SUPPLEMENT ARTICLE

Influenza Surveillance in 15 Countries in Africa, 2006–2010

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Background. In response to the potential threat of an influenza pandemic, several international institutions and governments, in partnership with African countries, invested in the development of epidemiologic and laboratory influenza surveillance capacity in Africa and the African Network of Influenza Surveillance and Epidemiology (ANISE) was formed.

Methods. We used a standardized form to collect information on influenza surveillance system characteristics, the number and percent of influenza-positive patients with influenza-like illness (ILI), or severe acute respiratory infection (SARI) and virologic data from countries participating in ANISE.

Results. Between 2006 and 2010, the number of ILI and SARI sites in 15 African countries increased from 21 to 127 and from 2 to 98, respectively. Children 0–4 years accounted for 48% of all ILI and SARI cases of which 22% and 10%, respectively, were positive for influenza. Influenza peaks were generally discernible in North and South Africa. Substantial cocirculation of influenza A and B occurred most years.

Conclusions. Influenza is a major cause of respiratory illness in Africa, especially in children. Further strengthening influenza surveillance, along with conducting special studies on influenza burden, cost of illness, and role of other respiratory pathogens will help detect novel influenza viruses and inform and develop targeted influenza prevention policy decisions in the region.

Influenza infection is a major cause of morbidity and mortality worldwide. At particular risk of severe disease are young children, pregnant women, the elderly, and persons with underlying medical conditions [1, 2]. The burden and epidemiology of influenza have been studied almost exclusively in developed settings, but influenza may have a different epidemiology in lesser resourced settings such as much of Africa

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due to lack of healthcare access, untreated comorbidities such as human immunodeficiency virus (HIV) and tuberculosis, malnutrition, and other factors.

The few investigations of outbreaks of seasonal influenza in Africa have reported alarmingly high case-fatality proportions [3–5]. Furthermore, pandemic influenza strains can emerge and/or spread undetected in settings with less extensive surveillance systems, and pandemic influenza has the potential to cause relatively greater morbidity and mortality in resource-poor countries. In 2003, avian influenza A(H5N1) spread to several countries in Asia and eventually reached Africa [6], infecting humans in 3 countries on the continent (Djibouti, Egypt, and Nigeria) [7]. Analysis of mortality data from the 1918 pandemic found that increased mortality was associated with lower income countries such as those found in the African region [8].

In response to this pandemic threat, beginning in 2006, several international institutions and governments, in partnership with African countries, invested in the development of epidemiologic and laboratory influenza surveillance capacity in Africa. This expanded surveillance allowed for detection and monitoring of influenza A(H1N1)pdm09, but, to date, neither pandemic nor seasonal influenza have been fully described in the region. A recent review of literature published from 1980 to 2009 found that most countries in sub-Saharan Africa have inadequate data for informing influenza public health policies. Substantive data on influenza incidence, case-fatality ratios, seasonality, economic burden, and the contribution of influenza to adult hospitalizations for acute respiratory infection are very limited [9].

In this article, we document influenza surveillance capacity from 2006 to 2010 in 15 African countries that received financial and/or technical support from the US Centers for Disease Control and Prevention (CDC) as well as from other sources. In 2009, efforts to generate and disseminate data on the burden and epidemiology of influenza disease in Africa were formalized into the African Network for Influenza Surveillance and Epidemiology (ANISE). We summarize surveillance data collected through ANISE to describe influenza age distribution, seasonality, strain circulation, and percent of respiratory disease in which influenza virus was detected.

METHODS

We used a standardized form to collect data on surveillance system characteristics, including the date surveillance started and the number of sites conducting surveillance for influenza like illness (ILI) and/or severe acute respiratory infection (SARI). We also collated information on the number of ILI and SARI specimens collected and tested, the percentage of these that tested positive for influenza by age and by month, and information on influenza seasonal and pandemic strains. Surveillance data from the World Health Organization's (WHO) influenza reporting system, FluNet, was aggregated to understand how reporting to WHO increased over time [10]. For the purposes of this article, the term "African countries" refers to all 54 countries on the continent, irrespective of WHO region.

We reviewed the case definitions used in each country and compared them to the following case definitions that have been recommended by the WHO and the Pan American Health Organization (PAHO) as follows:

> ILI: Any person with sudden onset of fever >38°C AND cough or sore throat in the absence of other diagnosis [11].
> SARI: Persons >5 years old presenting with symptoms of acute lower respiratory infection with sudden onset of fever >38°C, AND cough or sore throat, AND shortness of breath or difficulty breathing, AND requiring hospitalization [11, 12].
> Persons ≤5 years: Integrated Management of Childhood Illnesses case definition for pneumonia and severe pneumonia [11, 13].

South Africa used case definitions that varied slightly from the standard definitions described above; persons 3 months to 5 years of age were classified as a SARI case if they had a physician-diagnosed lower respiratory tract infection irrespective of signs and symptoms and persons 2 days to 2 months were classified as a SARI case if they had a diagnosis of suspected sepsis or a physician-diagnosed lower respiratory tract infection irrespective of signs and symptoms.

Ministries of health and other partner institutions were contacted in Angola, Côte D'Ivoire, Democratic Republic of Congo (DRC), Egypt, Ethiopia, Ghana, Kenya, Madagascar, Morocco, Nigeria, Rwanda, South Africa, Tanzania, Uganda, and Zambia. To examine how surveillance capacity changed over time, we aggregated countries into 5 separate subregions: North Africa (Egypt and Morocco), West Africa (Côte D'Ivoire, Ghana, and Nigeria), East Africa (Ethiopia, Kenya, Rwanda, Tanzania, and Uganda), and South/Central Africa (Angola, DRC, Madagascar, South Africa and Zambia), and plotted the number of surveillance sites, specimens collected, and number of positive influenza samples by year in these subregions. To assess the role of influenza as a cause of ILI and SARI, we calculated the percentage of specimens positive for influenza during complete years of surveillance in each country and by age group. Where known, we excluded outbreak-related cases from the analysis. We distinguished between private sector surveillance systems with dedicated staff and national ILI surveillance systems by networks of private physicians. To describe seasonality, we plotted the monthly number and proportion of influenza-positive specimens for each of the subregions but

described South Africa separately as it is a temperate country with characteristic Southern Hemisphere seasonality. We aggregated data using the same subregions to describe influenza circulation by seasonal and pandemic strains. All countries used reverse transcription polymerase chain reaction (RT-PCR) methods to test patient specimens.

RESULTS

From 2006 through 2010, the number of ANISE countries conducting surveillance increased from 6 to 15 (Figures 1 and Supplementary Figure 1). During that same time period, these countries increased the number of ILI sites from 21 to 127, the number of ILI private practitioner sites from 210 to 290, and the number of SARI sites from 2 to 98 (Figure 1 and Table 1). Most of the countries (11 of 15) had ILI and SARI surveillance sites inside and outside the capital city or economic center (Supplementary Table 1). From 2006 to 2010, the number of specimens tested in these 15 countries per year increased from 4623 to 44 763 and the number of influenza-positive specimens increased from 1474 to 6240 (Figure 1). Similarly, from 2006 to 2010, the number of African countries that reported data to WHO's FluNet increased from 8 to 26. The 15 countries featured in this article reported to FluNet; they reported 1047 influenza-positives out of 3157 specimens tested in 2006 and 8488 influenza-positives out of 45 891 specimens tested in 2010 [10].

Among the 15 countries that conducted at least 1 complete year of surveillance for ILI between 2006 and 2010, 21.7% of ILI cases (5165/69 860) tested positive for influenza, ranging from 6.7% in Angola to 40.4% in Madagascar. Overall, 10.1% of SARI cases (4427/43 620) tested positive for influenza, ranging from 4.6% in Ethiopia to 25.5% in Côte D'Ivoire (Table 1).

The highest number of cases tested was among children <5 years of age, among which 27 135 ILI cases and 27 029 SARI cases were tested for influenza. Children <5 years of age accounted for 48% (54 164/113 164) of all ILI and SARI cases tested and 39% (8155/21 090) of all influenza-positive cases. The ILI percent positive was highest (34%) in the 10–14 year age group but was also high among other age groups, with the lowest ILI percent positive (17%) among those >65 years. The SARI percent positive was highest (12%) in children 10–14 years but was also high among the other young age groups, with the lowest SARI percent positive (3%) among those >65 years (Figure 2).

Seasonal patterns were difficult to discern because relatively few specimens were collected before 2009. The North African subregion (Egypt and Morocco) and the country of South Africa had the most clearly defined seasons, and they

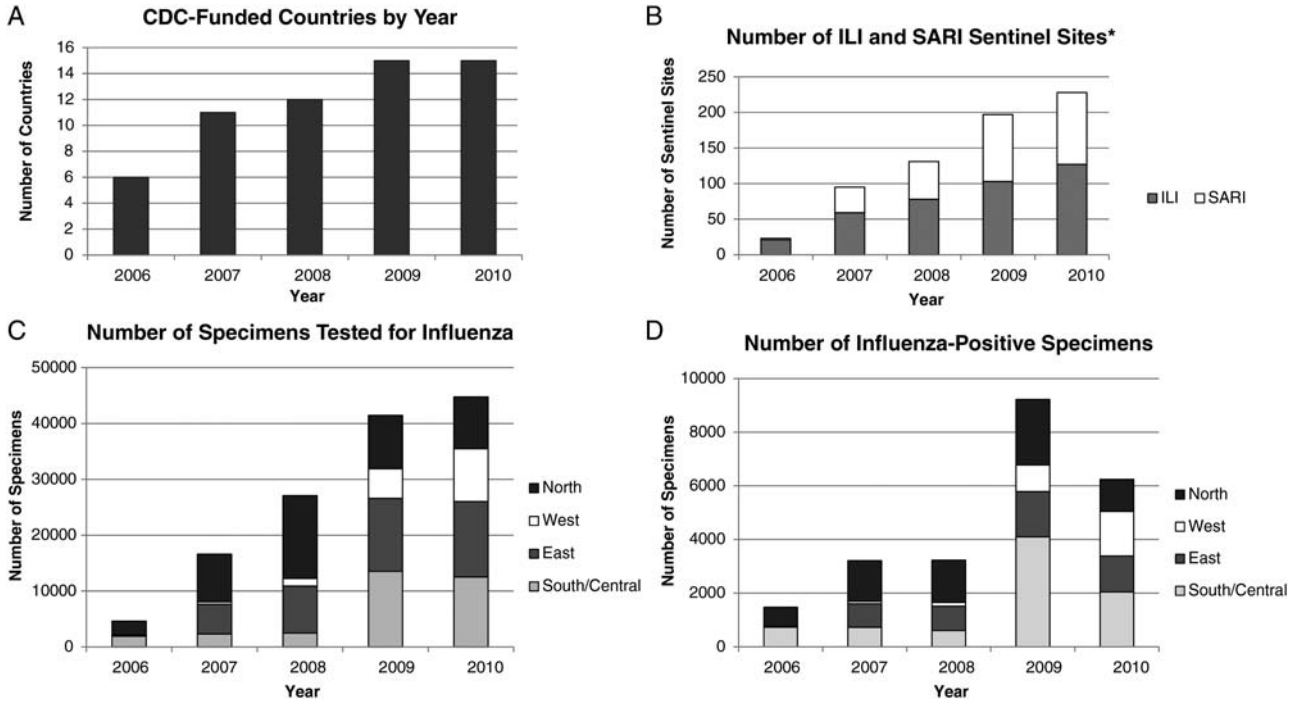

Figure 1. Number of ANISE countries funded by the Centers for Disease Control and Prevention (CDC), sentinel sites, specimens tested for influenza, and influenza-positive specimens in 15 African countries, 2006–2010. *Excludes influenza-like illness (ILI) private practitioners in Morocco and South Africa. Abbreviation: SARI, severe acute respiratory infection.

are both temperate. In North Africa, the number and percentage of influenza-positive specimens were usually highest between November and January of each year. In South Africa, the number and percentage of influenza-positive specimens were usually highest between June and August of each year. The West, East, and South/Central African subregions had less clearly defined seasonal peaks. East Africa had a higher prevalence of influenza in July through October (Figure 3).

Substantial cocirculation of influenza A and B occurred most years in most subregions. In 2006, 2007, and 2009, 3 of the 4 subregions had the same predominant influenza type or subtype. In 2006 and 2007, B was the predominant type in every region except South/Central Africa where H3N2 predominated in 2006 and H1N1 in 2007. In 2008, strain predominance varied across subregions. In 2009, influenza A (H1N1)pdm09 was the predominant subtype in every region except West Africa where H3N2 predominated. In 2010, type and subtype predominance varied across subregions: H3N2 predominated in East Africa, B predominated in South/Central Africa and North Africa, and influenza A (H1N1)pdm09 predominated in West Africa. Of note, predominance of influenza A(H1N1)pdm09 in West Africa occurred 1 year after it was predominantly circulating in the other African sub-regions (Supplementary Figure 2).

DISCUSSION

We show that, since 2006, substantial progress has been made to improve surveillance of influenza in Africa. The number of countries conducting surveillance, the number of sentinel sites, and the number of specimens tested have increased sharply, which has allowed for better understanding of seasonal influenza and the recent pandemic. The addition of sites conducting surveillance for SARI has allowed us to understand the role of influenza in hospitalized patients, a group of patients that are especially relevant from a clinical and public health perspective. Our data show that, as in the rest of the world, seasonal influenza is a substantial cause of respiratory disease in persons of all ages, associated on average with 22% of ILI and 10% of SARI. Influenza was consistently detected in a higher percentage of ILI cases than in SARI cases, which likely reflects the higher specificity of the ILI case definition for influenza compared to the SARI case definition [14]. Our findings regarding the percentage of influenza-positive ILI and SARI specimens are slightly higher than those reported by

Table 1. Number of Specimens Tested and Number of Influenza-Positive Specimens by ILI and SARI

Country	Date Surveillance Started	No. of Sentinel Sites (2006–2010)		Complete years of surveillance	No. of Specimens Tested for Influenza		No. (%) of Influenza-Positive Specimens	
		ILI	SARI		ILI	SARI	ILI	SARI
Angola	Apr 2008	0–6	0–6	2010	478	371	32 (6.7)	37 (10.0)
Côte D'Ivoire	Jan 2003	5–9	0–8	2006–2010	4620	94	890 (19.3)	24 (25.5)
DRC	Jan 2007	0–5	0–2	2009–2010	2510	662	404 (16.1)	77 (11.6)
Egypt	Feb 1999	8–8	0–8	2006–2010	10777	9368	984 (9.1)	993 (10.6)
Ethiopia	Nov 2008	0–3	0–2	2008–2010	115	131	11 (9.6)	6 (4.6)
Ghana	Sept 2007	0–19	0–3	2008–2010 (2009–2010 for SARI)	7669	688	1619 (21.1)	61(8.9)
Kenya	Oct 2006	2–10	2–10	2007–2010	11577	17388	1739 (15.0)	1814 (10.4)
Madagascar	1972	6–31	0–17	2006–2010	5712	NA	2310 (40.4)	NA
Morocco	Feb 1996	0–16 (99–110)[a]	0–16	2006–2010	7516	2323	2033 (27.0)	420 (18.1)
Nigeria	Apr 2008	0–4	0–4	2009–2010	2748	755	225 (8.2)	43 (5.7)
Rwanda	Jul 2008	0–6	0–6	2009–2010	1081	1471	273 (25.3)	96 (6.5)
South Africa	Feb 1984 (ILI)	(111–180)[a]	0–4	2006–2010	10164	8052	4089 (40.2)	701 (8.7)
	Feb 2009 (SARI)							
Tanzania	May 2008	0–5	0–5	2009–2010	1097	713	97 (8.8)	57 (8.0)
Uganda	May 2007	0–3	0–5	2008–2010	3359	642	421 (12.5)	41 (6.4)
Zambia	Apr 2009	0–2	0–2	2010	437	962	38 (8.7)	57 (5.9)
Total		21–127 (210–290)[a]	2–98		69860	43620	15165 (21.7)	4427 (10.1)
Median % positive							15.6	8.9

Abbreviations: DRC,Democratic Republic of Congo; ILI, influenza-like illness; NA, not available; SARI,severe acute respiratory infection.

[a] ILI Private Practitioners. In Morocco, ILI Private Practitioners only collect data from October through April.

other resource-limited countries outside of Africa; a study in Bangladesh found that 10% of ILI cases and 6% of SARI cases seeking care between May 2007 through December 2008 tested positive for influenza by real-time RT-PCR [15]. Studies in Cambodia and Indonesia found that 10% and 11% of ILI cases tested positive for influenza, respectively [16, 17].

In our study, the burden of respiratory disease and influenza was highest in children <5 years of age; approximately 48% of all ILI and SARI cases and 39% of all influenza-positive cases reported in these surveillance systems were from this age group. This finding is consistent with other studies in the region that have found that influenza is commonly identified in young children who suffer from acute respiratory illness [18–20]. Of note is in this study is that although children may be overrepresented in the surveillance, the role of influenza as a possible cause of 10%–12% of respiratory disease hospitalizations is substantial. In the United States, young children bear a heavy burden of respiratory disease [21] and of influenza-associated hospitalizations [22], similar to our findings from Africa. Nonetheless, the age distribution of influenza-associated ILI and SARI in our study was likely influenced by the low number of specimens collected previous to 2009, when seasonal influenza circulated, compared to 2009 and 2010, when influenza A(H1N1)pdm09 predominated. In other parts of the world such as the United States, Mexico, and China, younger adults were disproportionately affected by influenza A(H1N1)pdm09, an age distribution that differed from other years dominated by seasonal influenza, when young children and the elderly tend to be the most affected age groups [23–25]. The age distribution of influenza in Africa may be affected by the high prevalence of HIV in adults. In Kenya, HIV infection predominately affects those <65 years and was found to be a substantial risk factor for hospitalization for influenza disease [26]. In similar manner, HIV-infected persons hospitalized with influenza infection in South Africa have an increased risk of death compared to noninfected persons [27].

In our study, influenza peaks in the North African subregion and in the country of South Africa corresponded to the northern and southern hemisphere's winter season, respectively. The West, East, and South/Central African subregions had relatively undefined influenza transmission patterns. Several factors are likely to drive influenza seasonality, including climate, host distribution, and behavior patterns. Laboratory studies have identified cold temperature, low relative humidity, and, most recently, absolute humidity as important drivers of influenza transmission [28, 29]. It is unclear how these factors contribute to the lack of seasonality we observed in most of Africa. Our ability to interpret seasonality in this study is limited. Except for the country of South Africa, we do not present data on seasonality by country, and large climatic differences exist between and within countries. In addition, few specimens were collected during certain time periods in some countries.

The predominant influenza strain each year tended to be the same across most of the 4 subregions in Africa. Cocirculation of nearly all of the strains also occurred each year excluding 2006, which had minimal data. One regional strain

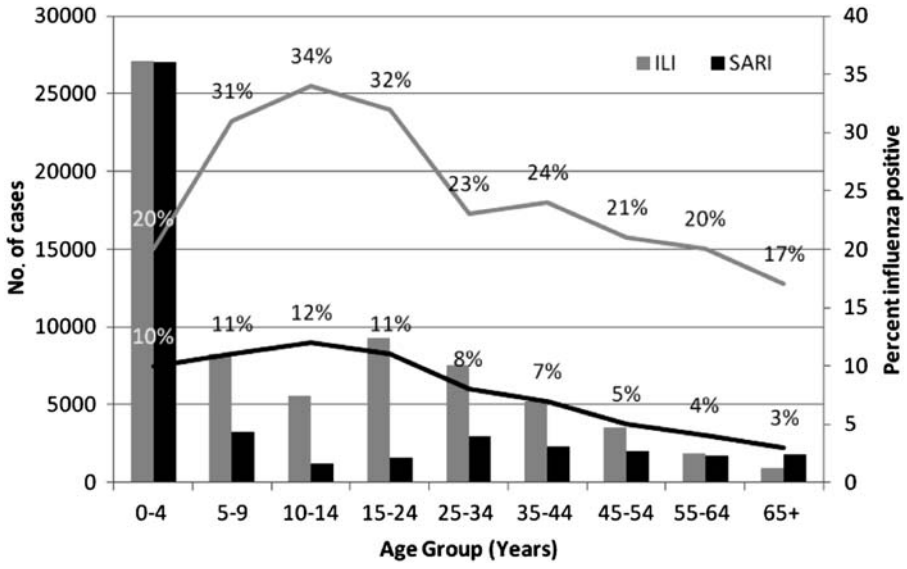

Figure 2. No. of influenza-like illness (ILI) and severe acute respiratory infection (SARI) cases tested and proportion positive for influenza in 14 African countries* by age group, 2006–2010. *Excludes Angola because their data could not be classified into the age group categories used in this figure.

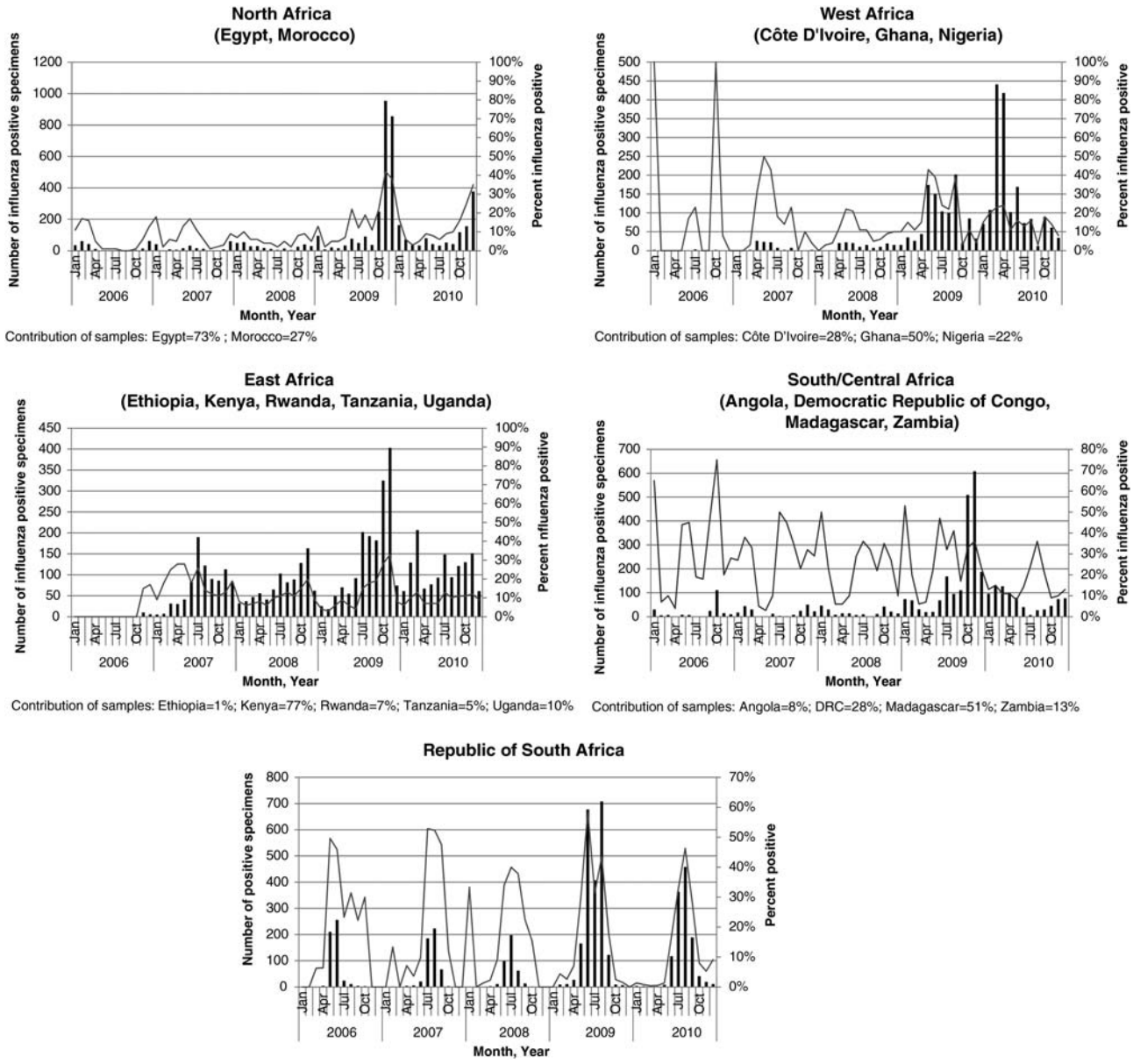

Figure 3. No. and percent of influenza-positive specimens in North, West, East, and South/Central African subregions and the country of South Africa, 2006–2010.

difference of interest occurred in 2009, when influenza A (H1N1)pdm09 spread quickly through the African continent except West Africa. Influenza A(H1N1)pdm09 transmission did not become predominant in West Africa until 2010, at which time it was declining and not predominant in the other subregions [30, 31].

Our findings have several limitations. These data only represent 15 of the 54 countries in the African continent. In addition, we cannot make conclusions about the absolute burden of influenza, only the potential contribution of influenza to respiratory disease because these are sentinel surveillance data. Moreover, we could not examine the true relative burden of influenza among children compared to older adults because samples may have been disproportionately collected from children because some sites were pediatric hospitals. Therefore, the relative burden of all-cause ILI and SARI in the <5-year age group compared to older children and adults may not be accurately represented here. We were also unable to compare the percent influenza-positivity of different subtypes by age. Nevertheless, the percentage of influenza-positive specimens in ILI and SARI cases likely reflects the relative contribution of influenza to illness in different age groups. The case definitions for SARI that were used also may not capture all patients with severe respiratory disease nor those who presented with

nonrespiratory symptoms (ie, congestive heart failure) that may be have been influenza-related. Countries may also have different sampling strategies for testing ILI and SARI cases, and despite the use of standard case definitions, sampling may be biased toward collection of more specimens from patients who are suspected on clinical grounds to have influenza. The increase in influenza-positive specimens in 2009 and 2010 may reflect specimens collected outside regular surveillance during the pandemic that were more likely to be positive for influenza, such as those gathered from contacts of confirmed cases.

Our analysis is only a first step to better understand influenza burden and epidemiology in Africa. Although this region faces substantial challenges in several areas of health, maintaining surveillance for respiratory illnesses, especially those associated with hospitalization, is critical for global health security and to help support interventions to prevent such illnesses. Moreover, it is important to identify circulating viruses and evaluate how well they match with global vaccines to assess the value of vaccination. Young children in sub-Saharan Africa, bear a disproportionately high burden of acute respiratory infections compared to the rest of the world [32]. Maternal immunization may protect pregnant women, who are at high risk of severe influenza illness, and newborns for the first 3–6 months of life [33], when the risk of severe influenza illness is elevated [34].

Since the global emergence of avian influenza A(H5N1), efforts by countries, CDC, Institut Pasteur, WHO, and other organizations have been instrumental in increasing surveillance efforts in the region [35]. It is not possible to attribute the increase in surveillance to any one effort.

This multi-institutional commitment to respiratory disease surveillance will likely remain for the time being, although it will not be indefinite, and individual countries' governments and institutions need to take steps now toward sustainability: to strengthen, and if necessary, resize these surveillance systems to provide nationally relevant data on influenza circulation, risk groups, and burden. Some degree of international support will likely be needed for some time, although as the burden of influenza is documented, this may garner support from other partners in the global health community. Leveraging efforts to conduct surveillance for other vaccine-preventable diseases and priority diseases will likely be necessary to help ensure sustainability. Further strengthening of influenza surveillance in Africa, along with conducting special studies on influenza burden, risk groups, cost of illness, the role of other respiratory pathogens, and the efficacy and applicability of new vaccine technologies and strategies remains critical to determine the epidemiology and relative importance of influenza in Africa, and to monitor for novel influenza strains. Very little is known on the role of comorbidities such as malaria, tuberculosis, and HIV on influenza severity in Africa, nor on the burden among children who may not have access to healthcare. Annual, universal vaccination in Africa is clearly not an option in the foreseeable future; however, as global manufacturing capacity increases and new vaccines and vaccination strategies are developed, surveillance and other data can inform policy decisions on targeted vaccination of risk groups even if only for a short high-risk period such as during pregnancy or early infancy.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Disclaimers. This publication and its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention.

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