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Trends in drug use-associated infective endocarditis and heart valve surgery, 2007 to 2017

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Abstract

Background: Drug use-associated infective endocarditis (DUA-IE) is rising during the opioid epidemic. Infective endocarditis (IE) can require valve surgery, but surgical treatment of DUA-IE has invoked controversy and the extent of its use is unknown.

Objective: To examine hospitalization trends for DUA-IE, the proportion with surgery, patient characteristics, length of stay and charges.

Design: Ten-year analysis of a statewide hospital discharge database.

Setting: North Carolina hospitals, 2007–2017.

Patients: All patients hospitalized for IE aged ≥ 18 years.

Measurements: Annual trends in all IE hospitalizations and those with valve surgery, stratified by patients' drug use. Characteristics of DUA-IE surgical hospitalizations including demographics, length of stay, disposition and charges.

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Results: Of 22,825 IE hospitalizations, 2,602 (11%) were for DUA-IE. Valve surgery was performed in 1,655 (7%) IE hospitalizations, including 285 (17%) for DUA-IE. Annual DUA-IE hospitalizations increased from 0.92 to 10.95 per 100,000, and DUA-IE hospitalizations with surgery rose from 0.10 per 100,000 to 1.38 per 100,000. In the final year, surgeries for DUA-IE comprised 42% of IE valve surgeries. Compared to other IE surgical patients, DUA-IE patients were younger (median age 33 vs. 56), more commonly female (47% vs. 33%) and White (89% vs. 63%), and primarily insured by Medicaid (38%) or uninsured (35%). Hospital stays for DUA-IE were longer (median 27 vs. 17 days) with higher median charges (\$250,994 vs. \$198,764). Charges for 282 DUA-IE hospitalizations exceeded \$78,000,000.

Limitations: Reliance on administrative data and billing codes.

Conclusions: DUA-IE hospitalizations and valve surgeries increased over twelve-fold and DUA-IE approached half of all IE valve surgeries. The swell of DUA-IE patients is reshaping the scope, type, and financing of healthcare resources needed for effective IE treatment.

Introduction:

Infective endocarditis (IE), an infection of one or more heart valves, is a severe complication of injection drug use (IDU), which can occur through inoculation of bacteria or fungi into the blood or by hematogenous spread from localized infections. Concurrent with rising IDU and overdose deaths, IE associated with drug use (DUA-IE) has increased markedly in the United States (US) since 2000 (1–4).

The rising incidence of DUA-IE aligns with the rapid growth of the opioid epidemic. For the period of 2000 to 2013, Wurcel et. al. estimated a greater than two-fold increase in DUA-IE admissions nationwide, a trend generally seen in other national studies from recent years (1,2,5,6). However, a report from North Carolina (NC) for 2010 to 2015 described a twelve-fold increase in hospitalizations for DUA-IE, with the sharpest increase beginning in 2013 (7).

The standard of care for IE is a prolonged course of intravenous antibiotics, often accompanied by surgical valve replacement. Yet the use of valve surgery for DUA-IE has invoked controversy because of concern about postoperative IDU and the associated risk of prosthetic valve infection. Despite the lengthy and expensive course of treatment for DUA-IE, drug use disorders (DUDs) and harm reduction often go unaddressed during hospitalizations, and the outpatient infrastructure for DUD treatment nationwide is often inadequate (8,9). As a result, clinicians have debated practical and ethical considerations of valve surgery for DUA-IE (10–13). No recent large-scale research has examined the rate of valve surgery for DUA-IE, or characterized DUA-IE patients undergoing surgery and their hospitalizations.

To quantify the impact of rising drug injection on the use of valve surgery for IE, we examined the case of NC. As of 2016, NC has continued to see rising overdose deaths, which are increasingly driven by heroin and synthetic narcotics, and are disproportionately distributed in different regions of the state (14,15). While our study focuses on one state, findings in NC may be reflective of trends nationwide. Past year misuse of pain relievers or

heroin (16) and the overdose death rate in NC align closely with US averages (17). The healthcare and political landscape of NC harbors many complexities that shape the opioid epidemic, including suboptimal but growing access to opioid treatment and syringe programs and a large uninsured population that remains in the wake of Medicaid non-expansion (14,18–20).

In this study, we used statewide NC data to examine the annual trends, characteristics and charges for DUA-IE hospitalizations with valve surgery, and we updated overall DA-IE hospitalization trends through mid-year 2017. Our findings can frame national discussions about the medical consequences of DUDs, contemporary management of IE and long-term care following valve replacement in young persons.

Methods:

Study Design and Data:

We conducted a retrospective study using the NC Hospital Discharge Database, which is comprised of demographic, diagnostic, procedural and billing data from all short-term, nonfederal, acute care NC hospitals, covering roughly one million hospitalizations yearly. The units of analysis were individual hospitalizations, not unique persons, as personal identifiers were not available for the entire study period.

The study population consisted of all NC hospitalizations for IE occurring from July 1, 2007, to June 30, 2017, among patients aged 18 years or older at the time of hospitalization.

Operationalization of IE, DUA-IE, and Valve Surgery:

Hospitalizations for IE were defined as those with an *International Classification of Diseases, Clinical Modification [ICD-9-CM and ICD-10-CM]* diagnosis code indicating IE, excluding those due to rare pathogens (e.g. *Histoplasma spp.*).

DUA-IE was identified among IE cases by the presence of a diagnosis code for recreational drug use, withdrawal, dependence or poisoning, excluding diagnoses for marijuana or unspecified drug use. Persons born after 1965 diagnosed with hepatitis C (HCV) were also coded for DUA-IE, given the high propensity of HCV to be transmitted through recreational injection and the common method of utilizing HCV as a criterion in identifying DUA-IE (1,21). All IE hospitalizations not meeting these criteria were classified as non-DUA-IE. Drugs were classified as opioids (inclusive of opiates), cocaine, amphetamines or other drugs (benzodiazepines, hallucinogens or unspecified drugs).

Among all IE hospitalizations, we used ICD procedure codes to determine whether valve surgery was performed.

We generated the list of diagnosis and procedure codes used to operationalize IE, DUA-IE, and valve surgery by reviewing published literature and directly examining ICD-9-CM and ICD-10-CM code lists. We used the General Equivalence Mappings from the Center for Medicare and Medicaid Services, employing forward-mapping (22–24). This strategy

ensured that we identified all ICD-10-CM codes that correspond (“map”) to included ICD-9-CM codes. We assessed the appropriateness of including each code (Appendix Tables 1–3).

Data Analysis:

For all IE hospitalizations and for IE hospitalizations with surgery, we examined annual trends in aggregate and stratified by drug use. Yearly rates were calculated for the number of IE hospitalizations per 100,000 NC residents aged 18 years or older, using state population data obtained from the US Census Bureau.

We described the distribution of demographic characteristics (age, race/ethnicity, gender), insurance payer, valve targets of surgery, length of stay (LOS), disposition location and hospital charges. Distributions among DUA-IE and non-DUA-IE groups were compared using Wilcoxon rank-sum tests for continuous variables or chi-squared tests for categorical variables, with statistical significance defined as $p < 0.01$.

To evaluate the influence of our assumption that HCV-infected patients born after 1965 acquired IE through IDU, despite having no specific drug-related diagnoses, we conducted a sensitivity analysis restricting our DUA-IE definition to include only hospitalizations with a diagnosis code specific to drug use.

Analyses were performed with SAS v9.4. The study was approved by the institutional review board at the University of North Carolina, Chapel Hill.

Role of the Funding Source:

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Results:

Annual Trends of all IE Hospitalizations and IE Hospitalizations with Valve Surgery:

Over the ten-year period, there were 22,825 hospitalizations for IE in NC. Of these, 2,602 (11%) were DUA-IE, while 20,223 (89%) were non-DUA-IE (Table 1). Among all IE hospitalizations, valve surgery was performed in 1,655 (7%). Among hospitalizations with valve surgery, 285 (17%) were DUA-IE and 1370 (83%) were non-DUA-IE (Table 2).

Annual IE hospitalizations increased during the study period, from 1,936 to 2,992, corresponding to 27.74 per 100,000 NC residents in the first year and 37.80 per 100,000 in the final year (Figure 1). Annual hospitalizations for DUA-IE rose from 64 (0.92 per 100,000) in 2007–2008 to 867 (10.95 per 100,000) in 2016–2017, an increase of approximately twelve-fold. Non-DUA-IE hospitalizations were generally stable across the period (26.84 per 100,000 in the final year), but greater numbers were observed in 2015–2016.

For all IE hospitalizations with valve surgery, annual hospitalizations rose from 1.62 per 100,000 in 2007–2008 to 3.26 per 100,000 in 2016–2017 (Figure 2). For DUA-IE, there were fewer than ten yearly hospitalizations with surgery until mid-2013 (representing 0.01–

0.10 per 100,000). Annual hospitalizations then rose to 109 (1.38 per 100,000) by 2016–2017, an overall increase of thirteen-fold. Non-DUA-IE hospitalizations with surgery increased from 106 (1.52 per 100,000) in the first year to 149 (1.88 per 100,000) in the last year. In the final year, DUA-IE accounted for 42% of all hospitalizations for IE where surgery was performed (109 of 258 hospitalizations) (Appendix Tables 4–5).

DUA-IE hospitalizations for all drug categories increased across the period, with opioids the most commonly implicated drugs in the final study year for hospitalizations overall (6.71 per 100,000), as well as for hospitalizations with surgery (0.80 per 100,000).

Characteristics of All Hospitalizations, by Drug Use Status:

Persons hospitalized for DUA-IE were younger than those with non-DUA-IE (median age 35 (interquartile range, IQR, 28–45) vs. 67 (54–79)). Female gender was slightly more common among DUA-IE than non-DUA-IE (51% vs 48% female). Race-ethnicity differed by drug use status: DUA-IE cases were 81% White/non-Hispanic and 10% Black/non-Hispanic, while non-DUA-IE cases were 61% White/non-Hispanic and 22% Black/non-Hispanic. Medicaid and self-pay/uninsured were the most frequent payers for DUA-IE (35% and 34%, respectively), while Medicare and private insurance were most common for non-DUA-IE (67% and 16%). The most common drugs observed were opioids, which appeared in 1,626 (62%) of DUA-IE cases (Table 1).

Characteristics of All Hospitalizations with Valve Surgery, by Drug Use Status:

Among hospitalizations for IE where valve surgery was performed, persons with DUA-IE were younger than those with non-DUA-IE (median age 33 (IQR 27–42) vs. 56 (44–66)). Persons with DUA-IE were more commonly female than those with non-DUA-IE (47% vs. 33% female). DUA-IE patients were 89% White/non-Hispanic and 6% Black/non-Hispanic, compared with 63% White/non-Hispanic and 22% Black/non-Hispanic among non-DUA-IE (Table 2).

The distribution of payers between DUA-IE and non-DUA-IE notably differed. Payers for DUA-IE with surgery were predominantly Medicaid or self-pay/uninsured (38% and 35%, respectively), whereas the most common payers for non-DUA-IE hospitalizations with surgery were Medicare and private insurance (42% and 31%).

Of the 285 hospitalizations with surgery for DUA-IE, opioids were the most commonly identified drug, reported in 176 (62%) (Table 2). 52 persons (18%) were coded for DUA-IE due to having HCV without a drug use diagnosis. Overall, 171 (60%) had HCV.

Target of Valve Surgery:

The most common surgical target was the aortic valve (55%), followed by the mitral (47%) and tricuspid (16%). Unlike the aortic and mitral valves, tricuspid involvement was significantly more common for DUA-IE (39% of DUA-IE vs. 11% of non-DUA-IE). The pulmonary valve was involved in 1% of surgeries. For 328 hospitalizations (20%), multiple valves were targeted for surgery (Table 2).

Length of Stay and Disposition:

Among all hospitalizations, LOS was longer for DUA-IE than non-DUA-IE (median 11 days (IQR 5–26) vs. 7 (4–13) days, $p<0.001$). Fewer DUA-IE hospitalizations resulted in discharge home, compared with non-DUA-IE (43% vs 49%), and inpatient mortality or hospice discharge was lower among DUA-IE (8% vs 14%). Discharge against medical advice occurred in 13% of DUA-IE hospitalizations, compared with 1% in non-DUA-IE (Table 3).

Of hospitalizations with surgery, median LOS was significantly longer for DUA-IE compared with non-DUA-IE (27 (17–44) vs. 17 (11–26) days, $p<0.001$). Distributions of discharge disposition differed significantly by drug use. Compared with non-DUA-IE, a lower proportion of DUA-IE were discharged home (51% vs. 59%) and a greater proportion were transferred to another facility (38% vs 31%) (Table 3).

Hospital Charges:

Median hospital charges were higher for DUA-IE than non-DUA-IE (\$60,333 vs. \$34,968, $p<0.001$). Among surgical hospitalizations, total hospital charges were overall greater and remained higher for DUA-IE than non-DUA-IE (median \$250,994 vs. \$198,764, $p<0.001$). Overall charges for 282 DUA-IE hospitalizations with surgery for DUA-IE over the ten-year period were \$78,781,627. Charges for 1,361 non-DUA-IE hospitalizations with surgery totaled \$333,536,647 (Table 3).

Sensitivity Analysis for Definition of Drug Use:

Restricting DUA-IE to those only with drug use diagnoses yielded 2,240 (10%) hospitalizations for DUA-IE and 20,585 (90%) for non-DUA-IE. Of hospitalizations with surgery, 233 (14%) were DUA-IE and 1,422 (86%) non-DUA-IE. Trends and the characteristics of all IE hospitalizations and those with surgery were similar to those in the main analysis, with total charges of \$65,493,939 for the 233 DUA-IE hospitalizations with surgery.

Conclusions:

In this large, statewide study, we observed a marked increase in overall hospitalizations and valve surgeries among patients with DUA-IE. Rates of hospitalizations for DUA-IE with valve surgery in NC rose thirteen-fold from 2007 to 2017. In the final study year, DUA-IE comprised 42% of all surgeries for IE, indicating a dramatic shift in the demographic and clinical profile of patients undergoing IE surgery.

Our findings are generally consistent with trends reported in earlier studies of hospitalizations and surgeries for IE due to drug use (1,2,7,25). However, in the context of quickly-evolving drug epidemics, prior studies do not fully capture the magnitude of the rise in DUA-IE, which increased notably in 2013–2014. Our study, which extends through mid-2017, illustrates that the sharply upward trend previously observed in NC is continuing (7). Additionally, the observed trend, which is largely attributable to opioids, aligns with

increasing deaths from heroin and synthetic narcotics in NC, which began an acute upward trajectory in 2014 (26).

The young age of surgical patients with DUA-IE raises concerns about their need for subsequent surgeries, which may be indicated for either recurrent IE or normal valve deterioration. Recent estimates of recurrent endocarditis after surgery for DUA-IE are based on small studies and vary from a low of 13% at a mean of 32 months postoperatively (27), to a high of 52% at a median of 18 months post-operation (28). In order to mitigate the risk of reinfection from IDU, the underlying drug use disorder (DUD) must be addressed as a root cause of acquiring IE. In our study nearly two-thirds (62%) of DUA-IE hospitalizations involved opioid use. Effective pharmacotherapies exist for opioid use disorder (OUD). Yet, in the absence of OUD treatment, many patients are detoxified during their hospitalization for IE. Detoxification without pharmacotherapy for OUD is ineffective, with 6–12 month relapse rates reported at 60–81%, suggesting that patients who do not receive OUD treatment are likely to resume opioid use after discharge, putting them at risk of reinfection if they inject drugs (29–31). DUDs other than OUD pose additional challenges in treatment as therapeutic options are more limited. Inpatient addiction consultation is a promising tool to address the multifaceted needs of patients with DUDs, potentially reducing further infections and overdose by offering patients pharmacotherapy for OUD and linking patients to post-discharge care (32,33).

Discharge against medical advice (DAMA), which occurred in 13% of DUA-IE hospitalizations overall, is a dangerous outcome that puts patients at risk of an inadequately treated, potentially life-threatening infection and is linked to increased mortality and readmissions (34). In addition, DAMA may also represent of a symptom of the lack of addiction care provided. Substance and alcohol use disorders are among the conditions most strongly associated with DAMA (34,35) and it is conceivable that untreated drug withdrawal is a contributing factor (36). OUD has been associated with an increased odds of DAMA from detoxification admission (37). One study of persons who inject drugs reported that receipt of methadone was associated was linked with a reduced odds of DAMA (38), a finding that suggests that, for opioid-tolerant patients, opioid substitution may be beneficial in curtailing DAMA. Another study found that, among persons who use illicit drugs, unemployment and incarceration were predictors of DAMA (39). While the reasons for this association are not totally clear, it highlights the importance of multidisciplinary efforts in addressing the needs of medical inpatients with DUDs.

Beyond the risk of reinfection, structural degeneration of prosthetic valves over time is a common indication for further valve surgery (40). The 15-year reoperation risk due to prosthetic valve degeneration (regardless of indication) for a 40 year-old person is 30% and, for a 20 year-old, the risk is 50% (41). Among persons who underwent surgery for DUA-IE, we found that 186 (65%) were under 40. Without advances in prosthetic valve longevity, many of these young valvular surgery patients who remain free of reinfection are likely to require additional valve replacements. The anticipated need for future surgeries, whether for reinfection or structural degeneration, and long-term cardiac follow-up care is substantial and must be considered in assessing the total downstream costs of DUA-IE.

Persons who inject drugs are frequently not considered candidates for outpatient parenteral antibiotic therapy (OPAT) due to perceived risk of tampering with an intravenous catheter in an unsupervised setting. Therefore, it is likely that the longer LOS for DUA-IE stems from needing to receive prolonged antibiotics (typically six weeks) as inpatients (42,43). Recent injection drug use is not an absolute contraindication to OPAT. Emerging case series have reported favorable outcomes of OPAT for selected IDU-experienced patients (44–46) and one report found that home OPAT was at least equally safe to receiving antibiotics in a rehabilitation facility (47). Expanding OPAT eligibility amongst selected candidates may help offset long hospital stays for drug-associated infections. Pathophysiology may also explain, in part, the long LOS in DUA-IE. Unlike non-DUA-IE, the organism most commonly responsible for DUA-IE is *Staphylococcus aureus*, which is highly virulent, and can result in severe and complicated presentations (25,48,49).

The surge in DUA-IE is driving an overall increase in IE that also impacts hospitals and insurance payers. The observed LOS for DUA-IE, particularly for those requiring surgery (median 27 days), was over three weeks longer than the 4–5 day national average for all hospitalizations (50). Given the high proportion of Medicaid and uninsured patients, care for DUA-IE poses a large financial burden to state and federal budgets, which jointly finance Medicaid, and to individual hospitals, which rely in-part on Medicaid Disproportionate Share Hospital payments to offset the costs of uninsured patients (51). Our study did not include any hospitalizations that occurred immediately prior or subsequent to the hospitalization with surgery, underestimating the total charges in treating IE for the one-third of patients who were transferred between institutions. Given the considerable charges for IE hospitalizations with surgery (median \$250,994) and the costs of downstream care of a prosthetic valve, the expense of caring for DUA-IE almost certainly exceeds that of comprehensive outpatient treatment programs with pharmacotherapy for opioid use disorder (estimated at \$5,980–\$14,112 per year) (52). A rational public health approach will prioritize funding inpatient and outpatient DUD treatment, harm reduction and other activities to prevent future IE occurrences.

In our study, the proportion of IE hospitalizations resulting in surgery was low (7%) and noticeably below estimates of IE surgery published for other populations (31–57%) (53,54). Our method of examining IE hospitalizations using ICD codes is similar to that used in the recent studies describing the rise in DUA-IE (1,2,7). We postulate that examining hospital discharge records with IE diagnoses alone, as was done in ours and numerous previous studies of DUA-IE, is overly sensitive and may capture persons in multiple hospitalizations across transfers in care for a single episode of IE. Adding cardiac surgery procedure codes to IE codes, as in our analysis, may improve detection of incident IE episodes, minimize inclusion of multiple hospitalizations per episode of endocarditis and yield more conservative estimates of the number of unique patients with IE.

Our study utilized a statewide discharge database. Nearly all states maintain such databases, which can be a resource to public health practitioners examining DUA-IE locally (55). Each state faces unique challenges in addressing medical complications of drug use, owing to regional variation in drug use practices, DUD treatment infrastructure and political climate.

Studies examining other states and regions may build a more nuanced picture of DUA-IE that looks beyond large-scale national trends.

This study has several limitations. First, it used administrative data lacking granular clinical information and may have been subject to inaccurate coding of drug use or other diagnoses. Accordingly, we were unable to validate IE or drug use diagnoses with other clinical indicators or assess surgical indications. Second, increasing awareness of both HCV and opioid misuse may have enhanced their documentation during the later study years. Third, our use of HCV infection as an indicator of drug use could have artificially increased the number of DUA-IE cases detected, as its inclusion alone accounted for 18% of cases. However, even excluding that population, the increase in DUA-IE hospitalizations remains striking. Fourth, although we were concerned that the 2015 switch from ICD-9 to ICD-10 would have introduced error into our trend estimates, the relatively steady number of surgeries for non-DUA-IE over the study period suggests that this issue was likely negligible for hospitalizations with surgery. Fifth, certain hospitals are not included in our database, such as Veterans Affairs and military hospitals, leading to an underestimate of the prevalence of IE in NC. Young veterans have higher rates of pain reliever misuse, and thus may be at greater risk for DUA-IE than the general population (56). Last, our study examined hospitalization events and therefore was unable to assess the number of unique persons affected.

In summary, rates for both overall hospitalizations and valve surgeries for DUA-IE increased markedly from 2007 to 2017 and surgeries for DUA-IE are alarmingly approaching half of all IE surgeries in NC. DUA-IE is a critical emerging public health issue that is affecting the lives of young persons, burdening health systems and public insurance payers, and fundamentally reshaping the epidemiology and management of endocarditis. Enhancing the multidisciplinary infrastructure to address treatment and prevention of DUA-IE should be an urgent priority, including improved provision of addiction care in the inpatient and outpatient setting (37,57). Further studies are needed to characterize long-term outcomes for DUA-IE after discharge, such as reinfection, reoperation and mortality, and to understand the role of addiction treatment, harm reduction and other interventions in improving DUA-IE outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1: Rates of hospitalization for infective endocarditis in North Carolina, by drug use status, 2007 to 2017*†

IE = infective endocarditis

*Rates are hospitalizations per 100,000 North Carolina residents, 18 years of age or older.

†North Carolina population as per US Census Bureau estimates of residents aged 18 years or older on July 1. Because annual estimates in this study incorporated two calendar years (July 1 to June 30), the average of the two years was used as the population denominator.

Figure 2: Rates of hospitalization for infective endocarditis in North Carolina treated with valve surgery, by drug use status, 2007 to 2017*†

IE = infective endocarditis

*Rates are hospitalizations per 100,000 North Carolina residents, 18 years of age or older.

†North Carolina population as per US Census Bureau estimates of residents aged 18 years or older on July 1. Because annual estimates in this study incorporated two calendar years (July 1 to June 30), the average of the two years was used as the population denominator.

Table 1:
Characteristics of infective endocarditis hospitalizations in North Carolina, by drug use status, 2007 to 2017.

	Total	DUA-IE	Non-DUA-IE
	n (%)	n (%)	n (%)
Total	22,825	2,602 (11)	20,223 (89)
Age, Median (IQR)	65 (49–77)	35 (28–45)	67 (54–79)
Gender			
Male	11,765 (52)	1,281 (49)	10,484 (52)
Female	11,060 (48)	1,321 (51)	9,739 (48)
Race/Ethnicity			
Black/non-Hispanic	4,638 (20)	269 (10)	4,369 (22)
White/non-Hispanic	14,411 (63)	2,108 (81)	12,303 (61)
Hispanic	743 (3)	32 (1)	711 (4)
Other or unknown	3,033 (13)	193 (7)	2,840 (14)
Insurance Payer			
Private	3,648 (16)	317 (12)	3,331 (16)
Medicare	14,077 (62)	444 (17)	13,633 (67)
Medicaid	2,629 (12)	903 (35)	1,726 (9)
Self-Pay/Uninsured	1,880 (8)	873 (34)	1,007 (5)
Other/Unknown	591 (3)	65 (3)	526 (3)
Drug Use Related Diagnosis *			
Opioid		1,626 (62)	
Cocaine		545 (21)	
Amphetamines		294 (11)	
Benzodiazepines, Hallucinogens or Others		486 (19)	
Hepatitis C and born after 1965		1,206 (46)	

DUA-IE = drug use-associated infective endocarditis; Non-DUA-IE = infective endocarditis not associated with drug use.

* Each drug was assessed independently, as hospitalizations may have been coded for numerous drugs

Table 2:
Characteristics of hospitalizations for infective endocarditis treated with valve surgery in North Carolina, by drug use status, 2007 to 2017.

	Total	DUA-IE	Non-DUA-IE
	n (%)	n (%)	n (%)
Total	1,655	285 (17)	1,370 (83)
Age, Median (IQR)	52 (39–64)	33 (27–42)	56 (44–66)
Gender			
Male	1,070 (65)	151 (53)	919 (67)
Female	585 (35)	134 (47)	451 (33)
Race/Ethnicity			
Black/non-Hispanic	317 (19)	16 (6)	301 (22)
White/non-Hispanic	1,124 (68)	255 (89)	869 (63)
Hispanic	30 (2)	0	30 (2)
Other or unknown	184 (11)	14 (5)	170 (12)
Insurance Payer			
Private	466 (28)	40 (14)	426 (31)
Medicare	605 (37)	32 (11)	573 (42)
Medicaid	285 (17)	109 (38)	176 (13)
Self-Pay/Uninsured	242 (15)	99 (35)	143 (10)
Other/Unknown	57 (3)	5 (2)	52 (4)
Drug Use Related Diagnosis *			
Opioid		176 (62)	
Cocaine		55 (19)	
Amphetamines		24 (8)	
Benzodiazepines, hallucinogens or others		48 (17)	
Hepatitis C and born after 1965		159 (56)	
Target of Valve Surgery †			
Aortic	910 (55)	126 (44)	784 (57)
Mitral	786 (47)	103 (36)	683 (50)
Pulmonic	22 (1)	4 (1)	18 (1)
Tricuspid	260 (16)	110 (39)	150 (11)
Multiple valves	328 (20)	56 (20)	272 (20)

DUA-IE = drug use-associated infective endocarditis; Non-DUA-IE = infective endocarditis not associated with drug use.

* Each drug was assessed independently, as hospitalizations may have been coded for numerous drugs.

† Valves were assessed independently, as individuals may have had surgery on multiple valves.

Table 3:
Length of stay, disposition and charges for hospitalizations for infective endocarditis in North Carolina, by drug use status, 2007 to 2017.

	All Hospitalizations				Hospitalizations with Valve Surgery			
	Total	DUA-IE	Non-DUA-IE	p-value	Total	DUA-IE	Non-DUA-IE	p-value
	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	
Length of Stay, Median (IQR)	7 (4–14)	11 (5–26)	7 (4–13)	< 0.001	18 (12–29)	27 (17–44)	17 (11–26)	< 0.001
Disposition								
Home	10,983 (48)	1,108 (43)	9,875 (49)	< 0.001	953 (58)	144 (51)	809 (59)	< 0.001
Nursing facility, long term acute care hospital, inpatient rehabilitation or transfer to another hospital	7,748 (34)	861 (33)	6,887 (34)		528 (32)	108 (38)	420 (31)	
Discharge against medical advice	502 (2)	333 (13)	169 (1)		11 (1)	8 (3)	3 (<1)	
Died while inpatient or hospice	2,996 (13)	221 (8)	2,775 (14)	< 0.001	133 (8)	17 (6)	116 (8)	< 0.001
Other or unknown	596 (3)	79 (3)	517 (3)		30 (2)	8 (3)	22 (2)	
Hospital Charges, Median (dollars)[†]	36,946	60,333	34,968		208,361	250,994	198,764	
Total charges (dollars)[†]	1,667,725,169	266,419,261	1,401,305,908	-	412,318,275	78,781,627	333,536,647	-

DUA-IE = drug use-associated infective endocarditis; Non-DUA-IE = infective endocarditis not associated with drug use.

* Chi-square tests were performed for categorical variables. Wilcoxon rank sum tests were used to compare continuous variables.

[†] 32 hospitalizations overall (4 DUA-IE and 28 non-DUA-IE), including twelve with valve surgery (3 DUA-IE and 9 non-DUA-IE), had incomplete charge data and were excluded from charge analyses.