International Classification of Diseases (ICD) Codes Fail to Accurately Identify Injection Drug Use Associated Endocarditis Cases

Erin Barnes, MD, MS, James Peacock, MD, and Laura Bachmann, MD, MPH

Objectives: Infective endocarditis (IE) secondary to injection drug use (IDU-IE) is a disease with high morbidity, cost, and rapid demographic evolution. Studies frequently utilize combinations of International Statistical Classification of Diseases (ICD) codes to identify IDU-IE cases in electronic medical records. This is a validation of this identification strategy in a US cohort.

Methods: Records from January 1, 2004 to September 31, 2015 for those aged ≥18yo with any ICD-coded IE encounter (inpatient or outpatient) were retrieved from the electronic medical record and then manually reviewed and classified as IDU-IE by strict and inclusive criteria. This registry was then used to assess the diagnostic accuracy of 10 identification algorithms that combined substance use, hepatitis C, and IE ICD codes.

Results: IE was present in 629 of the 2055 manually reviewed records; 109 reported IDU within 3 months of IE diagnosis and an additional 32 during their lifetime (141 cases). In contrast, no algorithm identified more than 46 (33%) of these cases. Algorithms assessing encounters with both an IE and substance use code had specificities >99% but sensitivities ≤11% with negative predictive values of 83% to 84% and positive predictive values ranging from 75% to 91%. Use of a hepatitis C OR substance use code with an IE-coded encounter resulted in higher sensitivities of 22% to 32% but more false positives and overall positive predictive value of <70%.

From the Section on Infectious Diseases, Wake Forest Baptist Health, Winston Salem, NC. Received for publication January 28, 2020; accepted December 27, 2020. This work was supported by a K21 and the Wake Forest CTSI funded by the NCATS National Institutes of Health [UL1TR001420]. The authors report no conflicts of interest. All authors meet criteria for substantial contributions to this work consistent with ICMJE guidelines. Supplemental digital content is available for this article. Direct URL citation appears in the printed text and is provided in the HTML and PDF versions of this article on the journal’s Web site (www.journaladdictionmedicine.com).

Send correspondence to Erin Barnes, MD, MS, 1 Medical Center Blvd, Walthington Hall, Section on Infectious Diseases, Winston Salem, NC 27157. E-mail: ewbarnes@wakehealth.edu.

Copyright © 2021 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Society of Addiction Medicine. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

ISSN: 1932-0620/21/1601-0027
DOI: 10.1097/ADM.0000000000000814

This algorithm limited to age ≤45yo had the best, but still low, discrimination ability with an area under the receiver operating characteristic curve of 0.62.

Conclusion: Substance use and hepatitis C codes have poor ability to accurately classify an IE-coded encounter as IDU-IE or routine IE.

Key Words: endocarditis, epidemiology, injection drug use, opioid epidemic, validation

(J Addict Med 2022;16: 27–32)

The US opioid epidemic began in the late 1980s and early 1990s with changes to regulatory structures, reimbursement incentives, patient advocacy action, and aggressive drug marketing resulting in US use of 99% and 83% of the world’s hydrocodone and oxycodone supplies by 2010. Increases in overdose deaths, hepatitis A, B, C, and HIV followed. Overdose data followed by viral infectious disease reports were key in alerting the nation to the opioid crisis and then informing public health policy due to the clear definitions and regular mandated reporting of these events. Lagging behind these reports are studies on the rising trends of IDU-IE. Multiple papers have now been published establishing a steep rise in IEs associated with substance use in a variety of locations and settings. These descriptive studies have been vital in highlighting the lack of addiction medicine infrastructure and sharp divide between care for substance use disorders versus that for routine internal medicine care, particularly in rural areas. The high monetary costs and morbidity from IDU-IE have also been highlighted by these studies with hospitals struggling to absorb costs of this underinsured population. The growing body of literature on the barriers and effects of IDU-IE on patients, communities, and providers highlight the need for ongoing high quality, timely epidemiologic studies of this patient group and the outcomes of research focused on their care.

The opioid epidemic led to a shift in the epidemiology of IDU-IE in addition to changing health costs, impacted locations, and recognition of need for more evidence-based guidelines for clinical decision making. Wuerbel et al have provided one of the most comprehensive assessments of the epidemiology and morbidity of this disease through query of the National Inpatient Sample database. The search strategy used was an adapted strategy from Cooper et al and together these search strategies have formed the basis for many other studies by researchers assessing IDU-IE within their own institutions. However, the accuracy of ICD coding for...
IE in general and IDU-IE in particular is suspect. A recent British study found that fewer than 50% of cases with an IE code were true IE cases and that the incidence and characteristics of the disease varied depending on the quality of the coding algorithms used. A large US study similarly found that combinations of primary and secondary codes for IE were required to achieve a sensitivity above 25%. The largest IDU-IE code validation study is a recent Canadian study, which found that combining IE and substance use disorder codes achieve ~87% sensitivity and 64% specificity with more code combinations required to increase sensitivity above 90%. However, this conclusion was based on an ICD-10 system in use since 2000 in another country. How accurate these methods are in the United States for IDU-IE is unknown. We describe here the results and accuracy of ICD-9 code-based algorithms to identify IDU-IE cases as compared to a database created through manual review of every individual who had an endocarditis code associated with their chart in any context or setting.

METHODS

Before study initiation the research protocol was approved by the Wake Forest Baptist Health IRB. The medical records of all patients >18 years of age with at least one ICD-9 IE code (appendix 1, http://links.lww.com/JAM/A242) for any encounter type (inpatient or outpatient) during January 1, 2004 to September 30, 2015, as the US changed to ICD-10 on October 1, 2015, were identified resulting in a study cohort of 2055 unique individuals. ICD codes used are those cited in previous literature. Each record was individually reviewed (EWB) and the diagnosis of IE was either accepted or rejected utilizing “strict” or “inclusive” case definitions. Patients who had an implantable cardiac device were removed from the cohort and not considered further. Strict cases included those with possible or definite IE by the modified Duke Criteria. Inclusive cases encompassed those patients who did not meet Duke Criteria but who were diagnosed and treated as IE by their physicians and who would therefore be reasonable cases for an ICD-based algorithm to identify. Rarely, cases of IE were acquired in the hospital more than 72 hours after admission for a noninfectious indication. Given that the sole goal of this investigation was to identify IE associated with the injection of substances, these cases were only included in the inclusive case definition regardless of how many Duke criteria they fulfilled.

Strict and inclusive criteria were also developed for determining if a case was associated with IDU. Those who reported injection in the 3 months before admission met strict criteria whereas those with ANY history of IDU met inclusive criteria. We included coding which included amphetamines/stimulants as at our institution many patients report frequent injection of opioids mixed with methamphetamine or cocaine or alternative between periods of isolated stimulant and then isolated opioid use. Only self-reported IDU was relied upon to determine criteria fulfillment. Urine drug screens were not considered due to their variable drug detection profiles, provider bias in determining who receives these tests, and the inability to cross check positive results with prescribed medications or medications received in the ED before the screen was drawn. Those cases where physicians were merely suspicious of IDU but no confirmation ever was obtained from the patient were not counted as IDU-IE to avoid introducing provider bias.

All cases which were identified and classified through comprehensive review of the 2055 patients were then compared to the patients identified by 10 different ICD-based algorithm searches (Table 1, Appendix 2, http://links.lww.com/JAM/A242). Each individual was counted only once even if they had multiple IE admissions so that the algorithms were measured against their ability to identify an individual rather than specific encounters. The age cutoff of ≤45 years old is significantly younger than the cutoff of age 64 used by Cooper and Wurcel. This limitation is hoped to increase specificity and is 1.5 standard deviations above the mean age of 92 persons in the IDU-IE population examined previously. The total number of individuals identified and the number of IDU-IE cases identified by strict and inclusive criteria were assessed and compared to the findings from the comprehensive search. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the receiver operating characteristic curve (AUC-ROC) for both strict and inclusive case

| Algorithm | Description |
|-----------|-------------|
| Algorithm 1 | Time range January 1, 2004 to September 31, 2015 with ANY encounter associated with both an ICD for endocarditis and a substance use code in the same encounter |
| Algorithm 2 | Time range January 1, 2004 to September 31, 2015 with ANY encounter associated with both an ICD for endocarditis and an OPIOID use code in the same encounter |
| Algorithm 3 | Algorithm 1 limited to inpatient encounters |
| Algorithm 4 | Algorithm 2 limited to inpatient encounters |
| Algorithm 5 | Algorithm 1 if you limit the group to those age 45 or younger at time of the coded encounter |
| Algorithm 6 | Algorithm 2 if you limit the group to those age 45 or younger at time of the coded encounter |
| Algorithm 7 | Time range January 1, 2004 to September 31, 2015 with ANY encounter associated with both an ICD for endocarditis and a substance use code in the same encounter OR the substance use code being in the same encounter as the endocarditis code, they have a hepatitis C code in the same encounter as the endocarditis code |
| Algorithm 8 | Algorithm 7 limited to those aged 45 or younger at the time of encounter |
| Algorithm 9 | Time range January 1, 2004 to September 31, 2015 who EVER had an endocarditis code and substance use code appear on their chart. The codes no longer need to coincide in the same encounter but merely any type of encounter with an endocarditis code and any type of encounter when a substance use code was utilized |
| Algorithm 10 | Time range January 1, 2004 to September 31, 2015 who EVER had both an endocarditis code and OPIOID use code appear on their chart where the codes no longer need to coincide in the same encounter but merely have one encounter of any kind where there was an endocarditis code and another encounter of any kind where there was a substance use code |
definitions of IDU-IE were assessed for each algorithm. Individuals which were identified by the algorithms but did not have IE at all, much less IDU-IE, are reported but were not considered “true negatives” for the calculations of specificity, NPV, and AUC-ROC for the purpose of these calculations (the diseased state was classified as IDU-IE for “disease present” and IE without IDU for “disease absent”). However, leaving these cases out altogether in calculations artificially deflates the false positive rate while artificially inflating specificity, PPV, and AUC-ROC. A true calculation using these cases would require analogous true negatives to be all cases in the hospital that did not have IE during this time which is a calculation of dubious use and relevance to this study. For the purposes of transparency, additional calculations where the false positives included cases returned by the algorithm without IE were included in the appendix (Appendix 3, http://links.lww.com/JAM/A242) for readers to reference as they see fit.

**RESULTS**

Comprehensive case review identified 629 total IE cases with 1426 individuals failing to have IE by strict or inclusive definitions. Frequently, IE seems to have been erroneously associated with a patient who had valve surgery for chronic degenerative valve disease, a history of rheumatic carditis, or a case where endocarditis was considered in the differential diagnosis but ultimately ruled out consistent with the findings from Fawcett et al.17 One hundred nine patients met strict criteria for both IDU and IE and with that number increasing to 141 IDU-IE cases when inclusive definitions were used (Table 2). In contrast, the highest number of IDU-IE cases identified by any algorithm was 46 cases identified by algorithm 7.

Those algorithms which relied solely on both IE and substance use ICD codes occurring during an encounter (algorithms 1–6) had very high specificity \( \geq 99.2\% \) (Table 3). However, this group also had the highest number of true false negatives leading to sensitivities of only 9.3\% to 11.0\% for strictly-defined cases and 6.4\% to 9.2\% for inclusively-defined cases. Sensitivity improved when the codes for endocarditis and substance use were not required to coincide in the same encounter (algorithms 9 and 10) but remained <15\% while specificity remained \( \geq 95\% \). In this group of codes (1–6, 9–10), PPV was highest in algorithms 5 and 6 which restricted to ages \( \leq 45 \) at 85\% to 92\% and comparable

### Table 2. Number of Individuals and Cases Identified by Each Search Algorithm

| Cohort     | Total N | IDU-IE by Strict | IDU-IE by Inclusive | Strict IE Cases | Inclusive IE Cases | No IE by Strict or Inclusive | False Positives Strict | False Positives Inclusive | False Negatives Strict | False Negatives Inclusive |
|------------|---------|------------------|---------------------|-----------------|------------------|-----------------------------|------------------------|--------------------------|-------------------------|--------------------------|
| Comprehensive | 109     | 141              |                     |                 |                  | 1426                        | 3                      | 5                        | 5                       | 95                       | 127                      |
| Algorithm 1 | 19      | 14               | 14                  | 14              | 16               | 3                           | 5                      | 5                        | 5                       | 95                       | 127                      |
| Algorithm 2 | 14      | 11               | 11                  | 12              | 13               | 1                           | 3                      | 5                        | 3                       | 4                        | 95                       | 127                      |
| Algorithm 3 | 18      | 14               | 14                  | 14              | 15               | 3                           | 4                      | 3                        | 3                       | 95                       | 127                      |
| Algorithm 4 | 12      | 10               | 10                  | 11              | 11               | 1                           | 2                      | 2                        | 2                       | 99                       | 131                      |
| Algorithm 5 | 15      | 13               | 13                  | 13              | 13               | 2                           | 2                      | 2                        | 2                       | 96                       | 128                      |
| Algorithm 6 | 11      | 9                | 9                   | 10              | 10               | 1                           | 2                      | 2                        | 1                       | 10                      | 132                      |
| Algorithm 7 | 94      | 32               | 46                  | 71              | 77               | 17                          | 61                     | 47                       | 77                      | 95                       |                         |
| Algorithm 8 | 53      | 25               | 32                  | 41              | 45               | 8                           | 28                     | 21                       | 84                      | 109                      |                         |
| Algorithm 9 | 50      | 15               | 20                  | 31              | 36               | 13                          | 35                     | 30                       | 94                      | 121                      |                         |
| Algorithm 10| 37      | 17               | 19                  | 27              | 30               | 7                           | 20                     | 18                       | 92                      | 124                      |                         |

Two patients were identified in each of these cohorts with cardiac implantable devices. They were excluded from total counts and calculations.

Strict criteria: include those who report injection in the last 3 months before presentation and endocarditis fulfills at least possible Modified Duke criteria. Inclusive: includes those who report a lifetime history of injection drug use and additionally includes endocarditis cases that did not meet Modified Duke Criteria but were treated as endocarditis as well as hospital acquired cases.

IDU-IE indicates Injection drug use associated infective endocarditis.
NPVs of 79% to 84%. These algorithms resulted in an AUC-ROC no greater than 0.55, however, suggesting that when faced with an individual coded as IE, relying on a substance use code to determine if the case is IDU-IE fares no better than a coin-flip.

Including hepatitis C as an alternative to substance use codes at the time of an IE-coded encounter (algorithms 7 and 8) allowed the highest number of cases to be identified. This strategy produced the highest respective sensitivities of 28.4 and 22.0% for strictly defined cases. These algorithms identified more false positive cases as well, however, so their specificities are lower than for groups 1 to 6. Specificity was lowest for algorithm 7 at 91.2% but when limited to those under 45 years of age in algorithm 8, the specificity rose to 96.0%. PPV for these algorithms was <53% for strictly defined cases and <69% for inclusively defined cases which is significantly worse than for algorithms 1 to 6; the trade-off gains in NPV were mild in comparison, remaining no better than 85.9%. The AUC-ROC of algorithm 7 was the highest for all algorithms for both strict (0.60) and inclusive (0.62) criteria.

**DISCUSSION**

In this study we found that in this ICD-9 based cohort relying on simultaneous encoding of endocarditis and substance use was a highly specific but very insensitive measure of case identification with many IDU-IE cases missed. Hepatitis C codes used for identification in place of substance use likely much higher than previously reported. Each case of IDU-IE costs an estimated $47,899 to $180,314. As our study suggests that up to 3-fold as many cases exist as have been identified, a conservative correction would increase reports by a factor of 1.5-fold and would result in an additional 4265 patients in the 2000 to 2013 cohort reported by Wurcel et al with a corresponding additional $204,289,235 to $769,039,210 in unreported health care charges. An extra 250 people with IDU-related IE would also be included in the NC study from 2010 to 2015 with additional costs of 11 million dollars for the year of 2015 alone. Those diseases which are more common or costly receive more national attention, interagency collaboration, external grant funding, and internal resources so that our national underestimation of both cases and cost may have far reaching effects on our ability to effectively and comprehensively treat this population.

The larger and more concerning issue raised here is our possible inability to accurately identify all IDU-IE cases in real-time. At present, ICD-based coding methods are the standard for case identification. Yet the data presented here suggest these codes are a woefully inadequate tool to capture trends and changes in IDU-IE epidemiology. This observation has many implications. First, at least 1 study has identified IDU-IE case rise as a marker of increased IDU in a region. Real-time and accurate identification of an IDU-IE spike could then conceivably allow earlier and more targeted resource intensification to areas in need. Second, the opioid epidemic has continued to evolve with heroin and fentanyl analogs now playing a larger role than prescription opioids and methamphetamine injection steadily increasing. How these changing dynamics will affect the epidemiology and pathophysiology of IDU-IE or interact with the other overlapping infectious syndemics of hepatitis and HIV/AIDS needs further study.
sexually transmitted diseases is unclear. Timely and accurate IDU-IE case identification could alert agencies and community stakeholders to evolving infectious trends associated with changing substance use patterns which would further enhance stakeholder decision-making and resource development and deployment. Requiring IE or at least IDU-IE to be a reportable disease for health departments may be one way to better capture the epidemiology of this condition. Finally, accurate identification strategies are needed for researchers to extract sufficient cases from the electronic medical record to compare and identify effective infection and addiction treatment strategies in this group which is otherwise very difficult to study in adequate numbers in a prospective manner. It may be that the heterogeneity of coding behaviors amongst providers and the inherent data limitations within administrative coding will never allow coded data to fully meet these needs. Machine learning technologies such as natural language processing, which can process text and context within physician notes themselves, are advancing in the medical field and may provide a novel path forward to bridge these gaps.

There are many potential limitations to this study. First, it was a single center and retrospective review. The lack of precision in the coding which we identified may be limited to our institution alone and may not translate to external sites or national databases. However, as our medical center employs physicians who have trained and worked at institutions from all over the world, there would be no a priori reason to believe they would be a unique and isolated group in their coding practices. As noted in our comparisons to Ball et al’s study above, it is possible that a medical center with a dedicated addiction medicine consult group or robust inpatient psychiatric consult service for IDU-IE patients may have better coding for substance use related conditions than we had at our institution. Secondly, even though a very wide net was cast by seeking documentation of IE in any context in any encounter type to minimize the chances of missing a case, it is still possible that some cases of IE were missed, particularly if they were not coded for IE at all and given that we did not use “E” Codes to supplement the CM codes. Based on the hundreds of records reviewed that had no endocarditis but were associated with an IE ICD-9 code, we believe it is unlikely that any significant number of cases were missed. Third, this study was conducted on an Epic-based EMR system. How each electronic medical record stores and retrieves data is unique and results with different EMRs may differ. Fourth, the US transitioned to ICD-10 coding on October 1, 2015 and there are many additional codes available in that system which may increase the ability to identify these cases using ICD-coded strategies. However, there remains no dedicated code to signify substance use through an injected route in ICD-10 with some systems creating proxy codes, for example, F19.10 appears as a suggested code if “injection drug use” is typed into our EMR though that code is technically the code for “other psychoactive substance abuse, uncomplicated.” Regardless, it will be some time before the accuracy of the ICD-10 codes can be compared to ICD-9 for identifying cases of IDU-related IE in the US. Fifth, the scale of the data extraction from the comprehensive data set precluded having 2 individuals each rank the cases and compare results. Cases that did not clearly meet case definitions were adjudicated by a panel of 3 infectious diseases physicians but bias may still remain from having a single individual data extractor. Sixth, many more combinations of ICD codes than were tested here exist and could potentially prove useful; full assessment of larger numbers of codes and information from a wider range of fields is ongoing. Finally, some may disagree with the strictness of the case definitions used here including the decision to exclude those where the physicians strongly suspected IDU but it was never self-reported. The decision to use such strict criteria was made to prevent bias. It was also based on the belief that future studies may attempt to pull detailed and complex data from cases to test hypotheses and assess treatment responses where rigorous case definitions will be paramount. There is great need for a unified definition of IDU-IE to insure further internally consistent and comparable research in this field.

CONCLUSIONS

In the United States, using a combination of substance use, hepatitis C, and endocarditis ICD-9 coding is an insensitive strategy for identifying IDU-IE and may be no better than “flipping a coin” at distinguishing between IE cases which are associated with substance use from those which are not. To ensure that accurate and reproducible data are extracted for epidemiological and clinical studies which can be extrapolated across institutions, a standard case identification tool needs to be developed and validated.

REFERENCES

1. deShazo RD, Johnson M, Eriator I, Rodenmeyer K. Backstories on the US opioid epidemic. Good intentions gone bad, an industry gone rogue, and watch dogs gone to sleep. Am J Med. 2018;131(6):595–601.
2. Manchikanti L, Boswell MV, Hirsch JA. Lessons learned in the abuse of pain-relief medication: A focus on healthcare costs. Expert Rev Neurother. 2013;13(5):527–543.
3. National Center for Health Statistics. Drug Overdose Deaths in the United States, 1999-2016. Center for Disease Control and Prevention. Updated 2017-12-20T09:10:12Z. 2018. Available at: https://www.cdc.gov/nchs/products/databriefs/db294.htm. Accessed June 5, 2018.
4. Zibbell JE, Iqbal K, Patel RC, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged <18-30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. MMWR Mortal Mortal Wkly Rep. 2015;64(17):453–458.
5. Harris AM, Iqbal K, Schiller S, et al. Increases in acute Hepatitis B virus infections - Kentucky, Tennessee, and West Virginia, 2006-2013. MMWR Mortal Mortal Wkly Rep. 2016;65(3):47–50.
6. Peters PJ, Pontones P, Hoover KW, et al. HIV infection linked to injection use of oxymorphone in Indiana, 2014-2015. N Engl J Med. 2016;375(3):229–239.
7. Beck E. HIV outbreak now up to 66 cases. The Register Herald. Available at: https://www.register-herald.com/health/hiv-outbreak-now-up-to-cases/article_5a4dcc96-3c06-5321-a05f-19daa1419737.html. Accessed November 5, 2019.
8. Gray ME, Rogawski McQuade ET, Scheld WM, Dillingham RA. Rising rates of injection drug use associated infective endocarditis in Virginia with missed opportunities for addiction treatment referral: A retrospective cohort study. BMC Infect Dis. 2018;18(1):532.
9. Bates MC, Annie F, Jha A, Kerns F. Increasing incidence of IV-drug use associated endocarditis in southern West Virginia and potential economic impact. Clin Cardiol. 2019;42(4):432–437.
10. Rosenthal ES, Karchmer AW, Theisen-Toupal J, Castillo RA, Rowley CF. Suboptimal addiction interventions for patients hospitalized with injection drug use-associated infective endocarditis. *Am J Med*. 2016;129(5):481–485.

11. Leahey PA, LaSalvia MT, Rosenthal ES, Karchmer AW, Rowley CF. High morbidity and mortality among patients with sentinel admission for injection drug use-related infective endocarditis. *Open Forum Infect Dis*. 2019;6(4):ofz089.

12. Fleischauer AT, Ruhl L, Rhea S, Barnes E. Hospitalizations for endocarditis and associated health care costs among persons with diagnosed drug dependence - North Carolina. *MMWR Morb Mortal Wkly Rep*. 2017;66(22):569–573.

13. Wurcel AG, Anderson JE, Chui KK, et al. Increasing infectious endocarditis admissions among young people who inject drugs. *Open Forum Infect Dis*. 2016;3(3):ofw157.

14. Tookes H, Diaz C, Li H, Khalid R, Doblecki-Lewis S. A cost analysis of hospitalizations for infections related to injection drug use at a County Safety-Net Hospital in Miami, Florida. *PLoS One*. 2015;10(6):e0129360.

15. Wurcel AG. Drug-associated infective endocarditis trends: What’s all the buzz about? *Ann Intern Med*. 2019;170(1):68–69.

16. Cooper HL, Brady JE, Ciccarone D, Tempalski B, Friedman SR. Nationwide increase in the number of hospitalizations for illicit injection drug use-related infective endocarditis. *Clin Infect Dis*. 2007;45(9):1200–1203.

17. Fawcett N, Young B, Peto L, et al. Caveat emptor: The cautionary tale of endocarditis and the potential pitfalls of clinical coding data—an electronic health records study. *BMC Med*. 2019;17:169.

18. Toyoda N, Chikwe J, Itagaki S, Gelijns AC, Adams DH, Egorova NN. Trends in infective endocarditis in California and New York state. *JAMA*. 2017;317(16):1652–1660.

19. Ball LJ, Sherazi A, Laczko D, et al. Validation of an algorithm to identify infective endocarditis in people who inject drugs. *Med Care*. 2018;56(10):e70–e75.

20. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis*. 2000;30(4):633–638.

21. Moeller KE, Kissack JC, Atayee RS, Lee KC. Clinical interpretation of urine drug tests: What clinicians need to know about urine drug screens. *Mayo Clin Proc*. 2017;92:774–796.

22. Hartman L, Barnes E, Bachmann L, Schafer K, Lovato J, Files DC. Opiate injection-associated infective endocarditis in the southeastern United States. *Am J Med Sci*. 2016;352(6):603–608.

23. Shrestha NK, Sue J, Hussain ST, et al. Injection drug use and outcomes after surgical intervention for infective endocarditis. *Am Thorac Surg*. 2015;100(3):875–882.

24. Nguyen-Tran Tiakj MJ, Mori M, Bin Mahmood SU, et al. Recidivism is the leading cause of death among intravenous drug users who underwent cardiac surgery for infective endocarditis. *Semin Thorac Cardiovasc Surg*. 2019;31(1):40–45.

25. Kim JB, Ejislav J, Yammine M, et al. Surgical outcomes of infective endocarditis among intravenous drug users. *J Thorac Cardiovasc Surg*. 2016;152(3):832–841.e1.

26. Rabkin DG, Mokadam NA, Miller DW, Goetz RR, Verrier ED, Aldea GS. Long-term outcome for the surgical treatment of infective endocarditis with a focus on intravenous drug users. *Ann Thorac Surg*. 2017;93(1):51–57.

27. Huang G, Barnes EW, Peacock JE Jr. Repeat infective endocarditis in persons who inject drugs: “Take another little piece of my heart”. *Open Forum Infect Dis*. 2018;5(12):ofy304.

28. Alexander MJ, Kiang MV, Barbieri M. Trends in black and white opioid mortality in the United States. *Epidemiology*. 2018;29(5):707–715.

29. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths—United States, 2006–2015. *MMWR Morb Mortal Wkly Rep*. 2016;64(50–51):1378–1382.

30. Keeshin SW, Feinberg J. Endocarditis as a marker for new epidemics of injection drug use. *Am J Med Sci*. 2016;352(6):603–608.

31. O’Donnell JK, Gladden RM, Seth P. Trends in deaths involving heroin and synthetic opioids excluding methadone, and law enforcement drug product reports, by census region — United States, 2006–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(34):897–903. 2017-08-30T10:14:26Z.

32. Jones CM, Einstein EB, Compton WM. Changes in synthetic opioid involvement in drug overdose deaths in the United States. *JAMA*. 2018;319(17):1819–1821.

33. Ahmad FB EL, Rossen LM, Spencer MR, Warner M, Sutton P. Provisional Drug Overdose Death Counts. National Center for Health Statistics. Updated 2019-10-07T10:30:18Z. Available at: https://www.cdc.gov/nchs/nvss/vsr/drug-overdose-data.htm. Accessed November 5, 2019.

34. Glick SN, Burt R, Kummer K, Tinsley J, Banta-Green CJ, Golden MR. Increasing methamphetamine injection among non-MSM who inject drugs in King County, Washington. *Drug Alcohol Depend*. 2018;182:86–92.

35. Al-Tayyib A, Koester S, Langegger S, Raville L. Heroin and methamphetamine injection: An emerging drug use pattern. *Drug Alcohol Depend*. 2016;164(86–92).

36. Petch J, Batt J, Murray J, Mamdani M. Extracting clinical features from dictated ambulatory consult notes using a commercially available natural language processing tool: pilot, retrospective, cross-sectional validation study. *JMIR Med Inform*. 2019;7(4):e12575.

37. Chen M, Decary M. Artificial intelligence in healthcare: an essential guide for health leaders. *Healthc Manage Forum*. 2019;33:10–18.