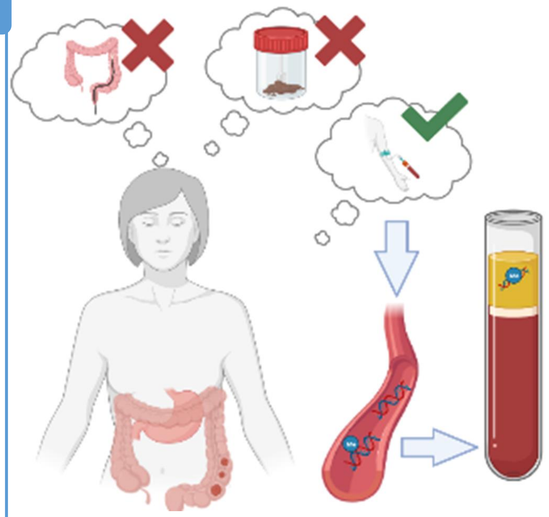
Colorectal cancer detected by liquid biopsy two years prior to clinical diagnosis in the HUNT study

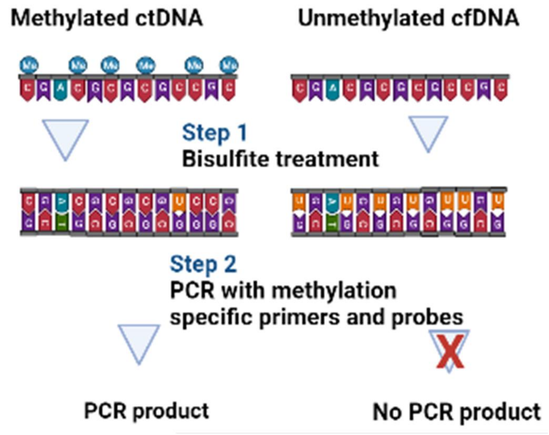
Siv S. Brenne [1, 2], Poul H. Madsen [3], Inge S. Pedersen [3, 4, 5], Kristian Hveem [2], Frank Skorpen [6], Henrik B. Krarup [3, 4, 5], Guro F. Giskeødegård [2], Eivor A. Laugsand [1, 2]

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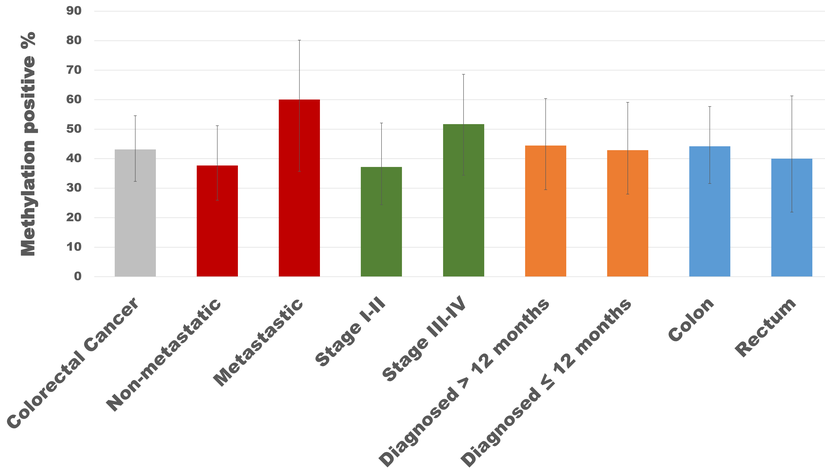
Objective

- Colorectal cancer (CRC) is often diagnosed in advanced stages.
- Circulating tumor DNA (ctDNA) has been proposed as an early diagnostic biomarker.
- However, as a screening tool, ctDNA has mainly been studied in selected populations at the time of clinical diagnosis.
- The aim of this study was to detect CRC by known ctDNA markers up to two years prior to clinical diagnosis.





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Design

- In this case-control study, methylated ctDNA markers were detected by a nested methylation-specific PCR assay in plasma samples from 106 healthy controls and 106 cases diagnosed with CRC within the 24 months following participation in The Trøndelag Health Study (HUNT).

Results

- Among the 42 markers analyzed, the most specific and significant single markers were *BMP3*, *FLI1*, *IKZF1*, *SFRP1*, *SFRP2*, *NPTX2*, *SLC8A1* and *VIM* (specificity >70%).
- When combining these into a panel (HUNT-CRC$_d$), the CRC sensitivity was 43% (95% CI 42.7 – 43.4) and the CRC specificity was 86% (95% CI 85.7 – 86.2), when two or more of the eight markers were positive.
- The findings were reproduced in an independent validation set of samples.

Diagnostic properties of HUNT-CRC$_d$ panel

	AROC analysis†			Sensitivity CRC		Specificity CRC	
	AUC	95% CI	p-value	%	95% CI	%	95% CI
HUNT-CRC$_d$*	0.669	0.580-0.759	**< 0.001**	43.1	42.7-43.4	85.9	85.7-86.2
HUNT-CRC$_d$* val	0.680	0.553-0.806	**0.010**	47.1	46.5-47.6	77.1	76.7-77.6

Conclusion

- Detection of known methylated ctDNA markers of CRC is possible up to two years prior to the clinical diagnosis in an unselected population resembling the screening setting.
- This study shows that some patients could be diagnosed earlier, if ctDNA detection was implemented as part of the CRC screening program.

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