UPMC
LIFE CHANGING MEDICINE

CAPER Collaborative Alliance for Pancreatic Education and Research

Coexistence of Alcoholic Liver Disease and Alcoholic Pancreatitis

AJAY SINGHVI

MENTOR: DHIRAJ YADAV

CAPER PANCREAS SCHOLAR PRESENTATION

Background

- Alcohol use is a common problem worldwide
- Alcohol use disorder affects approximately 6.2% or 15.1 million adults in the United States
- Long standing alcohol use is a known cause of liver and pancreatic damage, leading to cirrhosis or chronic pancreatitis respectively.
- Research has yielded variable results regarding the prevalence of the coexistent alcohol-related pancreatic and liver conditions

National Institute on Alcohol Abuse and Alcoholism, U.S. Department of Health and Human Services
J Gastroenterol. 2004 Sep;39(9):879-87.
World J Gastroenterol. 2008 Oct 28;14(40):6171-9.

Background

- In clinical practice, the coincidence of both liver cirrhosis and chronic pancreatitis is uncommon
- These diseases share few risk factors other than alcohol consumption
  - No significant overlap in risk factors in Japanese alcoholics.
  - Duration of alcohol use required for disease development is greater in liver cirrhosis than in chronic pancreatitis

J Gastroenterol. 2004 Sep;39(9):879-87.
Am J Gastroenterol. 1991 Feb;86(2):201-4.
J Gastroenterol. 2004 Sep;39(9):879-87.

Background

- However, asymptomatic alcoholic liver disease may be frequent in chronic alcoholic pancreatitis (and vice versa).
  - If hepatic pathology unrecognized, surgical procedures can lead to complications that aggravate the clinical course
- Development of ascites and varices as a sequela of portal hypertension increases morbidity and mortality in patients with both disease processes·

Mt Sinai J Med. 1997 Mar;64(2):125-9.
Ital J Gastroenterol. 1995 Mar;27(2):69-72.

Background

- Controversy exists regarding the frequency of coincident chronic pancreatitis and liver cirrhosis in alcoholic patients
- Conflicting findings may be due to differences in:
  - Variable definitions of alcohol related conditions studied
  - Methodology: retrospective vs prospective studies
  - Evaluation of diagnostic parameters (i.e. clinical, functional, radiographic, or histopathological criteria)

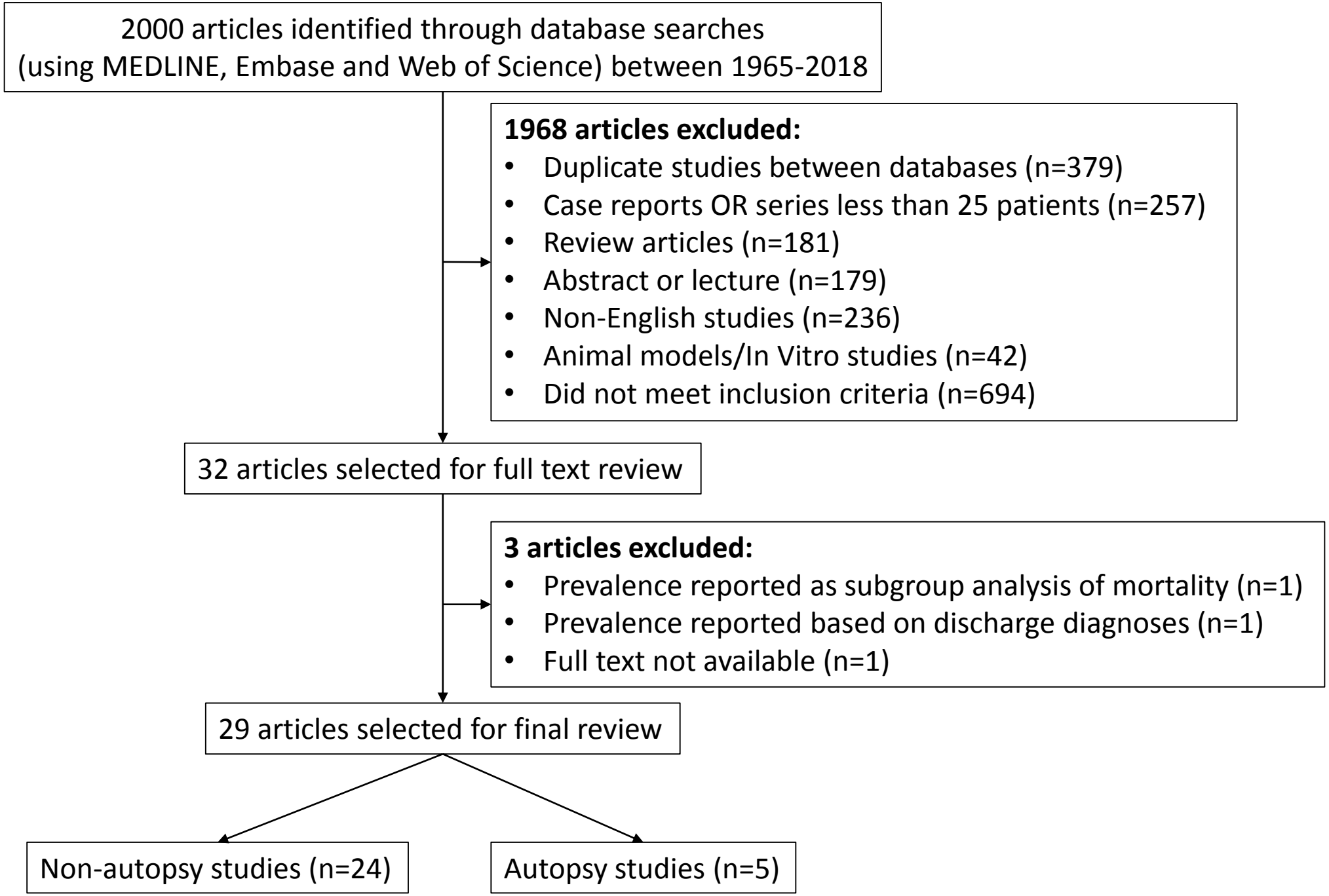
Digestion. 1992;51(2):86-94.
J Gastroenterol. 2004 Sep;39(9):879-87.
Dig Dis Sci. 1983 Dec;28(12):1089-93.
Gastrointest Endosc. 1999 Jun;49(6):705-9.
Dig Dis Sci. 1984 Jul;29(7):593-9.
Am J Gastroenterol. 1985 Dec;80(12):998-1003.

Aims: Systematic Review

- Determine robust prevalence estimates of coexistent
  - alcoholic cirrhosis and chronic pancreatitis
  - alcoholic liver disease and alcoholic pancreatitis among patients with a diagnosis of alcoholism
- Identify alcohol-related diseases that associate with alcoholic liver disease and alcoholic pancreatitis

Inclusion and Exclusion criteria

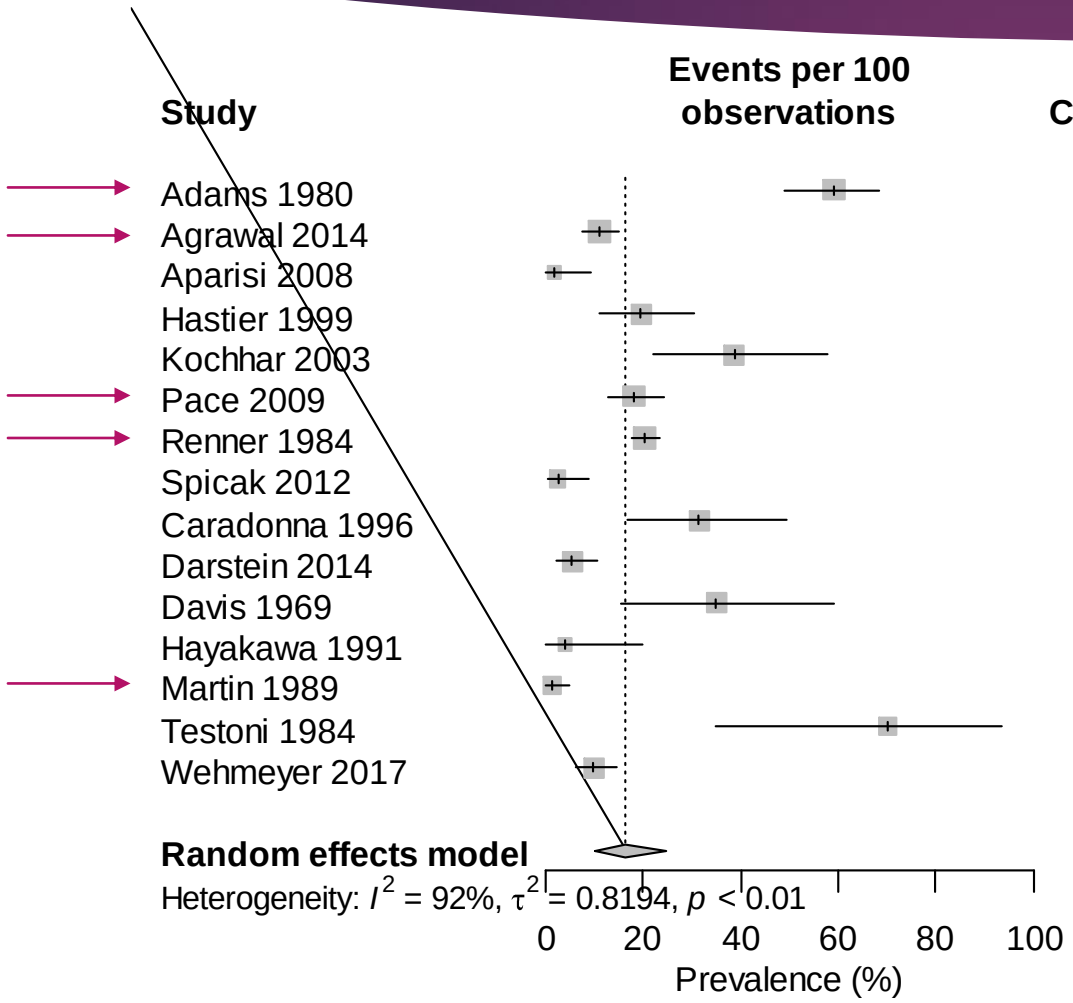
- Inclusion criteria
  - Studies that allowed for the calculation of prevalence of coexistent disease for alcoholic pancreatitis in alcoholic liver disease or alcoholic liver disease in alcoholic pancreatitis
  - Human studies
- Exclusion criteria
  - Non-English studies
  - Review articles and case studies/series < 25 patients
  - Abstracts without a full manuscript
  - Duplicate publications


2000 articles identified through database searches
(using MEDLINE, Embase and Web of Science) between 1965-2018
1968 articles excluded:
• Duplicate studies between databases (n=379)
• Case reports OR series less than 25 patients (n=257)
• Review articles (n=181)
• Abstract or lecture (n=179)
• Non-English studies (n=236)
• Animal models/In Vitro studies (n=42)
• Did not meet inclusion criteria (n=694)
32 articles selected for full text review
3 articles excluded:
• Prevalence reported as subgroup analysis of mortality (n=1)
• Prevalence reported based on discharge diagnoses (n=1)
• Full text not available (n=1)
29 articles selected for final review
Non-autopsy studies (n=24)
Autopsy studies (n=5)

Results

- Majority of studies were from Europe (59%) or North America (21%)
- Roughly 50% were published after year 2000
- Most included no or few female subjects
- Number of subjects
  - Alcoholic cirrhosis (n=2211 from 15 studies)
  - Chronic pancreatitis (n=652 from 11 studies)

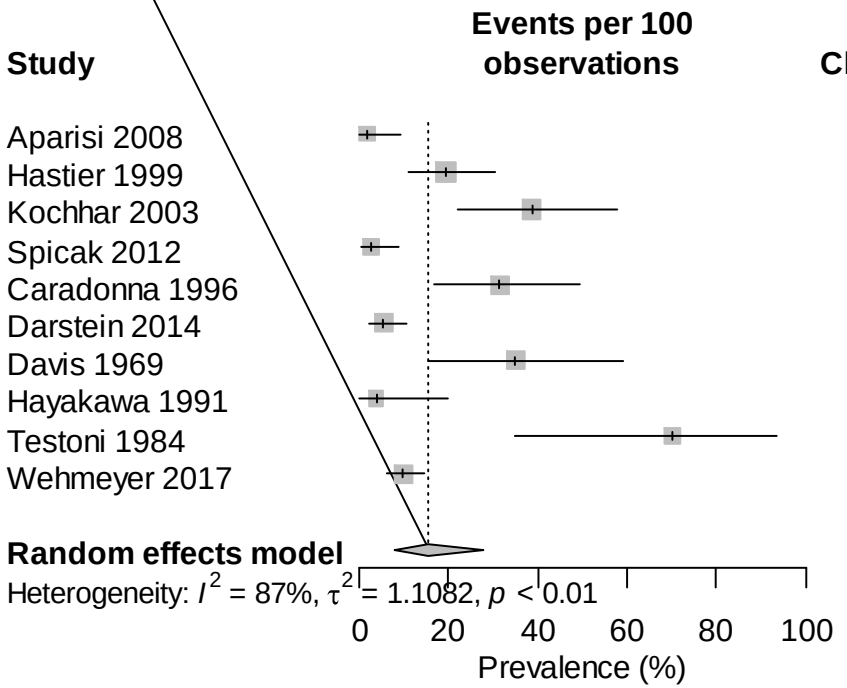
Prevalence of Alcoholic Chronic Pancreatitis in Alcoholic Cirrhosis



Study	Chronic Pancreatitis	Cirrhosis	Prevalence (%)	95% CI	Weight
Adams 1980	62	105	59.0	[49.0; 68.5]	9.3%
Agrawal 2014	32	292	11.0	[7.6; 15.1]	10.4%
Aparisi 2008	1	57	1.8	[0.0; 9.4]	0.4%
Hastier 1999	14	72	19.4	[11.1; 30.5]	4.1%
Kochhar 2003	12	31	38.7	[21.8; 57.8]	2.7%
Pace 2009	33	183	18.0	[12.8; 24.4]	9.9%
Renner 1984	159	783	20.3	[17.5; 23.3]	46.3%
Spicak 2012	2	80	2.5	[0.3; 8.7]	0.7%
Caradonna 1996	11	35	31.4	[16.9; 49.3]	2.8%
Darstein 2014	8	147	5.4	[2.4; 10.4]	2.8%
Davis 1969	7	20	35.0	[15.4; 59.2]	1.7%
Hayakawa 1991	1	26	3.8	[0.1; 19.6]	0.4%
Martin 1989	2	148	1.4	[0.2; 4.8]	0.7%
Testoni 1984	7	10	70.0	[34.8; 93.3]	0.8%
Wehmeyer 2017	22	222	9.9	[6.3; 14.6]	7.2%
Random effects model	**2211**		**16.2**	**[10.4; 24.5]**	**--**

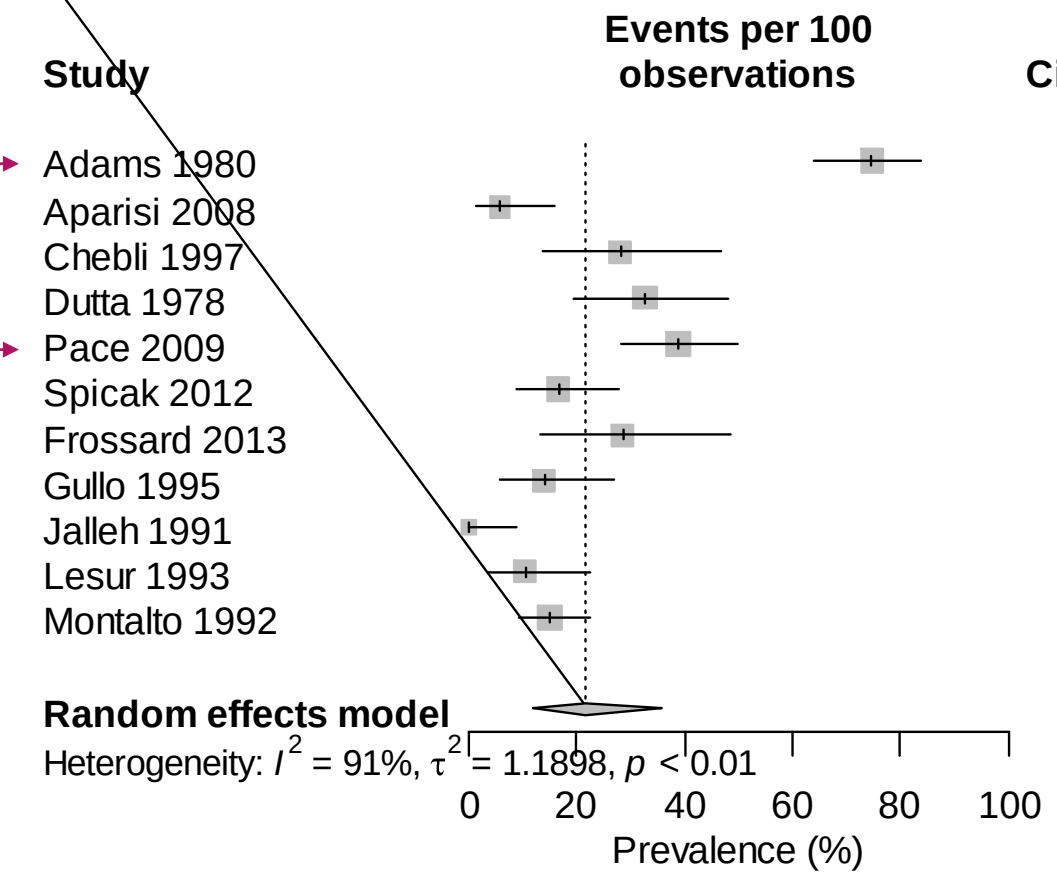
Heterogeneity: I^2 = 92%, τ^2 = 0.8194, p < 0.01

Prevalence of Alcoholic Chronic Pancreatitis in Alcoholic Cirrhosis (autopsy studies removed)



Study	Chronic Pancreatitis	Cirrhosis	Prevalence (%)	95% CI	Weight
Aparisi 2008	1	57	1.8	[0.0; 9.4]	1.5%
Hastier 1999	14	72	19.4	[11.1; 30.5]	17.6%
Kochhar 2003	12	31	38.7	[21.8; 57.8]	11.5%
Spicak 2012	2	80	2.5	[0.3; 8.7]	3.0%
Caradonna 1996	11	35	31.4	[16.9; 49.3]	11.8%
Darstein 2014	8	147	5.4	[2.4; 10.4]	11.8%
Davis 1969	7	20	35.0	[15.4; 59.2]	7.1%
Hayakawa 1991	1	26	3.8	[0.1; 19.6]	1.5%
Testoni 1984	7	10	70.0	[34.8; 93.3]	3.3%
Wehmeyer 2017	22	222	9.9	[6.3; 14.6]	30.9%
Random effects model	**700**		**15.5**	**[8.0; 27.7]**	**--**

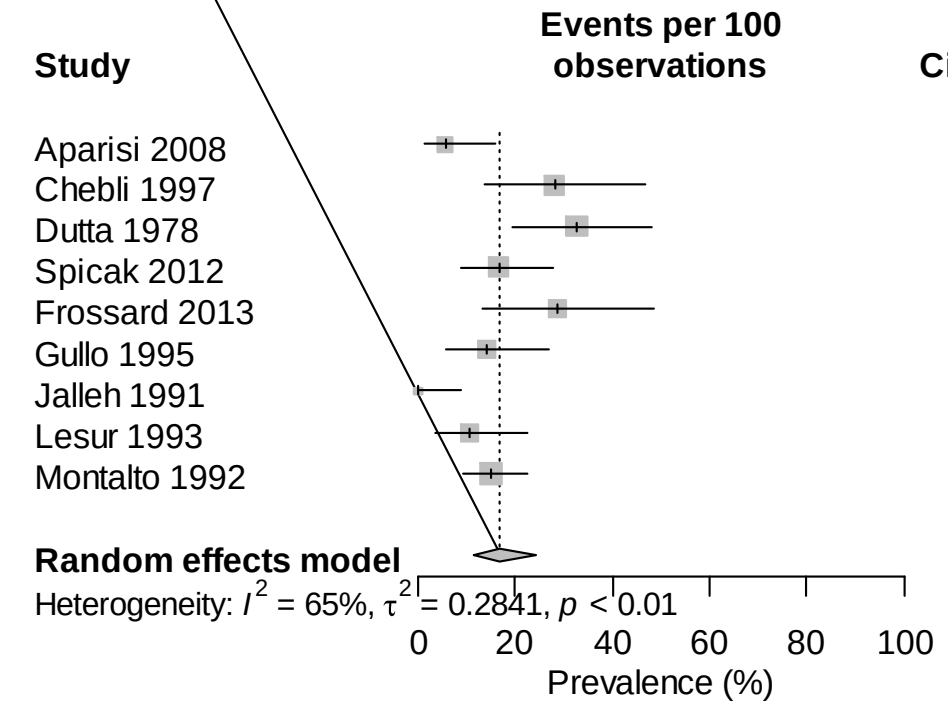
Prevalence of Alcoholic Cirrhosis in Alcoholic Chronic Pancreatitis



Study	Cirrhosis	Chronic Pancreatitis	Prevalence (%)	95% CI	Weight
Adams 1980	62	83	74.7	[64.0; 83.6]	16.3%
Aparisi 2008	3	53	5.7	[1.2; 15.7]	2.9%
Chebli 1997	9	32	28.1	[13.7; 46.7]	6.7%
Dutta 1978	15	46	32.6	[19.5; 48.0]	10.5%
Pace 2009	33	85	38.8	[28.4; 50.0]	20.9%
Spicak 2012	11	66	16.7	[8.6; 27.9]	9.5%
Frossard 2013	8	28	28.6	[13.2; 48.7]	5.9%
Gullo 1995	7	50	14.0	[5.8; 26.7]	6.2%
Jalleh 1991	0	40	0.0	[0.0; 8.8]	0.5%
Lesur 1993	5	48	10.4	[3.5; 22.7]	4.6%
Montalto 1992	18	121	14.9	[9.1; 22.5]	15.9%
Random effects model		**652**	**21.5**	**[12.0; 35.6]**	--

Heterogeneity: I^2 = 91%, τ^2 = 1.1898, p < 0.01

Prevalence of Alcoholic Cirrhosis in Alcoholic Chronic Pancreatitis (autopsy studies removed)



Study	Cirrhosis	Chronic Pancreatitis	Prevalence (%)	95% CI	Weight
Aparisi 2008	3	53	5.7	[1.2; 15.7]	4.7%
Chebli 1997	9	32	28.1	[13.7; 46.7]	10.7%
Dutta 1978	15	46	32.6	[19.5; 48.0]	16.7%
Spicak 2012	11	66	16.7	[8.6; 27.9]	15.1%
Frossard 2013	8	28	28.6	[13.2; 48.7]	9.4%
Gullo 1995	7	50	14.0	[5.8; 26.7]	9.9%
Jalleh 1991	0	40	0.0	[0.0; 8.8]	0.8%
Lesur 1993	5	48	10.4	[3.5; 22.7]	7.4%
Montalto 1992	18	121	14.9	[9.1; 22.5]	25.3%
Random effects model		**484**	**16.9**	**[11.5; 24.3]**	**--**

Summary of Results

- Pooled prevalence of Chronic Pancreatitis in overall Alcoholic Cirrhosis was 16.2% (95% CI 10.4-24.5)
  - After excluding autopsy studies was 15.5% (95% CI 15.5-27.7)
- Pooled prevalence of Alcoholic Cirrhosis in Chronic Pancreatitis overall was 21.5% (95% CI 12-35.6)
  - After excluding autopsy studies was 16.9% (95% CI 11.5-24.3)

Limitations of this systematic review

- Small sample sizes of individual studies
- Many of the studies were retrospective
- Geographical variation across countries and continents
- Comparing studies from different decades
- Variable criteria for defining alcoholic pancreatitis and alcoholic cirrhosis
  - Parameters used included clinical, functional, imaging, or histopathological criteria
- Few women

Administrative Data Study

- Study the prevalence of coexistent alcoholic pancreatitis and alcoholic cirrhosis
  - Larger sample sizes
  - Homogenous population
  - More female patients

Administrative Data Study

- Primary Aim: To determine the prevalence of alcohol-related comorbidities in patients with a diagnosis of alcoholism.
  - Alcoholic pancreatitis (acute/chronic)
  - Alcoholic hepatitis, Alcoholic cirrhosis
  - Coexistence of alcoholic cirrhosis + alcoholic pancreatitis
- Secondary Aim: To determine the prevalence of additional alcohol-related conditions (cardiomyopathy, withdrawal/DTs, Wernicke/Korsakoff, neuropathy) among patients with alcoholism

Study Design

- Retrospective cohort study
- Source population:
  - University of Pittsburgh Medical Center (UPMC) Medical Archival Retrieval System (MARS) to identify the patient cohort (2006-2015).
  - MARS collects all data from UPMC (outpatient, inpatient, billing)
- MARS will be used to screen all UPMC data using ICD-9/10 diagnosis codes

Disease groups

1. Group A: Alcoholism
   - Neuropsychiatric manifestations of Alcohol
   - Toxic Effects of Alcohol not otherwise specified
   - Sexual manifestations of alcohol
   - Cardiac manifestations of alcohol
   - Alcohol use disorder

Disease groups

2. Group B: Pancreatitis
   - Acute pancreatitis (unspecified etiology)
   - Acute pancreatitis, etiology biliary
   - Acute pancreatitis, etiology alcohol
   - Acute pancreatitis, etiology drug induced
   - Chronic pancreatitis, etiology alcohol
   - Chronic pancreatitis, (unspecified etiology)

Disease groups

3. Group C: Alcoholic Liver Disease
   - Alcoholic hepatitis
   - Alcoholic cirrhosis
   - Alcoholic liver disease (unspecified)
   - Alcoholic fatty liver
   - Alcoholic liver failure

Disease groups

- Group D: Other Liver Diseases
  - Hepatitis B (acute and chronic)
  - Hepatitis C (acute and chronic)
  - Hepatitis D
  - Unspecified viral hepatitis (acute and chronic)
  - Fatty liver disease
  - Hepatitis (not otherwise specified)
  - Cirrhosis not otherwise specified
  - Autoimmune hepatitis
  - Biliary cirrhosis
  - Liver failure, etiology not specified

Variables of interest

- Age at initial diagnosis
- Gender
- Race
- Inpatient admission (Y/N) for any of these diagnoses
  - Inpatient code that prompted admission
  - Number of inpatient admissions for each diagnosis
- Duration of contact with UPMC system
- Decompensated liver disease

Analysis Plan

- Calculate prevalence of individual condition and overlap
- Stratify prevalence results based on age, gender, and race
- Compare demographic and other relevant variables between groups
- Sensitivity analyses
  - Duration of follow-up in UPMC system, hospital type

Strengths and Limitations

- Strengths:
  - Large data set
  - Ability to provide data on women
- Limitations:
  - Use of ICD-9/10 diagnosis codes
  - Unable to capture data for some outpatient physician practices
  - Some hospitals came into UPMC system later during study period

Where are we now?

- We now have the data set
- Working on developing a detailed analysis plan

Questions?