imported cases of EVD have been reported in South Africa in 1996 and in Senegal, Nigeria and Mali in 2014. (Adapted from data available on http://www.cdc.gov/vhf/ebola/outbreaks/history/distribution-map.html).



*lab-confirmed cases only

Figure 2: Time-line indicating outbreaks by region/country of Ebola virus disease by year to date (19 October 2014 for West Africa and 23 October 2014 for DRC). Numbers of cases and numbers of deaths are indicated for each outbreak. (From data available on http://www.cdc.gov/vhf/ebola/outbreaks/history/distribution-map.html)

Aetiology and ecology

Ebola virus disease is caused by infection with ebola virus species which are members of the *Filoviridae* family. This family includes three genera: *Cuevavirus*, *Ebolavirus* and *Marburgvirus*. These filoviruses are named for their filamentous, pleomorphic shape (figure 3). A total of five species of *Ebolavirus* are recognized to date: *Zaire ebolavirus, Sudan ebolavirus, Bundibugyo ebolavirus, Tai Forest ebolavirus* and *Reston ebolavirus.*[2] *Zaire ebolavirus* and *Sudan ebolavirus* have been associated with the most sizeable and fatal outbreaks in humans. The virus causing the current outbreak in West Africa has been identified as *Zaire ebolavirus* although the genomes of the circulating isolates are only 97% homologous to isolates from previous outbreaks.[3] Genetic characterization and

molecular clocking analysis has estimated the introduction of this virus into West Africa in 2004. It has been evolving in its ecological niche there ever since and apparently spilled over into the human population for the first time in 2013.[4]

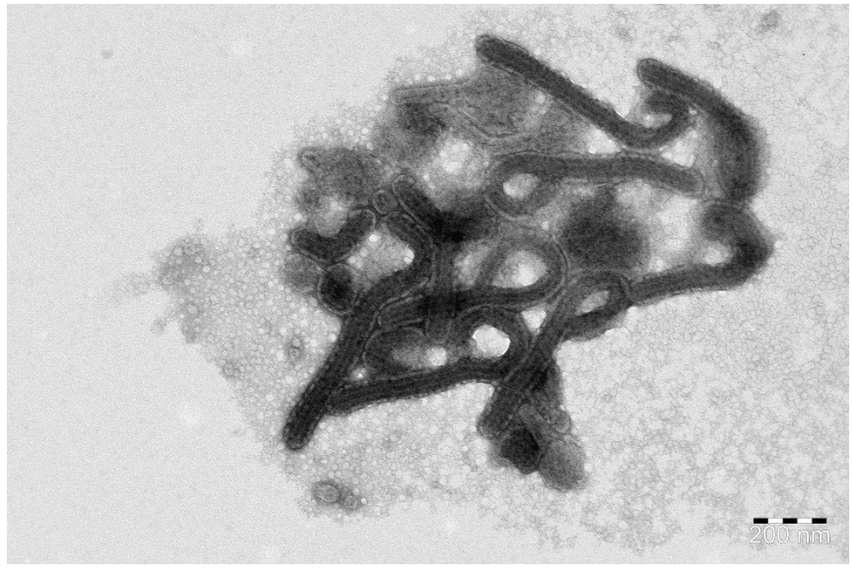


Figure 3: Electron micrograph of a cluster of Ebola virus virions
(Courtesy: Dr Monica Birkhead, NICD)

Current knowledge suggests that certain species of arboreal fruit bats are the natural reservoir for filoviruses.[5] The bats implicated as hosts are seemingly unaffected by infection with the ebola viruses but the exact mechanism of transmission within bat populations, and also from bats to other forest dwelling animals and humans, is not clear. Virus transmission through contact with infected blood and tissues of these bats, as well as other infected animals, is considered a major risk factor for spill over to the human population. Human-to-human transmission in turn occurs through direct contact with the blood and bodily fluids of a person infected with EVD - hence the propensity of outbreaks to perpetuate amongst families and in the healthcare setting. The World Health Organization estimates that up to 60% of cases reported during the 2014 West Africa outbreak are directly linked to exposures incurred through performing burial rites and ceremonies which include very intimate contact with the bodies of patients that died of EVD.[6]

Summary of the Ebola virus disease outbreak in West Africa to date

Case investigations have traced back the index case of the outbreak to a two year old child from the Guéckédou Prefecture in Guinea. The child died on the 6th December 2013.[3] The World Health Organization formally announced the outbreak in March 2014. This outbreak of EVD is unprecedented in many ways. Firstly, it is the first outbreak of EVD in this region of West Africa (figure 1). Secondly, it is the largest outbreak of EVD recorded to date with recorded cases (as of 19 October 2014) four times (at time of writing) the total number for all outbreaks prior to 2014 (figure 4). There are many socio-economic and public health related drivers that are fuelling the outbreak and thwarting conventional efforts to contain it.[7-9] The affected West African countries are some of the most impoverished in Africa with highly dysfunctional health care systems. In the aftermath of the civil conflicts that have characterized the recent histories of these

countries, the health and other infrastructure remains dilapidated. Hospitals are ill equipped and, in Liberia, one medical doctor is available per 100,000 of the population.[10] The poor health system correlates with a poor disease surveillance capacity and inability to recognize disease outbreaks and trends. In addition, the literacy rates of these countries are amongst the worst in Africa which in turn complicates effective communication to communities and social mobilization, which are integral parts of outbreak control and prevention measures. Mobility between communities in the region is common with people travelling for social and economic reasons in-country as well as across borders. These factors, including the late recognition of the outbreak, contribute to the wide and increasing distribution of EVD cases in affected countries.

Although the outbreak has remained largely confined to Guinea, Liberia and Sierra Leone, a total of four cases have been exported outside of these borders since July 2014. The first case involved a Liberian national travelling to Lagos, Nigeria. The patient was identified and isolated but set off a nosocomial outbreak resulting in a total of 20 cases. The outbreak has since been contained.[11] A case of EVD was confirmed in Dakar, Senegal, involving a Guinea national who travelled via bus to the city, with no secondary cases. In September 2014, a person travelling from Liberia to the USA was diagnosed and hospitalised for EVD. To date, two additional cases of EVD have been noted in nurses who tended to this patient. Likewise, there has been a secondary infection involving a nurse who cared for a patient evacuated for treatment of EVD in Spain. In October 2014, a young child whose mother died of EVB in Guinea was brought back to Mali. This child consequently developed and died of EBV.

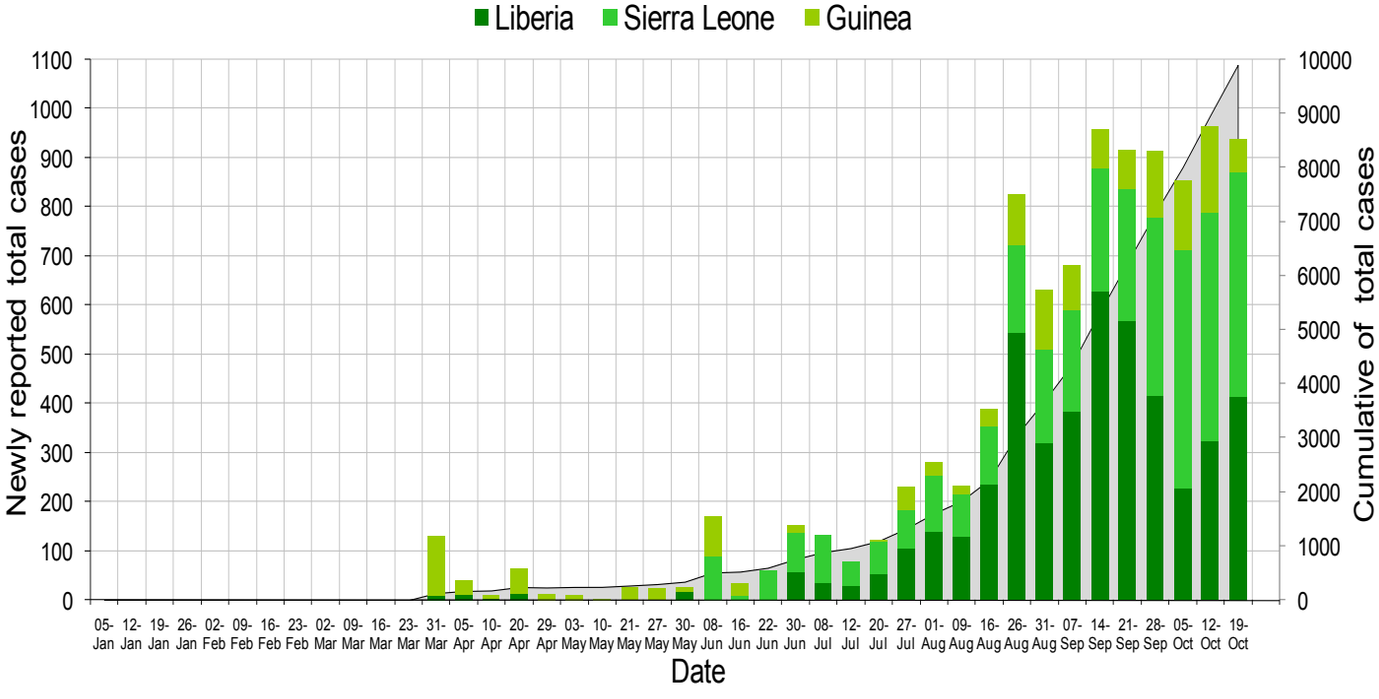


Figure 4: Epidemic curve for the current Ebola virus disease outbreak in Guinea, Liberia and Sierra Leone by date from the initial announcement of the outbreak in March 2014 (adapted from total case data reported by the Centers for Disease Control and Prevention and World Health Organization as of 19 October 2014).

Summary on Ebola virus disease outbreak in the Democratic Republic of Congo to date (19 October 2014)

A total of six EVD outbreaks were recorded in the Democratic Republic of Congo (DRC) from 1976 to 2012. Three of these outbreaks have occurred since 2007. It is noteworthy that more than 40% of all EVD cases reported before 2014 occurred in the DRC during these outbreaks. In August 2014 the World Health Organization was notified of an EVD outbreak in the Equateur Province of the DRC. The index patient was a pregnant female who was involved in the slaughtering and handling of bush meat prior to her death. A total of 68 cases of which 49 had a fatal outcome have been reported to date. Molecular sequencing analysis has shown that the ongoing outbreaks in the DRC and West Africa are unrelated.[17]

South African laboratory capacity for responding to the Ebola virus disease outbreak

The National Institute for Communicable Diseases (NICD) has a long-standing history of conducting laboratory investigations of potential haemorrhagic fever cases in South Africa and the southern African region. After the first reports of Lassa, Ebola and Marburg fevers in the 1960s and 1970s, a decision was made to establish a Biosafety Level 4 (BSL4) facility in South Africa. This laboratory was commissioned in 1980 as a strategic national and regional facility for responses to African haemorraghic fevers. It is currently managed by the Centre for Emerging and Zoonotic Diseases (CEZD) of the NICD and is the only maximum security facility operating in Africa (figure 5). CEZD is recognized as a World Health Organization Collaborating Center for Reference and Research of Viral Haemorrhagic Fevers and Arboviruses. It is also a member of the WHO Emerging and Dangerous Pathogens Laboratory Network to perform diagnosis and investigation of outbreaks caused by highly dangerous pathogens. Apart from the laboratory capacity to diagnose such cases, the NICD is also providing support to the National Department of Health in terms of contributions to the development of relevant guidelines, testing of potential cases, identification of risk cases and outbreak response measures. CEZD has confirmed nearly 200 cases of CCHF in South Africa since 1981[10], and has also been involved in the investigation and confirmation of imported haemorrhagic fever cases over several decades (table 1).[12-15] Since April 2014, a total of 18 suspected cases of haemorrhagic fever were tested for EVD in South Africa. At time of writing no cases of EVD have been confirmed in South Africa.

Figure 5: Scientists working in the Biosafety Level 4 facility at the National Institute for Communicable Diseases (NICD), Sandringham, Johannesburg.

Table 1: Summary of sporadic imported cases of viral haemorrhagic fever in South Africa, 1975 to date (October 2014).

Year	Brief outbreak history	Number of secondary cases identified	Viral haemorrhagic fever diagnosed	Reference #
1975	Australian backpacker travelled from Zimbabwe to South Africa. Possible exposure to bats during trip. Patient died	Two cases (nurse and travel companion), resulting in one fatality	Marburg virus disease	13
1996	Gabonese healthcare worker travelled to South Africa and presented to a Johannesburg hospital Patient recovered	One case (nurse), resulting in one fatality	Ebola virus disease	14
2007	Nigerian healthcare worker treated in South African hospital for presumptive diagnosis of typhoid fever. Patient died	No secondary cases	Lassa fever	Unpublished
2008	Index case from Zambia evacuated to South Africa for medical treatment with presumptive diagnosis of tick bite fever. Patient died	Three secondary cases (paramedic, nurse and hospital cleaner, all fatal) and one tertiary case (nurse, not fatal)	Lujo fever	15

Field laboratory support in Sierra Leone

Laboratory diagnosis of suspected EVD cases plays an integral part in the effort to combat the ongoing EVD outbreak in West Africa. Rapid confirmation of Ebola virus infectious status of individuals is critical for patient management and isolation, but also for contact tracing and identification of probable new transmission chains. Owing to a lack of capacity and expertise in EVD diagnosis within the health care systems of the affected countries, mitigation of this problem can be achieved by deployment of mobile laboratories from institutions and agencies that do have the necessary experience. The National Institute for Communicable Disease Mobile Laboratory Unit (NICD MLU) was deployed through the mechanism of the Global Outbreak Alert and Response Network (GOARN) of the World Health Organization (WHO) on the 17th of August, 2014, in order to set up Ebola diagnostic capacity in Freetown, Sierra Leone. As of the 23rd of October, 2014, the NICD MLU had tested a total of 2,497 submissions from suspected EVD cases, amounting to an average of 42 samples tested daily during 9 weeks of operation (figure 6).

An additional duty of the NICD MLU is to strengthen Sierra Leone's capacity to deal with the current and future outbreaks of EVD. Training and integration of Sierra Leonean laboratory personnel in operation of the MLU is ongoing. The continued operation of the NICD MLU is highly appreciated by Sierra Leonean authorities and organizations involved in controlling the outbreak, particularly the World Health Organization, and it is expected to play an important role in the coming months to support containment efforts.

Figure 6: Professor Janusz Paweska and Dr. Petrus Jansen van Vuren performing inactivation of blood specimens submitted from suspected EVD patients in Freetown, Sierra Leone.

Conclusion

The intervention strategies designed to contain the outbreak of EVD in West Africa have still to bear fruit. The World Health Organization stipulates in its roadmap the goal of containing the outbreak in the next six to nine months.[16] The NICD is providing an expert laboratory diagnostic service for EVD nationally as well as regionally for the SADC community. The NICD is also supporting international efforts to contain the EVD outbreak in West Africa by providing much needed laboratory diagnosis of EVD in Sierra Leone.

Acknowledgments

Acknowledgement is due to the staff of the Center for Emerging and Zoonotic Diseases and extended staff of the NICD, in particular the Division for Public Health Surveillance and Outbreak Response, who are playing an integral role in providing an uninterrupted and reliable diagnostic service for EVD in South Africa. A special thanks to all staff members that have contributed to the work being done in Sierra Leone.

References

1. World Health Organization. Ebola haemorrhagic fever in Zaire, 1976. *Bull World Health Org* 1978; 56: 271-93.
2. Carrol SA, Towner JS, Sealy TK et al. Molecular evolution of viruses of the Family Filoviridae based on 97 whole-genome sequences. *J Virol* 2013; 87(5): 2608-2616.
3. Baize S, Pannetier D, Oestereich L et al. Emergence of Zaire Ebola virus disease in Guinea – preliminary report. *NEJM* 2014; DOI:10.1056/NEJMoa1404505.
4. Gire SK, Goba A, Andersen KG et al. Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. *Science* 2014; DOI: 10.1126/science.1259657.
5. Groseth A, Feldmann H, Strong, JE. The ecology of Ebola virus. *Trends Microbiol* 2007: 15(9): 408-416.
6. World Health Organization. Sierra Leone: A traditional healer and a funeral. http://www.who.int/csr/disease/ebola/ebola-6-months/sierra-leone/en/ (Accessed: 24 October 2014).
7. Weyer J, Blumberg LH, Paweska JT. Ebola virus disease in West Africa – an unprecedented outbreak. *SAMJ* 2014; 104 (8): 555-556.

8. Fauci AS. Ebola – underscoring the global disparities in health care resources. *NEJM* 2014; 371(12): 1084-1086.
9. Chan M. Ebola virus disease in West Africa – no early end to the outbreak. *NEJM* 2014; 371: 1183-1185.
10. World Health Organization. Ebola situation in Liberia – non-conventional interventions needed. http://www.who.int/mediacentre/news/ebola/8-september-2014/en/ (accessed 24 October 2014).
11. World Health Organization. WHO declares end of Ebola outbreak in Nigeria. http://www.who.int/mediacentre/news/statements/2014/nigeria-ends-ebola/en/ (accessed 24 October 2014).
12. Kemp A, Msimang V, Weyer J, Paweska JT. Crimean-Congo haemorrhagic fever and tick bite fever in South Africa, 2012-2014. *Communicable Diseases Surveillance Bulletin* 2014; 12(3):59-62.
13. Gear JSS, Cassel GA, Gear AJ, et al. Outbreak of Marburg virus disease in Johannesburg. *BMJ* 1975; 4:489-493.
14. Richards GA, Murphy SRN, Jobson R. Unexpected Ebola virus in tertiary setting: Clinical and epidemiological aspects. *Crit Care Med* 2000; 28(1):240-244.
15. Paweska JT, Sewlall NH, Kziasek TJ, et al. Nosocomial outbreak of novel arenavirus infection, southern Africa. *Emerg Infect Dis* 2009; 15(10):1598-1602.
16. World Health Organization. Ebola response roadmap. https://extranet.who.int/ebola/# (accessed 24 October 2014).
17. World Health Organization. Virological analysis: no link between Ebola outbreaks in West Africa and Democratic Republic of Congo. http://www.who.int/mediacentre/news/ebola/2-september-2014/en/ (accessed on 27 October 2014).

MONITORING HIV-RELATED MORTALITY IN SOUTH AFRICA: THE CHALLENGES AND URGENCY

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Background

It is estimated that 6.4 million persons were living with HIV/AIDS (PLHIVA) in South Africa in 2012, with 370,000–450,000 HIV infections newly acquired.[1] Global data demonstrate that antiretroviral therapy (ART) use has led to decreased morbidity and mortality from HIV-related causes.[2-5] South Africa has mounted a vigorous response to its HIV epidemic by massively scaling up the provision of ART. By the end of 2012, an estimated 2.1 million persons were on ART. This has led to a significant increase in life expectancy in South Africa. In rural South Africa, the expanded ART roll-out has been shown to reduce HIV-related mortality by approximately 22% in men and 29% in women.[6] This reduction occurred in a setting characterised by a very high HIV prevalence and a high mortality attributable to HIV. Furthermore, the success of the prevention of mother-to-child transmission of HIV programme, as witnessed by reductions in vertical HIV transmission rates (from approximately 14% in 2004 to <3% in 2011), has

resulted in major decreases in mortality in infants and children under 5 years.[7]

Reliable data that illustrate trends in HIV/AIDS mortality are critical for the measurement and tracking of the impact of ART roll-out and for the implementation of the national strategic plan.[8] In this report, the national reporting system and estimator models of HIV-mortality are critically reviewed, and recommendations to improve the accuracy of the data are given.

Under-reporting of HIV/AIDS-related deaths

Mortality reports released by Statistics South Africa have consistently indicated that 3.4% of deaths in South Africa are HIV/AIDS-related.[9,10] Deeper analysis of these data suggest that this is likely a significant under-estimate because other causes of death known to be associated with HIV/AIDS were also reported. In 2010, other viral diseases, tuberculosis (TB), influenza and pneumonia, and infectious intestinal diseases accounted for 2.3%, 12%, 7.2% and 5% of all deaths respectively. Furthermore, infectious and parasitic diseases were the leading causes of death in 2010 (134,678/543,856 = 24.8%). The rankings of the main infectious disease groups have remained stable since 2008, and it is probable that many of these are indicator diseases for HIV (table 1).

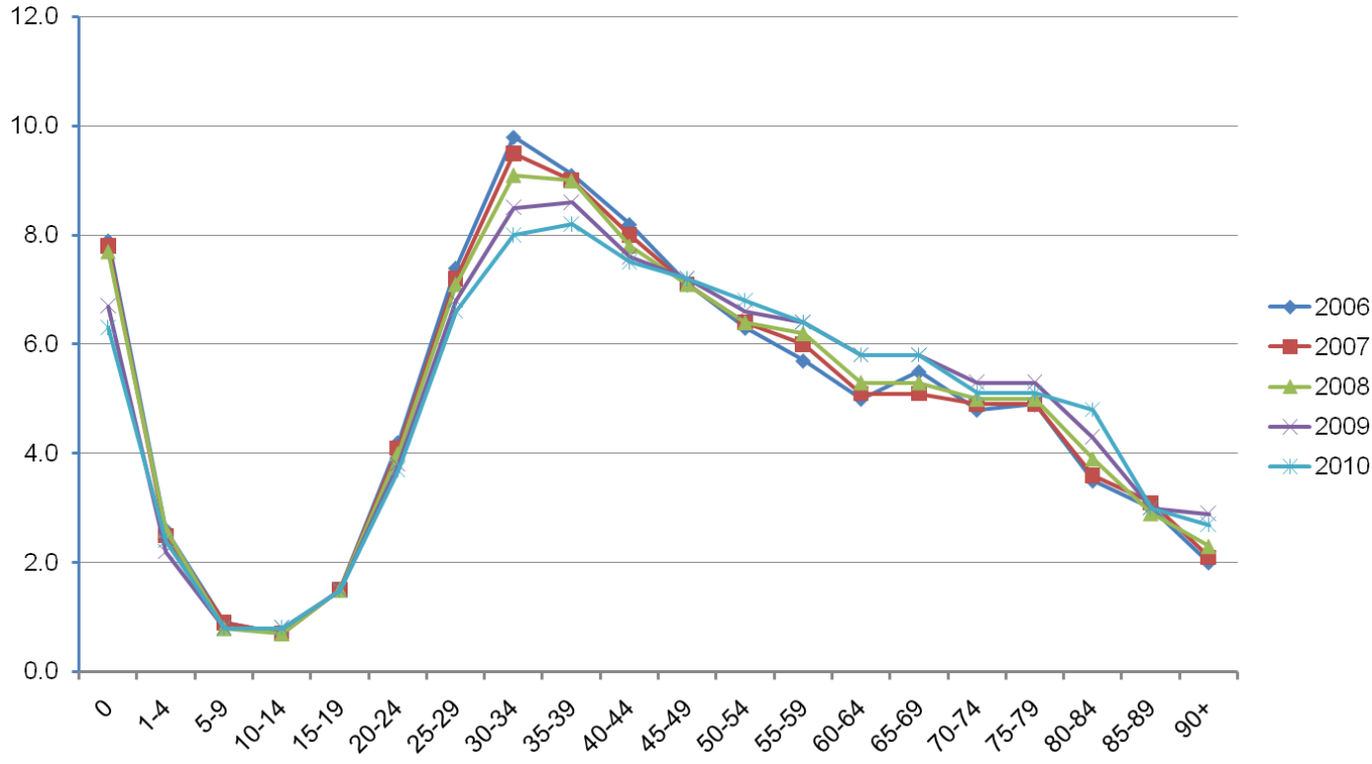
The mortality estimates show that the highest proportions of deaths occurred in the 30-39 year age group (16.2%) during the period 2006-2010, consistent for a region experiencing a generalised HIV epidemic. However, it should be noted that the proportion of deaths in this age group decreased steadily from 18.9%

Table 1: Causes of death by case incidence in South Africa by rank, 2008 to 2010. Table adapted from Statistics SA 2010 Mortality Estimates Report.

Causes of death (based on ICD-10)	2008			2009			2010		
	Rank	Number	%	Rank	Number	%	Rank	Number	%
Tuberculosis (A15-A19)*	1	75,281	12.6	1	69,791	12	1	62,827	11.6
Influenza and pneumonia (J09-J18)	2	45,826	7.7	2	43,449	7.5	2	39,027	7.2
Intestinal infectious diseases (A00-A09)	3	39,530	6.6	3	31,070	5.4	3	27,383	5
Other forms of heart disease (I30-152)	4	26,327	4.4	4	26,738	4.6	4	25,827	4.7
Cerebrovascular diseases (I60-I69)	5	24,473	4.1	5	25,062	4.3	5	24,664	4.5
Diabetes mellitus (E10-E14)	6	19,636	3.3	6	20,680	3.6	6	21,475	3.9
HIV disease (B20-B24)	7	15,179	2.5	7	17,785	3.1	7	18,325	3.4
Hypertensive diseases (I10-I15)	10	14,236	2.4	8	15,486	2.7	8	14,890	2.7
Chronic lower respiratory diseases (J40-J47)	9	14,338	2.4	9	14,334	2.5	9	13,099	2.4
Other viral diseases (B25-B34)							19	12,332	2.3
Certain disorders involving the immune mechanism (D80-D89)	8	14,728	2.5	10	13,256	2.3			
Other natural causes		252,720	42.4		251,777	43.4		235,630	43.3
Non-natural causes		53,350	9		50,283	8.7		48,377	8.9
All causes		**596,624**	**100**		**579,711**	**100**		**543,856**	**100**

*including deaths due to MDR-TB and XDR-TB

Figure 1: Percentage distribution of death by age and year, South Africa, 2006-2010. Adapted from Statistics SA 2010 mortality estimates report.



While the proportion of completed death registrations is high (estimated to be 93%, with late registration ~2%), HIV/AIDS-related deaths are substantially under-reported. Data quality hampers the utility of the database because up to 45% of death certificates contain errors.[11] Stigma associated with HIV infection, low HIV testing uptake, fears over health insurance benefit loss and confidentiality have been identified as causes for poor data quality.

Groenewald et al.[12] attempted to estimate the degree of misclassification of HIV/AIDS deaths in the vital registration system by examining increases in age-specific mortality patterns over time for HIV indicator illnesses that matched the age-specific mortality pattern of HIV deaths. Nine other diseases were found to match the age pattern of HIV deaths.[12] The misclassified deaths were added to those classified as HIV related through vital registration.

The Medical Research Council Burden of Disease Research Unit (MRC BoD) assists with the collation and analysis of South African mortality reports. They have made great strides in adjusting reported figures using different approaches in order to improve the outputs.[13-16] Substantial errors on the death notification forms (DNF) have been identified, with a third of these serious enough to affect the identification of underlying cause of death. In another study the MRC BoD compared information obtained from medical records against cause-of-death on the DNF and found that only 50% were in agreement.[17] By introducing correction factors for key diseases, it became apparent that HIV had been under-reported by 53.6% (12% vs. 18.4% cause-of-death from DNF vs medical records respectively) and that TB had been over-reported by 26.8% (5.8% vs. 4.3%). It was also established that a cause of death could be allocated in 81% of cases where no cause had been defined.

Modelling HIV mortality

There are three different models that have been used to estimate HIV mortality across South Africa. These models rely on prevalence data from the antenatal and household surveys as well as programme data as inputs. The latest Actuarial Society of South Africa (ASSA) estimates released in 2011 and using the 2008 model estimated that HIV/AIDS-related mortality decreased from 257,000 in 2005 to 194,000 in 2010.[18] This differs from the UNAIDS SPECTRUM model that estimated AIDS-related mortality stabilising at ~350,000 deaths per annum until 2010 and then declining rapidly to 24,000 in 2011.[19] The Thembisa model estimated 145,000 (95% CI: 134,000-156,000) AIDS-related deaths in 2011/2012.[20] These three models vary because of differing assumptions, but, importantly, they are only as good as the data that inform them. They all rely on estimates of the number of people receiving ART to calculate estimates of mortality rates. For these models to be accurate, it is critical that the underlying data used are accurate, and that they take into account patients accessing ART from more than one site, ART adherence, and retention in ART programmes.

Comparison of national mortality reports and modelled estimates

Compared to all three modelling estimates, the Stats SA / vital registration system reported HIV mortality numbers that were approximately 10-20 times lower than expected for 2010. Even after assuming all 134,678 (24.8%) deaths from infectious diseases and 73,149 (13.5%) deaths due to unspecified causes were attributable to HIV, this number is still far short of the 190,000 to 340,000 deaths predicted/estimated by mathematical models for 2010.

Conclusion and recommendations

The number and proportion of HIV/AIDS related deaths has been and is likely to be substantially underestimated. There are significant disparities between the estimates of HIV-AIDS related mortality in South Africa. This true for comparisons between the modelled estimates as well as comparisons between modelled estimates and vital registration sources.

Measurement of HIV/AIDS related deaths is critical for monitoring the impact of HIV/AIDS public health interventions. Building locally enhanced mortality surveillance systems with a focus on data quality is necessary in order to improve cause-of-death reporting in South Africa. In addition, training of doctors in death certification, a review of the confidentiality of HIV-related death notifications as well as an exploration of societal barriers to accurate vital death registration are necessary steps to improve cause-of-death reporting. It is also important to review the accuracy of the ART coverage data that inform models that estimate mortality so as to ensure accuracy.

References

1. Shisana O, Rehle T, Simbayi LC, Zuma K, Jooste S, Zungu N, Labadarios D, Onoya D et al. (2014) South African National HIV Prevalence, Incidence and Behaviour Survey, 2012. Cape Town, HSRC Press.
2. Hogg RS, Heath KV, Yip B, Craib KJP, O'Shaughnessy MV, Schechter MT, et al. Improved survival among HIV-infected individuals following initiation of antiretroviral therapy. *JAMA* 1998; 279: 450-4 doi: 10.1001/jama.279.6.450 pmid: 9466638.
3. The Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration. ART Cohort Collaboration (ART-CC) groups. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet* 2006; 367: 817-24 doi: 10.1016/S0140-6736(06)

68337-2 pmid: 16530575.

4. Abbas UL, Anderson RM, Mellors JW. Potential impact of antiretroviral therapy on HIV-1 transmission and AIDS mortality in resource-limited settings. *J Acquir Immune Defic Syndr* 2006; 41: 632-41 doi: 10.1097/01.qai.0000194234.31078.bf pmid: 16652038.
5. Blacker J. The impact of AIDS on adult mortality: evidence from national and regional statistics. *AIDS* 2004; 18: S19-26 pmid: 15319740.
6. Herbst AJ, Cooke GS, Bärnighausen T, KanyKany A, Tanser F, Newell M. Adult mortality and antiretroviral treatment roll-out in rural KwaZulu-Natal, South Africa. *Bull World Health Organ* 2009; 87:754-762. doi: 10.2471/BLT.08.058982.
7. Goga AE, Dinh TH, Jackson DJ for the SAPMTCTE study group. Evaluation of the effectiveness of the national Prevention of Mother-to-Child Transmission (PMTCT) programme measured at six weeks postpartum in South Africa, 2010. South African Medical Research Council, National Department of Health of South Africa and PEPFAR/US Centers for Disease Control and Prevention, 2012.
8. National Strategic Plan on HIV, STIs and TB: 2012-2016, National Department of Health of South Africa, 2012.
9. Mortality and causes of death in South Africa, 2010: Findings from death notification. Statistics SA, 2013.
10. Statistics SA 2011 Mortality Estimates. Statistics South Africa, Pretoria, South Africa.
11. Birnbaum JK, Murray CJ, Lozano R. Exposing misclassified HIV/AIDS deaths in South Africa. *Bull World Health Organ*. 2011; 89(4):278-85. doi: 10.2471/BLT.11.086280.
12. Groenewald P1, Nannan N, Bourne D, Laubscher R, Bradshaw D. Identifying deaths from AIDS in South Africa. *AIDS* 2005; 19(2):193-201.
13. 2008 Cause of Death by Province, MRC. Medical Research Council, Pretoria, South Africa.
14. 2010 Cause of death statistics for South Africa: Challenges and possibilities for improvement. Available from: http://www.mrc.ac.za/bod/cause_death_statsSA.pdf.
15. Nojilana B, Groenewald P, Bradshaw D, Reagon G. Quality of cause of death certification at an academic hospital in Cape Town, South Africa. *S Afr Med J* 2009; 99(9):648-52.
16. 2010 Western Cape Mortality Profile. Available from: http://www.mrc.ac.za/bod/WC2010Report.pdf. Accessed 16 August 2014.
17. Bradshaw D. Cause of Death certificates for South Africa: challenges and possibilities for improvement. MRC BoD, 2010.
18. Actuarial Society of South Africa. ASSA 2008 AIDS and Demographic Model; 2011. Available from: http://aids.actuarialsociety.org.za/models-3145.htm. Accessed 16 August 2014.
19. Stover J. Updates to the Spectrum/Estimation and Projection Package (EPP) model to estimate HIV trends for adults and children. *Sex Transm Infect* 2012; 88:11–i16. doi:10.1136/sextrans-2012-050640.
20. Johnson L. THEMBISA version 1.0: A model for evaluating the impact of HIV/AIDS in South Africa, University of Cape Town, 2014.

MICROBIOLOGICAL SURVEILLANCE OF SEXUALLY TRANSMITTED INFECTIONS IN JOHANNESBURG, GAUTENG PROVINCE, 2013-2014

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Introduction

According to 2008 WHO estimates, 499 million new cases of curable sexually transmitted infections (STIs) occur annually throughout the world in adults aged 15-49 years.[1] In developing countries, STIs and their complications rank in the top five disease categories for which adults seek health care. Surveillance of the prevalence of STIs is as a key priority in public health. Accurately monitoring the incidence and prevalence of STIs among the population and particularly STI patients is important in terms of measuring the effects of disease control and prevention.

The syndromic approach to the treatment of STIs has been vital in rationalizing and improving the management of these infections.[2] STI control in low-income countries is shaped by case management guidelines promoting syndromic management. The syndromic approach does not require identification of the underlying aetiology. Instead, it is based on the identification of a syndrome ie., a group of symptoms and easily recognizable signs associated with a number of well-defined aetiologies. Treatment is provided locally for the majority of the organisms responsible for each syndrome.[2,3]

The common STI syndromes are vaginal discharge syndrome (VDS) – women presenting with genital discharge, male urethritis syndrome (MUS) – males presenting with penile discharge, and genital ulcer syndrome (GUS) in both men and women. Syndromic management is simple, assures rapid, same-day treatment, and avoids the expensive diagnostic tests that are often unavailable in resource-limited settings. Periodic aetiological surveillance of STI syndromes is a critical component of the syndromic management approach of STIs as it validates existing algorithms and ensures that all major pathogens are covered in treatment algorithms.

The aim of this survey in Johannesburg, South Africa, was to determine a) the aetiology of the male urethritis syndrome (MUS), vaginal discharge syndrome (VDS) and genital ulcer syndrome (GUS); b) the prevalence of HIV co-infection in patients with these STI syndromes; and c) the antimicrobial susceptibility of Neisseria gonorrhoeae isolates to cefixime, ceftriaxone and ciprofloxacin. A total of 437 consecutive STI patients were recruited (186 VDS, 196 MUS and 55 GUS). Pathogens were detected by multiplex polymerase chain reaction (M-PCR) on swabs collected from these cases. Smears from VDS cases were examined for the presence of bacterial vaginosis (BV) and candidiasis by microscopy.

Aetiology of common STI syndromes

During the 2013 and 2014 surveys, *Neisseria gonorrhoeae* remained the most common aetiological agent detected (80.1%, 157/196) followed by *Chlamydia trachomatis* (28.6%, 56/196) among males with male urethritis syndrome, and among females with vaginal discharge syndrome, bacterial vaginosis was the most common aetiological agent followed by *Candida* sp. and *Trichomonas vaginalis* (102/184 - 55.4%; 41/184 - 22.3%; and 37/186 - 19.9%, respectively). These data are shown in tables 1 and 2. In both the 2013 and 2014 surveys, herpes remained the most frequent cause of genital ulceration, accounting for 68.1% (32/47) and

61.8% (34/55) of GUS cases detected by M-PCR respectively. Syphilis was the second most frequent cause of genital ulceration. No lymphogranuloma venereum (LGV), chancroid and donovanosis cases were detected in 2014 (table 3). There was a statistically significant decrease in the relative prevalence of *Trichomonas vaginalis* (TV) in women between 2013 and 2014. Syphilis remained an infrequent but important cause of genital ulceration and no cases of lymphogranuloma venereum were observed.

HIV co-infection amongst STI patients remained relatively high in 2014. In 2014, HIV co-infection was 30.1% among those with male urethritis syndrome, 40.3% among those with vaginal discharge syndrome and 46.3% among those with genital ulcer syndrome. HIV co-infection rates in 2014 were not significantly different from those in 2013 (table 4).

Table 1: The prevalence (%) of STI pathogens in patients presenting with male urethritis syndrome in Johannesburg during 2013 and 2014.

Pathogen	2013 (n=111)	2014 (n=196)	*P value
Neisseria gonorrhoeae	83.9	80.1	0.45
Chlamydia trachomatis	28.8	28.6	1.00
Mycoplasma genitalium	7.2	6.1	0.53
Trichomonas vaginalis	4.5	3.1	0.81

* P values reflect significance of difference between 2013 and 2014 data based on Fischer's exact tests.

Table 2: The prevalence (%) of STI pathogens and bacterial infections in patients presenting with vaginal discharge syndrome in Johannesburg during 2013 and 2014.

Pathogen or condition	2013 (n=190)	2014 (n=186)	*P value
Neisseria gonorrhoeae	17.9	17.7	1.00
Chlamydia trachomatis	16.8	19.9	0.51
Trichomonas vaginalis	31.6	16.1	**0.001**
Mycoplasma genitalium	13.8	11.3	0.53
Bacterial vaginosis	55.3	55.4	0.16
Candidiasis	18.9	22.3	0.90

* P values reflect significance of difference between 2013 and 2014 data based on Fischer's exact tests.

Table 3: The prevalence (%) of STI pathogens amongst patients with genital ulcer syndrome in Johannesburg during 2013 and 2014.

Pathogen	2013 (n=47)	2014 (n=55)	P value
Herpes simplex virus	68.1	61.8	0.54
Treponema pallidum	4.3	3.6	1.00
Haemophilus ducreyi	0.0	0.0	-
Chlamydia trachomatis L1-L3	2.1	0.0	0.46
Klebsiella granulomatis	0.0	0.0	-
No pathogens detected	27.7	34.6	0.52

* P values reflect significance of difference between 2013 and 2014 data based on Fischer's exact tests.

Table 4: HIV seroprevalence (%) amongst patients presenting with male urethritis syndrome (MUS), vaginal discharge syndrome (VDS) and genital ulcer syndrome (GUS) in Johannesburg during 2013 and 2014.

Syndrome	2013	2014	P value
MUS	31.5	30.1	0.80
VDS	41.8	40.3	0.06
GUS	57.5	46.3	0.32

* P values reflect significance of difference between 2013 and 2014 data based on Fischer's exact tests.

Antimicrobial Susceptibility

All isolates of *Neisseria gonorrhoeae* were susceptible to the cephalosporin antibiotics cefixime and ceftriaxone. Above forty percent of *Neisseria gonorrhoeae* isolates (41.7%, 71 /151) were resistant to ciprofloxacin. This was similar to data from 2013 (43.9%, 40/92).

Conclusions

Gonorrhoea remained the commonest cause of male urethritis syndrome whereas bacterial vaginosis showed the highest prevalence among females with vaginal discharge syndrome. Amongst females, *Neisseria gonorrhoeae*, *chlamydia trachomatis*, *trichomonas vaginalis* and *mycoplasma genitalium* all showed a prevalence range of 11-20%. These findings support current STI syndrome treatment algorithms for each pathogen.[4]

Oral cefixime is the current first line antibiotic of choice in South Africa for the treatment of gonorrhoea. Intramascular ceftriaxone is the recommended alternative. In this survey, all *Neisseria gonorrhoeae* isolates (100%) were susceptible to these cephalosporins. Conversely, above 40% of *Neisseria gonorrhoeae* isolates (41.7%) were resistant to the oral flouroquinolone ciprofloxacin. Ciprofloxacin is no longer recommended in South Africa as part of the treatment regimen for any genital discharge syndrome.

HIV co-infection was high amongst the survey participants. Sexually transmitted infections facilitate the transmission and acquisition of HIV-1.[5] In addition, HIV-1 infected persons with STIs are at increased risk of transmitting HIV-1 because genital tract shedding of HIV -1 is elevated in the presence of genital tract inflammation.[6,7] STI control programmes need to be embedded in HIV care and treatment programmes and vice-versa in order to achieve optimal benefit in ameliorating the impact of HIV/AIDS and STIs.

Acknowledgements

Special thanks to the STI Unit surveillance clinical team: Melt Ndlovu, Alex Vezi, Valentia Kekana and Mr. Maluleke as well as staff at the Alexandra Health Centre and Laboratory staff at the STI Unit. This surveillance programme is funded by the Centre for HIV & STIs, NICD/NHLS and the National Department of Health.

References

1. Global incidence and prevalence of selected curable sexually transmitted infections – 2008. World Health Organization, Dept. of Reproductive Health and Research. Available: http://www.who.int/reproductivehealth/publications/rtis/stisestimates/en/. Accessed 30 0ctober 2014.
2. World Health Organization. Guidelines for the management of sexually transmitted infections. Available at: http://www.who.int/reproductive-health/publications/mngt_stis/index.html Accessed 30 0ctober 2014

3. Vuylsteke B. Current status of syndromic management of sexually transmitted infections in developing countries. *Sex Transm Infect* 2004; 80:333-334 doi:10.1136/sti.2004.009407.
4. National Department of Health. First line comprehensive management and control of sexually transmitted infections (STIs): protocol for the management of a person with a sexually transmitted infection according to the Essential Drug List. Pretoria: National Department of Health, 2008: 1-18.
5. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Infect* 1999; 75(1):3-17.
6. Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Daly CC, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. AIDSCAP Malawi Research Group. *Lancet* 1997; 349(9096):1868-73.
7. Johnson LF, Lewis DA. The effect of genital tract infections on HIV-1 shedding in the genital tract: a systematic review and meta-analysis. *Sex Transm Dis* 2008; 35(11):946-59.

SMALL-SCALE FIELD TESTING AND EVALUATION OF THE EFFICACY AND RESIDUAL ACTION OF A NEW POLYMER-ENHANCED SUSPENSION CONCENTRATE DELTAMETHRIN FORMULATION FOR MALARIA VECTOR CONTROL IN MPUMALANGA PROVINCE, SOUTH AFRICA

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Introduction

Malaria vector control is primarily based on the use of insecticides. These are applied by indoor residual spraying (IRS) or by the treatment of fabrics, especially bed nets.[1] Both methods rely heavily on the pyrethroid class of insecticides.

Malaria vector control by indoor house spraying first began in the Tzaneen area, South Africa, in the early 1930s.[2,3] The first insecticide used for this purpose was pyrethrum dissolved in kerosene which was used as an indoor spray once per week. Its proven efficacy led to IRS formulations based on the organochlorine insecticide DDT in the 1940s, followed by the organochlorine dieldrin and the organophosphate insecticides malathion and fenitrothion in the 1950s, the carbamate insecticides propoxur and bendiocarb in the 1960s and 1970s respectively, and by the pyrethroids in the 1970s and 1980s.[4]

Indoor residual spraying for malaria control involves the treatment of indoor wall surfaces and eaves of dwellings in malaria affected regions with an appropriate long-lasting, residual insecticide formulation.[5] In this way indoor resting mosquitoes, including malaria vector species, are targeted. The specific objectives of IRS are to reduce the lifespan of malaria vectors, to reduce vector density and to reduce human-vector contact.[6]
The use of IRS for malaria control globally has recently been scaled up from 5% of malaria affected countries in

2005 to 11% in 2011.[7] The increasing adoption of this technology necessitates continued product and formulation development. Testing new insecticide products or new formulations under field conditions is a major step that is needed before making recommendations for their use in prevention and control of malaria. It allows such products to be assessed under natural conditions (e.g. different substrates, temperature and humidity) as well as testing their acceptability to local communities.

The aim of this project was to assess the residual activity of a new deltamethrin SC-PE formulation compared with a deltamethrin WG formulation (250 g/kg WG) and lambda-cyhalothrin CS (100 g/l CS). The deltamethrin formulations were supplied by Bayer (Pty.) Ltd. and the lambda-cyhalothrin CS was purchased commercially. Assessments were conducted on two different local indoor surfaces (mud and cement), using pyrethroid susceptible malaria vectors.

Specific objectives were:

- To evaluate the efficacy of deltamethrin SC-PE at a dose of 25 mg ai/m^2 and compare it with deltamethrin WG at a dosage of 20 mg ai/m^2 as well with lambda-cyhalothrin CS at a dose of 25 mg ai/m^2 on mud and cement indoor surfaces using a susceptible strain of the malaria vector *Anopheles arabiensis.*
- To determine the persistence over time of deltamethrin SC-PE compared with deltamethrin WG and lambda-cyhalothrin CS against *An. arabiensis*.

Methods

Study site

The study was carried out in Mpumalanga Province, South Africa. Jeppe's Reef village (25°43'9.76"S; 31° 27'43.82"E), near the Swaziland border, was identified as a suitable site for these assessments. The village is in a low malaria risk area with sporadic cases and is strip sprayed (ie houses in low lying areas adjacent to streams or other water bodies). It is a semi-urban settlement with a mix of traditional mud and western-style cement houses.

Selection of participant households

Heads of households were consulted for permission to spray their dwellings. They were informed of what the study comprised.

In order to obtain the minimum number of replicates needed for statistical analysis at the end of the trial (i.e. 3 per insecticide per substrate/surface), the indoor surfaces of 24 structures were sprayed at the dosages indicated, whilst 4 were left unsprayed as controls (2 per surface type) (table 1).

Table 1: Numbers of structures sprayed by insecticide/formulation and surface type.

Indoor surface	Spray cohort (active ingredient)	Dosage mg ai/m^2	No. of structures included in the study
Mud-plastered wall	deltamethrin SC-PE	25	4
	deltamethrin WG	20	4
	lambda-cyhalothrin CS	25	4
	control	-	2
Cement wall	deltamethrin SC-PE	25	4
	deltamethrin WG	20	4
	lambda-cyhalothrin CS	25	4
	control	-	2

Spraying and safety precautions

Spraying was carried out on 12 September 2012. 15L Hudson Xpert pumps with 8002 nozzles for porous surfaces were used. Sachets and waste water were disposed of according to WHO guidelines.[5]

Only one round of spraying was done. Three spray pumps were calibrated to obtain uniform and good quality spraying for the targeted dose, and one pump was assigned for spraying each insecticide/formulation. Spray operators were persons who routinely conduct spraying for the Mpumalanga malaria vector control programme. Protective clothing, goggles, gloves, etc. are routinely provided to each operator for their general safety. Householders were informed in advance about the spraying. The spraying technique of each operator was assessed prior to the commencement of spraying. The same spray operator was responsible for all 8 structures sprayed per insecticide/formulation.

Bioassays

A laboratory colony of *Anopheles arabiensis* housed and maintained at the National Institute for Communicable Diseases (NICD) in Johannesburg was used for the bioassays. This colony (designated KGB) was established in 1975 from wild females collected in Kanyemba, Zimbabwe. It is fully susceptible to all the approved classes of insecticides.

Standard WHO cone bioassays[8] were carried out seven days post spraying and once a month thereafter for twelve months or until <80% mortality was recorded for two consecutive months, with the exception of assays on mud surfaces treated with deltamethrin WG which were continued beyond this point because mortalities remained below but close to 80% for four consecutive months. Five cones were placed on each wall at differing heights ie one cone at head height (R1), 3 cones at waist height (R2, R3, R4) and one cone below knee height (R5). Ten unfed, 2-4 day old, female mosquitoes were exposed for 30 minutes in each cone. Knockdown was recorded immediately post-exposure, again at 60 min post-exposure and final mortality recorded 24 hours post-exposure. Wads of cotton wool soaked in a 10% sucrose solution were made available to all of the test mosquitoes from the time they were removed from the cones until the 24 hour post exposure assessment.

Data recording and analysis

Bioassay results were recorded on a standard form in the field and transferred to an Excel spreadsheet in the laboratory. Data are presented as overall 24 hr post exposure percentage mortality for each insecticide/dose/ substrate per time interval post spraying.

Results

Overall percentage mortalities for unsprayed control structures by surface at each time interval post-spraying were suitably low (<20%) throughout the test period (table 2).

Table 2: Overall percentage mortalities for unsprayed control structures by surface at each time interval post-spraying of test structures. W = week; M = month.

Surface	1W	1M	2M	3M	4M	5M	6M	7M	8M	9M	10M	11M	12M
Cement	5.6	8.2	2	0	6.5	0	2.9	1	12.4	0	9.8	0	0
Mud	2.05	3.5	2.1	11.3	0	8.5	0	0	4.5	0	0	2	1

Overall percentage mortalities vs time interval post spraying for all insecticides/formulations on both surfaces are shown in table 3 and figure 1. Based on WHOPES guidelines (<80% mortality for 2 consecutive months), bioassays on all lambda-cyhalothrin CS sprayed surfaces were discontinued 2 months post spraying. Bioassays on deltamethrin WG cement surfaces were discontinued 5 months post spraying, and bioassays on deltamethrin WG mud surfaces were discontinued 8 months post spraying. Bioassays on all sprayed surfaces were conducted at 12 months post spraying.

Table 3: Overall percentage mortalities (24 hours post exposure) induced by each insecticide/formulation by surface sprayed at each time interval post-spraying. W = week; M = month. Note that the lambda-cyhalothrin CS and deltamethrin WG formulations were re-assayed at 12 months post spraying.

Treatment/ surface	1 W	1 M	2 M	3 M	4 M	5 M	6 M	7 M	8 M	9M	10M	11 M	12 M
Lambda-cyhalothrin CS Mud	95.0	78.1	57.8										58.1
Lambda-cyhalothrin CS Cement	97.2	78.5	50.0										15.1
Deltamethrin WG Mud	98.1	99.1	84.1	75.6	76.4	73.1	80.0	63.8	31.1				49
Deltamethrin WG Cement	99.5	97.5	94.7	89.0	59.4	61.1							11.7
Deltamethrin SC-PE Mud	99.5	98.1	97.3	94.8	96.1	97.5	97.9	71.3	84.7	95.1	93.9	94.8	81.8
Deltamethrin SC-PE Cement	100.0	94.9	96.4	91.9	95.6	86.3	95.9	90.8	85.5	73.5	96.9	96.9	82.8

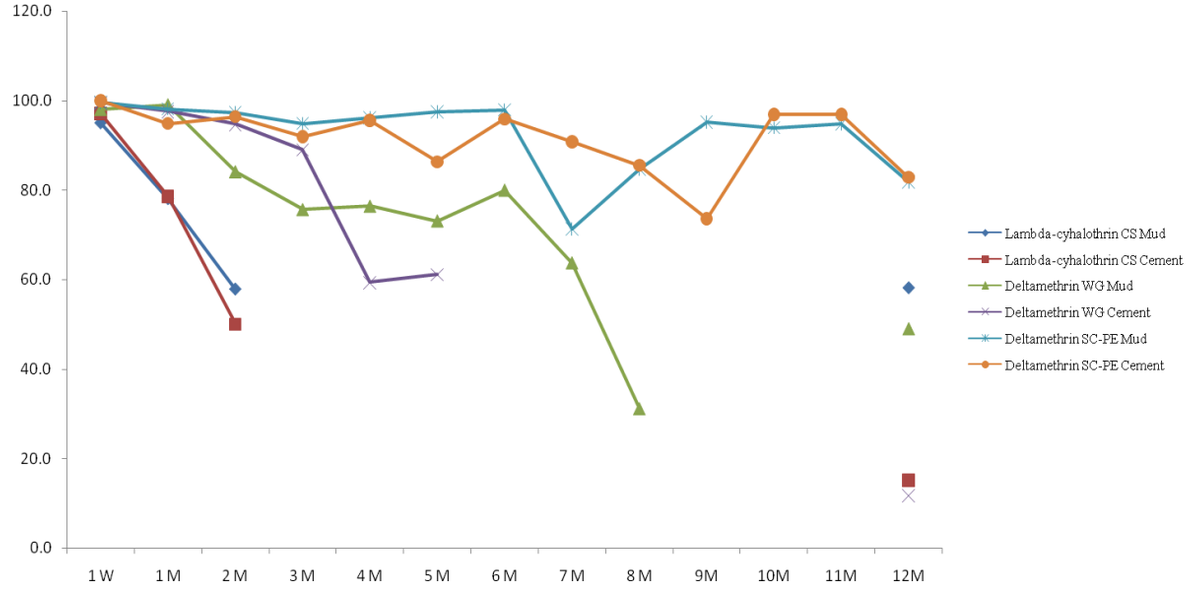

Figure 1: Overall percentage mortality induced by each insecticide/formulation by surface sprayed (mud or cement) at each time interval post spraying. W = week; M = month. Note that the lambda-cyhalothrin CS and deltamethrin WG formulations were re-assayed at 12 months post spraying.

Based on linear regression, there was no significant decrease in overall induced mortality with time post spraying for the deltamethrin SC-PE cement surfaces (F=3.01; P=0.11), nor for the deltamethrin SC-PE mud surfaces (F=3.26; P=0.1) at 12 months post-spraying. There was a significant and pronounced decrease in overall induced mortality with time post spraying for the deltamethrin WG mud surfaces (F=21.6; R^2=0.75; P=0.002) at 8 months post-spraying, and for the deltamethrin WG cement surfaces (F=20.78; R^2=0.8; P=0.01) at 5 months post-spraying.

Overall mortality induced by the deltamethrin SC-PE mud surfaces was significantly higher than that induced by the deltamethrin WG mud surfaces up to and including 8 months post spraying (ANOVA F=5.46; P=0.03). There was no significant difference in overall induced mortality between the deltamethrin SC-PE mud surfaces and the deltamethrin SC-PE cement surfaces up to and including 12 months post spraying (ANOVA F=0.15; P=0.7).

The lambda-cyhalothrin CS mud surfaces induced a similar level of mortality at 12 months post spraying to that recorded at 2 months post spraying (57.8% at 2 months vs 58.1% at 12 months). The deltamethrin WG mud surfaces induced a higher mortality at 12 months post spraying to that induced at 8 months post spraying (31.1% at 8 months vs 49% at 12 months). Conversely, mortality induced by the lambda-cyhalothrin CS cement surfaces was substantially lower at 12 months than at 2 months post spraying (50% at 2 months vs 15.1% at 12 months). Similarly, mortality induced by the deltamethrin WG cement surfaces was substantially lower at 12 months than at 5 months post spraying (61.1% at 2 months vs 11.7% at 12 months).

Discussion

Although it was not possible to assay every sprayed structure every month owing either to lock-outs (i.e. structure locked and owners absent) or destruction of mud structures, at least three structures were assayed per formulation per surface type each month as required. Furthermore, at least one unsprayed control structure per surface type was assayed on each day that assays on sprayed structures were conducted.

It should be noted that the lambda-cyhalothrin CS product had almost reached its expiry date at the time of spraying, which might account for its poor performance.

The long lasting deltamethrin SC-PE formulation significantly outperformed deltamethrin WG and lambda-cyhalothrin CS in terms of inducing mosquito mortality during the 12 month period post-spraying. Furthermore, the long lasting formulation performed equally well on mud and cement surfaces through 12 months post-spraying, without any significant decrease in efficacy over time on both surfaces during this period. However, data obtained from the lambda-cyhalothrin CS and deltamethrin WG sprayed structures showed that mud surfaces significantly outperformed the cement surfaces in terms of insecticide efficacy over time. This was especially apparent at 12 months post spraying. This is likely to prove important to future IRS operations in regions where brick and cement structures are rapidly replacing mud-walled structures.

The increasing sophistication of houses in malaria affected regions necessitates the development of malaria vector control products and technologies that are adapted to the needs of modern communities. The deltamethrin SC-PE formulation was evaluated by the WHO Pesticides Evaluation Scheme and was granted recommendation in 2013. The Report of the 16th WHOPES Working Group meeting[9] recommends the

use of deltamethrin SC-PE for indoor residual spraying against malaria vectors at a target dose of 20-25mg AI/ sqm with an expected residual efficacy of 6 months. This is valid for all surfaces, whereas lambda-cyhalothrin CS was recommended[10] with expected residual efficacy for 3-6 months, and it is not recommended for use on cement plastered surfaces.

It should be noted that new insecticide products and formulations for malaria vector control are only indicated for use in regions where the target vector population/s show full susceptibility to the active compounds. The increasing incidence of resistance to pyrethroids in malaria vector populations[11] essentially means that pyrethroid based IRS needs to be incorporated into a broader vector control scheme in accord with the principles of the global plan for insecticide resistance management (GPIRM).[12]

It is concluded that the deltamethrin (K-OthrineR Polyzone) long lasting formulation showed undiminished insecticidal efficacy up to 12 months post spraying under field conditions, was equally effective on mud and cement surfaces, and is therefore likely to prove highly effective for malaria vector control in regions where the occurrence of mud-walled structures is rapidly declining, assuming that pyrethroid resistance is not a confounding factor.

Acknowledgements

Staff of the Mpumalanga malaria vector control programme are thanked for their assistance with the field assessments and for the use of the satellite malaria control facility at Hectorspruit. Mr. Mark Edwardes is thanked for overseeing the spraying of structures. Miss Allison Gilbert is thanked for maintaining the *An. arabiensis* KGB laboratory colony and for providing female mosquitoes for the cone bioassays. Dr. Belinda Spillings, Ms Shune Oliver and Ms Maria Kaiser are thanked for their assistance with the bioassays.

References

1. Hemingway J. The role of vector control in stopping the transmission of malaria: threats and opportunities. *Philos Trans R Soc Lond B Biol Sci* 2014; 369 (1645): 20130431. doi: 10.1098/rstb.2013.0431.
2. De Meillon B. The control og malaria in south Africa directed against adult mosquitoes in habitations. *Quart Bull Hlth Org L o N* 1936; 5: 134-137.
3. Coetzee M, Kruger P, Hunt RH, Durrheim DN, Urbach J, Hansford CF. Malaria in South Africa: 110 years of learning to control the disease. *S Afr Med J* 2013; 103 (10 Suppl 2): 770-778.
4. Nauen R. A challenge for effective vector control. *Public health* 2006; 18: 9-15.
5. WHO. 2007. Manual for indoor residual spraying. Application of residual sprays for vector control. Available at: http://whqlibdoc.who.int/hq/2007/WHO_CDS_NTD_WHOPES_GCDPP_2007.3_eng.pdf
6. WHO. 2013. An operational manual for indoor residual spraying (IRS) for malaria transmission control and elimination. World Health Organization. Available at: http://apps.who.int/iris/bitstream/10665/80126/1/9789241505123_eng.pdf
7. WHO. 2012. World Malaria Report. World Health Organization, Geneva. Available at: www.who.int/**malaria**/publications/**world_malaria_report_2012**/en/
8. WHO. 2006. Guidelines for testing mosquito adulticides for indoor residual spraying and treatment of mosquito nets. WHO/CDS/WHOPES/GCDPP 2006.3, World Health Organization, Geneva. Available at: http://whqlibdoc.who.int/hq/2006/WHO_CDS_NTD_WHOPES_GCDPP_2006.3_eng.pdf

9. Report of the 16th WHOPES working group meeting. Available at: www.who.int/iris/bitstream/10665/90976/1/9789241506304_eng.pdf

10. Report of the 10th WHOPES working group meeting. Available at: www.who.int/whopes/.../WHO_CDS_NTD_WHOPES_2007_1.pdf

11. Ranson H, Nguessan R, Lines JL, Moiroux N, Nkuni Z, Corbel V. Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control? *Trends Parasitol* 2011; 27: 91–99.

12. WHO. 2012. Global plan for insecticide resistance management. World Health Organization, Geneva. Available at: www.who.int/malaria/publications/atoz/gpirm/en/

ROTAVIRUS SURVEILLANCE REPORT, SOUTH AFRICA, 2013

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Introduction

South Africa introduced the rotavirus vaccine into the national immunization program in August 2009. Since then, monitoring of the rotavirus vaccine has continued at six sentinel surveillance sites in four provinces. The main objectives of the surveillance programme are to describe the epidemiology of rotavirus infection and to monitor the impact of the rotavirus vaccine since introduction on the incidence of diarrhoeal disease.

Between 2009 and 2011, analysis from three of the six sites indicated that the vaccine reduced rotavirus hospitalizations in children under five years by 54%-58% and lowered all-cause diarrhoea hospitalization by a third.[1] Data from a vaccine effectiveness case-control study conducted between 2010 and 2012 showed that the vaccine was 40% effective after one dose and 57% effective after two doses in preventing rotavirus diarrhoea.[2] The study also revealed that vaccine effectiveness was similar in HIV-exposed versus HIV-unexposed children, an encouraging result for the introduction of the vaccine in high-HIV prevalent countries in Africa. Results from the rotavirus surveillance for 2013 are reported below.

Methods

The programme enrolled children under five years of age who were admitted to the sentinel hospitals with symptoms of three or more loose stools within a 24 hour period, following informed consent. The sentinel hospitals included Chris Hani Baragwanath Hospital, Mapulaneng Hospital, Matikwane Hospital, Dr George Mukhari Hospital, Edendale Hospital and Red Cross Children's Hospital. Case investigation forms including

patient demographic, socioeconomic and clinical information were completed by surveillance officers. A stool sample was collected from each case for rotavirus screening.

Testing of stool samples was performed at the Virology Division, Centre for Enteric Diseases (CED), NICD, and at the Diarrhoeal Pathogens Research Unit (DPRU), University of Limpopo Medunsa Campus. The stool samples were screened with the ProSpecT™ Rotavirus Microplate Assay (Oxoid, Basingstoke, UK).

Rotavirus positive samples were further characterized to determine the G and P genotype of each strain. Rotavirus dsRNA was extracted from each stool sample using the QIAamp Viral RNA Mini kit (Qiagen, Hilden, Germany) and genotyped using standardized real-time polymerase chain reaction (RT-PCR) methods and primers for G-specific (G1, G2, G3, G4, G8, G9, G10, G12) and P-specific (P[4], P[6], P[8], P[9], P[10], P[11], P[14]) genotypes.[3]

Results

A total of 1,224 stool samples was collected in 2013 (table 1). Laboratory screening could not be performed in 15% (183/1,224) of diarrhoea cases owing to insufficient collection of stool. Rotavirus was detected in 28% (292/1,041) of cases, ranging from 19% (26/134) at Dr George Mukhari Hospital to 31% at Edendale (21/68) and Red Cross Children's Hospitals (131/417).

Table 1: Total stools from diarrhoea cases collected for rotavirus detection (children under five years), number of stools insufficient for testing and rotavirus results for 2011–2013 by sentinel hospital.

Site	Total	Insufficient (%)	Rotavirus positive		
			2013 (%)	2012 (%)	2011 (%)
Chris Hani Baragwanath	311	72 (23)	71/239 (30)	39/213 (18)	45/288 (16)
Mapumaleng	84	10 (12)	16/74 (22)	16/70 (23)	12/48 (25)
Matikwane	120	11 (9)	27/109 (25)	25/139 (18)	20/99 (20)
Dr George Mukhari	161	27 (17)	26/134 (19)	27/156 (17)	45/198 (23)
Edendale	76	8 (11)	21/68 (31)	13/57 (23)	28/93 (30)
Red Cross Children's	472	55 (12)	131/417 (31)	70/359 (19)	152/497 (31)
Total	1,224	183 (15)	292/1,041 (28)	190/994 (19)	302/1,223 (25)

The start of a rotavirus season is defined as a rotavirus detection rate of above 20% for two consecutive weeks. The end of a season is defined as a rotavirus detection rate of below 20% for two consecutive weeks. The 2013 rotavirus season started in week 12 (18th March 2013) and ended in week 39 (23rd September 2013), with the peak in week 30 (22nd July 2013) during which 61% (22/36) of stools collected were positive for rotavirus (figure 1). A higher proportion of rotavirus cases was detected in the 2013 season (30%; 292/1,041) compared to 2012 (19%; 190/994).

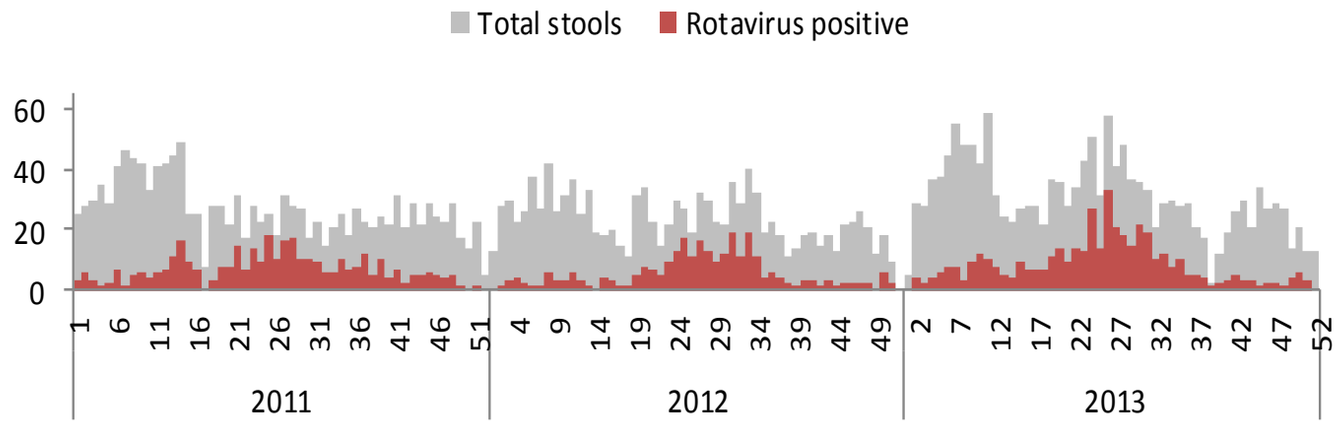

Figure 1: Total number of stool specimens screened for rotavirus and positive rotavirus cases by epidemiological week, 2011-2013.

The age of the children affected in 2013 ranged between 0 and 58 months with the majority of children affected between 4 and 9 months of age (table 2). The ages of children infected by rotavirus have remained relatively constant although differences are evident in the 0-3 age group in high rotavirus years (2011 and 2013). Preliminary analysis of the vaccination status of children with rotavirus detected in their stool revealed that 70% (203/292) had received two doses of vaccine prior to the diarrhoeal episode. Other enteric viruses were detected in 2% to 15% of rotavirus-positive cases (data not shown)

Table 2: Age distribution of children with rotavirus infections, 2011–2013, and predominant rotavirus genotypes by year.

Age range (in months)	Rotavirus positive (%)		
	2013	2012	2011
0-3	34 (12)	16 (8)	45 (15)
4-6	60 (21)	35 (18)	54 (18)
7-9	63 (22)	38 (20)	65 (22)
10-12	51 (17)	41 (22)	40 (13)
13-18	47 (16)	34 (18)	64 (21)
19-24	16 (5)	13 (7)	18 (6)
>24	17 (6)	12 (6)	13 (4)
Unknown	4 (1)	1 (1)	3 (1)
Total	292 (28)	190 (19)	302 (25)
Predominant genotypes	G2P[4] G9P[8]	G12P[8] G8P[4] G2P[4]	G12P[8] G9P[8]

The genotyping of the rotavirus strains revealed that the G2P[4] (47%; 137/292) and G9P[8] (39%; 115/292) strains were predominant (table 3). With the exception of Red Cross Children's Hospital, G2P[4] strains predominated in all sites in 2013.

Table 3: Rotavirus strains (G and P genotypes) detected at sentinel sites in South Africa, 2013. The predominant strains at each site are shaded grey. CHBH = Chris Hani Baragwanath Hospital, MP = Mapulaneng, MK = Matikwana, DGM = Dr. George Mukhari, EdH = Edendale Hospital and RCCH = Red Cross Children's Hospital.

Genotype	CHBH		MP		MK		DGM		EdH		RCCH		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
Rotavirus strains covered by the monovalent vaccine													
G1P[4]	1	1	0	0	0	0	0	0	0	0	0	0	1
G3P[8]	0	0	0	0	0	0	0	0	0	0	7	5	7
G9P[8]	9	13	2	13	1	4	1	4	1	5	101	77	115
Total	10	14	2	13	1	4	1	4	1	5	108	82	123
Rotavirus strains not covered by the monovalent vaccine													
G2P[4]	49	69	14	88	22	81	22	85	19	90	11	8	137
G2P[6]	4	6	0	0	0	0	0	0	0	0	4	3	8
G3P[4]	1	1	0	0	0	0	0	0	0	0	0	0	1
G8P[4]	0	0	0	0	0	0	0	0	1	5	2	2	3
G9P[4]	0	0	0	0	0	0	0	0	0	0	1	1	1
G9P[6]	0	0	0	0	0	0	1	4	0	0	3	2	4
Total	54	76	14	88	22	81	23	88	20	95	21	16	154
Mixed and non-typeable rotavirus strains													
Mixed	3	4	0	0	0	0	1	4	0	0	0	0	4
Not typed	0	0	0	0	0	0	1	4	0	0	0	0	1
Negative	4	6	0	0	4	15	0	0	0	0	2	2	10
Total	7	10	0	0	4	15	2	8	0	0	2	2	15
Grand total	71		16		27		26		21		131		292

Discussion

The incidence of rotavirus cases recorded during the 2013 South African rotavirus season increased by 54% compared to the 2012 season (292 cases versus 190 cases) but was 3% less than the 2011 season (292 cases versus 302 cases). Most of the children affected were between 4 and 9 months of age (42%; 123/292) even though 70% of them had received two doses of the vaccine. Various factors including reduced vaccine effectiveness, the genotype of the circulating strain and the presence of concomitant enteric pathogens may have contributed to diarrhoeal disease in this age group. Initially, these results were a cause for concern. However, further investigation of rotavirus epidemiology following vaccine introduction in other countries allayed fears concerning vaccine performance. The rotavirus vaccine was introduced into the national immunization programme in the United States (US) in 2006. Since vaccine introduction, the number of rotavirus-positive tests declined by 74%-90% compared to pre-vaccine baseline data. A trend that emerged during the monitoring of five post-vaccine seasons in the US (2007 -2012) was a pattern of biennial increases in rotavirus activity. These increases were, however, substantially below pre-vaccine rotavirus levels. The average rotavirus detection rate in the US varied between 10% in "high" years and 4% in "low" years. Some areas of the US have reported differences in rotavirus prevalence between high and low years of up to 12%.[4] Similarly, the 2013 rotavirus season in South Africa may represent a

biennial "high" season. The South African "high" season may also be greater than the "high" seasons recorded in the US because the vaccine effectiveness in South Africa is only 57% after two doses.[2] This is substantially lower than the 91-92% vaccine effectiveness reported in the US.[4]

The recent case-control study described by Groome et al.[2] demonstrated vaccine effectiveness of 71% against G12P[8] strains, 62% against strains with the G or P in the vaccine formulation and 52% against strains without a G or P in the vaccine formulation. The circulation of the G2P[4] strains in 2013 may have resulted in slightly lower vaccine effectiveness compared to the 2012 season. This case-control study also found little difference in vaccine effectiveness between cases where only rotavirus was detected versus cases where rotavirus and an additional enteric virus was found.[2] These results suggest that concomitant infections were not erroneously attributed to rotavirus and that reduced vaccine effectiveness is due to other factors. However, the study did not evaluate the effect of bacterial and parasitic enteric pathogens on vaccine effectiveness calculations and this line of investigation should be pursued in future.

Conclusion

It is likely that the South African 2013 rotavirus season signified the biennial "high" season, similar to trends seen in the US after rotavirus vaccine introduction. However, due to lower vaccine efficacy and effectiveness, the excess in the number of rotavirus cases and prevalence may be greater than the levels in the US. Continued monitoring of the rotavirus seasons between 2014 and 2017 will allow calculation of excess rotavirus cases that can be expected during "high" seasons in the South African population. Health facilities in South Africa are advised to be prepared for the 2015 rotavirus season, predicted to reach a peak in June 2015.

Acknowledgements

The following are thanked for their contributions to the Rotavirus Surveillance Programme:

National Institute for Communicable Diseases, NHLS:

- Centre for Opportunistic, Tropical and Hospital Infections: John Frean, Desiree du Plessis, Benjamin Mogoye, Bhavani Poonsamy
- Centre for HIV and STIs: Deirdre Greyling, Adrian Puren
- Centre for Enteric Diseases: Karen Keddy, Sandrama Nadan, Rembuluwani Netshikweta, Anthony Smith
- South African Field Epidemiology Training Programme (SA-FETP): Lazarus Kuonza, Alfred Musekiwa, Carl Reddy, Dorothy Southern, Seymour Williams
- Dr George Mukhari Hospital/Diarrhoeal Pathogens Research Unit, University of Limpopo Medunsa Campus: Gloria Ngubane, Jeff Mphahlele
- Edendale Hospital: Meera Chhagan, Halima Dawood, Sumayya Haffejee, Douglas Wilson
- MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt): Kathleen Kahn, Stephen Tollman, Rhian Twine
- Red Cross Children's Hospital: Earl Dietrich, Heather Zar
- South African National Department of Health - EPI programme: Ntombenhle Ngcobo, Johan van den Heever

In addition we wish to thank the surveillance officers, research assistants, data entry team and patients who participated in the surveillance programme.

References

1. Msimang VM, Page N, Groome MJ, Moyes J, Cortese MM, Seheri M, Kahn K, Chagan M, Madhi SA, Cohen C. Impact of rotavirus vaccine on childhood diarrheal hospitalization after introduction into the South African public immunization program. *Pediatr Infect Dis J.* 2013; 32(12):1359-64.
2. Groome MJ, Page N, Cortese MM, Moyes J, Zar HJ, Kapongo CN, Mulligan C, Diedericks R, Cohen C, Fleming JA, Seheri M, Mphahlele J, Walaza S, Khan K, Chagan M, Duncan Steele A, Parashar UD, Zell ER, Madhi SA. Effectiveness of monovalent human rotavirus vaccine against admission to hospital for acute rotavirus diarrhoea in South African children: a case-control study. *Lancet Infect Dis* 2014; 8 Oct doi:10.1016/S1473-3099(14)70940-5 [Epub ahead of print].
3. Gentsch J, Gray J, Iturriza-Gómara M, Klena J, Kirkwood C, Armah G, Page N. Manual of rotavirus detection and characterization. *World Health Org* 2009; www.who.int/vaccines-documents/
4. Tate JE, Haynes A, Payne DC, Cortese MM, Lopman BA, Patel MM, Parashar UD. Trends in national rotavirus activity before and after introduction of rotavirus vaccine into the national immunization program in the United States, 2000 to 2012. *Pediatr Infect Dis J.* 2013; 32(7):741-4.

SURVEILLANCE FOR *BORDETELLA PERTUSSIS*, ATYPICAL BACTERIAL CAUSES OF PNEUMONIA, *HAEMOPHILUS INFLUENZAE* AND *STREPTOCOCCUS PNEUMONIAE* WITHIN THE SEVERE RESPIRATORY ILLNESS SURVEILLANCE PROGRAMME, 2013

Maimuna Carrim, Cheryl Cohen, Mignon du Plessis, Fahima Moosa, Jocelyn Moyes, Anne von Gottberg, Sibongile Walaza, Nicole Wolter for the SARI surveillance network

Centre for Respiratory Diseases and Meningitis, NICD

Introduction

The National Institute for Communicable Diseases (NICD) has been conducting active, prospective, hospital-based sentinel surveillance for severe acute respiratory illness (SARI) since February 2009, initially in three of South Africa's provinces:

- Gauteng Province: Chris Hani-Baragwanath Hospital (CHBH) (this site stopped enrolling patients in December 2013)
- KwaZulu-Natal: Edendale Hospital
- Mpumalanga: Matikwana and Mapulaneng Hospitals.

Patients were enrolled based on a standardised clinical case definition. The programme initially focused on the detection of influenza, but included testing for other respiratory viruses and *Streptococcus pneumoniae*. In June 2010, Klerksdorp-Tshepong Hospital Complex (KTHC), North West Province, was included as a new site and the case definition was expanded to include cases with severe respiratory illness (SRI) irrespective of symptom duration, as well as to include patients with a clinician admission diagnosis of suspected tuberculosis. In 2012, the surveillance was further enhanced at two sites (Edendale and KTHC) to include expanded testing of specimens (naso- and oropharyngeal swabs and aspirates) and collection of additional specimens (induced sputum and oral washes) from patients with SRI. Respiratory samples were tested for the following pathogens: *Haemophilus influenzae*, *Streptococcus pneumoniae, Bordetella pertussis, Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and

Legionella species. Induced sputum specimens were tested for the following pathogens: *Mycobacterium tuberculosis*, *H. influenzae*, *S. pneumoniae, B. pertussis, M. pneumoniae*, *C. pneumoniae* and *Legionella* species. In addition, influenza-like illness (ILI) surveillance at two primary health care clinics serviced by the these two enhanced sites (Edendale and KTHC) was started in 2012. A sample of individuals without respiratory symptoms was enrolled at ILI sites.

The primary objectives of the surveillance for additional respiratory pathogens were:

- To estimate the prevalence and proportions of patients with *M. tuberculosis*, *S. pneumoniae, B. pertussis, H. influenzae* and atypical bacterial causes of pneumonia (*Legionella species, C. pneumoniae* and *M. pneumoniae*) in HIV-infected and HIV-uninfected adults and paediatric patients hospitalised SRI, and to describe the factors associated with positivity for these infections
- To describe the burden and aetiology of outpatient influenza-like illness in children and adults in selected sites in South Africa, in HIV-infected and HIV-uninfected populations

This report presents the findings from this surveillance programme for the year 2013 for the pathogens *S. pneumoniae, B. pertussis, H. influenzae* and atypical bacterial causes of pneumonia (*Legionella species, C. pneumoniae* and *M. pneumoniae*). Data from this surveillance programme from May 2012 to June 2013 have been previously reported.[1] Data are presented from Edendale Hospital and KTHC and the associated ILI sites. Data on individuals without respiratory symptoms are not included in this report.

Methods

Hospitalised patients meeting the clinical case definition for SRI and outpatient cases meeting the case definition for ILI were prospectively enrolled from January to December 2013. Clinical and epidemiological data were collected using standardised questionnaires. Information on in-hospital management and outcome was also collected.

Sample collection and processing

Upper respiratory tract samples (oropharyngeal and nasopharyngeal swabs in patients ≥5 years or nasopharyngeal aspirates in patients <5 years of age) were collected from hospitalised patients (SRI) and outpatients (ILI). Induced sputum, blood and oral washes were collected from hospitalised patients only. In those patients where tuberculosis testing was not conducted as part of clinical care, an expectorated sputum or second induced sputum sample (in patients who could not expectorate), was collected and tested at the local laboratory for tuberculosis. In patients <5 years, the first induced sputum was tested at the surveillance site laboratory for *M. tuberculosis* using GeneXpert and a second sample was tested at the NICD for *M. tuberculosis* and bacterial pathogens. Collections of induced sputum started in June 2012 and November 2012 for adult and paediatric patients respectively.

Collected upper respiratory specimens were placed in 4 ml cryovials containing virus transport medium. Oral washes and sputum were collected in universal containers. Whole blood samples were collected in EDTA-containing vacutainer tubes within 24 hours of hospital admission.

Following collection, respiratory and blood samples were kept at 4°C at the local laboratory, and were transported to the NICD on ice within 72 hours post-collection. At the start of the programme, sputum samples were transported together with the oropharyngeal/nasopharyngeal samples. From July

2013 sputum samples were stored separately at -20^{0}C at the local laboratory before being transported to the NICD on dry ice on a weekly basis.

Laboratory procedures

DNA was extracted from the clinical specimens and tested for bacterial pathogens by real-time polymerase chain reaction (PCR).

Detection of bacterial pathogens

Induced sputum and nasopharyngeal samples were tested for *M. pneumoniae*, *C. pneumoniae, Legionella* spp. and *B. pertussis.* A specimen was considered positive for *M. pneumoniae* if the *MP181* target was detected (Ct<45), *C. pneumoniae* if the *CP-Arg* target was detected (Ct<45) and *Legionella* spp. if the Pan-Leg target was detected (Ct<45).[2] This multiplex real-time PCR assay is only able to identify *Legionella* spp., but further assays are required to identify samples to species level. Any specimen that was positive for the *MP181*, *CP-Arg* or Pan-Leg targets was re-extracted and the PCR was repeated in duplicate. If there was an insufficient amount of primary specimen, the initial DNA extract was repeated in duplicate. A specimen was only reported as positive if the PCR result was positive in at least 2 of the 3 reactions i.e. identified through two extracts. A positive result for pertussis was obtained when a specimen was positive for *IS481* and/or *ptxS*1 genes.[3] A specimen was considered negative if the organism-specific targets (*MP181*, *CP-Arg* and Pan-Leg)[1] were not detected (Ct≥45) and the *RNAse P* target was positive (Ct <45).

Blood specimens were tested using quantitative real-time PCR for the presence of pneumococcal DNA (*lyt*A gene), and for *H. influenzae* targeting *IgA, bexA* and region II of the *cap* locus of *H. influenzae.* For *lytA* testing, specimens with a *lytA* Ct-value <40 were considered positive.[4]

Determination of HIV status

HIV status data was obtained from two data sources. Firstly, for some patients HIV testing was requested by admitting physicians as part of clinical management. This included HIV enzyme-linked immunosorbent assay (ELISA) testing with confirmation by ELISA on a second specimen for patients ≥18 months of age, and qualitative HIV PCR testing for confirmation of HIV-infection status in children <18 months of age. Secondly, for consenting patients, linked anonymous HIV PCR testing for children <18 months of age or ELISA for patients ≥18 months of age was performed using a dried blood spot or whole blood specimen.

Data management

Data management was centralised at the NICD where laboratory, clinical and demographic data from enrolled patients were recorded on a Microsoft Access database.

Ethical considerations

The protocol was approved by the Research Ethics Committees of the University of the Witwatersrand and University of KwaZulu-Natal.

Results

Characteristics of patients with severe respiratory illness (SRI) and influenza-like illness (ILI) enrolled at enhanced surveillance sites

For the period 1 January 2013 to 31 December 2013 a total of 1206 hospitalized individuals with SRI and 1,065 individuals with ILI were enrolled at the two sites.

Influenza-like illness (ILI) patients

Of the patients with ILI, 307/1,065 (29%) were <5 years, and 301/1,065 (28%) were in the age group 25-44 years (table 1). More than half the patients were female (661/1,057, 63%). The HIV prevalence in patients with ILI was 28% (264/934). The highest prevalence was in the age group 25-44 years 160/284 (56%), followed by

43% (40/94) in the age group 45-64 years (figure 1). The majority of patients with ILI were enrolled at the Edendale Gateway clinic (848/1,076, 79%).

Severe respiratory illness (SRI) patients

Most of the patients who were admitted with SRI were in the age group 25-44 years (533/1,206, 44%) and half were female (597/1,206, 50%) (table 1). The HIV prevalence in patients with SRI was 70% (752/1,081). The highest prevalence was in the 25-44 years age group (440/497, 92%) (figure 1). The KTHC site accounted for 820/1,206 (79%) of patients enrolled with SRI.

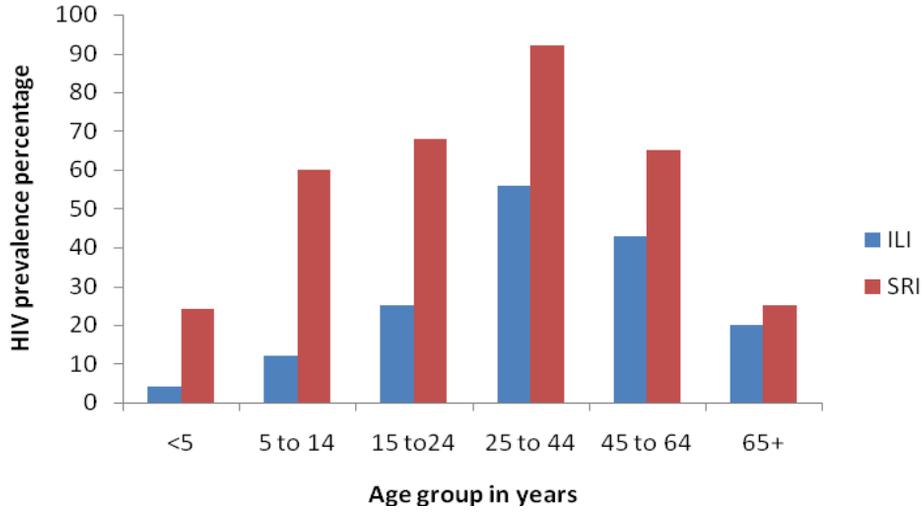

Figure 1: HIV prevalence by age group, influenza-like illness (ILI) and severe respiratory illness (SRI), at enhanced surveillance sites, South Africa, 2013.

Table 1: Characteristics of patients enrolled with severe respiratory illness and influenza-like illness at enhanced surveillance sites, South Africa, 2013.

Characteristic	Influenza-like illness n/N (%)	Severe respiratory illness n/N (%)
Age Group (years)		
0-4	307/1,065 (29)	151/1,206 (13)
5-14	192/1,065 (18)	32/1,206 (3)
15-24	150/1,065 (14)	87/1,206 (7)
25-44	301/1,065 (28)	533/1,206 (44)
45-64	104/1,065 (10)	317/1,206 (26)
≥65	11/1,065 (1)	86/1,206 (7)
Female sex	661/1,057 (63)	597/1,206 (50)
Hospital/Clinic name		
Edendale Hospital	n/a	386/1,206 (32)
KTHC	n/a	820/1,206 (68)
Edendale Gateway clinic	848/1,065 (80)	n/a
Jouberton Gateway clinic	217/1,065 (20)	n/a
HIV prevalence	264/934 (28)	752/1,081 (70)
Underlying illness	45/1,055 (4)	130/1,206 (11)
In-hospital death	n/a	130/1,148 (11)

Bordetella pertussis

ILI patients

Of the enrolled patients 81% (866/1,065) were tested for *B. pertussis*. The prevalence of *B. pertussis* was 1% (5/866). The patients were all aged <25 years (figure 2). Of the five cases, four occurred in the winter months (figure 3) and three were identified at the Jouberton clinic (figure 4). The majority were female (4/5, 80%) and 20% (1/5) tested positive for HIV.

SRI patients

Of the enrolled patients, 91% (1,101/1,206) were tested for *B. pertussis* and 13/1,101 (1%) tested positive for *B. pertussis.* Three of the 13 cases (23%) were aged <5 years, 8/13 (62%) were 25-44 and 2/13 (15%) were 45-64 years (figure 2). The HIV prevalence in *B. pertussis* patients with SRI was 75% (9/12). More than half were female 7/13 (54%) and more than half were enrolled from the Edendale site 7/13 (54%).

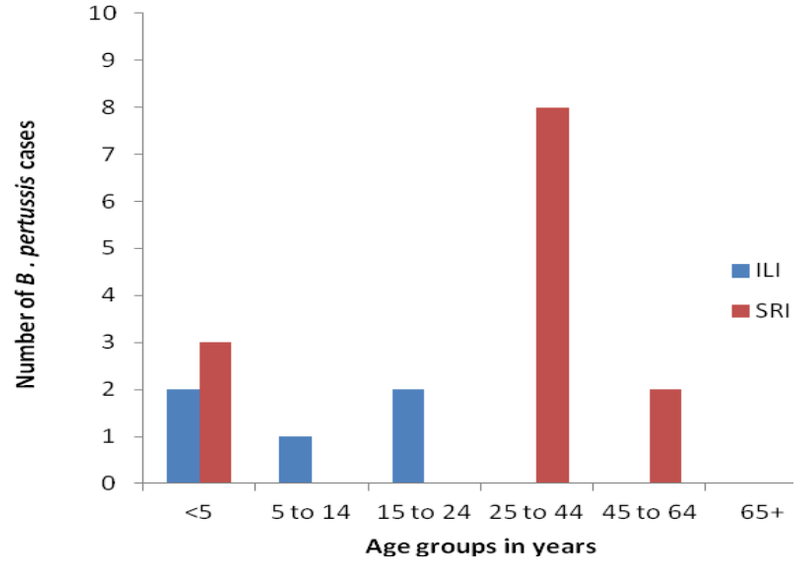

Figure 2: Detection rate of *Bordetella pertussis* among patients with severe respiratory illness (SRI) and influenza-like illness (ILI) by age group at enhanced sites, South Africa, 2013.

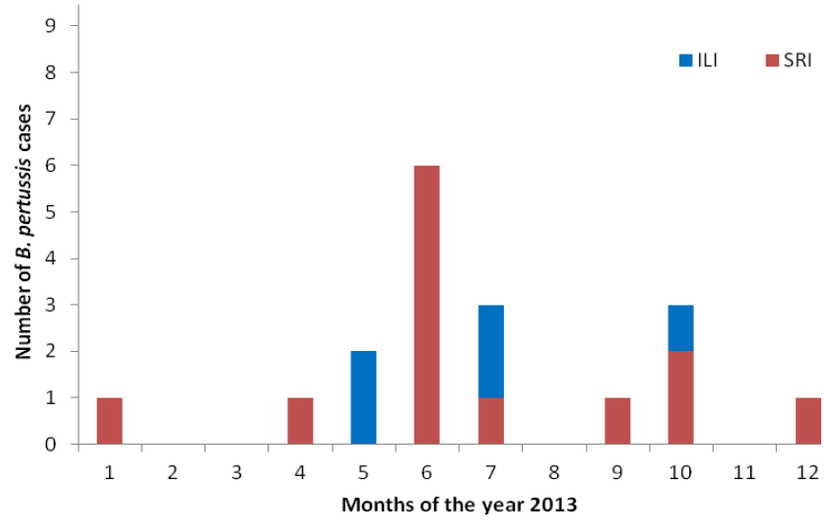

Figure 3: Numbers of cases of *Bordetella pertussis* among patients with severe respiratory illness (SRI) and influenza -like illness (ILI) by month and year at enhanced sites, South Africa, 2013.

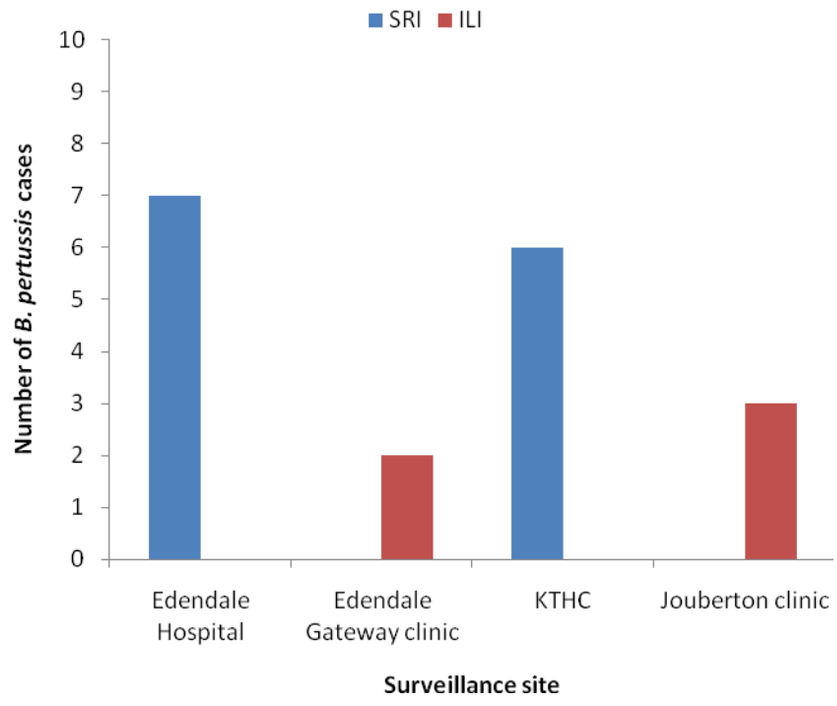

Figure 4: Numbers of cases of *Bordetella pertussis* among patients with severe respiratory illness (SRI) and influenza -like illness (ILI) by study site at enhanced sites, South Africa, 2013.

Atypical pneumonia-causing bacteria

ILI patients

Of the 1,065 patients enrolled, 863 (81%) were tested for *M. pneumoniae*, *C. pneumoniae* and *Legionella* spp. Of these, 1% (12/863) tested positive for *M. pneumoniae,* 0.3% (3/863) tested positive for *C. pneumoniae* and none tested positive for *Legionella* spp (figure 6). Cases of *M. pneumoniae* were detected all year round (figure 5), while cases of *C. pneumoniae* were detected between April and September (figure 7). Half of the *M. pneumoniae* cases were under the age of 5 years (6/12, 50%) (figure 8). Only one case was HIV infected. Two of three patients with *C. pneumoniae* were aged 5-14 years and 1 case was under the age of five (figure 10). No *C. pneumoniae* cases were HIV infected.

SRI patients

Of the 1,206 enrolled patients, 91% (1,094) were tested for *M. pneumoniae*, *C. pneumoniae* and *Legionella* spp. Among SRI cases, 21/1,094 (2%) were positive for *M. pneumoniae*, 5/1094 (0.5%) were positive for *Legionella* spp. and 1/1,094 (0.1%) were positive for *C. pneumoniae*. A third of the *M. pneumonia* SRI cases were in the 25-44 age group. The *Legionella* spp cases were all aged >15 years (figures 6 & 9). The majority of *M. pneumoniae cases* were detected at Edendale hospitals (13/21, 62%) (figure 11), whereas all five *Legionella* spp. cases were detected at KTHC hospitals and there were no cases of *Chlamydia* at KTHC (figure 12).

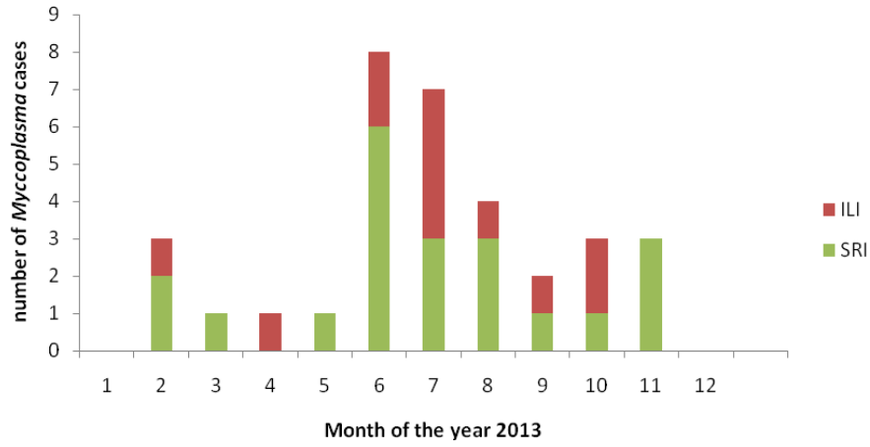

Figure 5: Numbers of cases of *Mycoplasma pneumoniae* among patients with influenza-like illness (ILI) and severe respiratory illness (SRI) by month at enhanced sites, South Africa, 2013.

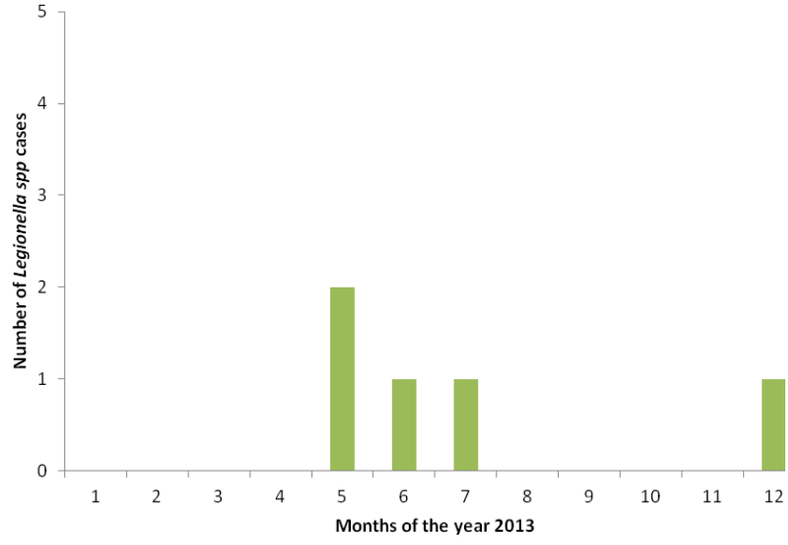

Figure 6: Numbers of cases of *Legionella* spp among patients with severe respiratory illness by month and year at enhanced sites, South Africa, 2013.

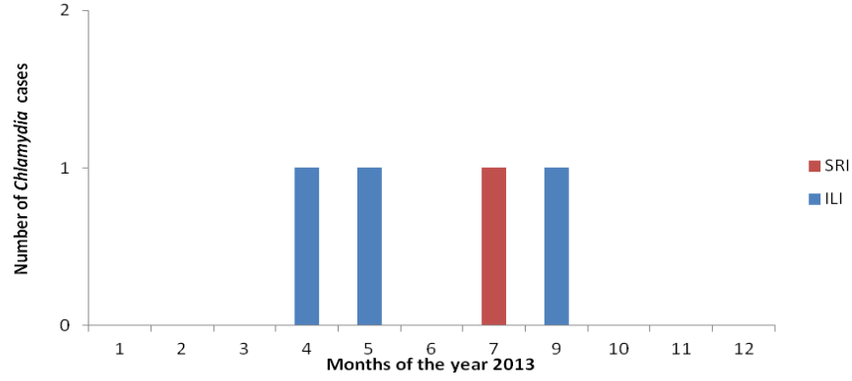

Figure 7: Numbers of cases of *Chlamydia pneumonia* among patients with influenza-like illness (ILI) and severe respiratory illness (SRI) by month and year at enhanced sites, South Africa, 2013.

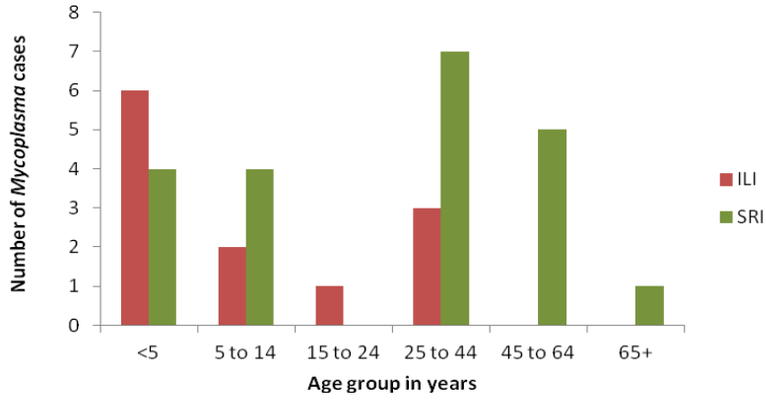

Figure 8: Numbers of cases of *Mycoplasma pneumonia* among patients with influenza-like illness (ILI) and severe respiratory illness (SRI) by age group at enhanced sites, South Africa, 2013.

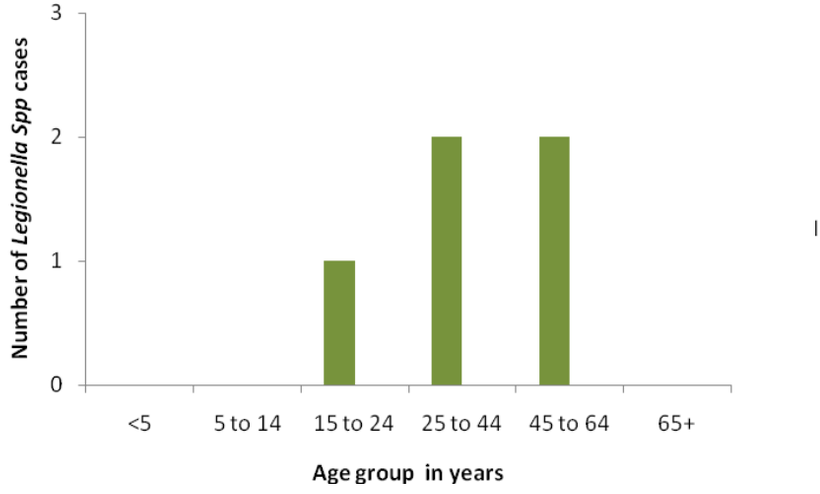

Figure 9: Numbers of cases of *Legionella spp* among patients with severe respiratory illness by age group at enhanced sites, South Africa, 2013.

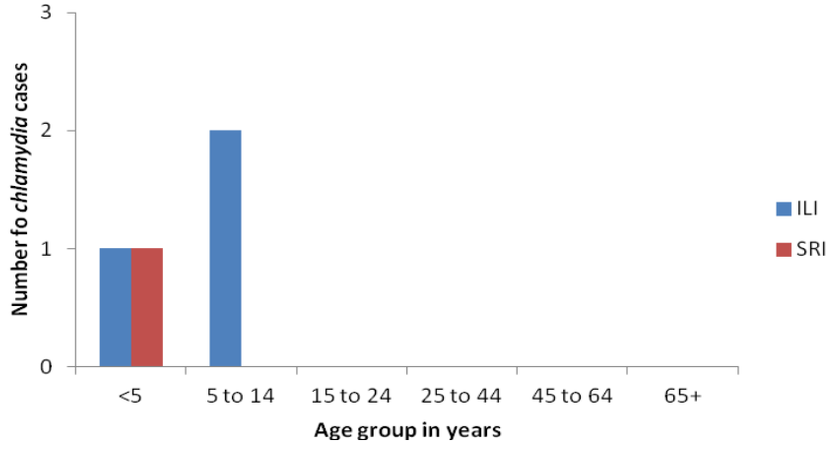

Figure 10: Numbers of cases of *Chlamydia pneumonia*e among patients with influenza-like illness (ILI) and severe respiratory illness (SRI) by age group at enhanced sites, South Africa, 2013.

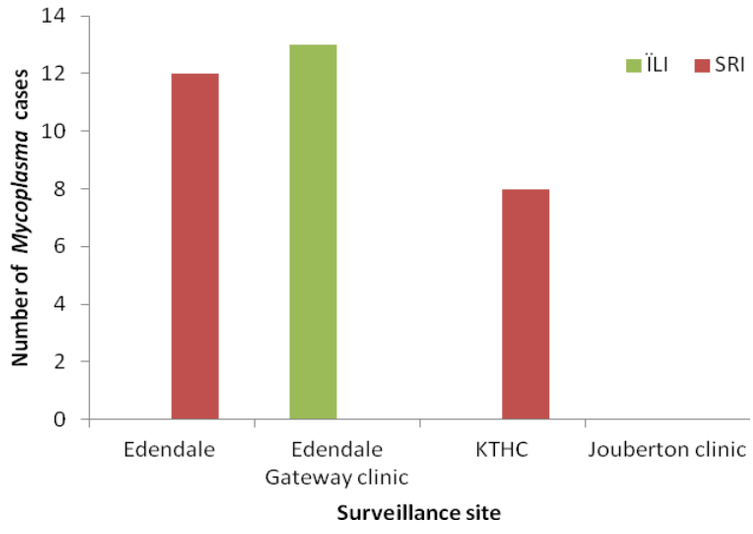

Figure 11: Numbers of cases of *Mycoplasma pneumoniae,* among patients with influenza-like illness (ILI) and severe respiratory illness (SRI) by study site at enhanced sites, South Africa, 2013

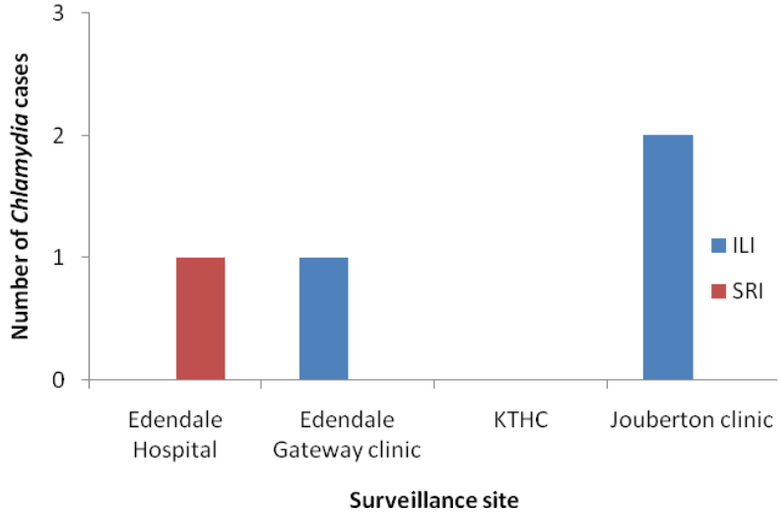

Figure 12: Numbers of cases of *Chlamydia pneumonia* among patients with influenza-like illness (ILI) and severe respiratory illness (SRI) by study site at enhanced sites, South Africa, 2013.

Streptococcus pneumoniae and *Haemophilus influenzae*

Blood specimens were tested for *S. pneumoniae* for 85% (1,637/1,961) of SRI patients enrolled in 2013 and 126 (11%) were positive for *S. pneumoniae*. Pneumococcal infection was detected throughout the year with peaks in the winter and spring months (figure 13). Cases were distributed between the two study sites (figure 14). The detection rate of *S. pneumoniae* ranged from 9% (9/96) in the <5 year age group to 13% in both the 15-24 year (11/84) and the 46-64 year (40/299) age group (figure 15). Of the 1105 SRI cases who had blood specimens tested for *H. influenzae,* 44 (4%) were positive. *Haemophilus influenzae* cases were detected throughout the year (figure 16) and at both hospitals (Edendale 21/44 (48%) and Klerksdorp 23/44 (52%) (figure 17). Of the 44 *H. influenzae* cases, three *H. influenzae* serotype b (Hib) cases were identified and all three were enrolled at the Klerksdorp hospital and were in the age group 25 to 44 years (figure 18).

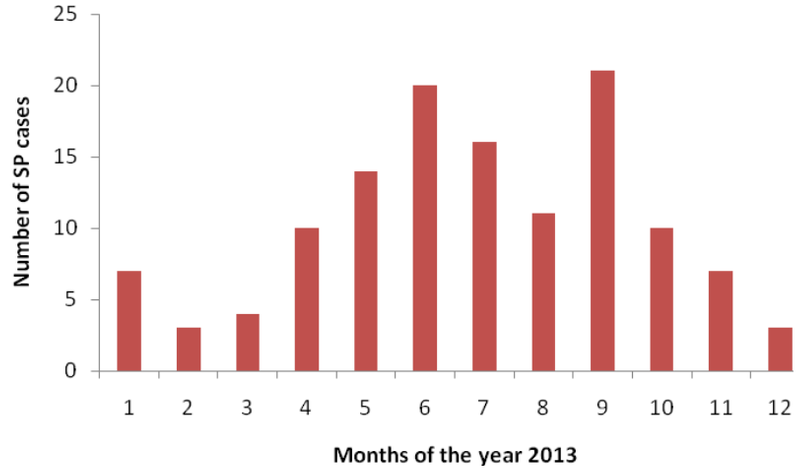

Figure 13: Numbers of cases of *Streptococcus pneumoniae* from patients with severe respiratory illness (SRI) by month and year at enhanced sites, South Africa, 2013.

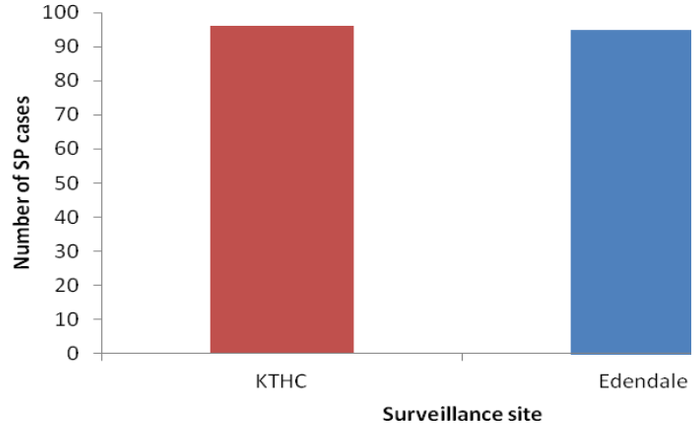

Figure 14: Numbers of cases of *Streptococcus pneumonia* from patients with severe respiratory illness by surveillance site, South Africa, 2013.

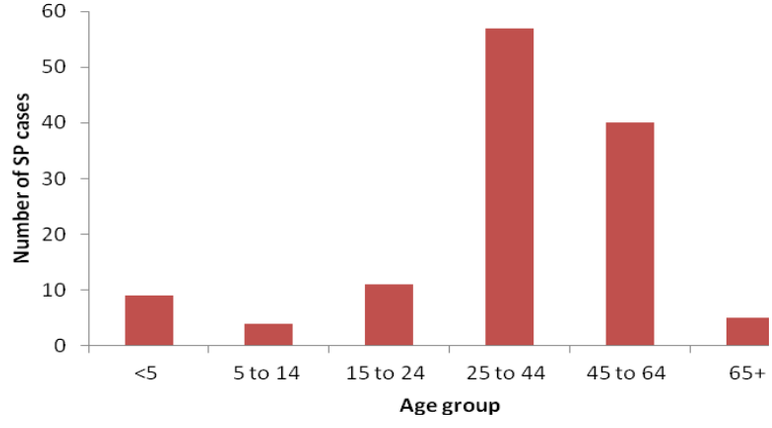

Figure 15: Numbers of cases of *Streptococcus pneumoniae* from patients with severe respiratory illness by age group at enhanced sites, South Africa, 2013.

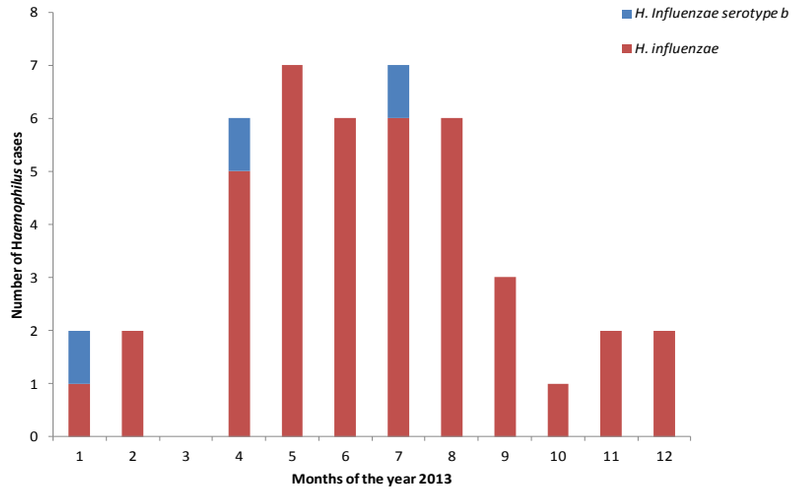

Figure 16: Numbers of cases of *Haemophilus influenzae and Haemophilus influenzae* serotype b from patients with severe respiratory illness by month and year at enhanced sites, South Africa, 2013.

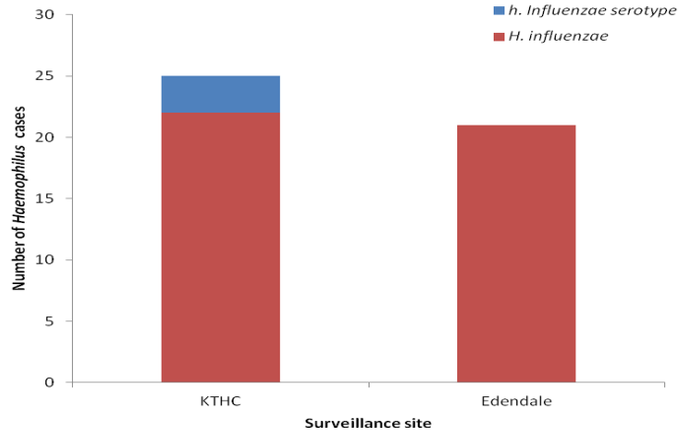

Figure 17: Numbers of cases of *Haemophilus influenzae* and *Haemophilus influenzae* serotype b among patients with severe respiratory infection by study site at enhanced sites, South Africa, 2013.

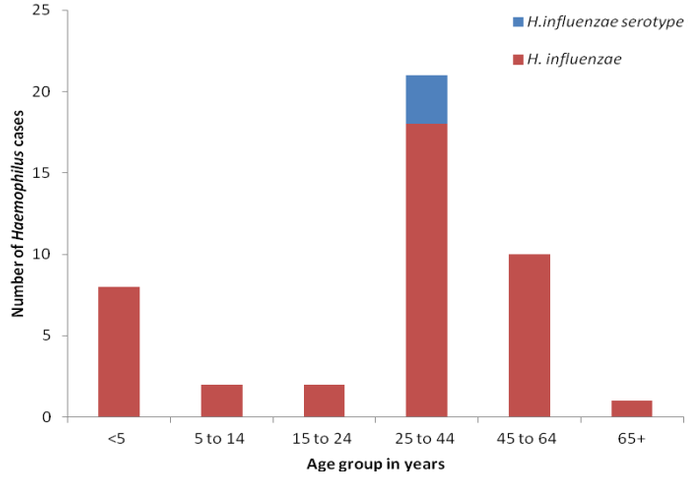

Figure 18: Numbers of cases of *Haemophilus influenzae* and *Haemophilus influenzae* serotype b among patients with severe respiratory infection by age group at enhanced sites, South Africa, 2013.

Discussion

By expanding the existing respiratory surveillance to include additional bacterial pathogens common in South Africa's high HIV prevalence setting and by including surveillance for milder infections, this surveillance programme has enabled descriptions of the prevalence of additional respiratory pathogens in patients with different clinical presentations at the enhanced sites. These pathogens are not routinely tested for in the public hospital setting due to cost and the difficulty in getting appropriate specimens.

Atypical bacterial pathogens were uncommonly identified: *M. pneumoniae* was found in 2% of cases, *Legionella* spp. in 1% and *C. pneumoniae* in 0.2% of cases. The highest detection rate of *M. pneumoniae* was in children aged 1 to 4 years of age and all positive *Legionella* cases were detected in adult patients in the 15-64 years age category. During the one year period of this survey, 18 (1%) pertussis cases among patients with SRI and ILI were detected. Most clinicians do not consider pertussis in adults and although it is a notifiable condition it is seldom reported. The highest number of pertussis cases was detected in patients with SRI and was similar between the two sites. While disease was identified in all age groups, disease burden was greatest in the 25-44 year age group. ILI cases were spread across the following age groups: <5, 5 to 14 and 25 to 44 years. With the change from whole-cell to acellular pertussis vaccine in the routine immunisation schedule from 2009, it is important that monitoring for a possible increase in case numbers continues. Further analysis of data gathered from this surveillance programme will allow for the identification of risk groups to be targeted for interventions and to describe how co-infections with these pathogens relate to patient outcome.

Acknowledgements

Special thanks to the following: Patients from participating sites who agreed to enroll in our study; surveillance officers from all the participating sites; clinicians from the sites and the data teams that work on the project.

References

1. Communicable Diseases Surveillance Bulletin. National Institute for Communicable Diseases, 2013: 11 (4): 101-114.
2. Thurman KA, Warner AK, Cowart KC, Benitez AJ, Winchell JM. Detection of *Mycoplasma pneumoniae, Chlamydia pneumoniae*, and *Legionella* spp. in clinical specimens using a single-tube multiplex real-time PCR assay. *Diagn Microbiol Infect Dis* 2011; 70:1-9.
3. Tatti KM, Wu KH, Tondella ML, Cassiday PK, Cortese MM, Wilkins PP, Sanden GN. Development and evaluation of dual-target real-time polymerase chain reaction assays to detect *Bordetella* spp. *Diagn Microbiol Infect Dis* 2008; 61: 264-72.
4. Carvalho MG, Tondella ML, McCaustland K, Weidlich L, McGee L, Mayer LW, Steigerwalt A, Whaley M, Facklam RR, Fields B, Carlone G, Ades EW, Dagan R, Sampson JS. Evaluation and improvement of real-time PCR assays targeting lytA, ply, and psaA genes for detection of pneumococcal DNA. *J Clin Microbiol* 2007; 45: 2460-246.

Table 1: Provisional number of laboratory confirmed cases of diseases under surveillance reported to the NICD - South Africa, corresponding periods 1 January - 30 September 2013/2014*

Disease/Organism	1 Jan to 30 Sep, year	EC	FS	GA	KZ	LP	MP	NC	NW	WC	South Africa
Anthrax	2013	0	0	0	0	0	0	0	0	0	0
	2014	0	0	0	0	0	0	0	0	0	0
Botulism	2013	0	0	0	0	0	0	0	0	0	0
	2014	0	0	0	0	0	0	0	0	0	0
Cryptococcus spp.	2013	505	184	1496	1308	109	260	34	198	400	4494
	2014	533	150	957	1084	75	211	29	144	459	3642
Haemophilus influenzae, invasive disease, all serotypes	2013	20	13	93	39	2	10	4	3	83	267
	2014	24	12	78	43	0	15	4	4	77	257
Haemophilus influenzae, invasive disease, < 5 years											
Serotype b	2013	3	1	11	5	0	2	0	0	4	26
	2014	2	1	6	1	0	0	1	0	9	20
Serotypes a,c,d,e,f	2013	0	1	5	0	0	0	1	0	7	14
	2014	0	1	4	2	0	0	0	0	3	10
Non-typeable (unencapsulated)	2013	0	2	17	4	0	0	1	1	20	45
	2014	1	0	11	5	0	1	0	0	13	31
No isolate available for serotyping	2013	1	3	18	6	1	5	1	0	5	40
	2014	4	3	21	14	0	3	1	3	8	57
Measles	2013	1	0	1	0	0	0	0	0	0	2
	2014	1	2	8	3	0	1	0	0	1	16
Neisseria meningitidis, invasive disease	2013	30	11	51	30	1	3	2	4	37	169
	2014	32	5	46	15	0	2	0	2	43	145
Novel Influenza A virus infections	2013	0	0	0	0	0	0	0	0	0	0
	2014	0	0	0	0	0	0	0	0	0	0
Plague	2013	0	0	0	0	0	0	0	0	0	0
	2014	0	0	0	0	0	0	0	0	0	0
Rabies	2013	0	2	0	1	3	1	0	0	0	7
	2014	2	0	0	0	1	0	1	1	0	5
*Salmonella typhi***	2013	1	1	21	10	0	10	0	1	12	56
	2014	1	3	32	12	0	8	0	0	17	73
Streptococcus pneumoniae, invasive disease, all ages	2013	233	140	743	372	43	92	63	100	352	2138
	2014	176	127	742	391	26	92	28	82	396	2060
Streptococcus pneumoniae, invasive disease, < 5 years	2013	34	29	172	54	5	9	4	27	53	387
	2014	21	16	145	61	6	12	5	14	57	337
Vibrio cholerae O1	2013	0	0	0	0	1	0	0	0	0	1
	2014	0	0	2	0	0	0	0	0	0	2
Viral Haemorrhagic Fever (VHF)											
Crimean Congo Haemorrhagic Fever (CCHF)	2013	0	2	0	0	0	2	0	1	0	5
	2014	0	1	0	0	0	0	2	0	0	3
Other VHF (not CCHF)	2013	0	0	0	0	0	0	0	0	0	0
	2014	0	0	0	0	0	0	0	0	0	0

Footnotes

*Numbers are for cases of all ages unless otherwise specified. Data presented are provisional cases reported to date and are updated from figures reported in previous bulletins.

Provinces of South Africa: EC – Eastern Cape, FS – Free State, GA – Gauteng, KZ – KwaZulu-Natal, LP – Limpopo, MP – Mpumalanga, NC – Northern Cape, NW – North West, WC – Western Cape

0 = no cases reported

**Laboratory-based surveillance for *Shigella* and *Salmonella* spp other than *typhi* has been discontinued as of 2014

Table 2: Provisional laboratory indicators for NHLS and NICD, South Africa, corresponding periods 1 January - 30 September 2013/2014*

Programme and Indicator	1 January to 30 September, year	EC	FS	GA	KZ	LP	MP	NC	NW	WC	South Africa
Acute Flaccid Paralysis Surveillance											
Cases < 15 years of age from whom specimens received	2013	44	13	46	58	36	26	5	20	30	278
	2014	37	18	61	56	35	34	8	17	31	297

Footnotes

*Numbers are for all ages unless otherwise specified. Data presented are provisional numbers reported to date and are updated from figures reported in previous bulletins.

Provinces of South Africa: EC – Eastern Cape, FS – Free State, GA – Gauteng, KZ – KwaZulu-Natal, LP – Limpopo, MP – Mpumalanga, NC – Northern Cape, NW – North West, WC – Western Cape

Monitoring for the presence of polio in a country is based on AFP (acute flaccid paralysis) surveillance – the hallmark clinical expression of paralytic poliomyelitis. The clinical case definition of AFP is an acute onset of flaccid paralysis or paresis in any child under 15 years of age. AFP is a statutory notifiable disease and requires that 2 adequate stool specimens are taken as soon as possible, 24 to 48 hours apart, but within 14 days after onset of paralysis, for isolation and characterisation of polio virus. The differential diagnosis of AFP is wide, the most common cause of which is Guillain-Barre Syndrome. The incidence of AFP in a population has been studied in a number of developing countries and WHO have determined, as a result of these studies, that the criterion for adequate surveillance of AFP is 2 cases per 100 000 population of children less than 15 years of age (it was formerly 1 per 100,000 but this was thought to be inadequately sensitive).

The Communicable Diseases Surveillance Bulletin is published by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory Services (NHLS), Private Bag X4, Sandringham, 2131, Johannesburg, South Africa.

Suggested citation: [Authors' names or National Institute for Communicable Diseases (if no author)]. [Article title]. Communicable Diseases Surveillance Bulletin 2014; 12(4): [page numbers].

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