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# Neural Tube Defects in Pregnancies Among Women With Diagnosed HIV Infection — 15 Jurisdictions, 2013–2017

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In May 2018, a study of birth defects in infants born to women with diagnosed human immunodeficiency virus (HIV) infection in Botswana reported an eightfold increased risk for neural tube defects (NTDs) among births with periconceptional exposure to antiretroviral therapy (ART) that included the integrase inhibitor dolutegravir (DTG) compared with other ART regimens (*1*). The World Health Organization* (WHO) and the U.S. Department of Health and Human Services† (HHS) promptly issued interim guidance limiting the initiation of DTG during early pregnancy and in women of childbearing age with HIV who desire pregnancy or are sexually active and not using effective contraception. On the basis of additional data, WHO now recommends DTG as a preferred treatment option for all populations, including women of childbearing age and pregnant women. Similarly, the U.S. recommendations currently state that DTG is a preferred antiretroviral drug throughout pregnancy (with provider-patient counseling) and as an alternative antiretroviral drug in women who are trying to conceive.§ Since 1981 and 1994, CDC has supported separate surveillance programs for HIV/acquired immunodeficiency syndrome (AIDS) (*2*) and birth defects (*3*) in state health departments. These two surveillance programs can inform public health programs and policy, linkage to care, and research activities. Because birth defects surveillance programs do not collect HIV status, and HIV surveillance programs do not routinely collect data on occurrence of birth defects, the related data have not been used by CDC to characterize birth defects in births to women with HIV. Data from these two programs were linked to estimate overall prevalence of NTDs and prevalence of NTDs in HIV-exposed pregnancies during 2013–2017 for 15 participating jurisdictions. Prevalence of NTDs in pregnancies among women with diagnosed HIV infection was 7.0 per 10,000 live births, similar



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* https://www.who.int/medicines/publications/drugalerts/Statement_on_DTG_18May_2018final.pdf.

† https://aidsinfo.nih.gov/news/2094/statement-on-potential-safety-signal-in-infants-born-to-women-taking-dolutegravir-from-the-hhs-antiretroviral-guideline-panels; https://aidsinfo.nih.gov/news/2109/recommendations-regarding-the-use-of-dolutegravir-in-adults-and-adolescents-with-hiv-who-are-pregnant-or-of-child-bearing-potential.

§ https://www.who.int/news-room/detail/22-07-2019-who-recommends-dolutegravir-as-preferred-hiv-treatment-option-in-all-populations; https://aidsinfo.nih.gov/guidelines/html/3/perinatal/224/whats-new-in-the-guidelines.

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to that among the general population in these 15 jurisdictions, and the U.S. estimate based on data from 24 states. Successful linking of data from birth defects and HIV/AIDS surveillance programs for pregnancies among women with diagnosed HIV infection suggests that similar data linkages might be used to characterize possible associations between maternal diseases or maternal use of medications, such as integrase strand transfer inhibitors used to manage HIV, and pregnancy outcomes. Although no difference in NTD prevalence in HIV-exposed pregnancies was found, data on the use of integrase strand transfer inhibitors in pregnancy are needed to understand the safety and risks of these drugs during pregnancy.

In the United States, many aspects of adult HIV surveillance are standardized across all 50 states, the District of Columbia, and six territories, but surveillance for pregnancy outcomes among women with diagnosed HIV infection varies across jurisdictions (*2*). A comprehensive national surveillance approach for birth defects does not exist. Not all jurisdictions have birth defects surveillance programs, and among those that do, there is variability in surveillance methods and in the program's authority to ascertain cases that end in a stillbirth or termination. Active birth defects surveillance programs send abstractors to hospitals and other data sources to identify pregnancies affected by birth defects; passive birth defects surveillance programs receive notifications from hospitals and health care practitioners about pregnancies affected by birth defects, and some passive surveillance programs use a hybrid method where notifications lead to abstractions for verifying reported cases (*4*).

CDC contacted the 20 jurisdictions with the highest numbers of women of reproductive age living with diagnosed HIV infection that also had birth defects surveillance programs with data available from 2013 to 2017. This period was chosen to ascertain birth defects during the 5 years after DTG was approved for use in the United States by the Food and Drug Administration in 2013. Certain jurisdictions were not able to obtain the required legal agreements between the different governmental departments responsible for each program to perform the data linkage or were otherwise not able to contribute to this effort.

After obtaining required agreements, the birth defects surveillance programs in 15 jurisdictions (including 11 states, Atlanta metropolitan area, New York City, Philadelphia, and Puerto Rico) identified pregnancies affected by NTDs (on the basis of *International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code range 740–742.0 and ICD-10-CM codes Q00.0–Q01.9, Q05.0–Q05.9, Q07.01, and Q07.03) for the period 2013 through 2017. U.S. jurisdictions have varying levels of authority to ascertain nonlive births. For this report, pregnancies include live births, stillbirths, and induced terminations. Identifying data for the mothers was matched to HIV surveillance records, using locally established linking algorithms, to ascertain whether any data related to the women with an NTD-affected pregnancy were also available in the HIV surveillance system.

Total population prevalence estimates for NTDs were calculated by dividing the number of pregnancies affected by

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NTDs by the total number of live births during 2013–2017 in the reporting jurisdictions. Denominators for prevalence calculations of HIV-exposed births were the number of live births that occurred during 2013–2017 among women with diagnosed HIV infection. To establish these denominators, most jurisdictions matched HIV surveillance data to birth certificates; one state used data from their comprehensive newborn HIV screening program. Variability was assessed using 95% confidence intervals (CIs) calculated with the Poisson methods. Nonoverlapping confidence intervals were used as a measure of statistical difference to acknowledge the imprecision of the estimate on the basis of small numbers. SAS (version 9.4; SAS Institute) was used to conduct all analyses.

Participating jurisdictions[¶] had surveillance information on 64,272 women aged 13–44 years with diagnosed HIV infection in 2015,[**] which represents approximately 70% of all women aged 13–44 years living with diagnosed HIV infection in the United States in 2015. Among 8,043,489 live births from these jurisdictions during 2013–2017, the prevalence of NTDs was 5.8 per 10,000 live births (Table). Data linkage between the two independent surveillance systems in each jurisdiction identified eight NTD cases, and there were 11,425 live births to women with diagnosed HIV infection during 2013–2017, for a prevalence of 7.0 per 10,000 HIV-exposed live births; this did not significantly differ from the general population prevalence, on the basis of the overlapping confidence intervals.

For the general population in these 15 jurisdictions, the NTD prevalence was higher when the analysis was limited to active surveillance programs (7.0 per 10,000 live births), which have more complete data than do passive programs (4.7 per 10,000 live births) (Table). Among women with diagnosed HIV infection, the NTD prevalence estimates based on active and passive surveillance had overlapping confidence intervals, suggesting no difference on the basis of case ascertainment. Surveillance systems that are not able to ascertain birth defects among nonlive births will usually underascertain NTDs because pregnancies affected by NTDs often lead to nonlive births. However, for these 15 jurisdictions, the NTD prevalence estimates for the general population and NTD prevalence estimates for pregnancies of women with diagnosed HIV infection were considered similar among programs that did or did not include nonlive births because the respective confidence intervals were wide and overlapped.

## Discussion

For the first time, linked data from HIV and birth defects surveillance programs were used to estimate the prevalence of birth defects among pregnancies among women with diagnosed HIV infection. The prevalence of NTDs among pregnancies among women with diagnosed HIV infection in these 15 jurisdictions (7.0 per 10,000 live births) does not appear to differ from all births in these jurisdictions and from the estimate for the U.S. population based on 24 states (approximately 8 per 10,000 live births) (*5*,*6*). However, an association between ART and NTDs could not be assessed because information about maternal ART use is not collected routinely.

Additional pregnancies were followed up in Botswana, and two studies (*7*,*8*) have reported that risks of NTDs are lower than suggested by the initial study (*1*) (threefold versus eightfold, respectively). WHO now recommends DTG as

[¶] Florida, Georgia (metropolitan Atlanta), Illinois, Louisiana, Maryland, Massachusetts, New Jersey, New York City, New York State, North Carolina, Pennsylvania, Philadelphia, Puerto Rico, South Carolina, and Texas.

[**] https://www.cdc.gov/nchhstp/atlas/index.htm.

**TABLE. Neural tube defect (NTD) prevalence among the general population of births and human immunodeficiency virus (HIV)–exposed births in 15 jurisdictions — United States, 2013–2017***

| Type of BD surveillance | General population births | | | HIV-exposed births | | |
|---|---|---|---|---|---|---|
| | Total no. of live births | NTDs | NTDs per 10,000 live births (95% CI[§]) | Total no. of live births | NTDs | NTDs per 10,000 live births (95% CI[§]) |
| **All jurisdictions[†]** | **8,043,489** | **4,656** | **5.8 (5.6–6.0)** | **11,425** | **8** | **7.0 (3.0–13.8)** |
| Active BD surveillance[¶] | 3,850,065 | 2,685 | 7.0 (6.7–7.2) | 4,697 | 3 | 6.4 (1.3–18.7) |
| Passive BD surveillance[¶] | 4,193,424 | 1,971 | 4.7 (4.5–4.9) | 6,728 | 5 | 7.4 (2.4–17.3) |
| Only ascertain BD in live births[**] | 2,194,646 | 1,261 | 5.7 (5.4–6.1) | 3,681 | 4 | 10.9 (3.0–27.8) |
| Ascertain BD in live births and nonlive births[**] | 5,848,843 | 3,395 | 5.8 (5.6–6.0) | 7,744 | 4 | 5.2 (1.4–13.2) |

**Abbreviations:** BD = birth defects; CI = confidence interval.

* Florida provided data from 2013 to 2015.

† Data from Philadelphia and New York City were included in the data for Pennsylvania and New York State, respectively; however, it is important to note that the majority of HIV-exposed pregnancies originated from the metropolitan jurisdictions. Data from the Metropolitan Atlanta Congenital Defects Program (MACDP) represents three counties in Georgia: DeKalb, Fulton, and Gwinnett; the other jurisdictions are statewide.

§ Calculated using exact Poisson methods because of the small number of cases.

¶ Jurisdictions with active BD surveillance: MACDP within Georgia, Louisiana, Massachusetts, North Carolina, Puerto Rico, South Carolina, and Texas; jurisdictions with passive BD surveillance: Florida, Illinois, Maryland, New Jersey, New York, and Pennsylvania.

** Jurisdictions that only ascertain BD in live births: Florida, Louisiana, New Jersey, and Pennsylvania; jurisdictions that ascertain BD in live births and nonlive births: MACDP within Georgia, Illinois, Maryland, Massachusetts, New York, North Carolina, Puerto Rico, South Carolina, and Texas.

a preferred treatment option for all populations, including women of childbearing age and pregnant women based on an evaluation of both risks and benefits.

The HHS Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission now recommends DTG as a preferred antiretroviral drug throughout pregnancy and as an alternative antiretroviral drug in women who are trying to conceive, and also strongly recommends that use of DTG be accompanied by appropriate counseling to allow joint decision-making between patients and providers. CDC is exploring data on ART and birth defects that can be compiled in the United States. The Antiretroviral Pregnancy Registry (*9*) has provided some data to assess this association, but the addition of a U.S. population-based estimate, not dependent on volunteer participation, would be an important addition to the literature. CDC is currently working with partners to use the linked data in this report to ascertain specific ART use before or during early pregnancy and specific NTD phenotypes as well as other birth defects.

The findings in this report are subject to at least five limitations. First, the birth defects surveillance data might have been incomplete because surveillance methods varied by jurisdiction, nonlive birth outcomes were not available in all jurisdictions, and 2017 data might have been incomplete because of delays in abstraction. Second, linkage of persons' data in two separate surveillance programs is never 100% complete because of differences in linking variables, such as names or birth dates, which could have resulted in underestimation of the total number of births and NTDs. Third, approximately one in nine women with HIV have not received a diagnosis and therefore are not monitored by HIV surveillance.[††] Fourth, because of data limitations, it was not possible to adjust for confounders. Finally, CIs were used as a measure of variability, and nonoverlapping CIs were considered statistically different. This analytical approach is considered a conservative evaluation of significance differences and infrequently can lead to the conclusion that estimates are similar, even when point estimates do differ significantly.

Because data on pregnancy and ongoing antiretroviral medication use are not routinely collected in many state HIV surveillance programs, and HIV treatment options are evolving, continued efforts to collect information on pregnancies affected by maternal HIV infection are needed to understand the association between HIV treatment and birth defects and other pregnancy outcomes. Linkage of data from other surveillance programs might help to assess possible associations between maternal disease or maternal use of medications, and pregnancy outcomes.

**Summary**

**What is already known about this topic?**

In 2018, an association between periconceptional dolutegravir exposure and neural tube defects (NTD) was reported in Botswana. Data from U.S. birth defects and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) surveillance programs had not previously been linked to assess NTD prevalence in births to women with HIV.

**What is added by this report?**

Linking of data from birth defects and HIV/AIDS surveillance programs in 15 jurisdictions was done for the first time. The NTD prevalence in HIV-exposed pregnancies during 2013–2017 was estimated to be 7.0 per 10,000 live births, similar to the prevalence in the general population in the 15 jurisdictions and the U.S. estimate.

**What are the implications for public health practice?**

Current U.S. recommendations state that dolutegravir is a preferred antiretroviral drug throughout pregnancy (with provider-patient counseling) and an alternative antiretroviral drug in women who are trying to conceive. Although no difference in NTD prevalence in HIV-exposed pregnancies was found, data on the use of integrase strand transfer inhibitors in pregnancy are needed to understand the safety and risks of these drugs during pregnancy.

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[††] https://www.cdc.gov/hiv/group/gender/women/index.html.

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# *Candida auris* Isolates Resistant to Three Classes of Antifungal Medications — New York, 2019

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*Candida auris* is a globally emerging yeast that causes outbreaks in health care settings and is often resistant to one or more classes of antifungal medications (*1*). Cases of *C. auris* with resistance to all three classes of commonly prescribed antifungal drugs (pan-resistance) have been reported in multiple countries (*1*). *C. auris* has been identified in the United States since 2016; the largest number (427 of 911 [47%]) of confirmed clinical cases reported as of October 31, 2019, have been reported in New York, where *C. auris* was first detected in July 2016 (*1*,*2*). As of June 28, 2019, a total of 801 patients with *C. auris* were identified in New York, based on clinical cultures or swabs of skin or nares obtained to detect asymptomatic colonization (*3*). Among these patients, three were found to have pan-resistant *C. auris* that developed after receipt of antifungal medications, including echinocandins, a class of drugs that targets the fungal cell wall. All three patients had multiple comorbidities and no known recent domestic or foreign travel. Although extensive investigations failed to document transmission of pan-resistant isolates from the three patients to other patients or the environment, the emergence of pan-resistance is concerning. The occurrence of these cases underscores the public health importance of surveillance for *C. auris*, the need for prudent antifungal prescribing, and the importance of conducting susceptibility testing on all clinical isolates, including serial isolates from individual patients, especially those treated with echinocandin medications. This report summarizes investigations related to the three New York patients with pan-resistant infections and the subsequent actions conducted by the New York State Department of Health and hospital and long-term care facility partners.

Clinical *C. auris* cases were defined as those in which *C. auris* was identified in a clinical culture obtained to diagnose or treat disease. Screening cases were defined as those in which *C. auris* was identified by polymerase chain reaction testing and culture, or by culture only, of a sample from an axilla, groin, or nares swab obtained for the purpose of state public health surveillance (*2*). To assess ongoing colonization with *C. auris,* additional swabs were collected over time from patients colonized with *C. auris*.

Wadsworth Center, the New York State public health laboratory, conducted testing to confirm presumptive *C. auris* isolates from various health care facilities in New York during August 2016–June 2019 by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, using both the manufacturer's and in-house validated library databases. The laboratory also performed antifungal susceptibility testing for azoles and echinocandins by broth microdilution and for amphotericin B, by E-test methods* as described previously, and categorized isolates as resistant based on CDC's tentative breakpoints (*1*,*2*). A pan-resistant isolate was defined as one with resistance to the triazole class (fluconazole minimum inhibitory concentration [MIC] ≥32 μg/mL), polyene class (amphotericin B MIC ≥2 μg/mL [E-test values of 1.5 rounded up to 2]), and echinocandins (anidulafungin MIC ≥4 μg/mL, caspofungin MIC ≥2 μg/mL, micafungin MIC ≥4 μg/mL), tested at Wadsworth Center with confirmation by the laboratory at CDC's Mycotic Diseases Branch (*1*,*2*).

Epidemiologic investigation of patients with pan-resistant cases included collecting clinical and exposure data, screening close contacts (persons who had an epidemiologic link to a patient in place or time), and assessing infection control practices in health care facilities that cared for the patients (*2*,*4*,*5*). When close contacts could be located, the New York State Department of Health attempted to obtain swabs for culture.

Site visits involved observations of infection control practices, on-site education, and point prevalence studies. During point prevalence surveys, samples were collected from the nares, axilla, and groin of consenting patients. When possible, samples from the environments of facilities where patients with pan-resistant infections were admitted or resided were collected, with priority given to frequently touched surfaces and objects in patients' rooms.

As of June 28, 2019, a total of 801 patients with *C. auris* were detected in New York, identified through clinical cultures (349) or skin or nares screening swabs only (452) (*3*). Testing of the first available clinical isolates with susceptibilities revealed that 276 of 277 (99.6%) were resistant to fluconazole, 170 of 277 (61.3%) were resistant to amphotericin B, and none was resistant to echinocandins (*1*,*6*). Testing of subsequent available isolates obtained from infected patients with susceptibilities revealed 330 of 331 (99.7%) were resistant to fluconazole,

* E-test, previously known as Epsilometer test, is a method for antimicrobial susceptibility testing that provides an MIC.

210 of 331 (63.4%) were resistant to amphotericin B, and 13 of 331 (3.9%) were resistant to echinocandins (*1*,*6*). Three patients' subsequent isolates were pan-resistant.

The first two patients with pan-resistant *C. auris* infections (patient A and patient B) were aged >50 years and residents of long-term care facilities; each had multiple underlying medical conditions, including ventilator dependence and colonization with multidrug-resistant bacteria (Table). The two patients developed *C. auris* infections in 2017 (patient A) and 2018 (patient B), and multiple samples obtained from them had *C. auris*-positive cultures. Patient A had *C. auris* isolated from a central venous catheter tip and later from blood and urine cultures; patient B had *C. auris* isolated from a urine sample and a tracheal aspirate. All isolates were resistant to fluconazole; seven of 13 (54%) isolates from patient A and three of five (60%) isolates from patient B were resistant to amphotericin B; no isolates were initially resistant to echinocandins. Neither patient was known to have received antifungal medications before the diagnosis of *C. auris* infection, but both patients were treated with prolonged courses of echinocandins after *C. auris* was identified. Patient A was also treated with amphotericin B. Cultures taken after echinocandin therapy from both patients yielded *C. auris* isolates resistant to fluconazole, amphotericin B, and echinocandins. Both patients died; the role of *C. auris* in their deaths is unclear.

No epidemiologic links were found between the two patients. They resided in and were patients at different health care facilities in the same borough of New York City, and neither patient had any known domestic or international travel. Point prevalence surveys, environmental sampling, and infection control assessments were performed at facilities where the two patients had resided to determine whether spread of the resistant isolates occurred (*2*,*4*,*5*). No pan-resistant isolates were identified among contacts or on environmental surfaces from the index patients' rooms or common equipment (after discharge and terminal cleaning) at the three facilities that had cared for these two patients; however, non–pan-resistant *C. auris* was isolated from other patients and the environment at two of these facilities and from the environment at the third facility. Additional infection control and cleaning interventions

**TABLE. Characteristics of three *Candida auris* cases with emergence of pan-resistance to antifungal agents — New York, 2019**

| Characteristic | Patient A | Patient B | Patient C |
|---|---|---|---|
| **Underlying condition** | Chronic ventilator dependence | Chronic ventilator dependence, alcohol dependence | Acute mechanical ventilation, alcohol dependence, chronic skin condition |
| **Antifungal medication received** | Echinocandin, amphotericin B | Echinocandin | Echinocandin |
| **Date pan-resistance confirmed** | February 2019 | March 2019 | June 2019* |
| **Sample type for pan-resistant isolate** | Blood | Urine | Rectal swab |
| **Time from first isolation of *C. auris* to collection of pan-resistant sample** | 22 mos | 13 mos | 2 mos |
| **Time from isolation of pan-resistant *C. auris* to patient's death** | 2 wks | 3–4 wks | 10 mos |
| **MICs for pan-resistant isolates (μg/mL)†** | | | |
| Triazole class | | | |
| Fluconazole | >256 | >256 | >256 |
| Voriconazole | 2 | 2 | 2 |
| Posaconazole | 0.25 | 0.5 | 0.25 |
| Polyene class | | | |
| Amphotericin B | 2 | 2 | 2 |
| Echinocardin class | | | |
| Caspofungin | 16 | 2 | 16 |
| Anidulafungin | 4 | 4 | 4 |
| Micafungin | 4 | 4 | 4 |
| **No. of facilities at which screening was conducted** | 1 | 2 | 1§ |
| **No. of contacts with *C. auris*/No. tested (%)** | 4/35 (11) | 2/50 (4) | 0/15§(0) |
| **No. of contacts with pan-resistant *C. auris*** | 0 | 0 | 0§ |
| **No. of environmental surfaces and equipment with *C. auris*/No. tested (%)** | 14/36 (39) | 3/28 (11) | 1/11§ (9) |
| **No. of environmental surfaces with pan-resistant *C. auris*** | 0 | 0 | 0§ |

**Abbreviation:** MIC = minimum inhibitory concentration.

* Isolate was from April 2017.

† Tentative CDC MIC breakpoints (μg/mL): fluconazole, ≥32; voriconazole: N/A; amphotericin B, ≥2; caspofungin, ≥2; anidulafungin ≥4; micafungin, ≥4. https://www.cdc.gov/fungal/candida-auris/health-professionals.html.

§ Data from an assessment of contacts and environments in March 2017, approximately 1 month before collection of the pan-resistant isolate; laboratory surveillance of a sampling of *Candida* isolates from urine was also conducted.

**Summary**

What is already known about this topic?

*Candida auris* is an emerging yeast that is often drug-resistant.

What is added by this report?

Three chronically ill patients in New York were identified as having pan-resistant *C. auris* after receipt of antifungal medications. No transmission of the pan-resistant isolates was found in patient contacts or the facility environments.

What are the implications for public health practice?

Three years after the first identification of *C. auris* in New York, pan-resistant isolates remain rare. Continued surveillance for *C. auris*, prudent antifungal use, and susceptibility testing for all *C. auris* clinical isolates (especially after patients have been treated with antifungal drugs) are needed.

were implemented by the facilities based on gaps identified during infection control assessments.

After identification of patients A and B in 2019, a retrospective review of all New York *C. auris* isolates and additional antifungal susceptibility testing at CDC identified a third patient (patient C), from whom a *C. auris* isolate from 2017 was found to be resistant to the three major antifungal classes. Patient C was also aged >50 years and had multiple comorbidities and a prolonged hospital admission and long-term care admission at facilities that were different (including in another borough) from those that cared for patients A and B. The initial isolate of *C. auris* from patient C was from a February 2017 blood culture; treatment with an echinocandin for 2 weeks followed. Serial isolates obtained from February to early April 2017 were resistant to fluconazole, had varying susceptibility to amphotericin B (11 of 17 [65%] total isolates resistant), and were initially susceptible to echinocandins; the isolate resistant to all three classes of antifungals was obtained from a rectal swab collected in late April 2017 to assess ongoing colonization following resolution of active infection. Patient C was discharged to a long-term care facility (different from the facilities that cared for patients A and B) on contact precautions. Subsequent serial surveillance cultures from several body sites were obtained, and all remained negative for >6 months until the patient died from underlying medical conditions. Patient C was not known to have had any recent foreign or domestic travel and did not have any known contact with patient A or patient B.

Isolates from all three patients were initially sensitive to echinocandins; resistance was detected after treatment, indicating that it emerged during treatment with the drugs. No evidence of transmission of the resistant isolates following these events was found.

## Discussion

The precise mechanism of resistance in these isolates is unknown, although echinocandin resistance in other species of *Candida* is linked to mutations in the drug target protein Fks1 (*7*). Approximately 3 years into the New York outbreak, these pan-resistant isolates still appear to be rare, but their emergence is concerning. In other countries with earlier emergence of *C. auris,* higher levels of echinocandin resistance and pan-resistance have been reported (*8*). An isolate from Illinois with development of echinocandin resistance after echinocandin treatment was recently described, although that isolate was susceptible to azoles (*9*). The pan-resistant cases reported here were all from New York, where the South Asia clade (clade 1) predominates (*5*). This clade is known to exhibit increased antifungal resistance compared to other clades of *C. auris* (*8*). Surveillance for additional pan-resistant isolates in New York is ongoing.

Echinocandins are the treatment of choice for *C. auris* infections (*1*). Most New York *C. auris* strains are fluconazole-resistant, and most strains of C. *auris* have been susceptible to echinocandins (*1*). However, because of the potential for development of resistance, patients on antifungal treatment for *C. auris* should be monitored closely for clinical improvement, and follow-up cultures should be obtained. Repeat susceptibility testing should also be conducted, especially in patients previously treated with echinocandins. Consultation with an infectious disease specialist is recommended, especially given the possibility of emergence of pan-resistance.

These findings illustrate the need to continue surveillance for *C. auris,* encourage prudence in the use of antifungal medications, and conduct susceptibility testing on all clinical isolates, including serial isolates from a single patient, especially those treated with echinocandins.

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## *C. auris* Investigation Work Group

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# Population Movement Patterns Among the Democratic Republic of the Congo, Rwanda, and Uganda During an Outbreak of Ebola Virus Disease: Results from Community Engagement in Two Districts — Uganda, March 2019

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Tailoring communicable disease preparedness and response strategies to unique population movement patterns between an outbreak area and neighboring countries can help limit the international spread of disease. Global recognition of the value of addressing community connectivity in preparedness and response, through field work and visualizing the identified movement patterns, is reflected in the World Health Organization's declaration on July 17, 2019, that the 10th Ebola virus disease (Ebola) outbreak in the Democratic Republic of the Congo (DRC) was a Public Health Emergency of International Concern (*1*). In March 2019, the Infectious Diseases Institute (IDI), Uganda, in collaboration with the Ministry of Health (MOH) Uganda and CDC, had previously identified areas at increased risk for Ebola importation by facilitating community engagement with participatory mapping to characterize cross-border population connectivity patterns. Multisectoral participants identified 31 locations and associated movement pathways with high levels of connectivity to the Ebola outbreak areas. They described a major shift in the movement pattern between Goma (DRC) and Kisoro (Uganda), mainly through Rwanda, when Rwanda closed the Cyanika ground crossing with Uganda. This closure led some travelers to use a potentially less secure route within DRC. District and national leadership used these results to bolster preparedness at identified points of entry and health care facilities and prioritized locations at high risk further into Uganda, especially markets and transportation hubs, for enhanced preparedness. Strategies to forecast, identify, and rapidly respond to the international spread of disease require adapting to complex, dynamic, multisectoral cross-border population movement, which can be influenced by border control and public health measures of neighboring countries

During March 15–25, 2019, IDI and CDC, on behalf of MOH Uganda, assessed population movement patterns using the Population Connectivity Across Borders (PopCAB) toolkit,* a CDC innovation, in Uganda's southwestern Kanungu and Kisoro districts bordering DRC and Rwanda (*2*). Qualitative and spatial data were collected using community-level focus group discussions and key informant interviews with participatory mapping to characterize cross-border population movement patterns, through which participants helped facilitators annotate points of interest and travel routes on printed maps scaled to show the tricountry area (DRC, Rwanda, and Uganda). The team purposively sampled participants and event locations to ensure multisectoral representation and incorporate principal locations along community-level movement patterns based on contextual knowledge and discussions with district- and community-level leaders. The IDI-CDC team analyzed the qualitative data to identify themes addressing cross-border movement and border interventions and created and compiled spatial data for all identified locations and travel routes.

The IDI-CDC team conducted 12 data collection events with 52 participants, including border public health volunteers, health care providers, security officials, transportation officials, community leaders, army officers, and informal traders (Table). Participants described movement patterns across the DRC, Rwanda, and Uganda region associated with residents of DRC who were 1) seeking refugee status in Uganda; 2) conducting trade and other business; 3) seeking health care; or 4) visiting family. Participants identified 26 priority locations of interest, and five specific pathways connecting them, including refugee transit centers (two, including one that was also identified as a school), points of entry (eight), health care facilities (six), markets and entrepreneurial sites (nine), schools (one), and transportation hubs (one) (Figure). Participants also identified health care facilities that receive patients traveling from DRC to access cheaper and higher-quality medical care in Uganda. Although participants consistently described refugees as mostly women and children traveling by foot and traders as mostly adults traveling on motorbikes and trucks, the demographics and modes of travel for seeking health care and visiting family were inconsistent.

Five of the 12 events (three focus group discussions and two key informant interviews) described cross-border movements principally between DRC and Uganda, directly and through Rwanda. A main travel pathway linking the three countries was a bus route from DRC (Goma, Butembo, and

* https://www.cdc.gov/globalhealth/security/ghsareport/2018/cdc-innovation.html.

**TABLE. Population Connectivity Across Borders field events in Kanungu and Kisoro districts — Uganda, March 2019**

| Date | Type (no. of participants) | District | Target group | Event location |
|---|---|---|---|---|
| Mar 15 | Key informant interview (1) | Kisoro | Border screening volunteer | Nteko, unofficial POE |
| Mar 18 | Focus group discussion (8) | Kisoro | Transport personnel (motorcycle taxi drivers) | Bunagana, official POE |
| Mar 18 | Key informant interview (1) | Kisoro | Security personnel | Bunagana, official POE |
| Mar 19 | Key informant interview (1) | Kisoro | Health care worker | Nyakabande refugee transit camp |
| Mar 19 | Focus group discussion (4) | Kisoro | Health care workers | Kisoro Hospital |
| Mar 20 | Key informant interview (1) | Kanungu | Security personnel | Kanungu district health office |
| Mar 21 | Key informant interview (1) | Kanungu | District health personnel | Kanungu district health office |
| Mar 21 | Focus group discussion (10) | Kanungu | Community leaders | Butogota (also called Kyeshero), official POE |
| Mar 22 | Focus group discussion (8) | Kanungu | Traders | Ishasha, official POE |
| Mar 23 | Focus group discussion (8) | Kanungu | Health care workers | Bwindi Community Hospital |
| Mar 25 | Focus group discussion (8) | Kanungu | Military personnel at the border point | Kayonza Tea Factory |
| Mar 25 | Key informant interview (1) | Kanungu | Health care worker | Matanda refugee transit center |

**Abbreviation:** POE = point of entry.

other areas) through Rwanda (Gisenyi) and then into Uganda via the Cyanika ground crossing to Kisoro district (Figure). This bus route was mainly used to avoid the insecurity within DRC. However, after the border crossings at Cyanika and Katuna were closed indefinitely beginning February 28, 2019, passengers disembarked at the Rwanda-Uganda border, then walked to the Uganda side, where they rode motorcycle taxis (called "boda bodas") or other buses into Kisoro town (*3*). Some respondents also indicated that bus traffic was increasing on the more direct and insecure route through DRC from Goma, DRC, to Bunagana, Uganda, excluding Rwanda. Another multicountry pathway travelers followed was from DRC through Butogota ground crossing in Kanungu District followed by continued travel to Rwanda using two main routes: 1) southward through the Bwindi forest to Kisoro town and on to Rwanda through Cyanika ground crossing or 2) by bus through Kanungu District, eastward to Rukungiri District, then south to Kabale city, and into Rwanda through Katuna ground crossing. Respondents in the focus group discussions did not describe adjustments to the highlighted southward pathways into Rwanda following the Cyanika and Katuna ground crossing closures, in contrast to the shift in travel patterns from Goma to Uganda.

No seasonality was associated with general population movement, which was almost uniformly described as constant. However, increases in refugee movement were associated with more insecurity in DRC, and increases in trader movements were associated with agricultural cycles for a range of products.

The Uganda MOH National Task Force, which has led Ebola preparedness activities since DRC declared the Ebola outbreak on August 1, 2018, along with district leadership, used these findings to prioritize health facilities, points of entry, and villages for enhanced preparedness activities. These measures included public health screening of travelers, enhanced community-based surveillance procedures, targeted risk communication, and Ebola vaccination of frontline workers at facilities that were more likely to receive patients from outbreak-affected areas of DRC.

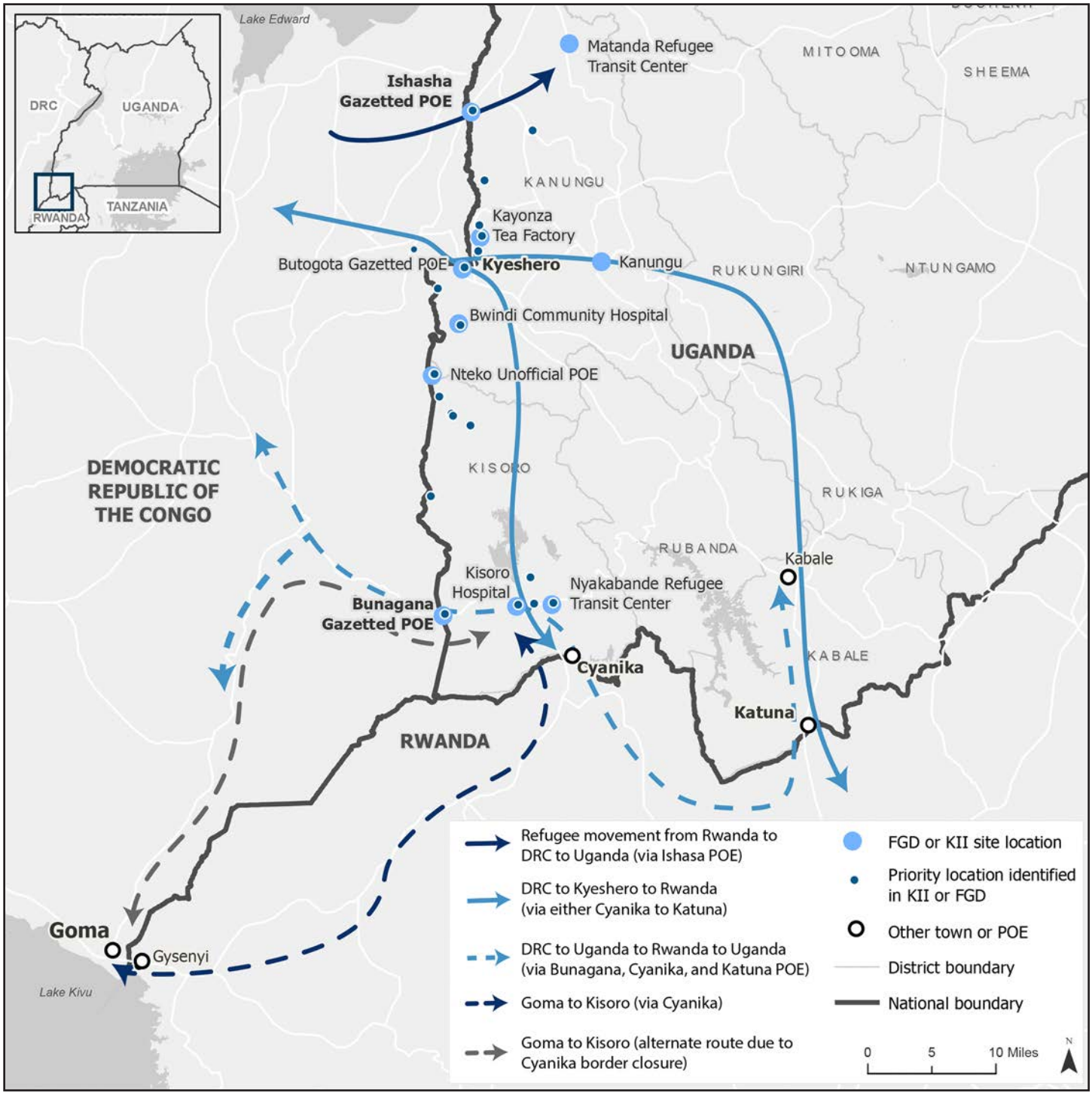
## Discussion

This population connectivity mapping exercise in two high-priority districts of southwestern Uganda helped national and district leadership identify locations and population groups to prioritize for preparedness efforts to avert or contain importation of Ebola from DRC. District-level stakeholders identified numerous locations within Uganda with high connectivity to the outbreak area in DRC. Additional locations within Uganda, such as the Kisoro bus park, were highlighted because of their risk for onward transmission to urban areas within southwestern Uganda and more distant locations, including the capital city of Kampala. The results illustrated the impact of border system interventions on population movement patterns, as evidenced by the major shifts in movement following border closures.

Goma, a large urban area in DRC, first reported an Ebola case on July 30, 2019, which led to a cluster with four confirmed cases (*4*). The multisectoral participants described high connectivity between Goma and southwestern Uganda, raising the need to address population movement and connectivity dynamics there. In response, District Health Officers in Kanungu and Kisoro used the PopCAB results to rapidly target preparedness activities and response capacity assessments to highly connected locations.

When adapting preparedness and response initiatives to the range of locations identified through this initiative, national and district leaders considered the unique characteristics of each location. Preparing workers in a marketplace to better identify persons with suspected Ebola cases follows a different process from that of preparing workers in points of entry or health care facilities. Market vendors who typically lack medical

**FIGURE. Population movement pathways and points of interest from 12 Population Connectivity Across Borders events — Kanungu and Kisoro districts, Uganda, March 2019**




**Abbreviations:** DRC = Democratic Republic of the Congo; FGD = focus group discussion; KII = key informant interview; POE = point of entry.

or public health training, require sensitization and training suitable to their backgrounds. Of note, the observed markets had multiple, nonuniform entry points, posing challenges to screening all market visitors. To increase the likelihood of identifying persons with possible Ebola at such busy locations or on inbound or outbound routes, preparedness efforts might require sensitizing not only stakeholders at the venues but also communities connected with them by proximity or travel patterns. National border health interventions must evolve to accommodate those implemented in neighboring countries as demonstrated by the highlighted shift in movement between countries caused by the Cyanika ground crossing closure.

The findings in this report are subject to at least one limitation regarding potential biases among the purposive participant sampling during the PopCAB implementation. To reduce the risk for bias, the team invited participants who represented multiple sectors and facilitated events in a range of locations across Kanungu and Kisoro districts.

This multisectoral, community-level engagement in southwestern Uganda helped to characterize the complexity of population movement and connectivity among DRC, Rwanda, and Uganda. National and district leadership in Uganda used the results to guide comprehensive border health strategies including identifying ground crossings for enhanced traveler screening and health facilities for surveillance, both along the border and within Uganda (*2*). In addition, the Uganda National Task Force used the results to tailor its surveillance, infection prevention and control, and risk communication strategies to address geographic areas at risk for importation of Ebola and to incorporate community-level sectors that interact with populations connected to the outbreak areas. This method was also adapted and applied to strengthen preparedness for mass gatherings and Ebola vaccination campaigns. Uganda's application of the PopCAB method to enhance Ebola preparedness and response initiatives could be adapted by other countries to better integrate multisectoral, cross-border population movement dynamics, especially in response to events in neighboring countries, into a broader response strategy to forecast, identify, and rapidly respond to the international spread of disease.

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**Summary**

What is known about this topic?

Understanding cross-border population movement patterns can help countries tailor public health interventions to limit international spread of communicable disease.

What is added by this report?

Land-based travel routes among the Democratic Republic of the Congo, Rwanda, and Uganda shifted as a result of formal border closures. Uganda assessed population movement patterns to tailor its surveillance, infection prevention and control, and communication strategies to address the risk for importation of Ebola virus disease from neighboring countries.

What are the implications for public health practice?

Strategies to forecast, identify, and rapidly respond to the international spread of disease require adapting to complex, dynamic, multisectoral cross-border population movement, which can be influenced by border control and public health measures used by neighboring countries.

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# Case Definitions Used During the First 6 Months of the 10th Ebola Virus Disease Outbreak in the Democratic Republic of the Congo — Four Neighboring Countries, August 2018–February 2019

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On August 1, 2018, the Democratic Republic of the Congo (DRC) declared its 10th Ebola virus disease (Ebola) outbreak in an area with a high volume of cross-border population movement to and from neighboring countries. The World Health Organization (WHO) designated Rwanda, South Sudan, and Uganda as the highest priority countries for Ebola preparedness because of the high risk for cross-border spread from DRC (*1*). Countries might base their disease case definitions on global standards; however, historical context and perceived risk often affect why countries modify and adapt definitions over time, moving toward or away from regional harmonization. Discordance in case definitions among countries might reduce the effectiveness of cross-border initiatives during outbreaks with high risk for regional spread. CDC worked with the ministries of health (MOHs) in DRC, Rwanda, South Sudan, and Uganda to collect MOH-approved Ebola case definitions used during the first 6 months of the outbreak to assess concordance (i.e., commonality in category case definitions) among countries. Changes in MOH-approved Ebola case definitions were analyzed, referencing the WHO standard case definition, and concordance among the four countries for Ebola case categories (i.e., community alert, suspected, probable, confirmed, and case contact) was assessed at three dates (*2*). The number of country-level revisions ranged from two to four, with all countries revising Ebola definitions by February 2019 after a December 2018 peak in incidence in DRC. Case definition complexity increased over time; all countries included more criteria per category than the WHO standard definition did, except for the "case contact" and "confirmed" categories. Low case definition concordance and lack of awareness of regional differences by national-level health officials could reduce effectiveness of cross-border communication and collaboration. Working toward regional harmonization or considering systematic approaches to addressing country-level differences might increase efficiency in cross-border information sharing.

Ebola case definitions provided by the MOHs in DRC, Rwanda, South Sudan, and Uganda were compared during the first 6 months of the DRC outbreak. Because Rwanda, South Sudan, and Uganda had no reported cases at the time, their case definitions were for the preparedness phase of emergency response. Three dates for comparison were chosen to assess definitions: the start of the DRC outbreak (August 1, 2018), the period before the peak (November 15, 2018), and 6 months into the outbreak (February 1, 2019).

Criteria for five Ebola case definition categories (community alert, suspected, probable, confirmed, and case contact) were reviewed, accommodating minor wording differences. For example, a confirmed case category might have had three criteria: "suspected case, laboratory-confirmed by reverse transcription–polymerase chain reaction (RT-PCR)," "suspected case, laboratory-confirmed by IgM (immunoglobulin M) antibody presence," or "suspected case with a positive laboratory test." Alerts at points of entry (where travelers were screened for Ebola) were considered an additional category; point of entry alerts were either an independent category or described within the "community alert" category.

The number of criteria present for each country was divided by the total number of possible criteria listed by all of the four countries to calculate the percentage of criteria present per category. The category percentage concordance (overlap) across the four countries was calculated by dividing the number of criteria used by all countries by the total number of possible criteria for that category. Countries that did not use a category were excluded from that category's analysis. Rwanda, South Sudan, and Uganda, the three countries bordering DRC, reported changing their Ebola case definitions in response to the context and perceived risk for an outbreak, especially during the early months of the DRC outbreak. During the 6 months from August 1, 2018, through February 1, 2019, each country revised its case definitions two to four times. The interval between revisions varied from 1 month to 5 months. All four countries revised their definitions in January 2019 after DRC's Ebola incidence peaked in December 2018. Uganda did not include the probable category throughout the 6 months, and South Sudan removed that category by November 2018 (Table 1). Rwanda's case definition did not include a community alert category until January 2019. Only Uganda included the case contact category consistently throughout the 6 months, although other countries defined case contact

**TABLE 1. Number of criteria per category for all major Ebola virus disease (Ebola) case definition categories at three dates during the first 6 months of the 10th Ebola outbreak in the Democratic Republic of the Congo (DRC), with the World Health Organization (WHO) standard Ebola case definition for reference — DRC, Rwanda, South Sudan, and Uganda, August 2018–February 2019**

| | Case definition category | | | | | |
|---|---|---|---|---|---|---|
| Date/Country | No. (%) suspected | No. (%) probable | No. (%) confirmed | No. (%) community alert | No. (%) case contact | No. (%) for POE |
| **August 1, 2018** | | | | | | |
| **Total no. of criteria used by all countries** | **12** | **3** | **5** | **9** | **14** | **1** |
| DRC | 6 (50) | 3 (100) | 2 (40) | 3 (33) | 8 (57) | 1 (100) |
| Rwanda | 6 (50) | 1 (33) | 2 (40) | None* | None | None |
| South Sudan | 3 (25) | 2 (67) | 2 (40) | 4 (44) | 5 (36) | None |
| Uganda | 6 (50) | None | 2 (40) | 4 (44) | 7 (50) | None |
| WHO | 4 (33) | 1 (33) | 3 (60) | 3 (33) | 9 (64) | None |
| **November 15, 2018** | | | | | | |
| **Total no. of criteria used by all countries** | **13** | **3** | **6** | **8** | **12** | **2** |
| DRC | 6 (46) | 2 (67) | 1 (17) | 3 (34) | None | None |
| Rwanda | 6 (46) | 1 (33) | 2 (33) | None | None | None |
| South Sudan | 7 (54) | None | 2 (33) | 6 (75) | None | 2 (100) |
| Uganda | 6 (46) | None | 2 (33) | 3 (34) | 7 (58) | None |
| WHO | 4 (31) | 1 (33) | 3 (50) | 3 (34) | 9 (75) | None |
| **February 1, 2019** | | | | | | |
| **Total no. of criteria used by all countries** | **20** | **3** | **7** | **10** | **13** | **8** |
| DRC | 6 (30) | 1 (33) | 1 (14) | 4 (40) | 6 (46) | 2 (25) |
| Rwanda | 6 (30) | 1 (33) | 1 (14) | 5 (50) | None | 2 (25) |
| South Sudan | 10 (50) | None | 4 (57) | 3 (30) | None | None |
| Uganda | 6 (30) | None | 2 (26) | 4 (40) | 7 (54) | 5 (63) |
| WHO | 4 (20) | 1 (33) | 3 (43) | 3 (30) | 9 (69) | None |

**Abbreviation:** POE = point of entry (a border crossing where travelers were screened for Ebola).
* "None" indicates that the country or WHO had no criteria for this category.

at one of the three dates or might have listed criteria in other surveillance documents.

Most countries listed nonbleeding symptoms of Ebola as criteria in suspected and community alert categories, except Uganda, where Ebola symptom criteria were limited to signs of unusual bleeding (Table 2). Some definitions had no thresholds for fever, and some had two thresholds concurrently in operation; where thresholds were defined, they ranged from ≥100°F (≥37.8°C) to 101.3°F (38.5°C). By the end of the 6 months, the suspected category included a higher proportion of fever-dependent criteria (65%) than did the community alert category (30%). The proportion of fever-dependent criteria for the community alert category declined from 56% at the start of the outbreak to 30% 6 months later. Except for the case contact and confirmed categories, all countries included more criteria per category than did the WHO definitions. From August 2018 to February 2019, the total number of criteria in the suspected category increased from 12 to 20. Concurrently, concordance decreased from 18% to 5% (Figure). The most consistent criteria for a suspected case among all countries were fever, unexplained bleeding, sudden death, and prior contact with a person with suspected, probable, or confirmed Ebola. However, fever was the only criterion consistently standing alone or upon which other criteria depended.

The probable category, present at least once for all countries except Uganda, always included the criterion deceased persons with a suspected case with an epidemiologic link to a case. For the DRC case definition, a probable case could be in a person alive with an epidemiologic link, and for DRC (at all three dates) and South Sudan (only at the start of the outbreak) a probable case could be based on a clinician's suspicion, even without an epidemiologic link. Percentage concordance for the probable category ranged from 33% to 100% (Figure). Laboratory confirmation by RT-PCR or detection of IgM antibody against Ebola virus in a suspected case were typically required for a confirmed case designation (Table 2).

Concordance in the criteria for case contact remained consistently low, increasing from 17% to 20% over the 6-month period (Figure). Initially there was zero concordance for community alerts; concordance increased to 25% in November 2018 but declined back to zero by February 2019. DRC defined point of entry criteria within the community alert category at the start of the outbreak. Rwanda and Uganda added point of entry categories by February 2019; Rwanda's

**TABLE 2. Ebola virus disease (Ebola) case definition criteria for five case definition categories and fever thresholds during the first 6 months of the 10th Ebola outbreak in the Democratic Republic of the Congo (DRC), with the World Health Organization (WHO) standard Ebola case definition for reference — DRC, Rwanda, South Sudan, and Uganda, August 2018–February 2019**

| Category/Criteria | DRC | Rwanda | South Sudan | Uganda | WHO |
|---|---|---|---|---|---|
| **Community alert** | | | | | |
| Unresponsive fever | Y | — | Y | Y | Y |
| Sudden onset fever | Y | — | — | — | — |
| Bloody diarrhea or bloody urine | Y | — | — | Y | — |
| Sudden death | Y | — | Y | Y | — |
| Unexplained bleeding | Y | — | Y | Y | Y |
| Sudden unexplained death and a persistent fever and unexplained bleeding | — | — | Y | — | — |
| Sudden death in the community of a person who had a strange illness | — | — | Y | — | — |
| Fever and international travel in the past 21 days | — | — | Y | — | — |
| Sudden onset fever and severe illness and unexplained bleeding | — | — | Y | — | — |
| Sudden death and travel to DRC in the past 21 days | Y | Y | — | — | — |
| Bleeding in the eyes or urine | Y | — | — | — | — |
| Fever and travel to an Ebola affected area | — | — | Y | — | — |
| Sudden and unexplained death | — | — | Y | — | Y |
| Travel to DRC in the past 21 days | — | Y | — | — | — |
| Travel to DRC in the past 21 days and fever or bleeding symptoms | — | Y | — | — | — |
| Fever that does not respond to typical treatments and one or more bleeding symptom at a point of entry | — | — | — | Y | — |
| Fever at a point of entry | Y | — | — | — | — |
| Unexplained bleeding at a point of entry with or without a fever | — | — | — | Y | — |
| Sudden death at a point of entry | — | — | — | Y | — |
| Fever at a point of entry and an epidemiologic link to a suspected, probable, or confirmed case of Ebola | — | — | — | Y | — |
| Visibly ill at a point of entry and travel to DRC in the past 21 days | — | Y | — | — | — |
| Signs of illness or bleeding at a point of entry | Y | — | — | — | — |
| Consistently high fever at a point of entry | — | — | Y | — | — |
| Fever at a point of entry and travel to DRC in the past 21 days | Y | Y | Y | Y | — |
| **Suspected case** | | | | | |
| Unresponsive fever | — | — | — | Y | — |
| Sudden fever and contact with a person with suspected, probable, or confirmed Ebola | — | — | Y | — | — |
| Sudden fever and an epidemiologic link to Ebola | — | — | Y | — | — |
| Alive or dead with fever and contact with a person with suspected, probable, or confirmed Ebola | Y | Y | Y | Y | Y |
| Alive or dead with a fever and contact with an ill or dead animal | Y | Y | Y | — | Y |
| Sudden onset fever and exposure to a mine or cave | — | Y | — | — | — |
| Sudden onset fever and three symptoms of Ebola | Y | — | Y | — | — |
| Sudden onset fever and one bleeding symptom | — | — | Y | Y | — |
| Unresponsive fever and one or more bleeding issue, such as a miscarriage | — | — | Y | — | — |
| Sudden fever and an epidemiologic link to Ebola | — | — | Y | — | — |
| Fever and travel to DRC and one or more symptoms of Ebola | — | Y | — | — | — |
| Fever and travel to DRC | — | — | Y | Y | — |
| Fever and travel to DRC and an epidemiologic link to Ebola | — | Y | — | — | — |
| Unexplained bleeding | Y | Y | Y | Y | Y |
| Unexplained bleeding and travel to DRC | — | — | Y | — | — |
| Unexplained bleeding and an epidemiologic link to Ebola | — | — | Y | — | — |
| Three or more symptoms of Ebola and DRC travel or an epidemiologic link to Ebola | — | — | Y | — | — |
| Sudden and unexplained death | Y | Y | Y | Y | Y |
| Sudden unexplained death and an epidemiologic link to Ebola | — | — | Y | — | — |
| Spontaneous miscarriage | Y | — | — | — | — |
| Fever and signs of Ebola in a person from the Ebola-affected area | Y | — | — | — | — |
| Sudden death after the person had a fever and bleeding symptoms | — | — | Y | — | — |
| Sudden fever that does not respond to typical treatment for fever and one or more symptoms of Ebola | — | — | Y | — | — |
| Fever and signs of Ebola in a person from the Ebola-affected area | Y | — | — | — | — |
| Fever and travel within 21 days to the affected area and contact with a dead or ill animal | — | Y | — | — | — |
| Sudden unexplained death and travel to DRC in the past 21 days | — | Y | Y | — | — |
| **Probable case** | | | | | |
| Clinician suspects Ebola | Y | — | Y | — | — |
| Suspected case in a person who is dead and has an epidemiologic link to Ebola | Y | Y | Y | — | Y |
| Suspected case in a person who is alive and has an epidemiologic link to Ebola | Y | — | — | — | — |
| Suspected case in a person who is dead with an epidemiologic link to a confirmed case | Y | Y | — | — | — |

See table footnotes on next page.

point of entry criteria were very similar to its criteria for community alert, and Uganda's were the same. South Sudan briefly included point of entry alert in October 2018 but removed it by February 2019.

## Discussion

Because of the high volume of cross-border population movement between DRC and neighboring countries, strengthening binational and multinational public health communication and coordination is a growing priority. The four contiguous countries are currently reviewing their case definitions and developing procedures to engage in cross-border and regional collaborations that respond to and accommodate differences in case definitions to prevent cross-border transmission of Ebola. Case definitions might not move toward concordance among countries responding to an outbreak and countries in different stages of preparation for possible outbreak spread

**Summary**

**What is already known about this topic?**

Whereas countries might initially base case definitions on global standards, historical context and perceived risk often affect why countries modify and adapt disease case definitions over time, moving either toward or away from regional harmonization.

**What is added by this report?**

Even with a regional risk for Ebola virus disease (Ebola) (i.e., importation into three countries bordering the Democratic Republic of the Congo), Ebola case definitions became increasingly complex and less concordant during a 6-month period.

**What are the implications for public health practice?**

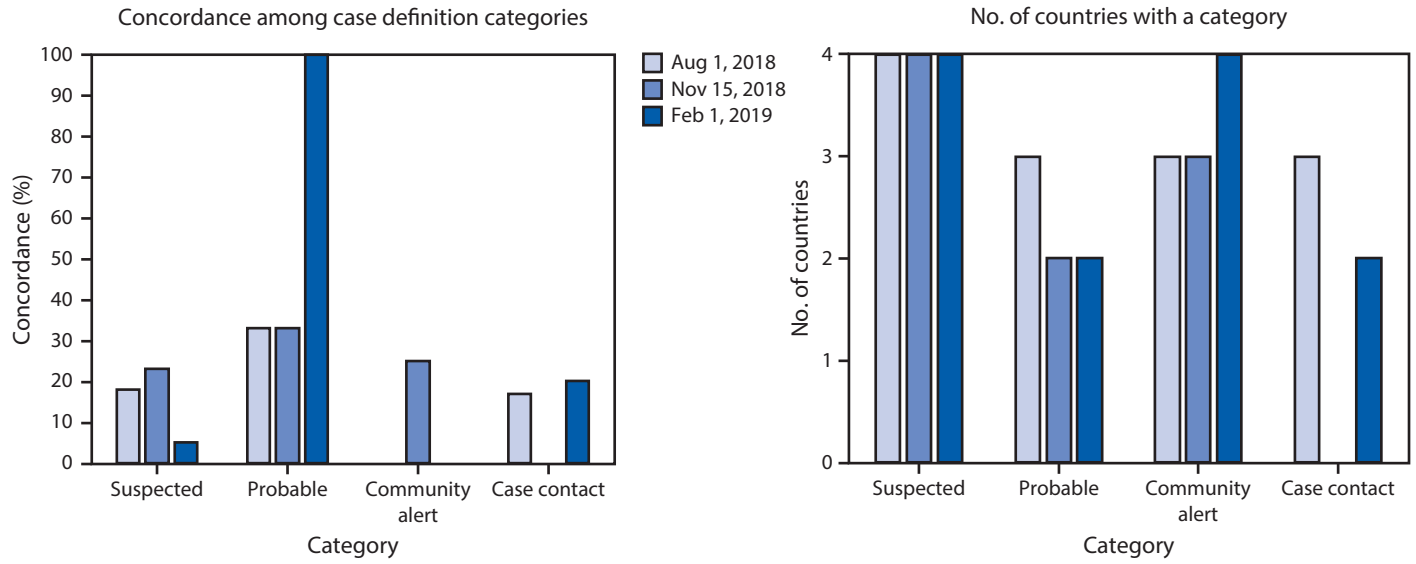
The low level of concordance in case definitions among countries, when case definitions are critical to many outbreak response and preparedness activities, indicates the need for routine evaluation of regional differences in case definitions and implementation of systematic approaches to advance harmonization.

**TABLE 2. (*Continued*) Ebola virus disease (Ebola) case definition criteria for five case definition categories and fever thresholds during the first 6 months of the 10th Ebola outbreak in the Democratic Republic of the Congo (DRC), with the World Health Organization (WHO) standard Ebola case definition for reference — DRC, Rwanda, South Sudan, and Uganda, August 2018–February 2019**

| Category/Criteria | DRC | Rwanda | South Sudan | Uganda | WHO |
|---|---|---|---|---|---|
| **Confirmed case** | | | | | |
| Suspected or probable case of Ebola with an RT-PCR positive result | — | Y | Y | — | — |
| Suspected or probable case of Ebola with IgM antibodies to Ebola virus | — | Y | Y | — | — |
| Suspected case of Ebola with an RT-PCR positive result | Y | — | Y | Y | Y |
| Suspected case of Ebola with IgM antibodies to Ebola virus | Y | — | Y | Y | Y |
| Suspected case with Ebola virus isolation | — | — | Y | — | Y |
| Suspected of probable case of Ebola with GeneXpert and RT-PCR positive results | — | Y | — | — | — |
| Suspected of probable case of Ebola with GeneXpert positive result | — | — | Y | — | — |
| Suspected case with a positive laboratory result | Y | — | — | — | — |
| **Case contact** | | | | | |
| Person was in the same household | Y | — | — | Y | Y |
| Had direct contact | — | — | — | Y | — |
| Shared the same room or bed | — | — | Y | — | — |
| Direct contact with a person with Ebola, alive or dead | Y | — | Y | — | Y |
| Touched body fluids | Y | — | Y | Y | Y |
| Direct contact with the body of a person with Ebola at a funeral | — | — | — | — | Y |
| Attended a burial ceremony of a person with suspected or confirmed Ebola | Y | — | — | Y | — |
| Gave patient care | Y | — | Y | — | — |
| Touched soiled linen | Y | — | Y | Y | Y |
| Was breastfed | Y | — | — | Y | Y |
| Shared transport | Y | — | — | Y | — |
| Had animal contact | Y | — | — | — | Y |
| Ate bushmeat | Y | — | — | — | Y |
| Had a laboratory exposure | Y | — | — | — | Y |
| **Fever threshold** | | | | | |
| ≥100°F (≥37.8°C) | — | — | Y | — | — |
| >100°F (>37.8°C) | — | — | Y | — | — |
| ≥100.4°F (≥38°C) | — | Y | — | Y | — |
| >100.4°F (>38°C) | Y | Y | — | — | — |
| 101.3°F (38.5°C) | — | — | Y | — | — |
| Elevated temperature | Y | — | — | — | — |
| Sudden onset fever | — | — | Y | — | Y |
| Sudden onset of a very high fever | — | — | Y | — | — |
| Persistently high fever | — | — | Y | — | — |
| Fever that does not respond to treatment for usual causes of fever | Y | — | Y | Y | — |

**Abbreviations:** Y = criterion present in category definition; — = criterion not present in category definition; IgM = immunoglobulin M; RT-PCR = reverse transcription–polymerase chain reaction.

**FIGURE. Percentage of concordance of Ebola virus disease category* case definitions and number of countries with case definition categories during the first 6 months of the 10th Ebola outbreak in the Democratic Republic of the Congo — four neighboring countries,† August 1, 2018–February 1, 2019**




* Not all countries had a case definition for all categories at any or all of the three time points. Concordance is indicated only for the countries that included the category.
† Democratic Republic of the Congo, Rwanda, South Sudan, and Uganda.

(*3*,*4*). This analysis found a sustained low level of concordance in Ebola case definitions among DRC and three neighboring countries throughout revisions made over the first 6 months of the outbreak. As the number of criteria increased, case definitions became more complex, and concordance among countries decreased.

DRC is operating in a response phase, and case definitions in the preparedness-phase countries might need to vary in sensitivity thresholds to identify cases based on available resources, perceived level of risk, and competing priorities (*5*). Complexity of and discordance in case definitions affect information sharing about alerts and cases across national borders. The potential risk associated with this discordance to cross-border communication and collaboration during an outbreak with a threat of cross-border spread might warrant a move toward regional harmonization or tailored binational and multinational communication strategies.

The findings in this report are subject to at least two limitations. First, although there was variation among countries in case definition sensitivity, this analysis did not evaluate the effect of discordance on surveillance; cases with in-country transmission have been limited to DRC. Second, MOH-approved case definitions are at the national level and might not represent those used by stakeholders at all levels, where local or cross-border informal information sharing might occur.

Awareness of differences in case definitions across the region provides critical fact-based support to national governments, regional or multinational bodies, and other public health stakeholders as they engage in or shift to preparedness and response initiatives with enhanced cross-border collaboration. Countries should consider routine evaluation of case definitions and implement systematic approaches to harmonization, when possible, and accommodate country-level differences when necessary. Revisiting these strategies throughout the continuum of preparedness and response might reduce the likelihood of cross-border transmission.

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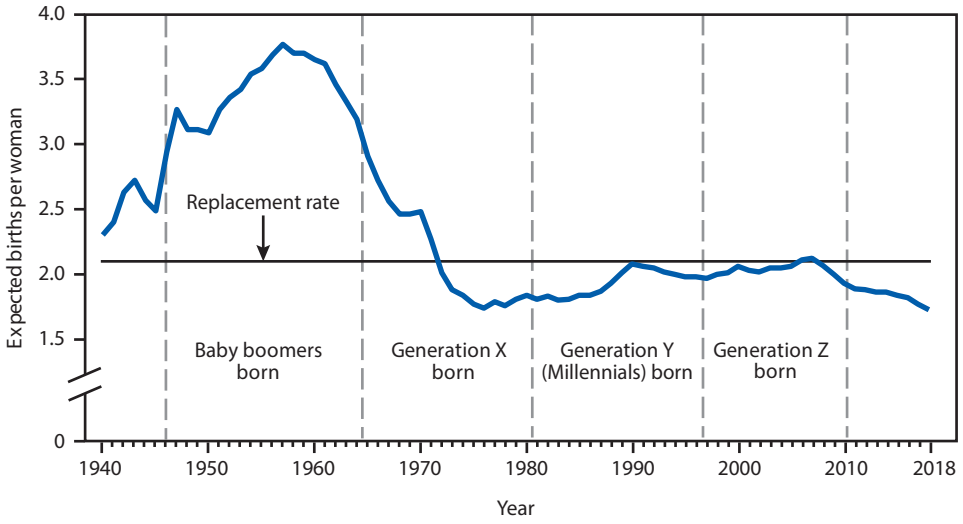
# QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Expected Number of Births over a Woman's Lifetime* — National Vital Statistics System, United States, 1940–2018




* The total fertility rate (TFR), the expected number of births that a woman would have over her lifetime, is the sum of the birth rates for women by 5-year age groups for ages 10–49 years in a given year, multiplied by 5 and expressed per woman.

During 1940–2018, the expected number of births a woman would have over her lifetime, the TFR, was highest for women during the post-World War II baby boom (births during 1946–1964). In 1957, the TFR reached a peak of 3.77 births per woman. The TFR generally declined for the birth cohort referred to as Generation X from 2.91 in 1965 to 1.84 in 1980. For the birth cohorts referred to as Millennials (Generation Y) and Generation Z, the TFR first increased to 2.08 in 1990 and then remained generally stable until it began to decline in 2007. By 2018, the expected number of births per women fell to 1.73, a record low for the nation. Except for 2006 and 2007, the TFR has been below the level needed for a generation to replace itself (2.10 births per woman) since 1971.

**Source:** National Vital Statistics System. Birth data, 1940–2018. https://www.cdc.gov/nchs/nvss/births.htm.

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