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## Putting It All Together: Lessons from the Jackson HIV Outbreak Investigation

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### Keywords

HIV; Southeastern United States; phylogenetic analysis; network analysis; men who have sex with men; African-Americans

One need only glance at a map of HIV prevalence in the United States to realize that the Southeast is disproportionately impacted (Figure). Though this region contains a little over one third of the national population, more than half of all newly diagnosed cases of HIV came from the South in 2010.<sup>1</sup> Inequity in the social determinants of health has served to concentrate a variety of communicable and non-communicable diseases among the South's poor and disadvantaged, of whom Blacks make up a outsized proportion.<sup>2, 3</sup> Recent estimates suggest that 1 in every 5 Southern Black men who have sex with men (MSM) are living with HIV infection, a number nearly 5 times that of Southern White MSM.<sup>4</sup> In the past several years, the epidemic has begun to affect young MSM more greatly. In 2011, the Centers for Disease Control and Prevention (CDC) reported that young, Black MSM aged 13–29 experienced a 48% increase in HIV incidence from 2006–2009.<sup>5</sup> Unfortunately, such statistics are no longer surprising for those of us living in the South and providing care for the scores of young, Black MSM being diagnosed with HIV each year. The real challenge for the future lies in identifying and addressing the root causes of this disparity, in order to effect meaningful reductions in HIV incidence among those at greatest risk.

The two-year investigation of an HIV outbreak among young, Black MSM in and around Jackson, Mississippi yields significant insights into this challenge. The study, coordinated by the CDC and the Mississippi State Department of Health (MSDH), was modeled on a 2004 investigation of multiple HIV diagnoses among Black MSM attending colleges and universities in central North Carolina.<sup>6, 7</sup> In five previous papers<sup>8–12</sup> and their article in this issue of *Sexually Transmitted Diseases*,<sup>13</sup> Oster and her colleagues from the CDC and MSDH provide us with a nuanced picture of the state of the HIV epidemic among Black MSM in the Deep South and a glimpse of how similar outbreak investigations could take place in the future.

In their work, Oster *et al.* present a portrait of the epidemic that is heavily influenced by stigma surrounding homosexuality and HIV in the Black community.<sup>14–16</sup> Young, Black MSM, ostracized by their families and support systems,<sup>12</sup> migrate to a handful of “safe” venues located in the more urban area of Jackson to socialize and meet new sex partners.<sup>11–13</sup> HIV-infected and uninfected men are both drawn to (or forced toward) the

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### Conflicts of Interest

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same few venues, characterized in the current paper<sup>11</sup> using an “affiliation” network.<sup>17</sup> This co-localization creates an overlapping social and sexual network with an enriched HIV prevalence – a phenomenon similar to recent observations in North Carolina, as well.<sup>18</sup> Black MSM in the resulting tight-knit system find safety in numbers, but may also have the mistaken impression that HIV prevalence is low among people with demographics like their own.<sup>19</sup> Evidence for this comes from two sources: over half of HIV-infected men thought they were “unlikely” or “very unlikely” to ever acquire HIV,<sup>8</sup> and participants reported less consistent condom usage with casual partners, compared to main partners.<sup>13</sup> Among Black MSM, intense stigmatization of persons living with HIV<sup>12</sup> further complicates efforts to have open, honest discussion about serostatus with sexual partners. When young men with less education about HIV and STI prevention<sup>10</sup> enter the sexual network and have sex with older partners, among whom the prevalence of HIV is greater, their odds of HIV infection are markedly increased.<sup>9, 10, 20</sup> Taken together, it becomes clearer why HIV infections are more frequent among young, Black MSM, despite no demonstrable differences in their risk behavior, compared to MSM of other racial/ethnic groups.<sup>21</sup> In a sexual network with high HIV prevalence, even a single lapse in preventive behavior has a much higher probability of resulting in a transmission event.<sup>18</sup>

In-depth investigations like the one conducted by CDC and MSDH are relatively rare in the HIV literature, given the enormous commitment of time and resources needed to successfully bring the data from field notes to published manuscripts. Perhaps the most unique aspect of the Jackson investigation was its use of molecular epidemiological methods in order to corroborate and extend the findings from “traditional” case-control,<sup>9, 10</sup> qualitative,<sup>12</sup> and network analyses (social and affiliation).<sup>13</sup> The study team analyzed genotypic sequence data from nearly 800 individuals diagnosed with HIV in Mississippi between 2005–2008, collected from CDC’s Variant, Atypical, and Resistant HIV Surveillance (VARHS) system and local surveillance specimens from Black MSM aged 16–25 diagnosed in early 2008.<sup>11</sup> Using sophisticated computational methods, they reconstructed phylogenetic trees depicting the genetic relatedness of the viruses, and then analyzed the characteristics of individuals whose viruses appeared in groups or “clusters” of highly similar sequences. Such clusters represent groups of individuals who likely share transmission of the same virus. It is important to note that only nucleotide sequences are included in phylogenetic analyses; tree structure is “solved” without considering the demographic or behavioral characteristics of individuals who supplied the viral specimens. Therefore, this method provides an additional way to understand transmission, independent of participant-reported history. Additional information can be gleaned by looking for patterns of shared characteristics among individuals identified in these clusters. Sequences from young Black MSM in Mississippi appeared in 21 out of 82 clusters, though these men contributed only 16% of the overall viruses studied. The members of these 21 clusters were all remarkably homogenous; of the 69 individuals in these clusters, all were men, 96% were Black, 88% were MSM, and 70% were under age 25. When examining the geographic locations from which the individuals came, most clusters involving young, Black MSM contained residents from two or more regions of Mississippi. Together, these findings strongly and independently support the conceptual framework of the epidemic among Southern Black MSM, as outlined above.

Phylogenetic analyses can complement traditional methods in other ways, as well. In the present paper,<sup>13</sup> Oster and colleagues were only able to obtain very limited identifying information concerning sex partners, such that the resulting sexual network was fractured into 20 separate components. Given the findings of the phylogenetic study, it seems likely this network would coalesce into fewer, larger groupings if the genetic relatedness of the participants’ viruses could be evaluated. Phylogenetic data can also shed light on broader patterns of HIV transmission, if large numbers of sequences are analyzed in conjunction

with clinical and demographic data. Two recent studies, one from North Carolina<sup>22</sup> and another from sites around the United States<sup>23</sup> both found homogeneity among Blacks within clusters of related sequences, suggesting the same assortative mixing or homophily seen among Black MSM in the Jackson investigation is true across the country. Phylogenetic analyses are not without their limitations, however. Individuals with closely related sequences could have directly transmitted HIV to one another – or they could have a common shared partner or multiple intermediaries. Neither the directionality nor exact date of transmission can be determined using sequences alone, but phylogenetic data can be used to support or refute information collected from putative partners.<sup>24–26</sup>

Molecular epidemiology’s role in assisting public health efforts and improving our understanding of HIV transmission in the United States undoubtedly will increase over time. HIV nucleotide sequence data from “baseline” or pre-treatment resistance testing are widely available, since such testing is recommended for all individuals entering care.<sup>27</sup> Phylogenetic analytical methods and computational speed have advanced markedly in the past decade, allowing large datasets to be analyzed more rapidly than ever before. As elegantly shown in the Jackson investigation, integrating these new methods with traditional, time-tested epidemiological approaches can deepen our understanding of the complex transmission dynamics of HIV in the United States.

Though the Jackson outbreak investigation has revealed much about HIV’s spread in young, Black MSM, we still must parlay these findings into more effective strategies for both primary and secondary prevention. Testing campaigns and sexual health messages ought to be directed at the “virtual” and physical venues frequented by these men, but we also need to address stigmatizing forces in their home communities through direct engagement and education. HIV treatment resources need to be available in rural and urban communities, to ensure access to the treatment we know will sustain individual health and reduce infectiousness to others. We must better understand why Black MSM living with HIV are shunned by their peers, and empower men to make discussions of serostatus more common. This will require bringing together an unlikely group of stakeholders for frank discussions about HIV and what can be done to prevent it. Urban and rural community and religious leaders, business and website owners, at-risk uninfected MSM, and men living with HIV all need to be a part of the effort. The stakes are as high, as are the barriers to success – but we really have no choice at this point but to rise to the challenge.

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### Sources of Support

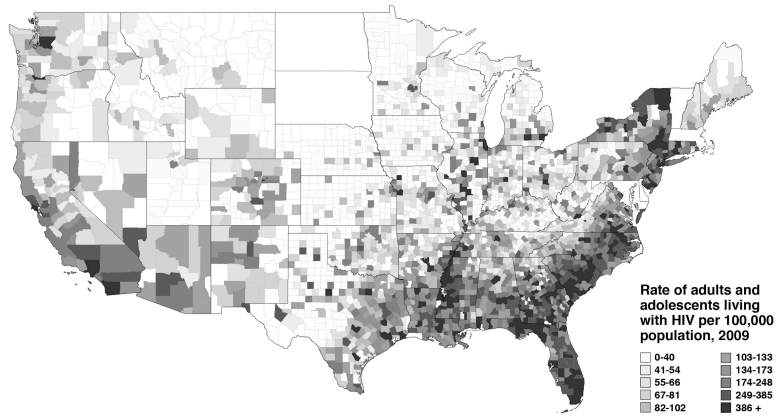
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**Figure 1. Prevalence of HIV infection in the United States, 2009**

Source: AIDS Vu (<http://www.aidsvu.org>). Emory University, Rollins School of Public Health. [Accessed December 10, 2012.] Data are not included for Delaware, Maryland, Massachusetts, North Dakota, South Dakota, Vermont, and the District of Columbia.