MSMR

MEDICAL SURVEILLANCE MONTHLY REPORT

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Characterizing the Contribution of Chronic Pain Diagnoses to the Neurologic Burden of Disease, Active Component, U.S. Armed Forces, 2009–2018

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In the annual *Medical Surveillance Monthly Report* (*MSMR*) burden of disease analysis, neurologic disorders represent the fifth most common category of diagnoses among active component service members within the Military Health System. One major subcategory of this disease group is "all other neurologic conditions." Incidence analysis from 2009–2018 revealed that the vast majority of diagnoses in this undefined subcategory were related to chronic pain and that such diagnoses have been increasing in burden by a considerable amount. Chronic pain diagnoses increased from a rate of 85.5 per 10,000 person-years (p-yrs) in 2009 to 261.1 per 10,000 p-yrs in 2018. Subgroup analysis by demographic characteristics demonstrated that female, non-Hispanic black, older, and enlisted personnel were at increased risk for chronic pain diagnoses. Among the branches of service, members of the Army were at the highest risk of a chronic pain diagnosis with a rate ratio of 4.8 compared to the Navy, the branch with the lowest risk. Future annual burden analyses should consider chronic pain as its own subcategory to better characterize its impact.

WHAT ARE THE NEW FINDINGS?

The crude annual incidence rates of any chronic pain diagnoses in the military increased steadily over the past decade, as has the associated burden of these conditions. Current findings also showed that the overall rates of chronic pain diagnoses varied by demographic and military characteristics.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

Chronic pain negatively impacts the ability of service members to perform their duties and limits their readiness. By understanding the burden of chronic pain and recognizing that its upward trend will likely continue, the Department of Defense may better allocate resources to combat chronic pain from a population-based perspective that focuses on prevention and mitigation.

Neurologic disorders are diseases of the central and peripheral nervous systems. In the past 5 annual burden of disease issues of the *Medical Surveillance Monthly Report* (*MSMR*), the major category "neurologic conditions" accounted for the fifth largest proportion of medical encounters among active component service members. In brief, these burden analyses classified healthcare encounters (outpatient visits and hospitalizations) by the primary (first-listed) diagnoses, which are subsequently grouped into 142 burden of disease-related conditions and 25 major categories based on a modified version of the classification system developed for the Global Burden of Disease Study.[1] Since 2016, these diagnoses have been recorded using International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes. In 2018, the neurologic conditions category accounted for over 680,000 medical encounters among active component service members.[2]

The neurologic conditions category consists of 6 burden-related conditions, which include organic sleep disorders, "all other neurologic conditions," other mononeuritis, epilepsy, multiple sclerosis, and Parkinson disease. In 2018, organic sleep disorders accounted for the most medical encounters among active component service members followed by "all other neurologic conditions." The latter grouping accounted for 113,050 medical encounters, affected 39,433 individuals, and was responsible for 3,046 bed days.[2]

Identifying the specific conditions that contribute to the burden of the disease-related condition category "all other neurologic conditions" would help to clarify the overarching composition of the burden of neurologic conditions within the military. A 2011 *MSMR* analysis evaluated the diagnostic codes associated with an observed increase in outpatient encounters for neurologic disorders among active component service members during 2005–2010.[3] This analysis demonstrated that chronic pain conditions accounted for a sizable proportion of the outpatient encounters within the "all other neurologic conditions" category. In addition, the rates of incident medical encounters with a primary diagnosis related to chronic pain among active component military members increased substantially from 2007 through 2014.[4]

This report summarizes the types of conditions included in the subcategory "all other neurologic conditions" at the 3-digit ICD code level, describes the temporal trends in the morbidity burden of these conditions, and examines the relative proportion of diagnoses in this category contributed by chronic pain diagnoses without a specific etiology (i.e., chronic pain diagnoses not attributed to trauma or a surgical or other procedure). Lastly, the current analysis updates the prior *MSMR* report on the incidence of chronic pain diagnoses among active component military members[4] and describes trends in the annual incidence rates of these chronic pain diagnoses in this population during 2009–2018.

METHODS

The surveillance population for this retrospective cohort study included all service members who served in the active component of the U.S. Army, Navy, Air Force, or Marine Corps at any point during the interval from 1 January 2009 through 31 December 2018. This analysis used data available from the Defense Medical Surveillance System (DMSS). The DMSS, maintained by the Armed Forces Health Surveillance Branch, contains longitudinal data on service members, including medical encounter records and demographic data. Diagnoses were ascertained from the administrative records of all medical encounters of individuals who received care in military medical treatment facilities, civilian facilities in the purchased care system, or in deployed settings as documented in the Theater Medical Data Store.

For the period between 2009 and 2018, all medical encounters were identified for which the primary listed diagnosis would have resulted in classification into the "all other neurologic conditions" subcategory of the annual *MSMR* burden analysis.[2] In the burden analysis, ICD codes for pain that specify an etiology (e.g., chronic postthoracotomy pain, chronic pain due to trauma) are classified into relevant condition subcategories and not the "all other neurologic conditions" subcategory. Medical encounters in the "all other neurologic conditions" subcategory were then further classified into 8 distinct and mutually exclusive subgroups based on conceptual organization and the disease conditions represented **(Table 1)**. These subgroups included pain not elsewhere classified (NEC), brain and brainstem, spinal cord, cranial nerves, peripheral nervous system, neuromuscular, paralytic, and "other." This initial classification schema provided a summary of diagnoses at the 3-digit ICD code level. For example, the pain NEC subgroup included both acute and chronic pain diagnoses that were not attributed to a specific etiology (ICD-9: 338.*; ICD-10: G89.*). In a more specific example, "other chronic pain" is represented by ICD-9 diagnosis code 338.29 and ICD-10 code G89.29. The ICD-9 and ICD-10 codes included in each subgroup are listed in **Table 1**. The numbers of medical encounters attributed to and individuals affected by diagnoses in each of the 8 subgroups were examined over time. Chronic pain-specific diagnoses were identified from within the subgroup of pain NEC diagnoses to determine the relative percentage of diagnoses attributable to chronic pain.

A second analysis was carried out in which the overall incidence of any chronic pain-specific diagnoses was calculated and examined by demographic and military characteristics. For this analysis, an incident case of chronic pain was defined as any inpatient or outpatient encounter with 1 of the qualifying chronic pain codes **(Table 2)** listed in the primary or secondary diagnostic position. An individual could only be counted as an incident case once during the surveillance period. The current analysis incorporated additional chronic pain diagnoses that were not included in the prior burden analysis, such as those attributed to a specific etiology. Annual incidence rates of any chronic pain diagnoses as well as annual rates of 6 types of chronic pain diagnoses were examined. The types of chronic pain diagnoses included chronic pain NEC, chronic pain due to trauma, chronic post-thoracotomy pain, other chronic post-procedural pain, other chronic pain, and chronic pain syndrome. Overall and annual rates of any incident chronic pain diagnoses were calculated per 10,000 person-years (p-yrs) of

TABLE 1. ICD-9 and ICD-10 codes used in the classification of medical encounters in the MSMR burden of disease subcategory "all other neurologic conditions"

Category	ICD-9[a]	ICD-10[a]
Pain NEC	338.*	G89.*
Brain and brainstem	323.*, 325.*, 326.*, 331, 348	G04, G08, G09, G23, G30, G31, G32, G91, G93, G94, G96
Spinal cord	333, 334, 335, 336, 341	G25, G26, G36, G37, G95
Cranial nerves	350, 351, 352	G50, G51, G52, G53
Peripheral nervous system	337, 353, 356, 357	G54, G55, G60, G61, G62, G63, G64, G65, G90
Neuromuscular	358, 359	G12, G13, G70, G71, G72, G73
Paralytic	342, 344	G81, G82, G83
Other	330, 343, 347, 349	E75, G10, G11, G21, G24, G47, G80, G97, G98, G99, H93

[a]An asterisk (*) indicates that any subsequent digit/character is included.
ICD, International Classification of Diseases; *MSMR, Medical Surveillance Monthly Report*; NEC, not elsewhere classified.

TABLE 2. ICD-9 and ICD-10 codes used for the identification of incident chronic pain cases

Description	ICD-9	ICD-10
Chronic pain NEC	338.2	G89.2
Chronic pain due to trauma	338.21	G89.21
Chronic postthoracotomy pain	338.22	G89.22
Other chronic postprocedural pain	338.28	G89.28
Other chronic pain	338.29	G89.29
Chronic pain syndrome	338.4	G89.4

ICD, International Classification of Diseases; NEC, not elsewhere classified.

active component service. Annual rates of the 6 types of chronic pain-specific diagnoses were calculated in the same manner. In addition, the total number of chronic pain-related encounters was determined and used to compute the average number of encounters per affected individual. All statistical analyses were carried out using SAS/STAT software, version 9.4 (2014, SAS Institute, Cary, NC).

RESULTS

Burden

In 2018, diagnoses falling under the ICD-9/ICD-10 parent code pain NEC accounted for 79.1% (92,711/117,279) of the medical encounters related to and 73.5% (29,307/39,896) of the individuals affected by conditions within the "all other neurologic conditions" burden subcategory **(Figure 1, 2)**. Although this group of codes included both acute and chronic pain diagnoses, almost all (99.9%) of the diagnoses were codes specifying chronic pain **(data not shown)**. As such, references to pain NEC can hereafter be interpreted as "chronic pain." Over the 10-year period, the number of medical encounters attributed to and individuals affected by diagnoses of pain NEC increased from 22,042 to 92,711 and 9,536 to 29,307, for increases of 320.6% and 207.3%, respectively **(Figures 1, 2)**. Moreover, the number of medical encounters per patient with chronic pain rose steadily from 2.3 in 2009 to 3.2 in 2018 **(Figure 3)**. In contrast, the number of medical encounters related to and individuals affected by diagnoses within the other 7 subgroups remained relatively stable from 2009 through 2018, with comparatively minor fluctuations in counts. **(Figures 1, 2)**.

Incidence

Between 2009 and 2018, 212,480 service members received an incident chronic pain diagnosis **(Table 3)**. The most frequent chronic pain diagnosis was "other chronic pain." This diagnosis represented 85.0% of incident chronic pain diagnoses during the 10-year surveillance period **(data not shown)**. In addition, approximately 1 in 6

FIGURE 1. Annual numbers of medical encounters by subgroup based on new classification schema for burden subcategory "all other neurologic conditions," active component, U.S. Armed Forces, 2009–2018
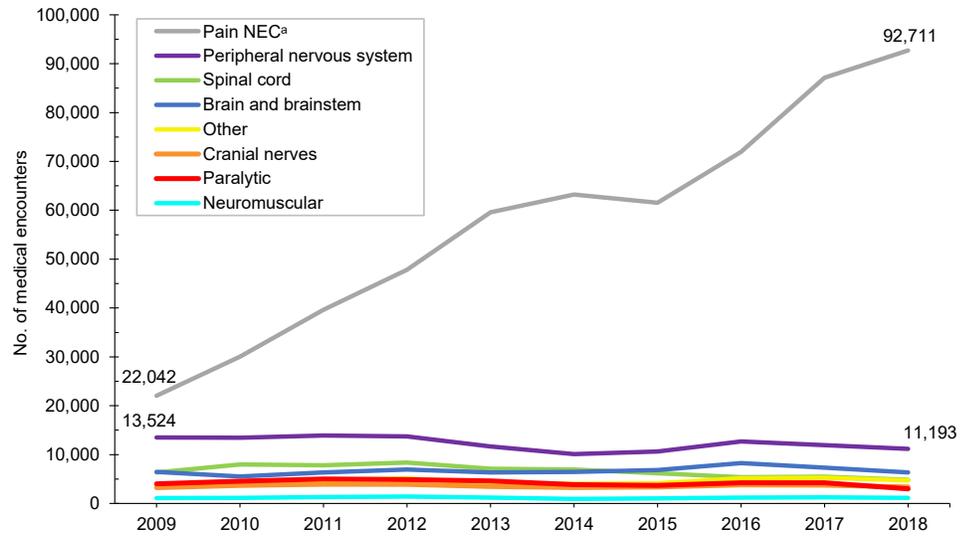
No., number; NEC, not elsewhere classified.
[a]The vast majority (99.9%) of pain NEC diagnoses were codes specifying chronic pain.

FIGURE 2. Annual numbers of unique individuals affected by subgroup based on new classification schema for burden subcategory "all other neurologic conditions," active component, U.S. Armed Forces, 2009–2018
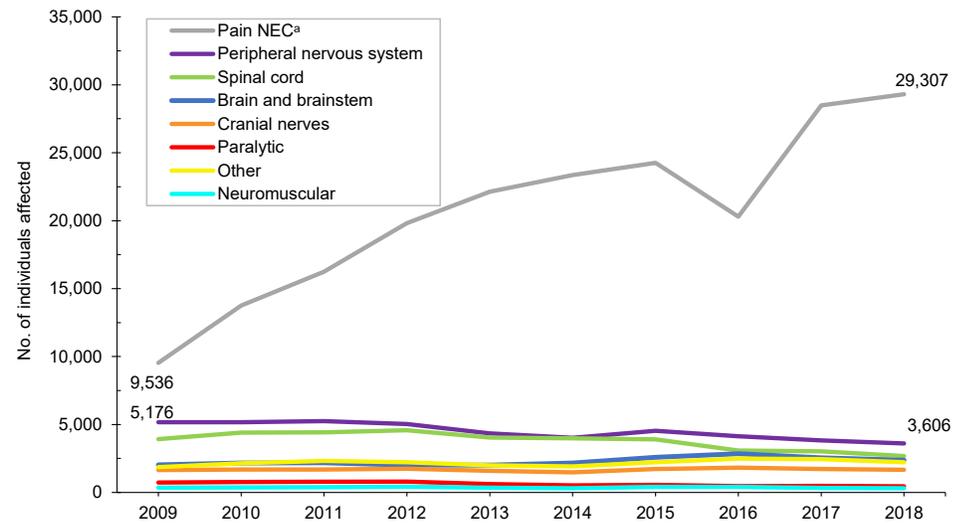
No., number; NEC, not elsewhere classified.
[a]The vast majority (99.9%) of pain NEC diagnoses were codes specifying chronic pain.

service members who qualified as an incident chronic pain case received more than 1 diagnosis of the chronic pain types examined in this analysis **(data not shown)**. The crude incidence rate of any chronic pain diagnoses increased from 85.5 per 10,000 p-yrs in 2009 to 261.1 per 10,000 p-yrs in 2018 **(Figure 4)**. This trend was largely driven

by increases in the rates of incident diagnoses of "other chronic pain," which increased from 58.0 per 10,000 p-yrs in 2009 to 233.1 per 10,000 p-yrs in 2018 **(Figure 4)**.

During the 10-year surveillance period, males received 79.7% (n=169,423) of incident chronic pain diagnoses during the surveillance period; however, the

FIGURE 3. Average number of medical encounters for chronic pain, active component, U.S. Armed Forces, 2009–2018
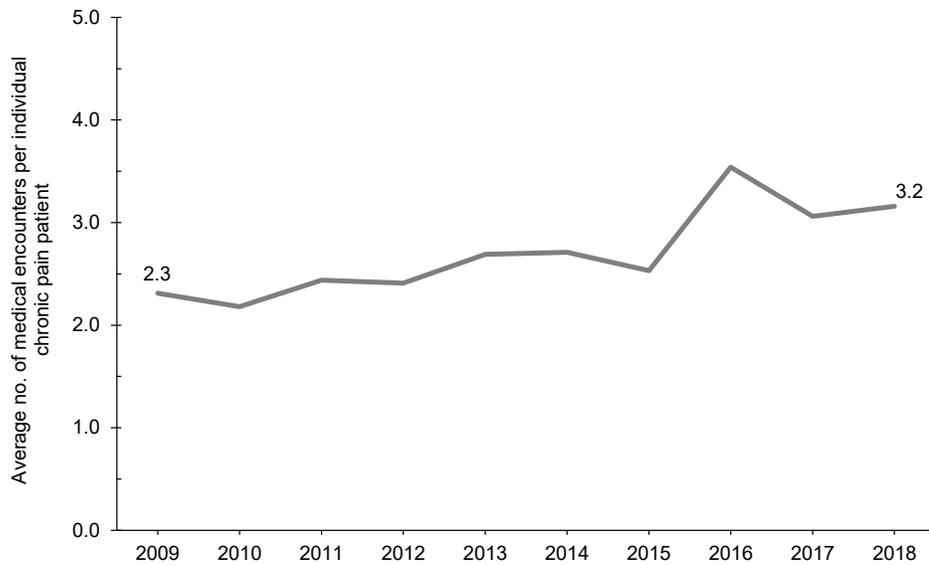
No., number.

TABLE 3. Incident cases and incidence rates of any chronic pain diagnoses, by demographic and military characteristics, active component, U.S. Armed Forces, 2009–2018

	Any chronic pain diagnosis		
	No.	Rate[a]	IRR
Total	212,480	157.3	--
Sex			
Male	169,423	147.8	ref
Female	43,057	211.0	1.4
Race/ethnicity group			
Non-Hispanic white	125,640	155.9	ref
Non-Hispanic black	41,714	191.9	1.2
Hispanic	26,961	149.3	1.0
Other/unknown	18,165	123.8	0.8
Age group (years)			
<20	4,054	46.1	ref
20–24	47,405	110.0	2.4
25–29	48,434	149.8	3.3
30–34	37,683	177.5	3.9
35–39	35,201	227.6	4.9
40–44	24,275	268.6	5.8
45+	15,428	302.9	6.6
Service			
Army	146,596	284.7	4.8
Navy	19,005	59.2	ref
Air Force	30,417	94.5	1.6
Marine Corps	16,462	85.6	1.4
Rank/grade			
Junior enlisted (E1–E5)	118,807	144.4	ref
Senior enlisted (E6–E10)	64,966	220.3	1.5
Junior officer (O1–O3)	15,563	108.3	0.7
Senior officer (O4–O10)	13,144	147.4	1.0

[a]Rate per 10,000 person-years.
No., number; IRR, incidence rate ratio; ref, reference.

overall rate of chronic pain diagnoses in females was 1.4 times that of their male counterparts (211.0 cases per 10,000 p-yrs versus 147.8 cases per 10,000 p-yrs, respectively) **(Table 3)**. In both sexes, the overall rate of any incident chronic pain diagnoses increased with increasing age **(Figure 5)**. The elevated incidence rate of any chronic pain diagnoses in females was evident across all age groups but the largest rate differences by sex were among the 3 oldest age groups. Across race/ethnicity groups, the overall rate was highest among non-Hispanic black service members (191.9 per 10,000 p-yrs) and lowest among those of other/unknown race/ethnicity (123.8 per 10,000 p-yrs) **(Table 3)**. The overall rate among non-Hispanic black service members was 1.2 times that of non-Hispanic white service members.

Service members in the U.S. Army had the highest overall incidence rate of chronic pain diagnoses as compared to their counterparts in other services **(Table 3)**. The overall rate of incident chronic pain diagnoses among Army members was 4.8 times that among Navy members (284.7 and 59.2 per 10,000 p-yrs, respectively). The overall rates among Air Force members and Marine Corps members were 94.5 and 85.6 per 10,000 p-yrs, respectively **(Table 3)**. Overall incidence rates of chronic pain diagnoses were highest among senior enlisted service members (220.3 per 10,000 p-yrs) and lowest among junior officers (108.3 per 10,000 p-yrs) **(Table 3)**.

EDITORIAL COMMENT

This analysis revealed a marked increase in the crude annual incidence rates of any chronic pain diagnoses, the numbers of chronic pain-related encounters, and the numbers of unique individuals affected by chronic pain during 2009–2018. The vast majority of encounters (79.1%) and individual patients (73.5%) associated with the burden subcategory "all other neurologic conditions" were attributable to diagnoses of chronic pain. In addition, chronic pain diagnoses were the only subgroup of diagnoses in this subcategory that demonstrated a steady

FIGURE 4. Crude annual incidence rates of chronic pain diagnoses by type, active component, U.S. Armed Forces, 2009–2018
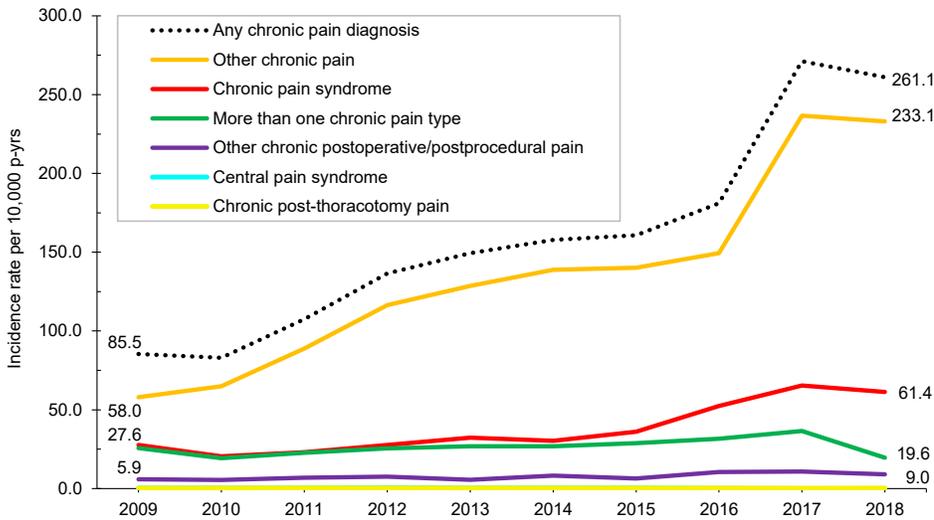
P-yrs, person-years.

FIGURE 5. Overall incidence rates of any chronic pain diagnoses, by sex and age group, active component, U.S. Armed Forces, 2009–2018
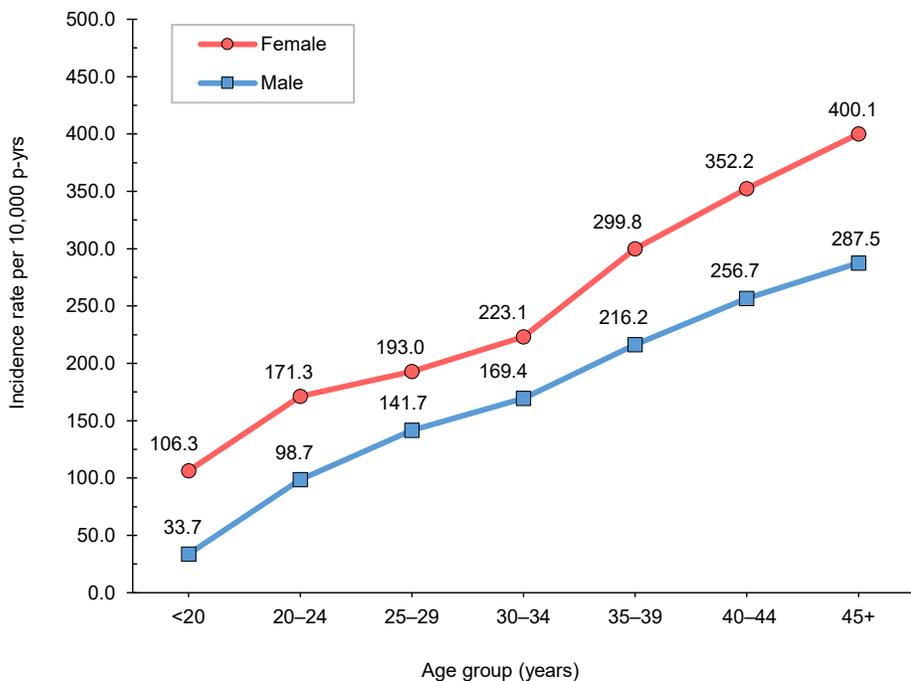
P-yrs, person-years.

and increasing trend in crude incidence rates over the 10-year period. It is uncertain whether this trend of crude rates of chronic pain diagnoses represents a true increase in the experience of chronic pain across the military over the course of the surveillance period, a change in diagnostic guidelines or methodologies, heightened awareness and acceptance for reporting chronic pain by patients, the expansion of integrated interdisciplinary pain management teams, or some other factors. However, it is notable that this increase in chronic pain diagnoses is not restricted to military populations; these trends have been documented in civilian populations in both the U.S. and globally.[5-7] The existence of similar patterns in other contexts suggests that the increases seen in this analysis reflect true increases in chronic pain. Further, not only are there increasing rates of chronic pain encounters and individuals affected by chronic pain, but the mean number of encounters per chronic pain patient also increased during the surveillance period. This increasing trend of healthcare utilization related to chronic pain has also been noted in U.S. civilian populations in patients with back pain.[8,9]

There were pronounced differences in the overall incidence of any chronic pain diagnosis by demographic characteristics as well, though they were all generally reflective of findings noted in U.S. civilian populations. With respect to sex, females were at higher risk of having a chronic pain diagnosis than men, which is well documented in civilian populations.[10] Although research on the causes of this difference is still underway, it is likely due to a combination of physiologic differences, societal conditioning, differences in healthcare interactions, and other possible factors. There was also a linear trend in the increase of rates of chronic pain diagnoses with age, a pattern that has been similarly noted in civilian literature.[5] This pattern is due to greater "wear and tear" on service members' bodies, more opportunities for some trauma to occur or medical conditions associated with pain to arise, and physiologic changes associated with aging. There were also notable differences by race/ethnicity group, with non-Hispanic black service members at higher risk of a chronic pain diagnosis compared to those in other race/ethnicity groups, as has been observed in U.S. civilian populations.[11]

Finally, notable differences in overall rates of incident chronic pain diagnoses were also observed by service; Army members had a much higher overall rate of chronic pain than members of any of the other services. There is no clear explanation for these differences. However, some

contributing factors may include the Army imposing a greater institutional focus on pain management and chronic pain identification, demographic differences across the services (e.g., age and sex), and differences in physical training methodologies. There were also differences in the overall rates between junior versus senior grades as well as enlisted personnel versus officers. The differences between enlisted and officers is likely due to the composition of their military duties, with enlisted personnel performing more physically burdensome and potentially harmful activities compared to their officer peers. The junior vs senior grade differences likely reflect the impact of age, as senior service members are more likely to be older and therefore at higher risk of chronic pain. Observed differences in overall rates of incident chronic pain diagnoses warrant further examination of adjusted (e.g., by age, sex, race/ethnicity) incidence rates among service members.

Performing surveillance epidemiology of this sort is critical, as an understanding of disease baseline rates, temporal trends, and demographic composition is vital for attempts to control chronic pain through clinical and public health measures. Management of neurologic conditions from preventive and readiness standpoints requires an understanding of the associated risk factors. Further, by examining the burden of chronic pain and recognizing that its marked upward trend will likely continue, the Department of Defense may better allocate resources to combat chronic pain from a population-based perspective with focuses on prevention and mitigation.

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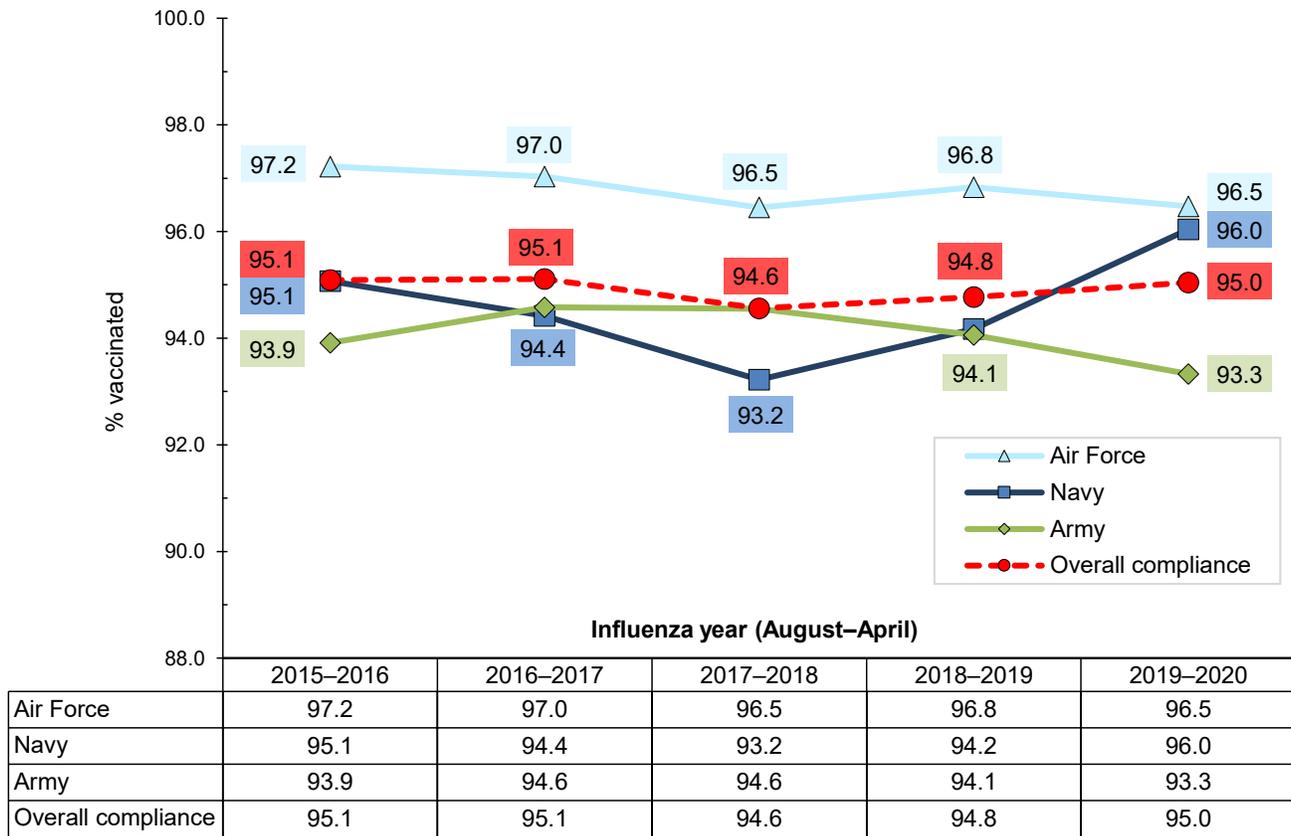9. Thorpe KE, Florence CS, Joski P. Which medical conditions account for the rise in health care spending? *Health Affairs*. 2004; W4-437–W4-445.

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Surveillance Snapshot: Influenza Immunization Among U.S. Armed Forces Healthcare Workers, August 2015–April 2020

FIGURE. Percentage of healthcare specialists and officers with records of influenza vaccination, by influenza year (1 August through 30 April) and service, active component, U.S. Armed Forces, August 2015–April 2020

	2015–2016	2016–2017	2017–2018	2018–2019	2019–2020
Air Force	97.2	97.0	96.5	96.8	96.5
Navy	95.1	94.4	93.2	94.2	96.0
Army	93.9	94.6	94.6	94.1	93.3
Overall compliance	95.1	95.1	94.6	94.8	95.0

The U.S. Advisory Committee on Immunization Practices recommends that all healthcare personnel be vaccinated against influenza to protect themselves and their patients.[1] The Joint Commission's standard on infection control emphasizes that individuals who are infected with influenza virus are contagious to others before any signs or symptoms appear. The Joint Commission requires that healthcare organizations have influenza vaccination programs for practitioners and staff and that they work toward the goal of 90% receipt of influenza vaccine. Within the Department of Defense, seasonal influenza immunization is mandatory for all uniformed personnel and for healthcare personnel who provide direct patient care and is recommended for all others (excluding those who are medically exempt).[2–4]

This snapshot covers a 5-year surveillance period (August 2015–April 2020) and presents the documented percentage compliance with the influenza immunization requirement among active component healthcare personnel of the Army, Navy, and Air Force. During the 2019–2020 influenza season, each of the 3 services had compliance rates of 93.3% or higher among healthcare personnel **(Figure)**. For all services together, the compliance rate was 95.0%, very similar to the rate from the previous year.

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Acute and Chronic Pancreatitis, Active Component, U.S. Armed Forces, 2004–2018

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Pancreatitis is an inflammatory disease of the pancreas resulting from the premature activation of digestive enzymes within the pancreas. Pancreatitis occurs in both acute and chronic forms. During 2004–2018, a total of 6,471 U.S. active component service members received incident diagnoses of acute pancreatitis (AP), for a crude overall incidence rate of 31.8 per 100,000 person-years (p-yrs). Compared to their respective counterparts, overall rates of AP diagnoses were highest among females, those in older age groups, non-Hispanic blacks, Army members, and those working in healthcare occupations. Crude annual rates of AP diagnoses increased by 25.5% over the 15-year period; this trend was driven largely by a rise in outpatient rates. Of the total incident cases of AP, 9.0% received a subsequent incident diagnosis of chronic pancreatitis (CP) during the surveillance period. Between 2004 and 2018, the crude overall incidence rate of CP was 4.4 per 100,000 p-yrs. Patterns of overall rates of CP by demographic and military characteristics were generally similar to those for AP. Crude annual rates of CP fluctuated between 3.7 per 100,000 p-yrs and 5.7 per 100,000 p-yrs during the surveillance period, with no pronounced overall trend over time. To inform preventive and therapeutic strategies, continued research is needed to understand the factors that increase risk of progression from AP to CP and the importance of the interaction between genetic and environmental factors in this transition.

WHAT ARE THE NEW FINDINGS?

This is the first *MSMR* report of the incidence of acute (AP) and chronic pancreatitis (CP) in the U.S. Armed Forces. Over the 15-year surveillance period, these relatively rare conditions were diagnosed in 6,471 and 893 active component service members, respectively. During the study period, approximately one-fifth (20.1%) of the incident AP cases experienced a recurrent attack of AP. A total of 581 (9.0%) of the AP cases received a subsequent incident diagnosis of CP during the study period.

WHAT IS THE IMPACT ON READINESS AND FORCE HEALTH PROTECTION?

AP and CP can significantly degrade the military operational capabilities of affected service members due to the various symptoms of the disorders. As a result, applicants for military service with a history of AP or CP are disqualified from service unless their AP was due to gallstones and was successfully treated by cholecystectomy. Furthermore, CP may result in long-term disability and predisposes patients to pancreatic cancer.

Pancreatitis is an inflammatory disease of the pancreas that causes significant morbidity and mortality worldwide.[1] Located behind the stomach, the pancreas is a long, flat gland that secretes digestive enzymes into the small intestine and releases insulin to regulate blood glucose levels. Clusters of pancreatic acinar cells produce inactive precursors of digestive enzymes that are converted to active forms once they reach the small intestine.[2] Pancreatitis results from the premature activation of digestive enzymes within the pancreas that leads to organ injury with or without subsequent destruction of the pancreatic acinar cell clusters.[2]

Pancreatitis occurs in acute and chronic forms. Acute pancreatitis (AP) is characterized by abdominal pain, nausea, vomiting, and elevated levels of pancreatic enzymes in the blood.[2] The course of AP is highly variable. Although AP is self-limiting with supportive treatment in up to 80% of patients, it results in severe fulminant disease with extensive necrosis, systemic inflammation, and life-threatening multi-organ failure in a minority of cases.[3,4]

Gallstones and chronic alcohol abuse are the most common causes of AP.[2,5] Gallstones account for an estimated 25 to 60% of AP cases in the U.S.[6–9] Obstruction of the pancreatic duct by gallstones and the resultant collection of pancreatic fluid leads to an inflammatory response within the pancreas.[2,4,10] In cases with a biliary etiology, recurrence of AP is prevented by cholecystectomy and removal of gallstones from the common bile duct.[11]

Approximately 25 to 35% of AP cases in the U.S. are attributable to long-term excessive alcohol consumption.[6–9] Limiting alcohol consumption or total abstinence from alcohol after the onset of alcohol-related AP greatly reduces the risk of recurrences.[11] Many of the damaging effects of alcohol on the pancreas are likely due to the direct effects of its toxic metabolites (e.g., acetaldehyde and fatty acid ethyl esters) on pancreatic cells.[12] Alcohol also increases the permeability of pancreatic duct cells and alters pancreatic secretions by increasing their protein content and decreasing their bicarbonate levels.[12] The conditions resulting from these changes can lead to the formation of protein plugs that block pancreatic outflow.[12] However, many aspects of the mechanisms of pancreatic injury as well as the environmental (e.g., cigarette smoking) and genetic factors that affect the development of AP in heavy alcohol drinkers are not fully understood.[5,12]

Leading risk factors for AP include cigarette smoking,[13] hypertriglyceridemia

(triglyceride levels above 1,000 mg/dL),[14,15] some medications,[16] having undergone endoscopic retrograde cholangiopancreatography (ERCP),[17] and certain genetic risk profiles.[18] The cause of AP is unknown in 10 to 30% of AP cases;[9] however, results of several studies suggest that as many as two-thirds of idiopathic AP cases may be due to biliary microlithiasis.[19–21] Other recent evidence indicates that the majority of idiopathic and recurring AP cases have underlying complex genetic risk profiles.[22,23]

AP is a leading gastrointestinal-related cause of hospitalization in the U.S. In 2014, AP accounted for over 275 thousand hospital admissions and nearly 1.3 million hospital bed days.[24] In the U.S. general population, estimates of the incidence of AP range from approximately 40 to 124 per 100,000 persons, depending on the population studied, type of data used, and the methods employed to identify cases.[25–27] Published data on the occurrence of AP among U.S. military personnel are sparse. One study of the incidence of AP among Military Health System beneficiaries hospitalized between 1 October 2008 and 30 September 2012 reported a cumulative incidence of approximately 25 per 100,000 patients.[28]

Chronic pancreatitis (CP) is characterized by recurrent or persistent abdominal pain caused by progressive fibrosis of the pancreas and destruction of acinar and islet cells.[29] Over the long-term, the progressive injury to the pancreas and surrounding structures generally results in loss of function.[29] Evidence suggests that AP, recurring AP, and CP are on a continuum of related conditions with no clear-cut clinical transition points.[30–32] The mechanisms of CP initiation and progression are complex and vary depending on underlying etiology, genetic risk profile, and environmental exposure.[30–32] The majority of CP cases have more than 1 underlying cause; moreover, many aspects of the mechanisms by which the most common etiologies (i.e., heavy alcohol consumption[5] and cigarette smoking[13]) cause CP remain unclear. The currently accepted view of CP pathophysiology holds that, following recurrent acute attacks, alcohol may trigger progression to chronic pancreatitis and pancreatic

cancer.[12] Such progression may occur as a result of the damaging effects of alcohol's metabolites on pancreatic cells; changes in cell signaling pathways; oxidative stress; activation of pancreatic stellate cells to produce fibrosis and the associated tissue damage; and other mechanisms.[33] Smoking is an independent risk factor for both AP and CP and evidence indicates it has synergistic pathogenic effects with alcohol.[5,12,25]

Population-based estimates of the epidemiology of CP are highly variable as there are no universally accepted diagnostic criteria for this condition.[27,30] However, limited evidence suggests that the incidence of CP in the U.S. general population ranges from 4 to 32 per 100,000 persons.[25,26,34]

AP and CP can significantly degrade the military operational capabilities of affected service members due to the various symptoms of the disorders. As a result, histories of AP, unless due to gallstones and successfully treated by cholecystectomy, and CP are disqualifying conditions for entrance into the U.S. military.[35]

This is the first *MSMR* article to report on the incidence rates of both AP and CP among U.S. active component service members. The current analysis describes the incidence of both forms of pancreatitis during 2004–2018 by demographic and military characteristics, examines the age of onset of both AP and CP, determines the median number of AP attacks per affected individual, and identifies the proportion of incident AP cases that progressed to CP.

METHODS

The surveillance population consisted of all individuals who served in the active component of the U.S. Army, Navy, Air Force, or Marine Corps at any time between 1 January 2004 and 31 December 2018. Diagnoses were ascertained from administrative records of all inpatient and outpatient encounters of individuals who received medical care in fixed (i.e., not deployed or at sea) medical facilities of the Military Health System (MHS) or civilian facilities in the purchased care system documented in the Defense Medical Surveillance System (DMSS). In addition, diagnoses from

healthcare encounters of deployed service members were ascertained from the Theater Medical Data Store (TMDS), which is incorporated into the DMSS.

An incident case of AP was defined by having 1) a case-defining diagnosis **(Table 1)** in the first or second diagnostic position of at least 1 record of an inpatient medical encounter, or 2) two or more outpatient or TMDS medical encounters occurring within 90 days of each other (but not on the same day), with any of the defining diagnoses of AP in the first or second diagnostic position. The selection of the latter criterion was informed by the results of Xiao and colleagues' recent meta-analytic examination of the diagnostic accuracy of various case definitions for identifying AP patients.[27] Results of this study showed that the positive predictive value (PPV) associated with estimates of AP in studies using this criterion was higher (0.81) than that associated with studies that required the AP diagnosis appear in the primary diagnostic position (0.75).[27] Cases of CP were defined by at least 1 inpatient or 2 or more outpatient or TMDS medical encounters within 12 months of each other, with any of the defining diagnoses of CP in the first or second diagnostic positions **(Table 1)**. For the purposes of identifying incident AP and CP cases, TMDS records were treated as outpatient encounters.

The incidence date was the date of the first case-defining hospitalization or outpatient medical encounter that included a diagnosis of AP or CP. An individual could be counted as a case of AP or CP once per lifetime. An individual could be considered an incident case of AP and subsequently considered an incident case of CP. However, if a case-defining diagnosis of CP occurred first, the case could not be considered a case of AP at a later time. Prevalent cases (i.e., cases occurring before the start of the surveillance period) were excluded from the incidence analysis, and person-time was censored at the time of the incident case diagnosis. Incidence rates were calculated as incident AP or CP diagnoses per 100,000 person-years (p-yrs) of active component service. If a service member had more than 1 case-defining AP- or CP-related encounter on the same day, inpatient encounters were prioritized over outpatient encounters, which were prioritized over TMDS encounters.

Consistent with published studies of AP incidence using data from electronic medical records, AP cases were classified by the presence of specific clinical etiologic risk factors.[9,36] The number of etiologic categories for ICD-9-coded AP was limited to idiopathic and mixed etiology (classification as idiopathic plus either alcohol- or biliary-related). ICD-10-coded AP cases were classified into 7 categories including drug-induced, idiopathic, biliary, alcohol-induced, mixed etiology, other, and unspecified. The ICD diagnostic codes used to classify AP cases into these groupings are presented in **Table 2**. Incident CP cases were classified by diagnosis code into 2 categories—alcohol-induced CP or other CP **(Table 1)**.

Median age at the time of case-defining diagnosis of AP was computed overall, by sex, and by race/ethnicity group. In addition, the number and percentage of total incident AP cases who underwent cholecystectomy after their incident diagnosis of AP was determined. An incident AP case was considered to have undergone a cholecystectomy if there was an inpatient encounter with a procedure code (PR code) for cholecystectomy in any position or an outpatient encounter with a Current Procedural Terminology (CPT) code for cholecystectomy in any position **(Table 3)**.

Because AP is often characterized by later attacks that each require medical attention, the number of AP attacks during the surveillance period was determined. The incident AP diagnosis counted as 1 attack. A subsequent AP attack was defined as having an inpatient, outpatient, or TMDS encounter with the ICD-9 diagnosis code 577.0 or ICD-10 code K85.* recorded in the first or second diagnostic position. A subsequent

TABLE 1. ICD-9 and ICD-10 diagnostic codes used to identify cases of acute and chronic pancreatitis

ICD-9[a]	ICD-10[a]
577.0 Acute pancreatitis	K85.* Acute pancreatitis
	K85.0* Idiopathic acute pancreatitis
	K85.1* Biliary acute pancreatitis
	K85.2* Alcohol induced acute pancreatitis
	K85.3* Drug induced acute pancreatitis
	K85.8* Other acute pancreatitis
	K85.9* Acute pancreatitis, unspecified
577.1 Chronic pancreatitis	K86.0 Alcohol-induced chronic pancreatitis
	K86.1 Other chronic pancreatitis

[a]An asterisk (*) indicates that any subsequent digit/character is included.
ICD, International Classification of Diseases.

TABLE 2. Clinical etiologic risk factors and associated ICD-9/ICD-10 diagnostic codes used to categorize acute and chronic pancreatitis cases

Etiology grouping	ICD-9	ICD-10	Code description
Biliary acute pancreatitis	574.*	K80.*	Calculus of the gallbladder or bile duct (cholelithiasis)
	575.0	K81.0	Inflammation of the gallbladder or bile duct (acute cholecystitis) Chronic cholecystitis; acute cholecystitis with chronic cholecystitis; cholecystitis, unspecified
	575.1*	K81.1, K81.2, K81.9	
	---	K85.1*	Biliary acute pancreatitis
Drug-induced acute pancreatitis	---	K85.3*	Drug-induced acute pancreatitis
Idiopathic acute pancreatitis	577	K85.0*	Idiopathic acute pancreatitis
Alcohol-related acute pancreatitis	291.*, 303.*, 305.0*	F10.*	Mental health and behavioral health disorders due to alcohol
	357.5	G62.1	Alcoholic polyneuropathy
	425.5	I42.6	Alcoholic cardiomyopathy
	535.3*	K29.2*	Alcoholic gastritis
	571	K70.0	Alocholic fatty liver
	571.1	K70.1*	Acute alcoholic hepatitis
	571.2	K70.3*, K70.2	Alcoholic cirrhosis of liver
	571.3	K70.9	Alcoholic liver damage, unspecified
	---	K70.4*	Alcoholic hepatic failure
	980	T51.*	Toxic effect of ethanol
	V11.3	Z71.4	Alcohol abuse counseling and surveillance
	---	K85.2*	Alcohol-induced acute pancreatitis
Other acute pancreatitis	---	K85.8*	Other acute pancreatitis
Unspecified acute pancreatitis	---	K85.9	Acute pancreatitis, unspecified

[a]An asterisk (*) indicates that any subsequent digit/character is included.
ICD, International Classification of Diseases.

TABLE 3. ICD codes for cholecystectomy

	ICD-9[a]	ICD-10[a]	Description
Inpatient PR codes			
	51.23, 51.24	0FT44ZZ, 0FB44ZZ, 0FB48ZZ	Laparoscopic cholecystectomy
	51.21, 51.22	0FB40ZZ, 0FB43ZZ, 0FT40ZZ	Open cholecystectomy
Outpatient CPT codes			
	47562, 47563, 47564		Laparoscopic cholecystectomy
	47600, 47605, 47610, 47612, 47620		Open cholecystectomy

[a]An asterisk (*) indicates that any subsequent digit/character is included.
ICD, International Classification of Diseases; PR, procedure; CPT, current procedural terminology.

TABLE 4. Incident cases and incidence rates of acute pancreatitis diagnoses by demographic and military characteristics, active component, U.S. Armed Forces, 2004–2018

	Total 2004–2018	
	No.	Rate[a]
Total	6,471	31.8
Encounter setting		
Inpatient	3,819	18.8
Outpatient	2,599	12.8
TMDS	53	0.3
Sex		
Male	5,193	30.0
Female	1,278	42.1
Age group (years)		
< 20	511	19.4
20–24	1,332	24.7
25–29	1,415	29.9
30–34	1,064	34.3
35–39	966	40.5
40–49	1,050	54.2
50+	133	69.1
Race/ethnicity group		
Non-Hispanic white	3,863	31.3
Non-Hispanic black	1,171	35.0
Hispanic	854	33.6
Asian/Pacific Islander	201	26.1
Other/unknown	382	27.9
Service		
Army	2,751	36.0
Navy	1,466	29.7
Air Force	1,584	32.0
Marine Corps	670	23.7
Rank		
Junior enlisted (E1–E4)	2,504	28.2
Senior enlisted (E5–E9)	3,136	39.0
Junior officer (O1–O3; W1-W3)	406	19.2
Senior officer (O4–O10; W4-W5)	425	32.0
Military occupation		
Combat-specific[b]	854	29.4
Motor transport	215	35.2
Pilot/air crew	146	18.9
Repair/engineer	1,848	31.0
Communications/ intelligence	1,547	34.3
Healthcare	691	39.4
Other/unknown	1,170	30.4

[a]Rate per 100,000 person-years
[b]Infantry/artillery/combat engineering/armor
No., number.

attack was counted once every 90 days following the incident AP diagnosis.

Among those AP cases with subsequent case-defining CP diagnoses during the surveillance period, the time between the incident AP diagnosis and the first CP diagnosis was calculated. Finally, the total numbers of inpatient and outpatient encounters with a case-defining AP diagnosis in the first diagnostic position (incident and prevalent cases) and the total number of unique individuals affected were computed for the 2018 calendar year. For the number of encounters, only 1 encounter was counted per individual per day. The number of individuals affected by AP was the number of unique service members with at least 1 inpatient, outpatient, or TMDS encounter with an AP diagnosis in the first diagnostic position during 2018. The same procedures were employed to determine the total number of medical encounters for and total number of unique individuals affected by CP in 2018.

RESULTS

Acute pancreatitis

Between 2004 and 2018, a total of 6,471 active component service members received incident diagnoses of AP, for a crude overall incidence rate of 31.8 per 100,000 p-yrs **(Table 4)**. Nearly three fifths (59.0%; n=3,819) of the incident AP

diagnoses were recorded in an inpatient setting; 40.2% (n=2,599) were recorded in an outpatient setting; and less than 1% (n=53) were associated with TMDS encounters **(Table 4)**.

The overall crude rate of incident AP diagnoses among women was 1.4 times that among men (42.1 per 100,000 p-yrs and 30.0 per 100,000 p-yrs, respectively). Overall rates of AP diagnoses increased with increasing age, with the rate among service members 50 years of age or older more than 3 times that among those in the youngest age group (less than 20 years) **(Table 4)**. Non-Hispanic black service members had the highest crude overall rate of incident AP diagnoses (35.0 per 100,000 p-yrs) compared to those in other race/ ethnicity groups. The lowest overall rate by race/ethnicity group was observed among Asian/Pacific Islander service members (26.1 per 100,000 p-yrs). Across the services, overall incidence rates of AP diagnoses were highest among Army members (36.0 per 100,000 p-yrs) and lowest among Marine Corps members (23.7 per 100,000 p-yrs) **(Table 4)**. The overall rates of incident AP diagnoses among junior enlisted service members and junior officers were lower than those among their respective senior counterparts. The overall rate of incident AP diagnoses was highest among those working in healthcare occupations (39.4 per 100,000 p-yrs) and lowest among pilots/air crew (18.9 per 100,000 p-yrs).

Crude annual incidence rates of AP increased from 25.1 per 100,000 p-yrs in 2004 to a peak of 38.2 per 100,000 p-yrs in 2010 after which rates decreased to 31.5 per 100,000 p-yrs in 2018 **(Figure 1)**. The 2010 peak in annual rates was reflected in the pattern of inpatient rates of AP over time. Over the course of the surveillance period, annual rates of incident AP diagnoses increased 25.5%. This change in AP rates was driven largely by a rise in outpatient rates which increased from 9.2 per 100,000 p-yrs in 2004 to 14.6 per 100,000 p-yrs in 2018 (59.6%). Throughout the 15-year period, annual rates of AP among active component service women were consistently higher than those among service men **(Figure 2)**. Rates among service women showed a marked increase in 2010, peaking at 63.0 per 100,000 p-yrs and then declining to 39.0 per 100,000 p-yrs in 2012. From 2013 onward, rates fluctuated between 38.6 per 100,000 p-yrs and 45.9 per 100,000 p-yrs. Rates among service men increased gradually from 23.2 per 100,000 p-yrs in 2004 to a peak of 35.4 per 100,000 p-yrs in 2011, after which

rates declined slightly to 29.8 per 100,000 p-yrs in 2018. Examination of annual rates of incident AP diagnoses by age group showed that rates increased over time in the 2 oldest age groups, those 41 years of age or older and those aged 31–40 years **(Figure 3)**. Annual rates of incident AP diagnoses among those aged 20–30 years increased from 20.6 per 100,000 p-yrs in 2004 to 35.2 per 100,000 p-yrs in 2010 and then decreased to 23.9 per 100,000 p-yrs in 2018. During 2004–2018, annual rates were comparatively stable among service members under 20 years old; however, the annual numbers of cases were relatively small in this age group. No pronounced patterns in annual rates over time were evident by race/ethnicity group or by service.

As expected, given the 15-year span of the surveillance period, the majority (79.6%; n=5,149) of the incident AP diagnoses were coded with ICD-9 diagnostic codes **(data not shown)**. Of those AP cases with ICD-9 coding, slightly more than half (55.4%) were categorized as idiopathic AP and the remainder as AP of mixed etiology (idiopathic with biliary- or alcohol-related

etiology) **(data not shown)**. Of the 1,322 incident AP diagnoses with ICD-10 coding, more than a third (37.5%) were classified as AP unspecified, followed by 23.5% classified as alcohol-induced, 19.6% as biliary, 7.4% as idiopathic AP, 7.3% as AP of mixed etiology, 3.4% as other AP, and 1.3% as drug-induced AP **(data not shown)**. A total of 1,149 incident AP cases (17.8%) underwent a subsequent cholecystectomy during the surveillance period **(data not shown)**.

Overall, the median age at case-defining AP diagnosis was 29 years (interquartile range [IQR]=24–37) **(data not shown)**. Female AP cases had a younger median age at incident AP diagnosis than their male counterparts (27 years, IQR=23–34 and 30 years, IQR=24–38, respectively) **(data not shown)**. Crude comparisons of age at incident AP diagnosis by race/ethnicity group showed that Hispanics and those in the other/unknown race/ethnicity group had the youngest median ages at diagnosis (28 years, IQR=23–35 and 28 years, IQR=24–36, respectively), while Asian Pacific/Islanders and non-Hispanic blacks

FIGURE 1. Crude annual incidence rates of acute pancreatitis diagnoses, by setting type, active component, U.S. Armed Forces, 2004–2018
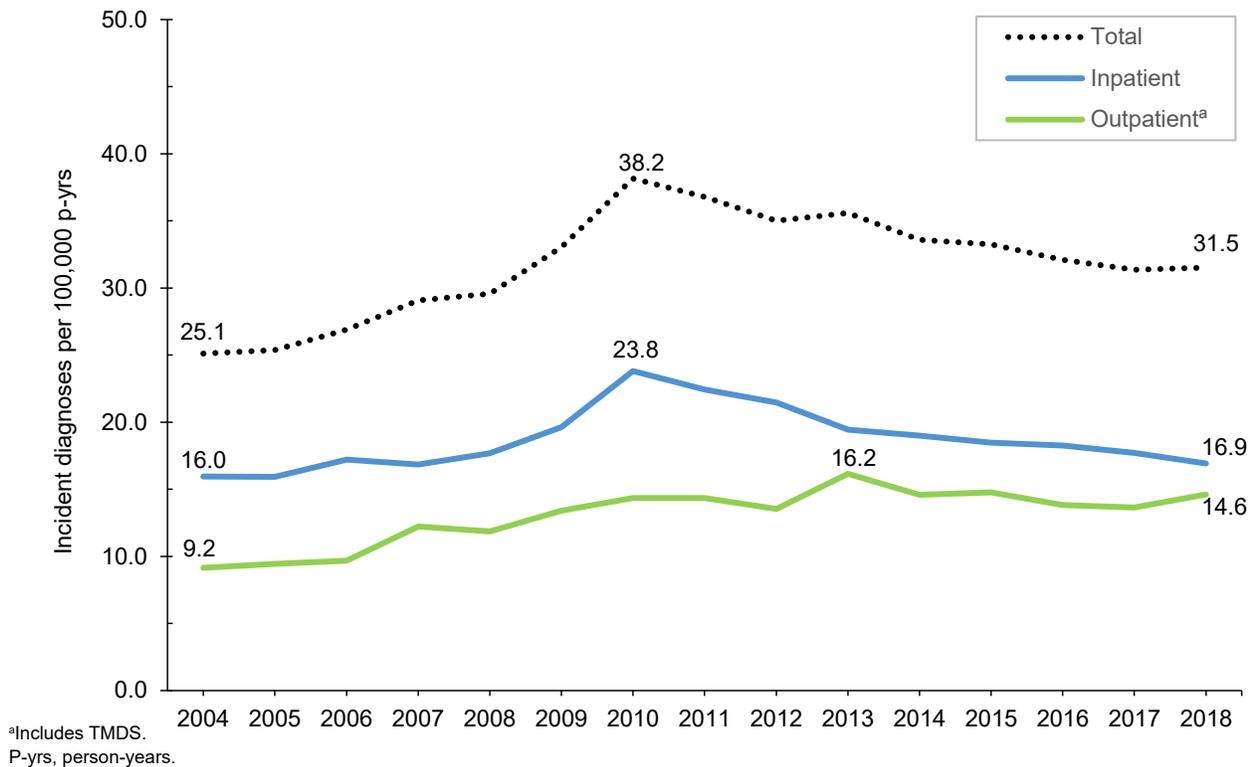
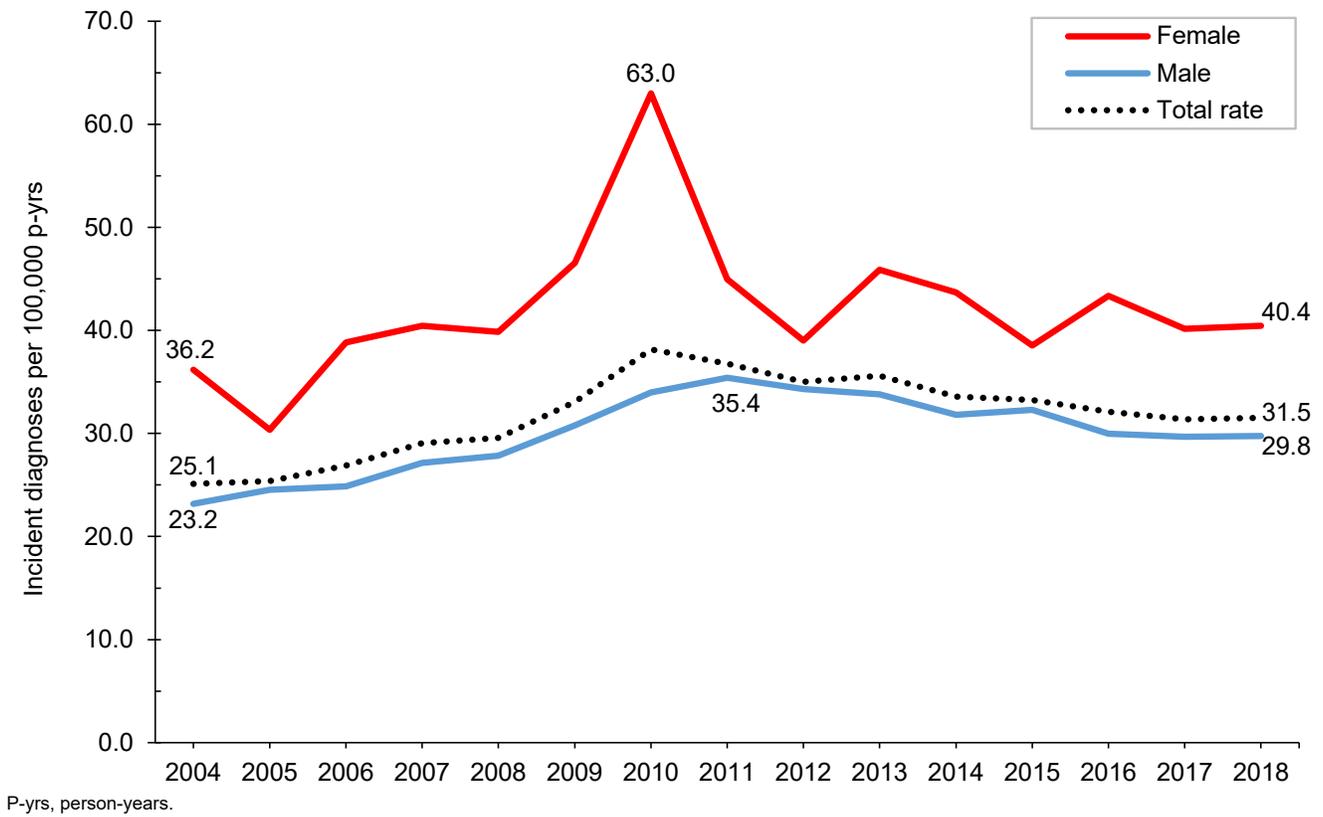**FIGURE 2.** Annual incidence rates of acute pancreatitis diagnoses, by sex, active component, U.S. Armed Forces, 2004–2018

P-yrs, person-years.

FIGURE 3. Annual incidence rates of acute pancreatitis diagnoses, by age group, active component, U.S. Armed Forces, 2004–2018
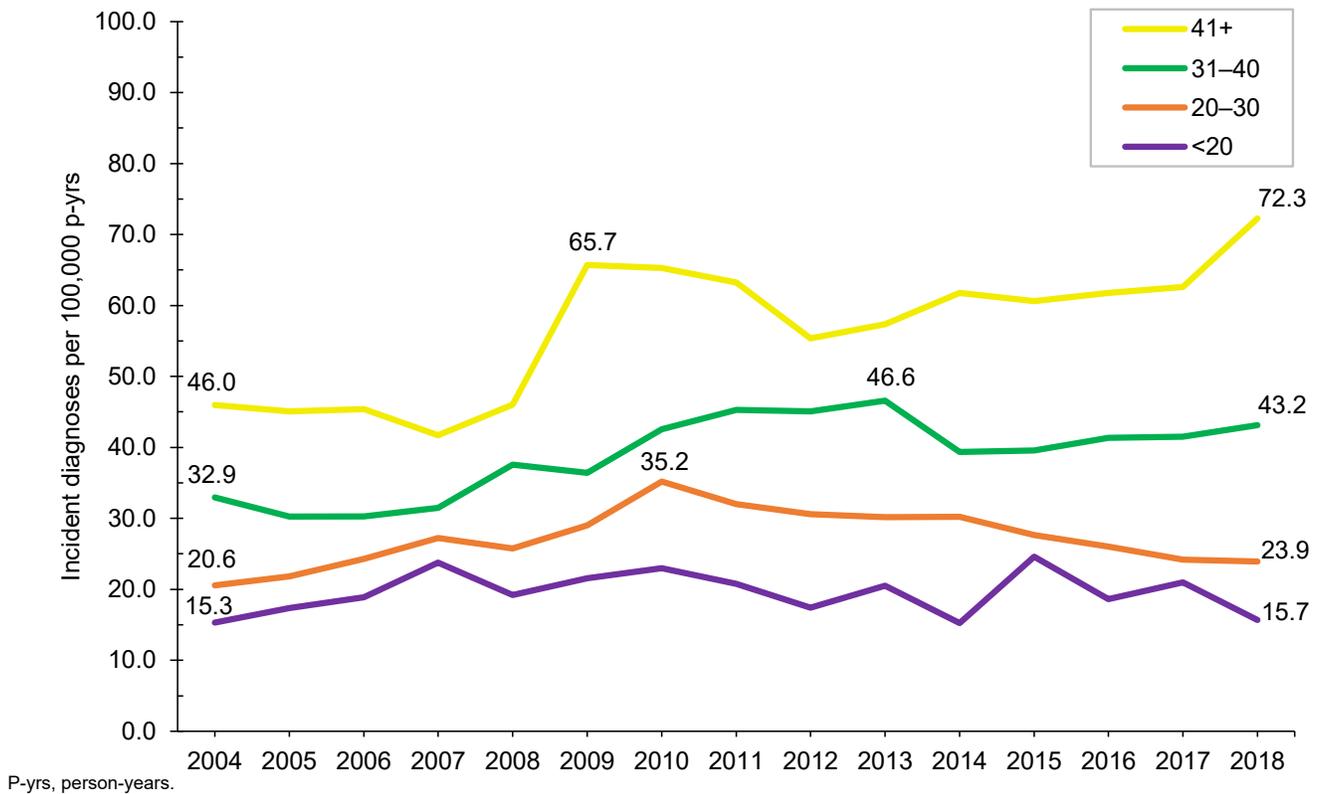

P-yrs, person-years.

TABLE 5. Incident cases and incidence rates of chronic pancreatitis diagnoses by demographic and military characteristics, active component, U.S. Armed Forces, 2004–2018

	Total 2004–2018	
	No.	Rate[a]
Total	893	4.4
Encounter setting		
Inpatient	225	1.1
Outpatient	664	3.3
TMDS	4	0.0
Sex		
Male	729	4.2
Female	164	5.4
Age group (years)		
< 20	32	1.2
20–24	135	2.5
25–29	187	3.9
30–34	180	5.8
35–39	151	6.3
40–49	186	9.6
50+	22	11.4
Race/ethnicity		
Non-Hispanic white	531	4.3
Non-Hispanic black	190	5.7
Hispanic	90	3.5
Asian/Pacific Islander	31	4.0
Other/unknown	51	3.7
Service		
Army	385	5.0
Navy	200	4.0
Air Force	230	4.6
Marine Corps	78	2.8
Rank		
Junior enlisted (E1–E4)	277	3.1
Senior enlisted (E5–E9)	480	6.0
Junior officer (O1–O3; W1-W3)	74	3.5
Senior officer (O4–O10; W4-W5)	62	4.7
Military occupation		
Combat-specific[a]	107	3.7
Motor transport	24	3.9
Pilot/air crew	22	2.9
Repair/engineer	246	4.1
Communications/ intelligence	227	5.0
Healthcare	122	6.9
Other	145	3.8

[a]Rate per 100,000 person-years
[b]Infantry/artillery/combat engineering/armor
No., number.

had the oldest median ages at diagnosis (32 years, IQR=26–39 and 32 years, IQR=25–38, respectively) **(data not shown)**.

Approximately four fifths (79.9%) of the incident cases had a single attack of AP during the surveillance period with the remaining 20.1% having had multiple attacks of AP **(data not shown)**. Incident cases with multiple AP attacks experienced an average of 3 attacks (median=2, IQR 2–3) during the 15-year surveillance period. Of the 6,471 total incident cases of AP, 581 (9.0%) received a subsequent incident diagnosis of CP during the surveillance period **(data not shown)**; among these cases, the median time between incident AP diagnosis and incident CP diagnosis was 4.6 months (IQR=1.2–16.7) (mean=12.7 months) **(data not shown)**.

Among active component service members in 2018, a total of 661 unique individuals (incident and prevalent cases) were affected by AP **(data not shown)**. These individuals contributed a total of 2,645 AP-related medical encounters, representing 4 medical encounters per affected individual. Slightly more than one-eighth (13.8%) of the total AP-related medical encounters in 2018 were in an inpatient setting with the remainder in an outpatient setting (85.6%) or recorded in TMDS (0.6%). In 2018, service members affected by AP who had 1 or more AP-related hospitalizations (n=297) contributed a total of 1,572 hospital bed days **(data not shown)**.

Chronic pancreatitis

During 2004–2018, a total of 893 active component service members received incident diagnoses of CP, for a crude overall incidence rate of 4.4 per 100,000 p-yrs **(Table 5)**. Nearly three quarters (74.4%; n=664) of the incident CP diagnoses were recorded in an outpatient setting; approximately one quarter (25.2%; n=225) were recorded in an inpatient setting; and less than 1% (n=4) were associated with TMDS encounters.

Compared to their respective counterparts, the overall rates of incident CP diagnoses were highest among women (5.4 per 100,000 p-yrs), senior enlisted service members (6.0 per 100,000 p-yrs), and those working in healthcare occupations

(6.9 per 100,000 p-yrs) **(Table 5)**. Overall incidence rates of CP increased with increasing age, with service members aged 50 years or older having an overall rate more than 4 times that of those aged 24 years or younger. Across race/ethnicity groups, the highest overall rate was among non-Hispanic black service members (5.7 per 100,000 p-yrs) and the lowest among Hispanic service members (3.5 per 100,000 p-yrs). The overall rate of CP among Army members was 1.8 times that of Marine Corps members (5.0 per 100,000 p-yrs and 2.8 per 100,000 p-yrs, respectively).

During the 15-year surveillance period, crude annual incidence rates of CP fluctuated between 3.7 per 100,000 p-yrs and 5.7 per 100,000 p-yrs with no pronounced overall trend over time **(Figure 4)**. Low case counts precluded the examination of annual incidence rates of CP diagnoses by demographic or military characteristics.

Of the total incident cases of CP, 36.1% had a case-defining diagnosis of alcohol-induced CP and 63.9% had a case-defining diagnosis of other CP **(data not shown)**. The median age at case-defining CP diagnosis was 32 years (IQR=26–39) **(data not shown)**. Examination of the age at incident CP diagnosis by sex showed that men had a higher median age at diagnosis than women (33 years, IQR=27–40 and 29 years, IQR=24–34, respectively) **(data not shown)**. Crude comparisons of age at incident CP diagnosis by race/ethnicity group showed that non-Hispanic black service members had the oldest median age at diagnosis (35 years, IQR=28–41), while Asian/Pacific Islanders had the youngest (30 years, IQR=26–39) **(data not shown)**.

Among active component service members in 2018, a total of 129 unique individuals (incident and prevalent cases) were affected by CP **(data not shown)**. These individuals contributed a total of 445 CP-related medical encounters, representing about 3 medical encounters per affected individual. The vast majority (96.2%) of total CP-related medical encounters in 2018 were in outpatient settings with the remainder in inpatient settings (3.1%) or recorded in TMDS (0.7%).

FIGURE 4. Crude annual incidence rates of chronic pancreatitis diagnoses, active component, U.S. Armed Forces, 2004–2018

P-yrs, person-years.

This study showed that the crude annual incidence rates of AP diagnoses increased by 25.5% over the course of the 15-year surveillance period; this trend was driven largely by a rise in outpatient rates. To date, only 1 published U.S. study of adult AP incidence rates over time has used data from records of both hospitalizations and ambulatory visits. In their analysis of commercial inpatient and outpatient insurance claims from 2007 through 2014, Sellers and colleagues found that adult AP incidence rates decreased from 123.7 per 100,000 persons in 2007 to 111.2 per 100,000 persons in 2014.[26] These estimates are 3 to 4 times higher than what was observed in the current study during a comparable time period. This difference is likely due, at least in part, to differences in the case definitions used (Sellers et al. identified case-defining ICD-9 codes in the first 4 diagnostic positions) and the demographic characteristics of the populations examined (Sellers et al.'s study population included more older adults [50+ years]).[26] However, the AP incidence estimate from Cunningham and colleagues' study of hospitalized Military Health System beneficiaries (25 per 100,000 persons) and the inpatient rate of incident AP diagnoses during a comparable time period from the current study (range 19.6–23.8 per 100,000 p-yrs) are relatively close in value.[28]

The crude overall rate of incident AP diagnoses increased with increasing age and was higher among females than males. Age and sex distributions of AP are known to differ by etiology.[25] The risk of AP increases progressively with age in both sexes, driven primarily by increasing incidence of biliary and idiopathic AP with increasing age.[25] The current findings by sex are in line with other studies of large administrative databases and may be explained, at least in part, by the fact that risk of biliary AP is higher in women, consistent with the demographic risk of gallstones.[9,25,26] Compared to their respective counterparts, non-Hispanic blacks had the highest overall incidence rate of AP.

The risk of hospitalization for AP in black patients has been reported to be 2–3 times greater than that of whites.[7,37–39] Moreover, compared to white patients, black patients are noted to have a greater risk of readmissions after an initial episode of AP.[40] Little is known about the reasons for the racial disparity in AP risk. Further research is needed to determine whether the observed differences result from dietary, lifestyle, genetic, or other factors.[25] Overall rates were highest among those in healthcare occupations and lowest among pilots and air crew. This finding warrants further analysis to examine adjusted (e.g., age. sex, race/ethnicity group) incidence rates among service members within these occupational categories.

Crude comparisons of the median age at incident AP diagnosis showed that service women had a younger median age at onset than service men. Evidence indicates that median age at onset of AP varies by etiology, with alcohol-related AP tending to have a younger age at onset compared to biliary AP.[25] Across race/ethnicity groups, Hispanics and those in the

other/unknown race/ethnicity group had the youngest median ages at AP diagnosis while Asian Pacific/Islanders and non-Hispanic blacks had the oldest median ages at diagnosis. However, these differences by race/ethnicity could be due, at least in part, to underlying differences in the age distributions of the groups.

In the current study, one-fifth (20.1%) of the incident AP cases experienced multiple AP attacks during the surveillance period. This finding is consistent with the results of a recent meta-analysis that reported a pooled prevalence of AP recurrence of 22% (95% CI: 18%–26%).[30] A similar estimate (22%) for the rate of readmission for primary diagnosis of AP was obtained by Yadav and colleagues using administrative information from the Pennsylvania Health Care Cost Containment Council (PHC4) dataset for the period from 1996 through 2005.[39]

Of the total incident cases of AP identified in the current study, 9.0% received a subsequent incident diagnosis of CP during the surveillance period. This percentage is similar to the pooled prevalence of CP in patients after their initial episode of AP reported by Sankaran et al. (10%; 95% CI: 6%–15%).[30] In their analysis of commercial inpatient and outpatient insurance claims from 2007 through 2014, Sellers and colleagues reported that 14.3% of incident AP cases went on to have a diagnosis of CP during the study period.[26]

Among the AP cases who later had a subsequent incident CP diagnosis during the surveillance period, the median time between incident AP diagnosis and incident CP diagnosis was 4.6 months (mean=12.7 months). From their study using PHC4 data, Yadav and colleagues reported a median duration from incident AP diagnosis to subsequent CP diagnosis of 10.4 months (IQR=2.6–28.9).[39] However, median duration of progression differed significantly by etiology, with the longest duration for alcoholic AP (14.8 months; IQR=4.3–37.8) and the shortest for biliary AP (3.7 months; IQR=0.7–16.9).[39] The rapid progression from AP to CP observed in the current study could suggest that existing CP may have initially been misdiagnosed as AP. The quantification of CP cases may be obscured by the continuum of disease between recurring AP and CP.

The current study documented that crude annual incidence rates of CP fluctuated between 3.7 per 100,000 p-yrs and 5.7 per 100,000 p-yrs during the 15-year surveillance period, with no pronounced overall trend over time. Sellers and colleagues' estimates of CP incidence decreased from 31.7 per 100,000 persons in 2007 to 24.7 per 100,000 persons in 2014.[26] As with the marked difference between Sellers et al.'s estimates of AP incidence and those of the current analysis, the difference in CP incidence estimates is likely attributable, at least in part, to differences in the case definitions used and the demographic characteristics of the populations examined. Of the few published U.S. estimates of CP incidence to date, the crude overall inpatient rate of CP observed in the current study (1.1 per 100,000 p-yrs) is most similar to the crude inpatient rate of CP reported by Yadav et al. for the period from 1997 through 2006 (3.95 per 100,000 persons).[34]

Patterns of overall incidence of CP diagnoses were similar to those observed for AP in terms of age, sex, race/ethnicity, and military characteristics. The differences in overall CP incidence rates by age and race/ethnicity group are consistent with known data.[37,38] One recent study of patients with CP prospectively enrolled from 26 U.S. centers during 2000–2014 demonstrated, that when compared with whites, black patients were almost twice as likely to receive a CP diagnosis due to alcohol and/or cigarette smoking and more likely to have a greater degree of disease-related disability.[37] Further research is needed to establish whether any greater genetic susceptibility to alcohol- and/or tobacco-induced disease and other features of CP is present based upon race/ethnicity.

Most previous U.S. studies of the occurrence of AP over time have relied solely on inpatient databases.[9,34,36,41,42] Hospital admission with AP is common given concerns about worsening course of illness even in initially mild AP cases and a lack of established home management practices/approaches. Also, when "nothing by mouth" was the main treatment for AP, hospital admission was necessary. However, with the current use of early enteral feeding, patients with mild AP who can tolerate oral hydration and pain control may be managed in an outpatient setting.[3] Thus, estimates of AP and CP based only on inpatient records do not completely capture all individuals with these conditions. This disparity may be even more pronounced for CP, where the management of chronic pain and nutrition primarily occur in an outpatient setting.[26] An important strength of the current study is that it drew on records of inpatient and outpatient encounters, likely resulting in increased accuracy of estimates of AP and CP incidence rates.

There are several limitations that should be considered when interpreting the results of the current analysis. First, miscoding may have led to miscategorization of some AP and CP cases. Recent studies have noted high variability in the reported PPV of diagnostic coding in AP and CP.[27,43,44] In their systematic review and meta-analysis of pancreatitis-focused diagnostic accuracy studies, Xiao and colleagues found that the pooled PPVs for AP and CP were 0.71[27]; that is, 71% of cases identified in the administrative data were likely true cases of AP or CP. It is important to note that these authors reported a PPV of 0.81 for studies that employed a case definition that included qualifying diagnoses in the first or second diagnostic position, as was done in the current analysis. Xiao and colleagues posited that the main clinical implication of the generally moderate PPVs of AP and CP (0.71) is that pancreatitis may be frequently overdiagnosed.[27] However, results of subgroup analyses by version of ICD showed that ICD-10 codes yielded a 10% higher PPV than that of ICD-9 codes.[27] This improvement in accuracy is partly attributable to improvements in diagnostic methods.[45] Also, ICD-10 coding requires classification by etiology, which would likely require more confidence in the diagnosis.[46] In the current analysis, the etiology of AP could not be appropriately categorized based on ICD-9 coding alone.

Another limitation of this study is that diagnoses that occurred after a service member left service, or were paid for

out of pocket, were not captured. Finally, medical data from sites that were using the new electronic health record for the Military Health System, MHS GENESIS, during 2017–2018 are not available in the DMSS. These sites include Naval Hospital Oak Harbor, Naval Hospital Bremerton, Air Force Medical Services Fairchild, and Madigan Army Medical Center. Therefore, medical encounter data for individuals seeking care at any of these facilities during 2017–2018 were not included in the current analysis.

As one of the only published studies of AP and CP incidence among U.S. active component service members, this study makes a useful contribution to the literature on temporal changes in the occurrence of these conditions in this population. Observed differences in overall incidence rates of AP and CP by race/ethnicity group and military occupation warrant further analysis to examine adjusted (e.g., by age, sex) incidence rates among service members within these groups. Results indicating that non-Hispanic blacks have higher incidence of AP and CP than non-Hispanic whites are consistent with recent civilian literature and highlight the importance of studying a racially and ethnically diverse population as findings may lead to important insights into the etiology and prognosis of both forms of the disease.

The current analysis identified 6,471 incident cases of AP among active component service members over a 15-year surveillance period. Factoring in the estimated PPV of the case definition employed in this study, about 1,230 of these cases may not have been true cases. Also, approximately four-fifths of the incident cases did not experience a recurrent attack of AP during the study period. However, any episode of AP experienced by a service member can result in significant periods of limited duty. The occurrence of CP reduces quality of life due to pain and inadequate digestion, may result in long-term disability, and predisposes patients to pancreatic cancer.[25] Furthermore, the management of AP and CP and their complications may impose considerable economic burden on the MHS. In the U.S. in 2014, AP and CP were associated with an estimated $2.7 billion dollars in direct costs, with hospital inpatient stays accounting for the majority of these costs.[24] To inform preventive and therapeutic strategies, continued research is needed to understand the factors that increase risk of progression from AP to CP and the importance of the interaction between genetic and environmental factors in this transition.

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