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Utilizing spatiotemporal analysis of influenza-like illness and rapid tests to focus swine-origin influenza virus intervention

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ABSTRACT

In the spring of 2009, a novel strain of H1N1 swine-origin influenza A virus (S-OIV) emerged in Mexico and the United States, and soon after was declared a pandemic by the World Health Organization. This work examined the ability of real-time reports of influenza-like illness (ILI) symptoms and rapid influenza diagnostic tests (RIDTs) to approximate the spatiotemporal distribution of PCR-confirmed S-OIV cases for the purposes of focusing local intervention efforts. Cluster and age adjusted relative risk patterns of ILI, RIDT, and S-OIV were assessed at a fine spatial scale at different time and space extents within Cameron County, Texas on the US–Mexico border. Space–time patterns of ILI and RIDT were found to effectively characterize the areas with highest geographical risk of S-OIV within the first two weeks of the outbreak. Based on these results, ILI and/or RIDT may prove to be acceptable indicators of the location of S-OIV hotspots. Given that S-OIV data is often difficult to obtain real-time during an outbreak; these findings may be of use to public health officials targeting prevention and response efforts during future flu outbreaks.

1. Introduction

In April 2009, a strain of novel H1N1 swine-origin influenza A virus (S-OIV) emerged in Central Mexico and the United States and was soon after declared a pandemic by the World Health Organization (Dawood et al., 2009; Fraser et al., 2009). By July 2009, the WHO was reporting 94,512 laboratory confirmed cases and 429 deaths worldwide (Organization, 2009). The limited studies on S-OIV to date have largely focused on global/macro-scale analyses (Fraser et al., 2009), historical/comparative analyses relative to the 1918 Spanish flu and other pandemics (Fraser et al., 2009; Morens et al., 2009; Zimmer and Burke, 2009) and phylogenetic analyses (Morens et al., 2009; Nava et al., 2009; Smith et al., 2009). Several critical research questions remain unanswered. First, there have been few studies outlining the spatial distribution of the disease at the community scale. Understanding the nature of the spatiotemporal patterns of S-OIVs at the local level will be critical in designing intervention and community outreach programs for future influenza outbreaks. Second, there has been little work examining the extent to which data on more easily diagnosed conditions like influenza may inform researchers and public health officials of the distribution in time and space of S-OIV cases (Ginocchio et al., 2009; Vasoo et al., 2009). During the pandemic of spring of 2009, there were few S-OIV tests available and extended lag times between the swab and the actual confirmed results. Tests often had to be routed through several levels of public health agencies (local, county, state and federal) before the results were returned to local public health officials, a process taking approximately six weeks locally, and results were often not available until the outbreak had retreated or was over. No work to date has focused on evaluating the ability of other, more cost-effective and time-efficient measures to spatially predict local clusters and patterns of disease for S-OIVs. Evaluation and comparison of these more convenient measures may also make it possible to identify the highest risk geographic areas at an early stage of an outbreak, rather than performing analysis after the outbreak has subsided. This temporal aspect has also not been explored to date. If more accessible measures could accurately reflect S-OIV patterns early on in an outbreak, our ability to respond in a timely and effective manner (Cohen, 2009) would be greatly improved, potentially mitigating the impacts of the disease and/or saving lives.

Our study takes place in Cameron County, Texas, which is located directly on the US–Mexico border at the mouth of the Rio

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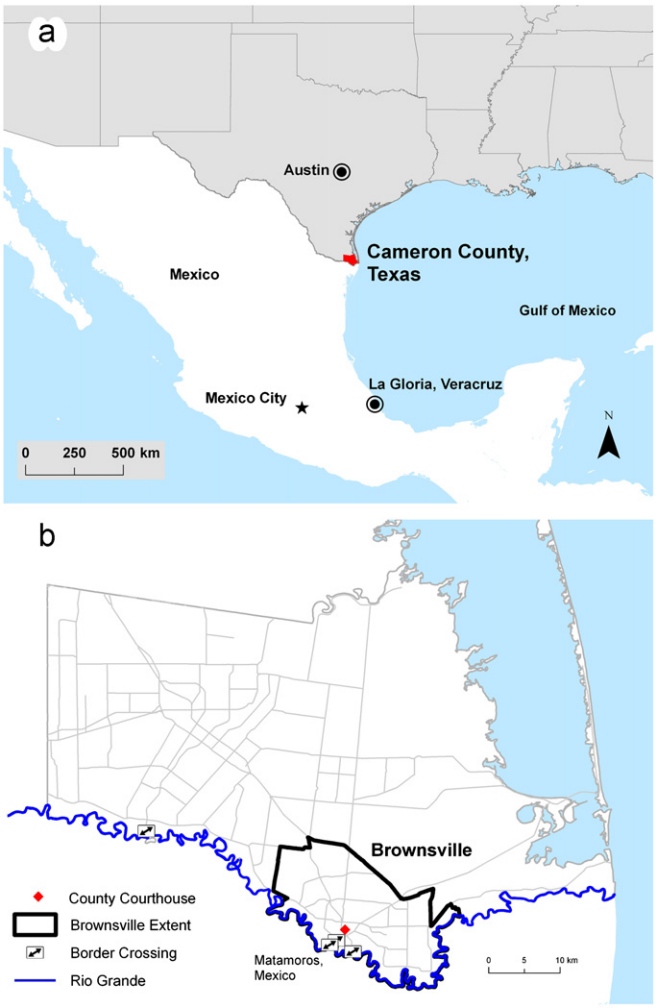

Fig. 1. Cameron County, Texas is situated directly on the US–Mexico border at the mouth on the Rio Grande River and is the nearest point of entry into the United States from the suspected origin of the H1N1 pandemic, La Gloria, in the state of Veracruz, Mexico (a). Brownsville, the largest city in Cameron County, sits directly on the border adjacent to the Mexican city of Matamoros, Tamaulipas (b). Border crossing points and the location of the Cameron County Courthouse are shown (b).

Grande River on the Gulf of Mexico (Fig. 1), an area known as the Lower Rio Grande Valley (LRGV). Brownsville is the closest point of entry by land into the United States from the likely origin of the S-OIV pandemic: the central Mexican town of La Gloria, Veracruz, which lies approximately 450 miles due south of Brownsville (Fig. 1) (Fraser et al., 2009). The local population is approximately 91% Hispanic (mostly of Mexican – American origin) and Cameron County is consistently ranked as among the most economically deprived counties in the entire United States (United States Census Bureau, 2003). Median per-capita income in Cameron County was estimated at $11,958 in 2006 with 32.1% of families below the poverty level, compared with 9.8% nationally (United States Census Bureau, 2007). The population is known to have exceptionally poor health, even relative to other communities with similar demographics (Fisher-Hoch et al., 2010). Cameron County also has four busy international crossing points and an appreciable amount of cross-border population mixing is present daily. In March 2009 alone, 258,796 vehicles, 205,582 pedestrians and 13,192 commercial trucks crossed into the US from Matamoros, Mexico and into Brownsville, the largest city in the County (Texas Center for Border Economic and Enterprise Development, 2009).

This paper aims to accomplish several objectives, namely: (i) to characterize the spatiotemporal nature of the S-OIV outbreak at a fine spatial scale within a US–Mexico border community; (ii) to systematically evaluate the effectiveness of ILI and RIDT in estimating the spatiotemporal nature of S-OIV cases at various time periods during the evolution of an outbreak; and (iii) comment on the suitability of utilizing ILI and RIDTs as surveillance measures to inform real-time outbreak surveillance in the absence of confirmed S-OIV results.

2. Materials and methods

2.1. Case definitions and data collection

The disease data in this study consists of three measures of influenza: ILI, RIDT, and S-OIV. The CDC defines Influenza-like-illness (ILI) as fever (temperature of 100 °F [37.8 °C] or greater) and a cough and/or a sore throat in the absence of a known cause other than influenza (CDC, 2009). RIDT represents a case of Influenza A or B that has been confirmed by a rapid test, generally conducted on-site in a clinic, physician office, or hospital. Results of the test are immediately available. Finally, S-OIV indicates a laboratory-confirmed case of novel influenza A (H1N1) virus infection, defined by the CDC as illness in any person who had a respiratory specimen that tested positive for novel influenza A (H1N1) by rRT-PCR (CDC, 2009). The majority of S-OIV cases internationally have been persons experiencing influenza-like illness with relatively mild effects (CDC, 2009) and ILI diagnoses have been shown to be strongly linked to contact with the earliest treated S-OIV positive cases in Mexico (Perez-Padilla et al., 2009).

ILI cases were recorded (per CDC definition) by hospitals and clinics throughout Cameron County as patients arrived, and for a portion of these cases, additional data was collected through official investigations conducted by the Cameron County Department of Health and Human Services (CCDHHS). RIDT cases were collected through these follow-up investigations. Confirmed S-OIV cases were recorded by Texas Department of State Health Services (DSHS) laboratories in Austin and San Antonio, following confirmatory testing of any ILI patient samples that were sent in from any Texas hospital or clinic (all confirmed S-OIV cases were initially ILI cases). Reports of ILI were faxed from healthcare providers to the Cameron County Department of Health and Human Services at the beginning of each day during the outbreak and reached a total of 1563 reports by May 13, 2009. These reports were classified as ILI for this analysis. Initial ILI reports contained the patient's home address, age, a date of report, and a date of onset, although date of onset was missing in approximately half (53%) of all reports. Investigations of these reports by CCDHHS staff ensued, consisting of a medical chart review and telephone questionnaire—this continued until June 5, at which point, the DSHS issued instructions to discontinue investigations. Of the 1563 ILI cases, a total of 498 cases (22.5%) were investigated. The medical chart review revealed that 405 of the 498 (81.3%) investigated cases had a positive influenza A RIDT result. These cases were classified as RIDT in this analysis. ILI patient respiratory samples collected by healthcare providers (clinics and hospitals) were sent directly to DSHS testing facilities (Austin and San Antonio) for rRT-PCR (polymerase chain reaction)-confirmatory testing. Due to the backlog in laboratory testing, results for 378 Cameron County cases sampled as early as April 26 were not received at CCDHHS until June 30. The rRT-PCR-confirmed cases were classified as S-OIV in this analysis. rRT-PCR testing continued on ILI patient samples also until June 5, when DSHS issued instructions to limit testing only to samples from hospitalized patients. All reports and investigation files were