

# Pancreatitis in Childhood: An Update

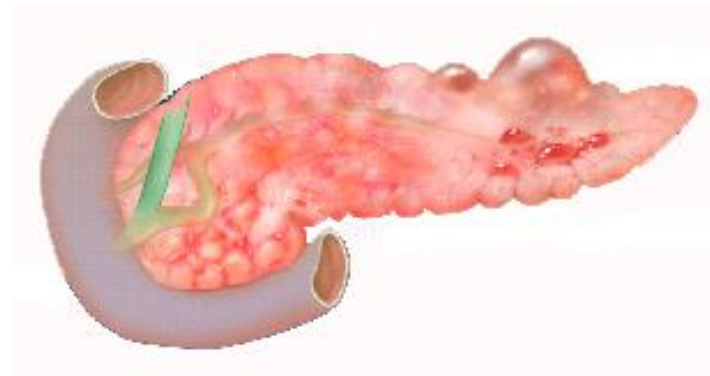
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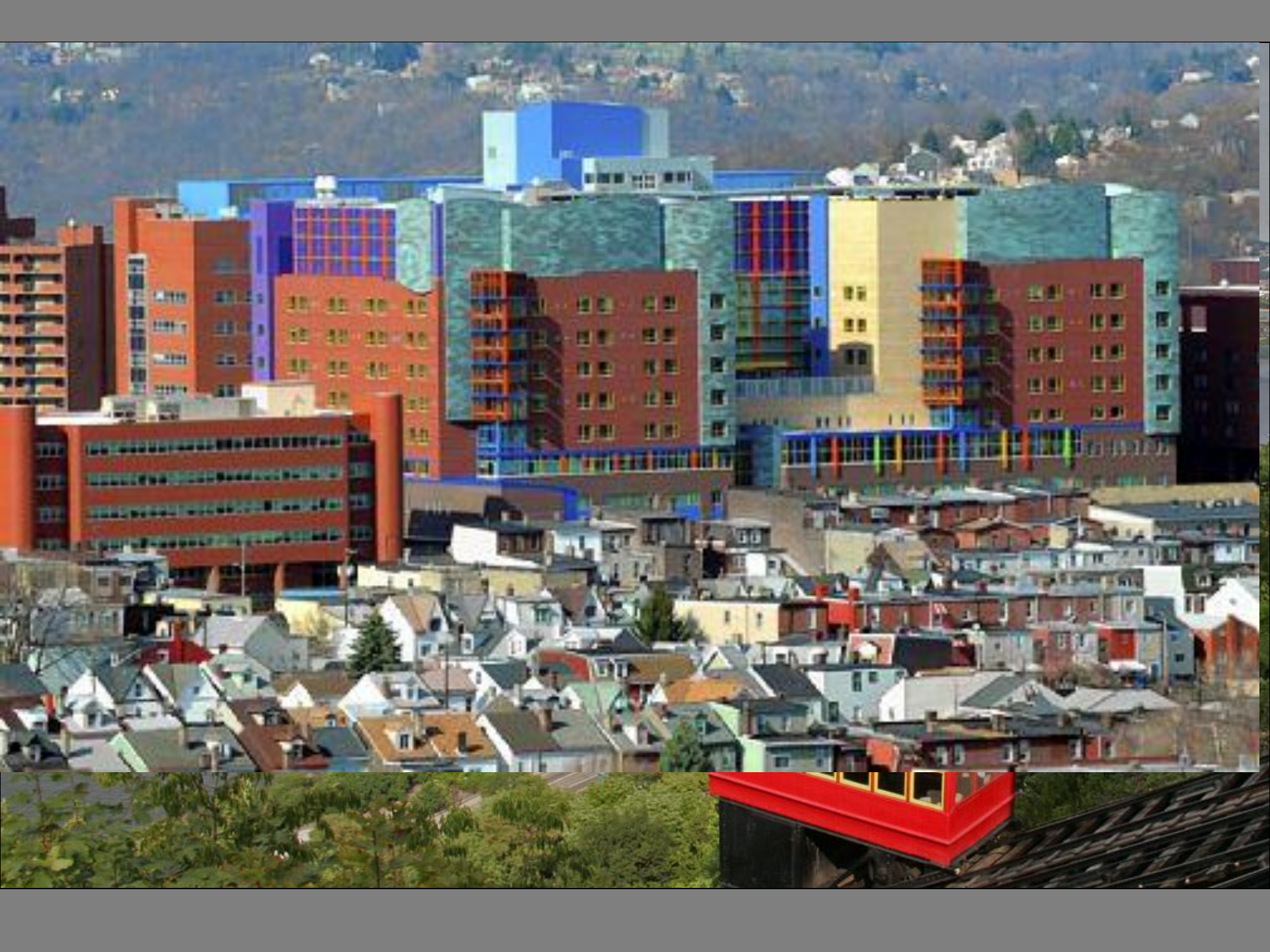


**Children's** | *of*  
Hospital of Pittsburgh | **UPMC**



# Author Disclosures

I have nothing to disclose that would create a conflict of interest.



# Definitions

- *Acute pancreatitis* is a reversible, inflammatory disease of the pancreas
  - Subpopulation have recurrent episodes
- *Chronic pancreatitis* is a destructive, inflammatory condition that irreversibly damages the pancreas.

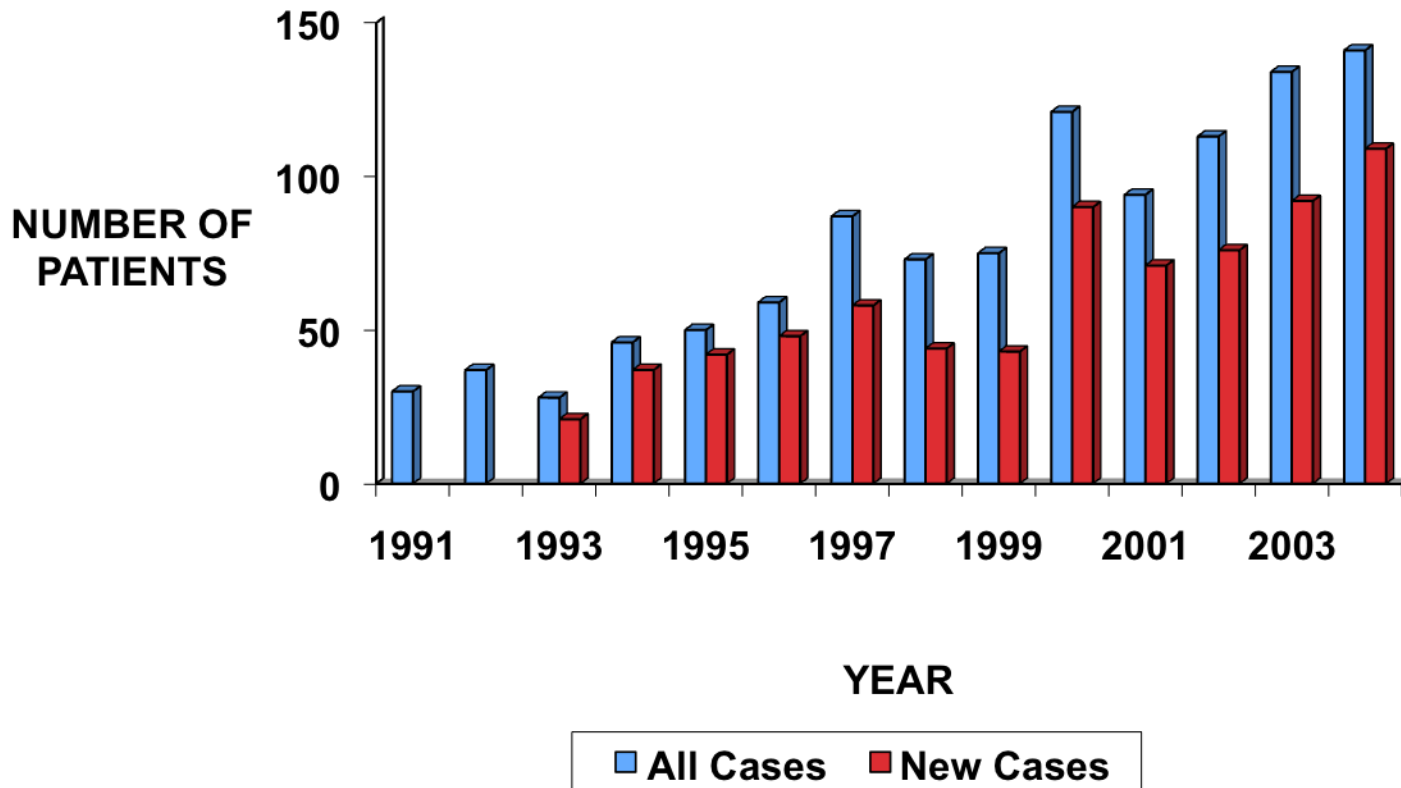
Thus, acute pancreatitis is an event whereas chronic pancreatitis is a process.

# The Incidence of Acute Pancreatitis has Increased in Childhood

- First reported by Lopez in a single institution study
- Subsequently confirmed in reports from other centers in the USA and Australia

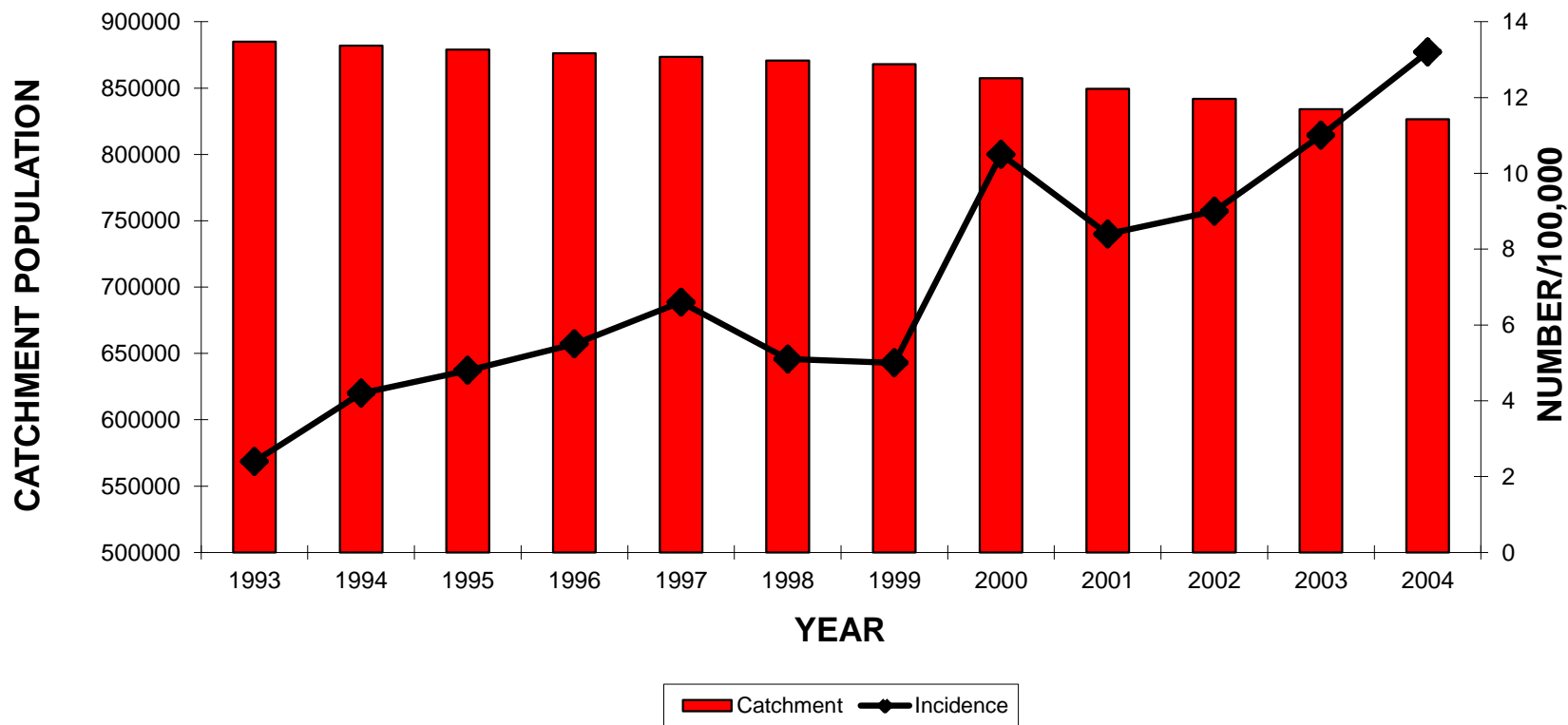
# Incidence of Childhood Pancreatitis

## CHP 1991-2004

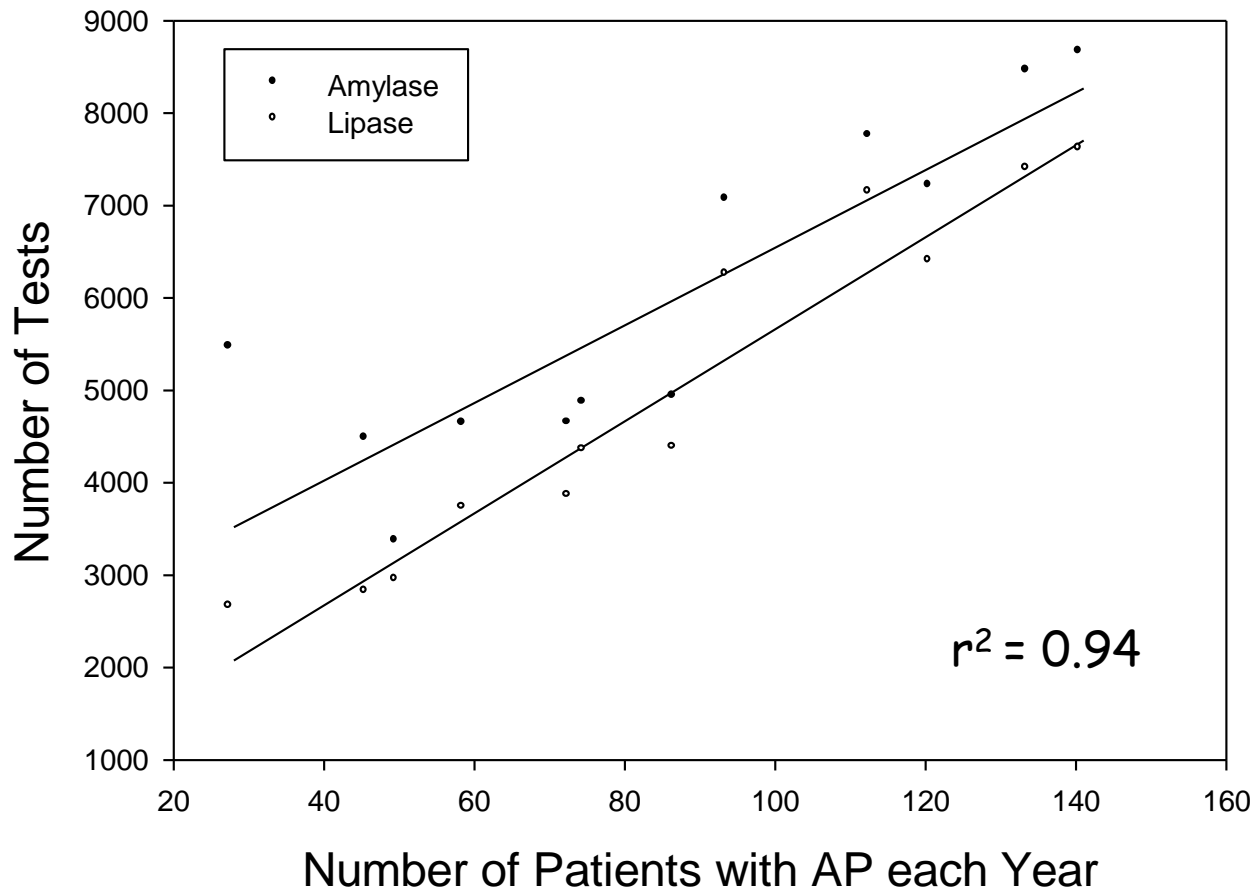


# Incidence Estimates at CHP

## First Known AP Admission



# Is Incidence Really Increasing?

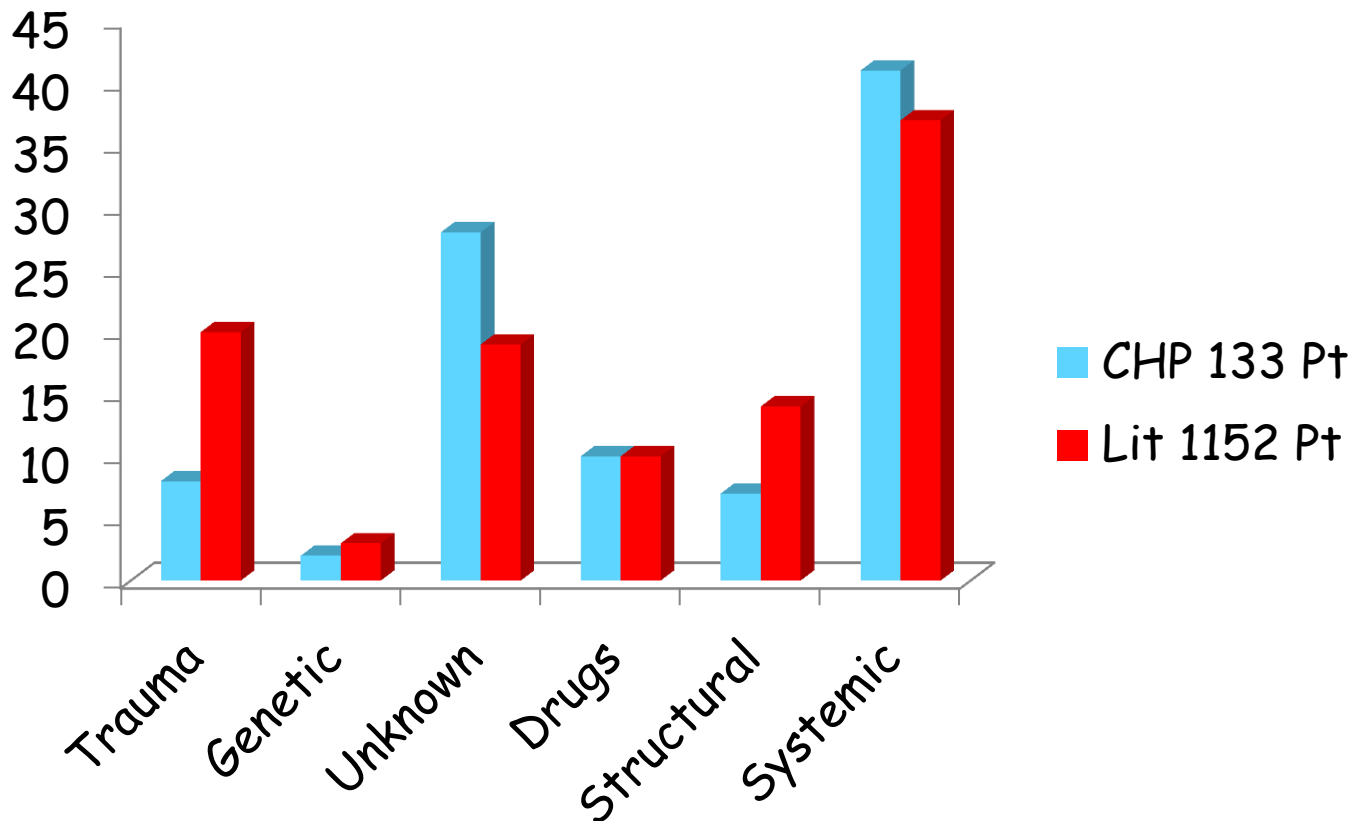


Not in Western PA. It's Increased Awareness!



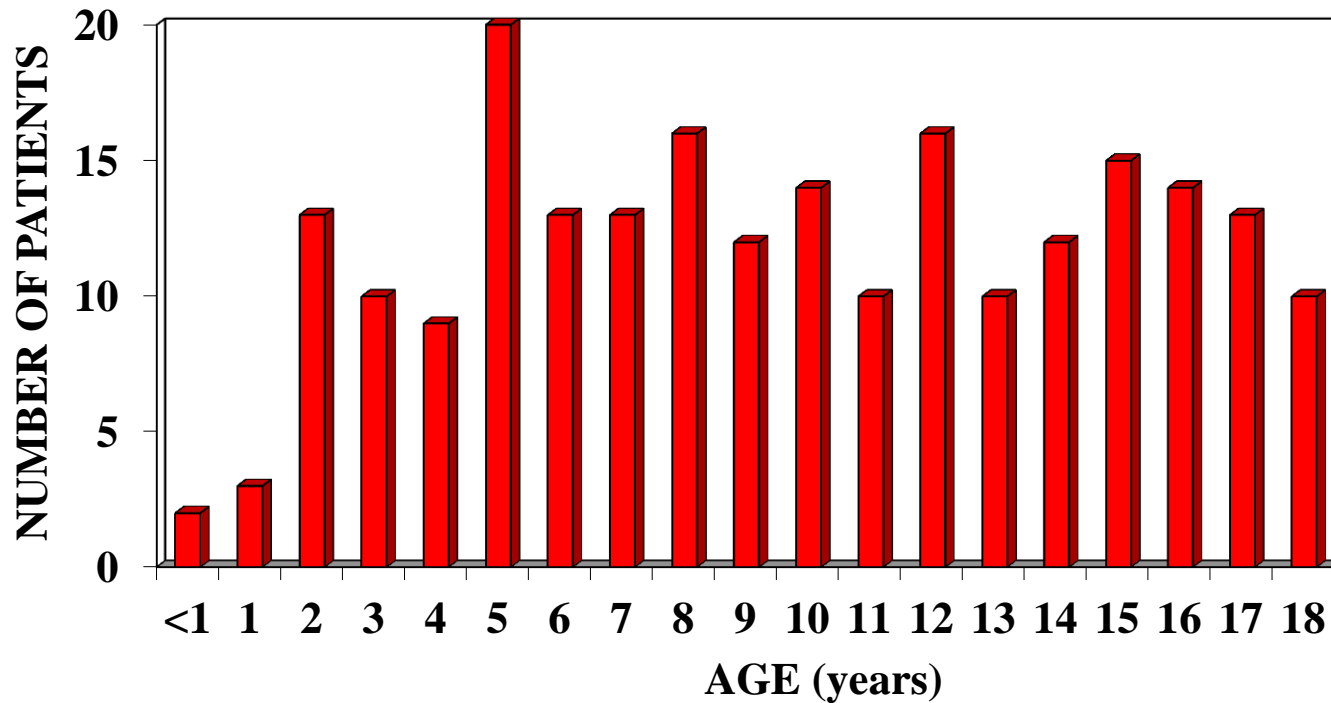
# Etiology of Acute Pancreatitis

## CHP and Literature



# Variation with Age

CHW 1996-2001



# Pancreatitis is a Clinical Diagnosis

- Need 2 out 3
  - Compatible history and symptoms
  - Amylase or lipase  $>3 \times$  URL
  - Radiographic evidence

# Clinical Presentation Varies by Age

## Children

- Vomiting 80%
- Abdominal pain 70%
- Back pain 8%

## Infants and Toddlers

- Vomiting 52%
- Fever 43%
- Irritability 43%
- Abdominal Pain 33%
- Distended Abdomen 16%

# Amylase and Lipase?

Should you do both?

- Majority of studies conclude that amylase improves the specificity of lipase
- Results in 369 pediatric patients
  - 93 had abnormal lipase alone
  - 19 had abnormal amylase alone
  - 257 had both

# Radiographic Studies

- Ultrasound
- CT scan
- Magnetic resonance  
cholangiopancreatography (MRCP)
- Endoscopic retrograde  
cholangiopancreatography (ERCP)

# Treatment of Acute Pancreatitis

- IV hydration at presentation
- Pain control
- Monitor for complications
- Nutrition support

# Pancreatic Rest as Therapy

## Dogma

Rest the inflamed pancreas.



# Is Pancreatic Rest Important?

## Fasting versus Oral Feeding

- Sixty patients with mild pancreatitis randomized to immediate oral feeding or fasting
- Two groups did not differ by clinical criteria at admission
- No differences in amylase, CRP, abdominal pain or number of GI symptoms during study
  - Oral feeding was safe and well-tolerated
- The length of hospital stay was shorter in the oral feeding group.
  - Oral feeding may be beneficial

# Is Pancreatic Rest Important?

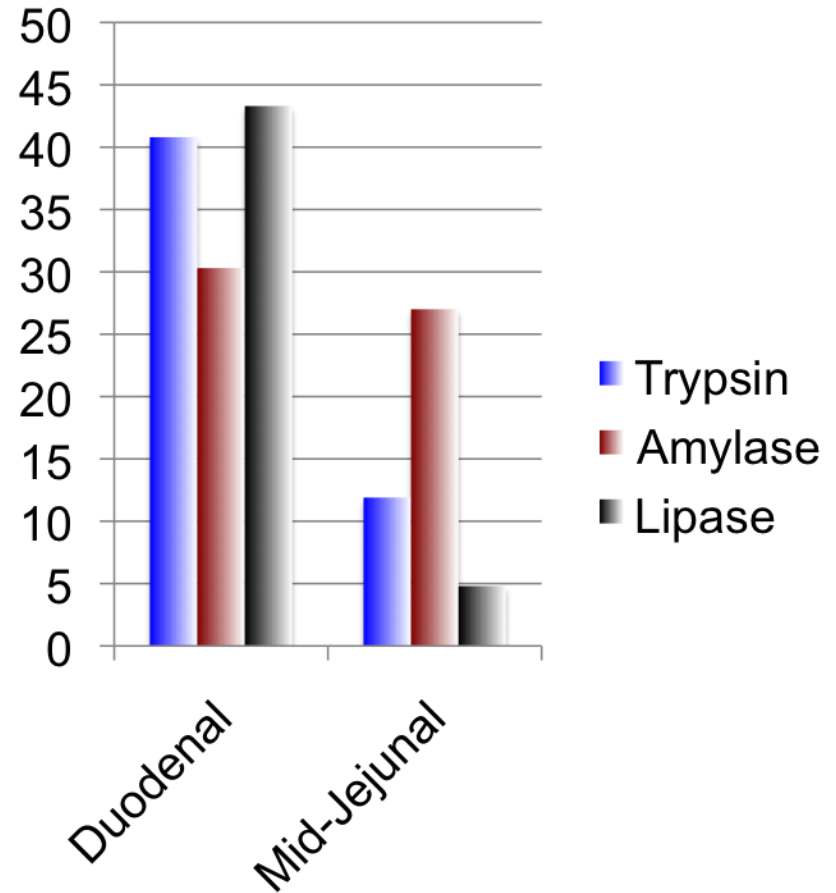
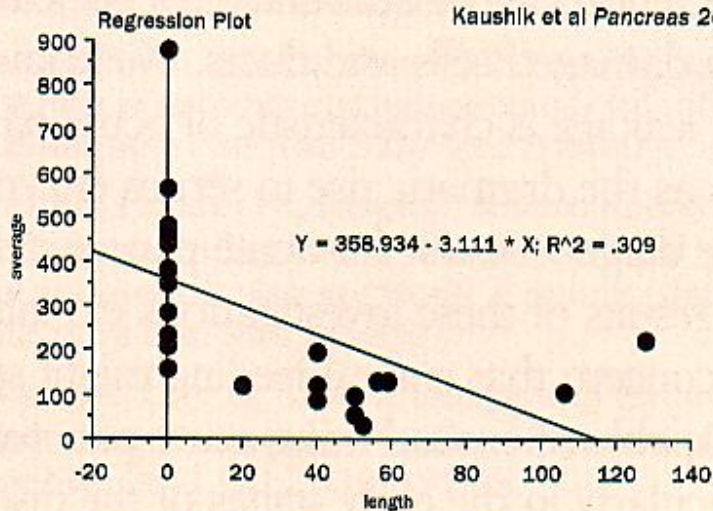
## Enteral Versus Parenteral Nutrition

- Eight separate, randomized studies reached similar conclusions
  - Enteral nutrition is associated with
    - Reduced mortality
    - Fewer episodes of multiple organ failure
    - Fewer infections
    - Fewer surgical interventions
    - Lower cost
- Resting the pancreas with parenteral nutrition did not improve outcomes

# Is Pancreatic Rest Important?

## Jejunal Feeds Decrease Pancreatic Secretion

Fig. 9: Relationship between Pancreatic Trypsin Secretory Response and Distance of Feeding down the Jejunum



# Randomized Trial of NG versus NJ

Eatock et al. *Am J Gastroenterol* 2005;100:432.

- NG 27 patients; NJ 22 patients
  - Location of NJ not given: "proximal jejunum"
- Low fat "semi-elemental" formula
- Severe pancreatitis by Glasgow and APACHE II scores
- No difference
  - Length of hospital stay
  - Length of stay in ICU
  - Mortality
  - Pain score or analgesia use

# Other Trials of NG versus NJ

- Kumar et. al., J Clin Gastroenterol, 2006
- Piciucchi et. al., World J Gastroenterol, 2010
  - Both found no difference in outcomes
- Chang et. al. Crit. Care, 2013
  - Metanalysis
  - No difference in outcomes
- Issues
  - Small numbers
  - Patient selection varies
  - Placement of tubes is not always documented
- Currently, a randomized, multi-center, NIH-funded study of NG versus NJ in patients with severe acute pancreatitis is in progress.

# When to Feed?

- Standard practice has been to wait 2-3 days with mild pancreatitis. Longer with severe pancreatitis
- Recent study compared patients
  - who were fed when they said they were ready
  - who were fed when the serum lipase was below 2x URL.

# Optimal timing of Oral Refeeding

- Randomized 143 patients with mild pancreatitis to lipase directed or patient directed feeding
- Time from admission to feeding
  - Patient selected: 2 days (1-3 days)
  - Lipase selected: 3 days (2-4 days)
- Findings
  - No difference in postprandial pain
  - No difference in LOS
  - Time to reach full calories was not different

# How to Start Feeding?

## **Dogma**

Start with clear liquids.



# Patients With Mild Pancreatitis Can Be Fed Solid Diet

- Jacobson et. al. *Clin Gastro Hep* 2007
  - Prospective, randomized trial of clear liquids versus a low-fat solid diet as the initial meal in mild acute pancreatitis.
  - Randomized 65 to clears and 55 to solids
- Moraes et. al., *J Clin Gastroenterol*, 2010
  - Prospective, randomized trial of clear liquids versus soft diet versus full solid diet
  - Randomized 70 patients to each meal
- In both studies
  - Medical team determined when to start feeds
  - Standard meals provided
  - Decisions about advancing diet and discharge made by medical team

# Findings

- No difference in pain relapse among the groups
- LOS the same in the first study, shorter for group receiving full solid diet in the second study
- Patients in the solid group consumed more calories and dietary fat
- Readmission rates similar for all groups

# What to feed?

**Dogma**

Low-fat diet is preferred.

# Fat or Lean?

- No direct data
- Two arguments for low fat
  1. Fatty acid-stimulated CCK release increases pancreatic inflammation
  2. High concentrations of serum lipids may cause pancreatic damage

# Serum Lipids

- Elevated serum triglycerides associate with pancreatitis
  - levels above 1000 mg/dl
    - Local hydrolysis of triglycerides in the pancreas may cause local toxicity to capillary membranes
    - High fatty acids may increase incidence of micro-thrombi leading to additional ischemic injury
- No evidence that post-prandial rise of TG exacerbates pancreatitis
- Intralipid infusion does not exacerbate pancreatitis

# CCK Argument

Premise

CCK stimulates pancreatic secretions

Premise

Pancreatic stimulation exacerbates  
pancreatitis

Premise

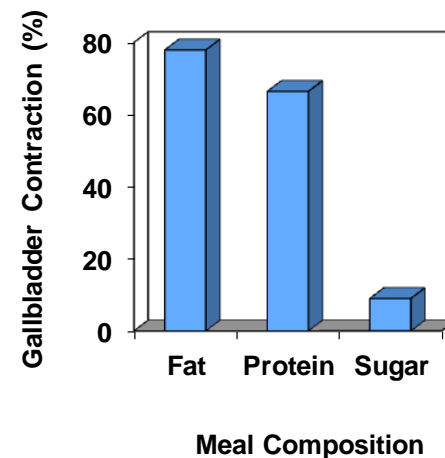
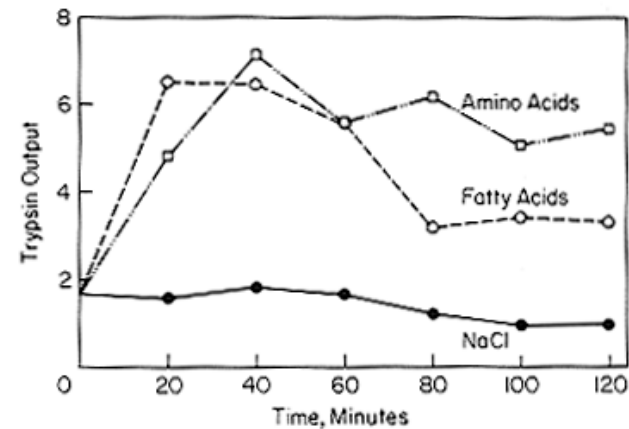
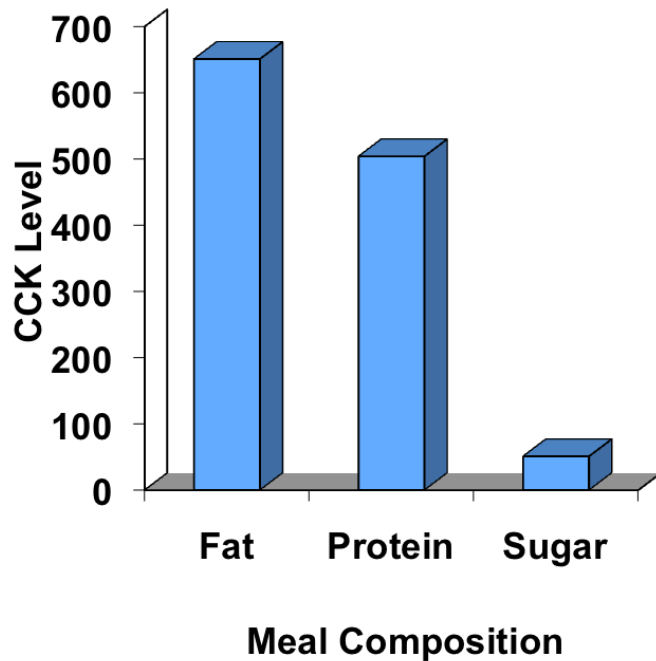
Dietary fat increases CCK secretion

Conclusion

Patients with pancreatitis should be fed a low  
fat diet.

# Is Fat the Only Worry?

## CCK Stimulation



# Low Fat Diet

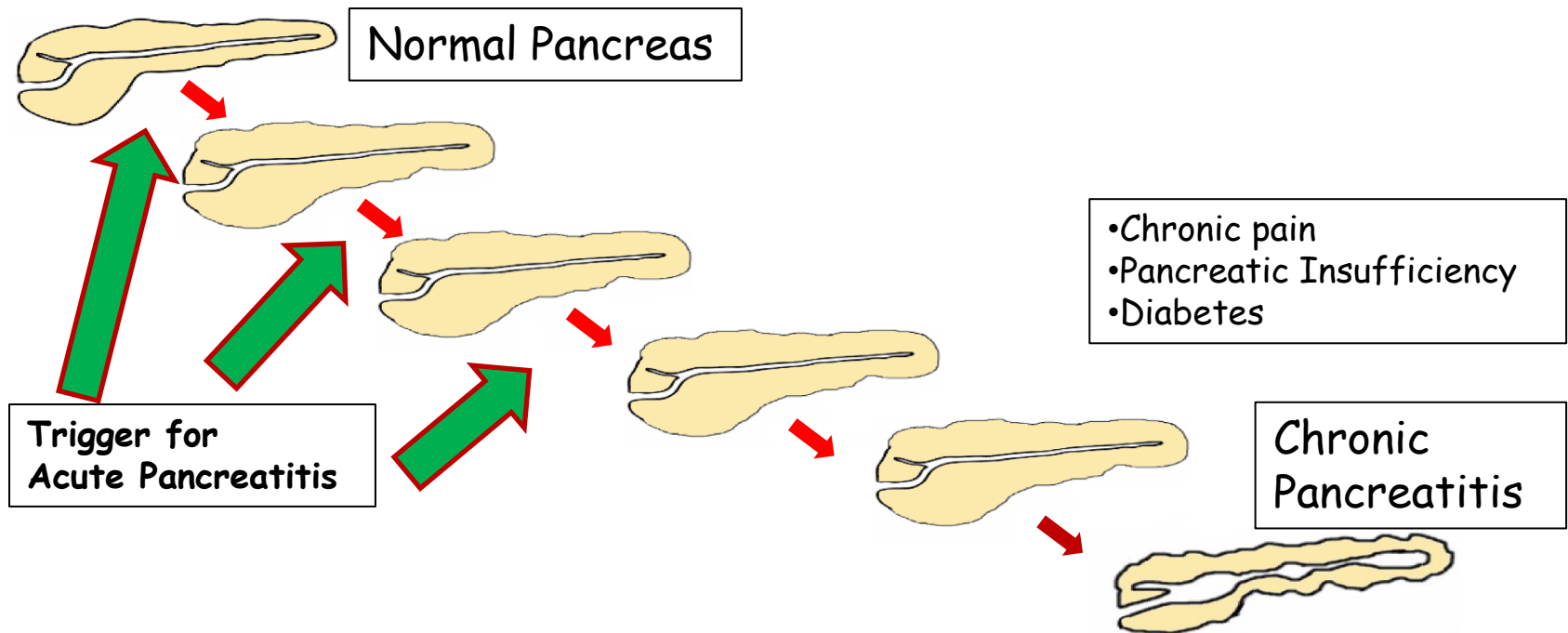
- The use of a low fat diet is based on “expert” opinion
  - If you say it often and loudly, it becomes true
- Does not make physiological sense
- Has not been directly tested
  - The little available data suggests it does not alter the course of pancreatitis



# Summary of Care in Acute Pancreatitis

- Fluid Resuscitation
- Pain control
- Nutrition
  - Start within 24-48 hours
    - No clinical parameters predict who will have increased pain
  - Oral feeding with solid diet in mild pancreatitis
  - Tube feeding with severe pancreatitis
    - NG versus NJ is still unclear
    - Parenteral nutrition already started?
  - Diet in severe pancreatitis
    - Moderate fat

# Acute Recurrent and Chronic Pancreatitis



# INSPPIRE

- Very little information in the literature
  - Few studies
  - Small sample sizes
- **INSPPIRE** (International Study Group of Pediatric Pancreatitis: In search for a cuRE) was created with the following objectives:
  - To better understand the epidemiology, etiologies, pathogenesis, natural history and outcome of pediatric pancreatitis.
  - To create a network of pediatric centers to engage in prospective studies and analyses of children with these disorders.

# INSPPIRE Centers

- USA
  - Univ of Iowa (CC)
  - Univ of Pittsburgh
  - UT Southwestern
  - Baylor Texas Children's
  - Nationwide Children's
  - Medical College of Wisconsin
  - Univ of Minnesota
  - UCSF
  - University of Utah
  - Seattle Children's
- Canada
  - Toronto Hospital for Sick Children
  - Montreal Children's
- Israel
  - Hadassah Medical Organization, Jerusalem
- Australia
  - UNSW, Sydney

# INSPPIRE

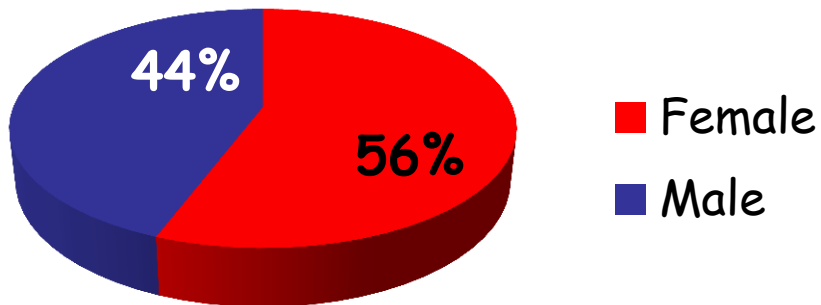
- September 2012-February 2014.
- 233 patients <19 y/o enrolled
  - 57% with ARP and 43% with CP
  - Data collected: demographics, past medical history, family and social history, medications, hospitalizations, risk factors, diagnostic work-up, treatments and outcome information.

# Demographics

## ARP and CP (233 Pt)

Age:  $12.1 \pm 4.6$

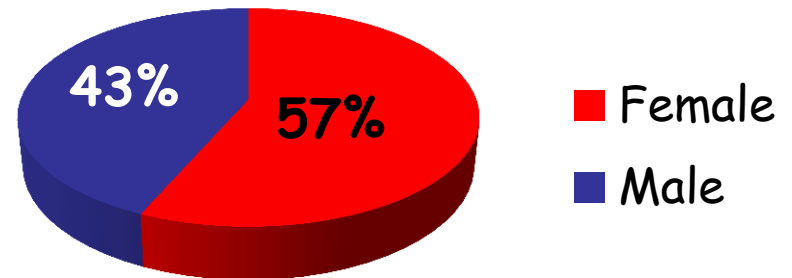
### Gender



## CP (76 PT)

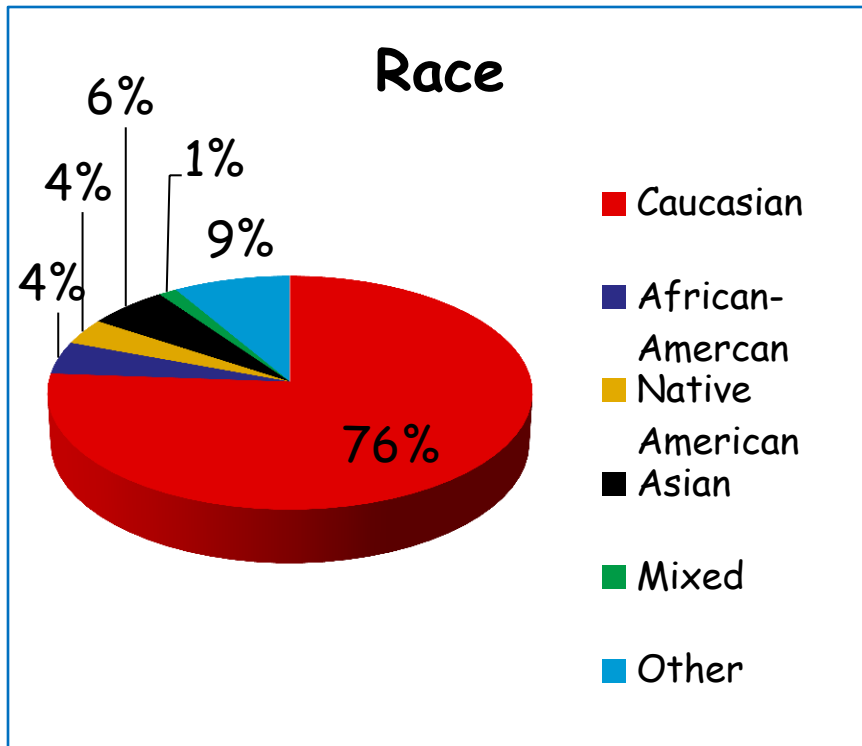
Age: Mean=13.0;  
Median=10.5; IQR=17.0

### Gender

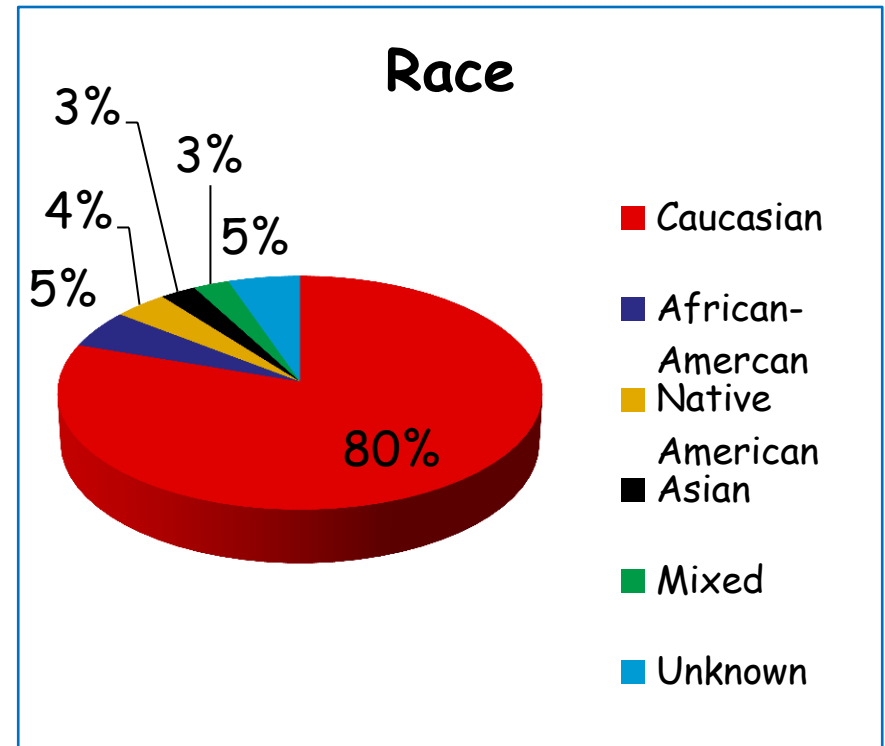


# Demographics

## ARP and CP (233 Pt)



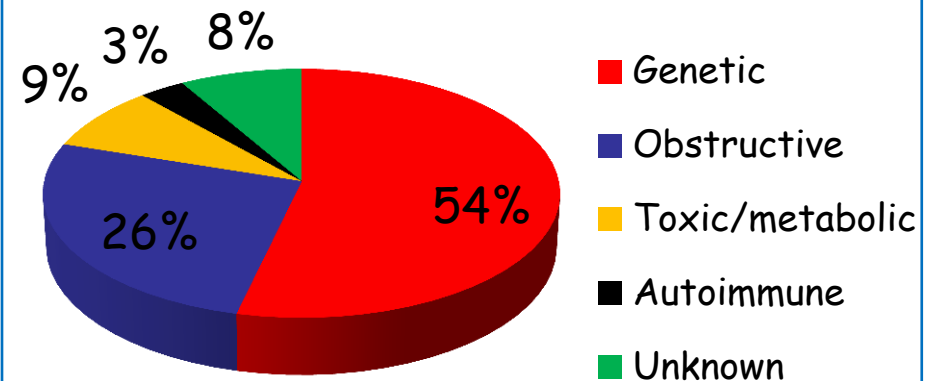
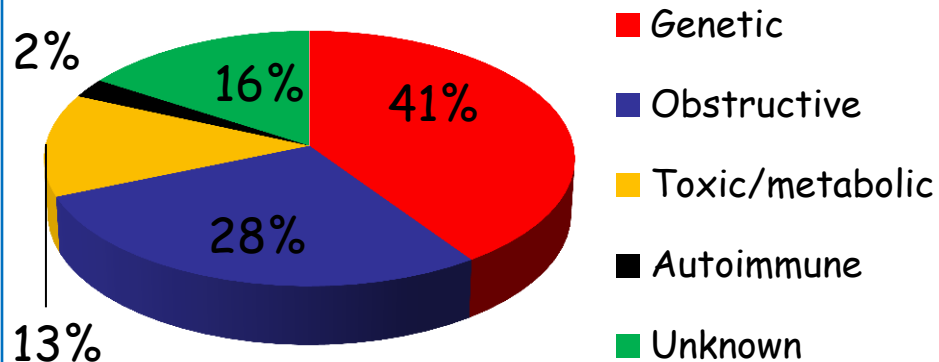
## CP (76 Pt)



# Etiology of ARP and CP

## ARP and CP (233 Pt)

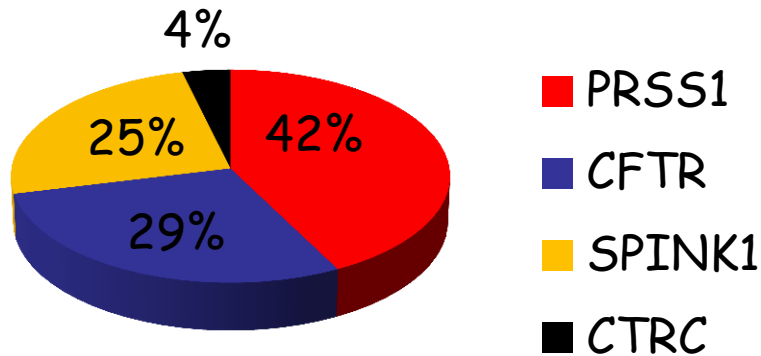
## CP (76 Pt)



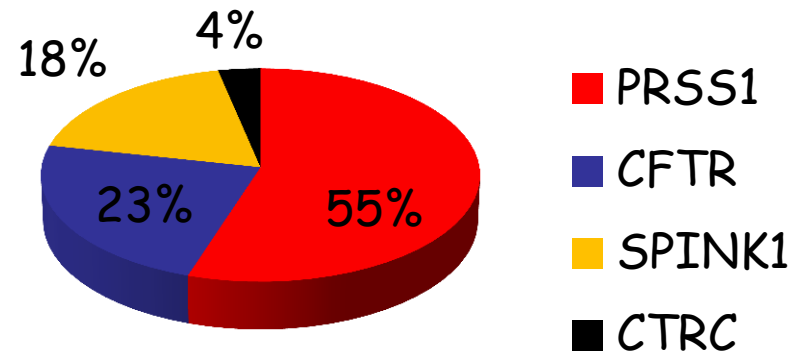


# Genetics of ARP and CP

ARP and CP (115 Pt)

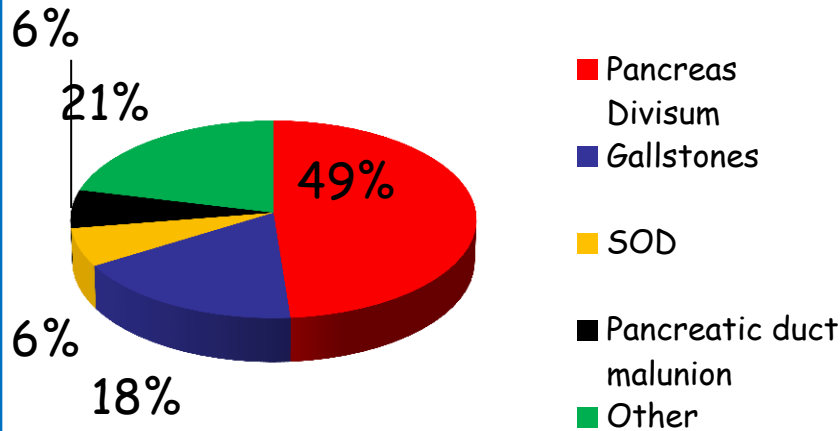


CP (51 Pt)

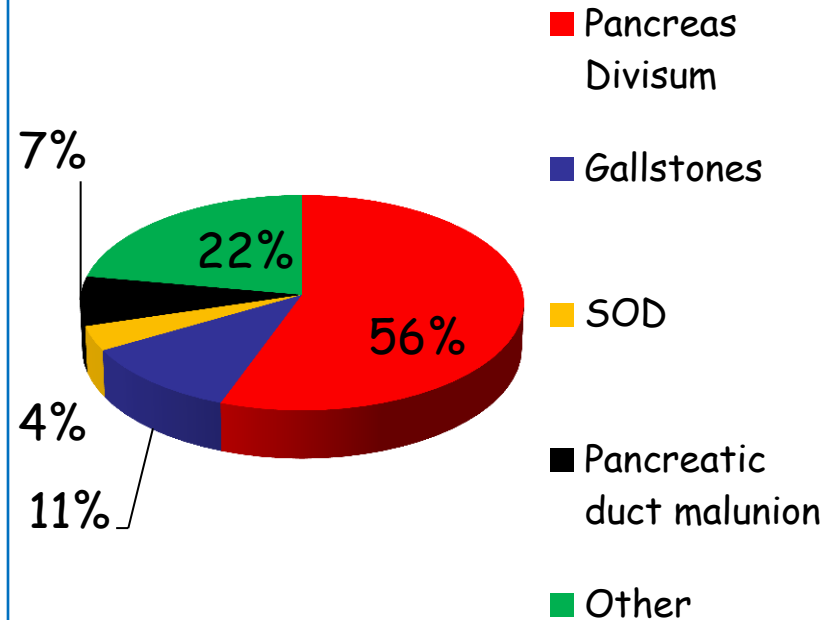


# Obstructive Etiologies

## ARP and CP (80 Pt)

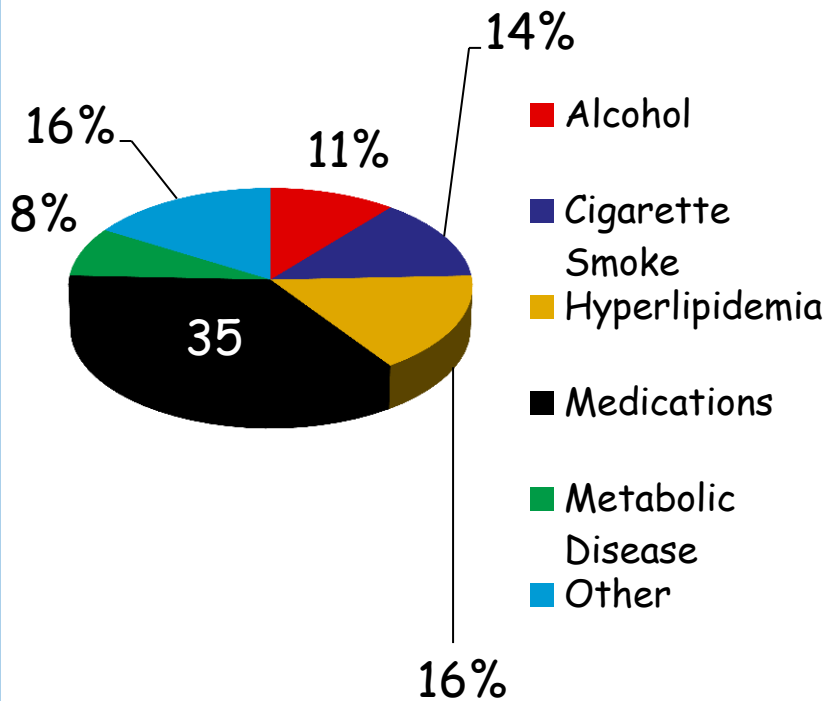


## CP (76 Pt)

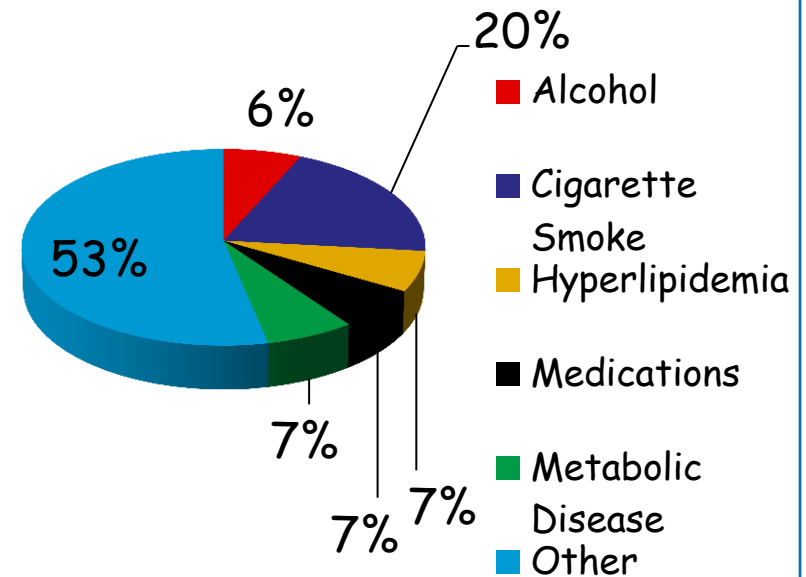


# Toxic/metabolic Etiologies

## ARP and CP (37 Pt)

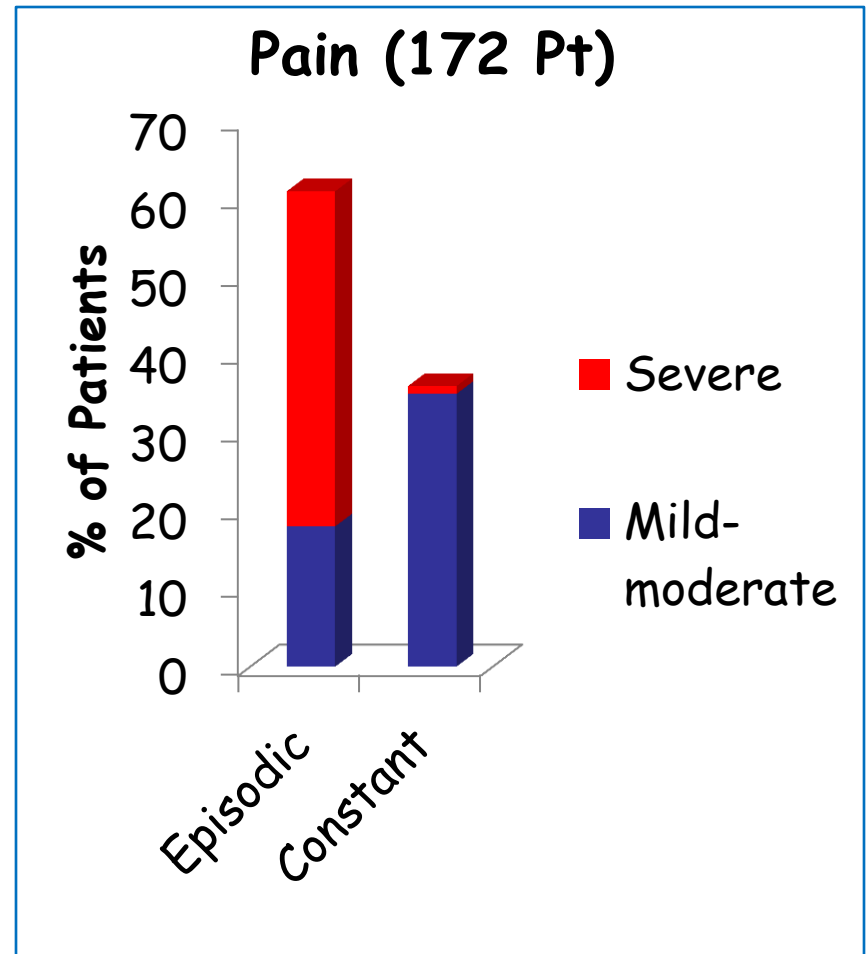


## CP (8 Pt)



# Disease Burden

- Median of 5 pancreatitis episodes per patient
- Median of 6 hospitalizations lifelong
- Pancreatitis interferes with enjoyment of life very much in 30%
- Patients miss an average of 5.4 school days a month
- 63% of patients with CP have surgery



# Conclusion

- Children have ARP and CP
- Unlike in adults, genetic and obstructive etiologies are the predominant causes of ARP and CP in children.
- ARP and CP significantly impact the lives of affected children.
- Novel approaches to treating ARP and CP are needed.

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