

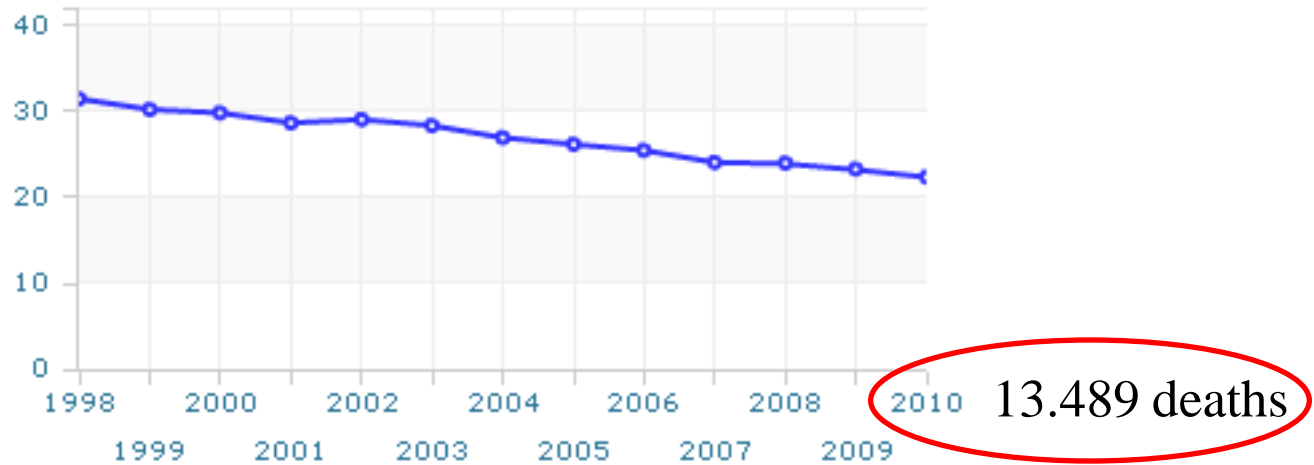
Bending down the mortality line: colonoscopy screening in Germany

Hermann Brenner

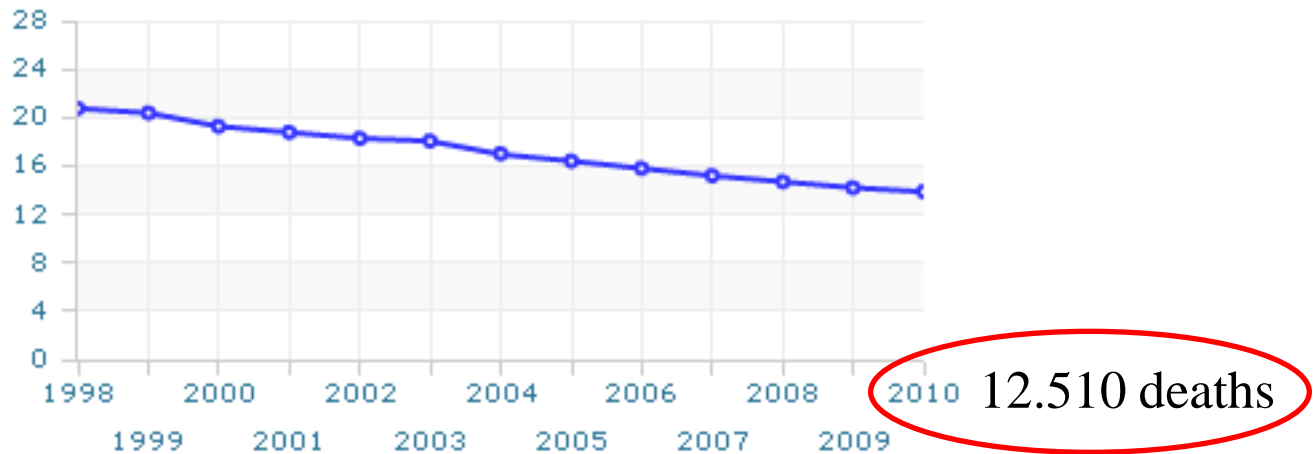
*Division of Clinical Epidemiology and Aging Research
German Cancer Research Center, Heidelberg*

Age standardized colorectal cancer mortality in Germany

Men



Women



Colorectal cancer screening offers in Germany

1977-September 2002:

45+: Annual fecal occult blood test (FOBT)

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

Colorectal cancer screening offers in Germany

1977-September 2002:

45+: Annual fecal occult blood test (FOBT)

October 2002 =>

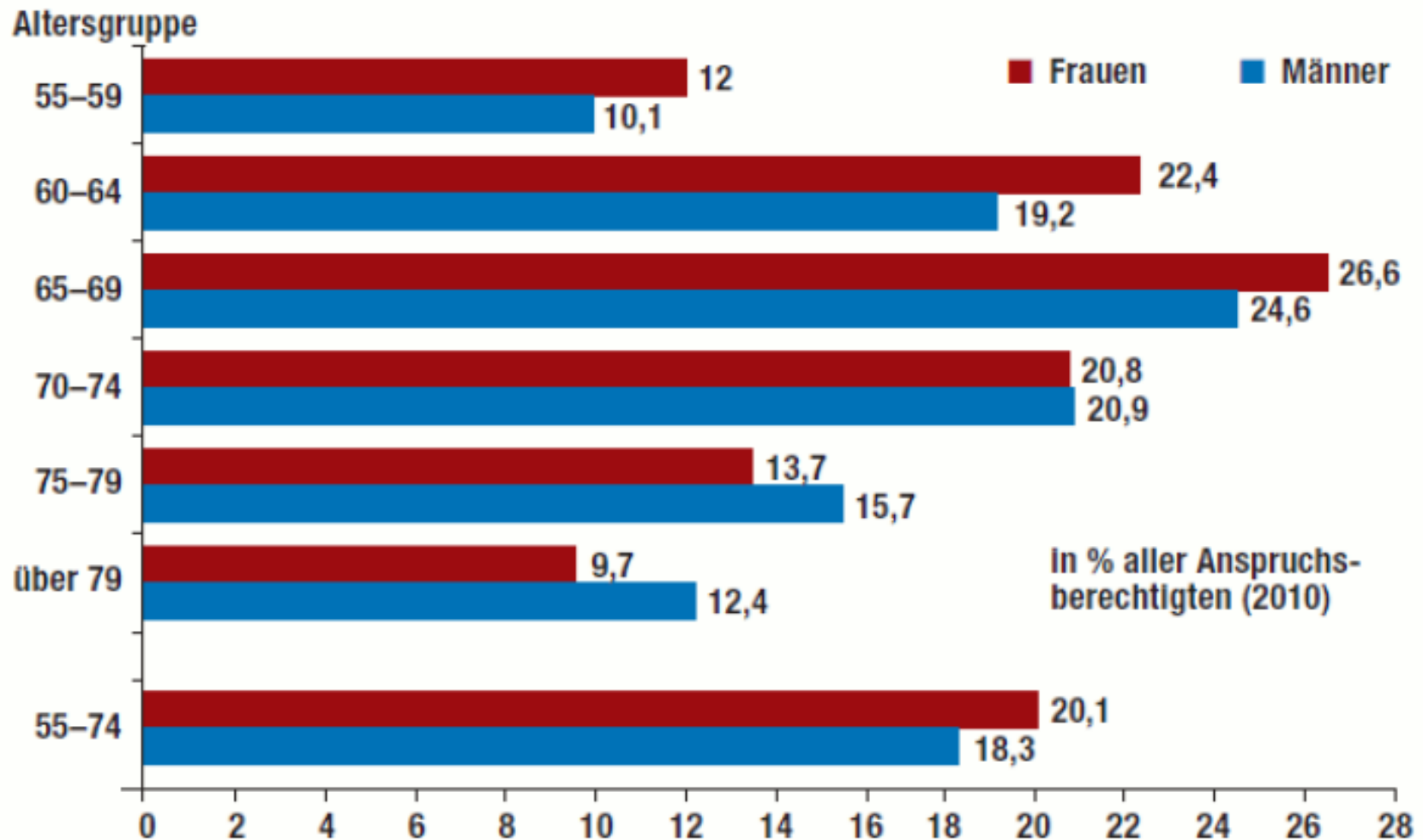
50-54: Annual FOBT

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

Opportunistic screening

Screening colonoscopy in Germany

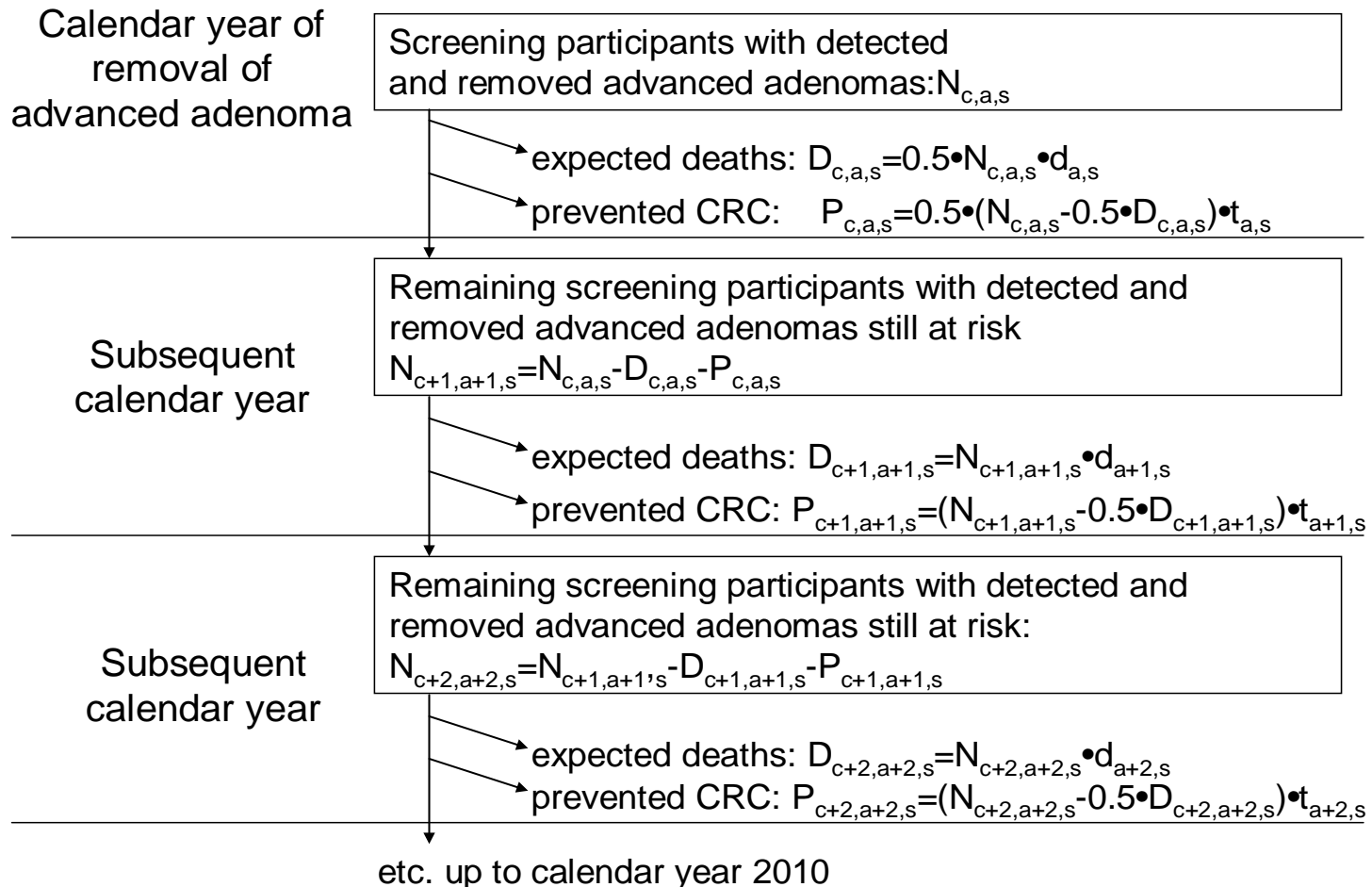
Cumulative participation 2003-2010



Schäfer, Altenhofen, von Stillfried, Dtsch Ärzteblatt 2012

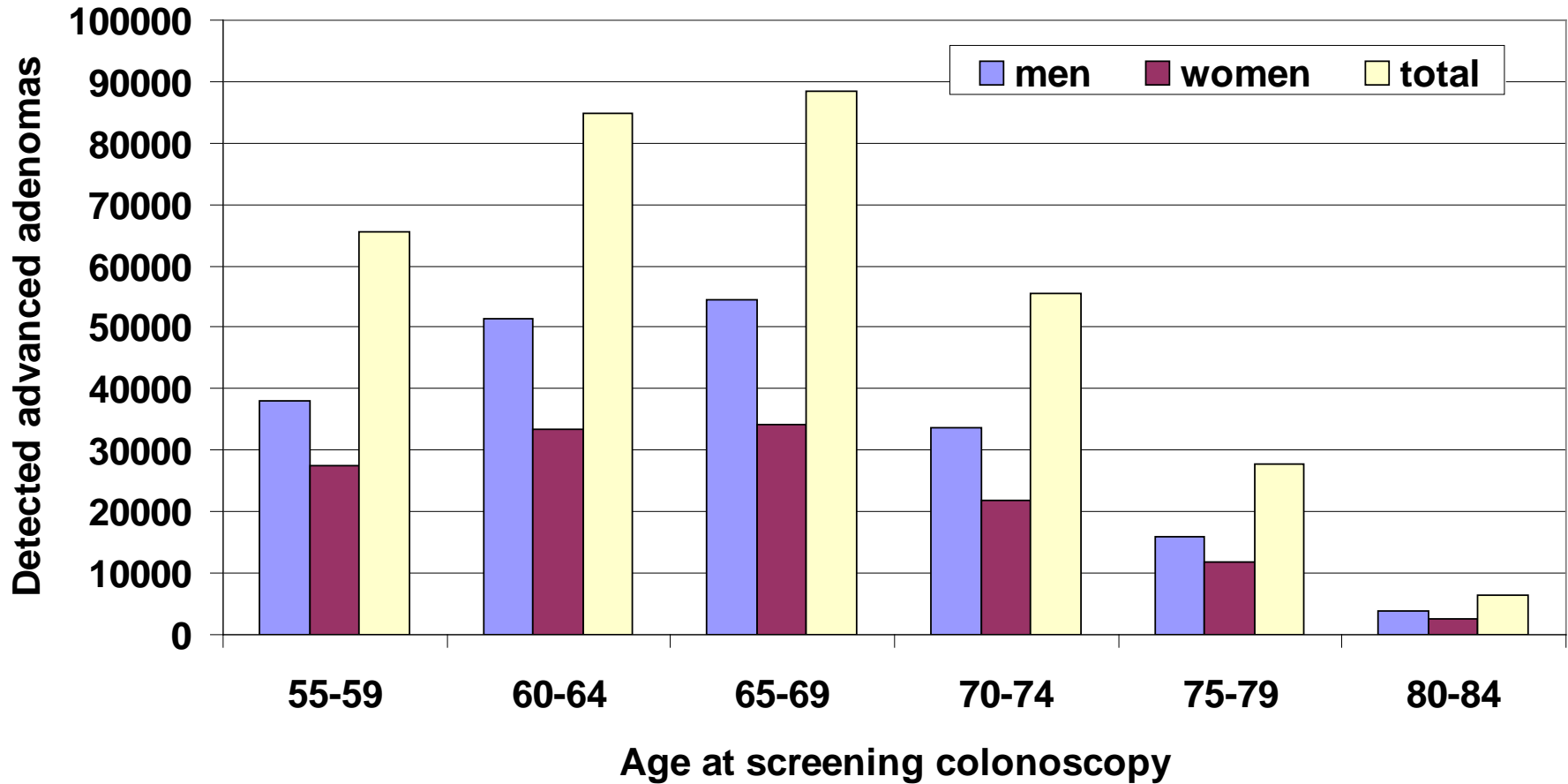
Screening colonoscopy:

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



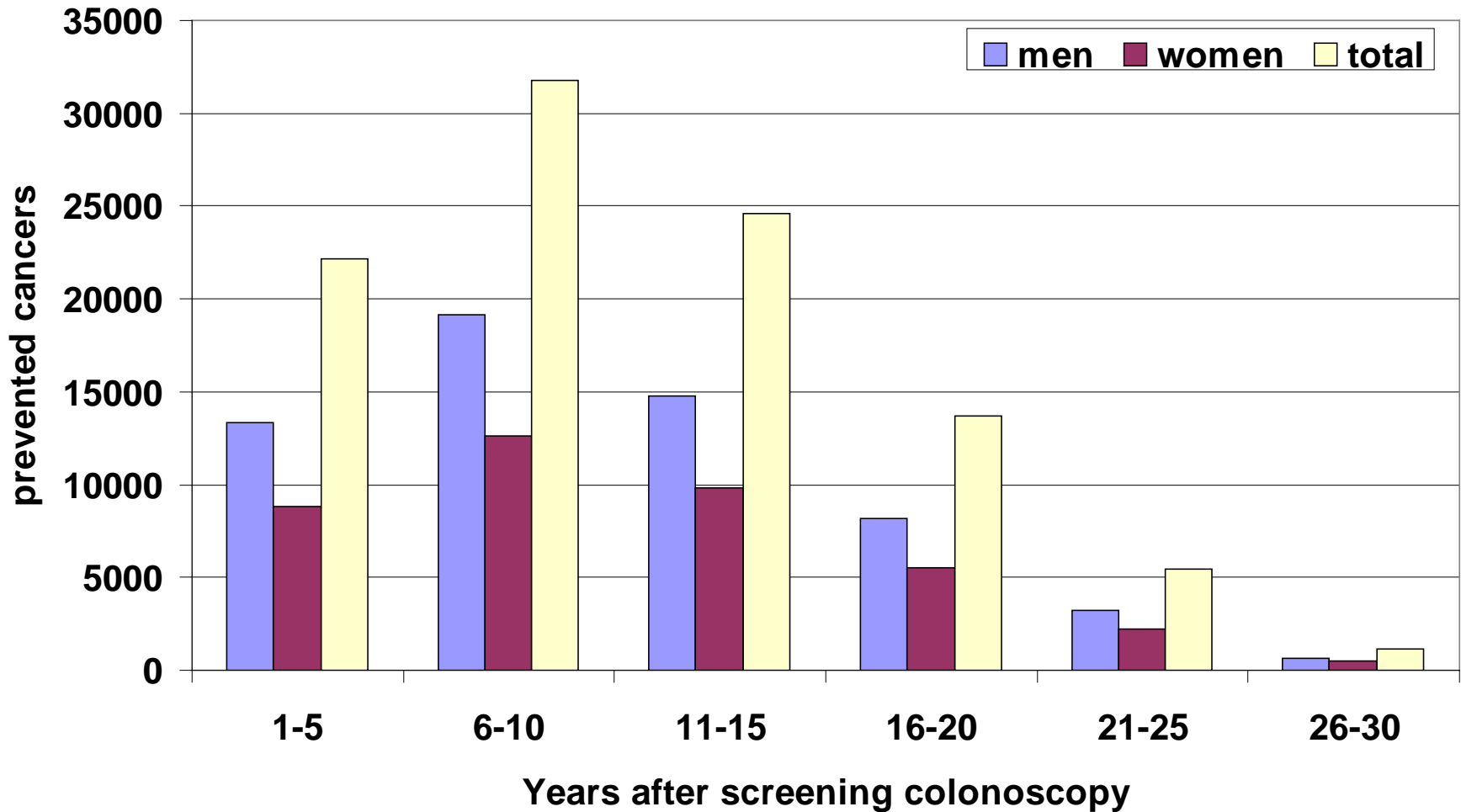
Brenner et al, Dtsch Ärztebl 2010

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



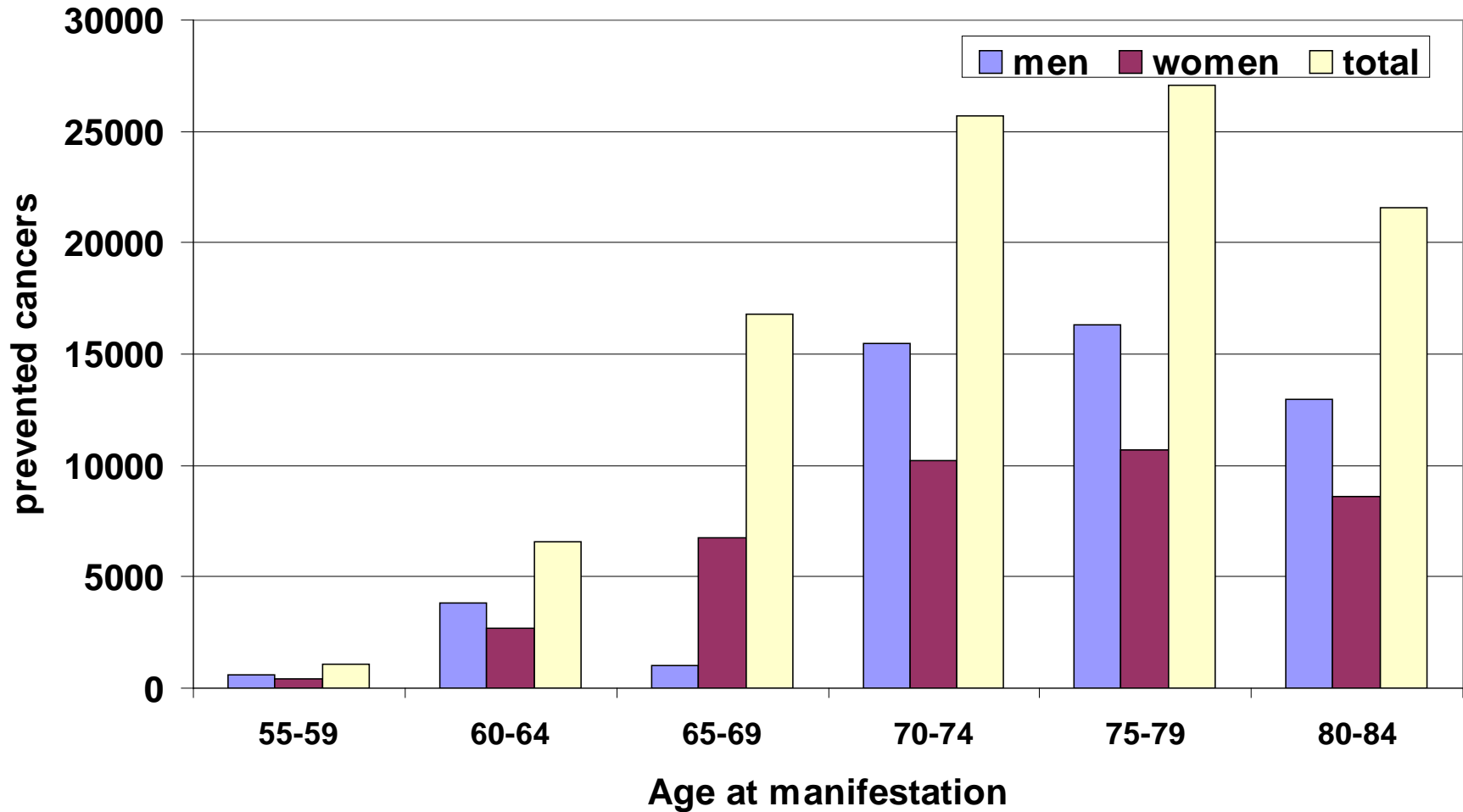
Brenner et al., Dtsch Ärztebl 2010

Estimated: almost 100.000 cancers prevented



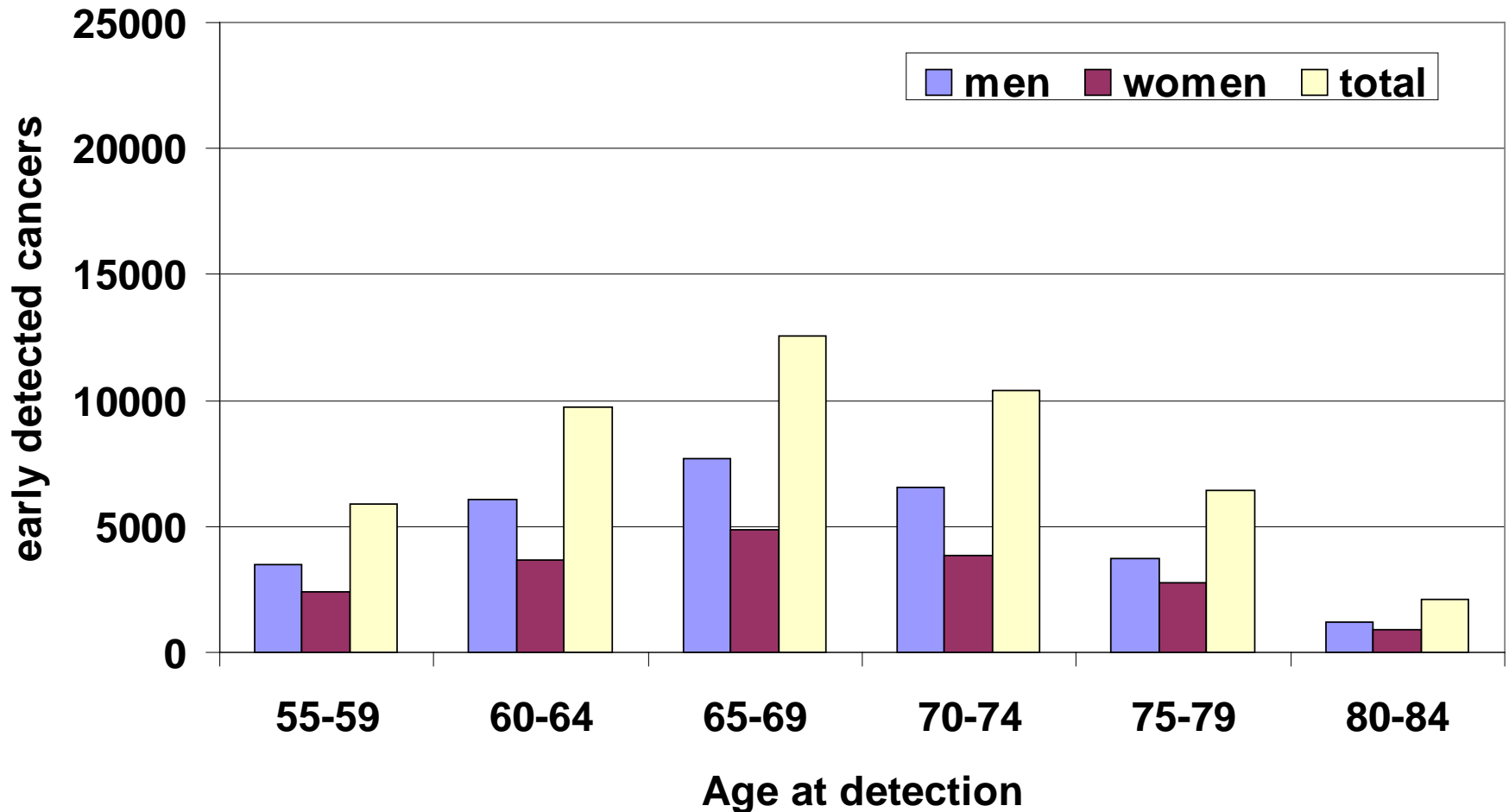
Brenner et al, Dtsch Ärztebl 2010

Estimated: almost 100.000 cancers prevented



Brenner et al, Dtsch Ärztebl 2010

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



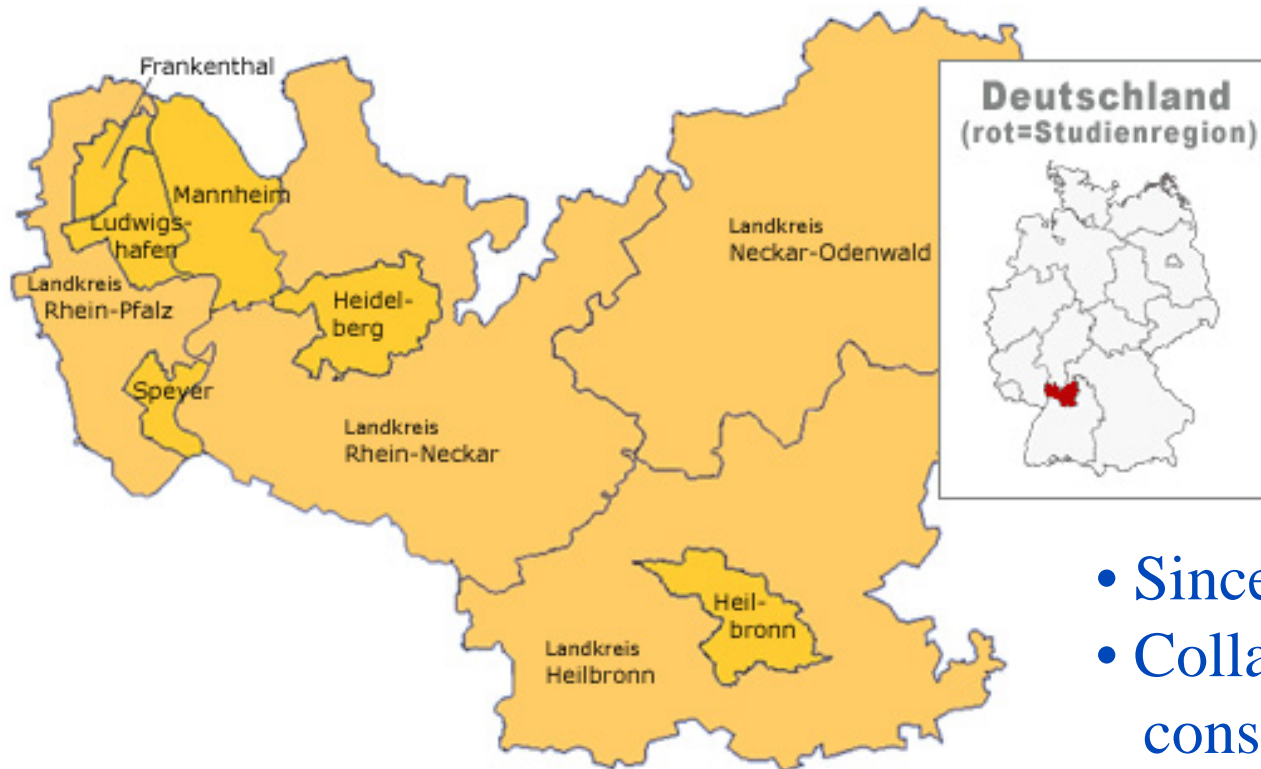
Brenner et al, Dtsch Ärztebl 2010

Effectiveness of colonoscopy in routine setting ?

DACHS

Darmkrebs: Chancen der Verhütung durch Screening

- **Population-based case-control study**
- 20 clinics, 3.800 cases, 3.800 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)

Brenner et al, 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)

Brenner et al, 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)

Brenner et al, 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)

Brenner et al, 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)

Brenner et al, 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)

Brenner et al, 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)

Brenner et al, 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)

Brenner et al, Ann Intern Med 2011;154:22-30

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

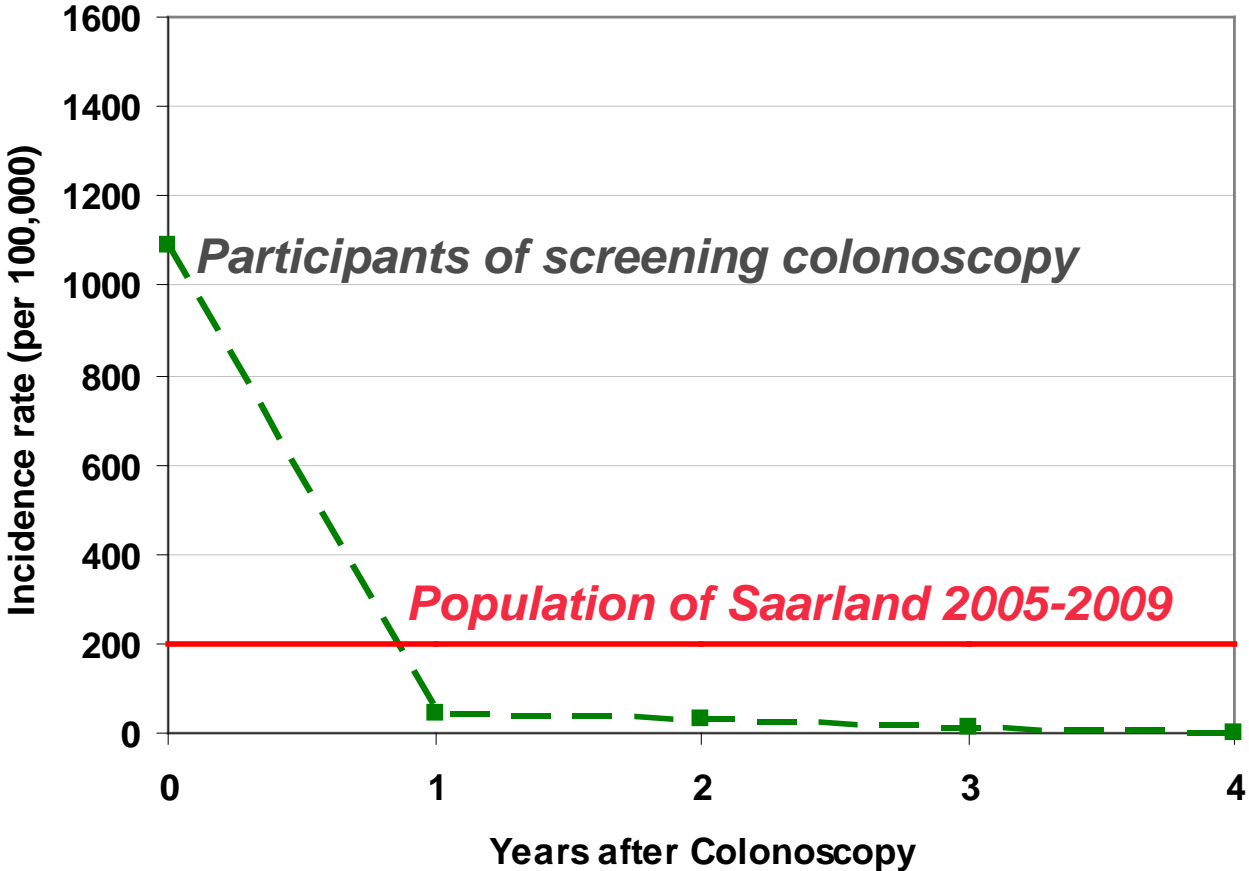
Long Term Follow-up !

**Preliminary
Data !**

Annual colorectal cancer incidence

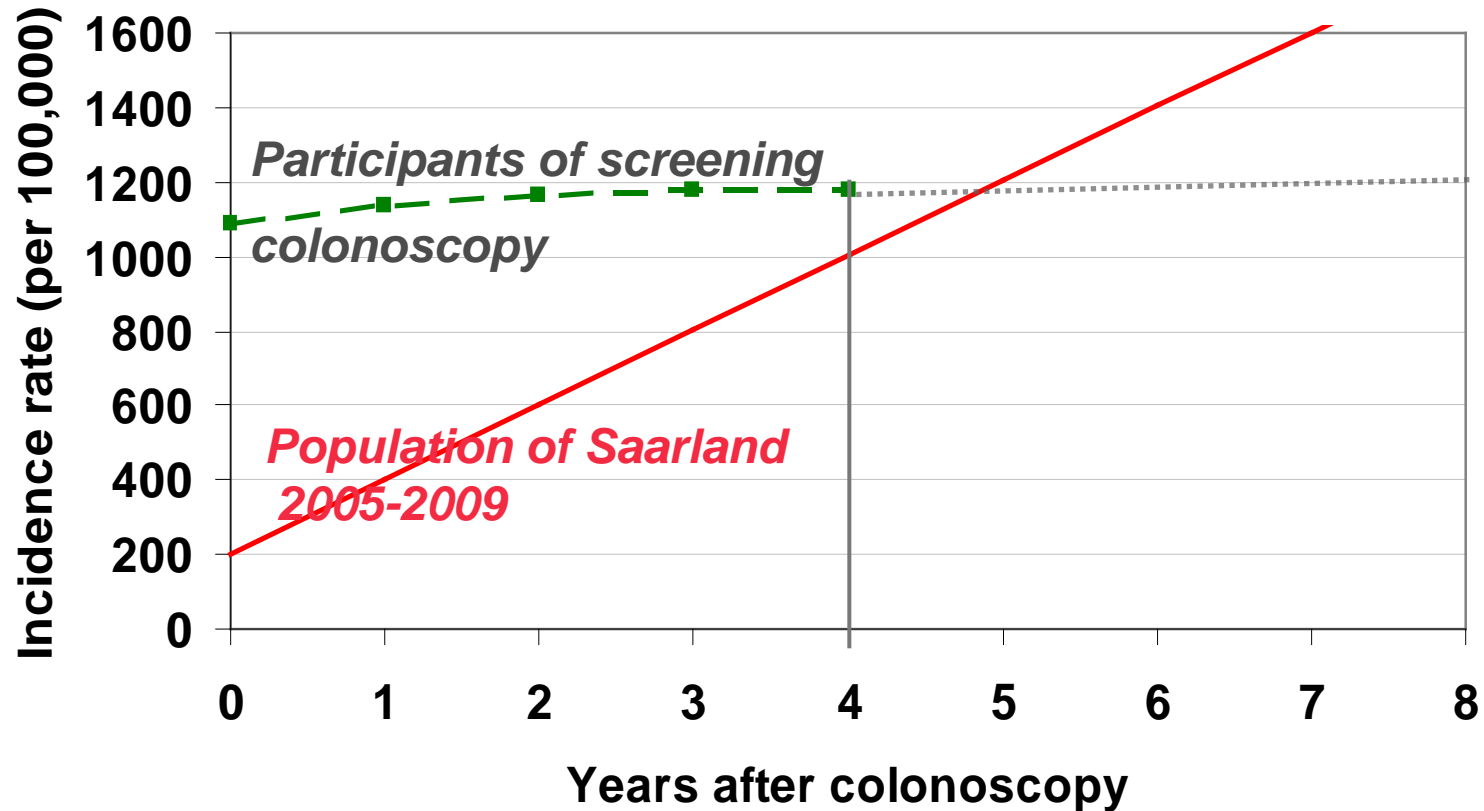
- Age- and sex-standardized incidence ratio (SIR)*

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



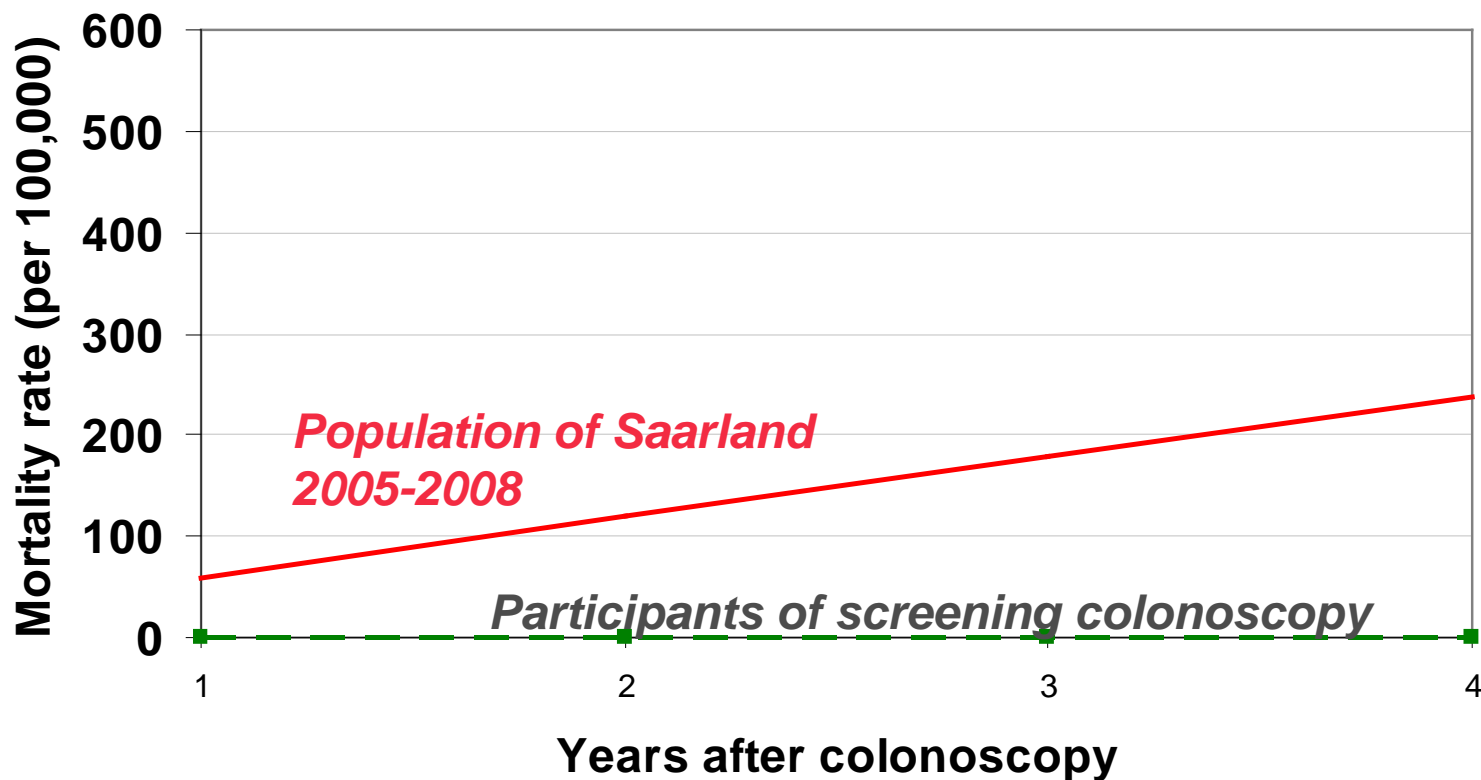
**Preliminary
Data !**

Cumulative colorectal cancer incidence



**Preliminary
Data !**

Cumulative colorectal cancer mortality



$$\text{SMR} = N \text{ observed} / N \text{ expected} = 0 / 21.9 = 0 \text{ (0.00-0.17)}$$

Summary

Colonoscopy highly effective in preventing CRC, especially left sided CRC, but also right sided CRC

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

Outlook

- **Major and accelerating reductions in colorectal cancer incidence and mortality expected in coming 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**
=> National Cancer Plan, model project in Saarland (SAMS study)

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

German Federal Ministry of Health

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	274 €

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

Savings

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

Z Gastroenterologie 2007;45:945-51

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]