

Outcome of 20 years of duodenal surveillance in FAP

The DAF II Study

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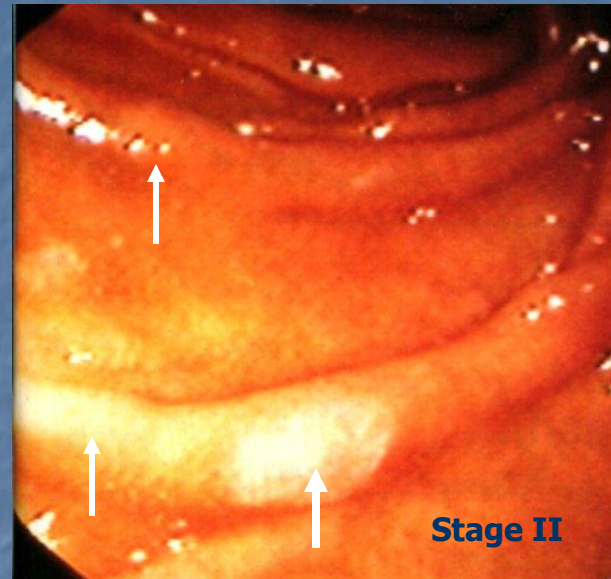
From The Danish, Swedish, Finnish and Dutch Polyposis Registries

Background

- The natural course and malignant potential of duodenal adenomatosis is well known
- The cancer risk increases by age and severity of the adenomatosis
- Regular endoscopic surveillance is recommended to identify high risk patients for close surveillance and prophylactic treatment -
- - but it has not yet been shown that surveillance will lead to a reduced cancer risk or improved survival

Duodenal adenomatosis

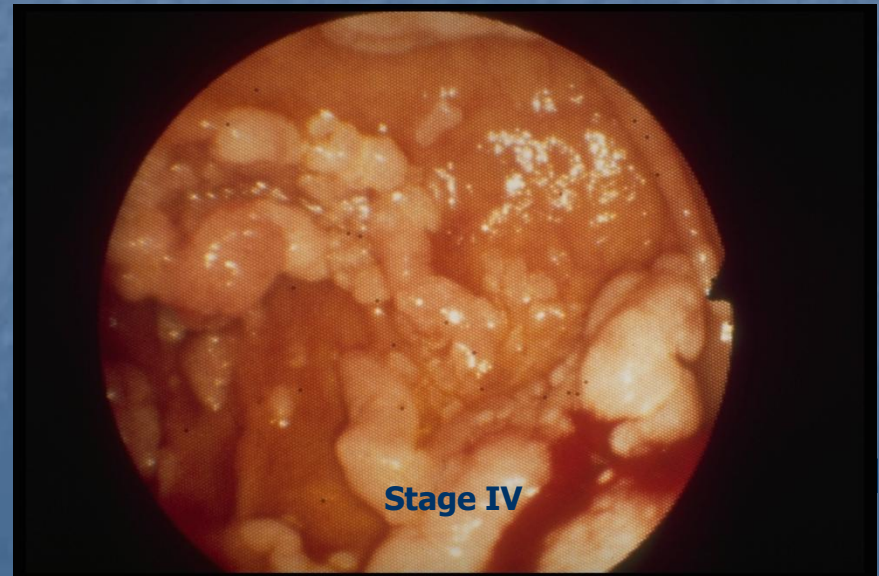
Multiple white sessile polyps on the mucosal folds in the 2nd and 3rd part



Spigelman Classification

Stage I - IV according to:

- Number of polyps
- Size of polyps
- Histological type
- Degree of dysplasia



Aim

Evaluation of the risk of severe adenomatosis and cancer after long-term duodenal surveillance

Methods and material

- Follow-up of patients in the DAF I Study *
- Data from the first and last duodenoscopy in the study period 1990 - 2010
- Update of vital statistics through public registries
- Statistical analysis including the chi²-test and Kaplan Meier analysis with log rank test and a significance level of 0.05

Data analysis

- Incidence of adenomatosis by age
- Incidence of adenomatosis Stage IV by age
- Changes in the severity of adenomatosis by time
- Incidence of cancer by age
- Over-all and cancer-specific survival after cancer (symptomatic vs. screen detected)
- Correlation between site of the *apc* mutation and development of adenomatosis stage IV and cancer

Results

306 patients	Denmark	105
	Finland	64
	Holland	35
	Sweden	102

Follow-up according to international guidelines *

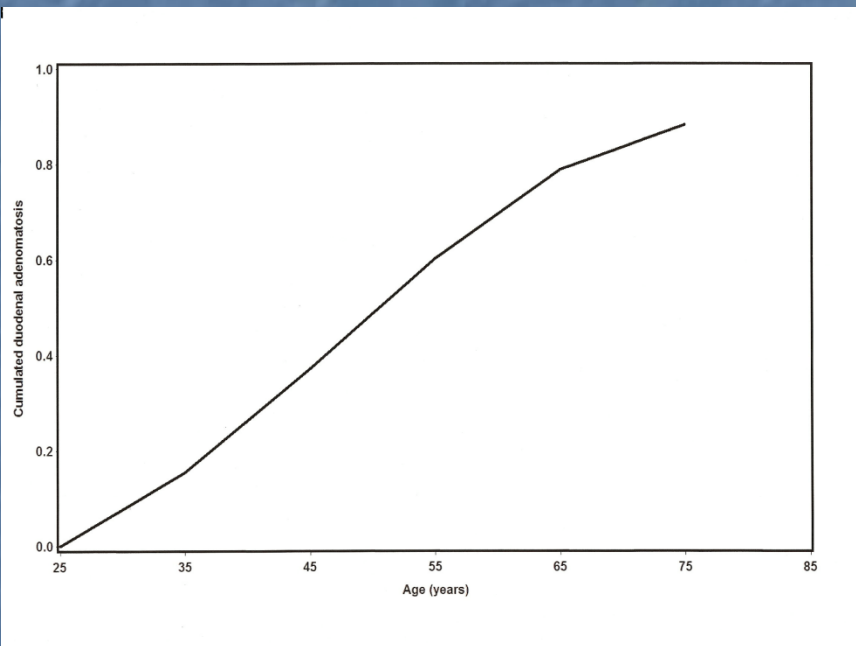
Median follow-up 14 years (range 1-20)

265 (87%) had at least two endoscopies

* Groves 2002, Bülow 2004, Gallagher 2006, Vasen 2008

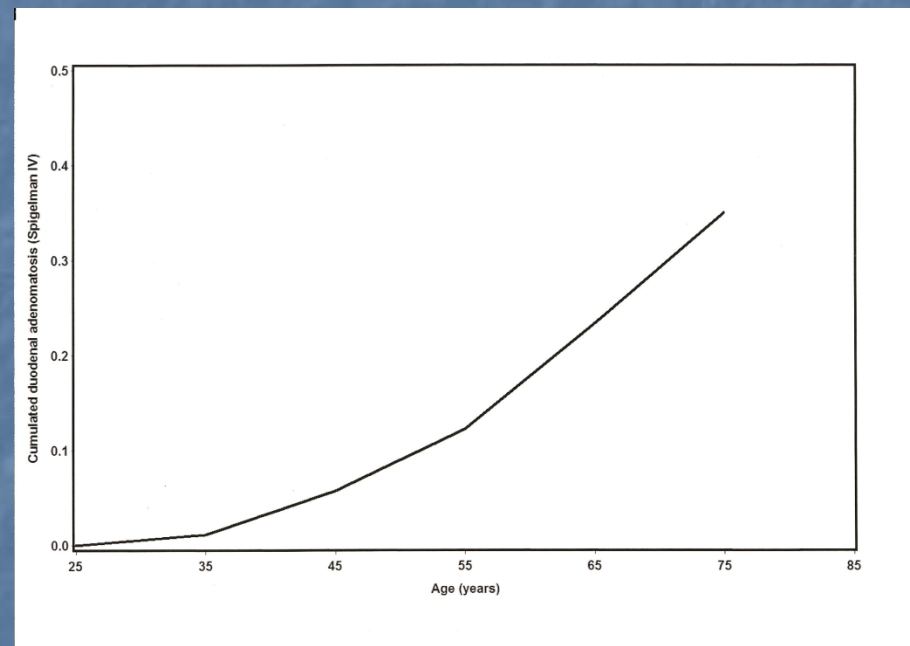
Adenomatosis by age

Cumulative adenomatosis



Life-time risk * **88%** (95% CI 84-93)

Cumulative Spigelman stage IV



Life-time risk * **35%** (95% CI 25-45)

* Cumulative incidence at age 75 y

Spigelman stage

Changes in Spigelman stage from the index endoscopy to the last endoscopy:

- by one or by two stages:

"Improvement"	33	(13%)
No change	88	(34%)
Worsening	116	(44%)
Unknown	25	(10%)

Cancer

N = 20

Two patients had a symptomatic cancer at the index endoscopy

During the study period 18 (6%) developed cancer at a median age of 56 years (range 44-82):

- 4 symptomatic interval cancers

- 9 screen-detected in asymptomatic patients

- 5 incidental findings in the operative specimen after prophylactic surgery for severe adenomatosis

Cancer

Location

True duodenal	4 (20%)
Periampullary	10 (50%)
Unknown	6 (30%)

UICC stage III or IV

Symptomatic cancer	5/6	
Screen-detected + incidental	0/14	(p<0.0001)

According to Spigelman stage at the index endoscopy

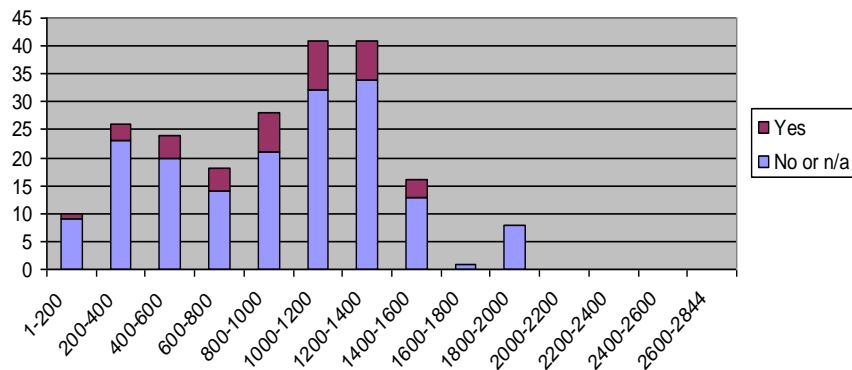
Stage 0-I	0	
Stage II-III	15/121 (12%)	
Stage IV	5/15 (33%)	(p<0.0001)

Mutation site

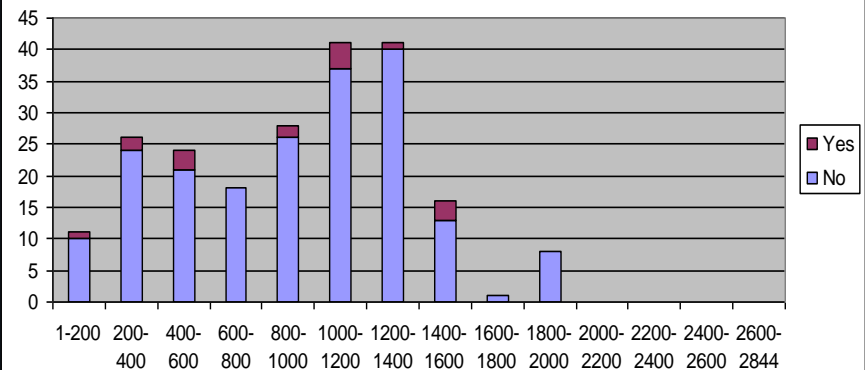
An *apc*-gene mutation was identified in 232 patients (76%):

Codon group	No.	Spigelman IV (p=0.46)	Cancer (p=0.83)
< 1250	164	32	12
1250-1464	32	5	2
> 1464	21	2	3
Promoter region	13	2	0
Entire gene	2	0	0

Spigelman IV



Duodenal cancer



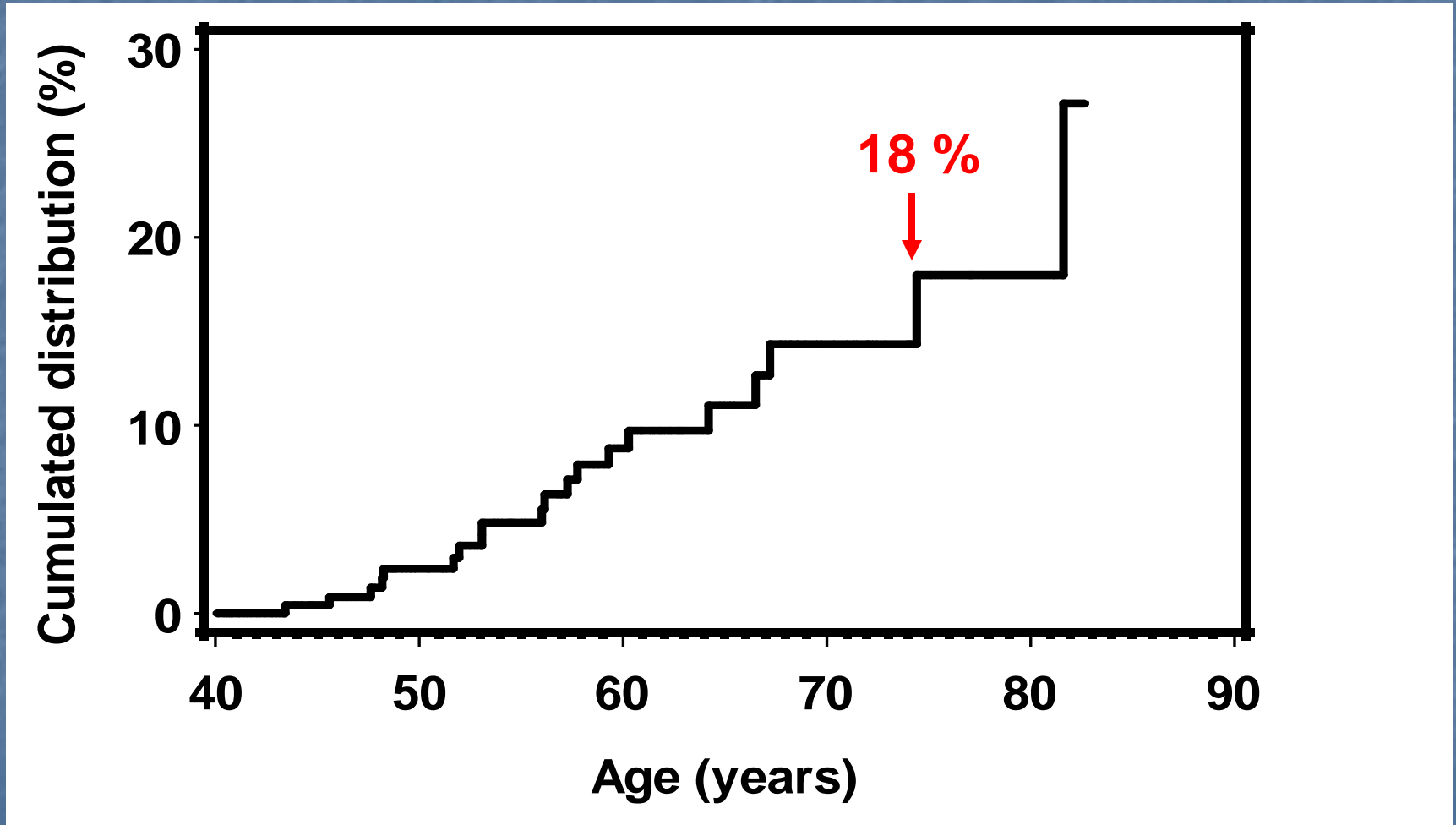
Surgery

N = 59

Pylorus-/pancreas sparing duodenectomy	23 *	
Whipple's operation:	26	11 for cancer 15 for adenomatosis
Open duodenectomy with polypectomy	10	
<hr/>		
Postoperative mortality	0	

* Invasive carcinoma found in the operative specimen in 5 (22%) patients

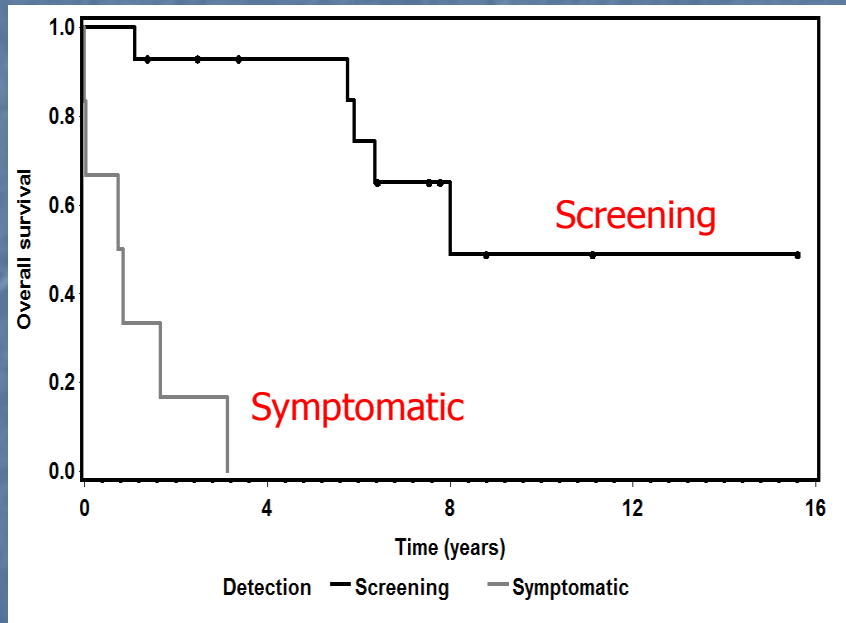
Life-time cancer risk*



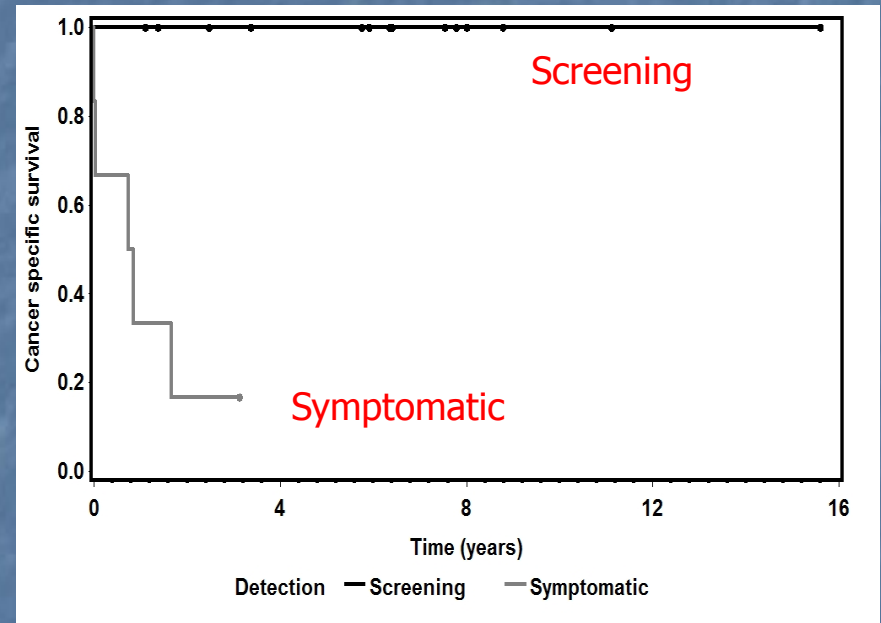
* Cumulative risk at age 75: 18% (95% CI 8-28)

Survival

Over-all survival



Cancer-specific survival



$p < 0.0001$

Conclusions

- The life-time risk of severe adenomatosis is 35%
- The life-time risk of cancer is 18%
- **Endoscopic surveillance can identify patients at high cancer risk**
- **Screen-detected cancer carries a good prognosis after surgery**