PancreasFest 2022

A Prospective Cohort Study Evaluating PAN-PROMISE To Detect and Risk-Stratify Post-ERCP Pancreatitis Symptoms

Nikhil Thiruvengadam MD

Assistant Professor of Medicine

Loma Linda University School of Medicine

Disclosures

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Background

Post-ERCP Pancreatitis

- Post-ERCP Pancreatitis (PEP) most common (3-8% overall) adverse event[1]
  - 35,000 cases occur with greater than 200 million dollars in healthcare expenditures[2]
- Cotton Consensus Criteria represents the current standard definition[2]
  - Typical symptoms, amylase/lipase > 3*ULN at 24 hours, Hospitalization > 48 hours
  - Severity of PEP based solely on length of stay
    - Mild – Hospitalization 2-3 days
    - Moderate – Hospitalization 4-10 days
    - Severe – Hospitalization for > 10 days/ need for endoscopic, surgical or percutaneous interventio

1. Testoni et al AJG 2010 2. Kochar et al GIE 2015 3. Cotton et al GIE 1991

Limitations of the Consensus Criteria

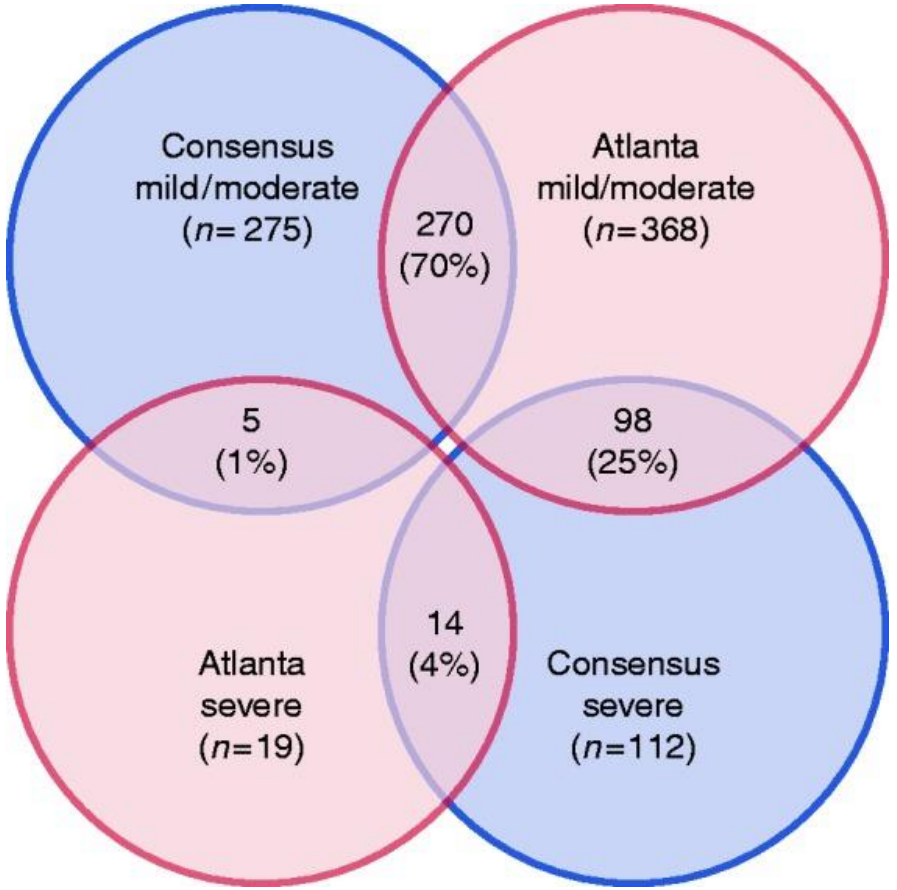
- Elevated amylase found in up to 75% of patients after ERCP[4]
  - Only 59% of patients with an amylase > 10* ULN had abdominal pain at 24 hours
- Post-procedure pain can be common (up to 40% of patients)[5]
  - bowel spasm, stent placement (particularly SEMS)
- Difficulty in identifying whether an admission was prolonged solely due to PEP[8]
- Reduced specificity in patients with chronic abdominal pain
- These limitations may lead to an inaccurate assessment of the effect size of PEP when studying PEP prophylactic therapies
  - Explains multiple discordant RCTs of PEP prophylactic measures

4. Testoni et al AJG 1999 5. Ito et al World J Gastro 2010 6. Freeman et a NEJM 1996
7. Elmunzer et al NEJM 2012 8. Ferreira et al World J Gastro 2010

Cotton Criteria Fails to Capture Pancreatitis Morbidity

- Abdominal pain is common post-ERCP
  - A substantial number of patients have unplanned short hospital stays (< 48 hours) for abdominal pain post-ERCP.[11]
  - Fails to capture patients with significant pain treated in ambulatory settings

- High discordance with revised Atlanta criteria
  - Clinical definitions requiring CT imaging[9]
  - Modified criteria using different amylase cut-offs[10]
  - Over-diagnosis for severe pancreatitis (LOS influenced by pain perception and comorbidities)



9. Artifan et al Pancreas 2010 10. Testoni et al Dig Liv Sci 2009
11. Ho et al GIE 2002 12. Smeets et al UEGJ 2019

PAN-PROMISE

- PAN-PROMISE is a survey instrument designed to quantify the severity of patient's symptoms in acute pancreatitis.
  - Seven-item scale based on the symptoms that cause the most discomfort and concern to patients with AP
  - Scores from 0 to 70
  - Mean score of 32 at 24-hours of admission -> 4.5 at 15 days post-discharge

- Constructed with input from patients, professionals and an expert panel[13]
  - Validated in an international multi-center prospective cohort study involving 524 patients with acute pancreatitis in 15 countries
  - Captures pancreatitis morbidity and patient's well being with good consistency, reliability, reproducibility

13 De Madaria et al Gut 2020

PAN-PROMISE

- Summation of each individual item is scored from 0 to 10 (worst score in the last 24 hours)
  - Pain, especially in the abdomen, chest or back.
  - Abdominal distention (bloating, sensation of excess gas).
  - Difficulty eating, sensation of food being stuck in the stomach.
  - Difficulty with bowel movements (constipation or straining on bowel movements).
  - Nausea and/or vomiting.
  - Thirst.
  - Weakness, lack of energy, fatigue, difficulty moving.

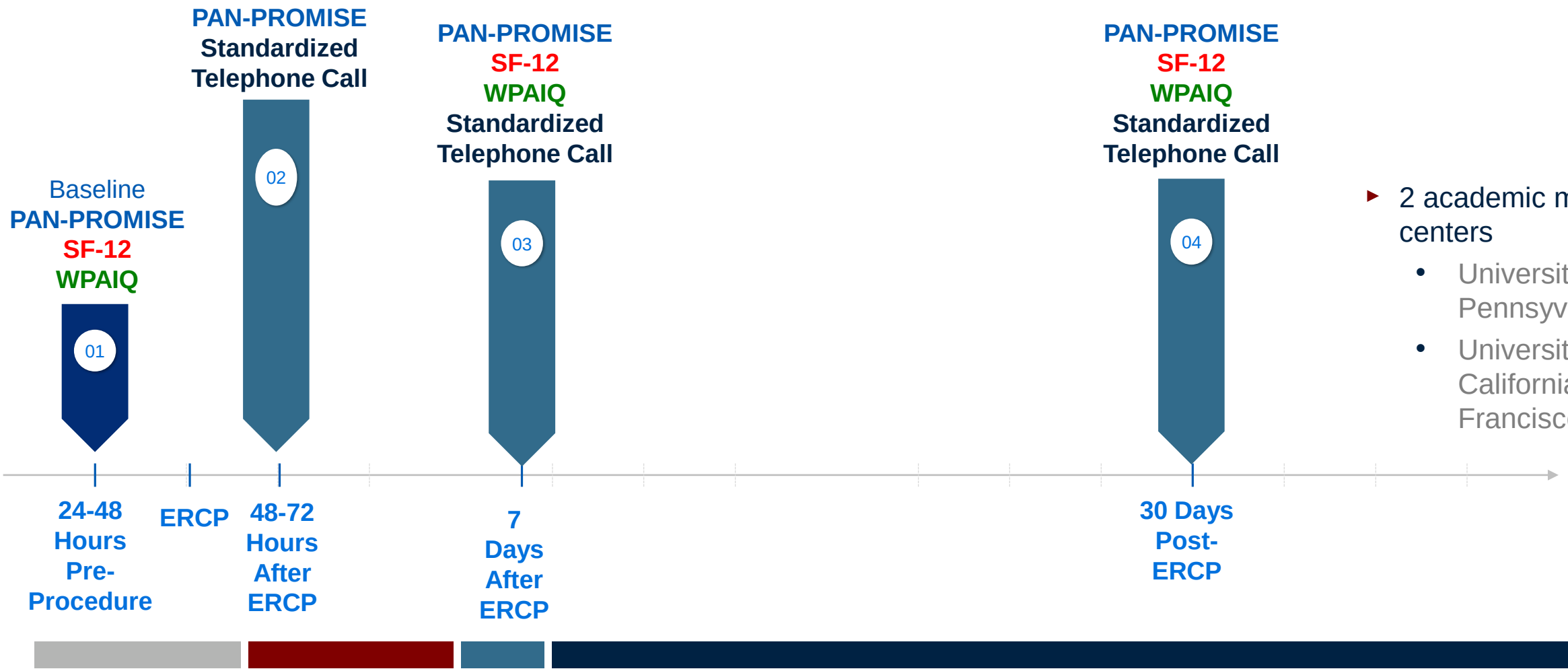
Study Design

Specific Aim/Hypothesis

- **Primary Aim**: To perform a prospective cohort study of patients undergoing ERCP comparing PAN-PROMISE to the Cotton Consensus Criteria for detection of post-ERCP pancreatitis symptoms

- **Primary Hypothesis**: The proportion of patients who have a PAN-PROMISE score > 7 at 7 days post-ERCP compared to baseline will be twice the proportion of patients who meet the Cotton Consensus Criteria.

Study Procedures



- 2 academic medical centers
  - University of Pennsylvania
  - University of California San Francisco

Inclusion and Exclusion Criteria

- Important Eligibility criteria include:
  - Planned cannulation of the bile duct and/or pancreatic duct
  - Major Papilla with or without prior sphincterotomy.
- Important Exclusion criteria include:
  - Surgical alteration of the major papilla or foregut
    - Example: Whipple or hepaticojejunostomy
  - Acute pancreatitis in the seven days prior to ERCP
  - Patients who do not complete 80% of the questions on the baseline or 48-72 hour surveys.

Statistical Analysis Plan

Primary and Secondary Outcomes

Primary Outcome

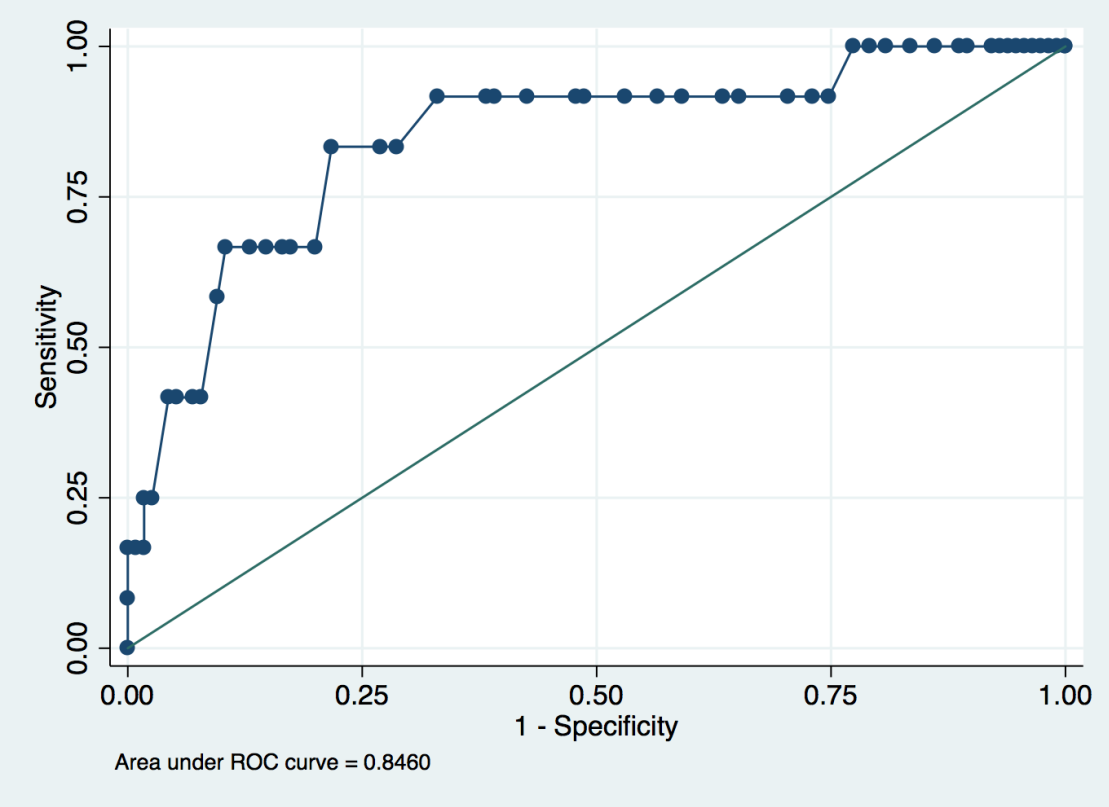
- PEP
  - Defined as PEP as defined by the Cotton Consensus Criteria
  - Requires symptoms, amylase/lipase > 3 * ULN at at least 24 hours after the procedure and hospitalization for at least 48 hours
- Elevated-PROM
  - Defined as a **change in the total PAN-PROMISE as compared to baseline** of > 7 at the 7 days.
  - > 7 cut-off was chosen based on our interim analysis demonstrating that it was an optimal cutpoint to distinguish unplanned healthcare encounters.

Secondary Outcomes

- Direct Healthcare costs in dollars using Medicare cost estimates and Indirect costs using WPAIQ and 2020 Bureau of Labor median hourly income estimates
- A blinded adjudication committee of three physicians was used to determine if the consensus criteria was met

Interim Analysis

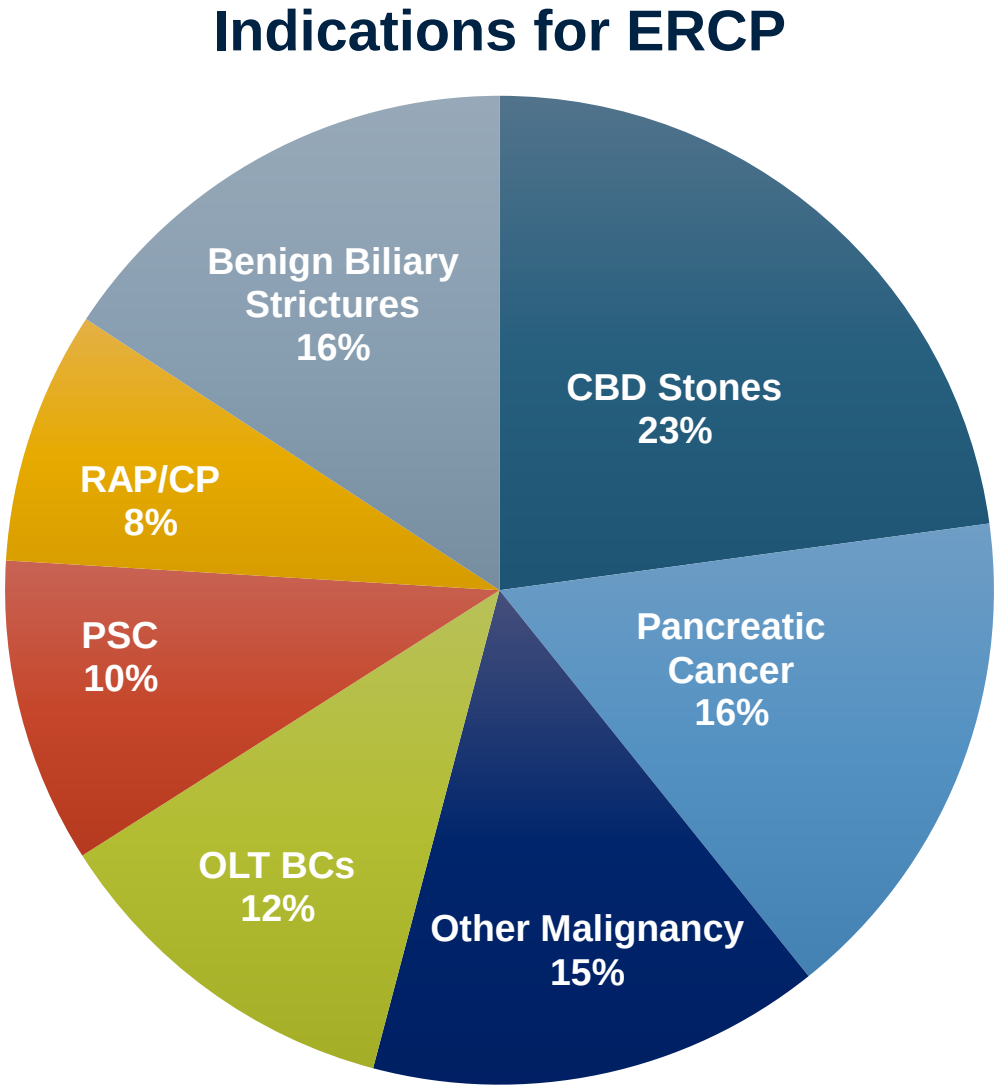
- After enrollment of 150 patients, an interim analysis was performed to identify the optimal cutpoint in change in PAN-PROMISE
  - Twelve patients (9.5%) had an unplanned inpatient or outpatient healthcare encounter in the seven days following ERCP with pancreatitis symptoms
- ROC analysis identified the optimal cutpoint in the change in PAN-PROMISE was an increase of >7 points, which had a sensitivity of 83% and specificity of 78% for an UHE with pancreatitis symptoms



Results

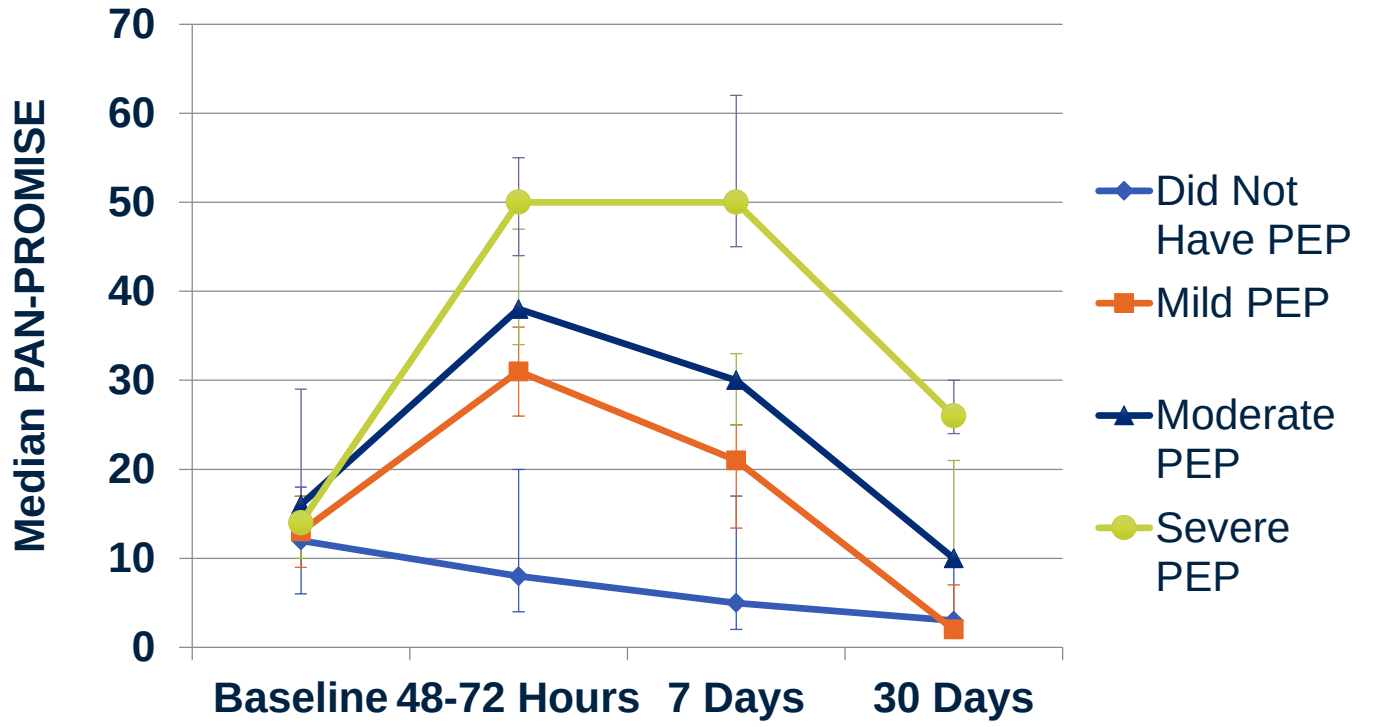
Results

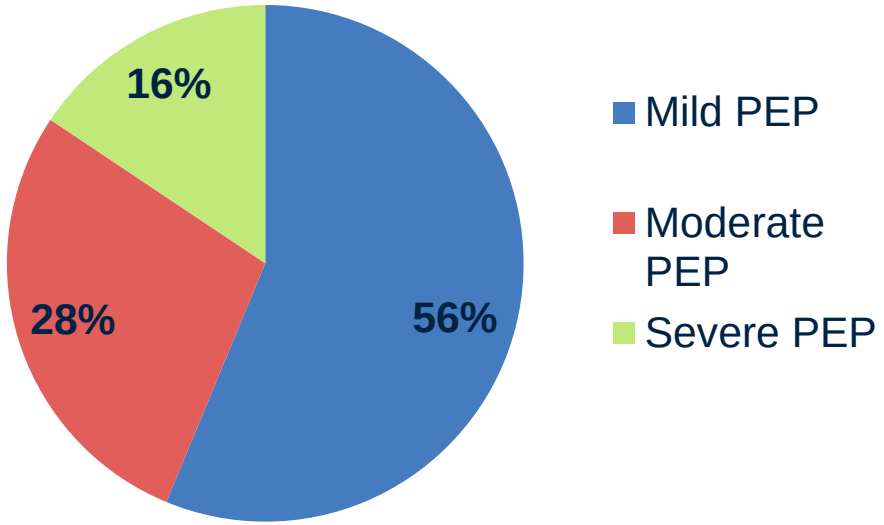
- 679 patients were enrolled from 10/20 to 08/21
- Median Age 63, 55% Male, 14% had a history of prior AP, 12% history of CP
- 441 (64.9%) had a native papilla
- 94.8% patients received rectal indomethacin, 29.5% received hydration with LR (median 1300 mL)



Post-ERCP Pancreatitis Outcomes

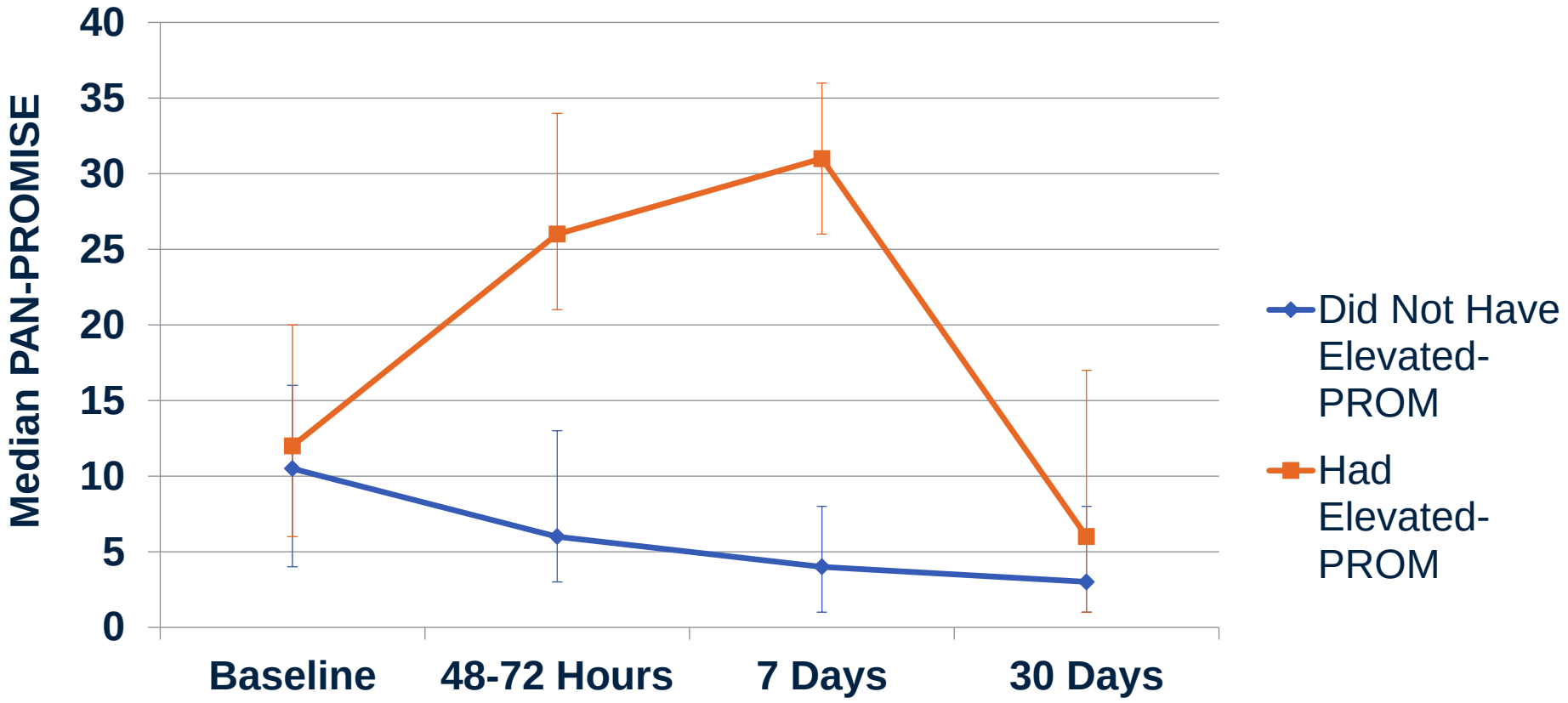
- 32/679 patients (4.72%) developed PEP by the Cotton Consensus Criteria after adjudication





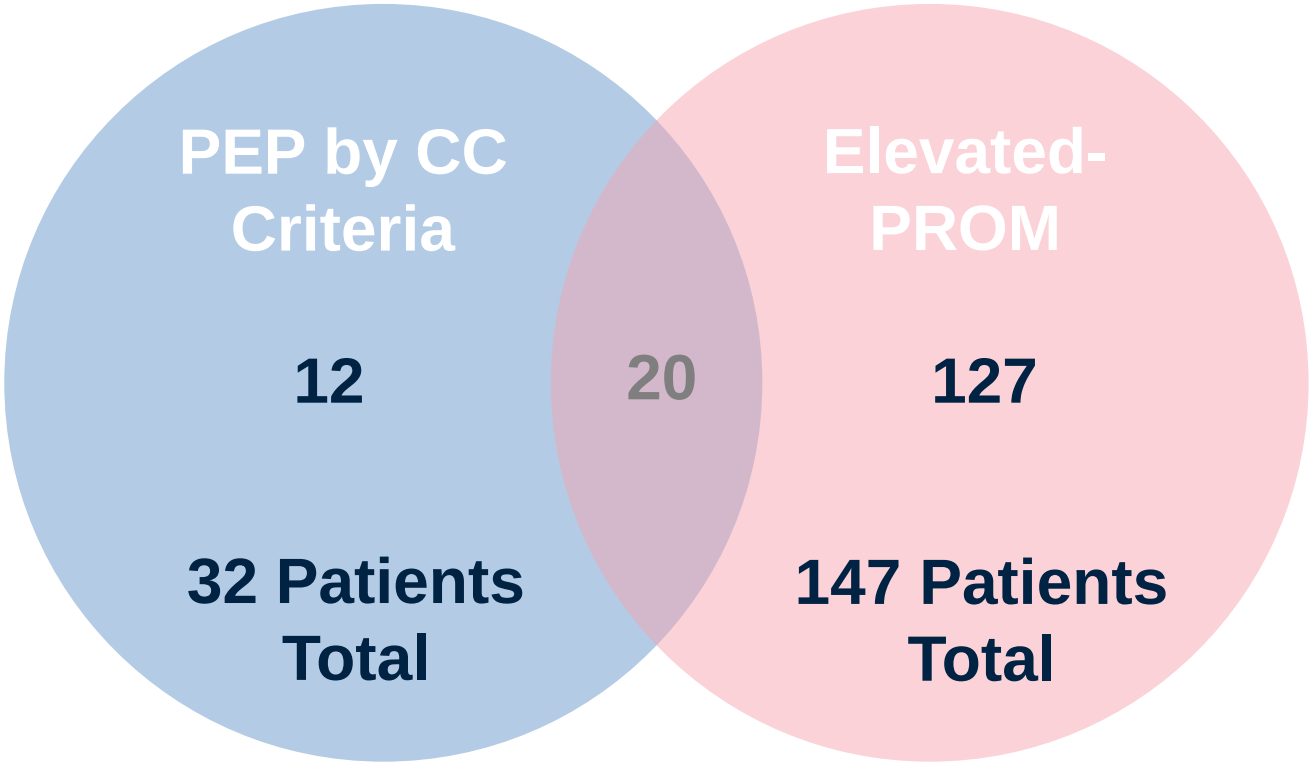
PAN-PROMISE Scores

147/679 (21.6%) had an elevated PROM at 7 days



Discordance between Consensus Criteria and Elevated-PROM

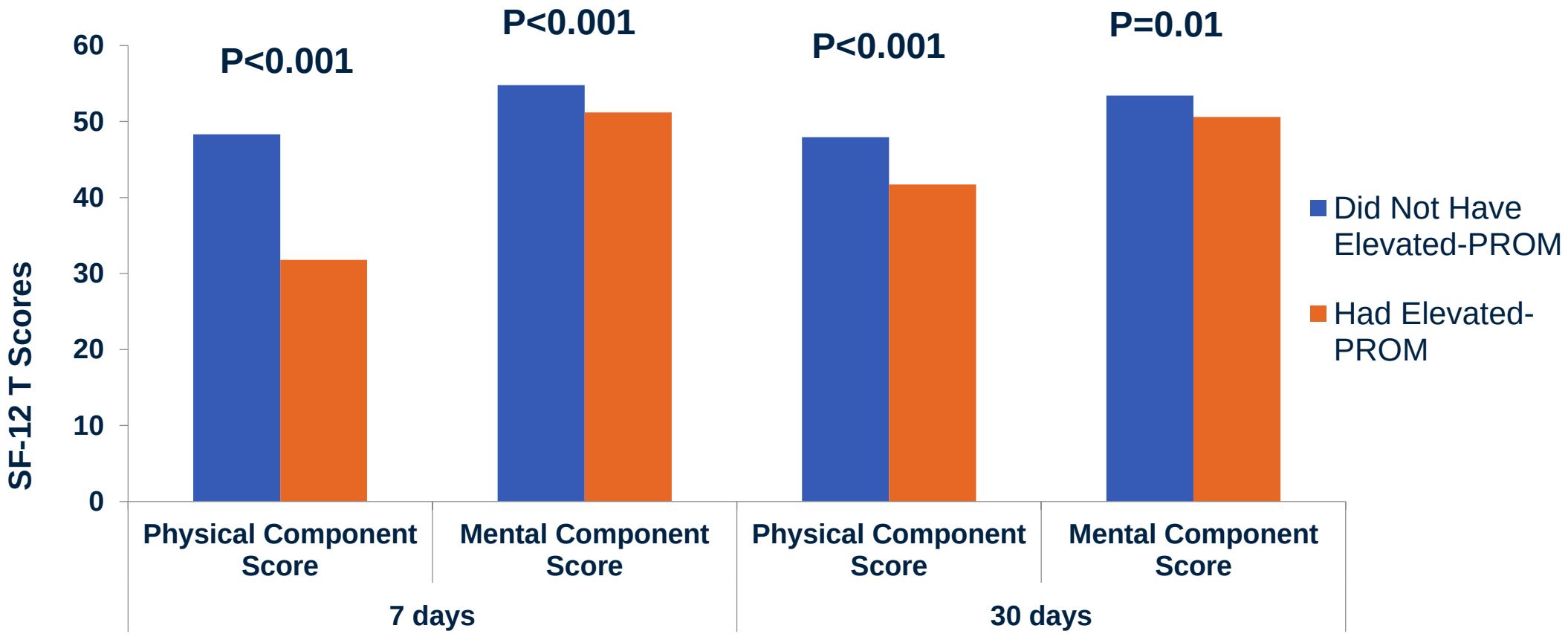
Total 679 Patients



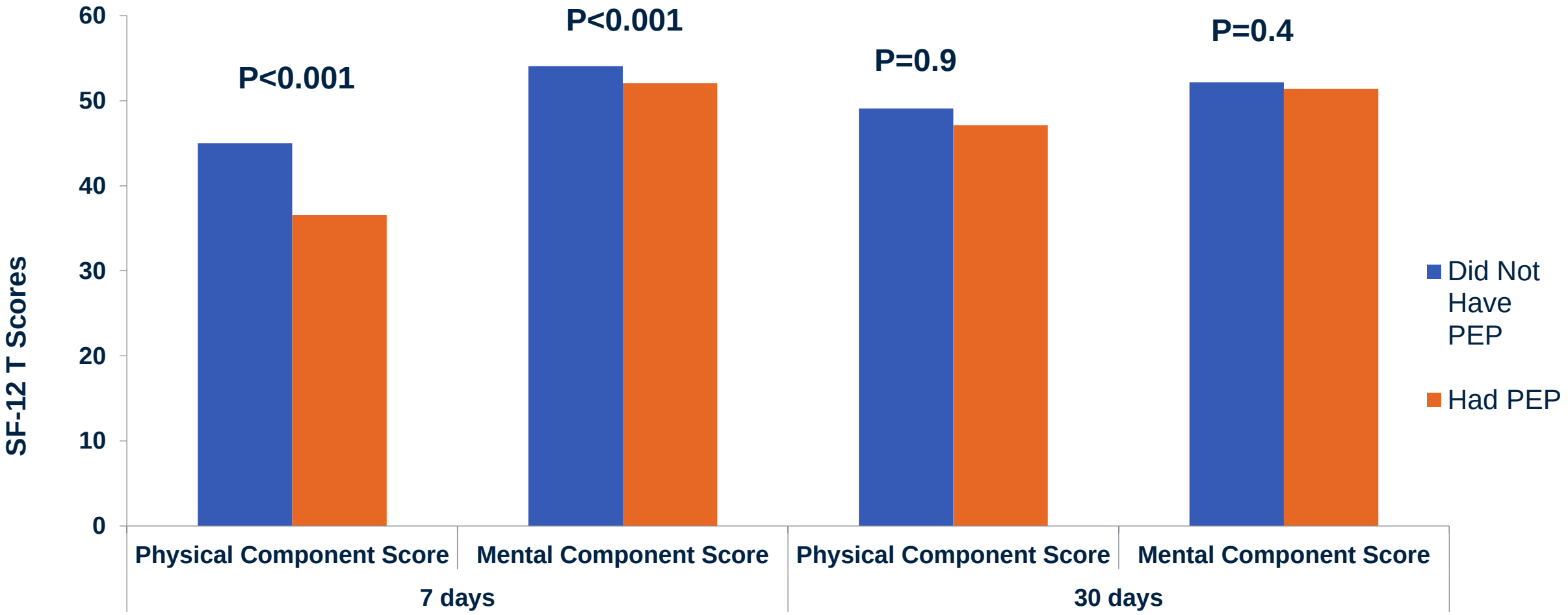
520 Patients Did Not Have PEP or Elevated-PROM

McNemar test for discordance: p-value < 0.001

Correlation of Elevated-PROM and Quality of Life

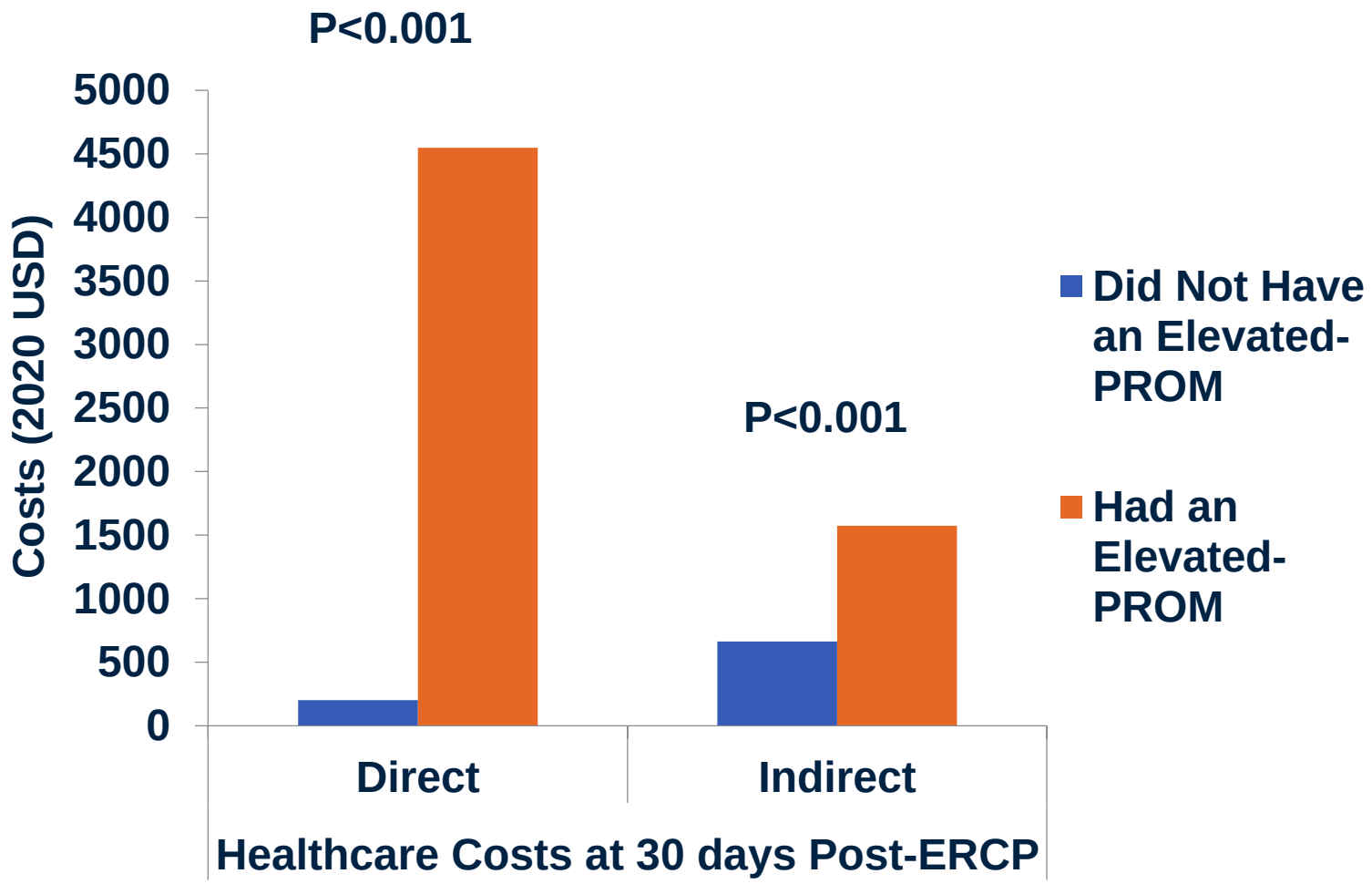


Correlation of PEP and Quality of Life

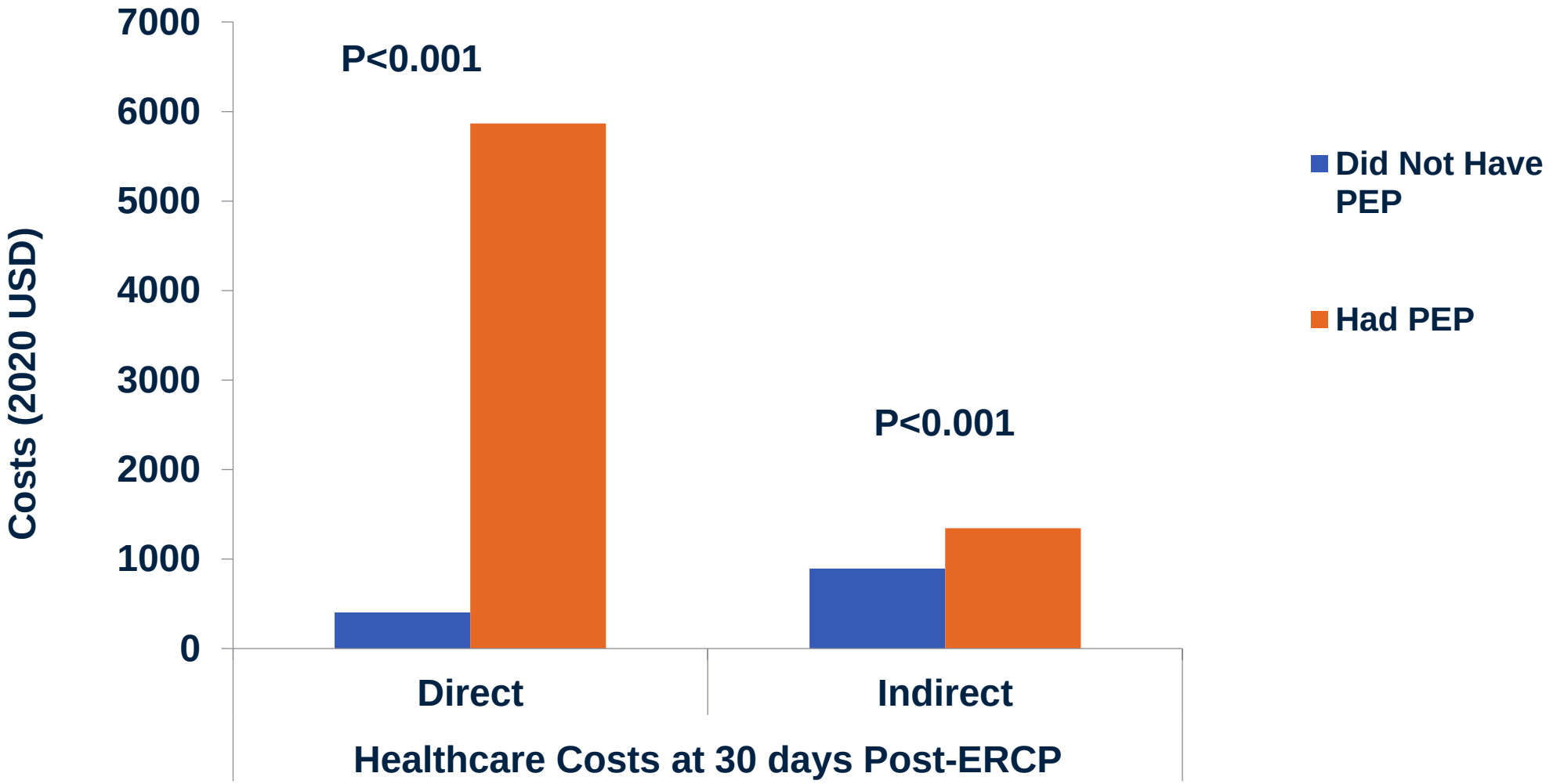


Correlation of Elevated-PROM and Healthcare Costs

- Every 1 point increase in PAN-PROMSE at 7 days was associated with a $80.86 increase in direct costs
- Every 1 point increase in PAN-PROMSE at 7 days was associated with a $25.40 increase in indirect costs



Correlation of PEP and Healthcare Costs



Risk Factors for Elevated-PROM

Variable	OR (95% CI)	P-value
Indication (compared to Choledocholithiasis)	--	--
Pancreatic Cancer	4.25 (1.68 – 10.74)	**0.002**
PSC	1.79 (1.29 – 2.45)	**0.005**
OLT BCs	0.69 (0.21 – 0.89)	**0.01**
Chronic Opiate Usage	2.74 (1.82 – 3.9)	**<0.001**
PD Accessed	1.52 (1.01 – 2.30)	**0.04**
SEMS Placement	2.27 (1.25 – 4.17)	**0.007**
Aggressive Hydration with LR	0.51 (0.31 – 0.83)	**0.007**
PD Stent Placement	0.56 (0.29 – 0.96)	**0.03**

Summary

Summary

- 147/679 (21.6%) Patients had Significant Symptoms Post-ERCP at 7 days
  - Strongly associated with lower QoL and increased healthcare costs
- 32/679 (4.7%) had PEP and only 20 (13.4%) of the 147 patients with an elevated PROM were classified as having PEP
  - This leads to an inaccurate assessment of the effect size for various PEP prophylactic methods and may explain why there are discordant study results for PEP prevention
- Legacy vs Evidence-based definition of PEP
  - New definition should incorporate symptoms defined by the patient, labs/biomarkers and imaging
- Pancreatic Cancer and PSC patients had the highest symptom burden

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