US, United States. The year of HepA vaccine introduction is mentioned next to each country. *For some states, the year of vaccine introduction was 1995. The incidence values represent the mean incidence during pre- and post-vaccination periods for Israel (Levine at al, 2015), the US (Averhoff et al, 2001; Wasley et al, 2005; Singleton et al, 2010) and Argentina (Vacchino et al, 2008; Vizzotti et al, 2014) ; range of annual incidence during pre- and post-vaccination periods for Panama (Estripeaut et al, 2015), the US (Daniels et al, 2009), Uruguay (Romero et al, 2012) and Brazil (Souto et al, 2019); annual incidence during pre- and post-vaccination periods for Israel (Belmaker et al, 2007; Chodick et al, 2008; Dagan et al, 2005) Saudi Arabia (Al-Mosa, 2011) and the US (Erhart & Ernst, 2012; Murphy et al, 2016). Two other studies included in our review (Fisenka et al, 2008 [Belarus]; Wang et al, 2019 [China]) do not present 'all ages' data.

Table 1. Anti-HAV antibody GMCs following vaccination with 2-dose and 1-dose schedules, data from studies included in our review

Conclusion. The implementation of 2- and 1-dose UMV programs against HAV induced decreases in disease incidence and related outcomes. Experience with 2-dose schedule is extensive, with wide geographical use, while evidence beyond 10 years for the 1-dose schedule has not yet been demonstrated. Continued and robust surveillance is needed to monitor the epidemiology, vaccine effectiveness, antibody persistence and protection (particularly in the absence of natural boosting) in order to have a strong, scientifically sound basis for decision makers when concluding on HepA prevention strategies in their countries.

	Country, study period (reference)	Time after vaccination, years (range)	Children tested	Clinical assay	Anti-HAV GMC mIU/mL (95% CI)	Persistence of HAV-antibodies % (n/N)
2-dose schedule	**China*** (Bian et al, 2010)	10	110	MEIA	61.59 (51.92–73.07)	≥5 mIU/mL: 99.09 (109/110) ≥10 mIU/mL: 90.0 (90/110)
	Argentina, 2008–2014 (Espul et al, 2017)	7	53 7**	ECLIA	712.5 (526.4–964.5) 257.2 (81.3–813.6)	≥3 mIU/mL: 100 (53/53) 100 (7/7)
	Argentina, 2007–2007 (Lopez et al, 2010)	10	48	Automated ELFA	261 (199–341)	≥20 mIU/mL: 97.9 (47/48)
	Argentina, 2010–2012 (Lopez et al, 2015)	14–15	30	Automated ELFA	253 (181–353)	≥20 mIU/mL: 100 (30/30)
	United States of America* (Raczniak et al, 2013)	11.1 (3.5–15.1)	101	Modified ELISA	NA	≥20 mIU/mL: 95 (96/101)
		≥7.5 to <9	1 (1–2 years old) 3 (3–6 years old) 3 (≥7 years old)		48 (NA) 115 (12–1114) 125 (11–1358)	NA
		≥9 to <11	10 (1–2 years old) 7 (3–6 years old) 17 (≥7 years old)		144 (78–263) 160 (94–271) 201 (117–343)	100 (7/7)
		≥11 to <13	26 (1–2 years old) 8 (3–6 years old) 11 (≥7 years old)		98 (66–147) 298 (51–1749) 211 (112–397)	100 (8/8)
		≥13 to <15	5 (1–2 years old) 5 (3–6 years old) 1 (≥7 years old		21 (6–77) 80 (40–159) 81	100 (5/5)
		≥15	1 (3–6 years old)		43	100 (1/1)
	Panama, 2016–2017 (Abadia et al, 2019)	Mean: 8.2 (7.0–9.7)	300	NA	123.9 (111.5–137.7)	≥15 mIU/mL 97.7% (293/300)
1-dose schedule	**Argentina**, 2013–2014 (Uruena et al, 2016)	Median: 7.7 (6.3–9.2)	1088	MEIA	170.5 (163.2–178.2)	≥10 mIU/mL: 97.4 (1060/1088)
	Argentina, 2008–2014 (Espul et al, 2017)	7	204	ECLIA	125.6 (118.8–141.1)	≥3 mIU/mL: 100 (204/204)
	Nicaragua, 2005–2012 (Mayorga et al, 2016)	7.5	97	MEIA	81 (64–101)	NA
	Panama, 2016–2017 (Abadia et al, 2019)	Mean: 8.1 (7.0–10.0)	300	ELISA	40.2 (34.2–47.4)	≥15 mIU/mL 74.3 (223/300)

HAV, hepatitis A virus; **GMC**, geometric mean concentration; **CI**, confidence interval; **NA**, not available; **MEIA**, microparticle enzyme immunoassay; **ECLIA**, electrochemiluminescence immunoassay; **ELFA**, enzyme-linked fluorescent assay; ELISA, enzyme-linked immunosorbent assay. *Study period not reported. ** This group received a vaccine dose and a booster dose

Funding: GlaxoSmithKline Biologicals SA

Disclosures. **Anar Andani, BSc**, **GSK group of companies** (Employee, Shareholder) **Eveline M. Bunge, PhD**, **GSK group of companies** (Research Grant or Support) **Fernanda Salgado, MD, MSc**, **GSK group of companies** (Employee) **Rosa C. van Hoorn, MSc**, **GSK group of companies** (Research Grant or Support) **Bernard Hoet, MD, FFPM**, **GSK group of companies** (Shareholder)

35. Missed and Unrecorded Drug Use Among Infective Endocarditis Cases Is Associated with Underestimated Burden of Disease and Fragmented Care: Evidence from Six States

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Background. Studies using national administrative data suggest that hospitalizations for drug use-associated infective endocarditis (DUA-IE) have increased over the last ten years. However, drug use as a contributing factor to IE hospitalizations is often missed or not included in coding documentation, resulting in undercount of DUA-IE. We assessed whether missed drug use during IE hospitalizations was associated with higher levels of fragmented care and underestimation of DUA-IE burden.

Methods. We analyzed data from State Inpatient Databases and State Emergency Department Databases from six states (FL, GA, IA, NY, UT, VT) from 2011–2015. Patients older than 16 with ICD-9/10 codes for admissions with IE were included. IE was categorized as DUA using ICD-9/10 codes for drugs/conditions associated with injection drug use. We labeled IE cases as a "missed" DUA-IE case if they had no diagnosis of drug use during their index hospitalization but received a drug use diagnosis during an ED visit or inpatient stay in the calendar year of their index IE hospitalization. We compared "missed" DUA-IE cases to DUA-IE cases where drug use was identified in the index hospitalization and non-DUE-IE cases with respect to demographics, length of stay (LOS) and total charges. To assess care fragmentation, we stratified IE groups by whether the patient was admitted to 1 or >1 hospital within 90-days of the index IE admission.

Results. There were 52147 non-DUA-IE cases, 6872 DUA-IE cases, and 2676 "missed" DUA-IE cases identified by linking drug use across multiple encounters. Missed cases represented a 39% increase in total DUA-IE cases. Compared to DUA-IE cases identified at index hospitalizations, missed cases were more likely to be older, Black, insured by Medicare, and from rural areas. They also had higher 30-day readmission rate (23.2% vs 14.5%, p< 0.001) and higher charges (p< 0.001), with similar LOS. Fragmented care was most common among patients with missed DUA-IE (33.3%), followed by DUA-IE cases identified during index hospitalization (20.5%) and non-DUA-IE cases (13.7%).

Table 1

Table 1: Characteristics of infective endocarditis (IE) episodes according to category of drug use, evidence from six states, 2011-2015[a]

Characteristic	Drug Use Category[b]			P-value[c]
	Non-DUA-IE	Index DUA-IE	Missed DUA-IE	
No. (%)	52147 (84.5)	6872 (11.1)	2676 (4.3)	
Age, median (IQR)	72 (23)	41 (24)	48 (26)	<0.001
Female, No. (%)	2505 (48.1)	3021 (44.4)	1205 (45.3)	<0.001
Race, No. (%)				
White	35463 (68.0)	4872 (70.9)	1696 (63.4)	<0.001
Black	8345 (16.0)	860 (12.5)	577 (21.6)	<0.001
Hispanic	4306 (8.3)	642 (9.3)	209 (7.8)	0.005
Other	4033 (7.7)	498 (7.3)	194 (7.3)	0.259
Insurance, No. (%)				
Medicare	36635 (70.3)	1427 (20.8)	1102 (41.2)	<0.001
Medicaid	4418 (8.5)	2621 (38.1)	784 (29.3)	<0.001
Private	8023 (15.4)	858 (12.5)	324 (12.1)	<0.001
Self-pay	1468 (2.8)	1368 (19.9)	319 (11.9)	<0.001
Other	1603 (3.1)	598 (8.7)	147 (5.5)	<0.001
Hospital Rurality, No. (%)[d]				
Large Urban	30341 (58.2)	4072 (59.3)	1497 (55.9)	0.013
Small Urban	14367 (27.6)	2107 (30.7)	839 (31.4)	<0.001
Rural	7439 (14.3)	693 (10.1)	340 (12.7)	<0.001
Drug/Condition Associated with IE, No. (%)				
Opiate	0 (0)	4390 (63.9)	1658 (62.0)	<0.001
Cocaine	0 (0)	2140 (31.1)	599 (22.4)	<0.001
Amphetamine	0 (0)	643 (9.4)	225 (8.4)	<0.001
Hepatitis C	0 (0)	4239 (61.7)	977 (36.5)	<0.001
Number of Hospitals per IE Episode, No. (%)[e]				
One	45028 (86.4)	5466 (79.5)	1786 (66.7)	<0.001
Two	6367 (12.2)	1122 (16.3)	683 (25.5)	<0.001
Three or more	752 (1.4)	284 (4.1)	207 (7.7)	<0.001

Abbreviations: IE = infective endocarditis; DUA = drug use-associated; IQR = interquartile range

[a] Data from State Inpatient Databases and State Emergency Department Databases from six states (FL, GA, IA, NY, UT, VT), pooled across years from 2011-2015. IE hospitalizations identified using ICD-9/10 codes.

[b] In accordance with prior studies, drug use categories defined by ICD-9/10 codes for drugs and conditions associated with injection drug use, including opiates, cocaine, amphetamines, and hepatitis C. Non-DUA-IE refers to IE episodes without any associated drug use. Index DUA-IE refers to IE episodes in which an ICD-9/10 code for drug use was used during the same episode. Missed DUA-IE refers to IE episodes in which an ICD-9/10 codes for drug use was not used during the IE episode, but was recorded during a different inpatient stay or ED visit within the same calendar year.

[c] P-values refer to global comparison for differences across drug use groups, with ANOVA for continuous variables and Chi-Square tests for categorical variables. Bonferroni corrected p-value using alpha 0.05 = 0.002.

[d] Hospital rurality defined using simplified adaptation of UIC codes as reported in state databases.

[e] Measure of number of hospitals at which a patient received care for a single episode of IE within 90 days of their index IE hospitalization. Transfers between hospitals (e.g. transfer for cardiac surgery) were counted as only one hospitalization, with the location assigned to the discharging hospital.

Table 2

Table 2: Hospital utilization and selected outcomes for IE episodes according to drug use category and care fragmentation, evidence from six states, 2011-2015[a]

Hospital Utilization / Outcome	Drug Use Category[b]			P-value[c]
	Non-DUA-IE	Index DUA-IE	Missed DUA-IE	
All Admissions				
No.	52147	6872	2676	
Episode LOS, days, median (IQR)	11 (17)	22 (30)	21 (32)	<0.001
Episode Total Charges, $, median (IQR)	84567 (158k)	154318 (229k)	164430 (268k)	<0.001
Discharged AMA, No. (%)	552 (1.1)	921 (13.4)	212 (8.9)	<0.001
30 Day Readmission, No. (%)	7694 (14.7)	1005 (14.6)	523 (23.3)	<0.001
Surgical Repair within 90 days, No. (%)	4374 (8.4)	1020 (14.8)	389 (14.5)	<0.001
Death within 90 days, No. (%)	7648 (14.7)	832 (12.1)	276 (10.3)	<0.001
IE Reoccurrence, No. (%)[e]	1288 (2.5)	534 (7.8)	534 (10.5)	<0.001
No Fragmented Care[d]				
No.	45028	5466	1786	
Episode LOS, days, median (IQR)	10 (15)	18 (29)	17 (27)	<0.001
Episode Total Charges, $, median (IQR)	73364 (134k)	139045 (207k)	138969 (232k)	<0.001
Discharged AMA, No. (%)	425 (0.9)	596 (10.9)	114 (6.4)	<0.001
30 Day Readmission, No. (%)	4881 (10.8)	465 (8.5)	271 (15.2)	<0.001
Surgical Repair within 90 days, No. (%)	3364 (7.5)	740 (13.5)	238 (13.3)	<0.001
Death within 90 days, No. (%)	6669 (14.8)	738 (13.5)	204 (11.4)	<0.001
IE Reoccurrence, No. (%)[e]	973 (2.2)	371 (6.8)	165 (9.2)	<0.001
Fragmented Care[d]				
No.	7119	1406	890	
Episode LOS, days, median (IQR)	24 (29)	31 (33)	31 (32)	<0.001
Episode Total Charges, $, median (IQR)	190202 (258k)	233384 (279k)	235568 (316k)	<0.001
Discharged AMA, No. (%)	127 (1.8)	325 (23.1)	98 (11.0)	<0.001
30 Day Readmission, No. (%)	2813 (39.5)	540 (38.4)	352 (39.6)	0.734
Surgical Repair within 90 days, No. (%)	1010 (14.2)	280 (19.9)	151 (17.0)	<0.001
Death within 90 days, No. (%)	979 (13.8)	94 (6.7)	72 (8.1)	<0.001
IE Reoccurrence, No. (%)[e]	315 (4.4)	163 (7.7)	116 (13.0)	<0.001

Abbreviations: IE = infective endocarditis; DUA = drug use-associated; IQR = interquartile range; LOS = length of stay; AMA = against medical advice

[a] Data from State Inpatient Databases and State Emergency Department Databases from six states (FL, GA, IA, NY, UT, VT), pooled across years from 2011-2015. IE hospitalizations identified using ICD-9/10 codes.

[b] In accordance with prior studies, drug use categories defined by ICD-9/10 codes for drugs and conditions associated with injection drug use, including opiates, cocaine, amphetamines, and hepatitis C. Non-DUA-IE refers to IE episodes without any associated drug use. Index DUA-IE refers to IE episodes in which an ICD-9/10 code for drug use was used during the same episode. Missed DUA-IE refers to IE episodes in which an ICD-9/10 codes for drug use was not used during the IE episode, but was recorded during a different inpatient stay or ED visit within the same calendar year.

[c] P-values refer to global comparison for differences across drug use groups, with ANOVA for continuous variables and Chi-Square tests for categorical variables. Bonferroni corrected p-value using alpha 0.05 = 0.002. Note that all P-values comparing across categories of care fragmentation within drug use categories were also <0.001, except for death within 90 days (p=0.018 for Non-DUA-IE, p=0.007 for Index DUA-IE), and IE reoccurrence (p=0.003 for Index DUA-IE).

[d] No fragmented care defined as hospitalization at only one hospital within a 90-day period, excluding inter-hospital transfers. Fragmented care defined as hospitalization at greater than one hospital for the same IE episode, i.e. within 90 days of their index IE hospitalization. Transfers between hospitals (e.g. transfer for cardiac surgery) were counted as only one hospitalization, with the location assigned to the discharging hospital.

[e] Reoccurrence defined as rehospitalization for IE more than 90 days after discharge from the index IE hospitalization.

Conclusion. Missed and/or unrecorded drug use and fragmented care are common features of DUA-IE. This results in underestimation of both DUA-IE prevalence and hospital utilization due to DUA-IE.

Disclosures. **All Authors**: No reported disclosures

36. Maternity-associated Infective Endocarditis in the United States: Similar Outcomes to Non-pregnant Patients

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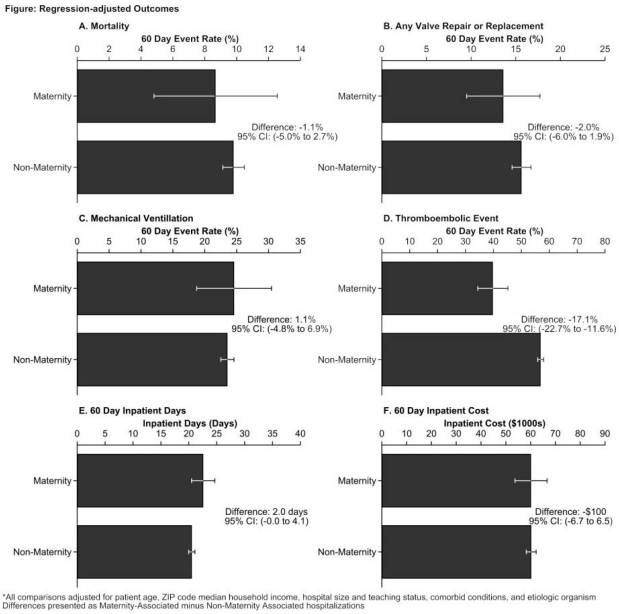
Background. Little is known about infective endocarditis (IE) occurring during pregnancy. In this analysis, we sought to define the patient characteristics, risk factors, and outcome of maternity-associated IE (maIE).

Methods. The National Readmissions Database was used to identify admissions for IE in female patients aged 12 – 55 years discharged between Oct. 2015 and Dec. 2017. Demographics, comorbidities, and outcomes were obtained. Differences between groups were analyzed using weighted Chi-squared test for categorical variables and weighted linear regression for continuous variables. Weighted multivariate regressions adjusted for demographics, hospital, etiologic organism, and comorbid conditions to assess the association between maternity status and outcomes.

Results. Out of 10,271 identified IE admissions (corresponding to a national estimate of 19,626 admissions), maIE accounted for 320 (national estimate 617) (3.1%). Of these maIE admissions, 41.2% were antepartum admissions, 26.3% resulted in delivery, 18.3% were postpartum, and 11.3% were an early or abnormal pregnancy. Patients with maIE were younger (28.4 ± 3.9 vs. 36.6 ± 8.0, $P < 0.001$) and more likely insured by Medicaid (73.3% vs. 46.6%, $P < 0.001$). Although generally healthier, patients with maIE had higher rates of drug abuse (75.7% vs. 58.5%, $P < 0.001$). In unadjusted comparisons maIE was associated with lower rates of 60-day mortality and thromboembolic events. In adjusted analysis only differences between rates of thromboembolic events were significant (adjusted incremental difference: -17.1%, 95% confidence interval: -22.7% to -11.6%). Differences in rates of valve procedures, mechanical ventilation, length of stay, and inpatient costs were not statistically significant (Figure).

Regression-adjusted Outcomes



Conclusion. Compared with other reproductive aged female IE patients, patients with maIE are younger, healthier, more likely insured by Medicaid, and report higher rates of drug abuse. After adjustment, they receive similar management and do not appear to be at higher risk for adverse outcomes including mortality.

Disclosures. **Vance G. Fowler, Jr., MD, MHS**, **Achaogen** (Consultant)**Actavis** (Grant/Research Support)**Advanced Liquid Logics** (Grant/Research Support)**Affinergy** (Consultant, Research Grant or Support)**Affinium** (Consultant)**Allergan** (Grant/Research Support)**Ampliphi Biosciences** (Consultant)**Basilea** (Consultant, Research Grant or Support)**Bayer** (Consultant)**C3J** (Consultant)**Cerexa** (Consultant, Research Grant or Support)**Contrafect** (Consultant, Research Grant or Support)**Cubist** (Grant/Research Support)**Debiopharm** (Consultant)**Destiny** (Consultant)**Durata** (Consultant)**Forest** (Grant/Research Support)**Genentech** (Consultant, Research Grant or Support)**Integrated Biotherapeutics** (Consultant)**Janssen** (Consultant, Research Grant or Support)**Karius** (Grant/Research Support)**Locus** (Grant/Research Support)**Medical Biosurfaces** (Grant/Research Support)**Medicines Co.** (Consultant)**Medimmune** (Consultant, Research Grant or Support)**Merck** (Consultant, Research Grant or Support)**NIH** (Grant/Research Support)**Novadigm** (Consultant)**Novartis** (Consultant, Research Grant or Support)**Pfizer** (Grant/Research Support)**Regeneron** (Consultant, Research Grant or Support)**Tetraphase** (Consultant)**Theravance** (Consultant, Research Grant or Support)**Trius** (Consultant)**xBiotech** (Consultant)

37. Bloodstream Infections in the United States and Europe: Etiology and Antimicrobial Susceptibility Results from the SENTRY Antimicrobial Surveillance Program (2016–2019)

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Background. The SENTRY Antimicrobial Surveillance Program monitored the etiology of bloodstream infections (BSI) and other infections worldwide since 1997. We evaluated the results for BSI in the United States (US) and Europe (EU).

Methods. Organisms were consecutively collected (1/patient) from 79 medical centers located in the US (n=12,748; 35 centers), western EU (W-EU; n=12,198; 29 centers from 10 nations: Belgium, France, Germany, Ireland, Italy, Portugal, Spain, Sweden, Switzerland, and the United Kingdom), and eastern EU (E-EU; n=3,297; 15 centers from 12 nations: Belarus, Croatia, Czech Republic, Greece, Hungary, Israel, Poland, Romania, Russia, Slovakia, Slovenia, and Turkey). Organisms were susceptibility tested by reference broth microdilution methods in a central laboratory.

Results. The most common organism found was *S. aureus* in the US and *E. coli* in W-EU and E-EU (Table). *E. coli, S. aureus,* and *K. pneumoniae* represented the top 3 organisms in all 3 regions and accounted for 53.9–54.8% of the collection. Gram-negative bacilli (GNB) represented 48.8% of organisms in the US, 59.8% in W-EU, and 65.6% in E-EU. MRSA rates were higher in US (41.6%) compared to W-EU (24.4%) and E-EU (24.6%). In contrast, susceptibility to ceftriaxone and levofloxacin among *E. coli* were lower in E-EU (66.4% and 55.8%, respectively) compared to W-EU (83.3% and 73.5%, respectively) and the US (83.0% and 65.8%, respectively). Among *K. pneumoniae*, susceptibility to ceftriaxone and meropenem were 86.6% and 98.7% in US, 64.3% and 84.7% in W-EU, and 30.2% and 72.5% in E-EU, respectively. CRE rates were lower in US (0.5%) compared to W-EU (2.8%) and very high in E-EU (10.4%). *P. aeruginosa* susceptibility to piperacillin-tazobactam and meropenem were 84.8% and 83.7% in US, 81.4% and 82.3% in W-EU, and 64.6% and 57.6% in E-EU,