

# **Supplemental Material**

**Table S1. ICD 10 codes used for Infective endocarditis.**

<b>I33 - Acute and subacute infective endocarditis</b>
<b>I33.9 - Acute and subacute endocarditis, unspecified</b>
<b>I38 - Endocarditis, valve unspecified</b>
<b>B37.6 – Candida endocarditis</b>

**ICD 10 codes used for substance use disorder**

B17.1 (Acute hepatitis C)
T40.0 (Opium)
T40.1 (Heroin)
T40.2 (Other opioids)
T40.3 (Methadone)
T40.4 (Other synthetic narcotics)
T40.6 (Other and unspecified narcotics)
F11 (Mental and behavioural disorders due to use of opioids)
F13 (Mental and behavioural disorders due to use of sedatives or hypnotics)
F14 (Mental and behavioural disorders due to use of cocaine)
F15 (Mental and behavioural disorders due to use of other stimulants, including caffeine)
F16 (Mental and behavioural disorders due to use of hallucinogens)
F19 (Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances)
X42 (Accidental poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified)

Comorbidities: immunodeficiency (D80-D84, Y43.4), diabetes(E10-E14), and CKD(N18)

**Table S2. Infective endocarditis mortality in different age groups.**

Age group	"AAPC"	"AAPC C.I. Low"	"AAPC C.I. High"	"Statistically Significant (0=No 1=Yes)"	"Test Statistic"	"P- Value"
"25-34 years"	5.4	3.1	7.7	1	4.7	<0.001
"35-44 years"	2.3	1.3	3.3	1	4.3	<0.001
"45-54 years"	0.5	-1.9	3	0	0.4	0.684
"55-64 years"	-0.4	-0.7	-0.2	1	-3.3	0.003
"65-74 years"	-1.9	-2.2	-1.6	1	-13.3	<0.001
"75-84 years"	-1.9	-2.4	-1.3	1	-6.8	<0.001
"85+ years"	-0.9	-1.4	-0.3	1	-3.1	0.002

AAPC: average annual percent change CI: confidence interval

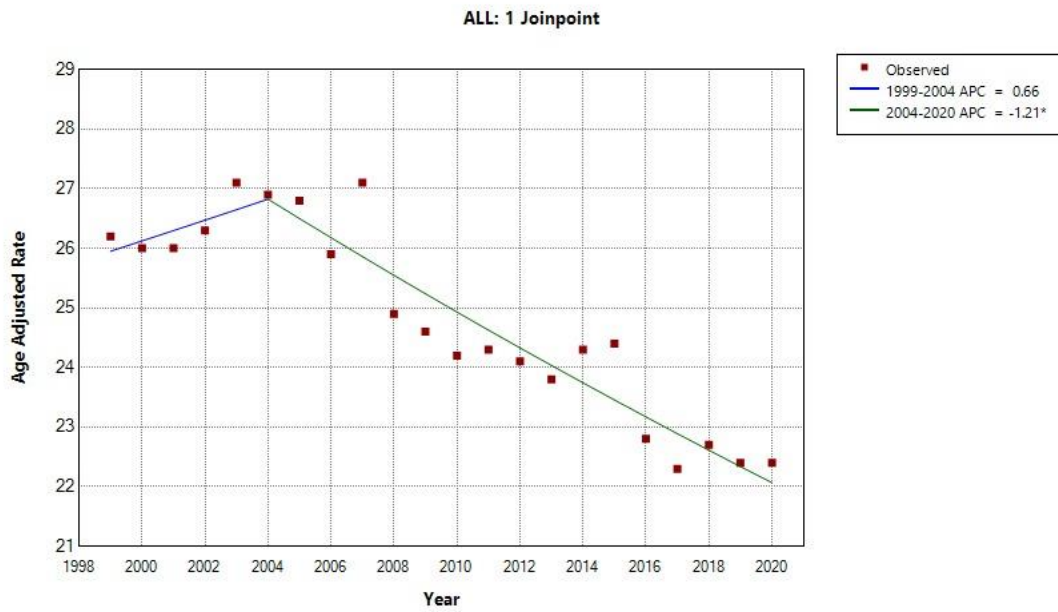
**Table S3. Average annual percent change in infective endocarditis age-adjusted mortality for each of the 50 states and District of Columbia between 1999 and 2020.**

state	AAPC	AAPC C.I. Low	AAPC C.I. High	Statistically Significant (0=No 1=Yes)	Test Statistic	P-Value
Alabama	-0.9	-1.9	0	1	-2.1	0.046
Arizona	-1.4	-3	0.3	0	-1.6	0.105
Arkansas	-1.2	-2	-0.4	1	-3.2	0.005
California	-2.5	-2.9	-2.1	1	-13.3	0
Colorado	0.4	-5.2	6.3	0	0.1	0.9
Connecticut	-1.6	-2.8	-0.4	1	-2.9	0.01
Delaware	-3.2	-6.2	-0.1	1	-2.3	0.043
Florida	0.2	-0.1	0.6	0	1.3	0.202
Georgia	-2.2	-3	-1.4	1	-5.9	0
Hawaii	-1.7	-2.8	-0.6	1	-3.4	0.005
Idaho	-2	-3.2	-0.8	1	-3.5	0.002
Illinois	-2.1	-2.6	-1.7	1	-9.7	0
Indiana	-0.3	-0.9	0.4	0	-0.8	0.414
Iowa	0.8	-1.8	3.4	0	0.6	0.56
Kansas	0	-0.7	0.7	0	0	0.978
Kentucky	1.2	0.7	1.7	1	5	0
Louisiana	-0.6	-2.3	1.1	0	-0.7	0.507
Maine	0.2	-0.7	1.2	0	0.5	0.636
Maryland	-1.6	-2.4	-0.8	1	-4.2	0
Massachusetts	-0.2	-1	0.6	0	-0.5	0.613
Michigan	-0.5	-1	0	1	-2.2	0.041
Minnesota	-0.2	-1	0.6	0	-0.5	0.589
Mississippi	1.2	0.3	2.2	1	2.8	0.01
Missouri	-0.8	-1.7	0.2	0	-1.5	0.136
Montana	-1	-2	0.1	0	-1.9	0.07
Nebraska	-0.5	-1.5	0.4	0	-1.2	0.245
Nevada	-3.2	-4.2	-2.2	1	-6.8	0
New Hampshire	-0.7	-2.3	0.8	0	-1	0.334
New Jersey	-1.1	-1.7	-0.5	1	-3.7	0.001
New Mexico	0.8	-0.3	2	0	1.5	0.157
New York	-0.7	-1.2	-0.3	1	-3.6	0.002

North Carolina	-0.6	-1.2	-0.1	1	-2.4	0.024
North Dakota	-0.3	-1.7	1.1	0	-0.5	0.658
Ohio	0.3	-0.1	0.7	0	1.8	0.095
Oklahoma	0.8	-0.1	1.8	0	1.8	0.093
Oregon	-1.3	-2.2	-0.3	1	-2.8	0.01
Pennsylvania	-0.9	-1.4	-0.5	1	-4.3	0
Rhode Island	-2.1	-4	-0.3	1	-2.6	0.03
South Carolina	-2	-2.6	-1.4	1	-6.9	0
South Dakota	-2	-3.4	-0.5	1	-2.9	0.012
Tennessee	0.8	0.2	1.4	1	2.9	0.01
Texas	-1.4	-2.7	-0.1	1	-2.1	0.039
Utah	-3.9	-5	-2.9	1	-7.9	0
Virginia	-1.6	-2.2	-1	1	-5.7	0
Washington	-1.2	-1.8	-0.6	1	-4.1	0.001
West Virginia	2	0.7	3.2	1	3.4	0.003
Wisconsin	-0.1	-0.6	0.4	0	-0.5	0.618

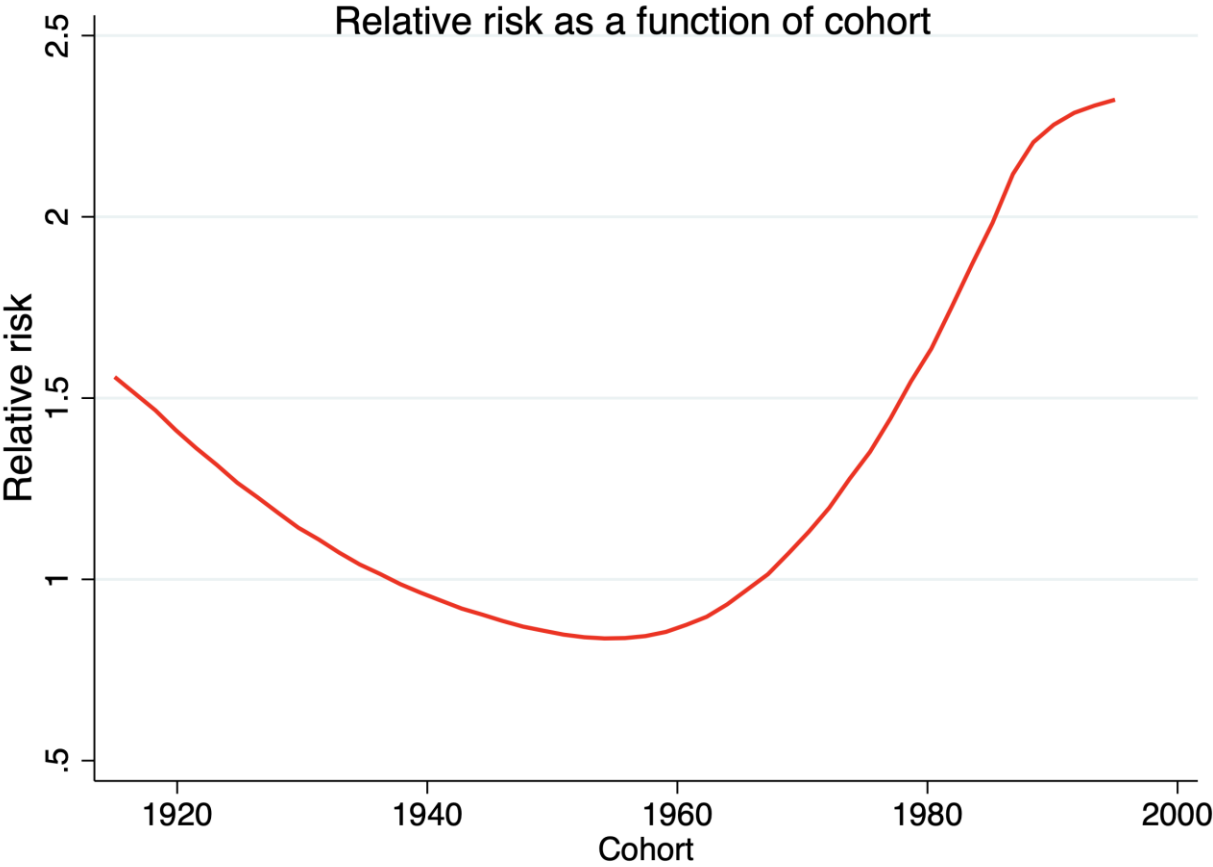
AAPC: Average annual percent change CI: confidence interval \*p-value significant

**Figure S1. Joinpoint analysis of trends in AAMR due to IE.**



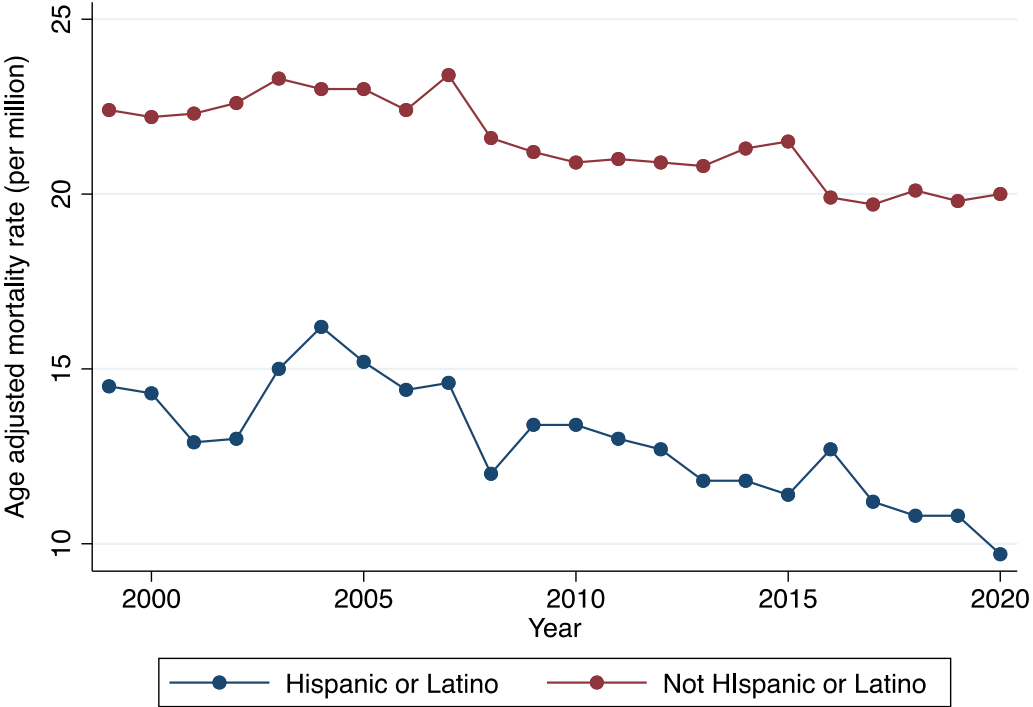
\* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.  
-- Test Statistic and P-Value not available for the Empirical Quantile method.  
Final Selected Model: 1 Joinpoint.

Figure S2. Age Period Cohort (APC) analysis of the IE cohort.



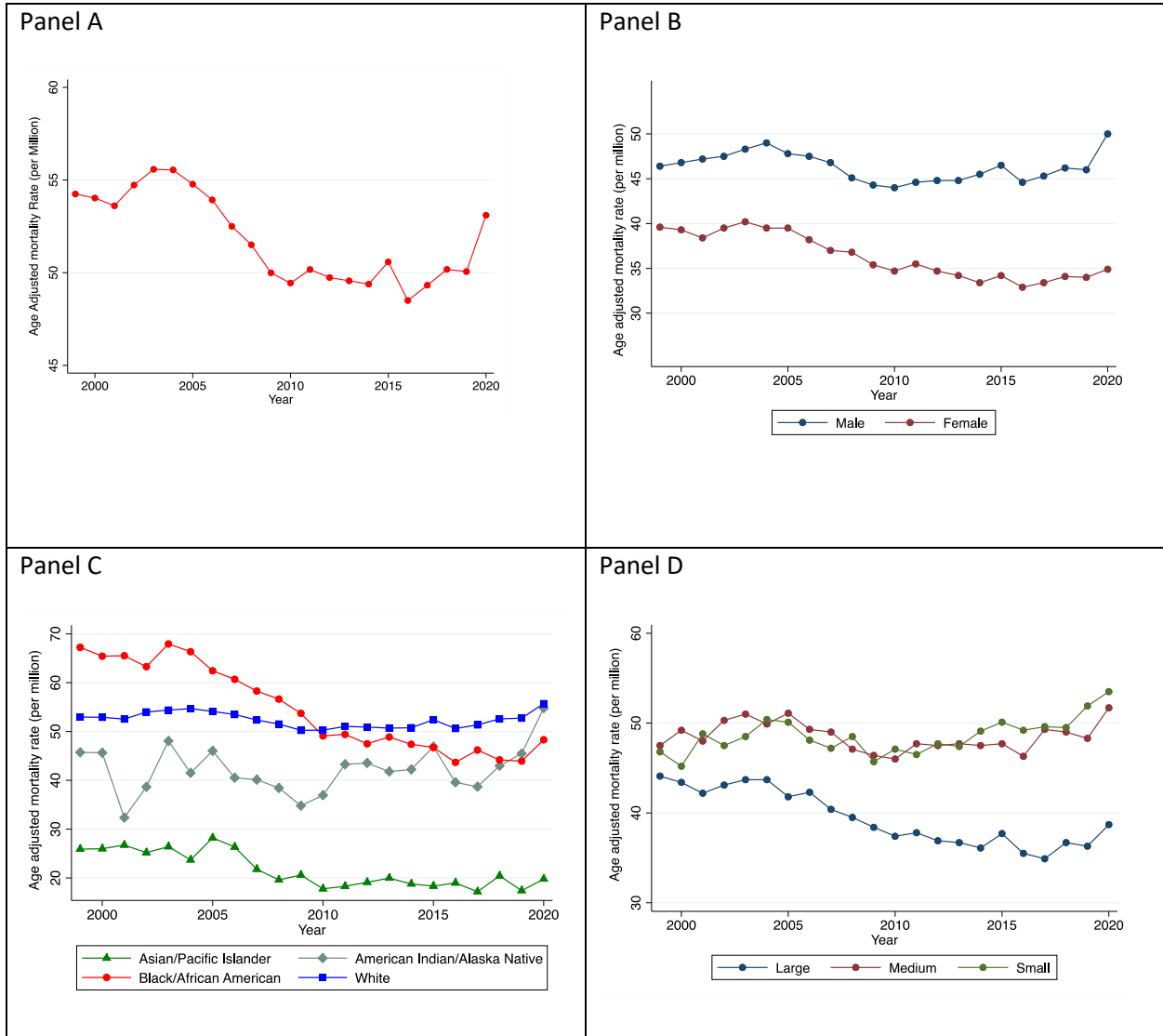
\*Birth cohorts on x axis

**Figure S3. Trends of age-adjusted mortality rates related to infective endocarditis in the US stratified by Hispanic origin.**





**Figure S4. Trend of age-adjusted mortality rates related to infective endocarditis(as contributing cause) in the US (Panel A) and stratified by sex (Panel B), race (Panel C), and urbanicity (Panel D) in the United States from 1999 to 2020.**



**Figure S5. Trend of age-adjusted mortality rates related to infective endocarditis (as contributing cause) in the US based on Hispanic origin**

