# What is the impact of population screening for CRC?

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#### **Conflicts of interest**



## **CRC** incidence

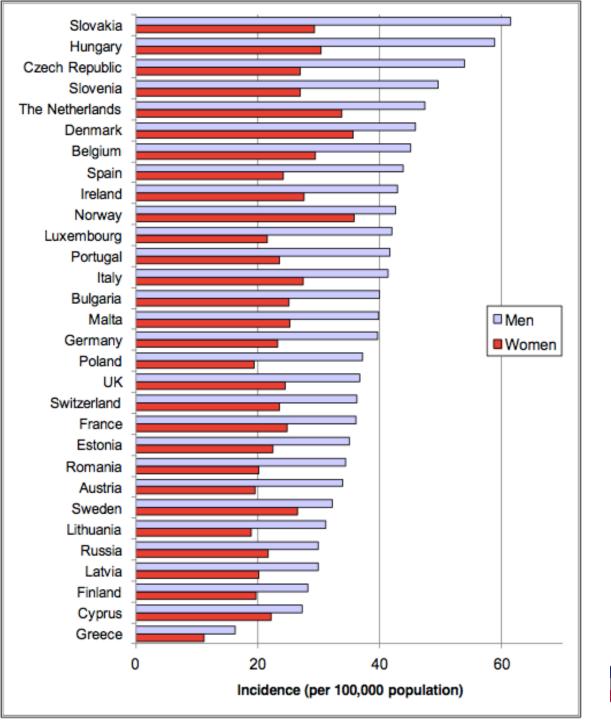
- CRC is the third most common cancer in Europe 342,000 new cases in 2012 (13% of all cancers)
- Overall incidence rate: 68 per 100,000 population
- Incidence in men:
- Incidence in women:
- 79 per 100,000
- 54 per 100,000





CRC Incidence 2012

#### Five-fold variation in IR



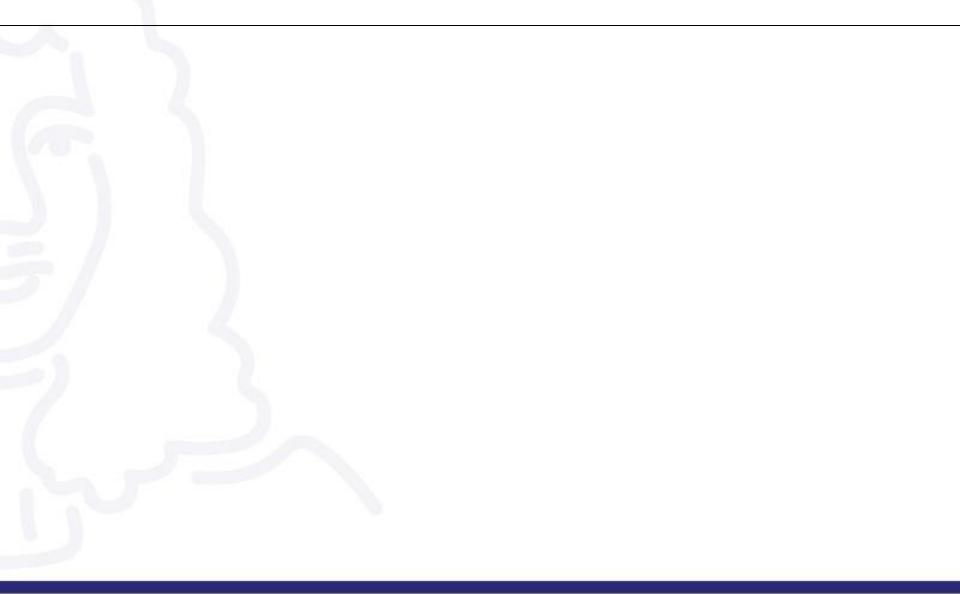
## **CRC** mortality

- CRC is the second most common cause of cancer related death in Europe
- 215,000 cases in 2012 (12-13% of all cancer deaths)

White book 2014, Ferlay Eur J Cancer 2013



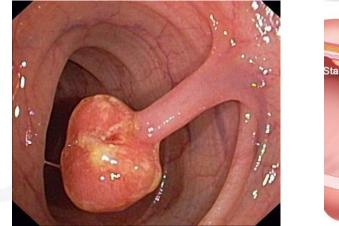
#### CRC screening

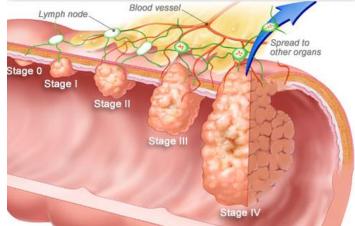


#### **CRC** screening

CRC is very suitable for screening

- Detectable and treatable pre-malignant lesions (adenomas)
- Early detection of CRC improves the prognosis
- Benefits outweigh the potential harms





Brenner, BMJ, 2014; Hewitson, Am J Gastro, 2008; Lansdorp-Vogelaar, Epi Rev, 2011

#### **Cost-effectiveness of CRC screening**

- CRC screening is cost-effective compared to no screening (cost-saving)
- No single strategy found to be the most effective or preferred for a given willingness to pay per LYG
- Reappraisal of CEA of CRC screening over time in light of rising treatment costs

Lansdorp-Vogelaar Epidemiol Rev 2011

#### **Cost-effective Screening methods**

#### FOBT

Chemical test (gFOBT) Immunochemical test (iFOBT) Stool DNA tests

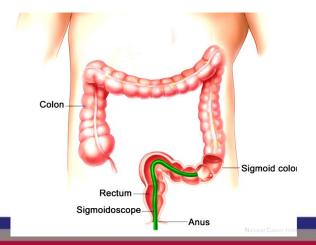
Endoscopy Sigmoidoscopy Colonoscopy

CTC Capsule endoscopy

Lansdorp-Vogelaar Epidemiol Rev 2011







## EU Counsel recommendation on cancer screening 2003

The Code against Cancer recommends:

# - faecal occult blood screening for colorectal cancer in men and women aged 50-74







No screening or unknown Opportunistic: gFOBT/FIT-based Opportunistic: colonoscopy (+gFOBT/FIT) Population-based organised, pilot Population-based organised, roll-out ongoing Population-based organised, roll-out complete

Schreuders Gut 2015 (WEO),

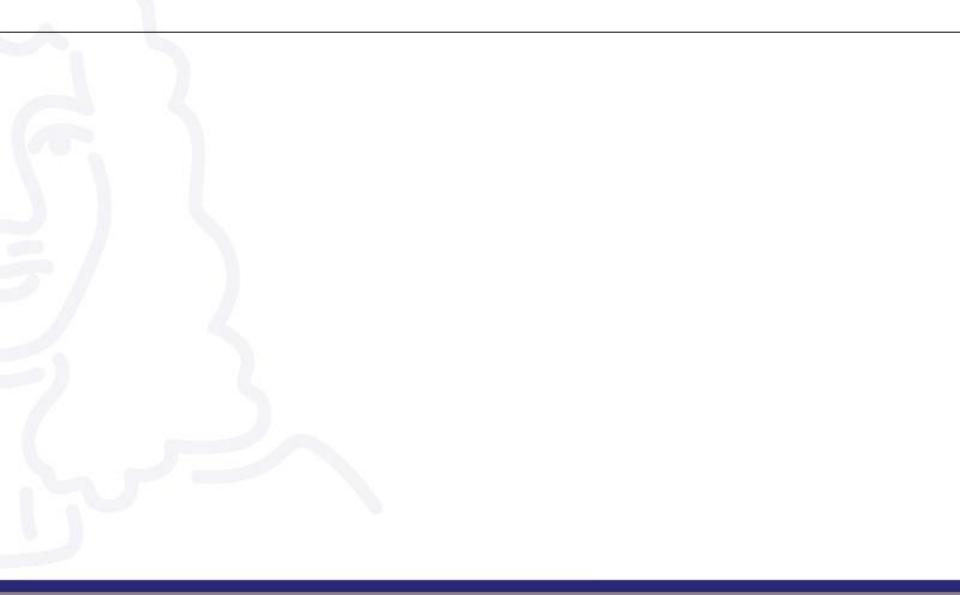
## **CRC** screening

Making screening effective depends on several factors;

- Solid organisation/ efficacy of the program
  - Uptake
- Quality assurance on all levels



#### Impact of CRC screening



## CRC screening; proven effect on mortality



**Cochrane** Database of Systematic Reviews



## Screening for colorectal cancer using the faecal occult blood test, Hemoccult (Review)

Hewitson P, Glasziou PP, Irwig L, Towler B, Watson E

#### CRC mortality; Hemoccult screening vs control

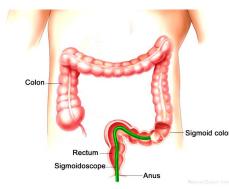
Study or subgroup	Screening	Control	Peto Odds Ratio	Weight	Peto Odds Ratio
, , ,	n/N	n/N	Peto,Fixed,95% Cl		Peto,Fixed,95% Cl
I Randomised controlled t	trials				
Funen 2004	362/30967	431/30966	-	26.2 %	0.84 [ 0.73, 0.96 ]
Goteborg 2005	252/34144	300/34164	-	18.3 %	0.84 [ 0.71, 0.99 ]
Minnesota 1999	269/31157	177/15394	•	13.1 %	0.74 [ 0.61, 0.90 ]
Nottingham 2002	593/76466	684/76384	-	42.4 %	0.87 [ 0.77, 0.97 ]
Total (95% CI)	172734	156908	•	100.0 %	0.84 [ 0.78, 0.90 ]
Total events: 1476 (Screen	ing), 1592 (Control)				
Heterogeneity: Chi <sup>2</sup> = 1.85	5, df = 3 (P = 0.60); I <sup>2</sup>	=0.0%			
Test for overall effect: $Z =$	4.89 (P < 0.00001)				
Test for subgroup difference	ces: Not applicable				
			0.1 0.2 0.5 1 2 5	10	
			Favours screening Favours contr	rol	

#### 16% mortality reduction

## CRC screening; proven effect on mortality



Cochrane Database of Systematic Reviews



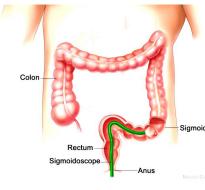
Flexible sigmoidoscopy versus faecal occult blood testing for colorectal cancer screening in asymptomatic individuals (Review)

Holme Ø, Bretthauer M, Fretheim A, Odgaard-Jensen J, Hoff G

#### CRC mortality; FS screening vs control

Study or subgroup	Screening	Control	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI
I Flexible sigmoidoscopy					
Atkin 2010	221/57099	637/112939	-	47.3 %	0.69 [ 0.59, 0.80 ]
Hoff 2009	24/13653	99/41092		5.5 %	0.73 [ 0.47, 1.14 ]
Schoen 2012	252/77445	341/77455	+	37.7 %	0.74 [ 0.63, 0.87 ]
Segnan 2011 (1)	65/17136	83/17136		9.2 %	0.78 [ 0.57, 1.08 ]
This-Evensen 1999	1/400	3/399	+ +	0.3 %	0.33 [ 0.03, 3.18 ]
Subtotal (95% CI)	165733	249021	•	100.0 %	0.72 [ 0.65, 0.79 ]
2011 - 1 2 2 2 2 2 2 1 S			1		

28% mortality reduction18% incidence reduction



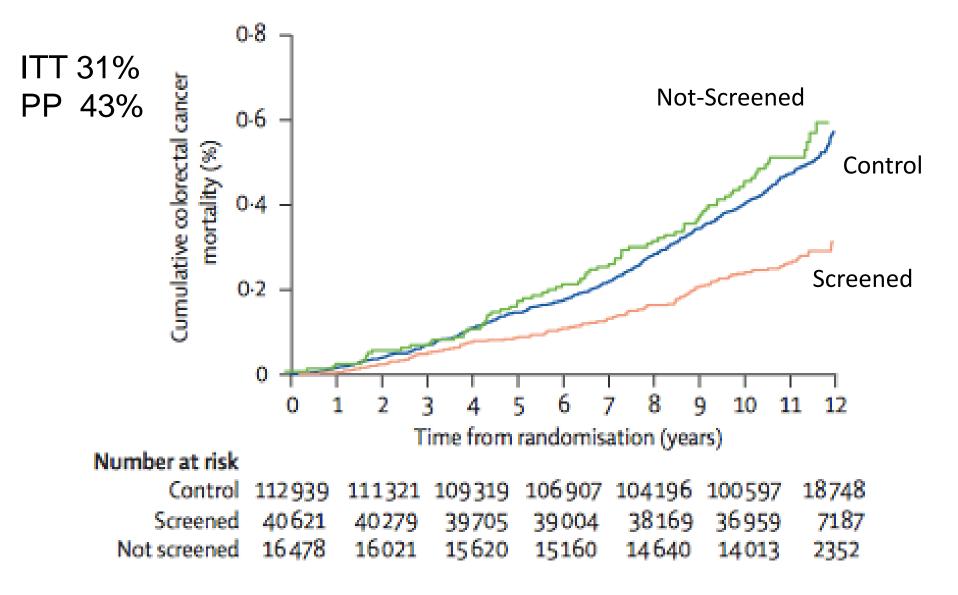
# CRC screening; proven effect on mortality and incidence

#### Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew RHart, John M A Northover, D M ax Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators

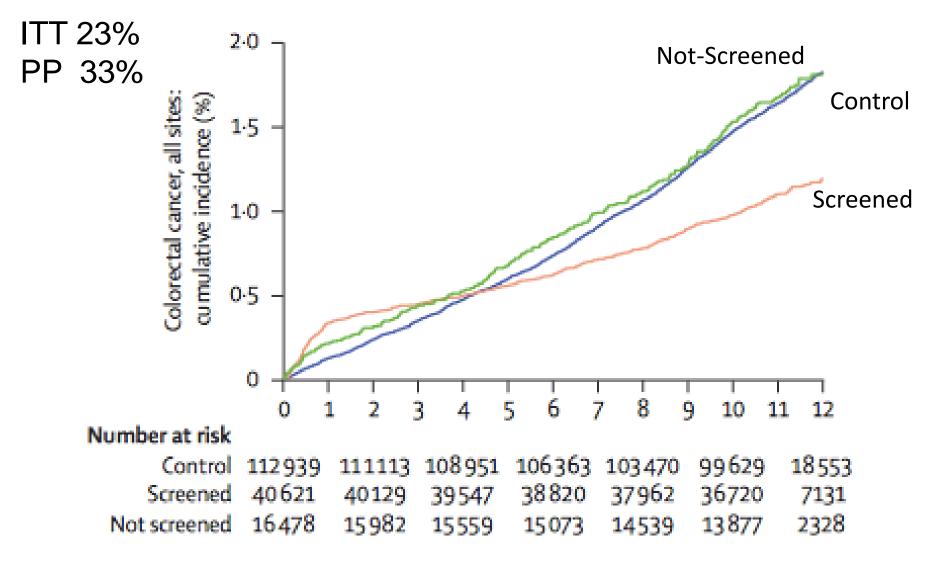
Atkin Lancet 2010,

## CRC screening; proven effect on mortality



Atkin Lancet 2010,

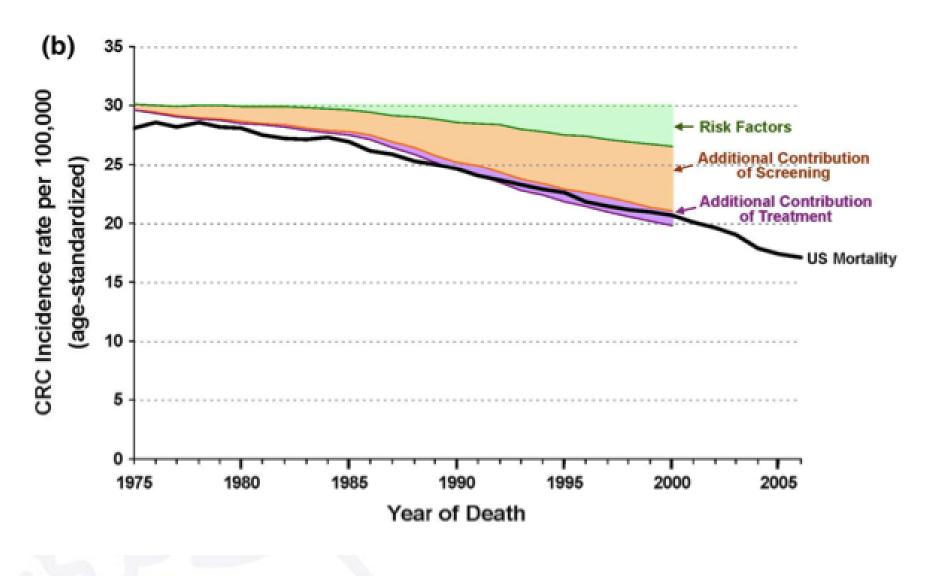
#### CRC screening; proven effect on incidence



Atkin Lancet 2010,

#### Impact of CRC screening

 Microsimulation modeling suggests that decline in CRC incidence and death in the USA are due to a relative large contribution from screening



Zauber Dig Dis Sci 2015

## CRC screening program

Effect on site and stage distribution



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#### Effect on site distribution

#### UK program (gFOBT) 1772 CRCs



Cancer site data were missing for 3.2%

Logan, GUT, 2012

#### Effect on stage distribution

#### • UK program (gFOBT) 1772 CRCs

Stage	%	
Malignant polyp	9.8%	ן
Dukes A	32.0%	71%
Dukes B	29.5%	
Dukes C	25.7%	
Dukes D	3.0%	

Cancer staging data were missing for 11.2%

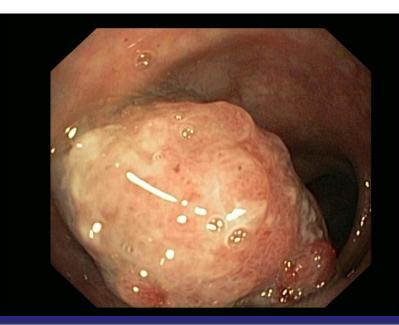
Logan, GUT, 2012

#### Effect on stage distribution

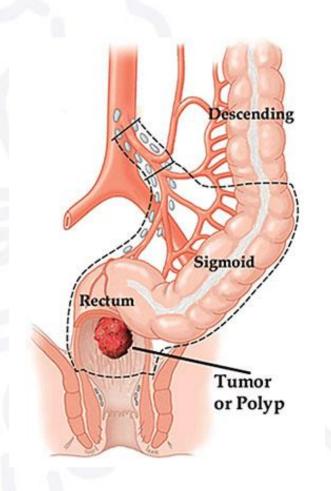
UK gFOBT program; 49% of screen-detected CRC pT1/T2N0

German colonoscopy screening program; 43% of screen-detected CRC pT1/T2N0

UK Colorectal Cancer Screening Pilot Group. BMJ 2004; Bokemeyer, Eur J Gastro&Hepatol 2009;21:650



## Colon/ Rectal preserving therapy?



**Postoperative mortality** 

Short term morbidity Anastomotic leakage

Long term morbidity Bowel dysfunction Bladder dysfunction Sexual dysfunction

## Colon/ Rectal preserving treatment

Complete clinical staging, discussion in MDT meeting, expertise mandatory

Endoscopic technique first choice (EMR,TEM, SILS port) for clinically low risk T1 cancers (< 3-4 cm)

High risk T1 of T2 after local excision: completion surgery

Dutch CRC guideline 2014



#### Median risk early Rectal Cancer?

T1/T2 N0 Rectal Cancer

Role for neo-adjuvant (chemo) radiotherapy?

Medium Risk Early Rectal Cancer T1 size 3-5 cm with any other histological characteristics, or size < 3 cm with poor differentiation and/or vascular invasion and/or lymphatic invasion. T2, well/moderate differentiated, No lymphatic or vascular invasion, size < 3cm

**TESAR** trial

#### Conclusions

CRC screening decreases CRC mortality and CRC incidence

Size and stage distribution changes with screening

Place for local excision for early CRC Place for organ preserving treatment of early Rectal Cancer???

#### Acknowledgement

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