

# Background rates of neuroinflammatory disorders and atrial fibrillation – conditions of interest for vaccine safety studies

Anna A. Agan<sup>1</sup>, Casie E. Horgan<sup>1</sup>, Sruthi Adimadhyam<sup>1,2</sup>, Vincent Lo Re III<sup>3,4</sup>, Dominique Luyts<sup>5</sup>, Quentin Deraedt<sup>5</sup>, Armina Omole<sup>5</sup>, Noelle Cocoros<sup>1,2</sup>

<sup>1</sup>Dept. of Population Medicine, Harvard Pilgrim Health Care Institute, Boston, MA, USA; <sup>2</sup>Harvard Medical School, Boston, MA, USA; <sup>3</sup>Dept. of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; <sup>4</sup>Dept. of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; <sup>5</sup>GSK, Belgium

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## Background

Guillain-Barré Syndrome (GBS), acute disseminated encephalomyelitis (ADEM), and atrial fibrillation/flutter (AF) are conditions of interest to vaccine safety, including the recently released respiratory syncytial virus (RSV) vaccines.<sup>1</sup>

## Specific Aims

We aimed to estimate the rates of new-onset GBS, ADEM, AF, and recurrent AF, and to assess the infection status and seasonality of these events among older adults in the US.

## Methods

**Study period:** January 2017 – December 2022

**Data source:** Merative™ MarketScan® Commercial and Medicare Databases (US claims)

**Cohort:** Adults aged ≥60 years with evidence of new-onset GBS, ADEM, or AF, or recurrent AF:

- 365 days of prior medical and drug coverage were required with a 45-day allowable coverage gap;
- 365-day washout was used to identify new-onset conditions.

**Data analysis:**

- Calculated rates per 10K member-years (MY), rates per 10K members, and 95% CIs for each condition overall and stratified by age, sex, and month/year.
- Assessed evidence of recent infections that might precipitate an event of interest and seasonality of the events.
- Day 0 (index date): date the individual met one of the definitions in **Table 1**.
- Event-defining algorithms used ICD-10-CM diagnosis codes (**Table 1**).

**Table 1: Definitions of events of interest**

Event	Definition
New-onset GBS/ADEM	≥1 inpatient principal discharge diagnosis, OR ≥1 inpatient diagnosis (any position) and an ambulatory diagnosis (outpatient or emergency department) within 7 days prior to hospital admission
New-onset AF	≥1 inpatient diagnosis in any position, OR ≥2 ambulatory diagnoses ≥7 days apart and within 90 days of one another
Recurrent AF	≥1 inpatient diagnosis in any position, AND history of ≥1 inpatient or ≥2 ambulatory diagnoses withing 365 days of admission

## Results

- We identified 437 GBS events, with a rate of 0.33 per 10K MY (95% CI 0.30-0.36) and 14 ADEM events, with a rate of 0.01 per 10K MY (95% CI 0.01-0.02).
- Rates of new-onset AF (n=199,540) and recurrent AF (n=153,725) were 160.8 (95% CI 160.1-161.5) and 2,660.5 per 10K MY (95% CI 2,647.2-2,673.8), respectively.
- GBS and new-onset AF rates were higher in males vs. females; recurrent AF was higher in females (**Table 2**).
- Increasing rates with older age were observed for both AF cohorts, while GBS rates peaked among those 70-74 years of age (**Table 2**).
- Evidence of infection on the event date was similar among those with GBS and ADEM; most were respiratory infections (**Table 3**).
- Most of the surgical procedures identified among those with new-onset and recurrent AF were related to cardiovascular care (data not shown).

**Table 2: Rates per 10K MY (with 95% CI) of GBS, ADEM, and AF, 2017-2022**

	New-onset GBS (N = 437)	New-onset ADEM (N = 14)	New-onset AF (N = 199,540)	Recurrent AF (N = 153,725)
Overall	0.33 (0.30-0.36)	0.01 (0.01-0.02)	160.8 (160.1-161.5)	2,660.5 (2,647.2-2,673.8)
Sex				
Female	0.26 (0.22-0.30)	0.01 (0.01-0.02)	127.4 (126.5-128.2)	2,846.6 (2,825.3-2,868.0)
Male	0.41 (0.36-0.46)	0.01 (0.00-0.02)	201.0 (199.8-202.2)	2,528.6 (2,511.7-2,545.6)
Age categories				
60-64 years	0.32 (0.29-0.37)	0.01 (0.00-0.02)	78.0 (77.4-78.6)	1,813.0 (1,791.7-1,834.6)
65-69 years	0.32 (0.24-0.41)	0.01 (0.00-0.04)	125.5 (123.8-127.3)	2,072.0 (2,035.7-2,109.0)
70-74 years	0.44 (0.34-0.56)	0.02 (0.01-0.07)	209.9 (207.4-212.4)	2,319.5 (2,286.8-2,352.7)
75-79 years	0.36 (0.26-0.49)	0.03 (0.01-0.09)	328.1 (324.3-331.8)	2,762.5 (2,728.9-2,796.5)
80-84 years	0.35 (0.23-0.52)	0.01 (0.00-0.10)	474.6 (468.9-480.3)	3,190.3 (3,152.3-3,228.6)
≥85 years	0.14 (0.08-0.26)	0.00 (0.00-0.00)	706.1 (699.0-713.3)	3,942.2 (3,904.8-3,979.9)

**Table 3: Characteristics of Patients with GBS, ADEM, and AF, 2017-2022**

Patient characteristics	New-onset GBS	New-onset ADEM	New-onset AF	Recurrent AF
	Number or Mean (% or std dev <sup>a</sup> )	Number or Mean (% or std dev <sup>a</sup> )	Number or Mean (% or std dev <sup>a</sup> )	Number or Mean (% or std dev <sup>a</sup> )
Unique patients	437 (100.0%)	14 (100.0%)	199,540 (100.0%)	153,725 (100.0%)
<b>Demographic characteristics</b>				
Age (years; mean and std dev)	67.5 (7.2)	69.2 (7.3)	74.4 (10.3)	77.7 (10.1)
Age categories				
60-64 years	250 (57.2%)	6 (42.9%)	58,488 (29.3%)	27,531 (17.9%)
65-69 years	55 (12.6%)	1 (7.1%)	20,710 (10.4%)	12,290 (8.0%)
70-74 years	61 (14.0%)	3 (21.4%)	26,573 (13.3%)	19,053 (12.4%)
75-79 years	37 (8.5%)	3 (21.4%)	29,482 (14.8%)	25,706 (16.7%)
80-84 years	24 (5.5%)	1 (7.1%)	26,644 (13.4%)	26,847 (17.5%)
≥85 years	10 (2.3%)	0 (0.0%)	37,643 (18.9%)	42,298 (27.5%)
Sex				
Female	185 (42.3%)	9 (64.3%)	86,212 (43.2%)	68,209 (44.4%)
Male	252 (57.7%)	5 (35.7%)	113,328 (56.8%)	85,516 (55.6%)
<b>Combined comorbidity score from day -365 through day -1<sup>2,3</sup></b>				
Mean score (std dev)	1.8 (2.8)	1.6 (2.6)	2.4 (3.1)	5.0 (3.3)
Score categories				
≤0	185 (42.3%)	7 (50.0%)	66,402 (33.3%)	8,936 (5.8%)
1-2	131 (30.0%)	3 (21.4%)	57,015 (28.6%)	30,632 (19.9%)
3-4	50 (11.4%)	1 (7.1%)	33,698 (16.9%)	37,449 (24.4%)
≥5	71 (16.2%)	3 (21.4%)	42,425 (21.3%)	76,708 (49.9%)
<b>Health characteristics from day -28 through day 0</b>				
Concomitant influenza and COVID-19 <sup>b</sup> vaccination	1 (0.2%)	0 (0.0%)	203 (0.1%)	112 (0.1%)
COVID-19 vaccination	7 (1.6%)	1 (7.1%)	1,922 (1.0%)	958 (0.6%)
Influenza vaccination	19 (4.3%)	1 (7.1%)	7,328 (3.7%)	4,693 (3.1%)
<b>Health characteristics on day of event</b>				
Gastrointestinal infection	13 (3.0%)	0 (0.0%)	1,822 (0.9%)	2,312 (1.5%)
Respiratory infection	89 (20.4%)	3 (21.4%)	27,799 (13.9%)	30,442 (19.8%)
Other infection	10 (2.3%)	0 (0.0%)	331 (0.2%)	263 (0.2%)
Unspecified viral infection	2 (0.5%)	0 (0.0%)	303 (0.2%)	319 (0.2%)
<b>Health characteristics on day -7 through day 28</b>				
Electrocardiogram	n/a	n/a	162,098 (81.2%)	123,557 (80.4%)
Electrophysiologic testing	145 (33.2%)	0 (0.0%)	n/a	n/a
Lumbar puncture	319 (73.0%)	10 (71.4%)	n/a	n/a
Magnetic resonance imaging	256 (58.6%)	12 (85.7%)	n/a	n/a
Telemetry	n/a	n/a	4,762 (2.4%)	1,240 (0.8%)
<b>Health characteristics on day 0 through day 14</b>				
Intravenous immunoglobulin	36 (8.2%)	1 (7.1%)	n/a	n/a
Plasmapheresis	78 (17.8%)	3 (21.4%)	n/a	n/a
<b>Health characteristics from day -30 through day 0</b>				
Any surgical procedure <sup>c</sup>	n/a	n/a	91,133 (45.7%)	83,989 (54.6%)

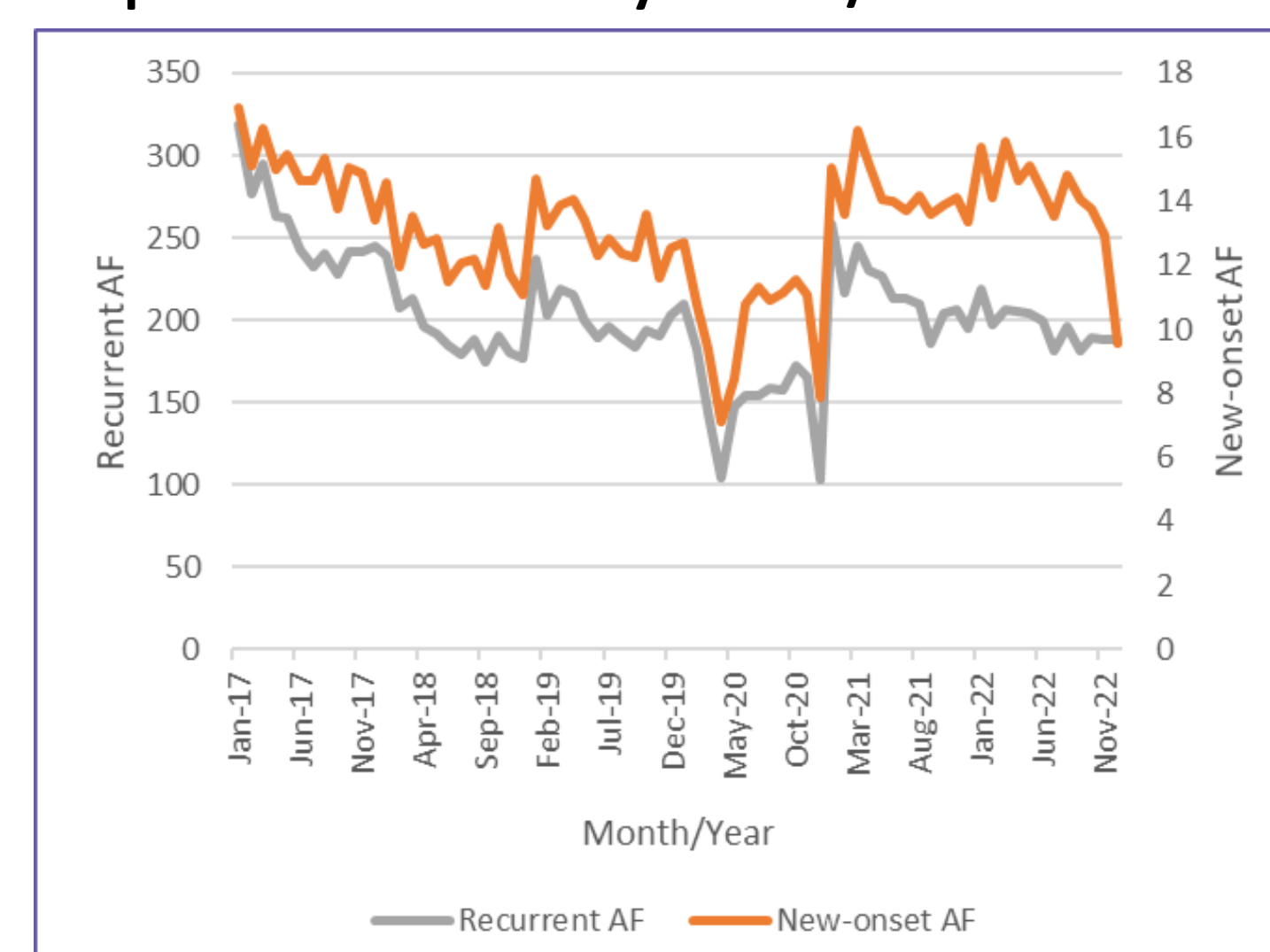
<sup>a</sup>std dev: standard deviation

<sup>b</sup>COVID-19: Coronavirus disease 2019

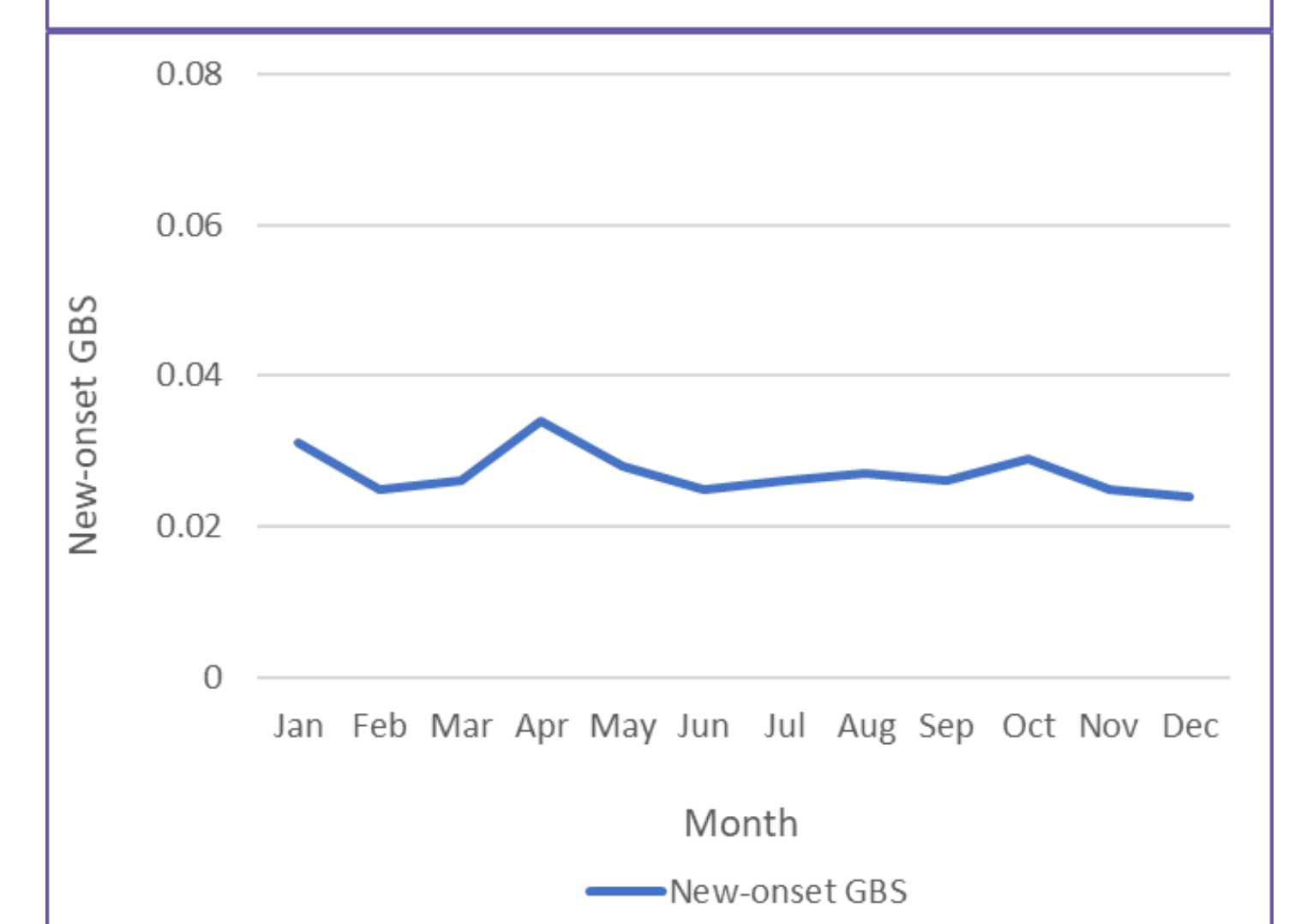
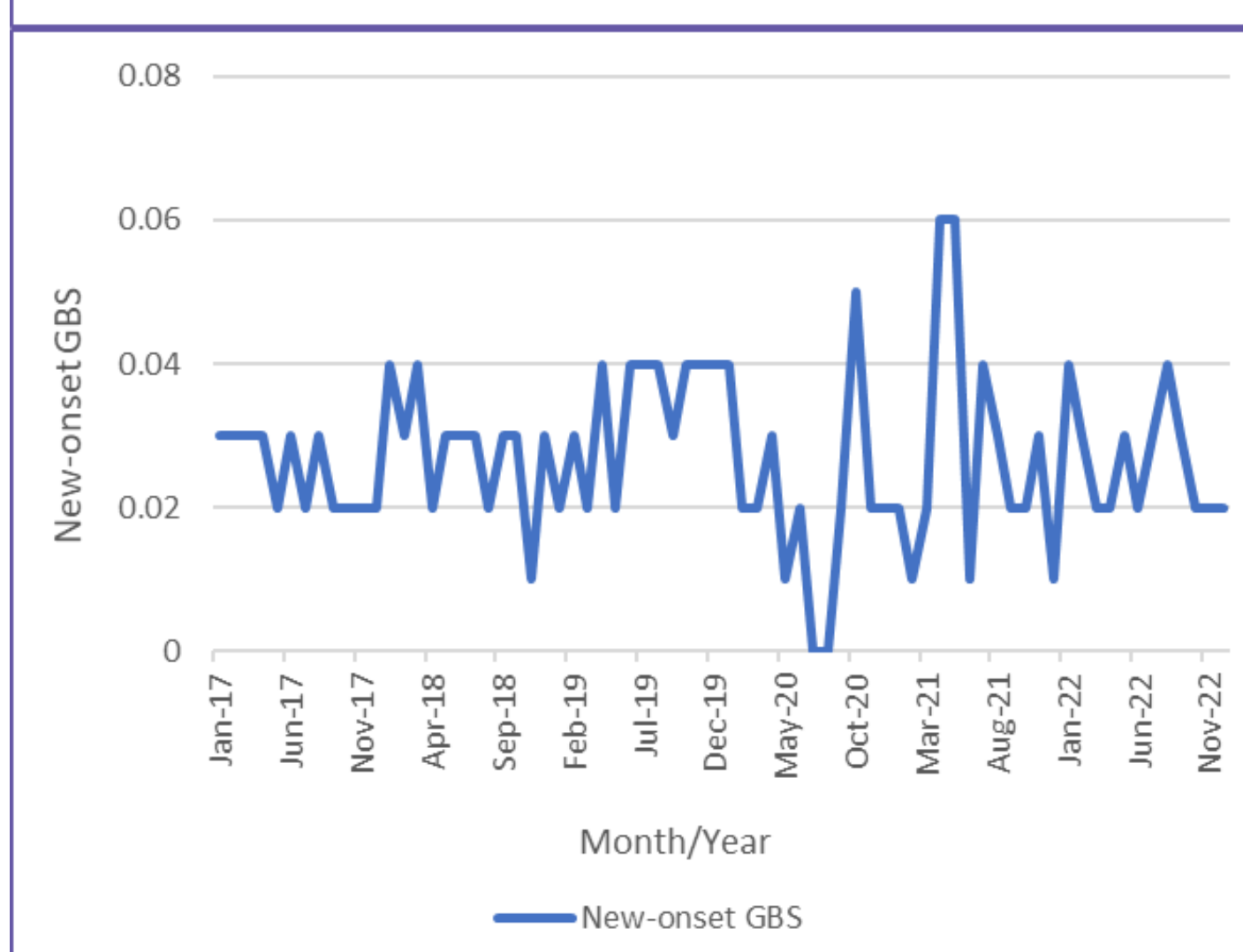
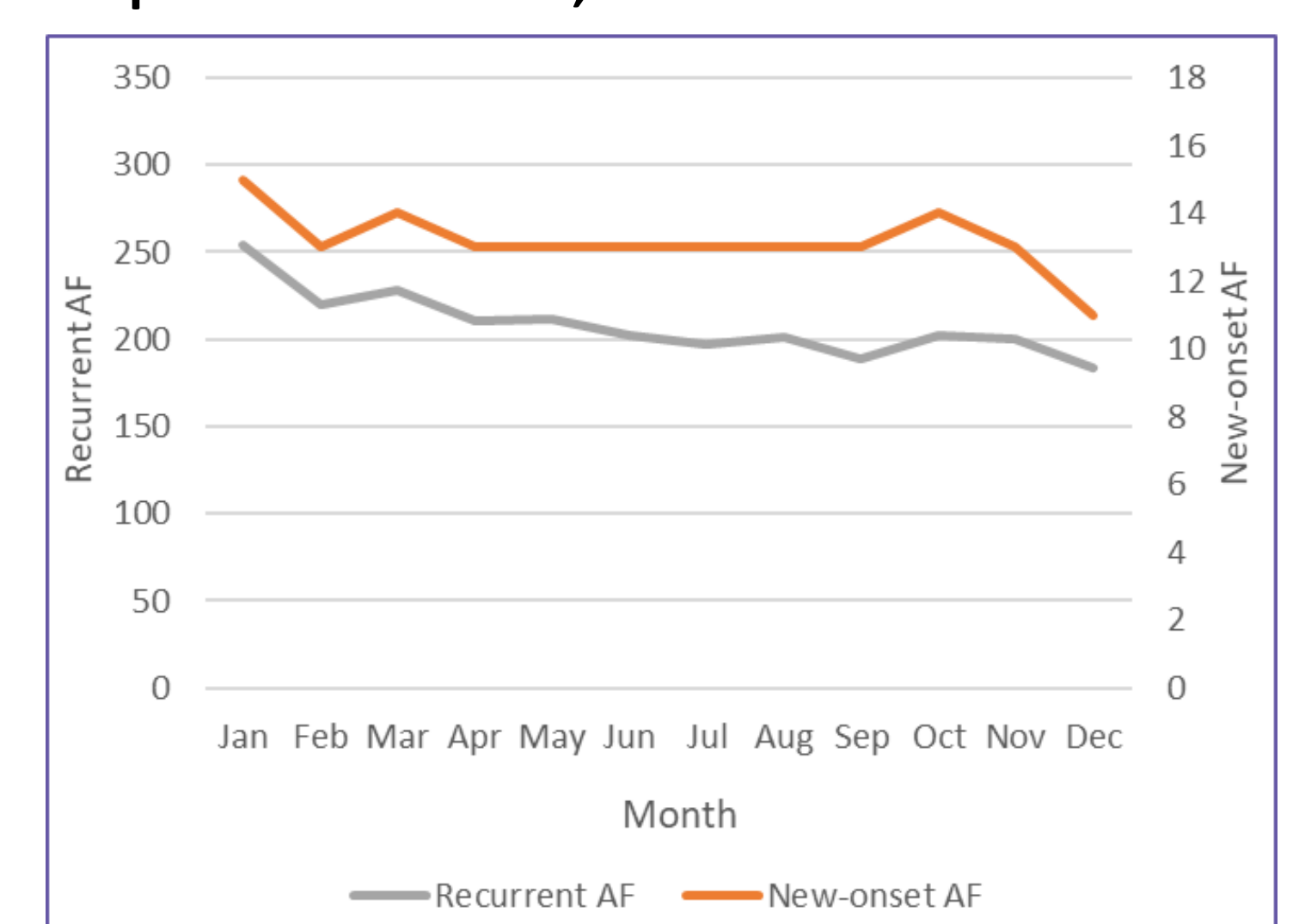
<sup>c</sup>Surgical procedures were identified by Current Procedural Terminology (CPT) codes only; CPT codes are for ambulatory/outpatient services and physician visits to inpatients.

- We observed decreases in the rates of new-onset and recurrent AF during the first year of the COVID-19 pandemic (**Figure 1**).
- Pre-pandemic, AF rates were highest January through May (2017-2019) (**Figure 1**).
- We did not observe evidence of seasonality for GBS or AF (**Figure 2**).

**Figure 1: Event Rates per 10K Members by Month/Year**



**Figure 2: Mean Monthly Event Rates per 10K Members, 2017-2022**



Note: New-onset ADEM is not shown in Figures 1 and 2 due to small counts.

## Conclusions

We observed rates of GBS and ADEM similar to those reported in the literature.<sup>4,5</sup> The rate of new-onset AF was higher than that observed in a recent study,<sup>6</sup> perhaps due to age differences between the populations included and/or the algorithms used.

Estimated rates of GBS, ADEM, and AF among older US adults, as well as the observed trends, can inform feasibility and sample size assessments for post-market studies of RSV and other vaccines and medical products.

## References

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