Menopausal hormone therapy and colorectal cancer: a linkage between nationwide registries in Norway

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New preventive strategies for colorectal cancer (CRC) are being explored.
We aimed to investigate if menopausal hormone therapy (HT) may have impact on CRC reduction

Materials and Methods

We selected from a nationwide population registry a cohort of 510 123 women born in Norway, aged 55-79 years, alive and resident in Norway as of January 1st 2004, and followed them until December 31st 2008.
The study was based on the linkage of Norwegian population registries. Each women contributed person-years at risk as non-user, current user or/and past HT user.
The outcome of interest was adenocarcinoma of the colorectal tract, overall, by anatomic site and stage at diagnosis. Poisson regression was used to evaluate the association between HT and CRC incidence.

510 123 women born in Norway between 1925 and 1949; registered in the Norwegian National Population Registry; alive and resident in Norway by 1st of January 2004

43 301 women excluded: history of CRC or any other cancer diagnosis, emigration or death before baseline 1st of January 2004

466 822 women free of cancer by 1st of January 2004 and fulfilling selection criteria for analyses

Strengths and limitations

- Detailed information on exposure of HT, including type of HT based on registry linkages with no risk of self-selection of women to participate
- Lack of information on recognized risk factors for colorectal cancer, e.g. family history of CRC, body mass index, physical activity, diet, alcohol use, smoking and aspirin use

Results

During the median follow-up of 4.8 years, 138 655 (30%) women received HT, and 3 799 (0,8%) were diagnosed with CRC. Characteristics of the study population were not homogenously distributed between HT users and non-users, and between ET users and EPT users. ET users were substantially older than EPT users. Median age was 64.0 and 60.0 years, respectively.

Current, but not past use of HT was associated with a lower risk of CRC as a whole and in regionally advanced and metastatic, but not in localized CRC.

Table 1. Use of hormone therapy and risk of colorectal cancer

	HT use	Women ≥ 55 years		
		PY	Cases	RR (95%CI)
Status	Non-use	2 126 753	3 020	Ref.
	Current	320 202	441	0.88 (0.80-0.98)
	Past	203 759	338	0.98 (0.87-1.09)
	Ever	523 961	779	0.92 (0.85-1.00)
HT type	Non-use	2 126 753	3 020	Ref.
	ET	159 495	252	0.91 (0.80-1.04)
	*Estradiol**	118 910	159	0.87 (0.74-1.03)
	*Estirol**	40 585	93	0.98 (0.79-1.21)
	Tibolone*	20 043	21	0.86 (0.56-1.32)
	EPT*	91 654	106	0.85 (0.70-1.03)
	Other*	49 010	62	0.86 (0.67-1.10)
Route	Non-use	2 126 753	3 020	Ref.
	ET Oral*	57 031	94	0.83 (0.68-1.03)
	ET Vaginal*	89 719	134	0.92 (0.77-1.09)
	ET Transdermal*	7 246	15	1.63 (0.98-2.71)
	EPT Oral*	90 126	106	0.86 (0.71-1.05)
	EPT Transdermal*	1 163	0	-
	Other*	74 917	92	0.86 (0.70-1.06)
Oral dose unit increase	Estrogen 1 mg/d*			0.87 (0.73-1.04)
	Progestin 10 mg/mth*			1.01 (0.86-1.19)

Table 2. Use of hormone therapy and risk of colorectal cancer by colorectal cancer stage, women ≥ 55 years

	HT use	Lokalized CRC	RR (95% CI)	Regionally advanced CRC	RR (95% CI)	Metastatic CRC	RR (95% CI)
Status	Non-use	548	Ref.	1 607	Ref.	598	Ref.
	Current	101	1.13 (0.91-1.41)	216	0.81 (0.70-0.94)	78	0.79 (0.62-1.00)
	Past	49	0.79 (0.59-1.06)	200	1.08 (0.93-1.26)	61	0.90 (0.69-1.18)
	Ever	150	0.99 (0.82-1.20)	416	0.92 (0.83-1.03)	139	0.83 (0.69-1.01)
HT type	Non-use	548	Ref.	1 607	Ref.	598	Ref.
	ET	67	1.33 (1.03-1.72)	125	0.84 (0.70-1.02)	34	0.64 (0.45-0.91)
	*Estradiol**	44	1.36 (0.99-1.85)	75	0.78 (0.62-0.98)	22	0.60 (0.39-0.93)
	*Estirol**	23	1.27 (0.83-1.94)	50	0.97 (0.73-1.30)	12	0.73 (0.41-1.29)
	Tibolone*	5	1.20 (0.50-2.90)	12	0.93 (0.52-1.64)	4	0.75 (0.28-2.01)
	EPT*	17	0.79 (0.49-1.29)	56	0.84 (0.64-1.10)	24	0.91 (0.60-1.37)
	Other*	12	0.94 (0.53-1.66)	23	0.60 (0.40-0.90)	16	1.09 (0.67-1.80)
Route	Non-use	584	Ref.	1 607	Ref.	598	Ref.
	ET Oral*	24	1.15 (0.76-1.73)	48	0.79 (0.59-1.06)	13	0.63 (0.36-1.10)
	ET Vaginal*	36	1.36 (0.97-1.91)	67	0.86 (0.68-1.10)	17	0.59 (0.37-0.96)
	ET Transdermal*	6	3.80 (1.70-8.50)	7	1.44 (0.69-3.04)	1	0.51 (0.07-3.65)
	EPT Oral*	17	0.81 (0.50-1.31)	56	0.86 (0.65-1.12)	24	0.86 (0.61-1.39)
	EPT Transdermal*	0	-	0	-	0	-
	Other*	18	0.96 (0.60-1.54)	38	0.67 (0.49-0.93)	23	1.05 (0.69-1.60)
Oral dose unit increase	Estrogen 1 mg/d*		1.13 (0.82-1.57)		0.75 (0.57-0.98)		0.97 (0.67-1.39)
	Progestin 10 mg/mth*		0.80 (0.57-1.13)		1.11 (0.88-1.41)		1.02 (0.74-1.42)

Incidence rate ratios (RR) were adjusted for age, number of births, highest level of education, marital status, use of antihypertensives, antidiabetics, statins and thyroid therapy.
*HT: hormone therapy, ET: estrogen only therapy, EPT: combined estrogen-progestin therapy, PY: person-years, CI: confidence interval, CRC: colorectal cancer, Ref: reference, mg: milligram, d: day, mth: month, * current use*

Conclusions

- Use of hormone therapy is associated with reduced risk of colorectal cancer
- HT protects against regionally advanced and metastatic colorectal cancer while it has no impact on localized CRC
- HT may play a key role in the inhibition of cancer progression