

**Effect of screening sigmoidoscopy and
screening colonoscopy on colorectal cancer
incidence and mortality:**

**Systematic review and meta-analysis of
randomised trials and observational studies**

Hermann Brenner

Division of Clinical Epidemiology and Aging Research

German Cancer Research Center, Heidelberg

Randomised Trials

=> Effects of screening offer under trial conditions

4 RCTs on screening sigmoidoscopy published in 2009-2012

RCT on screening colonoscopy started in 2009 (NORDICC)

Authors year	Country	N	Age	Inter- vention	Recruit- ment	Follow -up Years (Med.)	% with endoscopy	
							Inter- vention	Con- trol
Hoff et al 2009	NORWAY	55,736	55-64	1 x FlexSig	1999- 2000	7	64.8	?
Atkin et al 2010	UK	170,432	55-64	1 x FlexSig	1994- 1999	11.2	71.1	?
Segnan et al 2011	ITALY	56,532	55-64	1 x FlexSig	1995- 1999	10.5	58.3	?
Schoen et al 2012	USA	154,900	55-74	FlexSig T0 + 3-5 yr	1993- 2001	11.9	86.6	46.5

Brenner, Stock, Hoffmeister, BMJ 2014

RCT Colonoscopy: NORDICC Study, started in 2009

Bretthauer, DDW 2011



Poland



Netherlands



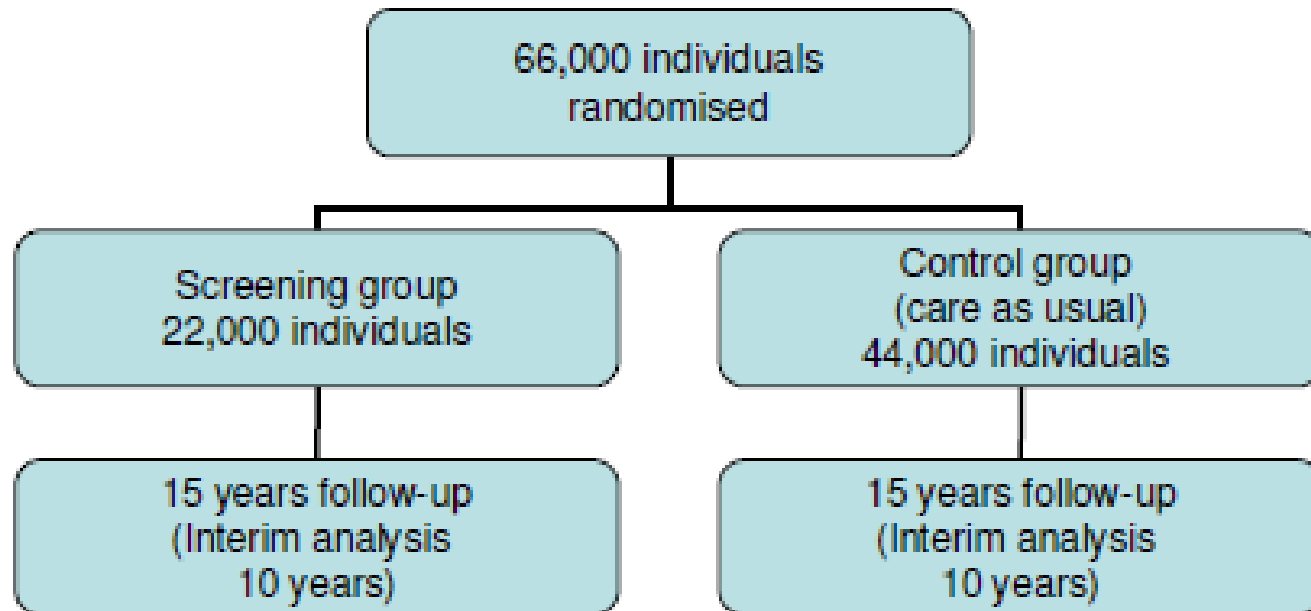
Norway



Sweden

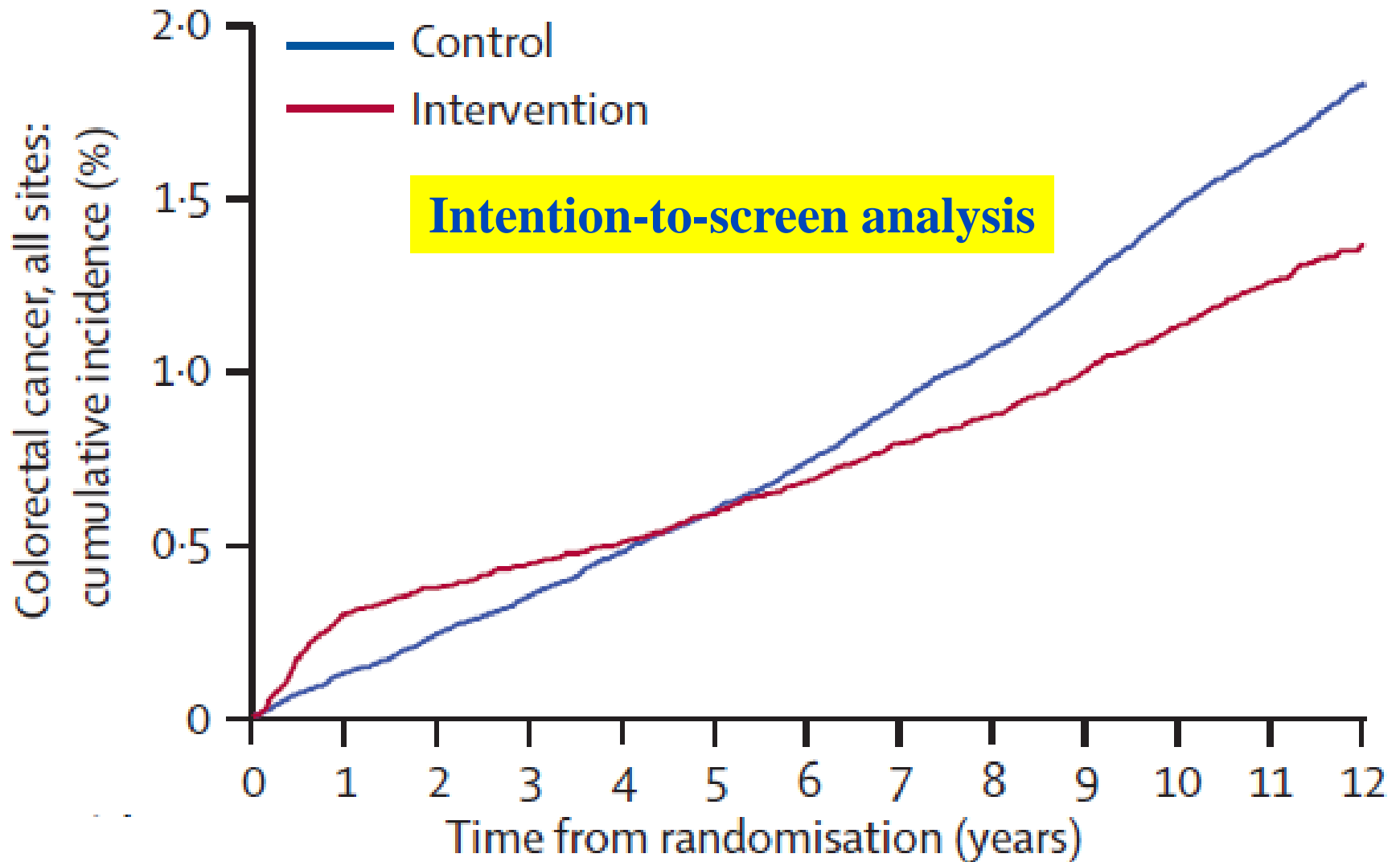


Iceland

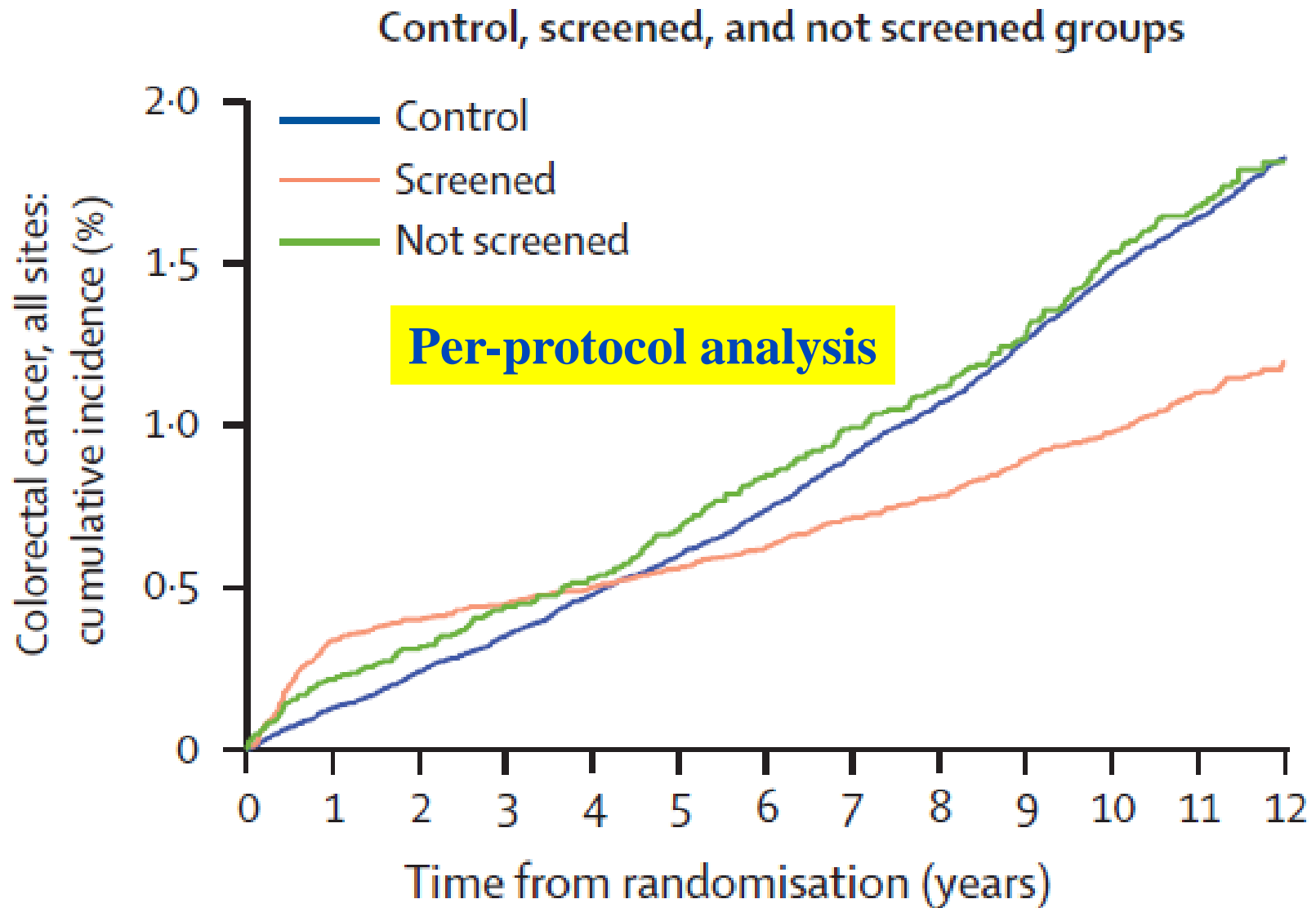


Main results on colorectal cancer mortality expected in 2030

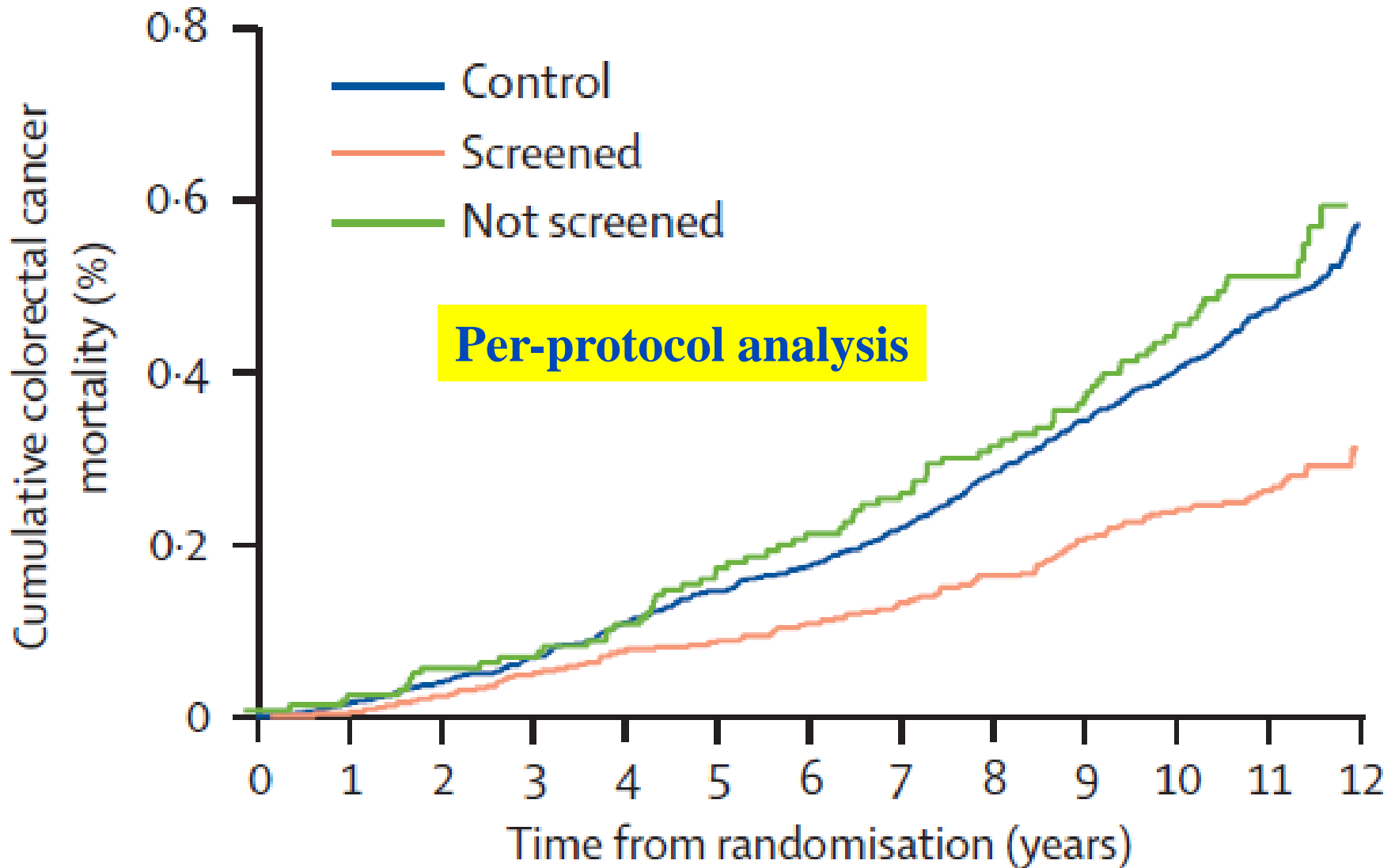
UK Trial, Atkin et al, Lancet 2010: Incidence



UK Trial, Atkin et al, Lancet 2010: Incidence



UK Trial, Atkin et al, Lancet 2010: Mortality



Sigmoidoscopy RCTs

Meta-analysis reduction of CRC incidence

Analysis	Site	Reduction of incidence
Intention-to-screen	Overall	-21%
	Proximal	- 9 %
	Distal	-31%
Per-protocol*	Overall	-33%
	Proximal	- 6 % n.s.
	Distal	-47%

* adjusted for non-compliance, but not for contamination

Sigmoidoscopy RCTs

Meta-analysis reduction of CRC mortality

Analysis	Site	Reduction of mortality
Intention-to-screen	Overall	-28%
	Proximal	- 5 % n.s.
	Distal	-46%
Per-protocol*	Overall	-44%
	Proximal	-22% n.s.
	Distal	-61%

* adjusted for non-compliance, but not for contamination

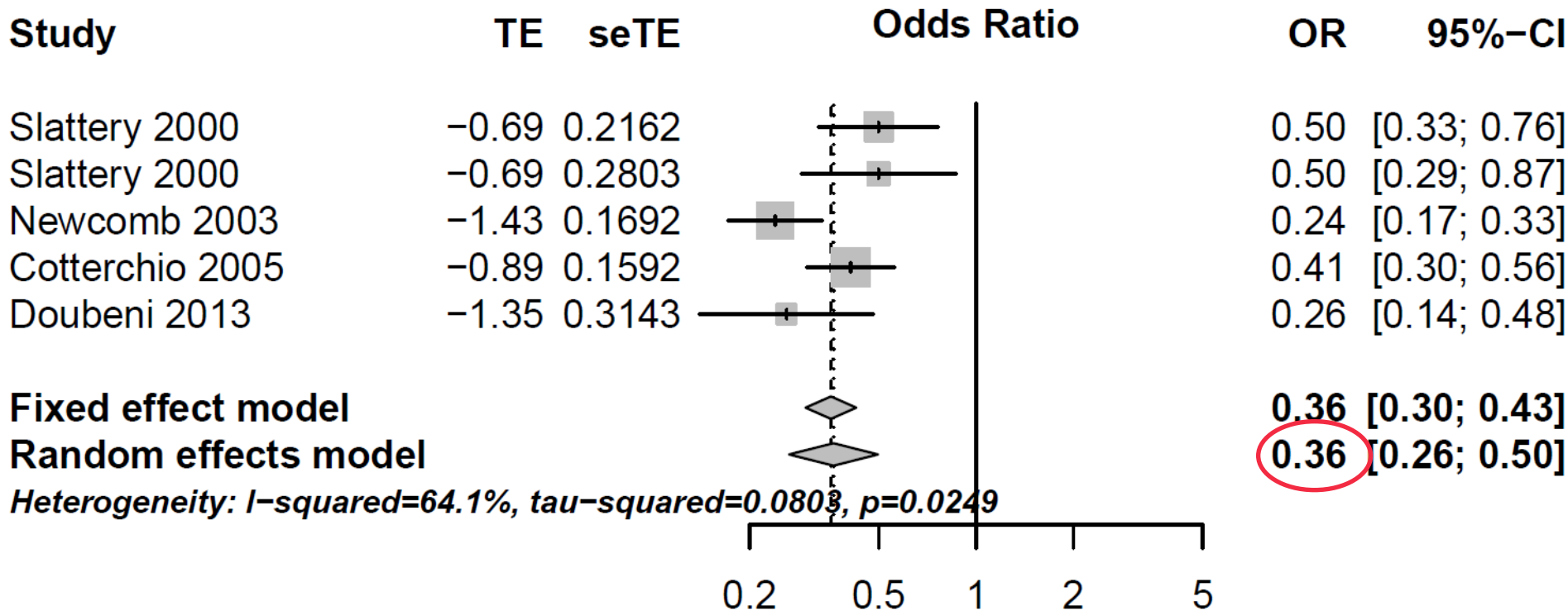
RCTs Sigmoidoscopy: Impact of non-adherence and contamination

Adherence proportion	Contamination proportion	True relative CRC incidence or mortality		
		RR=0.30	RR=0.50	RR=0.70
		Observed relative CRC incidence or mortality		
0.90	0.10	0.39	0.57	0.75
0.90	0.30	0.44	0.63	0.79
0.90	0.50	0.52	0.70	0.84
0.70	0.10	0.53	0.67	0.81
0.70	0.30	0.57	0.71	0.84
0.70	0.50	0.62	0.77	0.88
0.50	0.10	0.66	0.76	0.86
0.50	0.30	0.69	0.79	0.88
0.50	0.50	0.73	0.83	0.91

Brenner et al, J Clin Epidemiol 2014

Meta-Analysis Observational Studies

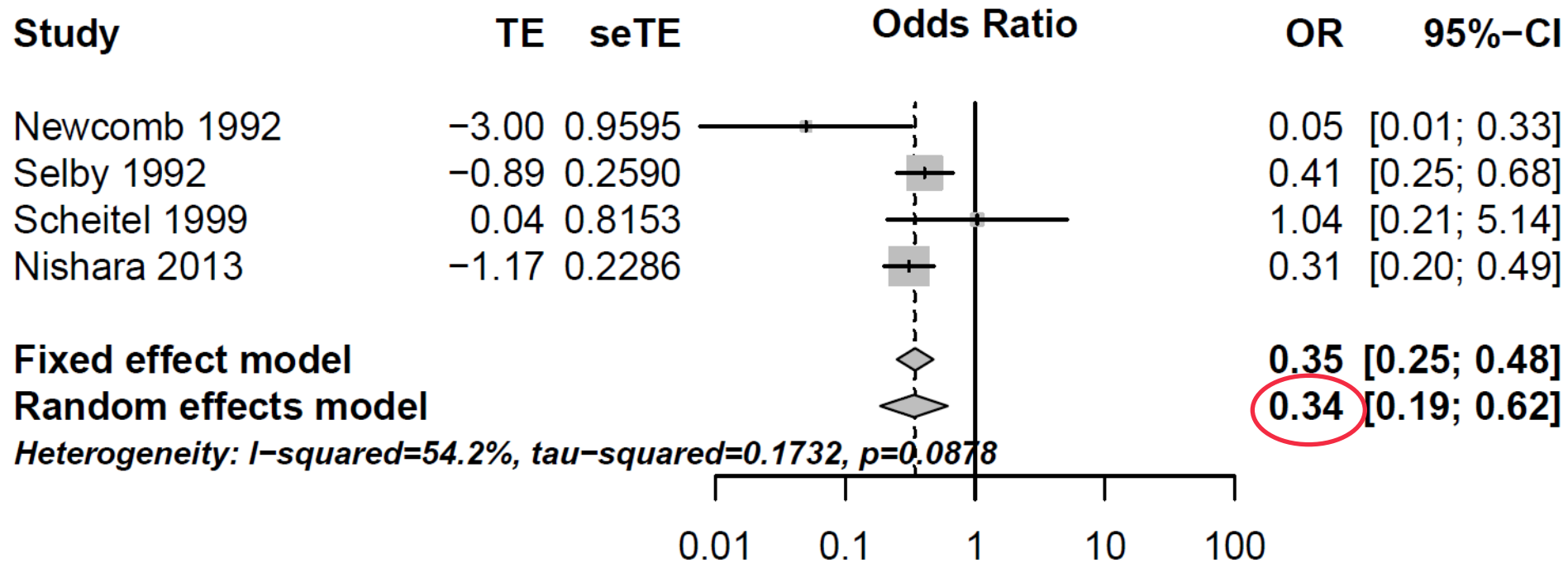
Previous screening sigmoidoscopy – distal CRC incidence



Brenner, Stock, Hoffmeister, BMJ 2014

Meta-Analysis Observational Studies

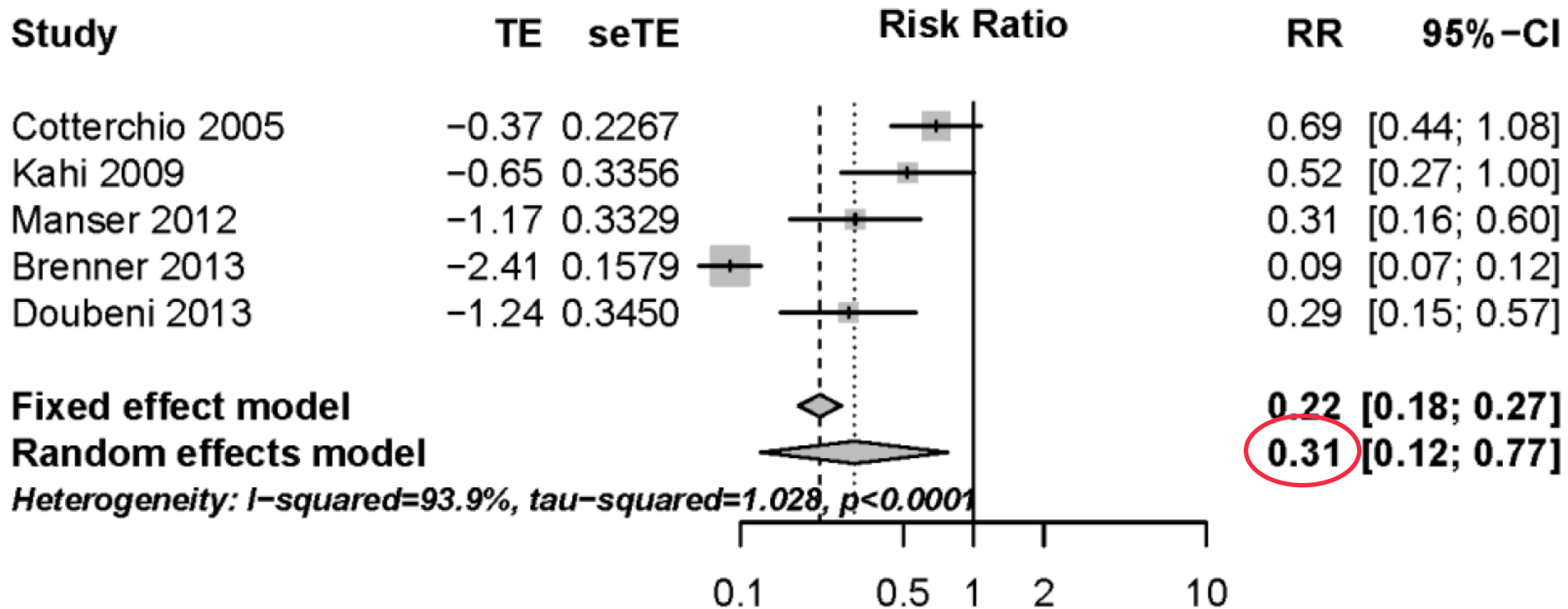
Previous screening sigmoidoscopy – distal CRC mortality



Brenner, Stock, Hoffmeister, BMJ 2014

Meta-Analysis Observational Studies

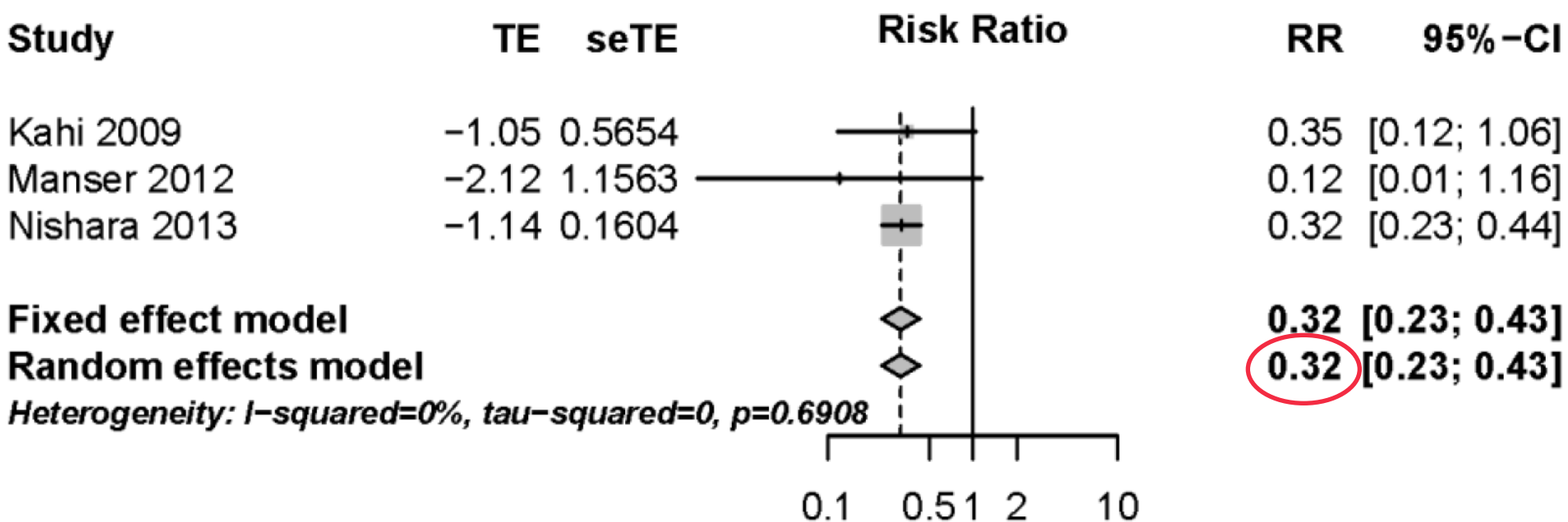
Previous screening colonoscopy – total CRC incidence



Brenner, Stock, Hoffmeister, BMJ 2014

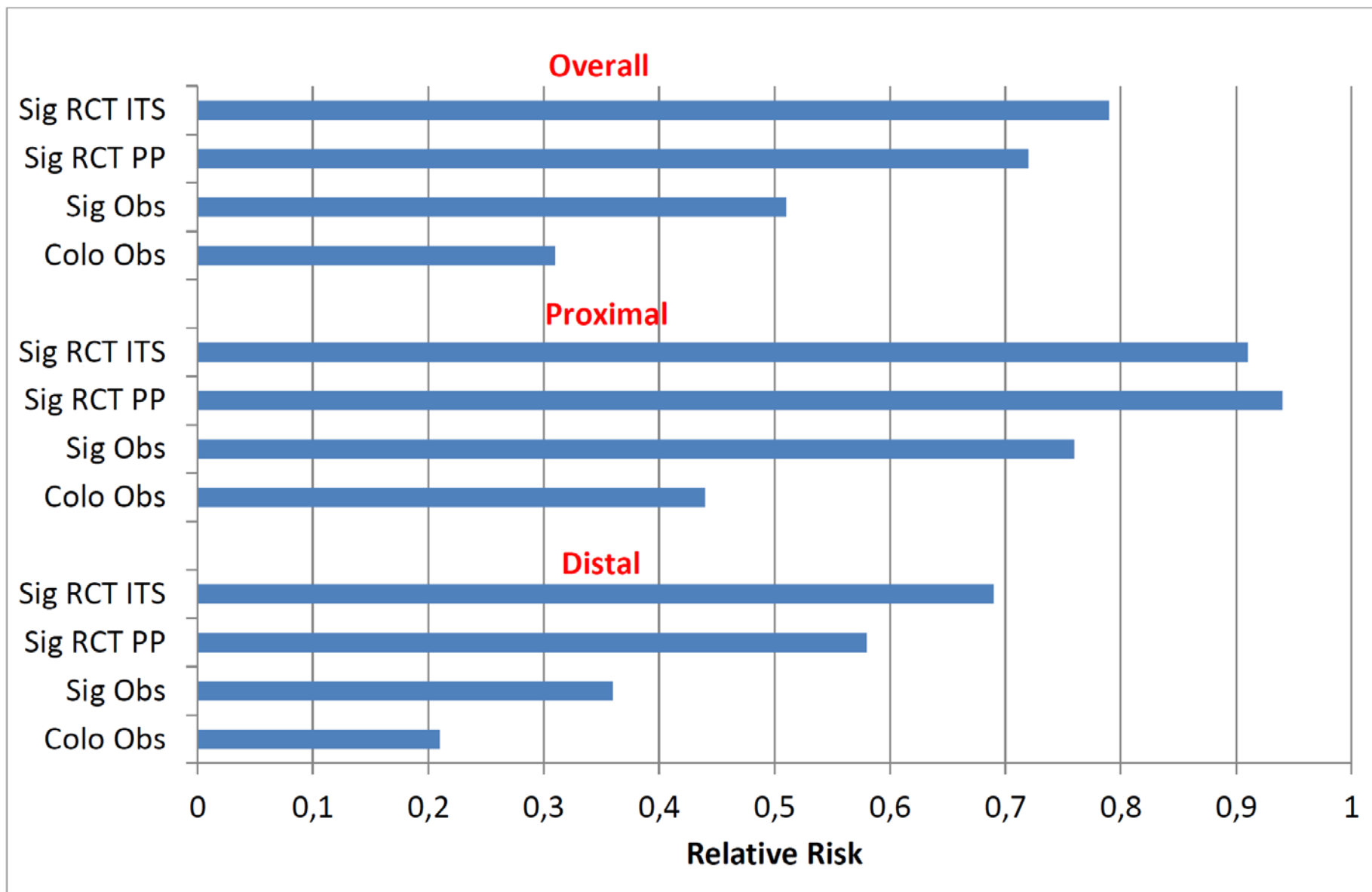
Meta-Analysis Observational Studies

Previous screening colonoscopy – total CRC mortality

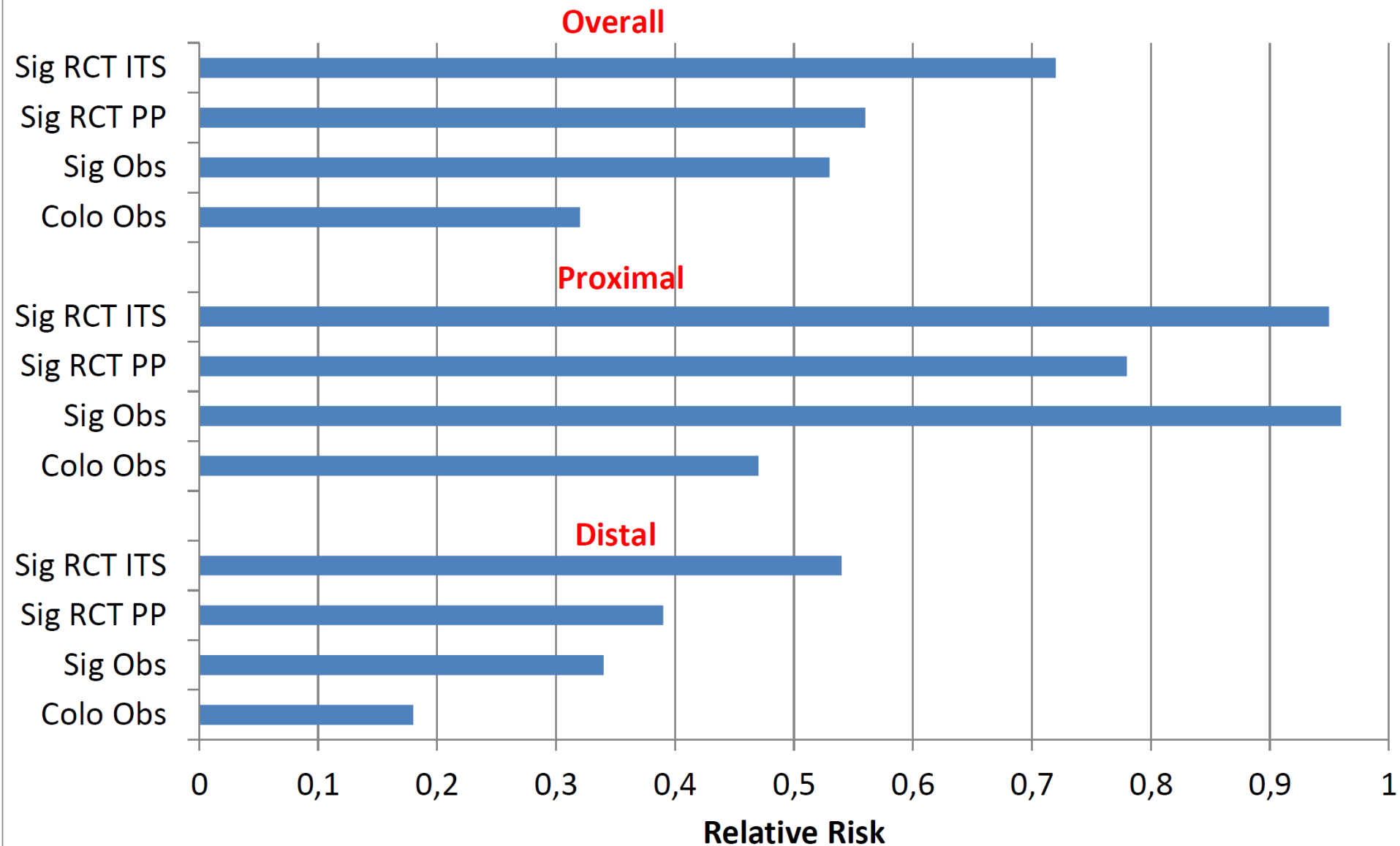


Brenner, Stock, Hoffmeister, BMJ 2014

Summary Meta-Analyses CRC Incidence



Summary Meta-Analyses CRC Mortality



Summary and Conclusions

RCTs ...

... provide most valid estimates of the effects of offering screening sigmoidoscopy or colonoscopy

(highly relevant for political / public health decisions)

... may strongly underestimate **effects of actually performed screening sigmoidoscopy or colonoscopy**

(most relevant for individual screening decisions)

due to non-adherence (overcome in per-protocol analyses:

47% / 61% reduction in distal CRC incidence/mortality)

due to contamination (not adjusted for in RCT publications)

... results are available for screening sigmoidoscopy only,
will not be available for screening colonoscopy for a very long time

Summary and Conclusions

Observational studies ...

... are prone to a number of potential biases
confounding, misclassification etc.
=> utmost care in design and interpretation

... provide effect estimates of actually performed
screening sigmoidoscopy or colonoscopy

(most relevant for individual screening decisions)

Sigmoidoscopy: 64%/69% reduction in distal CRC incidence/mortality

Colonoscopy: 69%/68% reduction in total CRC incidence/mortality

Summary and Conclusions

Important complementary information provided by RCTs and observational studies

They jointly provide strong evidence of very high potential of sigmoidoscopy/colonoscopy for reducing distal/total CRC incidence and mortality

Public health/political decisions and implementation should consider additional aspects

- availability of high quality resources
- adequate training and quality assurance
- adherence
- supplementary / alternative screening offers, such as FITs
- cost-effectiveness