

# Preventie door vroege diagnostiek van darmkanker

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# Disclosure

- Research funding by MDxHealth



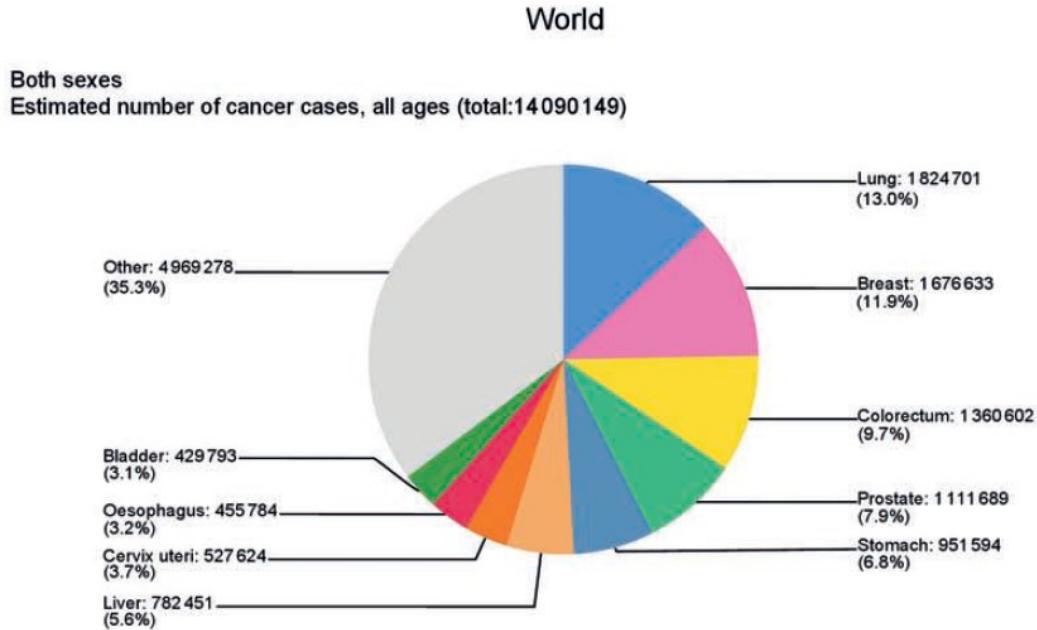
# Preventie

- **Primaire preventie:**
  - activiteiten die *voorkomen* dat gezonde mensen een bepaald gezondheidsprobleem/ziekte krijgen
- **Secundaire preventie:**
  - ziekten of afwijkingen in een *vroeg stadium opgespoord* bij personen die ziek zijn, een verhoogd risico lopen of een bepaalde genetische aanleg hebben
- **Tertiaire preventie:**
  - *Voorkomen van ziekteverergering en complicaties* in patiënten

# The problem

14 million new cases per year in 2012

>20 million new cases per year in 2025



IARC: *World Cancer Report 2014*

# Colorectal cancer: facts and figures

- Incidence: 1.360.000
- Mortality: 694.000
- Treatment has modestly improved disease outcome and extended survival in metastatic patients
- Markedly increased treatment costs
- 50% of patients diagnosed with CRC die as result of disease

*'Despite exciting advances...we cannot treat our way out of the cancer problem'*

*'More commitment to prevention and early detection is desperately needed in order to address the alarming rise in cancer burden globally'*

Prof. Christopher Wild  
Director IARC/WHO  
TEFAF Oncology Chair 2018



# Early detection of colorectal cancer

- Prevention by screening
  - High incidence
  - Long preclinical phase
  - Recognizable and treatable precursor lesion
  - High treatment costs
  - Correlation of mortality and disease stage
- International guidelines recommend screening for CRC
- CRC screening is only offered to a small proportion of target population
- Most preventable, yet least prevented cancer type



# The ‘ideal’ CRC screening test

- Low risk
  - directly: test must not cause harm
  - indirectly (risks resulting from need for subsequent testing)
- High sensitivity
- High specificity
- Widely available
- User friendly
- Cost-effective



# CRC screening methods

- Invasive imaging techniques
  - Flexible sigmoidoscopy
  - Colonoscopy
  - CT colonography (CTC) (virtual colonoscopy)
- Non-invasive screening test
  - gFOBTs (heme catalyzed chemical reaction)
  - FITs (immunological detection of human globin)



**Table 1** Test performance per screening test in asymptomatic, average-risk adults

	gFOBT	FIT	FS	CTC	Colonoscopy
Sensitivity (%) for detecting advanced neoplasia	9 to 24 <sup>43-48</sup>	32 to 53 <sup>43 44 47 49</sup>	90 to 92* <sup>50</sup>	88 <sup>35</sup> to 97 <sup>43</sup>	88 to 98 <sup>51</sup>
Sensitivity (%) for detecting CRC	13 to 50 <sup>44-46</sup>	79 <sup>52</sup>	90 to 92* <sup>50</sup>	100† <sup>53</sup>	92 to 99 <sup>50</sup>
Reduction in CRC incidence (%) intention-to-screen	No‡ <sup>19 54</sup>	Unknown	18 <sup>54</sup>	Unknown	69§ <sup>55</sup>
Reduction in CRC mortality (%) intention-to-screen	14 to 16 <sup>19</sup>	22¶ <sup>25</sup>	28 <sup>54</sup>	Unknown	68§ <sup>55</sup>

\*Sensitivity is given for the distal colon.

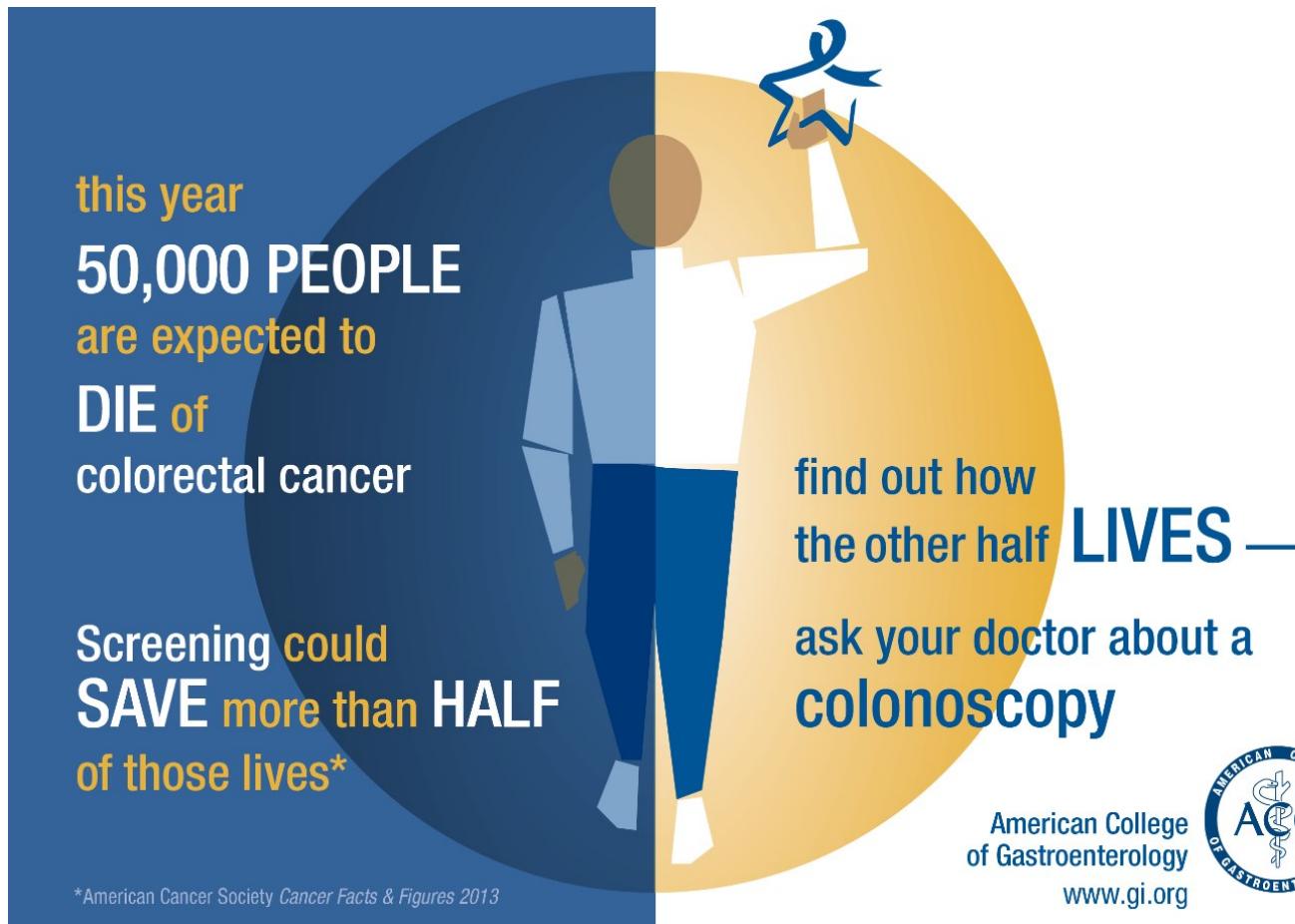
†No CRCs were missed by CTC in six screening trials.

‡No reduction in incidence was found in three of four RCTs included in meta-analysis.

§ Meta-analysis of observational studies, more results expected.

¶ Ecological study.

CRC, colorectal cancer; CTC, CT colonography; FIT, faecal immunochemical test for haemoglobin; FS, flexible sigmoidoscopy; gFOBT, guaiac faecal occult blood test; RCT, randomised controlled trial.



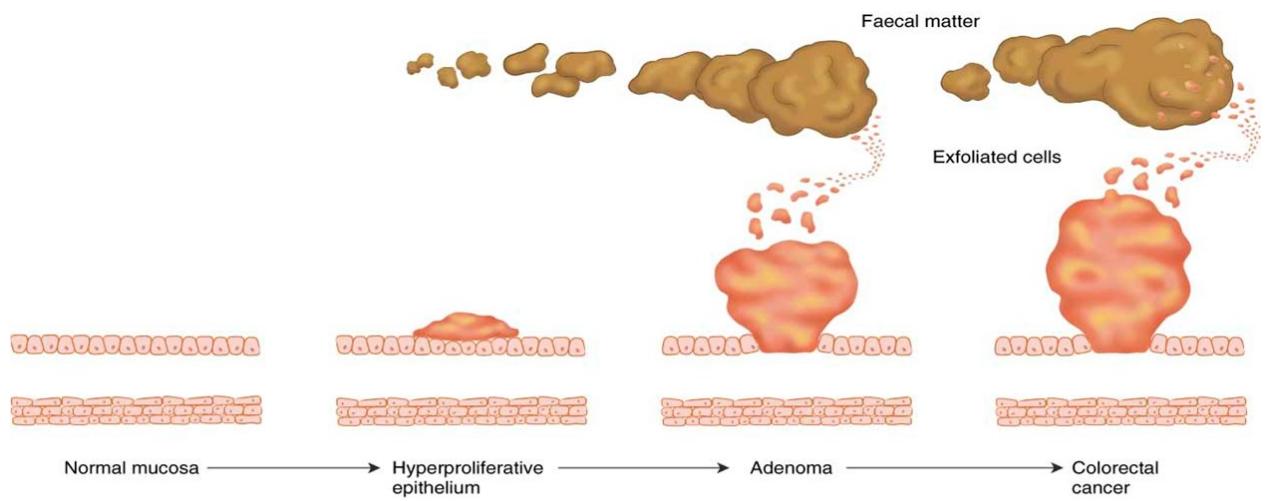
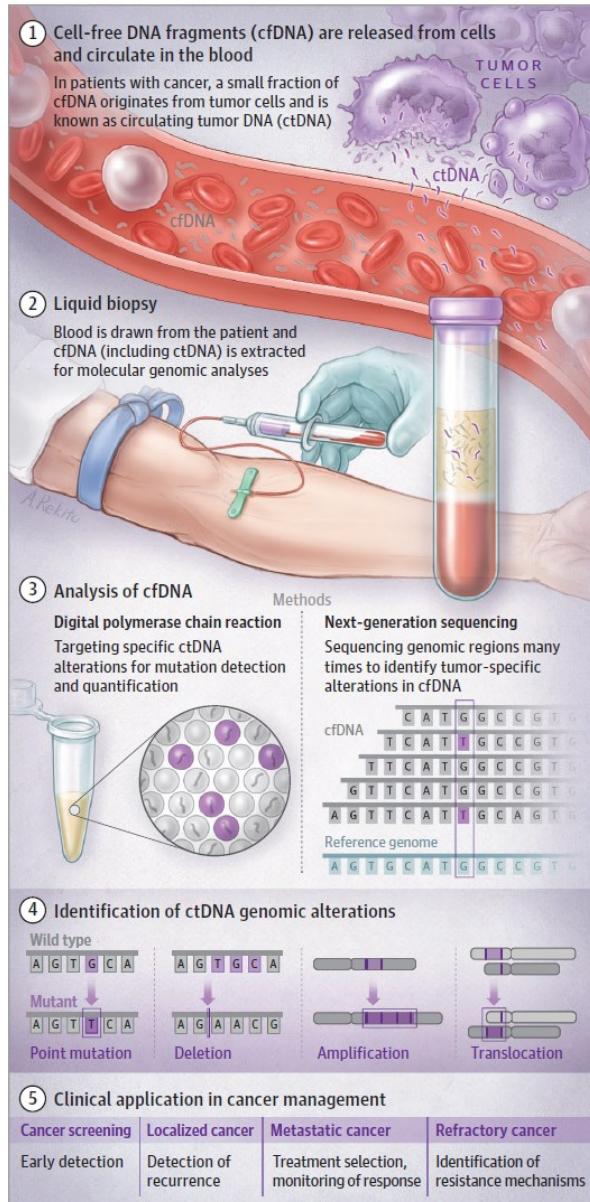
*Randomized controlled trials, observational studies and microsimulation models*



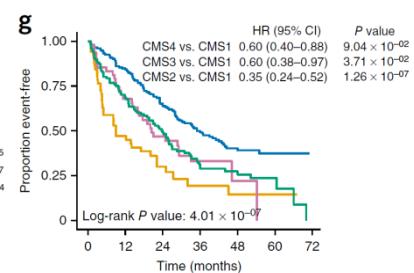
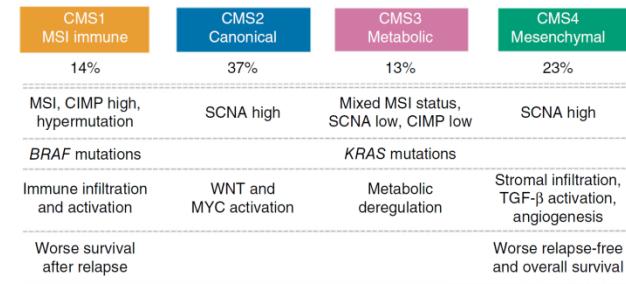
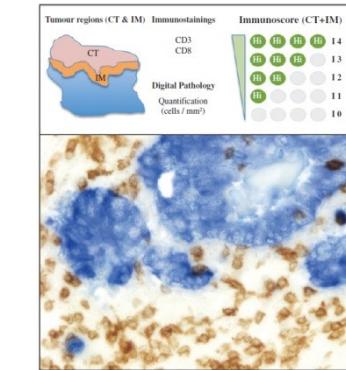
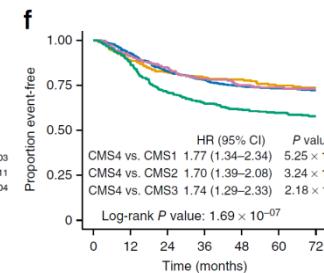
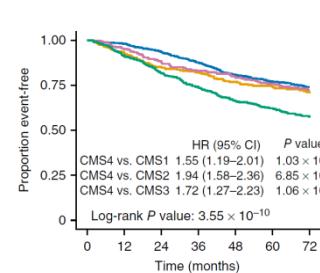
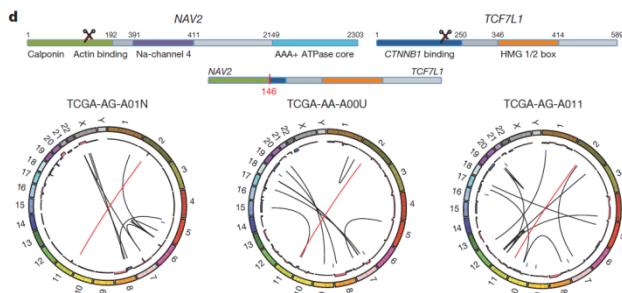
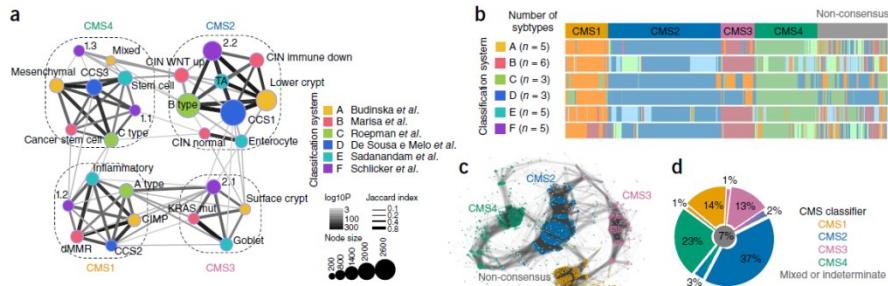
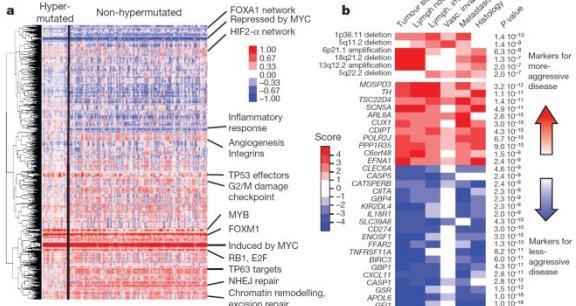
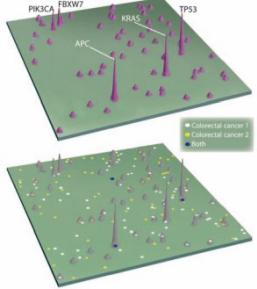
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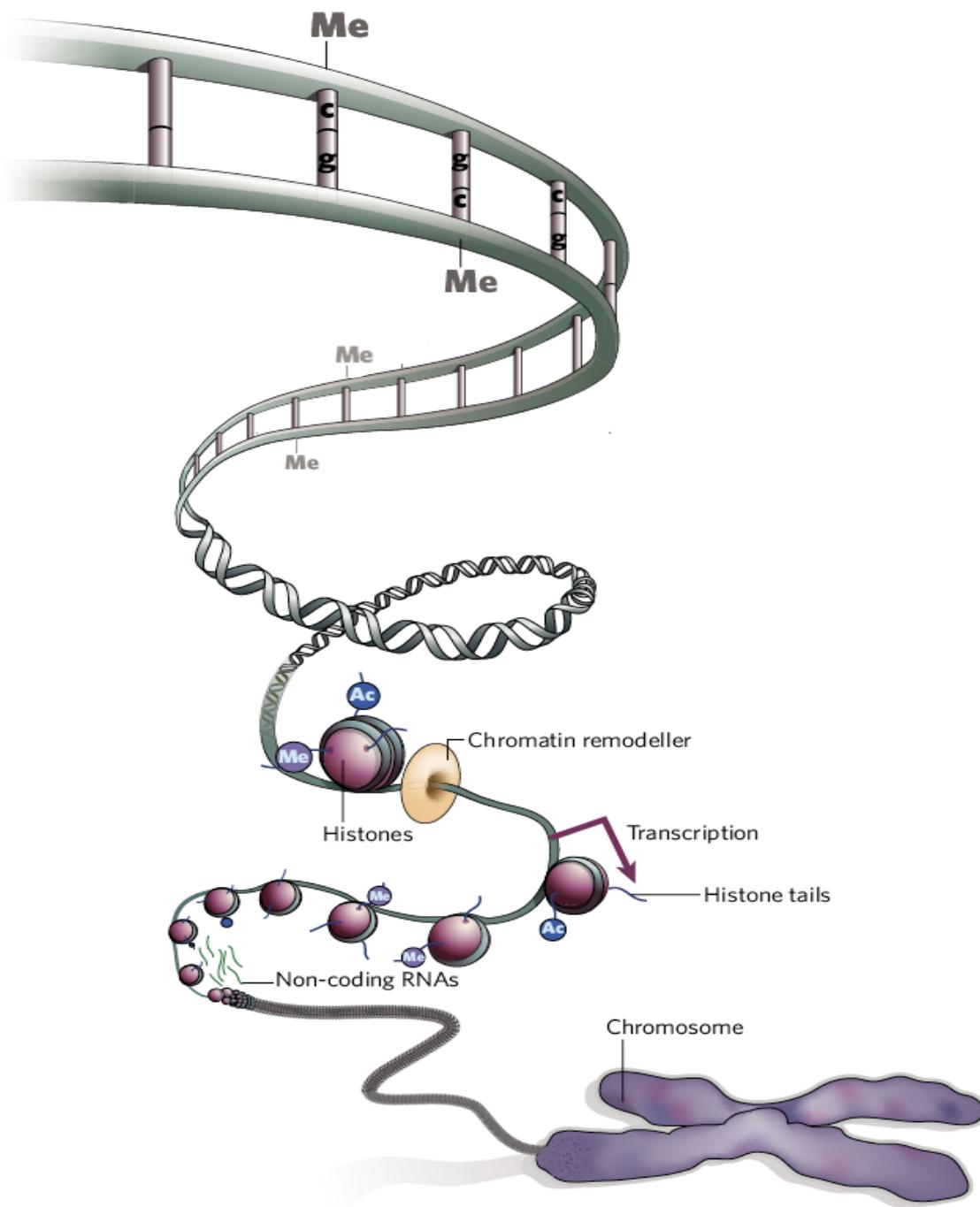
# CRC biology is rapidly being unraveled

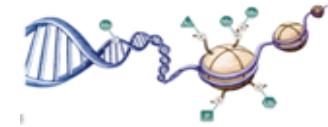
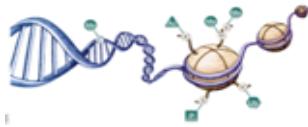
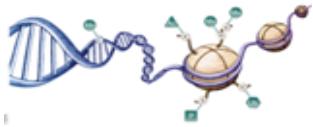




The lack of standardization in the collection and storage of medical specimens (pictured) can hinder subsequent research.

# Bring on the biomarkers





# **N-Myc Downstream-Regulated Gene 4 (*NDRG4*): A Candidate Tumor Suppressor Gene and Potential Biomarker for Colorectal Cancer**

Veerle Melotte, Marjolein H. F. M. Lentjes, Sandra M. van den Bosch, Debby M. E. I. Hellebrekers, Joep P. J. de Hoon, Kim A. D. Wouters, Kathleen L. J. Daenen, Iris E. J. M. Partouns-Hendriks, Filip Stessels, Joost Louwagie, Kim M. Smits, Matty P. Weijenberg, Silvia Sanduleanu, Carolina A. J. Khalid-de Bakker, Frank A. Oort, Gerrit A. Meijer, Daisy M. A. E. Jonkers, James G. Herman, Adriaan P. de Bruïne, Manon van Engeland



J Natl Cancer Inst 2009;101:916–927

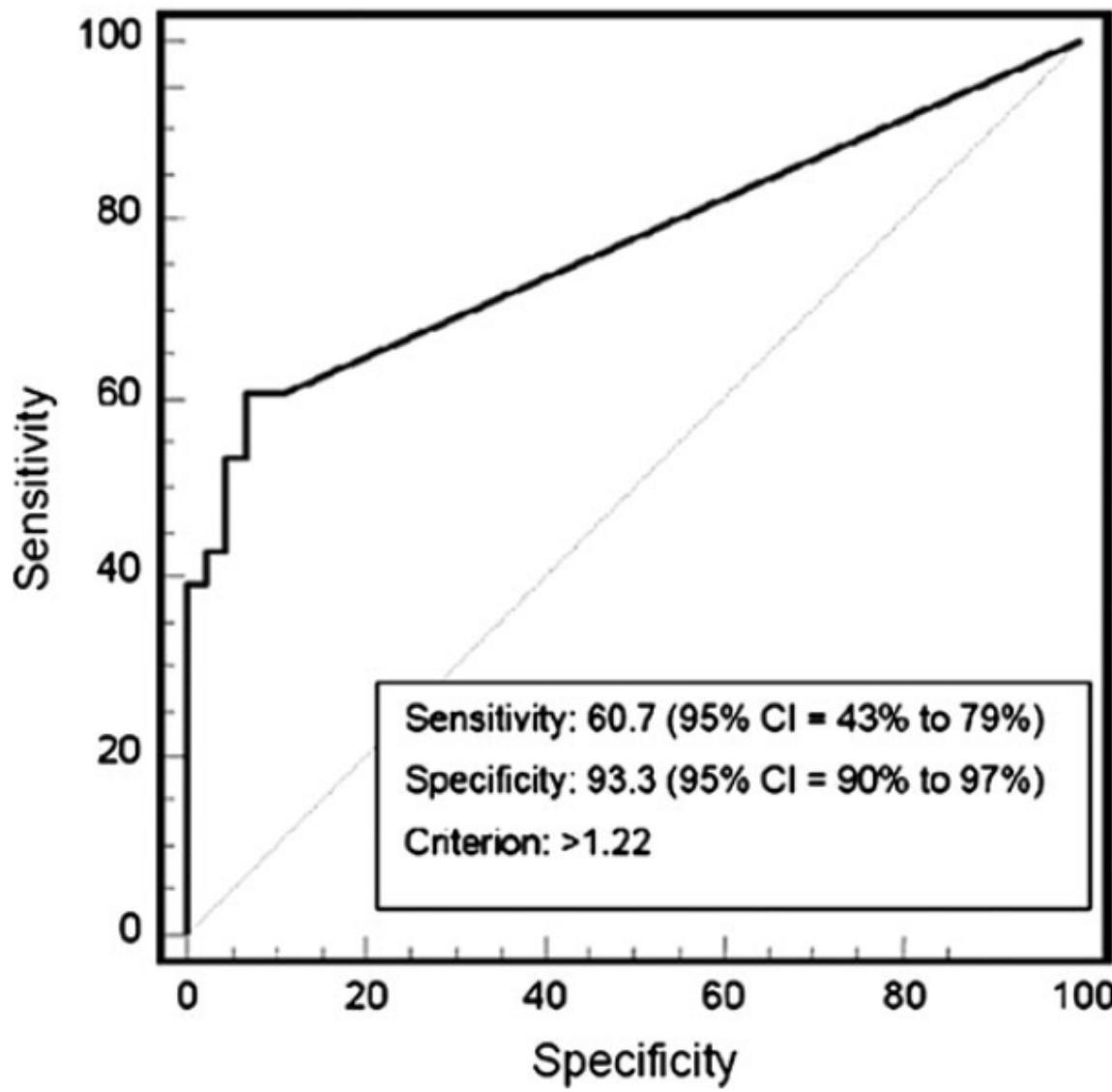


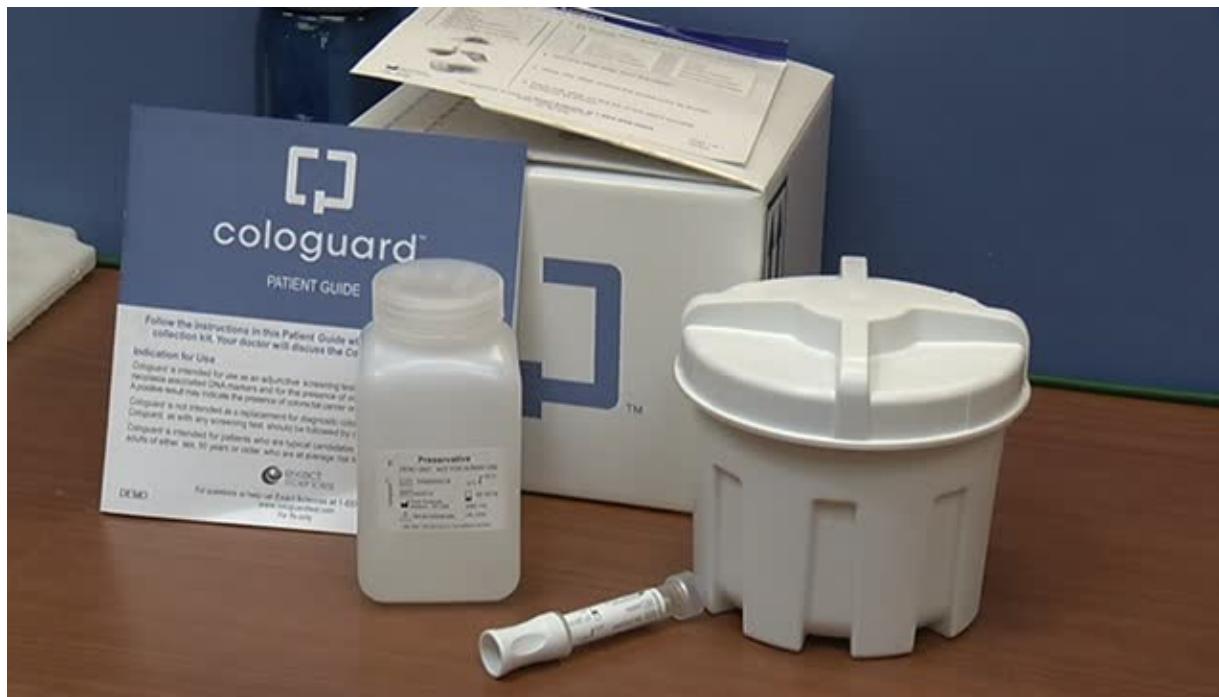
**Table 2.** Prevalence of *NDRG4* promoter methylation in colorectal cancer tissue in relation to clinicopathological features for two independent series\*

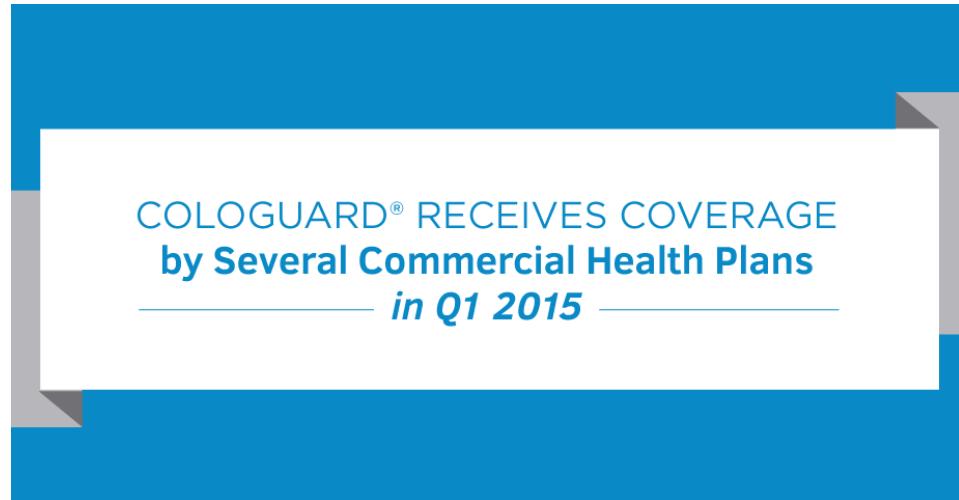
Characteristic	Hospital-based series†	Population-based series‡
TNM stage§		
I	11/12 (92)	30/42 (71)
II	23/28 (82)	42/57 (74)
III	29/32 (91)	39/56 (70)
IV	8/11 (72)	17/21 (81)
P	.431	.790
Tumor location		
Proximal	34/39 (87)	47/58 (81)
Distal	37/42 (89)	81/118 (69)
P	1.00	.141
Sex		
Male	34/41 (83)	71/95 (75)
Female	37/42 (88)	57/81 (70)
P	.548	.611
Age at diagnosis, y		
≤70	30/32 (94)	83/117 (71)
>70	41/51 (80)	45/59 (76)
P	.117	.453



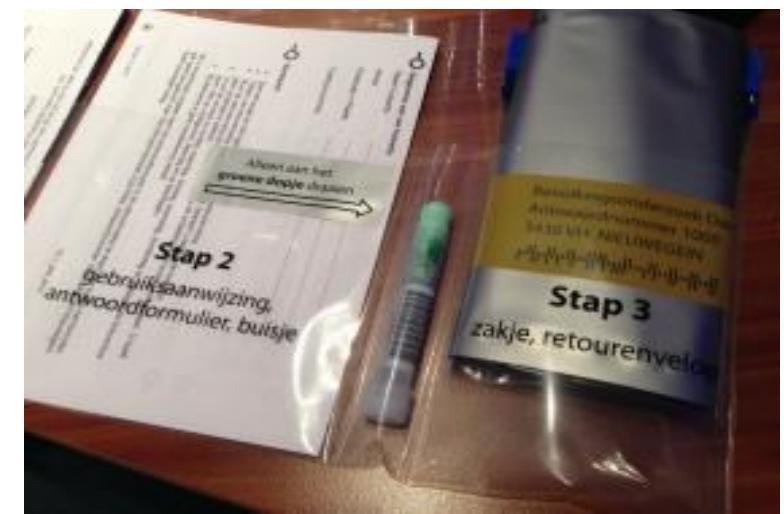
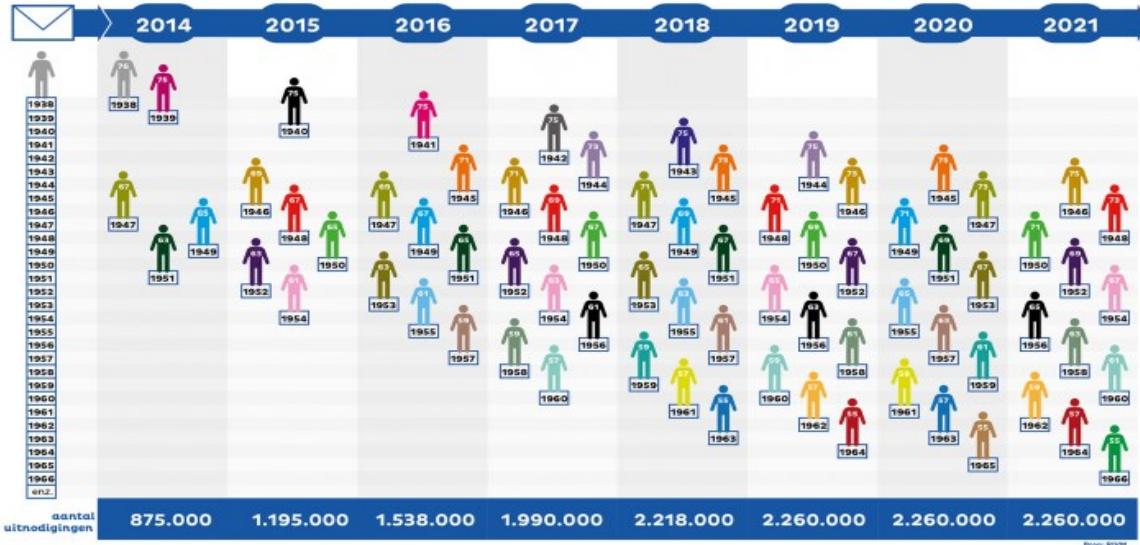








# Vroege detectie dikkedarmkanker in Nederland: bevolkingsonderzoek sinds januari 2014



# Huidige test bevolkingsonderzoek: FIT



- Kosten-effectief
- Voorkomt 2.400 sterfgevallen dikkedarmkanker per jaar
- Test is niet optimaal
  - 30% kankers niet gedetecteerd
  - 20-70% adenomen niet gedetecteerd
  - 50% positieve FIT geen afwijkingen

# The problem



# Conclusions

- CRC screening reduces CRC incidence and mortality
- Non-invasive stool testing will enhance screening uptake
- Novel molecular markers are being evaluated in stool/blood samples
- Cost-effectiveness and infrastructure



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Linda Bosch  
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Jeff Wang  
Tom Pisanic

