



Identification of high risk groups increases the effectiveness of colon cancer screening

European Conference on Colon Cancer Prevention
in Europe, Brussels, 8-9 May 2007

Hans FA Vasen

The Netherlands Foundation for the Detection of Hereditary Tumours

&

Department of Gastroenterology
Leiden University Medical Centre

The Dutch Hereditary Cancer Registry



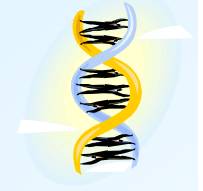
Start 1985 financially supported
by government

To promote early detection of
hereditary cancer syndromes



Outline presentation

- High risk groups
 - which groups?
 - CRC-risk?
 - frequency?
- Surveillance
 - protocols?
 - effectiveness?
- Identification



1. High risk groups

Hereditary CRC

Familial CRC

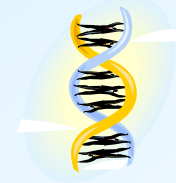
Personal history
CRC/CRA

other diseases

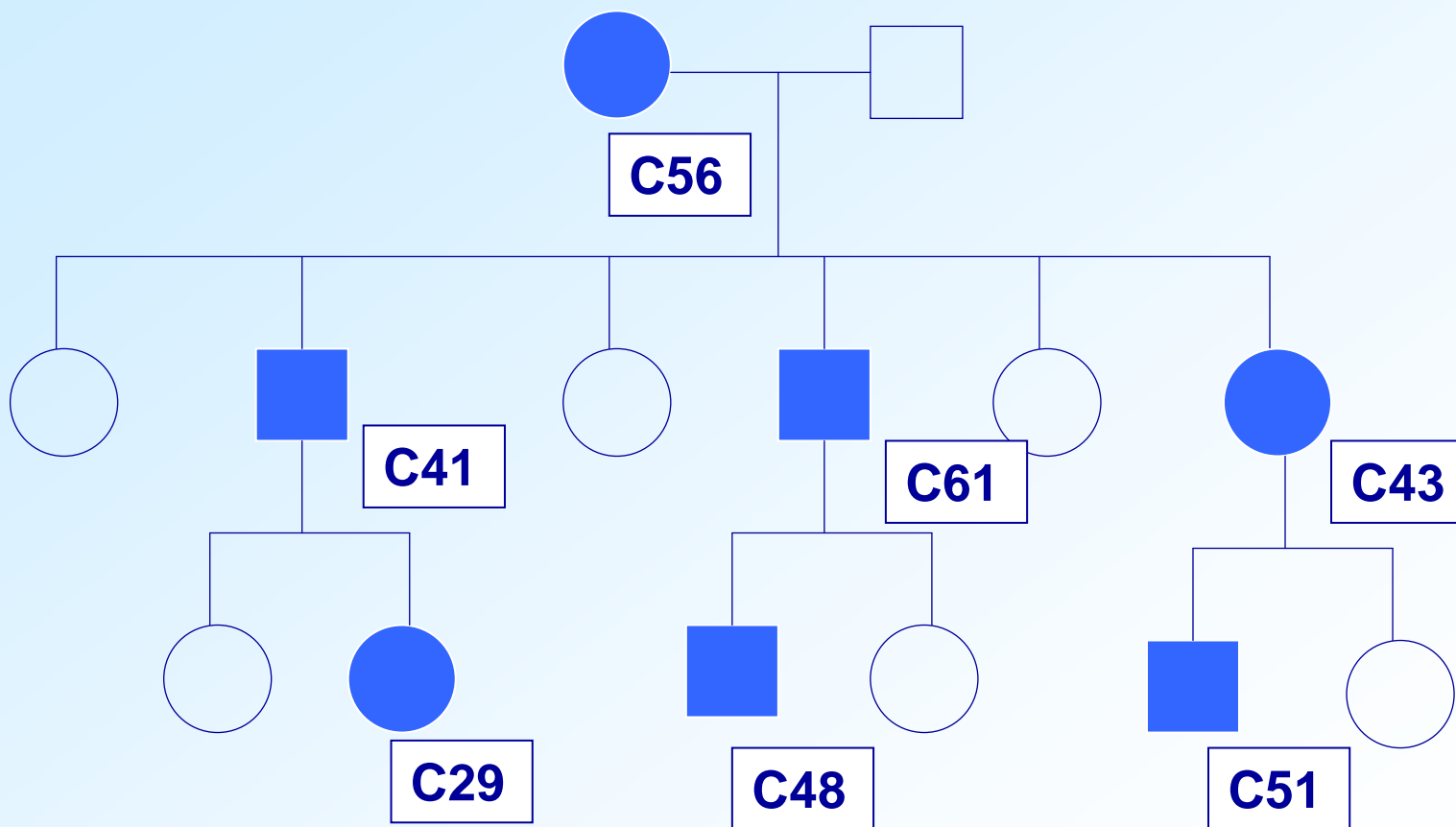


1. High risk groups

	CRC risk
Hereditary CRC	>50%
Familial CRC	20%
Personal history CRC/CRA	15-20%
other diseases	10-20%



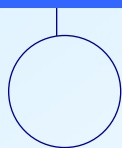
Hereditary colorectal cancer



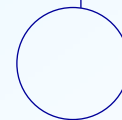


Hereditary colorectal cancer

Her. Non-Polyposis CRC (HNPCC) (MMR-genes)
Fam. adenomatous polyposis (APC/MUTYH-gene)
Peutz-Jeghers syndrome (STK11-gene)
Juvenile polyposis (SMAD4-gene)
Cowden syndrome (PTEN-gene)



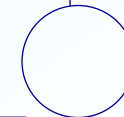
C29



C48

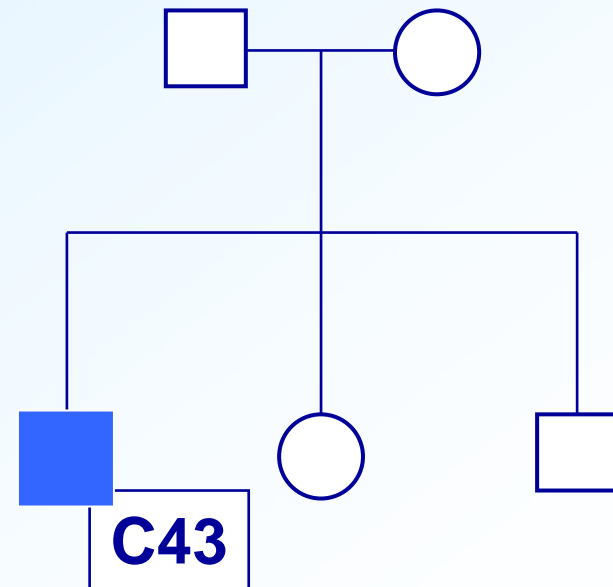
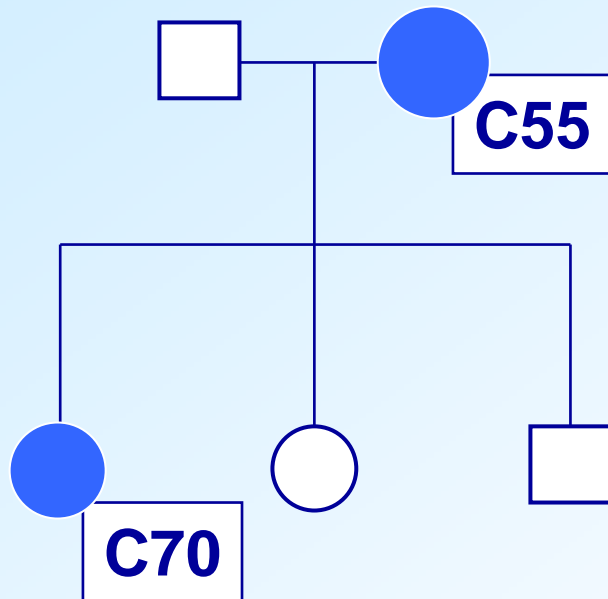


C51

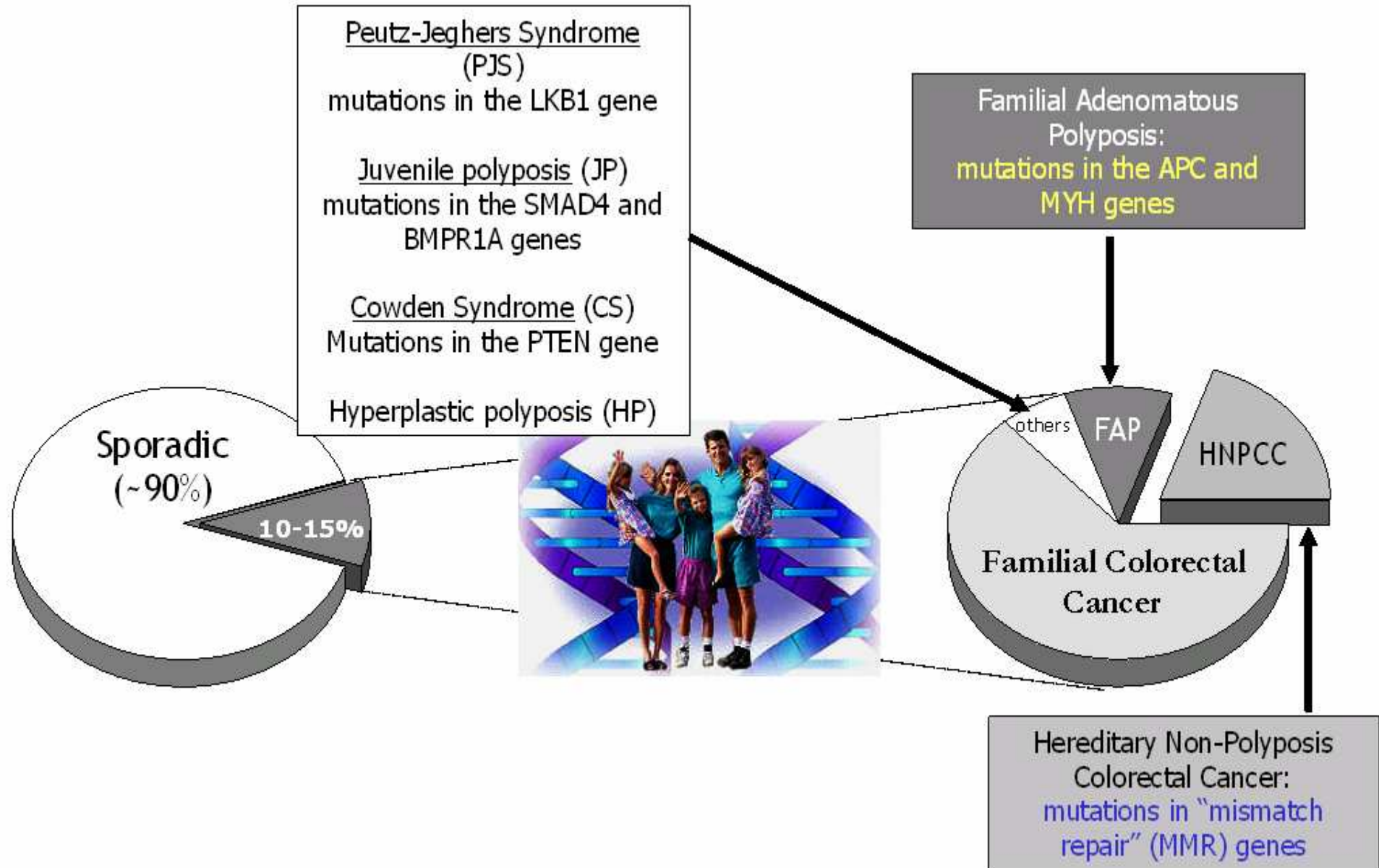




Familial colorectal cancer



Frequency of familial / hereditary CRC



The frequency of a positive family history for colorectal cancer: a population-based study in the Netherlands

A.E. de Jong, H.F.A. Vasen*

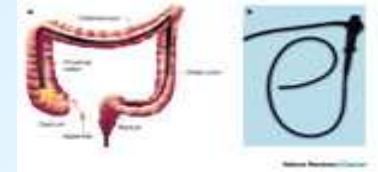
Questionnaires 5072 individuals 45<<70 yrs in Coevorden

First degree relatives with CRC	Number
≥ 1 CRC	438 (11.1%)
- 1 CRC < 50 jr	- 46
- 2 CRC	- 32
- ≥ 3 CRC	- 10
High risk groep (>20% CRC risk)	- 88 (2.2%)

The frequency of a positive family history for colorectal cancer: a population-based study in the Netherlands

Estimated number of high risk individuals (45<<70 yrs)

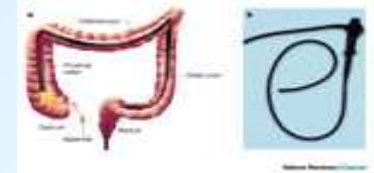
<u>Country</u>	<u>Number</u>
Germany	640.000
France	400.000
UK	400.000
Italy	400.000
Spain	260.000



2. Surveillance of high-risk groups

Advantages

- Compliance +++
- Young age hereditary CRC

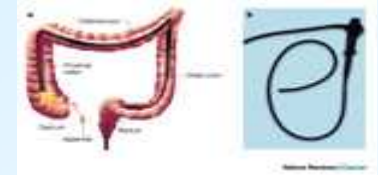


GASTROENTEROLOGY 2005;128:280-287

Screening Behavior of Individuals at High Risk for Colorectal Cancer

EVELINE M. A. BLEIKER,* FRED H. MENKO,[†] BABS G. TAAL,[§] IRMA KLUIJT,[¶]
LIDWINA D. V. WEVER,* MIRANDA A. GERRITSMA,* HANS F. A. VASEN,^{||} and
NEIL K. AARONSON*

Hereditary/familial CRC	149 subjects
Compliance	97%

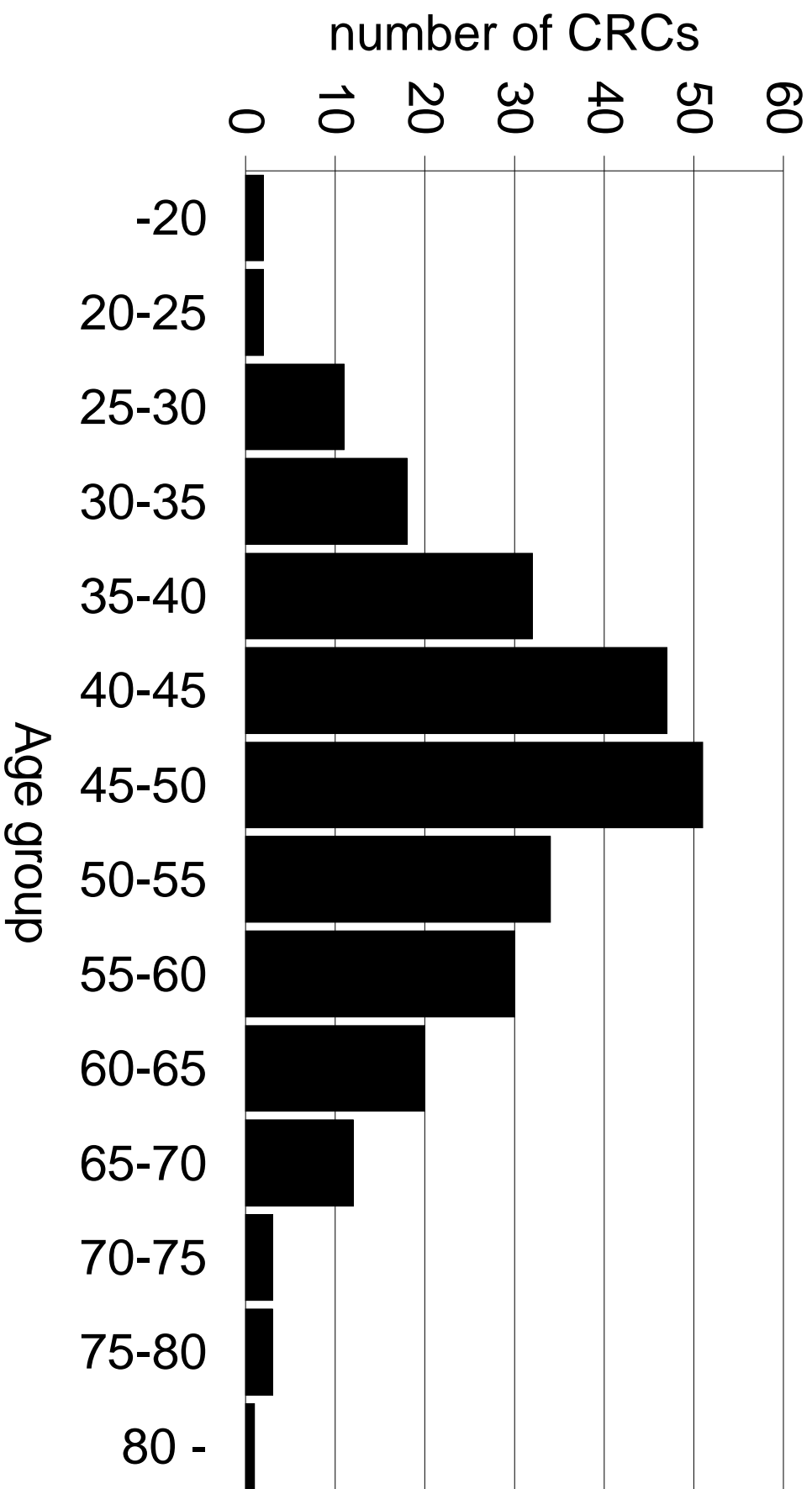


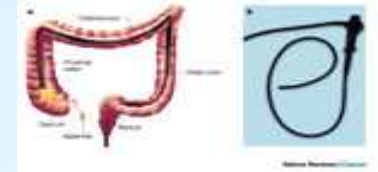
2. Surveillance of high-risk groups

Advantages

- Compliance +++
- Young age hereditary CRC

Age Distribution 264 CRC in hereditary CRC

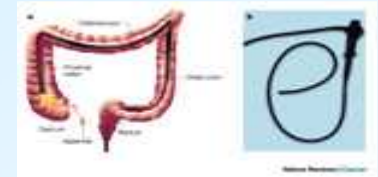




Familial / hereditary CRC surveillance protocol

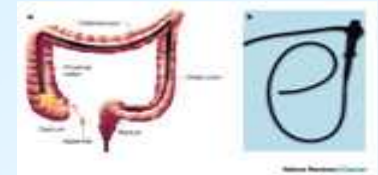
Hereditary CRC: colonoscopy 1x / 1- 2 yrs

Familial CRC: colonoscopy 1x / 3 - 6 yr



Effectiveness surveillance Hereditary CRC

- Hereditary Cancer Registries
 - UK, Denmark, Finland, Norway, Sweden, Netherlands, Italy, Germany, Belgium, other countries
- Aims
 - to promote surveillance
 - to guarantee continuity of lifelong surveillance
 - to evaluate effectiveness



Effectiveness surveillance

GASTROENTEROLOGY 2006;130:665–671

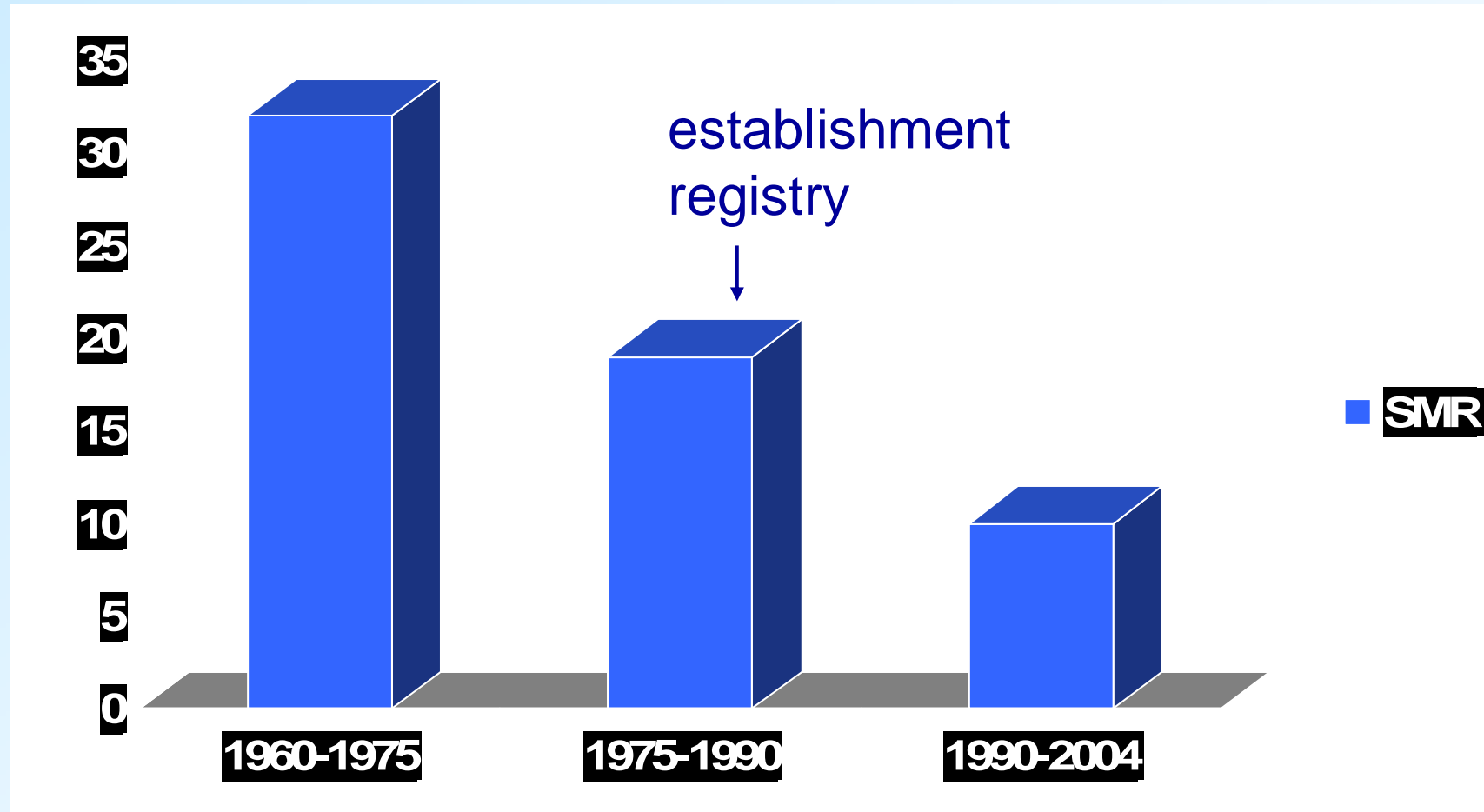
Decrease in Mortality in Lynch Syndrome Families Because of Surveillance

ANDREA E. DE JONG,^{*,†} YVONNE M. C. HENDRIKS,[§] JAN H. KLEIBEUKER,[¶]
SYBRAND Y. DE BOER,^{||} ANNEMIEKE CATS,[#] GERRIT GRIFFIOEN,[†] FOKKO M. NAGENGAST,^{**}
FRITS G. NELIS,^{††} MATTI A. ROOKUS,^{§§} and HANS F. A. VASEN^{*,†}

^{*}The Netherlands Foundation for the Detection of Hereditary Tumors, [†]Department of Gastroenterology and [§]Department of Human and Clinical Genetics, Leiden University Medical Center, Leiden; [¶]Department of Gastroenterology, University of Groningen and University Medical Center Groningen, Groningen; ^{||}Rijnstate Hospital Arnhem, Arnhem; [#]The Netherlands Cancer Institute, Amsterdam; ^{**}University Medical Center Nijmegen, Nijmegen; ^{††}Sophia Hospital Zwolle, Zwolle; and ^{§§}Department of Epidemiology, The Netherlands Cancer Institute, Amsterdam, The Netherlands

- 140 families: 2788 carriers and FDR
- 733 deaths: 445 cancer; 50% CRC

Standard mortality rate CRC in three time periods



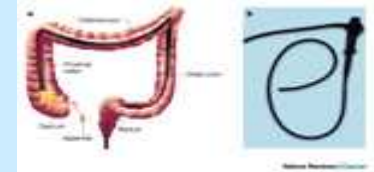
Costs

Her.Cancer Registry vs treatment CRC

■ Annual costs Registry:	350.000 euro
■ Costs treatment metastatic CRC (5-FU/leucovorin/irinotecan/avastin)	250.000 euro

Detecting 1.5 patient per year with CRC at stage A or B covers the costs of the registry

Effectiveness surveillance Familial CRC

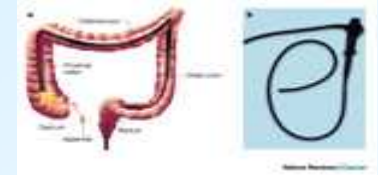


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Colonoscopy in Colorectal-Cancer Screening for Detection of Advanced Neoplasia

Jaroslawn Regula, M.D., Maciej Rupinski, M.D., Ewa Kraszewska, M.Sc.,
Marcin Polkowski, M.D., Jacek Pachlewski, M.D., Janina Orłowska, M.D.,
Marek P. Nowacki, M.D., and Eugeniusz Butruk, M.D.



Predictive factors for presence of advanced adenomas

- Age
- Sex
- Family history

	Total number	Nr needed to screen to find one AAP
<u>Negative FH</u>		
men	889	30
women	1503	52
<u>Positive FH</u>		
<u>FDR CRC>60</u>		
men	1171	23
women	1949	37
<u>FDR CRC<60</u>		
men	532	17
women	916	27
<u>2 FDR CRC</u>		
men	54	11
women	92	16

Appropriate interval?

The FACTS study 2003-2013

The National Familial Colorectal
Cancer Screening Study



Aims

Yield surveillance

Appropriate interval (3 or 6 yr)

Predictive factors

Association environmental factors

Costs



Protocol FACTS study

First colonoscopy:

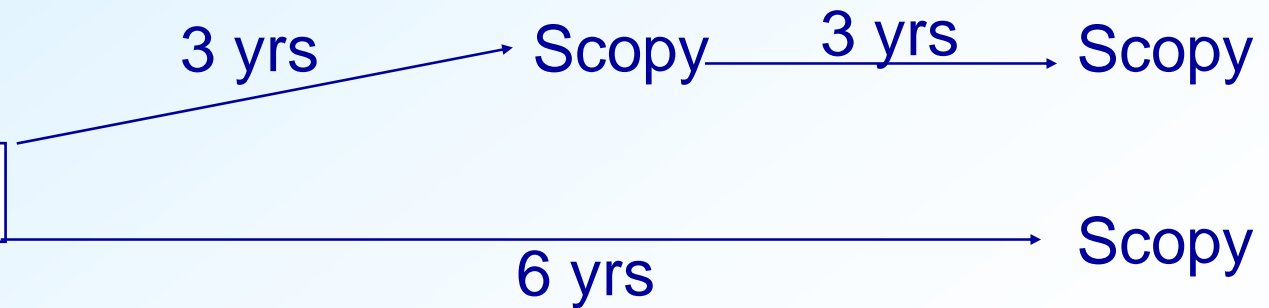
Group A

Multiple adenomas
(≥ 3)



Group B

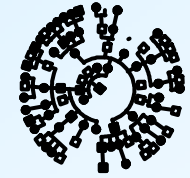
0,1,2 adenomas



2007: 550 patients (CRC risk 20%)

2013

3. Identification



1913 First family Hereditary CRC (Alfred Warthin)

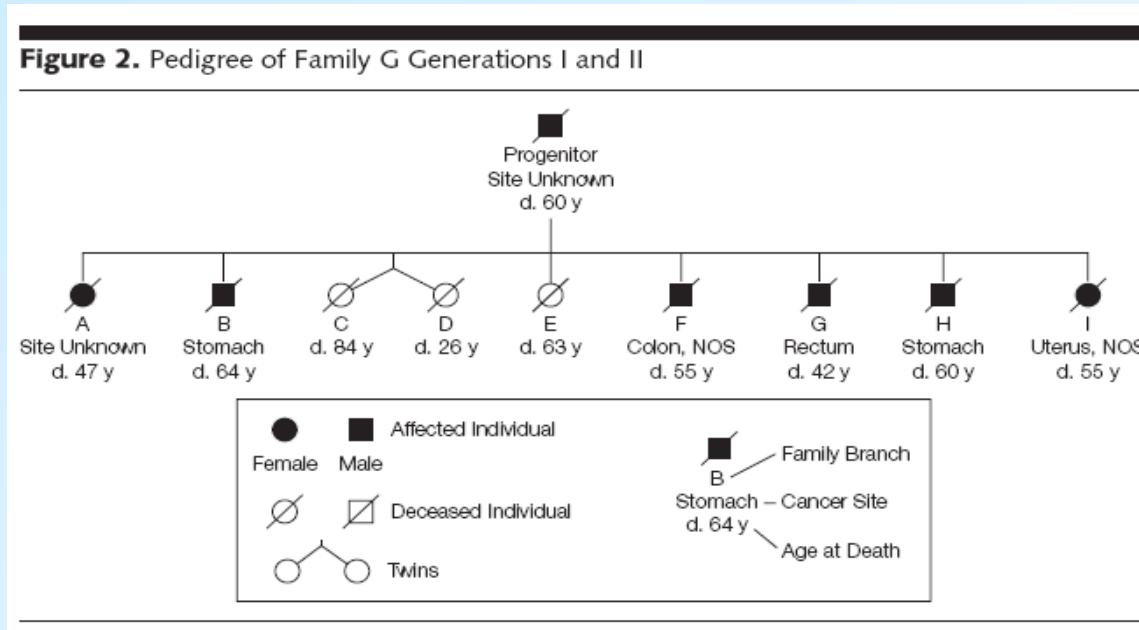
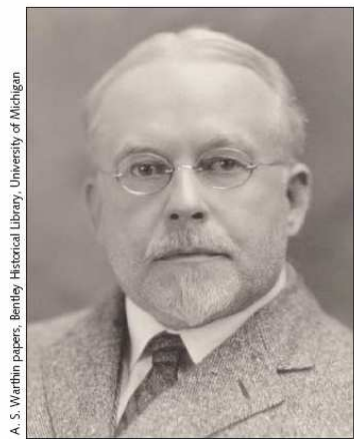
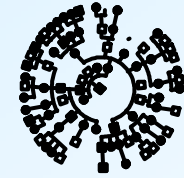


Figure 1. Aldred Scott Warthin, MD, PhD



1966 Two families (HT Lynch)

3. Identification

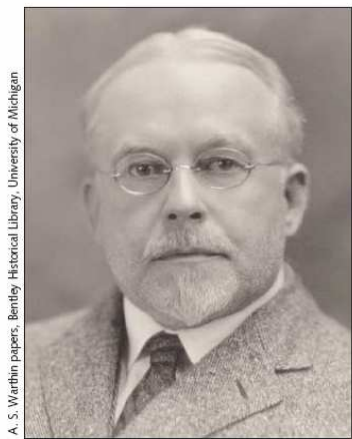


19

Hereditary CRC
denied by medical
community!

19

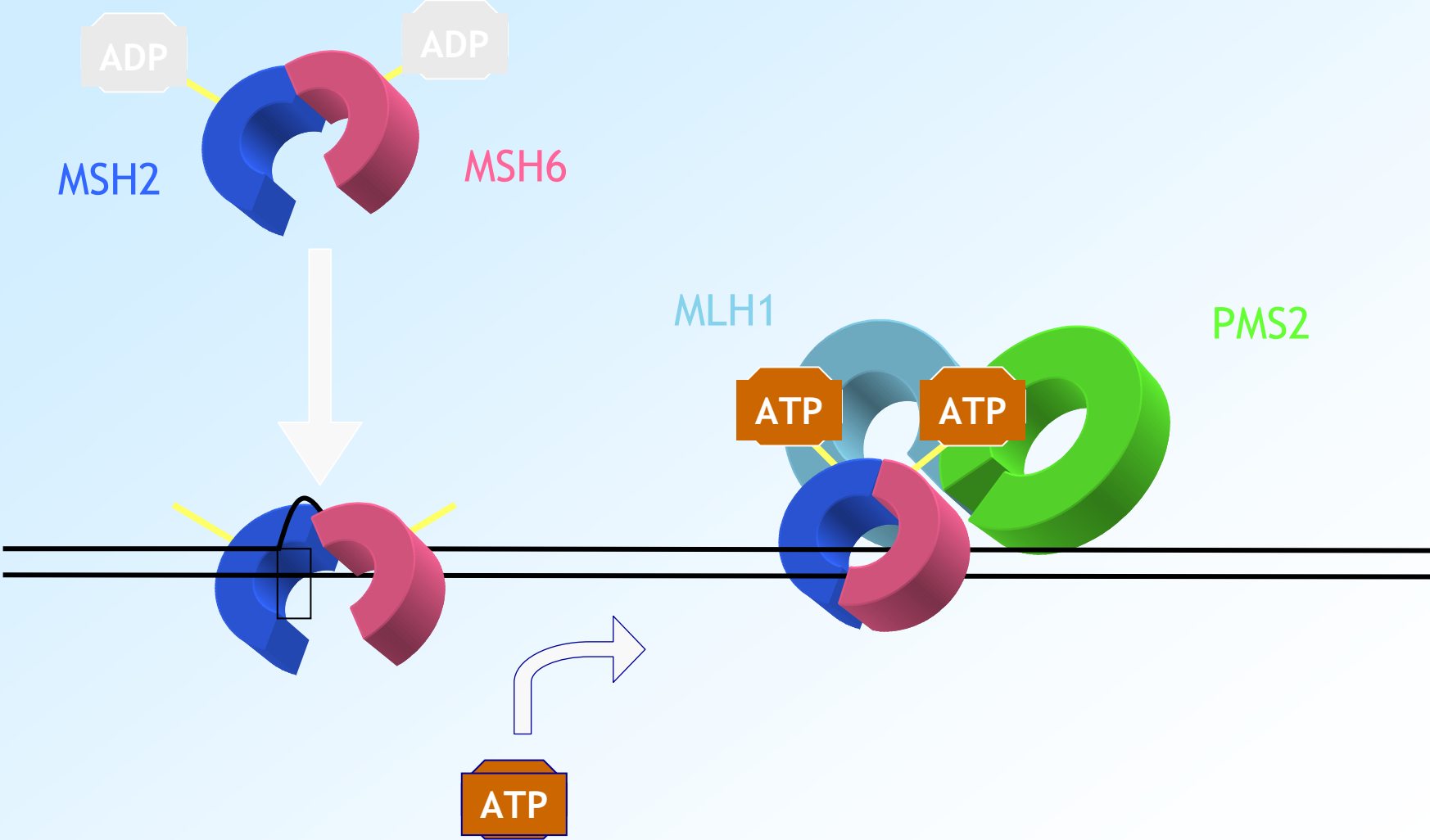
Figure 1. Aldred Scott Warthin, MD, PhD



A. S. Warthin papers, Bentley Historical Library, University of Michigan

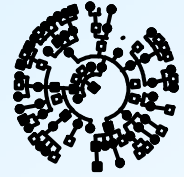


1993-1997 Mismatch repair genes identified



Adapted from R. Fishel

Identification



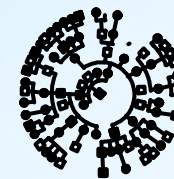
Familial Cancer (2007) 6:131–134

DOI 10.1007/s10689-006-9114-8

Family history is neglected in the work-up of patients with colorectal cancer: a quality assessment using cancer registry data

**D. A. van Dijk · M. J. Oostindiër · W. M. Kloosterman-Boele ·
P. Krijnen · H. F. A. Vasen · Hereditary Tumor Study Group of the
Comprehensive Cancer Centre West (CCCW)**

224 patients (7 hospitals) with CRC age < 50 or multiple CRC
Complete family history (type of cancer, age, number): 16%



How to improve identification?

■ General population

- Assess the family history for CRC at start of screening program
- Fam/her.CRC: advise colonoscopy, refer to genetic centres and her.cancer registry

■ CRC-patients

- Perform IHC analysis of all CRC to identify MMR gene defect
- Ask patient to complete questionnaire about family history



Conclusions

- Her/fam CRC: quantitatively important
- Surveillance attractive because of high compliance and large gain in life-expectancy
- Her.Cancer Registries important for coordination of surveillance
- Surveillance is effective
- Large proportion of families undetected because physicians pay hardly attention to family history