

# A Wake-Up Call: Outcomes Following Infective Endocarditis in Persons Who Inject Drugs

Asher J. Schranz

Division of Infectious Diseases, Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

(See the Major Article by Straw et al on pages 564–71.)

The opioid crisis in the United States has renewed concern around the intersecting epidemics of substance use disorders and infectious diseases [1]. While significant public health attention has been given to outbreaks of human immunodeficiency virus (HIV) and increasing hepatitis C diagnoses among persons who inject drugs (PWID), relatively less research has focused on the rising incidence of injection-related invasive bacterial and fungal infections, such as infective endocarditis (IE) [2–5]. IE can be a devastating, multisystem disease, resulting in heart failure, strokes, and death.

Short-term outcomes following IE in PWID (PWID-IE) are no worse—and are possibly better—than outcomes among people who acquired IE from other causes. In North Carolina, 8% of hospitalizations for IE thought to be due to drug use resulted in in-hospital deaths, compared with 14% for those with IE not due to drug use [6]. A recent meta-analysis demonstrated that there was no difference in 30-day mortality rates after valve surgery between those with PWID-IE and those with IE from other causes [7]. In response to the growing number of people with PWID-IE, there

has been interest in understanding and improving long-term outcomes.

In this issue of *Clinical Infectious Diseases*, Straw and colleagues contribute important data about mortality in the 10 years following PWID-IE treatment. Following 92 PWID in the United Kingdom across 105 episodes of IE during an 11-year period, the authors examined both short- and long-term mortality rates. The primary outcomes were mortality at 30 days after antibiotic completion, at 30 days postoperatively, and at 1, 3, 5, and 10 years.

Consistent with prior studies, Straw et al found that PWID-IE were generally young, with a median age of 36 years, and the majority of cases were due to *Staphylococcus aureus* (63%) [8–10]. Heart failure and stroke occurred in 49% and 15% of patients, respectively. Nearly one-half of patients underwent surgical management (47%). Mortality at 30 days occurred in 15% overall and in 8.5% of those who were surgically treated.

Long-term mortality rates among PWID-IE have not been well described in recent studies, and the results observed in Straw et al's report are stunning. Over a quarter of persons with PWID-IE (26%) died by 1 year, over a third (36%) by 3 years, and a majority (56%) were dead within 10 years. Driving home these dismal outcomes, in their Supplementary Tables, the authors reported a projected post-IE life expectancy of as little as 6.2 years following operative treatment for a 36-year-old man (the median age in the study).

The authors did not find an association between surgical treatment and mortality. However, as they noted in their

conclusions, comparisons between surgically treated and medically treated patients may be clouded by unmeasured dimensions of clinical severity, rendering the retrospective comparison fraught. In another recent study examining long-term outcomes, following 202 episodes of PWID-IE at 3 Canadian hospitals from 2007 to 2016, Rodger et al [10] reported a similar 1-year mortality rate to that in the study by Straw et al. However, in adjusted analyses, Rodger et al [10] found that undergoing surgery was one of only two factors that conferred a reduction in the mortality rate.

Straw and colleagues reported that mortality after PWID-IE was largely due to another infection, primarily IE, which was the cause of death in 21 of the 38 patients who had death information. A drug overdose, another relatively frequent cause, was responsible for 6 deaths in the study. These causes reflect the need for resources and infrastructure to treat underlying substance use disorders and engage patients in comprehensive care following a hospital discharge.

Effective medications exist to treat opioid use disorder, as do harm reduction services. These services include naloxone (the antidote to an opioid overdose), for which prescriptions have surged in the United States, and syringe programs, which can help PWID minimize nonsterility in injecting and may be linked to preventing HIV transmission [11, 12]. In the study by Rodger et al [10], the only factor besides surgery that improved mortality was referral to addiction treatment. In the present article, all patients received

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Correspondence: A. J. Schranz, Division of Infectious Diseases, Department of Medicine, University of North Carolina at Chapel Hill, 130 Mason Farm Road, CB #7030, Chapel Hill, NC 27599 (aschranz@med.unc.edu).

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a visit for substance use disorder services, but, as the authors noted, the study lacked detailed information about any addiction care delivered. Moving forward, such information will be essential in improving our understanding of the types and intensities of interventions needed to reduce mortality among PWID-IE patients.

Although the study by Straw et al described experiences in the United Kingdom, it calls attention to how care is delivered in the United States, where hospitalizations for drug-related infections are rising [5, 6, 13, 14]. US studies have documented opportunities for improving addiction care in the inpatient setting. A notable recent report of PWID hospitalized with *Staphylococcus aureus* bacteremia starkly contrasted the high quality of care delivered for the infection with the insufficient treatment received for addiction [15]. Nearly all patients had appropriate care for *Staphylococcus aureus* bacteremia, but almost half did not have a substance use disorder listed as a problem on the discharge summary, and under a quarter received a medication for opioid use disorder. The long hospitalizations for IE and other severe, drug-related infections can represent an opportunity to engage patients in addiction care. Addiction medicine consultation teams can be a valuable tool in this effort. A multidisciplinary model, combining clinicians, social workers, and peer support, has shown a significant effect in improving linkage to postdischarge substance use disorder treatment [16].

The present study by Straw and colleagues should be a wake-up call to clinicians, public health officials, and policy-makers, highlighting the extremely morbid threat of injection drug-related IE, the long-term harms facing

patients after such an infection, and the pressing opportunity to do more for our patients. The authors rightly concluded by calling for a holistic approach. Best practices in the care of PWID-IE are needed, incorporating multidisciplinary input from infectious diseases specialists, cardiac surgeons, and addiction medicine clinicians, as well as community members and people with lived experience with substance use disorders. Novel interventions should ensure that we address not only the infection, but also the underlying addiction, using harm reduction strategies and any modifiable psychosocial determinants, in order to ultimately improve outcomes. As this study shows us, there is a lot of room for improvement.

#### Note

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