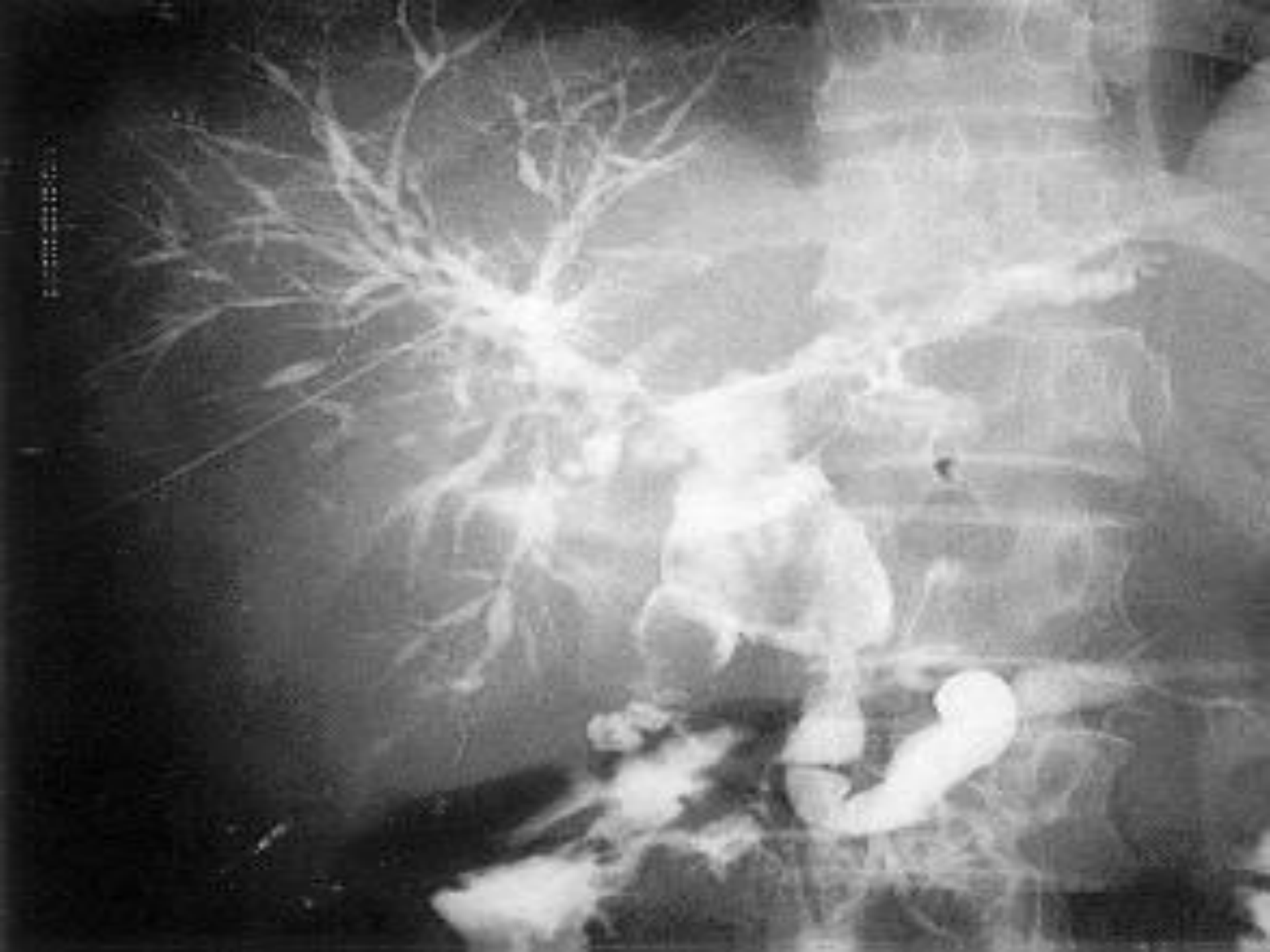


Prognosis of untreated  
Primary Sclerosing Cholangitis  
(PSC)

Erik Christensen  
Copenhagen, Denmark



# Study of Prognosis of PSC

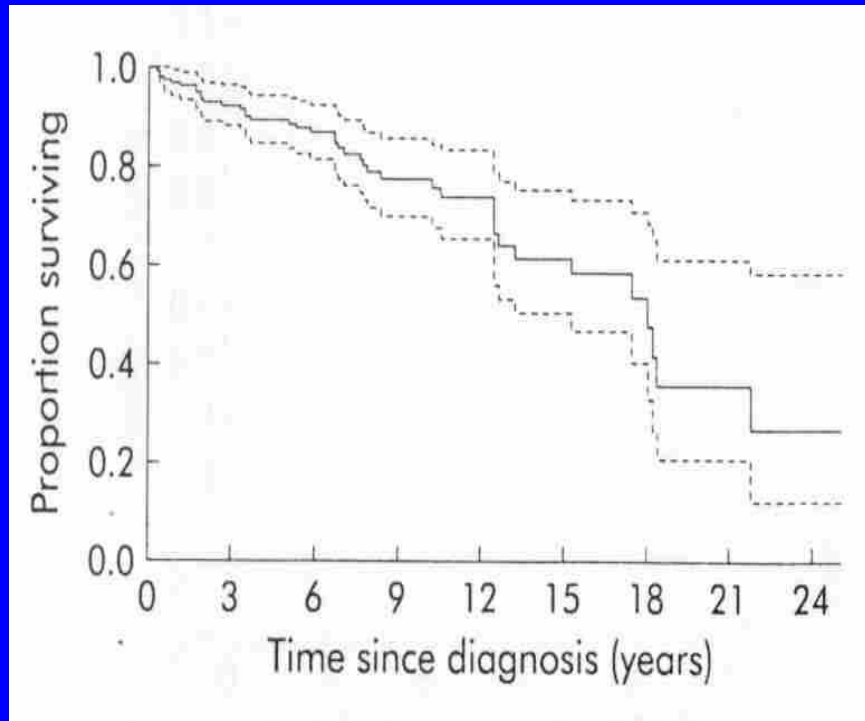
## Difficulties:

- Disease is rare
- The duration of the course of disease may be very long
- Course fluctuating
- Phases of improvement and deterioration
- Hard endpoints (death) delayed for many years
- No useful "soft" endpoints

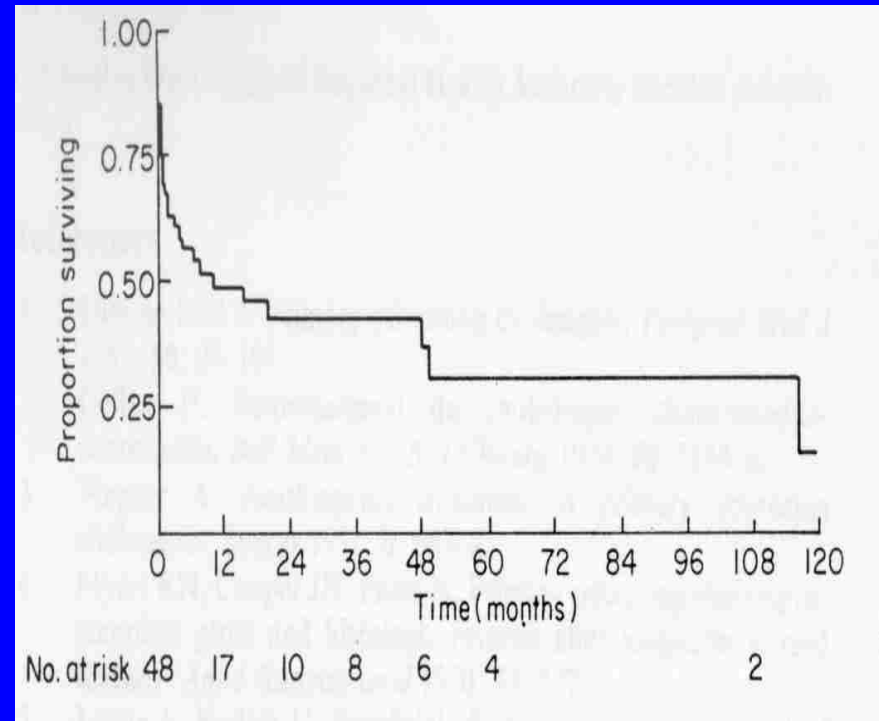
# Studies of Prognosis in PSC

	N =
• <b>Wiesner.</b> Hepatology. 1989;10:430-6.	174
• <b>Farrant.</b> Gastroenterology. 1991;100:1710-7.	126
• <b>Ismail.</b> Br J Surg. 1991;78:564-7.	48
• <b>Dickson.</b> Gastroenterology. 1992;103:1893-901.	426
• <b>Schrumpf.</b> J Hepatol. 1994;21:1061-6.	77
• <b>Broomé.</b> Gut. 1996;38:610-5.	305
• <b>Okolicsanyi.</b> Eur J Gastroenterol Hepatol. 1996;8:685-91.	117
• <b>Kim.</b> Mayo Clin Proc. 2000;75:688-94.	405
• <b>Boberg.</b> Hepatology. 2002;35:652-7.	330
• <b>Ponsioen.</b> Gut. 2002;51:562-6.	174

# Overall Survival in PSC



**Ponsioen.** Gut. 2002;51:562-6.



**Ismail.** Br J Surg. 1991;78:564-7.

# Prognostic variables in PSC – Univariate - Clinical 1

	Studies	P
Older Age	7	++ - +++
Long Duration of History	1	+++
Males	2	(+) - +
Presence of Symptoms	2	++
Inflammatory Bowel Disease	2	+

P: +++:  $p < 0.001$ ; ++:  $p < 0.01$ ; +:  $p < 0.05$ ; (+):  $p < 0.10$

# Prognostic variables in PSC – Univariate - Clinical 2

## *Early or Mild Symptoms and Signs*

	Studies	P
Pruritus	2	++ - +++
Fatigue	1	+++
Weight Loss	1	++
Fever	2	+
Abdominal Pain	2	+ - ++

P: +++:  $p < 0.001$ ; ++:  $p < 0.01$ ; +:  $p < 0.05$ ; (+):  $p < 0.10$

# Prognostic variables in PSC – Univariate - Clinical 3

## *Late or Advanced Symptoms and Signs*

	Studies	P
Ascites	5	++ - +++
Jaundice	4	+++
Varices	2	++ - +++
Variceal Bleeding	4	++ - +++
Hepatomegaly	5	+ - +++
Splenomegaly	5	+ - +++

P: +++:  $p < 0.001$ ; ++:  $p < 0.01$ ; +:  $p < 0.05$ ; (+):  $p < 0.10$



# Prognostic variables in PSC – Univariate – Biochemical Variables

	Studies	P
<b>Cholestasis</b>		
High Bilirubin	9	+ - +++
High Alkaline Phosphatase	6	(+) - ++
High Cholesterol	1	+++
<b>Liver Cell Destruction, Inflammation</b>		
High AST	6	(+) - +++
High Gamma Globulin	1	+
<b>↓ Liver Cell Function, Portal Hypertension, Hypersplenism</b>		
Low Albumin	7	(+) - +++
Prolonged Prothrombin Time	2	++ - +++
Low Haemoglobin	6	(+) - +++
Low Platelet Count	4	(+) - ++

P: +++: p<0.001; ++: p<0.01; +: p<0.05; (+): p<0.10

# Prognostic variables in PSC – Univariate – Structural Variables

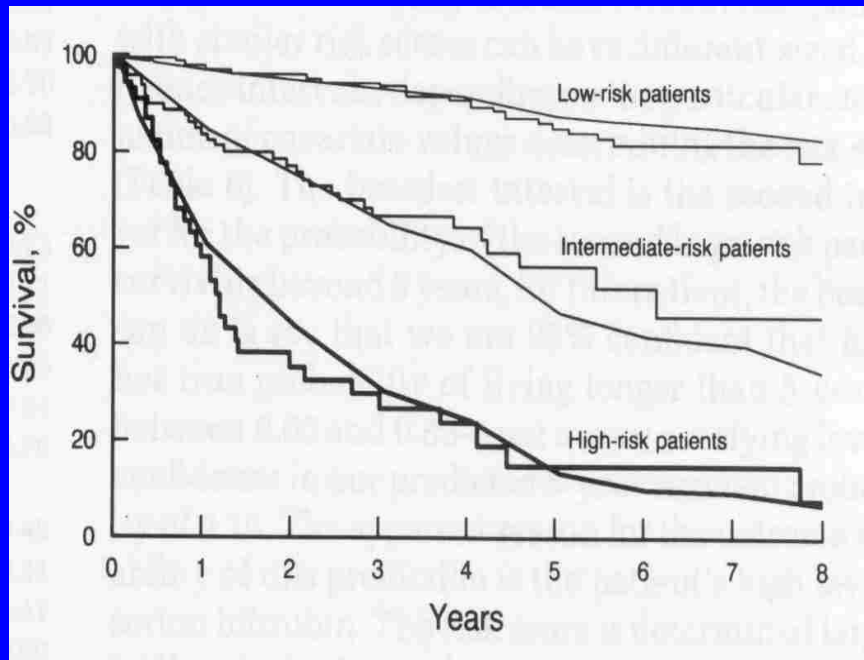
	Studies	P
<b>Macroscopic</b>		
Common bile duct stricture	1	+
Extrahepatic PSC	1	+++
High Cholangiographic Score	1	+++
<b>Microscopic - Early</b>		
Ductopenia	1	++
Cholestasis	2	++ - +++
Piecemeal Necrosis	1	+++
<b>Microscopic - Late</b>		
Portal Fibrosis	1	++
Advanced Histologic Stage	4	+++
Cirrhosis	1	++

P: +++: p<0.001; ++: p<0.01; +: p<0.05; (+): p<0.10

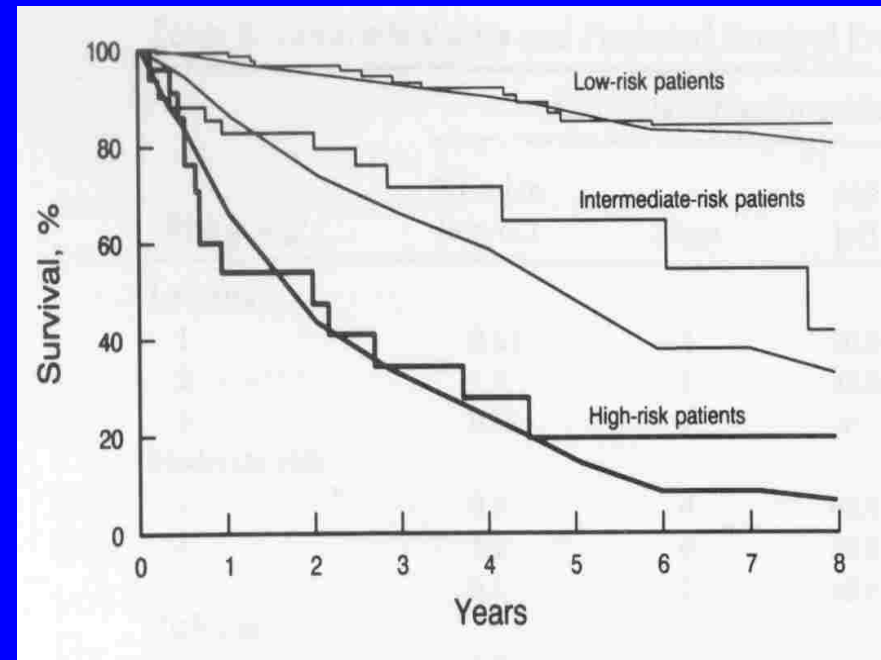


# Predicted and Observed Survival in High, Intermediate and Low Risk PSC Patients

Prediction in **Model Sample** Patients. N=426



Prediction in **Independent** Patients. N=199



**Dickson.** Gastroenterology. 1992;103:1893-901.

Model based on: Age, Splenomegaly, Bilirubin and Histological Stage.

# Cholangiographic scoring in PSC

Ponsioen. Gut. 2002;51:562-6.

Type of duct involvement/  
classification

Cholangiographic abnormalities

Intrahepatic (IHD)

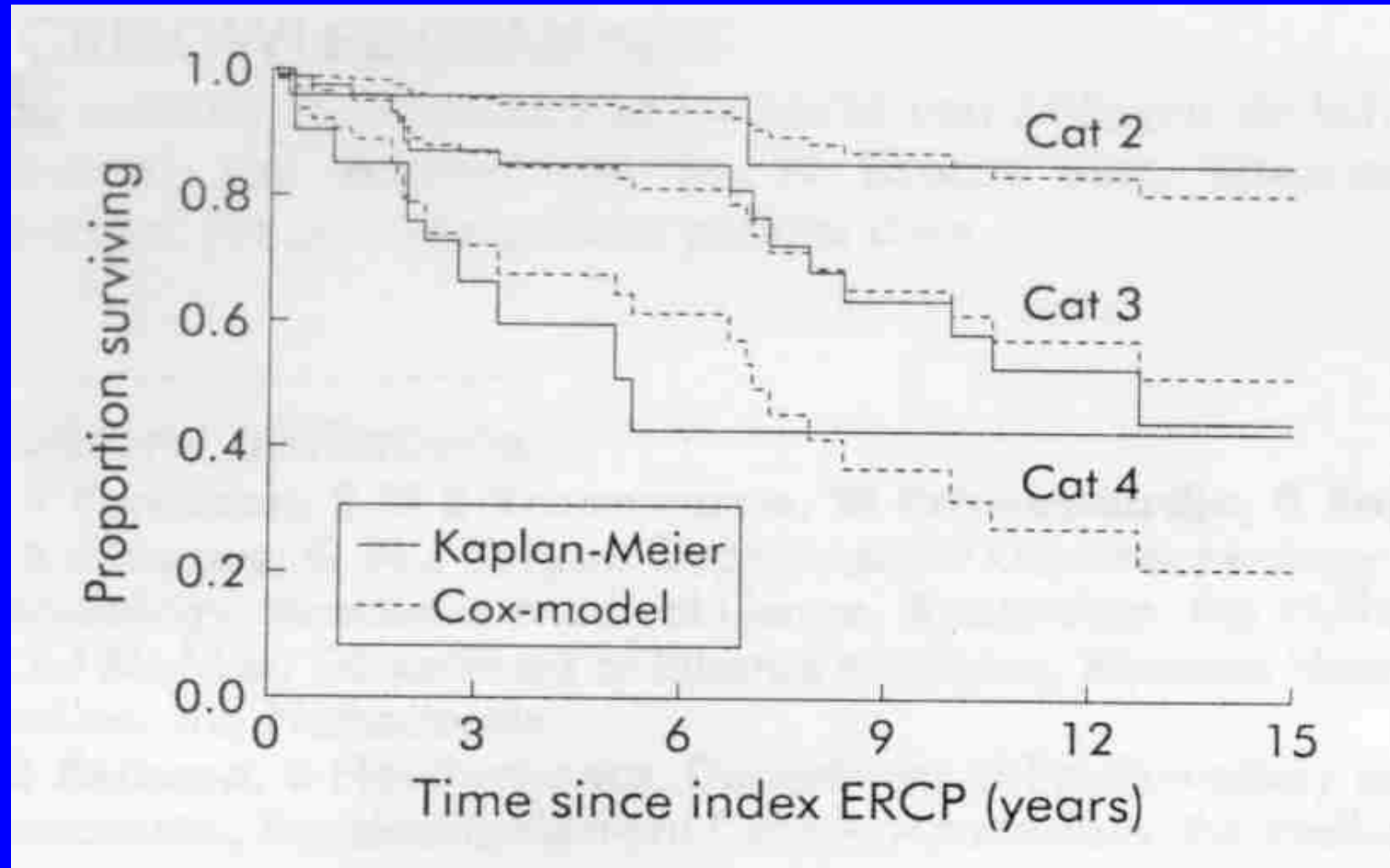
- |     |  |
|-----|--|
| 0   | No visible abnormalities   |
| I   | Multiple strictures; normal calibre of bile ducts or minimal dilatation        |
| II  | Multiple strictures, saccular dilatations, decreased arborisation              |
| III | Only central branches filled despite adequate filling pressure; severe pruning |

Extrahepatic (EHD)

- |     |  |
|-----|--|
| 0   | No visible abnormalities                                   |
| I   | Slight irregularities of duct contour; no stricture        |
| II  | Segmental stricture  |
| III | Stricture of almost entire length of duct                  |
| IV  | Extremely irregular margin; diverticulum-like outpouchings |

	IHD			
	0	I	II	III
EHD				
0	—	2	3	3
I	1	2	3	3
II	2	3	3	4
III	3	3	4	5
IV	3	3	4	5

# Survival Observed and Predicted from Combined Intrahepatic and Extrahepatic Cholangiographic Score



Ponsioen. Gut. 2002;51:562-6.

# Time-dependent Prognostic Model in PSC

Boberg. Hepatology. 2002;35:652-7.

Variable	Regression Coefficient	
	T-F	T-D
Ln (bilirubin)	0.411	1.044
Albumin	-0.089	-0.112
Age at diagnosis of PSC	0.027	0.013

The time-dependent model:

- Utilizes better the prognostic information
- Short-term prognostication is improved
- Better suited for monitoring of the patients

# Applicability of Prognostic Models in PSC

- *Guidance* to prognosis of individual patients
- Estimate *change* in short-term prognosis (time-dependent model)
- Assist in timing of liver transplantation (time-dependent model)
- Improved description of patient groups
- Illuminate pathogenesis
- Educational value



# Future development

- Further combination of data bases
- More widespread use of the time-dependent model
- Closer study of the correlation structure of the variables
- Inclusion of interaction terms
- Better variables (genetic, molecular) to describe the core problem(s) of the disease