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BRIEF REPORT

Increasing Infectious Endocarditis Admissions Among Young People Who Inject Drugs

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People who inject drugs (PWID) are at risk for infective endocarditis (IE). Hospitalization rates related to misuse of prescription opioids and heroin have increased in recent years, but there are no recent investigations into rates of hospitalizations from injection drug use-related IE (IDU-IE). Using the Health Care and Utilization Project National Inpatient Sample (HCUP-NIS) dataset, we found that the proportion of IE hospitalizations from IDU-IE increased from 7% to 12.1% between 2000 and 2013. Over this time period, we detected a significant increase in the percentages of IDU-IE hospitalizations among 15- to 34-year-olds (27.1%–42.0%; $P < .001$) and among whites (40.2%–68.9%; $P < .001$). Female gender was less common when examining all the IDU-IE (40.9%), but it was more common in the 15- to 34-year-old age group (53%). Our findings suggest that the demographics of inpatients hospitalized with IDU-IE are shifting to reflect younger PWID who are more likely to be white and female than previously reported. Future studies to investigate risk behaviors associated with IDU-IE and targeted harm reduction strategies are needed to avoid further increases in morbidity and mortality in this rapidly growing population of young PWID.

Keywords. hepatitis C virus; HIV; hospitalization; infective endocarditis; people who inject drugs.

Infective endocarditis (IE) has high rates of morbidity and mortality [1–3]. Although there are multiple risk factors for IE, including congenital and acquired valve abnormalities, approximately 16% of IE in North America is attributed to injection of illicit drugs [1]. Injection drug use (IDU) can lead to IE through direct injection of bacteria or through spread from skin and soft tissue abscesses into the bloodstream. Depending on the criteria used to define IE, it is estimated that anywhere between 5% and 20% of people who inject drugs (PWID) have had IE [4–6]. People with IDU-related IE (IDU-IE) have worse outcomes than people with non-IDU-IE, including higher mortality after valve replacement and increased frequency of repeat endocarditis [7, 8]. The most recent US study investigating trends in hospitalizations attributed to IDU-IE reported a 66% increase in admissions between 1996 and 2003 [9]. The study by Cooper et al [9] was published before the recent increase in opioid use in the United States, and it is limited because of likely underreporting of illicit drug use by patients. The goal of the current study was to determine whether the increasing opioid epidemic over the past decade was paralleled by increasing hospitalization trends for IDU-IE. In addition to using the *International Classification of Disease, 9th Edition* (ICD-9) for drug use, we used the ICD-9 codes for hepatitis C virus (HCV) to identify potential IDU-IE because 80% of PWID have HCV [10]. Based on recent evidence that overdose and HCV infection rates have increased most dramatically in young, white, females, our goal was to conduct trend analyses looking at changes in IDU-IE discharges by age, race/ethnicity, and gender [11–17].

METHODS

Data Sources

We analyzed data from the 2000–2013 Nationwide Inpatient Samples (NIS), which is the largest publicly available all-payer inpatient health care database in the United States [18]. The database was developed as a part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality. From 2000 through 2011, the NIS includes all discharges from 20% of community hospitals from participating states. From 2012 through 2013, the NIS includes a 20% stratified sample of all discharges from community hospitals from participating states. Community hospitals are defined by HCUP as short-term, non-Federal, general and other hospitals, excluding hospital units of other institutions (eg, prisons, rehabilitation and long-term hospitals). The sample was weighted in order to produce national estimate. Approximately 5–8 million discharges are recorded in the NIS annually. Information for each de-identified discharge includes age, race, gender, as well as diagnosis and procedure codes. The NIS has been used in many studies to estimate trends in hospitalizations for a variety of medical conditions including but not limited to HCV and mental and substance abuse disorders [17, 19–21]. We applied for and received an exemption

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from the Tufts Health Sciences Institutional Review Board because the data from NIS are de-identified.

Inclusion and Exclusion Criteria

We used ICD-9 codes 421.0, 421.9, 424.90, 424.91, and 424.99 to identify admissions with IE. First, we limited discharges to patients aged 15–64 in order to exclude older patients who may have contracted endocarditis from non-IDU risks such as degenerative valvular disease. Second, we classified each patient as presenting with IDU risks based on ICD-9 codes for (1) illicit drug use codes or diagnosis or (2) HCV (codes 70.40, 70.44, 70.51, 70.54, 70.70, 70.71, V0262).

We excluded discharges with any ICD-9 codes for specific endocarditis risk factors (rheumatic heart disease and congenital heart disease) that we speculated likely preceded initiation of IDU. Our inclusion and exclusion criteria were based on an algorithm published by Cooper et al [9] in 2007. We used diagnosis codes and procedures related to commonly injected illicit drugs (e.g., cocaine, heroin, and methamphetamine) that were identical to those used in Cooper's algorithm. We made slight modifications, including the following: (1) a lowered inclusion age from 16 to 15 years, (2) addition of HCV ICD-9 codes, and (3) inclusion of patients with a record of other heart problems (prior prosthetic valve, hemodialysis, pacemaker, heart catheterization, intracardiac balloon). We added the last modification because although these conditions could predispose the patient to endocarditis, they could also be complications of endocarditis [9]. Because the admissions to the database have separate identifications with no ability to link admissions to previous or subsequent admissions, it is impossible to know whether heart problems were the cause or the result of endocarditis.

Statistical Analysis

For statistical analysis, we first computed the rate of IDU-IE by year to observe the trend for the whole selected sample and then stratified by the following: (1) 3 age groups at 15–34, 35–54, and 55–64 years; (2) race/ethnicity, ie, white and non-white; (3) race/ethnicity aged 15–34; and (4) gender. We conducted statistical analyses using Stata 13.1 (StataCorp, College Station, TX) and SAS 9.3 (SAS Institute Inc., Cary, NC). Microsoft Excel was used to compose graphs. Statistical significance was determined based on the threshold of $P < .05$. We incorporated the sample weights provided by the NIS to generate representative estimates; all results presented are weighted unless otherwise specified.

RESULTS

We identified a total of 16 206 unweighted hospitalizations (76 126 weighted) with IE ICD-9 codes between 2000 and 2013. The weighted number of IE hospitalizations increased from 51 291 in 2000 to 70 740 in 2013, and the number of IDU-IE hospitalizations increased from 3578 to 8530 during this time (Figure 1A). The proportion of hospitalizations due to IDU-IE remained stable at approximately 7%–8% until 2008 when there was a decrease to 6.1% followed by an increase to 12.1% in 2013. The IDU-IE hospitalization trends, stratified by age group, are summarized in Figure 1B. We found that the percentage of IDU-IE hospitalizations among young adults (15–34 years) steadily increased from 2000 to 2013, with a steep increase from 2008 to 2013 (27.7%–42.0%; $P < .001$ using χ^2 test for trend in proportions). In contrast, IDU-IE rates among middle-aged adults (ages 35–54) steadily decreased between 2000 and 2013 (67.2%–39.9%; $P < .001$). Injection drug use-related IE increased in whites from 40.2% in 2000 to 68.9% in 2013 ($P < .001$) (Figure 1C). We also detected an increasing trend in younger whites, where the proportion of IDU-IE increased from 57.0% in 2000 to 80.3% in 2013 ($P < .001$) (Figure 1D). Female gender was less common when examining all the IDU-IE (female = 40.9%); however, in the 15- to 34-year-old age group, there is greater parity in IDU-IE distribution by sex (female = 53%). There were no significant changes in IDU-IE hospitalizations by gender over time (data not shown). We noted transition from a unimodal to bimodal age distribution of IDU-IE hospitalizations over time, indicating a shift toward increased proportions in younger populations (Figure 2).

DISCUSSION

The results of our study demonstrate that trends in IDU-IE hospitalizations appear to mirror those of the intertwined prescription opioid, heroin, HCV, and overdose epidemics throughout the country. The proportion of IDU-IE hospitalizations occurring in young, white people is increasing. It is noteworthy to mention that we identified a bimodal age distribution in IDU-IE similar to that of recent HCV age distributions in Massachusetts, with peaks in IDU-IE (and HCV) in younger and older populations [11]. The increase in infections seen in young PWID may represent (1) a stable IE risk in a growing subgroup of PWID or (2) behaviors specific to the younger populations that put them at higher risk.

It has been almost a decade since the last investigation into demographic trends in hospitalization attributed to IDU-IE. Our analysis has important clinical, financial, and public health implications. Infective endocarditis can vary in severity, but overall it is an extremely morbid disease with 11%–26% in-hospital mortality and estimated 12%–50% 5-year mortality [1, 22, 23]. Hospital officials and practitioners agree that care for IDU-IE is expensive and prolonged. It often involves multidisciplinary medical, surgical, nursing, and case-management collaborations. After hospitalization, the care continuum for PWID relies upon a myriad of public health organizations, social service agencies, corrections institutions, and emergency and outpatient clinicians. The cumulative expense of care for

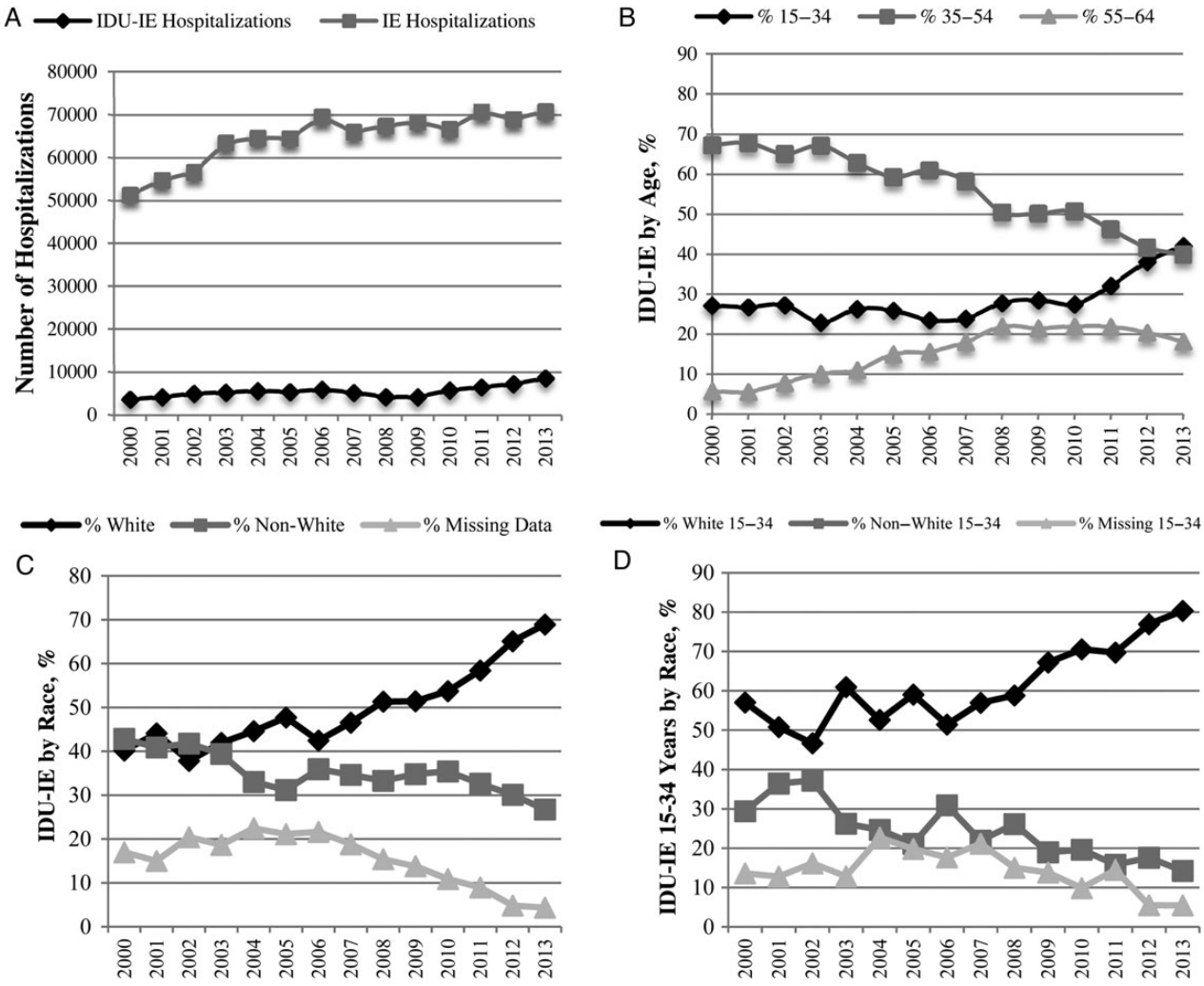

Figure 1. (A), Total annual number of injection drug use-related (IDU) infective endocarditis (IE) and IE hospitalizations between 2000 and 2013. (B) Annual percentage of IDU-IE hospitalizations by age, 2000 to 2013. (C) Annual percentage of IDU-IE hospitalizations by race, 2000 to 2013. (D) Annual percentage of IDU-IE hospitalizations among the 15–34 age group by race, 2000–2013.

IDU-IE poses increasing financial burdens for healthcare facilities and insurance companies, because the majority of patients with hospitalizations from IDU are unemployed or underemployed and are reliant on publically funded medical insurance [24, 25]. Rosenthal et al [26] showed that readmission rates in IDU-IE are high (approximately 50%), implying

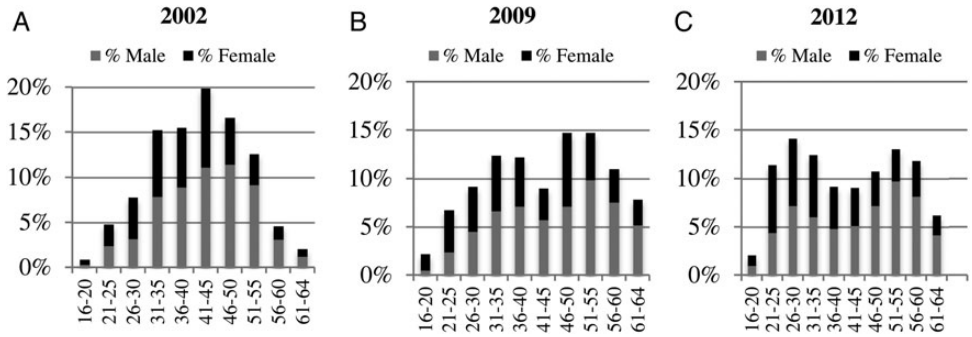

Figure 2. Age distribution of injection drug use-related infective endocarditis hospitalizations by gender in 2002 (A), 2009 (B), and 2012 (C).

increased costs and poorer outcomes. Rates of treatment for opioid addiction by opioid-replacement therapy after hospitalization are very low (<8%) [26]. Increasing awareness of the need and financial support for harm reduction services, including needle-exchange programs and opioid substitution programs, may not only reduce morbidity and mortality from IDU-IE but may also be cost-saving.

Our findings should be considered because of several limitations tied to analysis of health claims data. Our results are only generalizable to PWID who seek medical care in HCUP-participating hospitals. Our classifications are based on ICD-9 data extrapolated from clinical interactions. We expanded the criteria for the definition of IDU-IE from Cooper et al [27] by allowing for HCV-ICD-9 to serve as a proxy for IDU. Given that illicit drug use is underreported and is a major risk factor for HCV infection, expansion of the definition for PWID by the addition of HCV codes should better capture hospitalizations likely to be attributable to IDU-IE. However, there has been increased awareness of HCV among healthcare providers, so increases in IDU-IE diagnoses in this study may be partly attributed to increased testing for HCV during recent years. There was heterogeneity by age groups in how people met the inclusion criteria for IDU-IE. In the 15- to 34-year-old population, 90% were classified as IDU-IE based on presence of IDU diagnosis or procedure ICD-9 code, whereas older populations were more likely to be identified by HCV ICD-9 codes. Only 40% of 55- to 64-year-olds were classified as IDU-IE by IDU diagnosis or procedure codes. Thus, inclusion of HCV diagnosis in our operational definition did not appear to influence our key findings among younger white PWID.

CONCLUSIONS

Our findings add to the growing body of scientific literature that demonstrates increasing concerns about substance misuse, injection-mediated risks, and a constellation of comorbidities within younger populations [12–14, 16, 21, 28–33]. Our results provide additional insights into the complex mix of infectious diseases that face PWID and are a harbinger of healthcare utilization patterns to come among young adults in the throes of addiction. Future research efforts should include interventional studies with PWID that will facilitate identification of factors associated with IDU-IE, helping to inform future public health prevention and clinical policies.

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