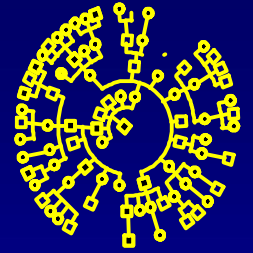




InSiGHT meeting,
Newcastle, United Kingdom
June 2005



Best surveillance protocol for Lynch syndrome?

Hans F.A.Vasen

The Netherlands Hereditary Cancer Registry

Leiden, The Netherlands

InSiGHT Surveillance protocol

(T. Weber, Lancet 1996; 348: 465)

<u>Site</u>	<u>Test</u>	<u>Age (yrs)</u>	<u>Interval</u>
Colon	Colonoscopy	20 – 25	2
Endometrium (ovaries)	Sonography CA125	30 – 35	1 - 2
<i>If cancer runs in the family:</i>			
Stomach	Gastroduodenoscopy	30-35	1 - 2
Urinarytract	Abdomen US Urine cytology	30-35	1 - 2

Validity and Grading of Recommendations

Validity		Grading
Meta-analysis	Ia	A
RCT	Ib	
Controlled trial without randomisation	IIa	B
Quasi-experimental	IIb	
Descriptive	III	
Expert opinion	IV	C

CRC surveillance (7 studies)

Author / year	Families	Type of study	Category of evidence
Love 1984	4	Descriptive	III
Mecklin 1987	22	Descriptive	III
Vasen 1989	22	Descriptive	III
Järvinen 1995	22	Clinical trial	IIb
Vasen 1995	50	Cohort study	III
Järvinen 2000	22	Clinical trial	IIb
De Vos 2002	114	Cohort study	III



Surveillance of 22 HNPCC families

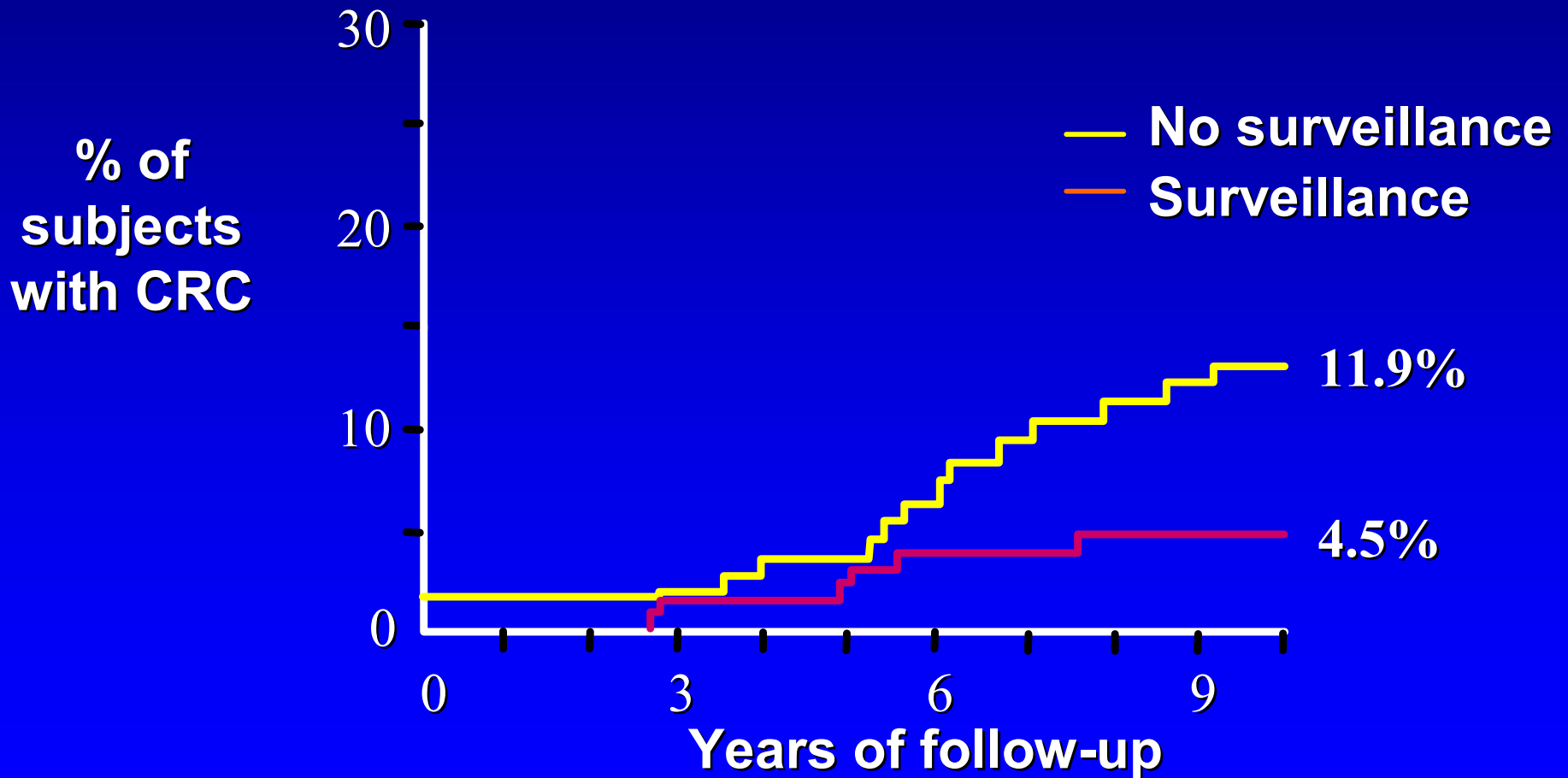
(Järvinen, Gastroenterology 1995; 108:1405)

- Clinical trial
- Colonoscopy 1x/3 yrs
- 133 accepted screening
- 118 refused/ could not be traced
- Follow up: 1985-1995



Surveillance of 22 HNPPCC families

(Järvinen, Gastroenterology 1995; 108:1405)



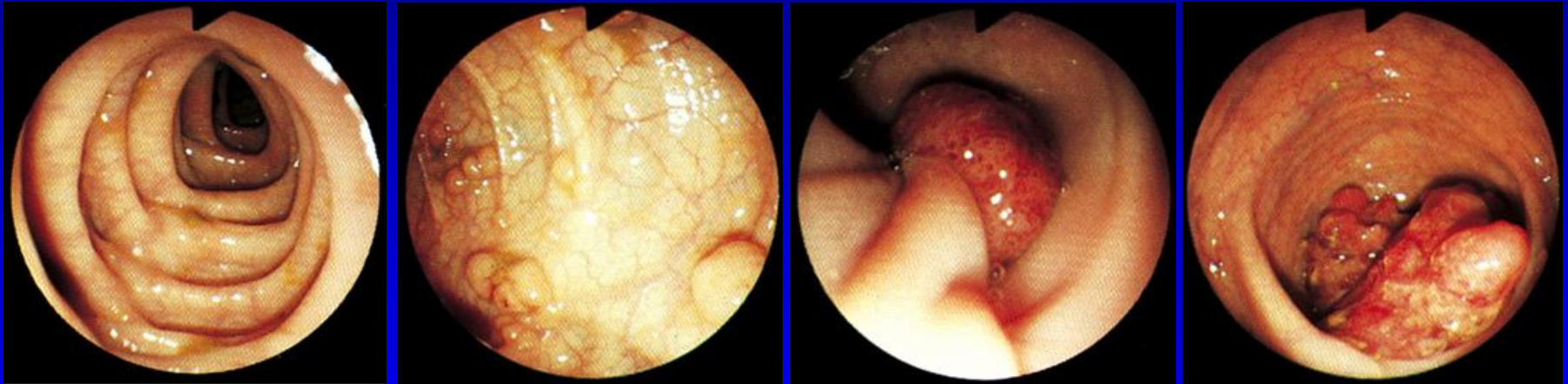


Reduction mortality in Lynch syndrome

(Järvinen, Gastroenterology 2000;118:829)

	Study group (133)	Control group (119)
CRC	-	9
Gastric cancer	1	-
Bile duct	-	1
Lymphoma	1	1
Brain tumor	1	-
Renal cancer	1	-
Other	6	15
Total	10	26

Accelerated carcinogenesis

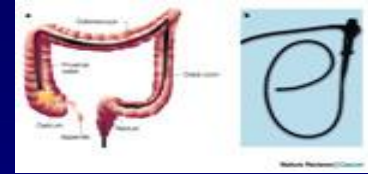


Jass JR. Mut Res 1994;310:125

Vasen HFA. Lancet 1995;345:1183

De Jong. Gastroenterology 2004;126:42

Does surveillance prevent
all deaths due to CRC?



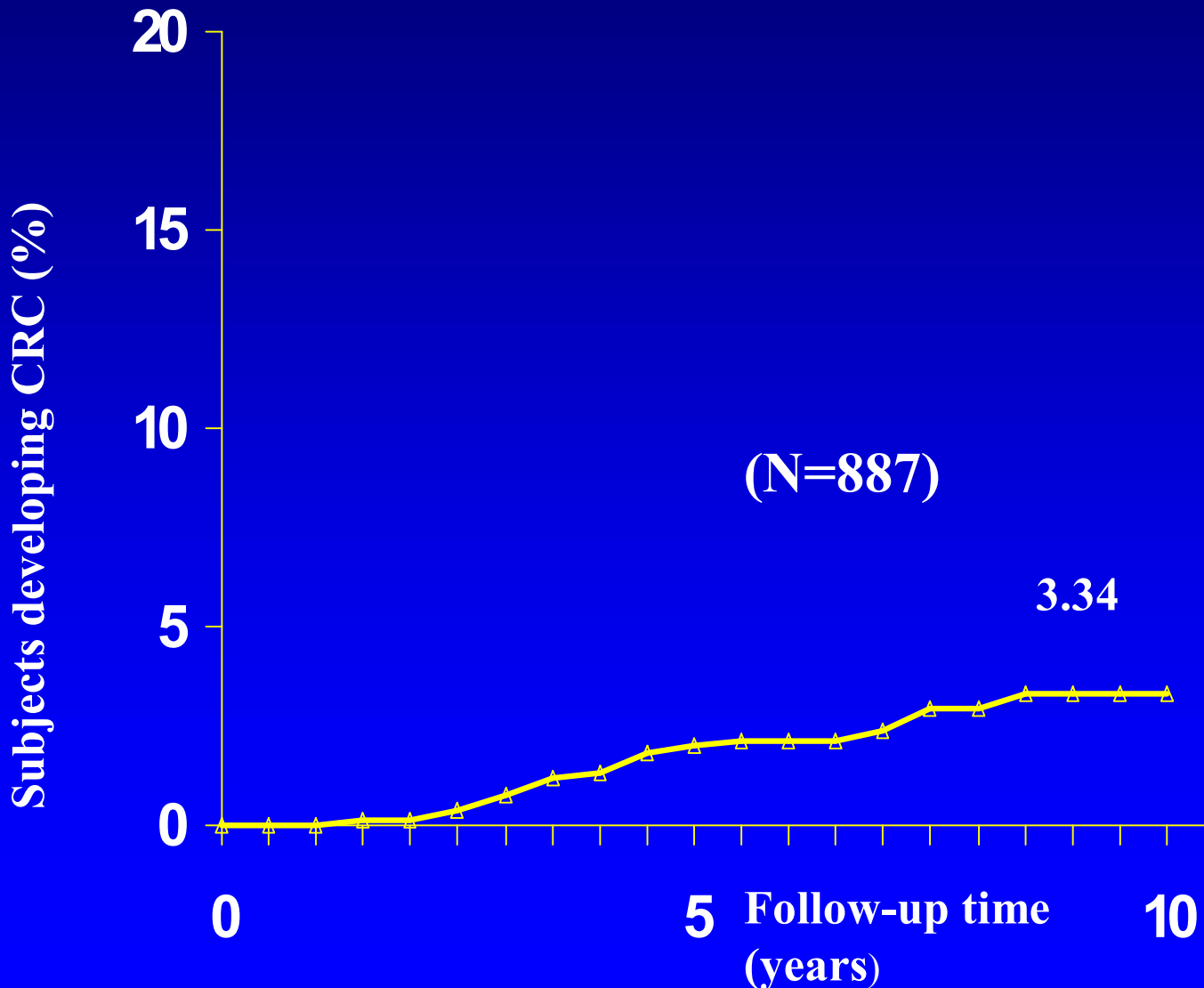
Surveillance for Lynch syndrome

(de Vos, Dis Colon Rectum 2002)

- 114 families (Adam or mutation)
- 887 relatives
- 199 mutation carriers
- Colonoscopy 1x/2-3 yrs
- Follow-up: 6.6 yrs

Surveillance of 114 HNPPC families

(De Vos et al. Dis Colon Rectum 2002;45:1588)



Stage of cancer in relation to interval since previous scopy (n=21)

Dukes Interval	A	B	C
0-1 yr	-	-	-
1-2 yrs	1	5	-
2-3 yrs	2	3	4
3-5 yrs	1	4	1

Conclusions

- With biennial screening risk developing Dukes B (~ 5%/10 yrs)
- Biennial screening probably does not prevent all CRC deaths
- Best interval one year?

Upper age limit surveillance?

(Dutch HNPPC database 2005)

	70 yrs	75 yrs	80 yrs
CRC free mutation carriers	56	39	25
P (CRC) next 10 years	10 %	10%	4%
Life expectancy (M/F)	12/15 yrs	9/11 yrs	6/8 yrs

Recommendations surveillance CRC

- Colonoscopy (grade B)
- Best interval between 1- 2 yrs (grade C)
- Upper age limit: 80 yrs ~ health status (grade C)

Surveillance: Other cancers in Lynch syndrome

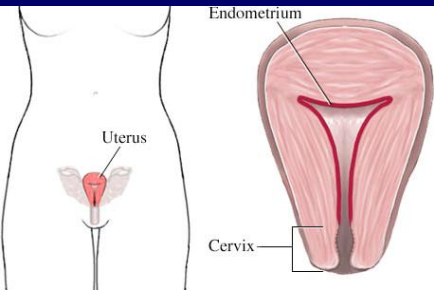
Endometrial cancer

Author / year	Subjects	Type of study	Category of evidence
Dove-Edwin 2002	269	Retrospective cohort study	III
Rijcken 2003	41	Retrospective cohort study	III

Gastric cancer

Renkonen-Sinisalo 2002	105	Controlled study	IIb
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Outcome endometrial carcinoma surveillance



UK / The Netherlands

(Cancer 2002;94:1708)

- 269 subjects
- 522 scans
- Two interval cancers:
 - symptoms <24 and 6 months after negative scan: both St I cancer

The Netherlands

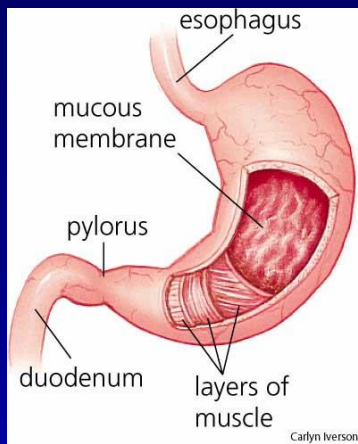
(Gyn.Oncology 2003;91:74)

- 41 subjects
- 179 scans (5 yrs)
- 3x (focal) complex atypia
- One interval cancer
 - symptoms 8 months after negative scan: Stage IB

EC-surveillance

Update Dutch HNPPC registry 2005

Subjects	200 (354 scans)	
Benign lesions	29	16x myomas 6x polyps 4x irregular 2x complex hyperplasia 1x dysplasia cervix
Malignant lesions	7	4x symptomatic after negative scan 2x screen-detected 1x hysterectomy ovarian cyst All Stage I



Endoscopic surveillance for gastric cancer in HNPPC

(L.Renkonen, Scand J Gastroenterol 2002; 37:574)

- 1x Gastroduodenoscopy
- 73 carriers, 32 controls
- Endpoints: HP, inflammation, atrophy, intestinal metaplasia, dysplasia
- No differences

Conclusions

Surveillance other cancers

- Endometrial cancer: no strong evidence for/ against surveillance
- Gastric/ urinary tract / ovarian cancer: no (longterm) studies
- BRCA-families: ovarian cancer surveillance not effective

Best recommendations for surveillance

Site	Test	Age (yrs)	Interval
Colon	Colonoscopy	20 – 25	2
Endometrium	Sonography	30 – 35	1 – 2
(ovaries)	CA125		

If cancer runs in the family:

Stomach	Gastroduodenoscopy	30-35	1 - 2
Urinarytract	Abdomen US	30-35	1 - 2
	Urine cytology		

Best recommendations for surveillance (personal view)

<u>Site</u>	<u>Test</u>	<u>Age (yrs)</u>	<u>Interval</u>
Colon	Colonoscopy	20 – 25	1 - 2
Endometrium	Sonography	30 – 35	1 - 2
<i>If cancer runs in the family:</i>			
Stomach	Gastroduodenoscopy	30-35	1 - 2
Urinarytract	Abdomen US	30-35	1 - 2
	Urine cytology		

Outcome survey (n=72)

CRC-surveillance

Target group surveillance	Carriers, first degree relatives of patients	66%
Lower age limit	20-25 yrs	>90%
Upper age limit	70 / 75 yrs	39%
	80 / 85 yrs	35%
Interval	1-2 yrs	39%
	2 yrs	22%
	Depending age	22%