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Original article

# Female and male differences in AIDS diagnosis rates among people who inject drugs in large U.S. metro areas from 1993 to 2007

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ABSTRACT

*Purpose:* We estimated female and male incident AIDS diagnosis rates (IARs) among people who inject drugs (PWID) in U.S. metropolitan statistical areas (MSAs) over time to assess whether declines in IARs varied by sex after combination antiretroviral therapy (cART) dissemination.
*Methods:* We compared IARs and 95% confidence intervals for female and male PWID in 95 of the most populous MSAs. To stabilize estimates, we aggregated data across three-year periods, selecting a period immediately preceding cART (1993–1995) and the most recent after the introduction of cART for which data were available (2005–2007). We assessed disparities by comparing IAR 95% confidence intervals for overlap, female-to-male risk ratios, and disparity change scores.
*Results:* IARs declined an average of 58% for female PWID and 67% for male PWID between the pre-cART and cART periods. Among female PWID, IARs were significantly lower in the later period relative to the pre-cART period in 48% of MSAs. Among male PWID, IARs were significantly lower over time in 86% of MSAs.
*Conclusions:* IARs among female PWID in large U.S. MSAs have declined more slowly than among male PWID. This suggests a need for increased targeting of prevention and treatment programs and for research on MSA level conditions that may drive differences in declining AIDS rates among female and male PWID.



## Introduction

After the introduction of combination antiretroviral therapy (cART), there was a substantial reduction in the number of AIDS diagnoses in the United States, particularly among people who inject drugs (PWID) [1]; however, national trajectories of change in AIDS diagnoses have not been the same for female and male PWID [1,2]. In 1995, PWID represented seven percent of persons diagnosed with AIDS among females and 19% among males [2]. In 2011, 20% of new AIDS diagnoses among females were injection related, whereas only 10% of AIDS diagnoses among males were from PWID [1]. During this time, we have estimated that PWID prevalence per 10,000 adult population in large U.S. metropolitan statistical areas (MSAs) also fell from 157 in the period from 1993 to 1995 to 133 in the period from 2005 to 2007 among males, and from 82 to 75 among females [3]. These data raise questions about changes in epidemiologic patterns of AIDS among female PWID and how these patterns may vary across geographic areas.

This article focuses on differences between female and male PWID in incident AIDS diagnosis rates (IARs) across MSAs. Analysis at the MSA level provides a useful lens through which to understand the historical and social factors that drive HIV burden in different locales. Several articles have found differences in HIV prevalence and AIDS mortality among PWID across MSAs, and this variation has been linked to MSA-level factors [4–6]. Previous research has also demonstrated that racial and/or ethnic disparities

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in AIDS diagnoses among PWID varied significantly across MSAs [7]. Although there is ample evidence demonstrating the success of cART in reducing morbidity and mortality in the United States [8,9], the diffusion of cART and other important services may not have been uniform across MSAs and may have reached male and female injectors at different times. Disparities in the availability of cART and HIV care, as well as its accessibility to female PWID, may have resulted in significant sex differences in AIDS diagnoses across MSAs among injectors. In this article, we assess changes in IARs among female and male PWID across large MSAs between a pre-cART period (1993–1995) and a period well after cART was available (2005–2007).

## Methods and materials

The unit of analysis in this article is the MSA, which is defined by the U.S. Census Bureau as contiguous counties containing a central city of 50,000 people or more and that form a socioeconomic unity [10]. Studying HIV among PWID at the MSA level [11] is useful because, as noted, each MSA has its own epidemic history and HIV prevalence rate. Analyses were conducted on a cohort of 95 of the largest MSAs in the continental United States. Preliminary analysis of trend lines over time from 1992 to 2007 (not shown) demonstrated that rates of AIDS diagnosis fell for both male and female PWID over time but fell more rapidly beginning in 1996 when cART was first introduced. In this article, we focus on long-term change between the period before cART and a time when cART was more widely available, treating these two time periods as summary end points of linear change. To minimize the potential impact of small numbers of diagnoses in some MSAs, we combined data from the 3-years immediately preceding cART dissemination (1993–1995) and compared this to a 3-year period (2005–2007) with the most recent available data.

We estimated metropolitan IARs among adult (aged 15–64 years) female and male PWID using Centers for Disease Control and Prevention's (CDC) National HIV Surveillance System data for 95 MSAs. Female PWID included females who reported injection drug use as a risk factor. Males who reported injecting drugs and males who were both PWID and men who have sex with men (MSM) were included as male PWID. For each MSA, period and sex, we calculated IARs by dividing the total number of AIDS diagnoses during that period by the estimated number of male or female PWID without AIDS. Methods for creating annual estimates of PWID for each MSA for females and males have been reported in detail elsewhere but involve calculating the number of PWID in the United States and then apportioning estimates to MSAs using multiplier methods [3,11–13]. These estimates were based on data on HIV counseling and testing, drug treatment, AIDS diagnoses, and estimates from published national and MSA-specific research studies [3,13]. PWID living with AIDS were excluded from the denominators to calculate incidence for the PWID population at risk for AIDS. PWID at risk for AIDS could be HIV infected or HIV uninfected. These estimates were then scaled (multiplied by 10,000) to provide IARs per 10,000 PWID for both females and males. At the time we conducted these analyses, our estimates of PWID prevalence were only available through 2007. Data on PWID AIDS diagnoses stratified by both sex and race were not available because of the suppression of CDC data with small cell sizes.

To facilitate comparisons, we calculated 95% confidence intervals (CIs) for each IAR. CIs were calculated using standard formulas when the number of new diagnoses in an MSA was 100 or more and using tabled values when the number of diagnoses was smaller [14]. The tabled values formula assumes that AIDS diagnoses are infrequent events relative to the size of the population and so can be viewed as occurring in a Poisson-distributed function [14]. As a result, the size of the CIs reflects both the rates and numbers of diagnoses so that MSAs with few diagnoses have relatively low rates and wide CIs and MSAs with many diagnoses have higher rates and more narrow CIs. We also present the dispersion of IARs across MSAs for female and male PWID using a measure of the coefficient of variation (CV).

We used various methods to assess absolute and relative disparities in IARs for female and male PWID. First, to assess important differences in IARs within a given MSA and time period, we compared the extent to which CIs overlapped for females and males: if the CI overlapped, the difference was considered to be not significant at the 95% level [14,15]. The CIs are based on standard error estimates that reflect only random error in the numerator. Comparing CIs for overlap is an absolute comparison that accounts for the precision of the IARs, allowing us to use all available data without excluding MSAs with small numbers of AIDS diagnoses and providing a way to assess the frequency and importance of sex differences across MSAs.

Second, we assessed the magnitude of sex differences in IARs among PWID in each period by calculating the rate ratio for female PWID compared with male PWID (female IAR/male IAR) for each MSA [16]. It is important to note that rate ratios are sensitive to small values so differences may appear to vary greatly within an MSA with small but changing numbers of diagnoses; therefore, we also provide a calculation of relative disparity, the percent difference between groups, which is more appropriate for MSAs with lower diagnosis rates [16].

Third, we present disparity change scores (DCSs) for each MSA to track differences in IARs for female and male PWID over time. The DCS indicates the change in the female-to-male rate ratio in each MSA between the early and late period by subtracting the rate of the health outcome at the later time point from the rate of the health outcome at baseline using the following formula: $DCS = |RR_{T1} - 1| - |RR_{T2} - 1|$ [16]. A negative DCS indicates that the gap in IARs between females and males is narrowing, with a larger DCS value indicating a greater change in the disparity [16]. We included the DCS as an additional tool with which to identify possible shrinking or growing disparities and to draw attention to those MSAs in which the service needs of female or male PWID may be greater.

The geographic distribution of differences was assessed by comparing IARs across region (Northeast, South, Midwest, and West). All analyses were conducted using IBM SPSS Statistics, version 19 [17].

## Results

AIDS diagnosis rates, 95% CIs, and significance of CIs for female and male PWID in each MSA and time period are listed in Table 1. Across all 95 MSAs, in the pre-cART period, IARs among females (per 10,000 female PWID) averaged 103 (SD = 124.1). In the later period, after the introduction of cART, the average IAR among females was 43 (SD = 44.9). Among males, the average IAR (per 10,000 male PWID) was 163 (SD = 138.6) in the pre-cART period and 53 (SD = 37.4) in the later period. IARs were more dispersed for female PWID (CV = 120%) than male PWID (CV = 85%) in the pre-cART period. Similarly, in the cART period, IARs were more dispersed for female PWID (CV = 105%) compared with male PWID (CV = 71%).

Differences between female and male IARs were present in both the pre-cART and cART periods. As seen in Table 1, in 94 of 95 MSAs, IARs in the pre-cART period were lower among female PWID than male PWID; differences between male and female IARs were significant in 65 of these 94 MSAs as indicated by nonoverlapping CIs. In the cART era, however, IARs among females were significantly