

Healthcare Costs of Recurrent Acute Pancreatitis and Hospitalizations

Nihar R. Desai,¹ Nathalie Kertesz,² Nathan Kleinman,³ Rohit Loomba,⁴ Robert S. Rosenson,⁵ Gerald F. Watts⁶

¹Yale School of Medicine, New Haven, CT, United States; ²Arrowhead Pharmaceuticals Inc., Pasadena, CA, United States; ³Kleinman Analytic Solutions, Paso Robles, CA, United States; ⁴Metabolism and Lipids Program, Mount Sinai Fuster Heart Hospital, Icahn School of Medicine at Mt Sinai, Mount Sinai, New York, NY, United States; ⁵UCSD School of Medicine, San Diego, CA, United States; ⁶School of Medicine, University of Western Australia and Department of Cardiology, Royal Perth Hospital, Perth, Australia

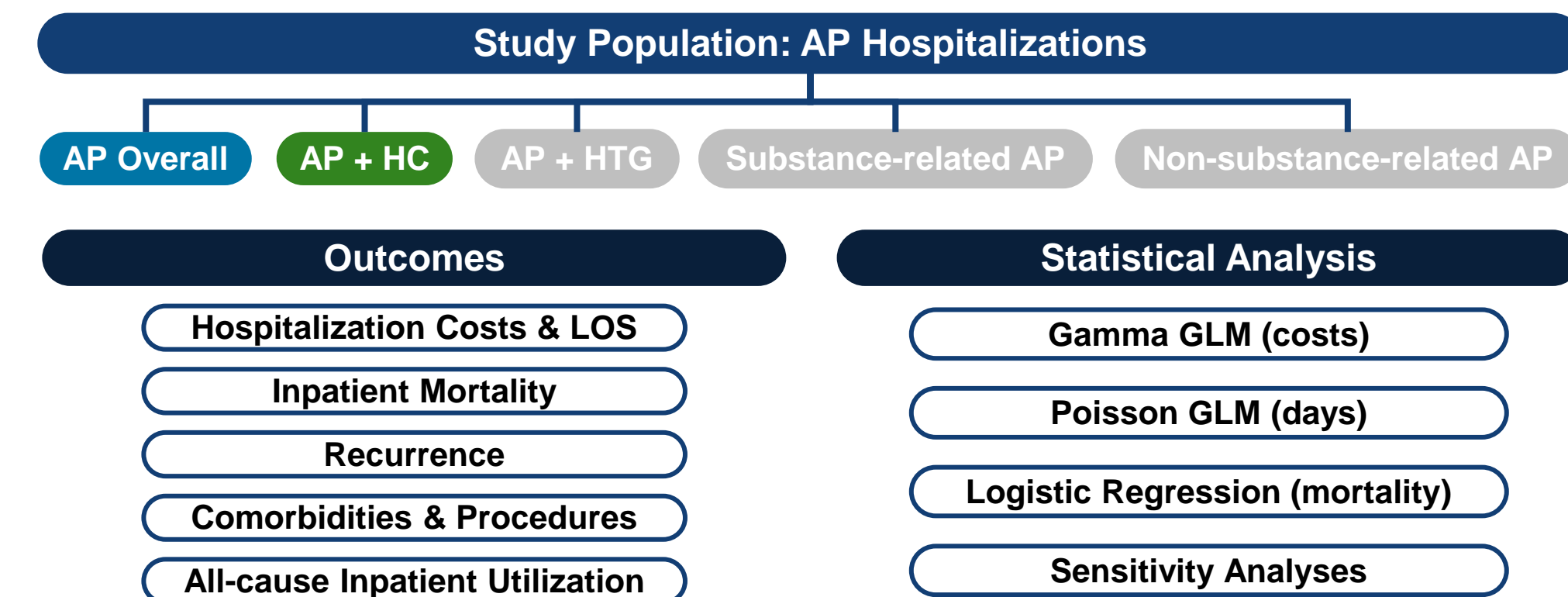
BACKGROUND

Persistent Chylomicronemia

- Patients with severe hypertriglyceridemia particularly due to hyperchylomicronemia (HC), are at especially high risk for acute pancreatitis (AP), which is often recurrent.
- Acute pancreatitis (AP) is a leading cause of gastrointestinal hospitalization in the U.S., with ~300,000 emergency visits per year;¹ incidence is rising globally² and severe disease carries mortality rates up to 30%.³ AP imposes substantial healthcare burden, with U.S. hospitalization costs reaching \$2.6B annually.⁴
- Hypertriglyceridemia (HTG) is a major AP risk factor and the third most common etiology, accounting for 5–22% of AP cases and up to 35% overall (and 56% in pregnancy).⁵
- HTG-induced AP (HTG-AP) is associated with more severe disease, including necrosis, persistent organ failure, and higher mortality compared with other causes.⁷ Extreme HTG (≥1000 mg/dL), often driven by chylomicronemia syndromes—and recurrent episodes may occur even with moderate elevations, particularly familial chylomicronemia syndrome (FCS) or multifactorial chylomicronemia (MCS)—confers especially high risk, with lifetime AP risk in FCS reported up to 76%.^{2,5,6,8,9,10-12}
- The current literature lacks data on recurring hospitalizations, hospitalization cost, time spent in the hospital, and a succinct breakdown of hospitalization-related outcomes by AP severity/cause.
- The objective of this study is to describe the real-world frequency, cost, duration, and mortality rates of patients' AP hospitalizations, focusing on AP hospitalizations overall and among HC patients.

METHODS

Retrospective observational cohort study using the 2017–2021 HCUP Nationwide Readmissions Database (NRD), a nationally representative dataset containing ~17 million annual discharges from all payer types. Data allowed multiple hospitalizations for a given patient to be identified within a calendar year. Any position AP ICD-10 codes used were K85.x, (K85.2x, K85.3x, K85.8x, or K85.9x, excluding K85.1). A subset of these AP hospitalizations were also studied, including those that also had diagnosis code for HC (ICD-10 code E78.3) (AP+HC). Hospitalization costs were adjusted for inflation to 2024 dollars.



ABBREVIATIONS

ApoC-III, apolipoprotein C3; AP, acute pancreatitis; CP, chronic pancreatitis; FCS, familial chylomicronemia syndrome; GLM, generalized linear model; HC, hyperchylomicronemia; HTG, hypertriglyceridemia; LOS, length of stay; MCS, multifactorial chylomicronemia; NRD, Nationwide Readmissions Database; N, number; SD, standard deviation; TIA, transient ischemic attack; TG, triglyceride.

DISCLOSURES

NR Desai: Contract Centers for Medicare and Medicaid Services. Research grants and consulting: Amgen, Arrowhead, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, CSL Behring, CSL Vifor, CytoKinetics, Merck, Milestone, Novartis, SCP Pharmaceuticals, Verve Therapeutics. N Kertesz: employed Arrowhead. N Kleinman: Arrowhead Pharmaceuticals, SeaStar Medical, CSL Vifor, Avidity, Exocruz and Pfizer. R Loomba: Consultant Aardvark Therapeutics, Altimmune, Anylam/Regeneron, Amgen, Arrowhead Pharmaceuticals, AstraZeneca, Bristol-Myers Squibb, CohBar, Eli Lilly, Galmed, Gilead, Glympe, Highside, Inpharma, Ionis, Intercept, Ionis, Janssen Inc., Madrigal, Mesance, Inc., NCM Biopharmaceuticals, Novartis, Novo Nordisk, Merck, Pfizer, Saginnet, Theratechnologies, 89bio, Terns Pharmaceuticals and Viking Therapeutics. Research grants from Arrowhead Pharmaceuticals, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galactin Therapeutics, Galmed Pharmaceuticals, Gilead, Intercept, Hammi, Intercept, Inventiva, Ionis, Janssen, Madrigal Pharmaceuticals, Merck, NCM Biopharmaceuticals, Novo Nordisk, Merck, Pfizer, Sonic Inxleyes and Terns Pharmaceuticals. Co-founder of LipiNexus Inc. RS Rosenson: grant/research support from: Amgen, Arrowhead, Novartis, Eli Lilly, Regeneron, consulting fees from Amgen, Arrowhead, CRISPR Therapeutics, Eli Lilly, Lipigon, Novartis, Precision Biosciences, Regeneron, UltraGenyx. Verve: non-promotional speaking fee from Amgen and Kowa; other support from MedMergent, LLC; and is an UpToDate, Inc. stock shareholder. GF Watts: grants and/or honoraria from Amgen, Novartis, Arrowhead, Esperion, AstraZeneca, Pfizer, Novo Nordisk, Silence Therapeutics, CSL Seqirus, and Sandi-Regeneron.

RESULTS

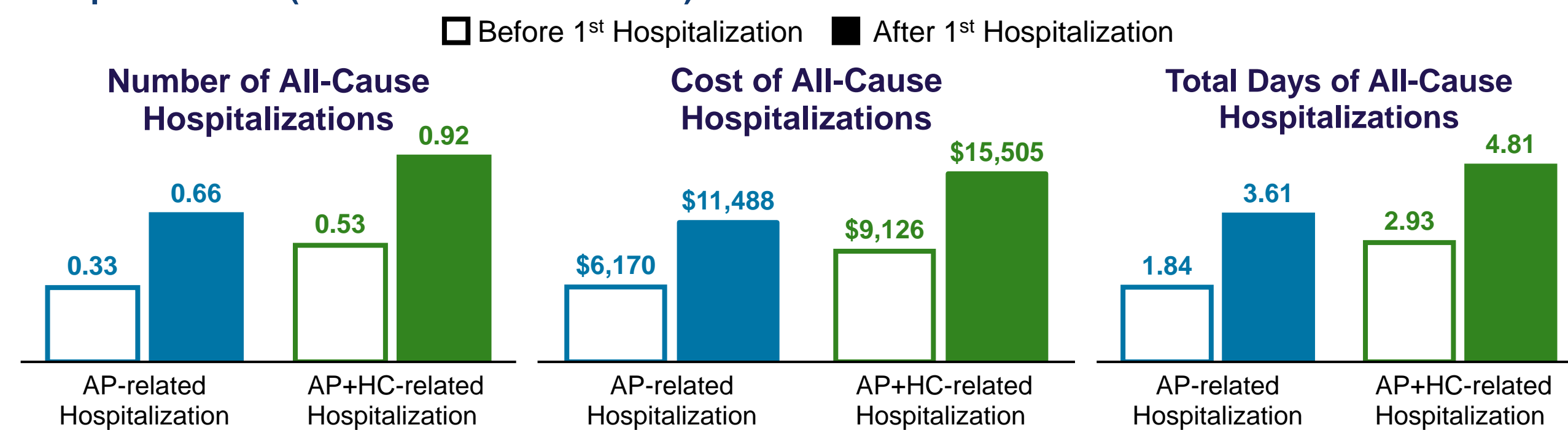
In a database of nearly one million AP hospitalizations from 788,715 patients, patients with AP+HC hospitalizations had 59% more annual AP hospitalizations, 66% higher annual AP hospitalization costs, and 71% more AP hospitalization days than overall AP hospitalization patients.

Table 1. Descriptive Characteristics of Patients with AP Hospitalizations and Patients with AP+HC Hospitalizations

Mean (SD)	Patients with AP Hospitalizations N=788,715	Patients with AP+HC Hospitalizations N=339
Number of AP hospitalizations per patient per year	1.2 (0.7)	2 (1.6)
Female	45.3% (49.8%)	44.0% (49.7%)
Total inflation-adjusted cost	\$24,387 (\$55,591)	\$40,440 (\$51,442)
Total length of stay	7.2 (10.9)	12.2 (13.9)
Died	3.3% (18.0%)	1.5% (12.1%)
Age	53.2 (17.2)	40.8 (11.5)

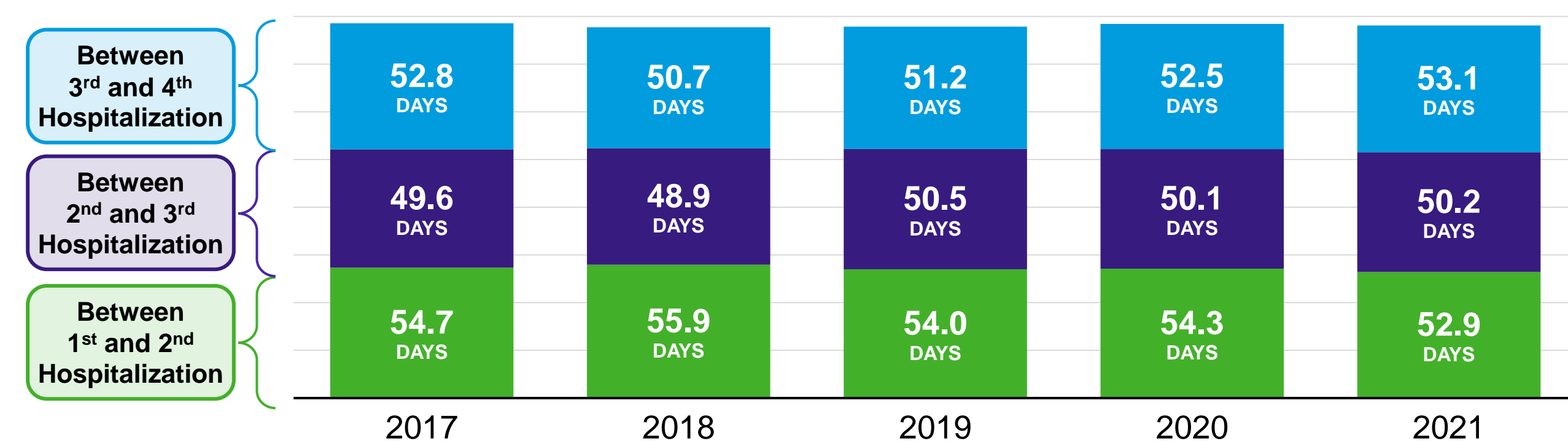
- Patients with HC and AP hospitalizations had 2.0 AP hospitalizations per year, compared with 1.2 in the AP cohort. Similarly, total costs were \$40,440 and had 12.2 hospitalization days and 1.5% mortality rates in the HC cohort compared to \$24,387 total costs, 7.2 days in the hospital, and 3.3% mortality rates in the overall AP cohort, respectively.
- The regression models for annual AP-hospitalization cost per patient, AP-hospitalization days per patient, and AP-hospitalization death rate found that a HC diagnosis had a significant increasing effect on both hospitalization cost and days and a non-significant effect on death rate.

Figure 1. All-Cause Hospitalizations, Costs, & Days Per Patient Before & After AP & AP+HC Hospitalizations (Within the Calendar Year)



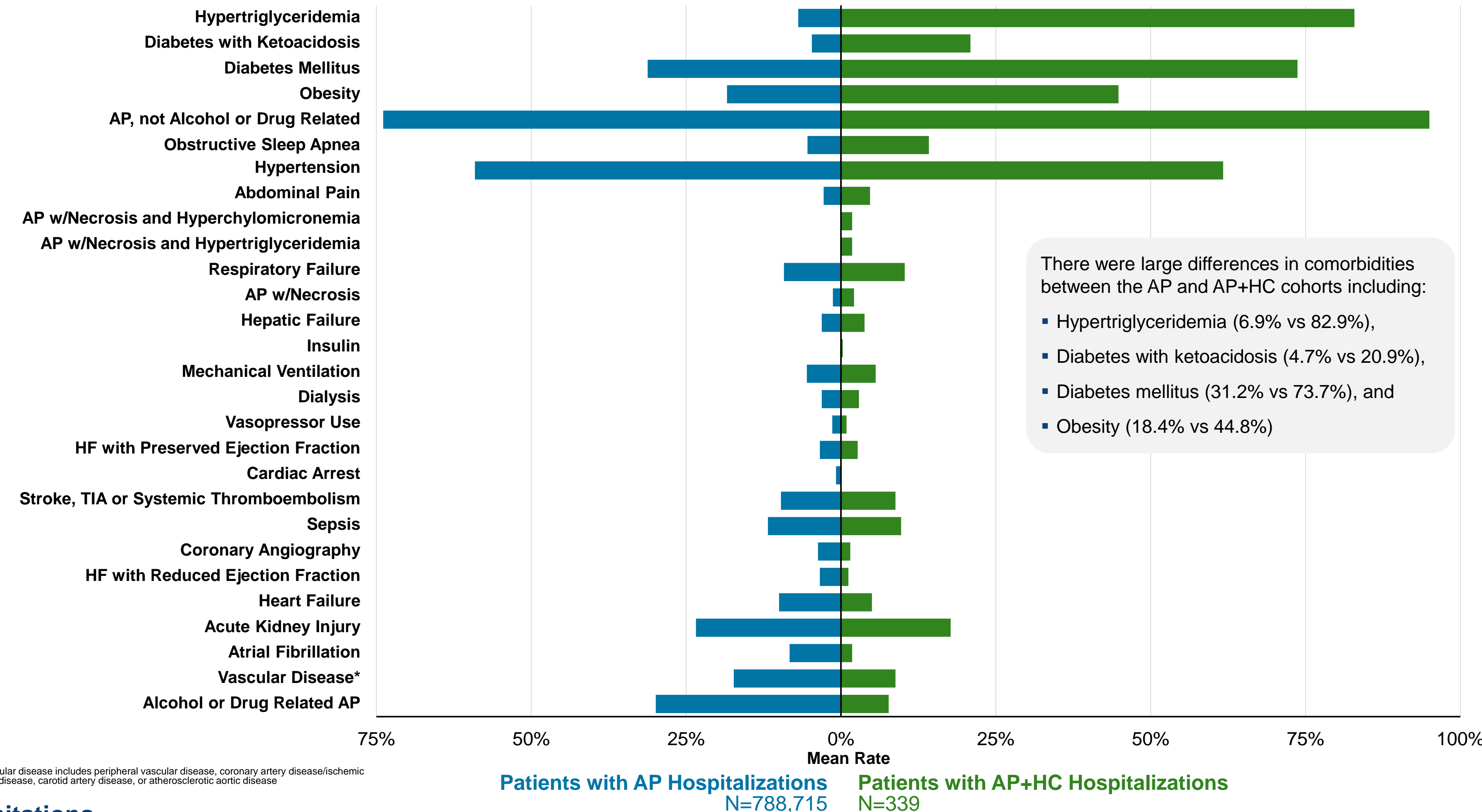
- Patients with an AP+HC hospitalization had greater all-cause hospitalizations, costs, and days per patient both before and after the index AP+HC hospitalization than the per-patient all-cause hospitalizations, costs, and days before and after AP patients' first AP hospitalization.

Figure 2. Average Days Between AP Hospitalizations Among Patients With 4+ AP Hospitalizations



- Average days between hospitalizations were similar between a patient's 1st and 2nd, 2nd and 3rd, and 3rd and 4th AP hospitalizations, averaging between 48.9–55.9 days.

Figure 3. Complicating Factors in Patients with AP Hospitalizations and Patients with AP+HC Hospitalizations



There were large differences in comorbidities between the AP and AP+HC cohorts including:

- Hypertriglyceridemia (6.9% vs 82.9%),
- Diabetes with ketoacidosis (4.7% vs 20.9%),
- Diabetes mellitus (31.2% vs 73.7%), and
- Obesity (18.4% vs 44.8%)

*Vascular disease includes peripheral vascular disease, coronary artery disease/ischemic heart disease, carotid artery disease, or atherosclerotic aortic disease

Limitations

- HCUP data does not include:
 - Outpatient services
 - Plasmapheresis or insulin/heparin therapy
 - Follow-up imaging and labs
 - Indirect costs (lost productivity, CP progression)
 - ED visits without admission
 - Precise U.S. ICU cost adders are not uniformly reported
 - May be missing readmissions costs due to average days between hospitalizations >30 days
 - Episode groupers which combine index admission, follow-up, and readmissions that capture full continuum of care are excluded.
- All of which result in higher per-episode costs and can push lifetime costs into tens of thousands per patient.

REFERENCES

1. Mederos MA, et al. *JAMA*. 2021;325(4):392–399. 2. Yadav D, Lowenfels AB. *Gastroenterology*. 2013;144(6):1252–1261. 3. Sohail Z, et al. *J Pak Med Assoc*. 2025;10(Suppl 1):e001798. 4. Cibran C, et al. *Trauma Surg Acute Care Open*. 2025;10(Suppl 1):e001798. 5. Coronado Arroyo JC, et al. *Rev Bras Ginecol Obstet*. 2021;43:220–224. 6. Pedersen SB, et al. *JAMA Intern Med*. 2016;176(12):1834–1842. 7. Yang AL, McNabb-Baltar J. *Pancreatology*. 2020;20(5):795–800. 8. Gagnon CA, Ashraf AP. *Curr Alcohol Relat Rep*. 2024;26(1):617–628. 9. Forsmark CE, et al. *N Engl J Med*. 2016;375(20):1972–1981. 10. Koutroumpakis E, et al. *Pancreatology*. 2017;17(1):32–40. 11. Lindkvist B, et al. *Pancreatology*. 2012;12(4):317–24. 12. Blom DJ, et al. *J Clin Lipidol*. 2018;12(5):1234–1243.e5. 13. Singh VK, et al. *Pancreatology*. 2022;22(8):1091–1098. 14. Watts GF, et al. *N Engl J Med*. 2024;392:127–137. 15. Gaudet D, et al. *JAMA Cardiol*. 2024;e240959. 16. Ballantray CM, et al. *N Engl J Med*. 2024;391:899–912. 17. Marston NA, et al. *N Engl J Med*. 2025; Nov; online ahead of print. doi:10.1056/NEJMoaz2512761.

CONCLUSIONS

This study provided a description of the costs, length of stay, and inpatient mortality in patients with AP hospitalizations and patients with AP+HC hospitalizations.

Additional outcomes included a wide array of complicating factors related to AP, giving a broad overview of AP+HC characteristics. All of these factors increase resource use.

Patients with AP+HC hospitalizations have significantly greater acute health care utilization with greater hospitalizations, LOS and cost.

Modifiable risk factors for preventing recurrence of AP attacks include managing contributing metabolic factors such as high TG levels.¹³

A new generation of therapies has emerged that potentially inhibit APOC-III production and reduce TGs to below threshold levels of AP, 500 mg/dL¹⁴⁻¹⁷, to address morbidity, mortality, and expenditure.