

**Protection from colorectal neoplasms  
after colonoscopy:  
results of epidemiological studies  
from Germany**

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# Colorectal cancer screening offers in Germany

**1977-September 2002:**

**45+: Annual fecal occult blood test (FOBT)**

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**October 2002 =>**

**50-54: Annual FOBT**

**55+** 

**Screening colonoscopy (55+, 65+)**

**FOBT every other year**

# Colorectal cancer screening offers in Germany

**1977-September 2002:**

**45+: Annual fecal occult blood test (FOBT)**

**October 2002 =>**

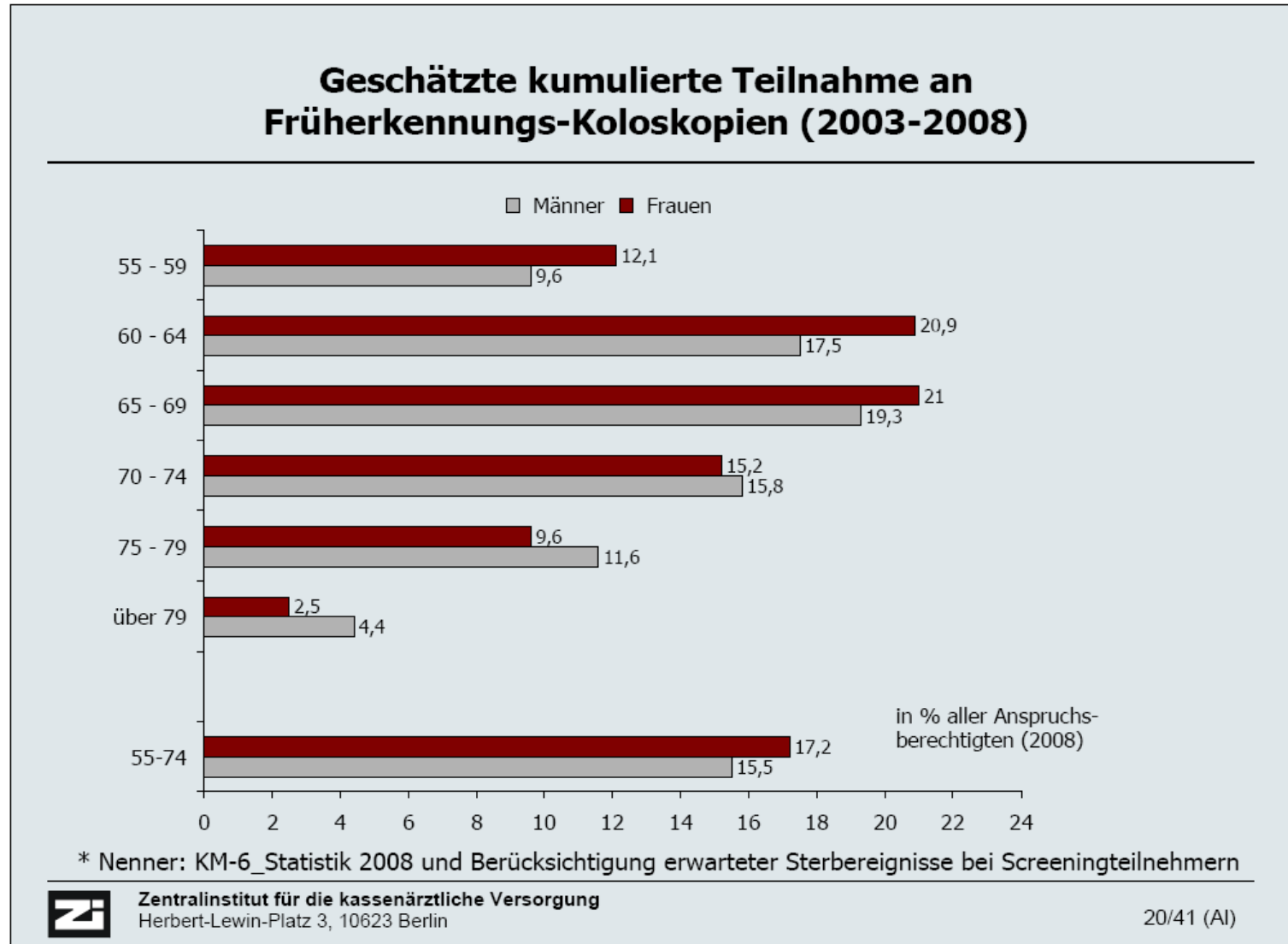
**50-54: Annual FOBT**

**55+** 

- Screening colonoscopy (55+, 65+)**
- FOBT every other year**

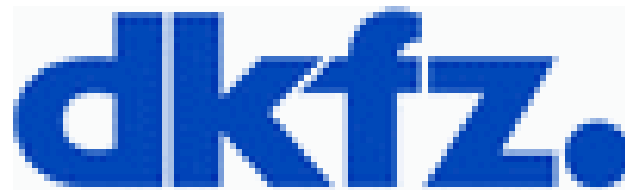
**Opportunistic screening**

# Participation in screening colonoscopy in Germany



## Cohort study of screening colonoscopy participants

### Partners



EPIDEMIOLOGISCHES  
Krebsregister  
SAARLAND



**LebensBlicke**  
Stiftung Früherkennung Darmkrebs



## Design

### State-wide cohort study in Saarland

#### Study Population

- 20.000 participants of screening colonoscopy 2005-2013

#### Data Collection

- 25 gastroenterology practices in Saarland
- Participant questionnaires
- Colonoscopy and pathology records
- Long-term follow-up (up to 20 years, cancer registry based)

## **Main Study Questions**

**Incidence + mortality of screening colonoscopy participants compared to general population / non-participants**

- overall, by age and sex**
- with careful consideration of potential confounding factors**

## Main Study Questions

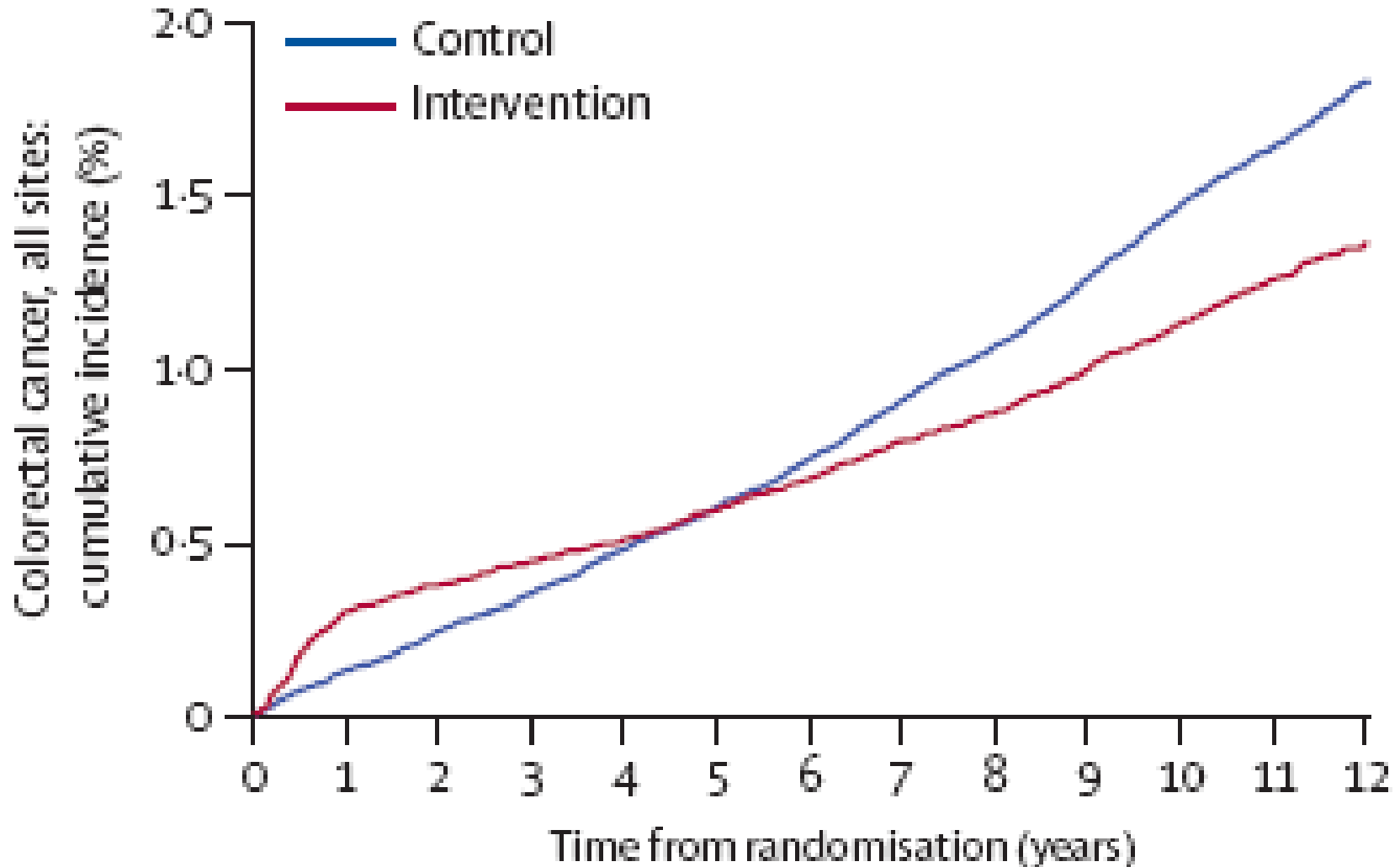
**Incidence + mortality of screening colonoscopy participants compared to general population / non-participants**

- overall, by age and sex
- with careful consideration of potential confounding factors

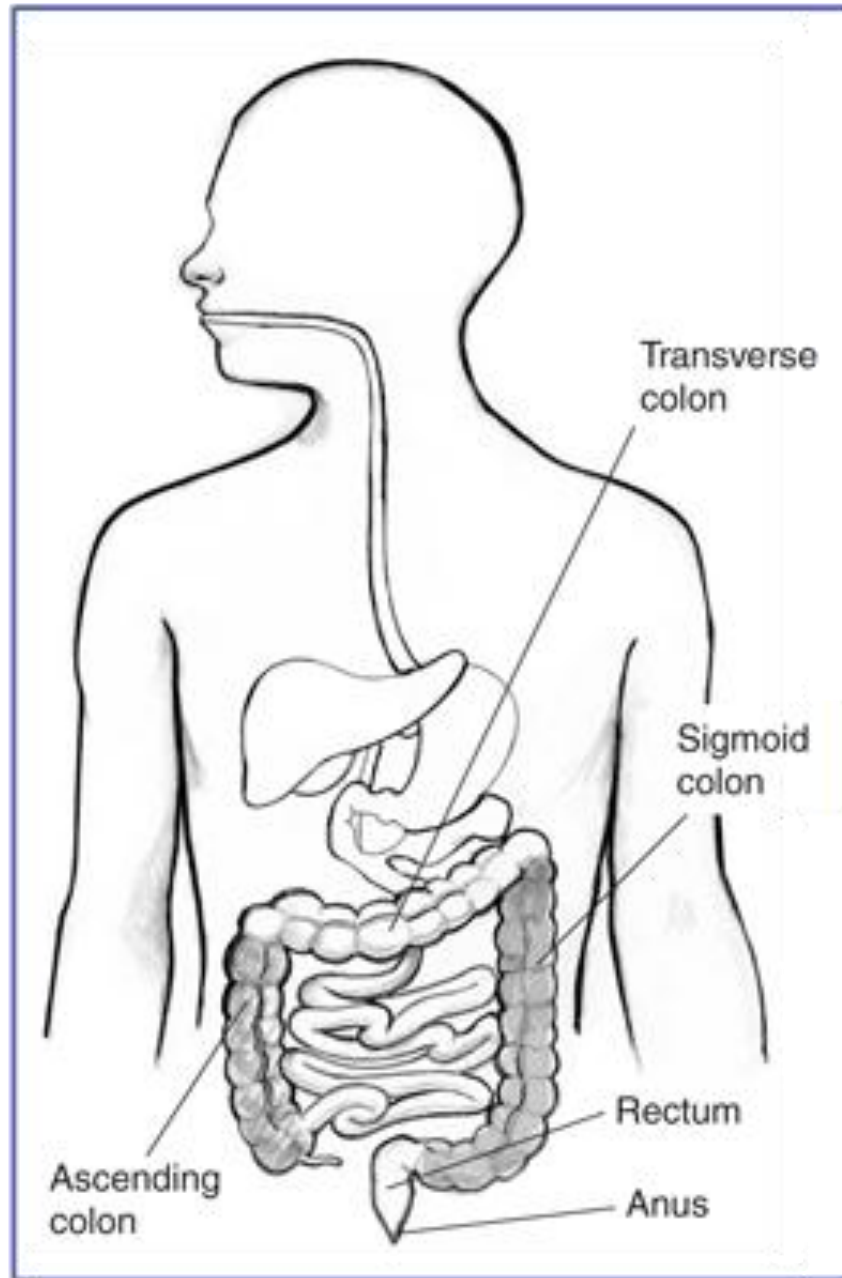
**Long Term Follow-up !**

# UK Trial on once only sigmoidoscopy screening

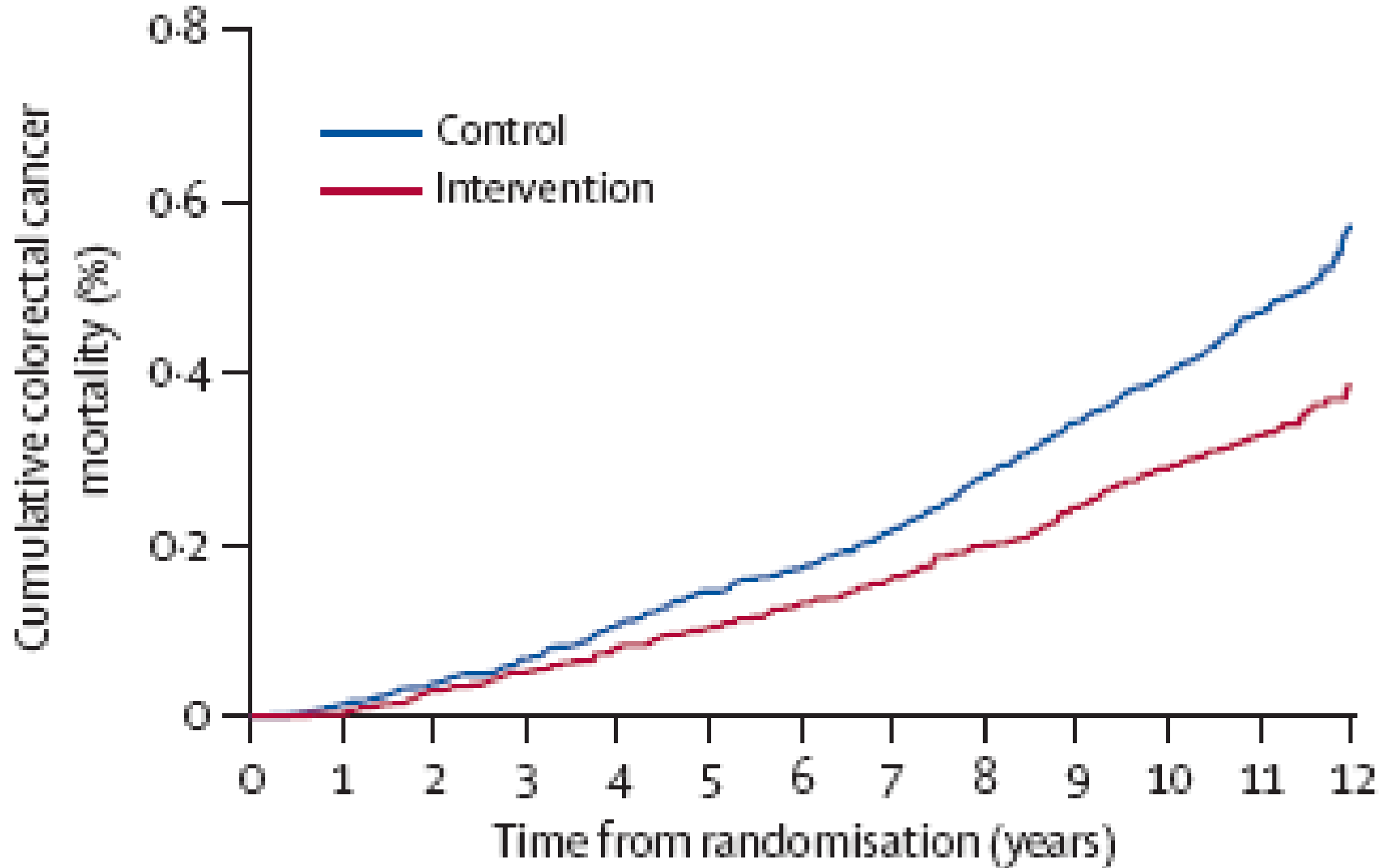
## Control and intervention groups



Atkin et al, Lancet 2010;375:1624-33



# UK Trial on once only sigmoidoscopy screening



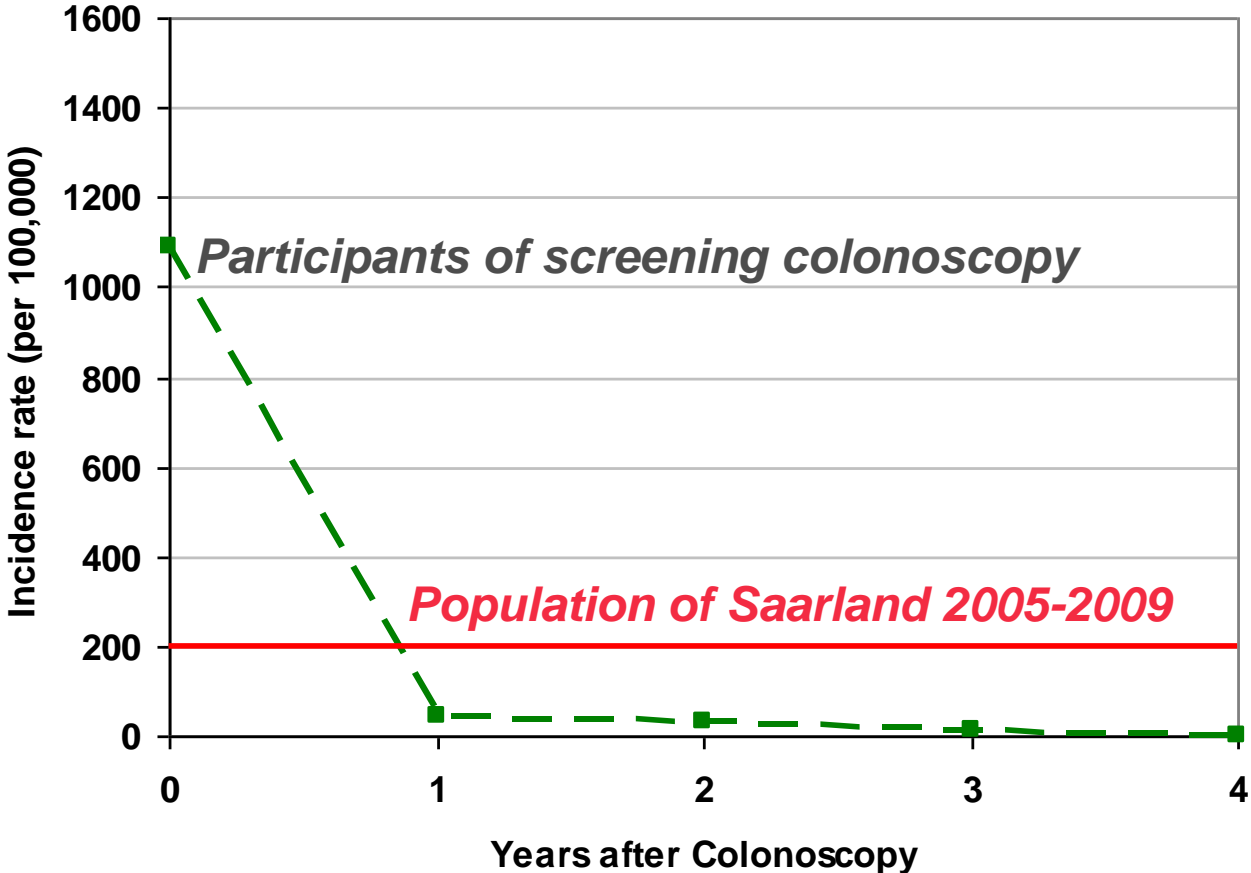
Atkin et al, Lancet 2010;375:1624-33

**Preliminary  
Data !**

# Annual colorectal cancer incidence

- Age- and sex-standardized incidence ratio (SIR)\*

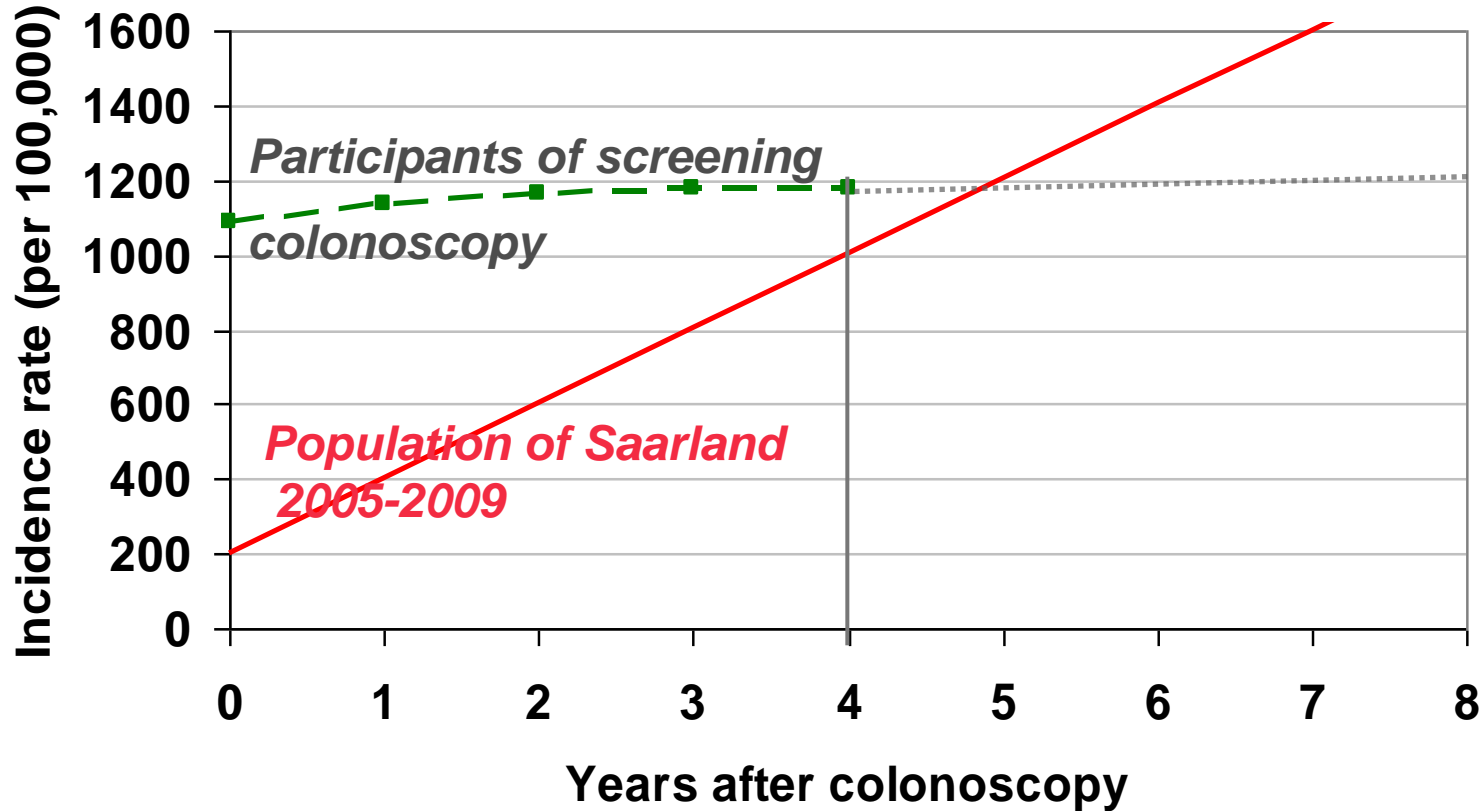
- Year 0: SIR=5.44
- Year 1: SIR=0.22
- Year 2: SIR=0.16
- Year 3: SIR=0.05
- Year 4: SIR=0.00



**Preliminary  
Data !**

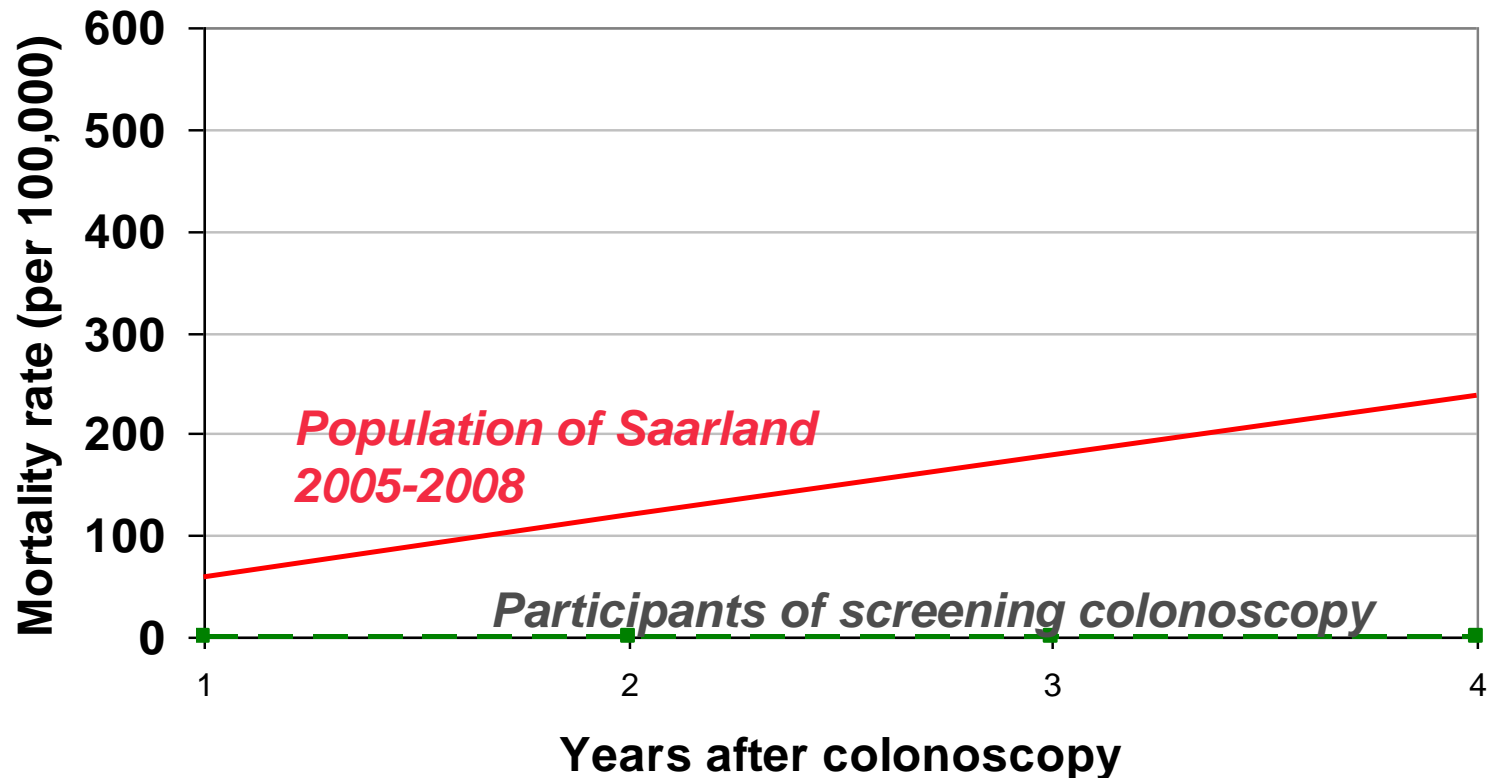


## Cumulative colorectal cancer incidence



**Preliminary  
Data !**

## Cumulative colorectal cancer mortality



**SMR = N observed / N expected = 0 / 21.9 = 0 (0.00-0.17)**

**First analyses baseline data:  
Risk reduction after colonoscopy ?**

Comparison of

- 2701 participants with no prior colonoscopy
- 586 participants with colonoscopy 1-10 years ago  
(validated by medical records)

with respect to

Prevalence of advanced neoplasms (cancer/advanced adenomas)

- overall
- by cancer site

controlling for potential confounding factors

J Natl Cancer Inst 2010;102:89-95

## Relative risk of advanced neoplasm after previous colonoscopy

Advanced neoplasm, Site	Relative Risk (95% confidence interval) after previous colonoscopy
Cecum, ascending, colon	0.99 (0.50-1.97)
Right flexure, transverse colon	1.21 (0.60-2.42)
Right colon combined	1.05 (0.63-1.76)
Left flexure, descending colon	0.36 (0.16-0.82)
Sigmoid colon	0.29 (0.16-0.53)
Rectum	0.07 (0.02-0.40)
Left Colon and rectum combined	0.33 (0.21-0.53)
Colon und rectum combined	0.52 (0.37-0.73)

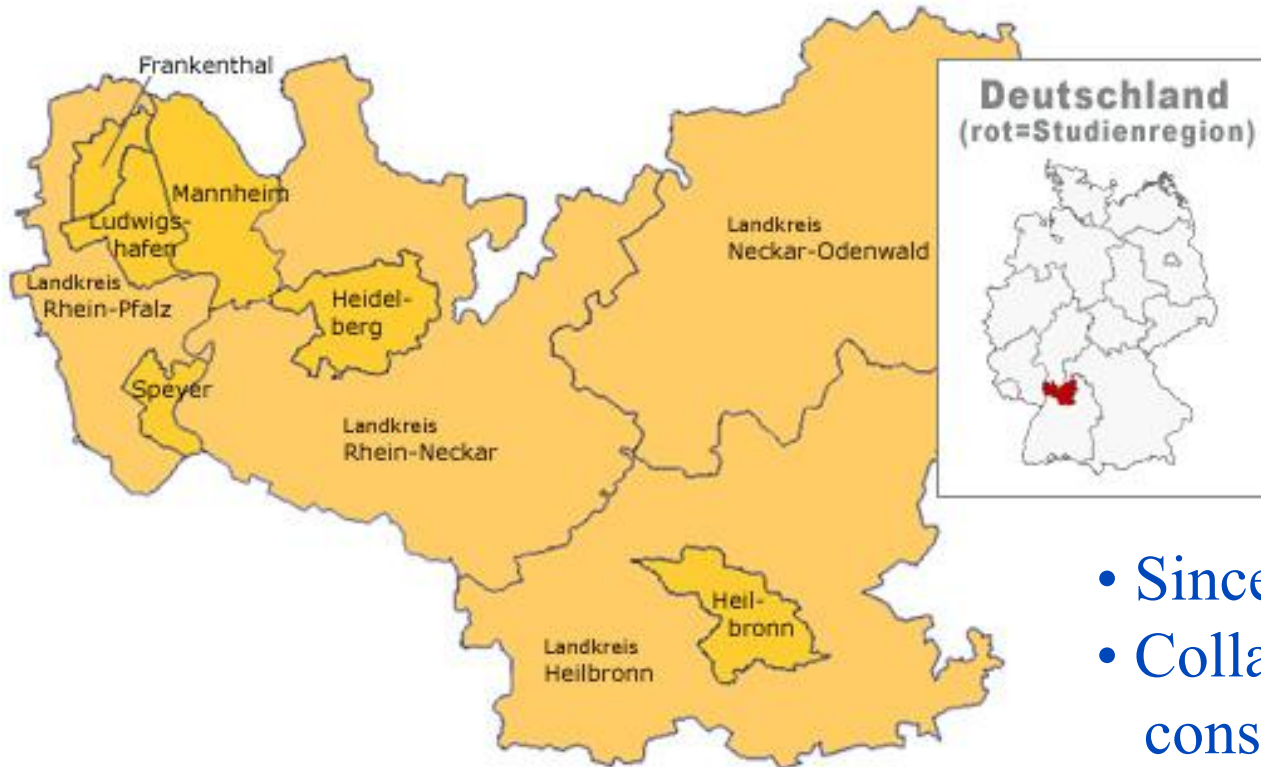
**J Natl Cancer Inst 2010;102:89-95**

# Effectiveness of colonoscopy in routine setting ?

## DACHS

Darmkrebs: Chancen der Verhütung durch Screening

- **Population-based case-control study**
- 20 clinics, 3.500 cases, 3.500 controls
- Personal interviews, medical records
- Blood and tissue samples (TMAs)
- Long-term follow-up of cases



- Since 2003
- Collaboration in nat./internat. consortia

# Effectiveness of colonoscopy in routine setting ?

## **DACHS**

Darmkrebs: Chancen der  
Verhütung durch Screening

### **Reduction of colorectal cancer risk by previous colonoscopy ?**

**=> Comparison of history of colonoscopy between cases – controls**

### **Key issues: avoidance / minimization of**

- **Selection bias**

**=> maximize response rates**

- **Misclassification of exposure**

**=> validation by medical records**

- **Confounding**

**=> questionnaires, multivariate analyses**

## Risk reduction after previous colonoscopy ?

Group	N	Colonoscopy 1-10 ys ago N [%]	Relative Risk (95% CI)
Controls	1932	793 (41.1%)	
Cases	1688	230 (13.6%)	0.23 (0.19-0.27)

Ann Intern Med 2011;154:22-30

# Dachs

Darmkrebs: Chancen der  
Verhütung durch Screening

Risk reduction **by cancer site ?**

Group	Site	N	Colonoscopy 1-10 ys ago N [%]	Relative Risk (95% CI)
Controls		1932	793 (41.1%)	
Cases	Right	537	125 (23.3%)	0.44 (0.35-0.55)
	Left	1060	101 (9.5%)	0.16 (0.12-0.20)

Ann Intern Med 2011;154:22-30

# DACHS

Darmkrebs: Chancen der  
Verhütung durch Screening

Risk reduction **by cancer site ?**

Site	Relative Risk (95% CI) after colonoscopy
Cecum	0.42 (0.28-0.61)
Ascending colon	0.58 (0.42-0.80)
Right flexure	0.31 (0.16-0.59)
Transverse colon	0.34 (0.18-0.65)
Right total	0.44 (0.35-0.55)

Ann Intern Med 2011;154:22-30

# DACHS

Darmkrebs: Chancen der  
Verhütung durch Screening

Risk reduction **by cancer site ?**

Cancer site	Relative Risk (95% CI) after colonoscopy
Left flexure	0.33 (0.15-0.73)
Descending colon	0.44 (0.25-0.79)
Sigmoid colon	0.14 (0.10-0.20)
Rectum	0.13 (0.09-0.18)
Left total	0.16 (0.12-0.20)

Ann Intern Med 2011;154:22-30

# DachS

Darmkrebs: Chancen der  
Verhütung durch Screening

Risk reduction **by cancer stage ?**

Cancer stage	Relative Risk (95% CI) after colonoscopy
I	0.27 (0.20-0.36)
II	0.23 (0.17-0.30)
III	0.22 (0.17-0.29)
IV	0.17 (0.11-0.27)

Ann Intern Med 2011;154:22-30

# DACHS

Darmkrebs: Chancen der  
Verhütung durch Screening

**Risk reduction by sex**

Sex	Relative Risk (95% CI) after colonoscopy
Women	0.24 (0.18-0.32)
Men	0.22 (0.18-0.28)

Ann Intern Med 2011;154:22-30

# Dachs

Darmkrebs: Chancen der  
Verhütung durch Screening

Risk reduction **by age**

Age	Relative Risk (95% CI) after colonoscopy
50-59	0.26 (0.15-0.43)
60-69	0.22 (0.16-0.29)
70-79	0.22 (0.16-0.29)
80+	0.23 (0.15-0.36)

Ann Intern Med 2011;154:22-30

# DachS

Darmkrebs: Chancen der  
Verhütung durch Screening

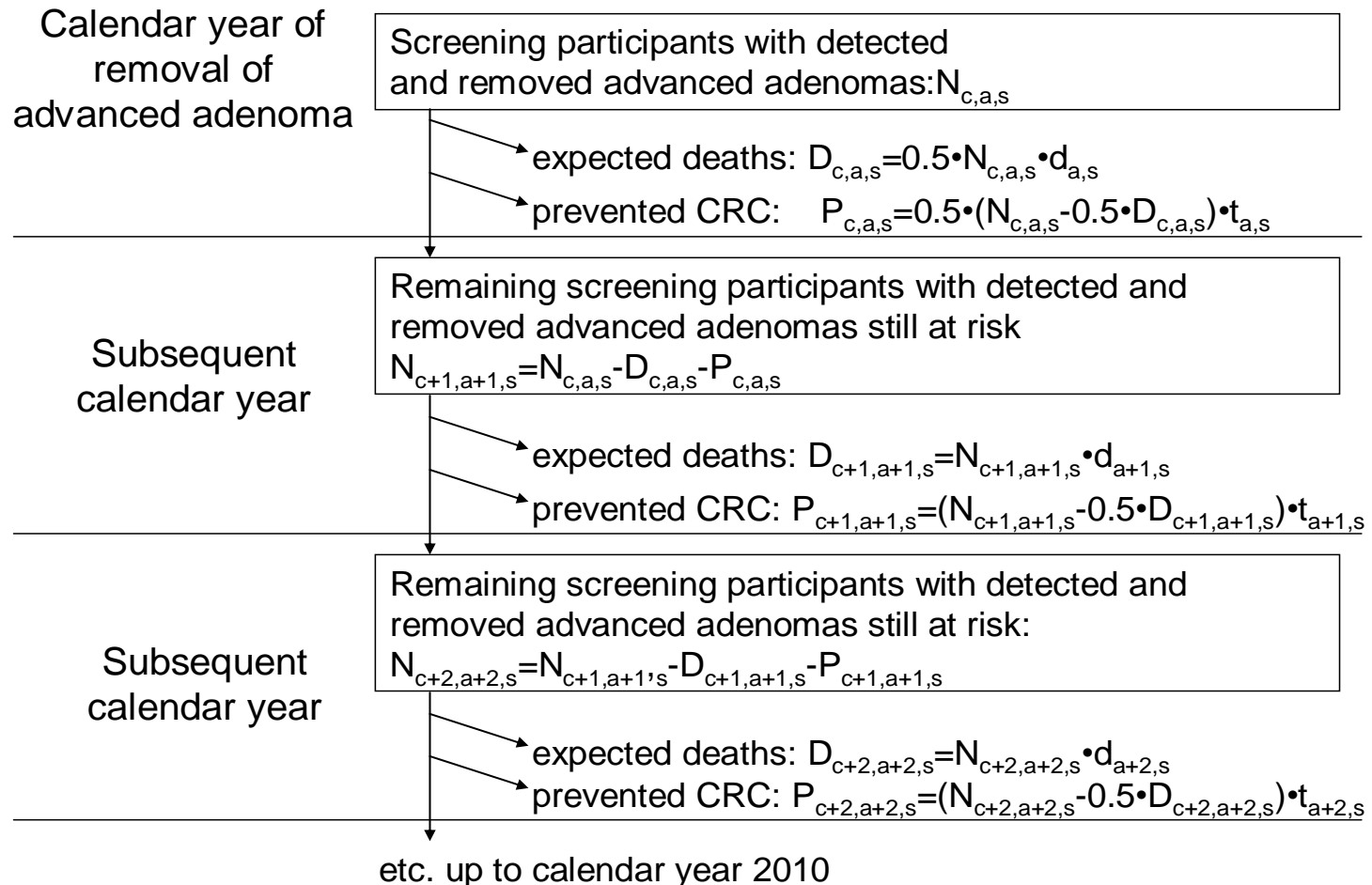
Risk reduction by **calendar year**

Age	Relative Risk (95% CI) after colonoscopy
2003-2004	0.37 (0.27-0.50)
2005	0.24 (0.16-0.36)
2006-2007	0.18 (0.14-0.25)

Ann Intern Med 2011;154:22-30

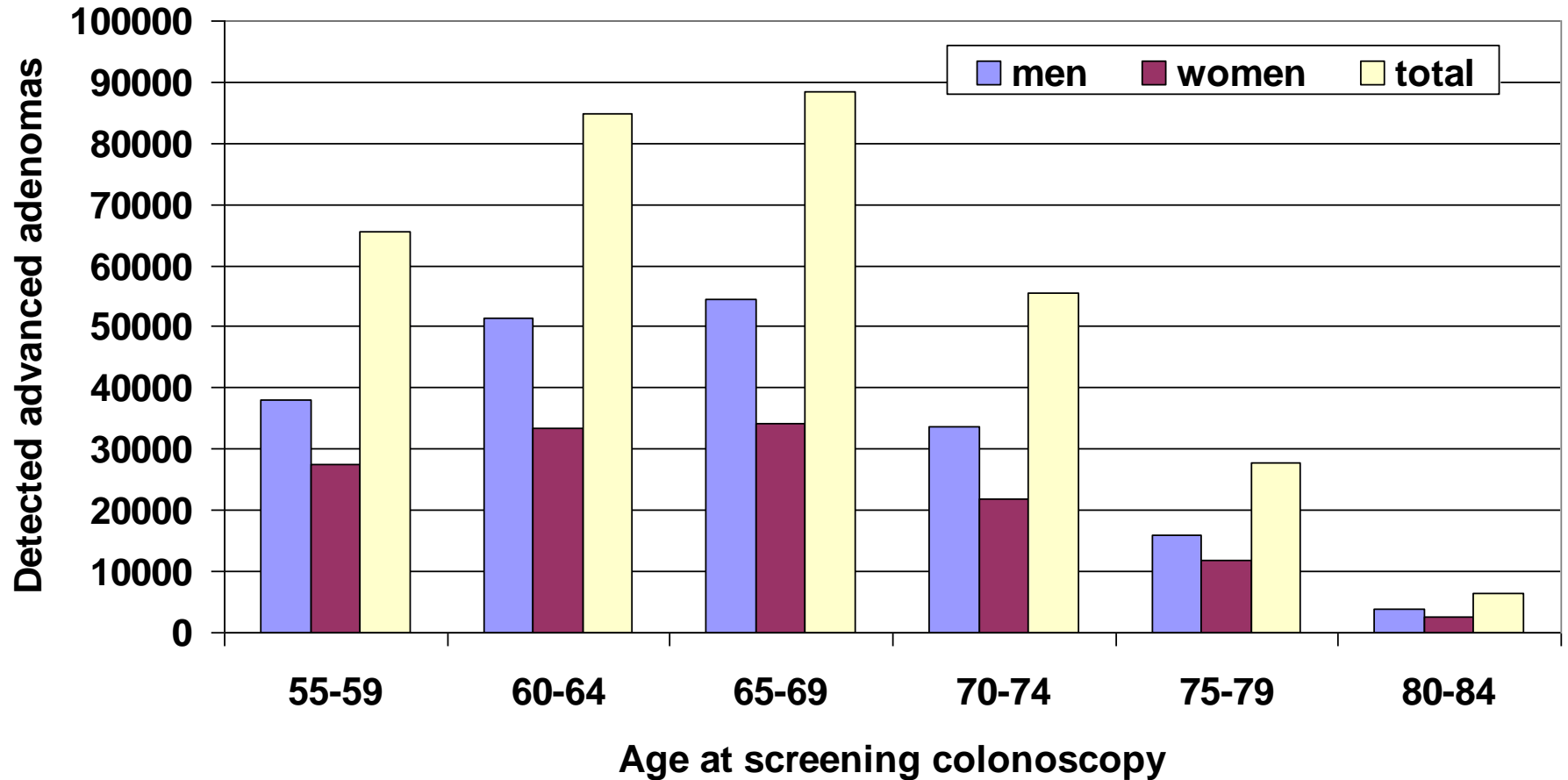
# Screening colonoscopy:

## Modeling of prevented colorectal cancer cases by detection and removal of advanced adenomas 2003-2010



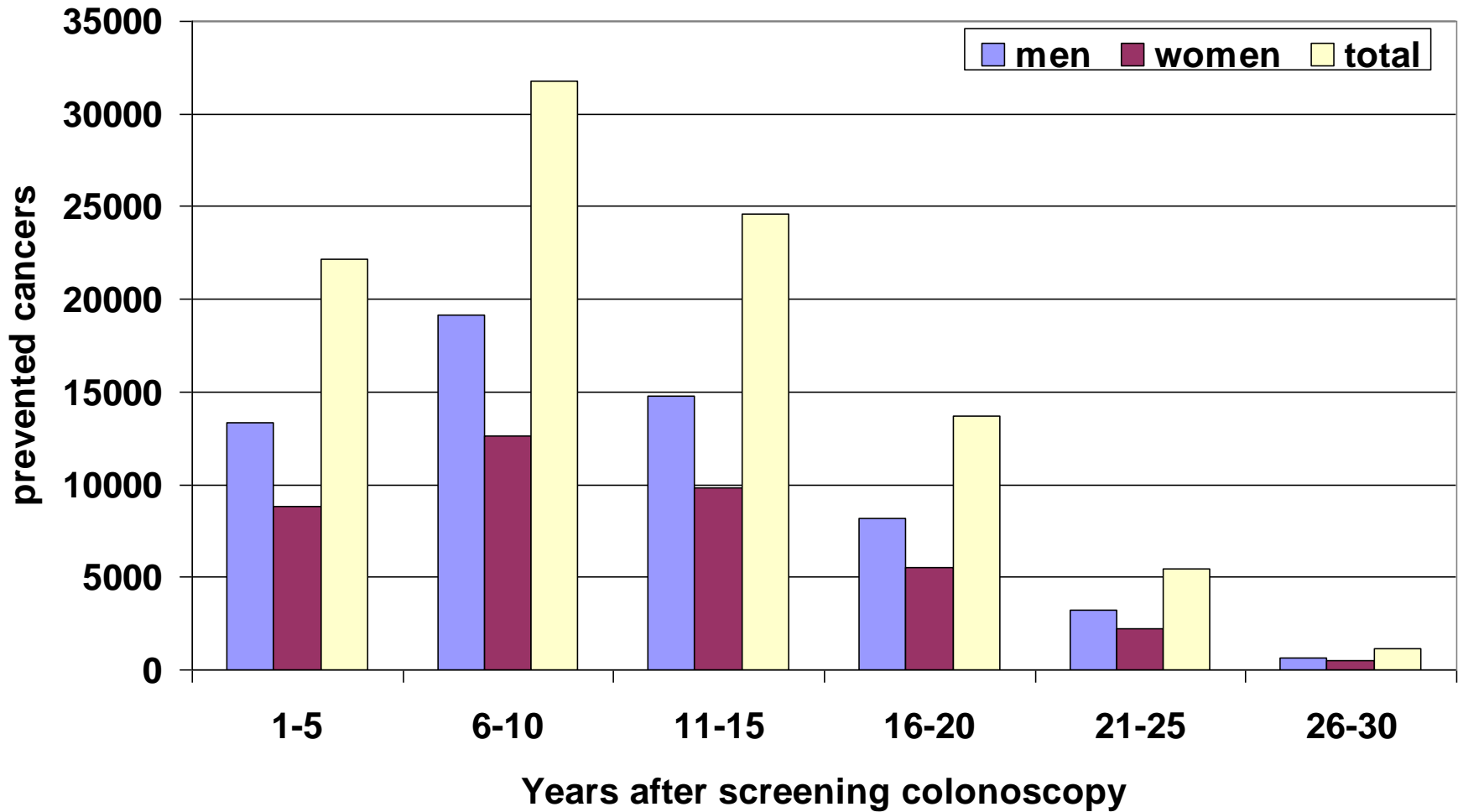
Deutsches Ärzteblatt 2010

**In 2003-2010:  
> 300.000 advanced adenomas detected and removed**



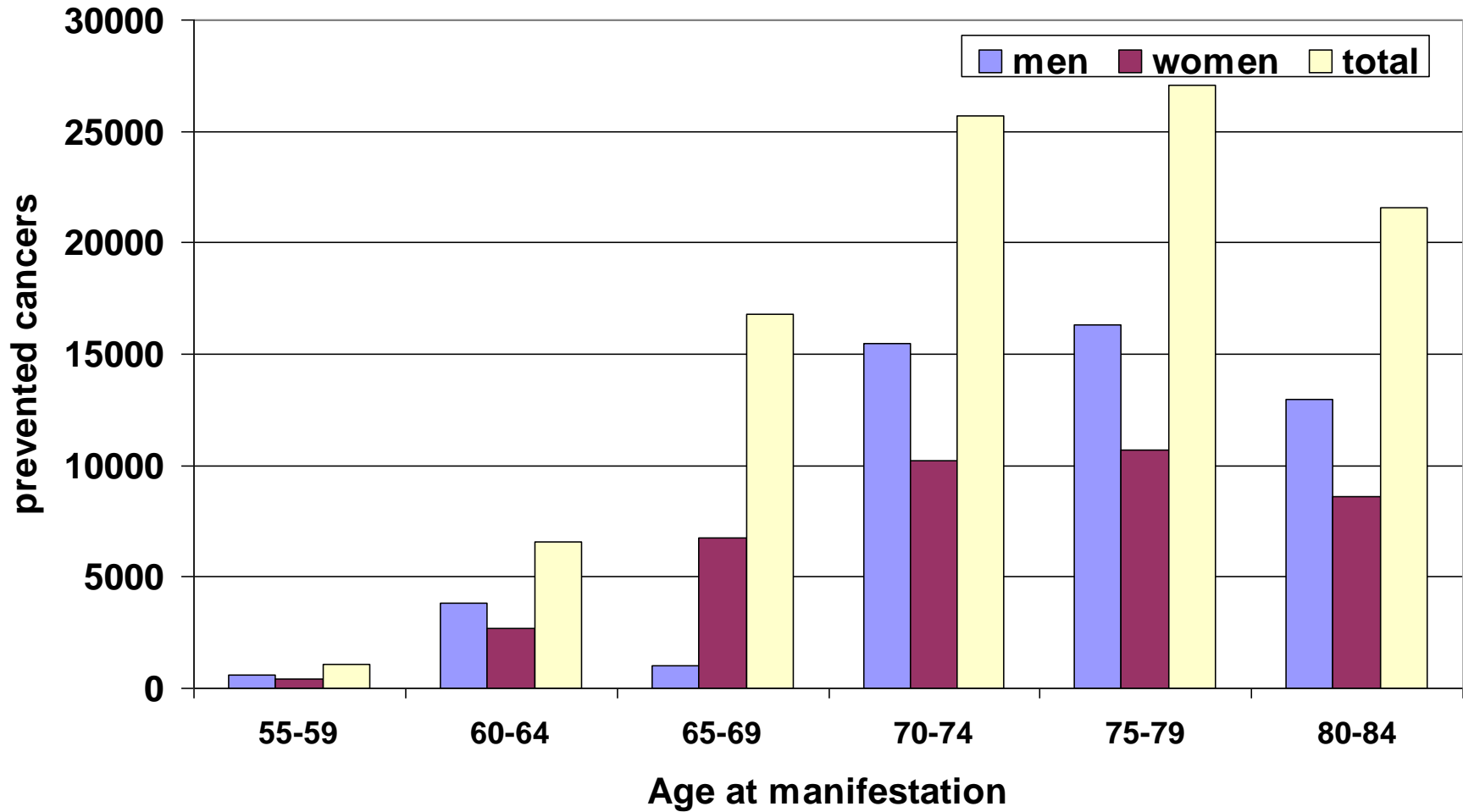
Deutsches Ärzteblatt 2010

# Estimated: almost 100.000 cancers prevented



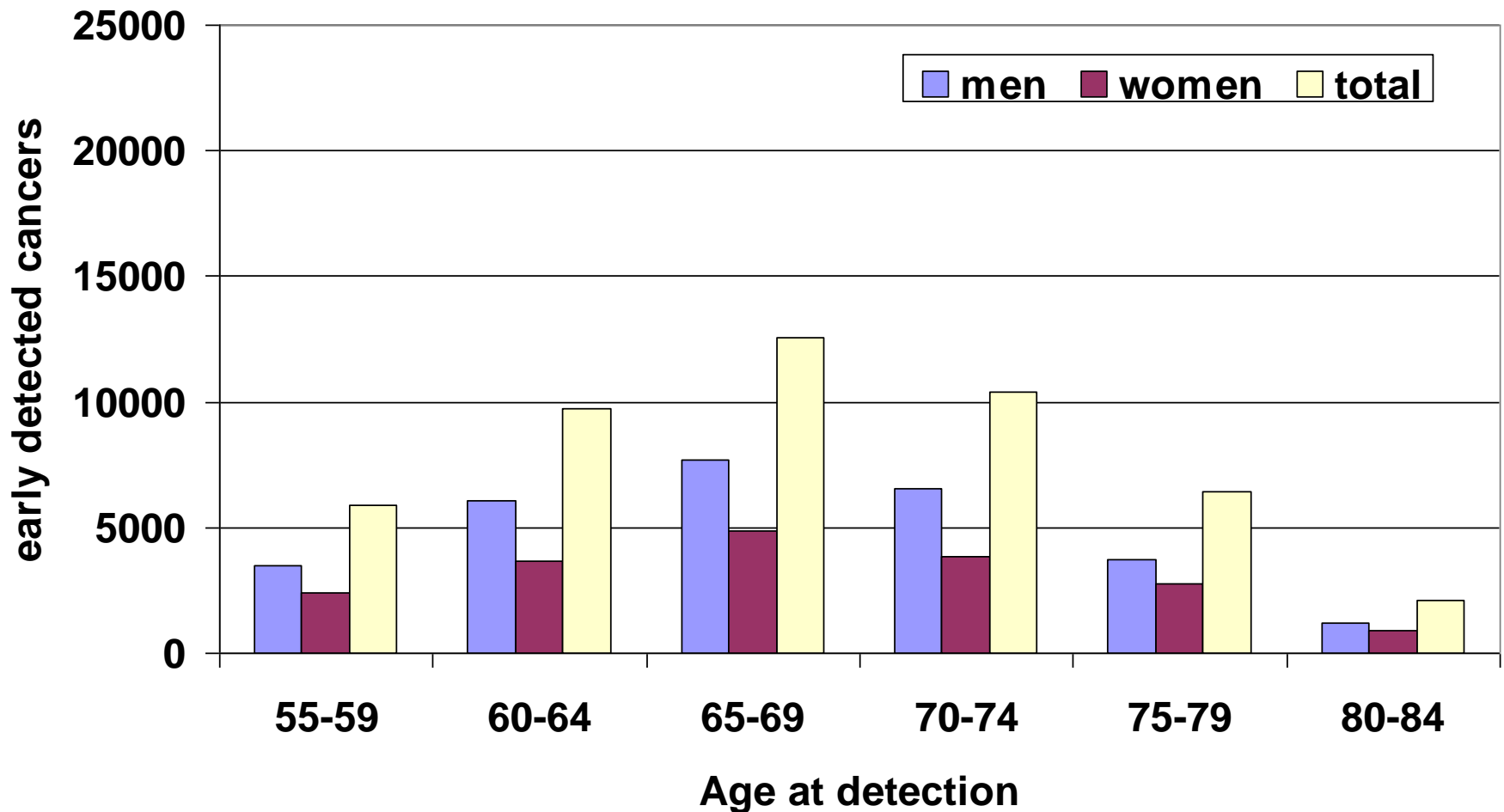
Deutsches Ärzteblatt 2010

## Estimated: almost 100.000 cancers prevented



Deutsches Ärzteblatt 2010

# In 2003-2010: Almost 50.000 cancers early detected and treated



Deutsches Ärzteblatt 2010

## Summary

**Colonoscopy highly effective in preventing colorectal cancer, especially for left sided CRC, but also for right sided CRC**

## Summary

**Colonoscopy highly effective in preventing colorectal cancer, especially for left sided CRC, but also for right sided CRC**

**Other promising screening options for reduction of incidence and mortality of colorectal cancer, such as iFOBT and sigmoidoscopy**

# Outlook

- **Major reductions in colorectal cancer incidence and mortality expected in the common years**
- **Even much larger effects would be possible with higher participation rates in colorectal cancer screening**
- **e.g. through organized screening with personal invitation and follow-up**

# Many thanks to

- **You for your attention**

- **Wonderful research groups and collaborators**

Michael Hoffmeister, Jenny Chang-Claude, Ute Handte-Daub  
Christa Stegmaier, Thomas Stolz, Isabel Lerch, Elke Fleck  
Lutz Altenhofen

- **Funding Agencies**

German Research Association (DFG)

German Cancer Aid

German Federal Ministry for Education and Research

Central Institute for Ambulatory Care in Germany



# Can we afford screening colonoscopy ?

## Cost-effectiveness ?

**Model calculations based on 109.989 screening colonoscopies**

### Costs

Direct costs screening colonoscopy	22.598.138 €
Costs surveillance colonoscopy	7.401.692 €
Costs complications	136.000 €
<hr/>	
Total costs	30.135.830 €
per participant	<b>274 €</b>

Z Gastroenterologie 2007;45:945-51

# Can we afford screening colonoscopy ?

## Cost-effectiveness ?

**Model calculations based on 109.989 screening colonoscopies**

### Costs

Direct costs screening colonoscopy	22.598.138 €
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Costs complications	136.000 €
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Total costs	30.135.830 €
per participant	<b>274 €</b>

### Savings

Removal of pT1 cancers at colonoscopy	6.131.420 €
Prevented cancers	47.713.016 €
Total savings	53.844.436 €
per participant	<b>490 €</b>

Z Gastroenterologie 2007;45:945-51

**First analyses baseline data:**

**II: Risk of advanced neoplasms by time since negative colonoscopy  
=> Screening intervals ?**

Comparison of

- 2701 participants with no prior colonoscopy
- 533 participants with previous negative colonoscopy

with respect to

Prevalence of advanced neoplasms (cancer/advanced adenoma)

- overall
- by time since negative colonoscopy

controlling for potential confounding factors

Gastroenterology 2010;138:870-876

**Relative risk of advanced neoplasm after negative colonoscopy**

Previous colonoscopy	Relative Risk (95% confidence interval)
No	1.00 (Reference)
Yes, ever	0.42 (0.25-0.68)
Yes, 1-5 years ago	0.38 (0.16-0.90)
Yes, 6-10 years ago	0.34 (0.15-0.74)
Yes, 11-15 years ago	0.38 (0.16-0.90)
Yes, 16+ years ago	0.53 (0.27-1.04)

Gastroenterology 2010;138:870-876

## „Satellite Projects“

### Complications

- Post-recruitment survey (self-reports, validation)  
(n = 5.000, 2010-2013)
- ⇒ Frequency and risk factors of complications during and within 4 weeks after screening colonoscopy

### Use and results of surveillance colonoscopies

- Follow-up survey (self reports, validation)  
5-6 years after screening colonoscopy (n=5,000, 2011-2014)
- ⇒ Guideline adherence, under- / overuse ?
- ⇒ Frequency and predictors of neoplasms

# DACHS

Darmkrebs: Chancen der  
Verhütung durch Screening

## Screening intervals after negative colonoscopy ?

History of screening colonoscopy		Adjusted OR (95% CI)	
No previous colonoscopy			1.00 Reference
Last negative colonoscopy			
	any time ago		0.19 (0.16-0.23)
	1-2 years ago		0.14 (0.10-0.20)
	3-4 years ago		0.12 (0.08-0.19)
	5-9 years ago		0.26 (0.18-0.39)
	10-19 years ago		0.28 (0.17-0.45)
	20+ years ago		0.40 (0.24-0.66)

J Clin Oncol 2011 [Epub 29 Aug]