

Shifting The Treatment Paradigm For Endocarditis Among People Who Use Drugs: Treat The Person, Not Just The Infection

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Disclosure Information



Joshua Barocas, MD

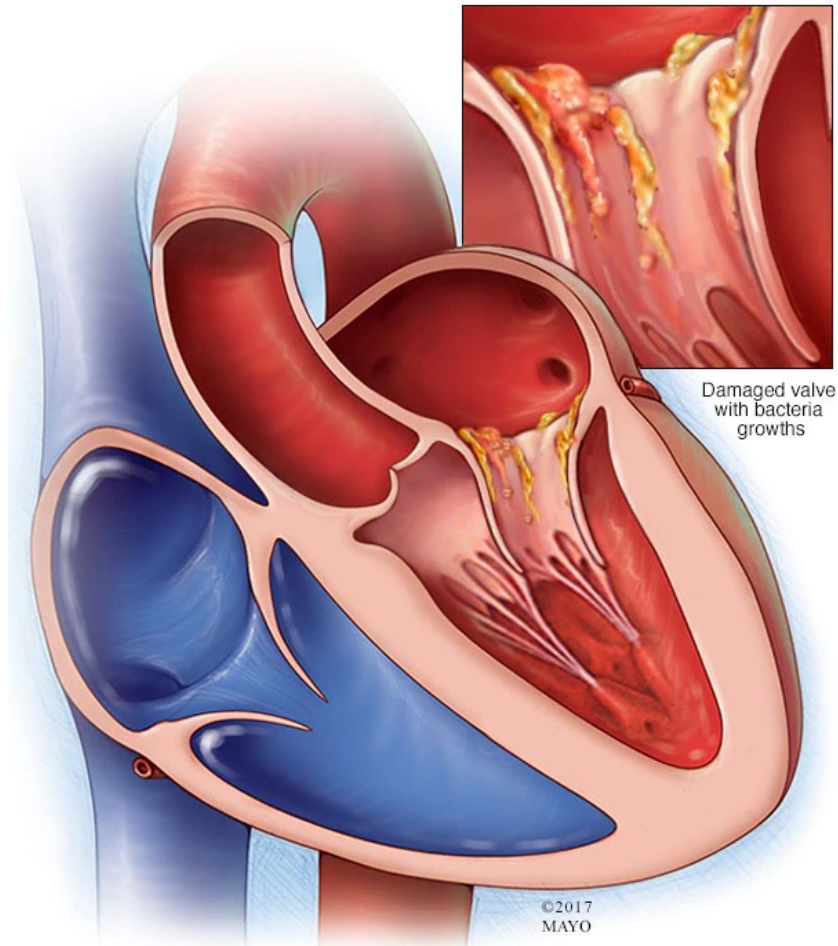
- Received consulting fees from eMed
- Received funding from National Institute on Drug Abuse

Session Learning Objectives

At the end of the session, you will be able to:

- List the diagnostic criteria for infective endocarditis.
- Describe and summarize the epidemiology of infective endocarditis in the U.S.
- Recognize the models of care for injection-related endocarditis.
- Determine if their practice approach fits into the new paradigm for care.

What is Infective Endocarditis?



- Caused by bacteria or fungi that enter the bloodstream and settle in the heart lining, a heart valve or a blood vessel

Clinical Presentation

Table 1. Clinical Signs and Complications of Infective Endocarditis

Sign	Patients, %
Fever	86-96
New murmur	48
Worsening of old murmur	20
Hematuria	26
Vascular embolic event	17
Splenomegaly	11
Splinter hemorrhages	8
Osler nodes	3
Janeway lesions	5
Roth spots	2
Complication	
Stroke	17-20
Nonstroke embolization	23-33
Heart failure	14-33
Intracardiac abscess	14-20
New conduction abnormality	8

- *Acute*
 - Advances rapidly, presenting with a sudden onset of high fever, rigors, sepsis, and systemic complications.
- *Chronic*
 - Nonspecific symptoms such as fatigue, dyspnea, or weight loss over several weeks to months. Usually fevers.

The Abbreviated-Modified* Duke Criteria

Major and minor criteria to diagnose endocarditis include:

- Positive blood cultures with organisms that seem like they could cause endocarditis (major)
- Something on imaging (usually TTE or TEE) that looks like endocarditis (major)
- Fever (minor)
- Predisposition to endocarditis (IDU) (minor)
- Vascular or immunologic phenomena (are emboli showering the patient?) (minor)
- A strange blood culture (minor)

**Not a real clinical criteria*

Changing Epidemiology

Then

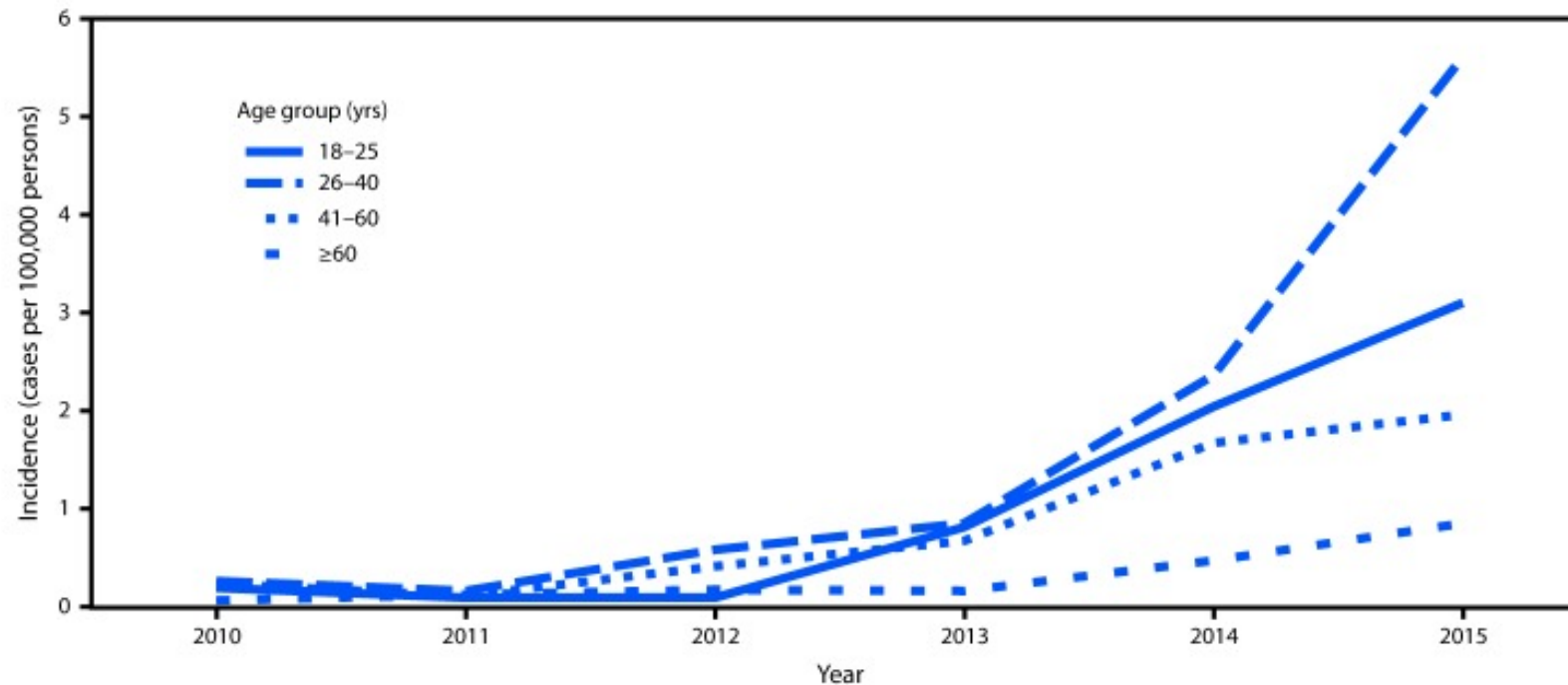
- Hospital admission for endocarditis was 25,511 in 1998
- Mean age prior to 2010 was 57.2 years (>one-third over the age of 70)
- Percent that were among PWID was ~3% (Olmstead County 1970-2006)

Now (ish)

- In North Carolina, 2.7 per 100,000 persons
- 2/3 less than 40 years
- Sharpest increase from 2010-2015 was among persons aged 18–25 years (IRR 2.1; 95% confidence intervals [CI] = 1.4–3.1) and 26–40 years (IRR 3.8; 95% CI = 2.8–5.1) compared with rates in persons aged >40 years

New Endocarditis Numbers

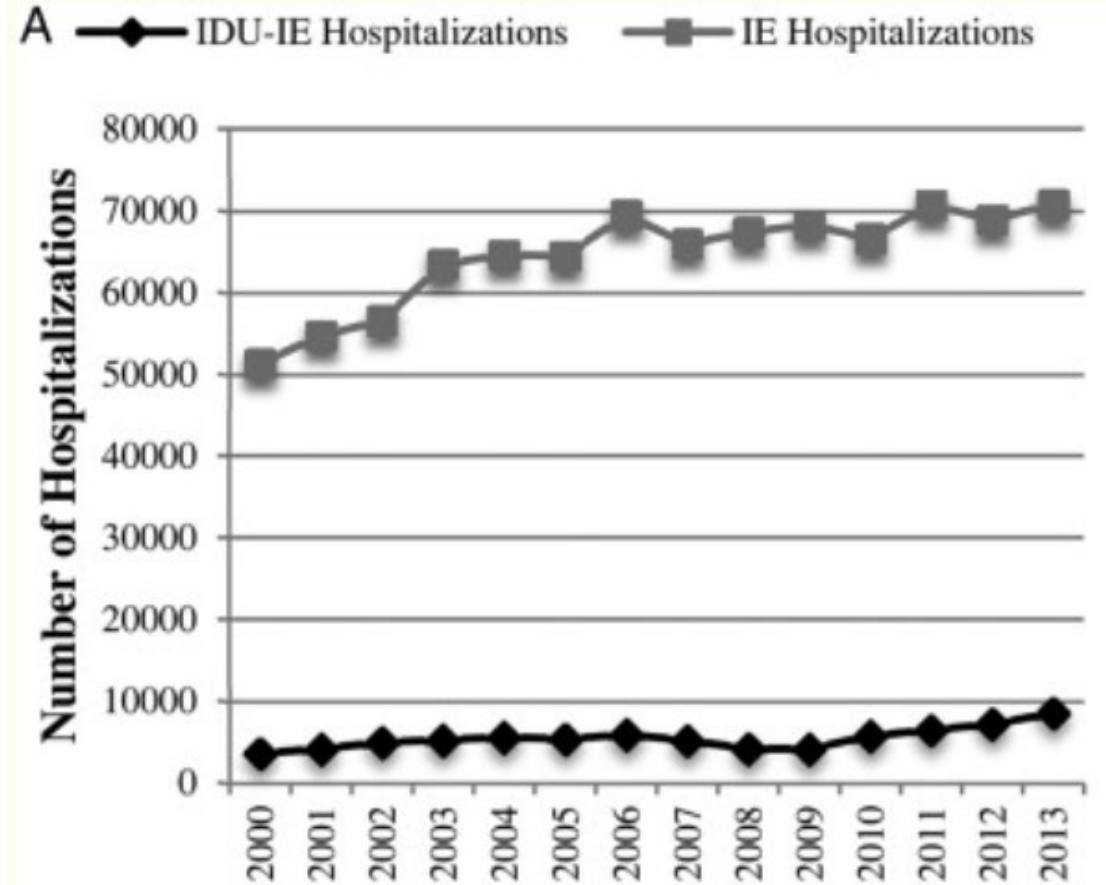
Hospitalizations for injection-related infective endocarditis increased twelve-fold between 2010 and 2015.



Incidence of hospital discharge diagnoses of drug dependence-associated endocarditis, by age group – North Carolina, 2010–2015

New Endocarditis Numbers: More IE Attributable To IDU

- Proportion of IE hospitalizations from IDU-IE increased from 7% to 12.1% between 2000 and 2013.
- Significant increase in the percentages of IDU-IE hospitalizations among 15- to 34-year-olds (27.1%-42.0%)



Trends in Hospitalization for Endocarditis

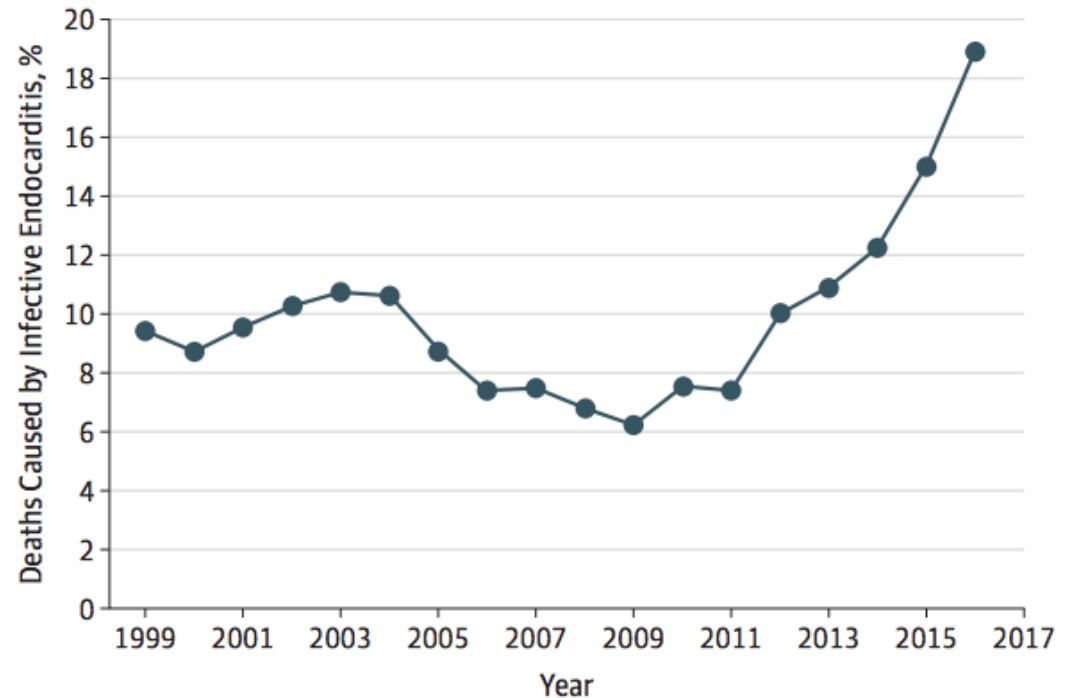
Characteristics of patients hospitalized with infective endocarditis as principal diagnosis, NIS 2009–2013

	2009	2010	2011	2012	2013	P value trend
Outcomes						
Length of stay	12.7 (0.3)	12.7 (0.4)	12.3 (0.4)	12.6 (0.3)	12.4 (0.3)	0.0058
Died	6.5 (0.5)	6.0 (0.5)	5.8 (0.5)	5.3 (0.1)	5.2 (0.4)	0.0528
Hospitalization charges (USD)	105,170 (6263.2)	105,385 (5990.2)	121,786 (7054.4)	121,907 (4161.1)	129,908 (4499.4)	0.0069



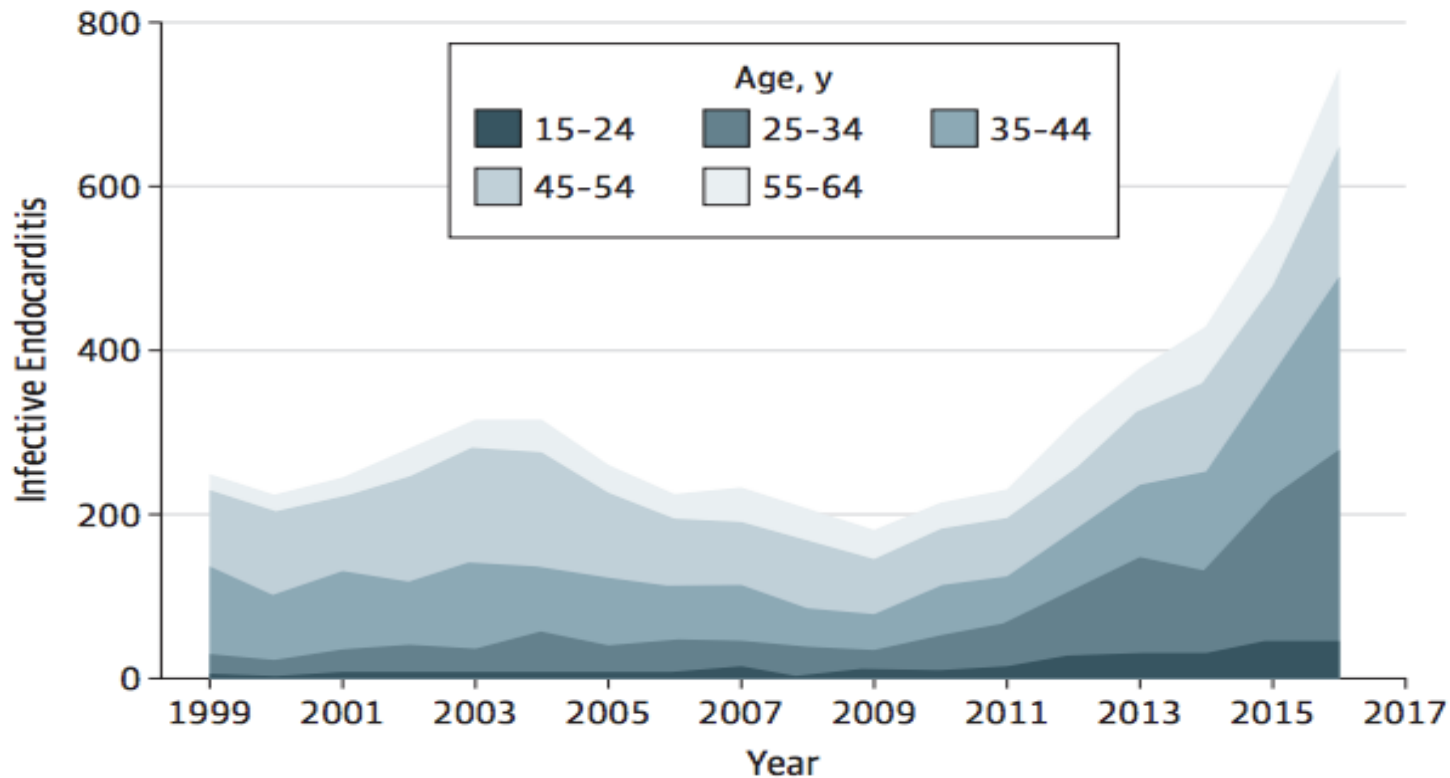
Mortality From Endocarditis

- Between 1999 and 2016, >55,000 deaths from endocarditis in the US
 - 10% occurred in PWID
 - 9% in 1999 to 19% in 2016
- Mortality among PWID increased 3-fold (249 in 1999 to 746 in 2016)
- Comparatively, endocarditis mortality among the general population increased 1.5-fold



Mortality From Endocarditis

A No. of deaths by age group



- The proportion of patients <35 who died of IE rose from 12.4% (n = 31/ 249) in 1999 to 37.4% (n = 279/746) in 2016

257,800 people who inject opioids are expected to die from endocarditis by 2030.

Typical Treatment For Bacterial Endocarditis

- Medical interventions
 - 6 weeks of intravenous antibiotics
 - Necessitates a PICC line and multiple doses per day
 - Toxicity ranges from possible hearing loss (gentamicin) to renal damage (vancomycin) to volume overload (oxacillin or nafcillin) to liver injury (daptomycin)
- Surgical
 - Debridement for associated septic arthritis, osteomyelitis, soft tissue abscesses, CNS abscesses, vitrectomy
 - Valve replacement

Barriers to Treatment for Injection-related Infections

- Typically, individuals with serious bacterial infections require days to weeks of intravenous antibiotics administered in the inpatient setting.
- Given their prolonged nature, these hospitalizations are costly and can only be shortened if transitional or outpatient options for antibiotic infusion exist or alternative antibiotic therapies are available
- Rehab facilities are reluctant to accept patients with active drug use
- Infusion companies are reluctant to offer home-based therapy

Changing Landscape of Antibiotics

Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N=199)	Oral Treatment (N=201)	Difference	Hazard Ratio (95% CI)
	<i>number (percent)</i>		<i>percentage points (95% CI)</i>	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (-1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (-3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (-2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (-3.1 to 3.1)	0.97 (0.28 to 3.33)

* Six patients, three in each group, had two outcomes.

† For details about relapse of the positive blood culture, see the Supplementary Appendix.

- POET Trial demonstrated that partial oral antibiotics was non-inferior to IV
- Several long-acting antibiotics are being used to finish treatment for endocarditis (e.g., dalbavancin, oritavancin)

Paired OPAT and SUD Treatment Models

- Treatment of endocarditis in people who use drugs should be viewed through a holistic lens that includes antimicrobial agents, treatment for their underlying substance use, and wrap around services (when necessary) through a multi-disciplinary approach

OPAT + BUP

- Pilot RCT of 20 patients at UKY, all of whom received SUD assessment by an addiction medicine physician + ID consultation
- Randomized to OPAT or usual care. Both received BUP in hospital and for 12 weeks post-discharge with frequent outpatient visits
- OPAT discharged when medically stable
- UC discharged after antibiotics completion

OPAT + BUP

- The average length of hospital stay for OPAT participants was 22.4 (standard deviation [SD] \pm 7.1) days compared to 45.9 (SD \pm 7.8) for UC participants
- All participants (100%) completed the recommended course of IV antibiotic therapy.
- For the 12 weeks posthospital discharge, the proportion of urine samples negative for illicit opioids was significantly greater in OPAT participants compared to UC participants
- Retention in outpatient treatment, measured by the proportion attending at least weekly outpatient physician visits, was similar in both groups
- OPAT participants reported no desire to inject in the indwelling catheter

Paired Treatment Improves Outcomes

- Among people with injection-related endocarditis:
 - MOUD receipt within 3 month of hospital discharge is associated with reduced mortality in the month that MOUD is received
 - MOUD receipt within 30 days of hospitalization reduces opioid overdose and 30-day, 90-day, and 1-year rehospitalization
 - MOUD decreases the chance of discharge against medical advice

Even Discharging to Residential Programs Works

- Jewell et al. cohort of 205 patients with opioid use disorder, who were discharged to a residential addiction treatment program with nurse-administered antibiotics via a PICC between 2006 and 2011.
 - 73% completed their course of antibiotics, 0 died during the program, and PICC misuse was not reported.
- However, Kimmel et al. found that people hospitalized with OUD frequently experience explicit discrimination when rejected from postacute care despite federal and state protections

Multi-Disciplinary Team Approach

- Several examples of a multi-disciplinary team that integrates infectious diseases, addiction medicine, hospital medicine, cardiology, cardiac surgery, and others
- Team approaches:
 - Are desired by cardiac surgeons
 - Decrease time to addiction medicine consult
 - Increase timely surgical intervention and may decrease AMA discharges
 - Can be supported by hospital administration

Final Takeaways

- Infective endocarditis have emerged as a significant cause of non-overdose mortality, morbidity, and cost among young PWID.
- Oral and long-acting injectable antibiotic regimens are being studied and represent new treatment modalities.
- MOUD during hospitalization or shortly thereafter improves outcomes.
- Hospitalization for injection drug use-related infections are unique opportunities to initiate MOUD and for multidisciplinary care teams to improve care.

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