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BACKGROUND

- Pericarditis is inflammation of the pericardium, the sac surrounding the heart.
 - It is diagnosed based on chest pain, fever, pericardial friction/rub, electrocardiographic changes, and pericardial effusion.¹
 - Pain associated with pericarditis can be debilitating, limiting physical activity and severely reducing quality of life.¹
 - Conventional therapy includes non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine, but no therapies are currently FDA-approved for the treatment of pericarditis. Cases of inadequate response are treated with corticosteroids, other exploratory immunosuppressants, and in the most severe cases, pericardiectomy.
- Recurrent pericarditis [RP] occurs when a second episode of pericarditis is experienced after a symptom-free period of ≥4-6 weeks.¹
 - Recurrence occurs in 15-30% of patients, presents with similar symptom(s) as the initial pericarditis episode, and can result in substantial clinical morbidity, chronic corticosteroid use, and impaired physical and mental quality of life (QoL).
- Complicated pericarditis refers to patients with multiple recurrent episodes and/or serious complications that necessitate a more involved treatment approach.¹
 - Understanding the long-term risk for recurrence in patients with complicated pericarditis is important when making treatment decisions.
- A review of the literature identified seven papers that report the incidence of pericarditis ranging from 3.3 to 168 cases per 100,000 persons per year; none of the studies reported incidence or prevalence of recurrent pericarditis or complicated pericarditis.
 - Further, while some studies have reported the portion of the population that experiences recurrence, little is understood of recurrence burden particularly in a contemporary population in the US.

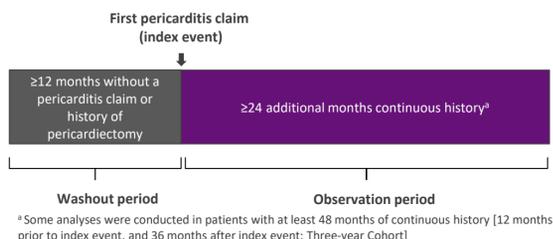
PURPOSE

- To better characterize size of the US recurrent pericarditis and complicated pericarditis populations and describe the clinical burden of pericarditis recurrence.

METHODS

- Study Design: Retrospective claims database analysis
- Data Source: PharMetrics Plus from IQVIA transactional database containing longitudinally linked records from ~90 million commercially insured patients in the US
 - Fully-adjudicated medical and pharmacy claims with dates of service between January 1, 2013 to March 31, 2018
 - A patient insurance coverage indicator (and therefore capture of associated claims) was included enabling a determination of continuous claims history
- Study Population: Newly-diagnosed pericarditis patients with at least 36 months of history were included in the study (Figure 1). These patients were identified by the presence of at least one ICD9/10 code (Table 1) for an office visit, emergency department visit or hospitalization following a washout period of at least 12 months without claims for pericarditis or pericardiectomy and preceding a period of at least 24 months of continuous history captured in the database. A newly-diagnosed patient's first pericarditis claim was considered the index event.

Figure 1: Inclusion criteria



- Pericarditis recurrence was defined as the presence of another ICD-9/10 codes for pericarditis (Table 1) at least 28 days after the index event. Patients with at least one recurrence were termed: recurrent pericarditis.
- Additional claims for physician office visits, emergency department visits or hospitalizations that were separated by at least 28 days were considered subsequent recurrences.
- Patients with complicated pericarditis were identified by having either qualifying events:
 - Multiple (two or more) pericarditis recurrences or
 - Less than two pericarditis recurrences but also a serious complication including constrictive pericarditis, cardiac tamponade or a large pericardial effusion which was further defined by the presence of at least one procedure code (CPT) for pericardiocentesis or a pericardial window (Table 2)

Estimate of disease persistence

- To approximate the duration that patients are impacted by recurrent pericarditis, annual disease persistence was calculated by determining the portion of patients with recurrence in the full calendar years following the index event. This was calculated in patients with at least three years of continuous history following their index event.

Calculations of incidence and prevalence

- Age-specific incidence of the initial pericarditis recurrence was calculated by dividing the number of patients experiencing their first recurrence by the enrolled population and standardized using the 2018 US Census to estimate the incident population. Prevalence was based on the sum of recurrent pericarditis patients from prior years plus the incident patients. This calculation assumed constant incidence and applied the annual disease persistence estimates from this study with the rate calculated in year three as the terminal value.
- Point prevalence estimates were calculated based on the incident and prevalent populations using the 2018 US Census.

Table 1: Pericarditis Coding

ICD-9		ICD-10		Mapping
Code	Description	Code	Description	
420.91	Acute idiopathic pericarditis	I30.0	Acute nonspecific idiopathic pericarditis	One to One
420.99	Other acute pericarditis	I30.8	Other forms of acute pericarditis	One to One
420.90	Acute pericarditis unspecified	I30.9	Acute pericarditis, unspecified	One to Many
		I30.1	Infective pericarditis	
423.90	Unspecified disease of pericardium	I31.9	Disease of pericardium, unspecified	One to One

Table 2: Serious Complication Coding

Type	Code	Description
ICD-CM	423.3, I31.4	Cardiac tamponade
ICD-CM	423.2, I31.1	Constrictive pericarditis
ICD-CM	423.9, I31.3	Large pericardial effusion
ICD-CM; CPT	37.0; 33010	Pericardiocentesis
CPT	33025	Pericardial window
ICD-CM; CPT	37.31; 33030, 33031	Pericardiectomy

RESULTS

Patient Demographics

- A total of 7,502 and 2,241 newly-treated patients with pericarditis were identified who had two (Two-year Cohort) and three (Three-year Cohort) years of continuous history following their index event, respectively (Table 3).
- Pericarditis patients were on average in their late 40s with 40-45% being female.
- Patients with complicated pericarditis had a mean age at the time of their index event that was slightly higher compared with the overall Two-year Cohort and patients with recurrent pericarditis.
- The portion of females was similar for recurrent pericarditis, complicated pericarditis, and the overall Two-year Cohort.

Table 3: Patient Demographics

	Pericarditis Patients Two-year Cohort N = 7,502	Pericarditis Patients Three-year Cohort N = 2,241	Recurrent Pericarditis Patients Two-year Cohort N = 2,096	Complicated Pericarditis Patients Two-year Cohort N = 1,508
Age; mean (SD)	48.2 (16.3)	47.3 (16.3)	48.6 (15.5)	50.5 (15.3)
Age; n (%)				
<45	2,633 (35.1)	846 (37.8)	714 (34.1)	439 (29.1)
45 to 54	1,802 (24.0)	541 (24.1)	534 (25.5)	390 (25.9)
55 to 64	2,215 (29.5)	608 (27.1)	619 (29.5)	478 (31.7)
65+	852 (11.4)	246 (11.0)	229 (10.9)	201 (13.3)
Female; n (%)	3,346 (45)	888 (40)	1,011 (48)	712 (47)

Complicated Pericarditis

- Of the 7,502 patients in the Two-year Cohort, 1,508 (20%) had complicated pericarditis.
- A total of 994 patients experienced two or more recurrences (66% and 13% of the complicated pericarditis and all pericarditis patient groups, respectively).
- A total of 514 patients had less than two recurrences but also experienced a serious complication considered as qualifying for the complicated pericarditis definition (34% and 7% of the complicated pericarditis and all pericarditis patient groups, respectively).

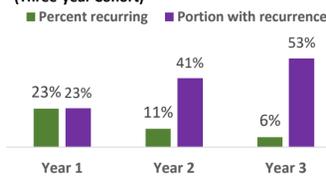
Table 4: Complicated Pericarditis Qualifying Events (Two-year Cohort)

Qualifying Event	Complicated Pericarditis Patients	Portion of Complicated Pericarditis Patients N = 1,508	Portion of Pericarditis Patients N = 7,502
≥ 2 recurrences	994	66%	13%
<2 recurrences and serious complication(s)	514	34%	7%
Total	1,508	100%	20%

Estimate of Disease Persistence

- Of the newly diagnosed patients in the Three-year Cohort, 23% experienced recurrence in the first calendar year following the index event (Figure 2).
 - 28% experienced at least one recurrence overall.
- Of the patients with at least one recurrence, 41% experienced recurrence in the second calendar year following the index event.
- Of the patients experiencing recurrence in the second calendar year following the index event, 53% experienced a recurrence in the third year. For 6% of patients who experienced an initial episode, the disease persisted into the third calendar year.

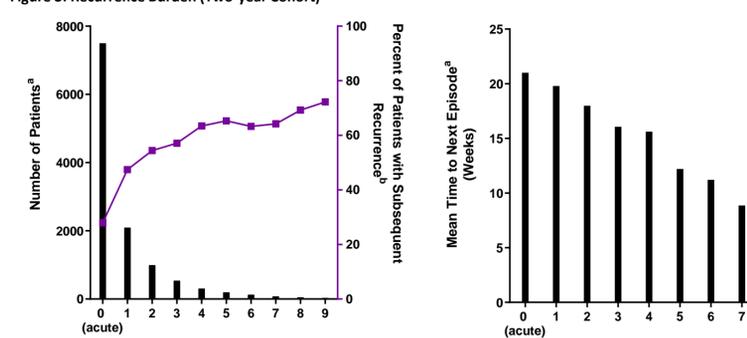
Figure 2: Estimate of Disease Persistence (Three-year Cohort)



Recurrence Burden

- Of 7,502 patients in the Two-year Cohort, 2,096 (28%) experienced at least one recurrence (Figure 3).
- Of 2,096 patients experiencing at least one recurrence, 994 (47%) go on to have a second recurrence; for each subsequent recurrence, the percent of patients progressing to an additional recurrence generally increases (of patients with 8 recurrences, 69% go on to have 9 recurrences).
- The average time between episodes decreases with increasing number of recurrences.
- Results of this analysis in the Three-year Cohort yielded consistent results.

Figure 3: Recurrence Burden (Two-year Cohort)



^aAll patients receiving at least that number of recurrences are included in each group. Groups are not mutually exclusive
^bFor example, of patients with 8 recurrences, 69% go on to have at least one additional recurrence
^cSmall numbers of patients have 10 or more (up to 22) recurrences

^aOf those progressing to another episode

Other Complications and Procedures

- Of the 7,502 pericarditis patients in the Two-year Cohort, 1,358 (18.1%) had pericardial effusion (Table 5).
- In the Two-year Cohort, 385 (5.1%) pericarditis patients had tamponade.

Table 5: Other Complications and Procedures (Two-year Cohort)

Complications/Procedures	Pericarditis Patients N = 7,502	Recurrent Pericarditis Patients N = 2,096	Complicated Pericarditis Patients N = 1,508
Pericardial effusion; n (%)	1,358 (18.1)	1,041 (49.7)	997 (66.1)
Cardiac tamponade; n (%)	385 (5.1)	186 (8.9)	385 (25.5)
Constrictive pericarditis; n (%)	129 (1.7)	82 (3.9)	129 (8.6)
Pericardiocentesis; n (%)	285 (3.8)	139 (6.6)	285 (18.9)
Pericardial window; n (%)	296 (3.9)	147 (7.0)	296 (19.6)
Pericardiectomy; n (%)	37 (0.5)	22 (1.0)	37 (2.5)

RESULTS, continued

Estimate of Recurrent Pericarditis Incident Patients

- Recurrent pericarditis incidence is estimated to be ~20,000 patients (Table 6).

Table 6: Estimated Incident Recurrent Pericarditis Population

Incidence of Recurrent Pericarditis (Claims analysis)			
0 – 17	18 – 39	40 – 64	65+
0.001%	0.005%	0.008%	0.01%

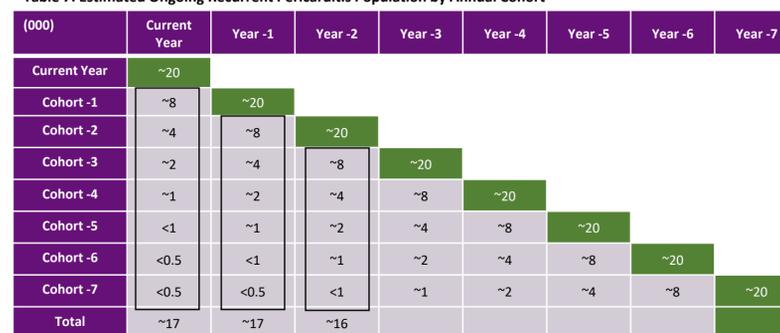
Standardized Incident Recurrent Pericarditis Patients (2018 US Census)

0 – 17	18 – 39	40 – 64	65+	Total
~0.4 K	~5 K	~8 K	~6 K	20 K

Patients with Ongoing Recurrent Pericarditis from Prior Years

- Using the disease persistence estimates, annual cohorts from the prior seven years were calculated as shown in Table 7.
- The sum of ongoing recurring patients from prior cohorts in the prior 6-7 years reaches ~17,000 patients, excluding the approximately 20,000 incident recurrent pericarditis cases.

Table 7: Estimated Ongoing Recurrent Pericarditis Population by Annual Cohort



Patients with ongoing recurrent pericarditis from prior years by age group

0 – 17	18 – 39	40 – 64	65+	Total
~0.3 K	~4 K	~7 K	~5 K	17 K

Estimate of Recurrent Pericarditis Prevalent Patients

- The total US prevalent recurrent pericarditis population is estimated to be ~37,000 patients (Table 8).

Table 8: Estimated Prevalent Recurrent Pericarditis Population by Age Group (Years)

US Prevalent Recurrent Pericarditis Population				
0 – 17	18 – 39	40 – 64	65+	Total
~1 K	~10 K	~15 K	~11 K	37 K

Point estimates of incidence and prevalence

- The prevalence of recurrent pericarditis was estimated to be 11.2 (95% CI, 10.6 – 11.7) per 100,000 population.
- The incidence of recurrent pericarditis was estimated to be 6.0 (95% CI, 5.6 – 6.3) per 100,000 persons per year.

CONCLUSIONS

- This is the first large claims database analysis focused on US recurrent pericarditis epidemiology and to our knowledge the first reported estimates of the incidence and prevalence of recurrent pericarditis in the US.
 - Observed recurrence rates coincide with prior studies for the first and second recurrence. The portion of patients experiencing each subsequent recurrence beyond second recurrence is higher than previously reported.
- Complicated pericarditis was found to impact approximately 20% of all patients with pericarditis. This is about two to three-fold more common than previously reported suggesting a higher disease burden in a greater portion of patients.
 - Approximately 2/3 of complicated pericarditis patients (13% of all patients) were found to experience multiple recurrences.
- Further investigation into the burden of disease of recurrent pericarditis is warranted.

Limitations

- Limitations inherent to retrospective database analyses are applicable such as a dependence on accuracy of administrative coding, interpretation of billed claims in the absence of physician notes, and lack of specificity in some of the diagnostic codes – specifically those that refer to 'other diseases of the pericardium.'
- There is no code for recurrent pericarditis. The methodology assumed recurrent pericarditis if a pericarditis code was noted after a first pericarditis event (after at least 28 days). There may be cases where follow-up visits or persistent pericarditis cases may appear to be recurrent cases.
- Duration of follow-up is insufficient to determine disease persistence in patients experiencing pericarditis episodes for greater than three years.

References

- Cremer PC et al. *J Am Coll Cardiol.* 2016;68(21):2311-2328

Disclosures

Allan Klein received research grants from Kiniksa Corp. and served as an advisory board member for Sobi. Paul Cremer served as an advisory board member for Sobi. Apostolos Kontzias served as a consultant for Novartis, Horizon, Sobi, and Kiniksa. Muhammad Furqan has nothing to disclose. Ryan Tubman and Mike Roy are employees of Clearview Health Partners. Matthew Magestro is an employee of Kiniksa Pharmaceuticals, Corp. This project was funded by Kiniksa Pharmaceuticals, Ltd. Medical writing support was provided by Emily Plummer, PhD, who is employed by Kiniksa Pharmaceuticals, Corp.