HNL I RIZIK RAKA JAJNIKA

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HORMONSKO NADOMJESNO LIJEČENJE

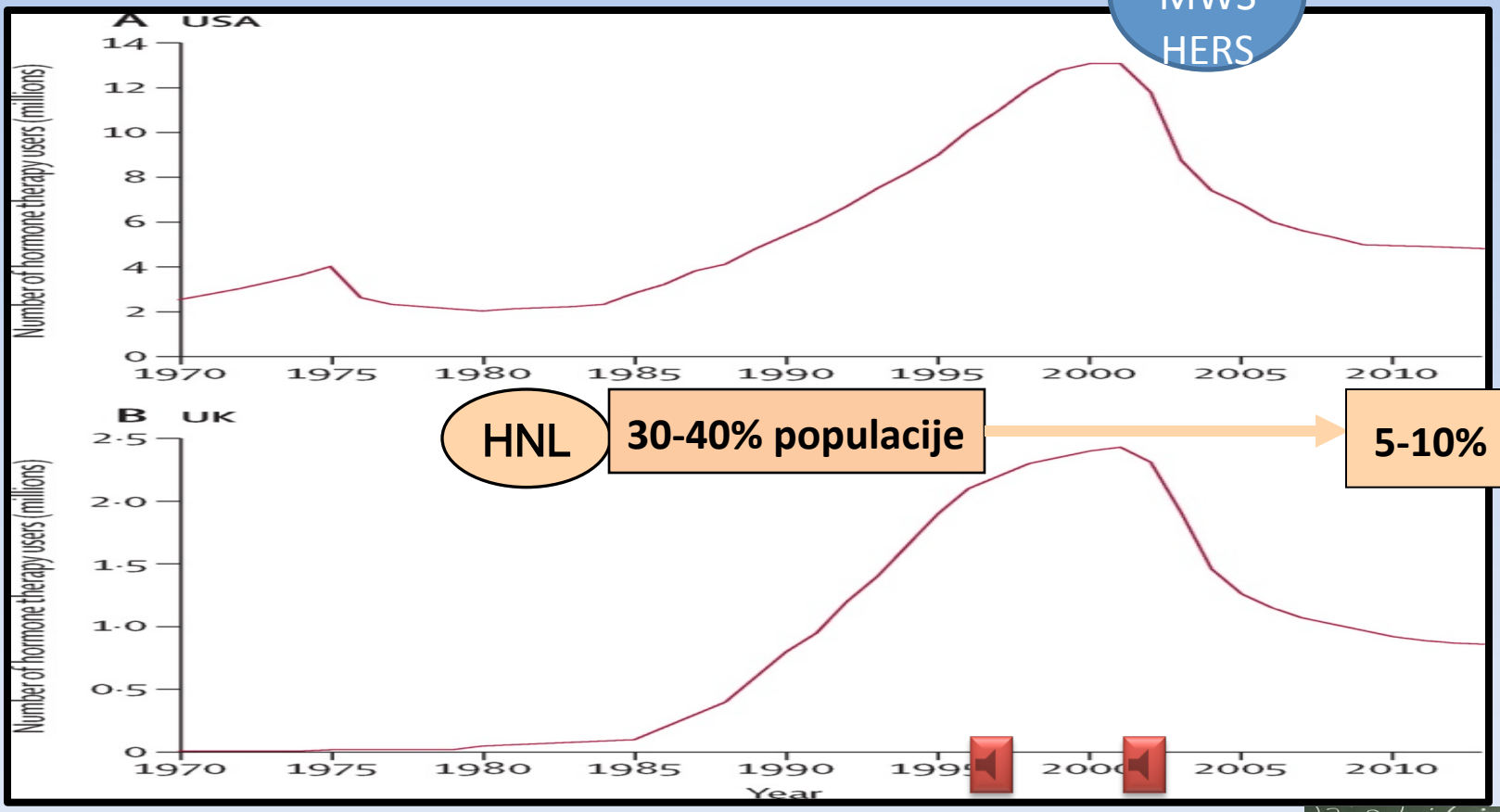
RAK DOJKE

RAK ENDOMETRIJA

RAK JAJNIKA

Trend korištenja HNL-a u SAD i UK

WHI
MWS
HERS



HNL

30-40% populacije → **5-10%**

Panacea
Femin.forever

Značajna korist
Minimalan rizik

> 1000 opservacijskih, eksperimentalnih studija, meta analiza

Hormonsko nadomjesno liječenje: korištenje u RH

X 1000

60

50

40

30

20

10

880.000
postmenopauza

335.000
perimenopauza

42.500 ž. HNL

4,8%

12,7%

- 62%

16.500 ž. HNL

1,9%

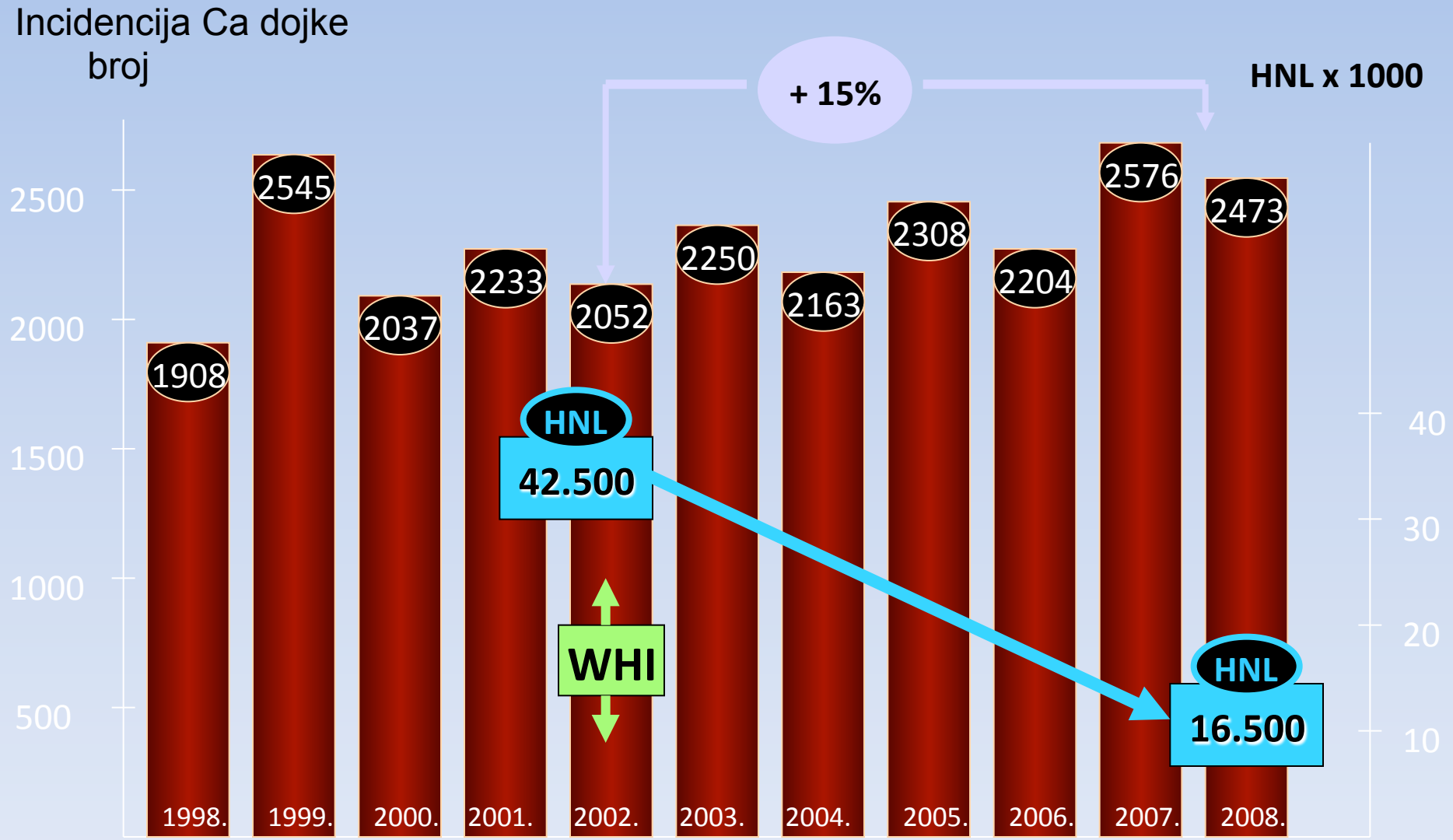
4,9%

2002.g

2010.g.

Izvori:
PharMiss
IMS
S. Roksandić (HZZJZ)

Učestalost raka dojke u RH: zadnjih 10 godina



- Učestalost raka dojke u postmenopauzi ⇒ 1,9‰ - 2,4‰

Izvori:
HZJZ, 2011.
Šimunić, 2011.

Menopausal hormone use and ovarian cancer risk: individual participant meta-analysis of 52 epidemiological studies

*Collaborative Group on Epidemiological Studies of Ovarian Cancer**

Summary

Background Half the epidemiological studies with information about menopausal hormone therapy and ovarian cancer risk remain unpublished, and some retrospective studies could have been biased by selective participation or recall. We aimed to assess with minimal bias the effects of hormone therapy on ovarian cancer risk.

Methods Individual participant datasets from 52 epidemiological studies were analysed centrally. The principal analyses involved the prospective studies (with last hormone therapy use extrapolated forwards for up to 4 years). Sensitivity analyses included the retrospective studies. Adjusted Poisson regressions yielded relative risks (RRs) versus never-use.

Findings During prospective follow-up, 12 110 postmenopausal women, 55% (6601) of whom had used hormone therapy, developed ovarian cancer. Among women last recorded as current users, risk was increased even with <5 years of use (RR 1·43, 95% CI 1·31–1·56; p<0·0001). Combining current-or-recent use (any duration, but stopped <5 years before diagnosis) resulted in an RR of 1·37 (95% CI 1·29–1·46; p<0·0001); this risk was similar in European and American prospective studies and for oestrogen-only and oestrogen-progestagen preparations, but differed across the four main tumour types (heterogeneity p<0·0001), being definitely increased only for the two most common types, serous (RR 1·53, 95% CI 1·40–1·66; p<0·0001) and endometrioid (1·42, 1·20–1·67; p<0·0001). Risk declined the longer ago use had ceased, although about 10 years after stopping long-duration hormone therapy use there was still an excess of serous or endometrioid tumours (RR 1·25, 95% CI 1·07–1·46, p=0·005).

Interpretation The increased risk may well be largely or wholly causal; if it is, women who use hormone therapy for 5 years from around age 50 years have about one extra ovarian cancer per 1000 users and, if its prognosis is typical, about one extra ovarian cancer death per 1700 users.

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See Editorial page 1804

See Comment page 1806

*Analysis and writing committee listed at end of paper

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17 prospektivnih i 35 retrospektivnih studija

Study (country)	Number of cases in current- or-recent users/never-users of hormone therapy	Relative risk for current- or-recent users vs never-users of hormone therapy (99% CI)*
Prospective studies		
Europe		
EPIC (eight European countries)	57/140	1·71 (0·96–3·06)
DaHoRS (Denmark)	600/1384	1·49 (1·31–1·69)
Million Women Study (UK)	1500/2500	1·28 (1·14–1·44)
Other (Netherlands, Norway, Sweden)	39/243	1·08 (0·54–2·18)
All Europe	**2196/4267**	**1·37 (1·26–1·50)**
North America		
BCDDP (USA)	85/120	1·40 (0·87–2·24)
CPS-II Mortality (USA)	23/485	1·21 (0·61–2·40)
CPS-II Nutrition (USA)	91/116	1·57 (0·99–2·51)
Nurses' Health Study (USA)	173/177	1·17 (0·84–1·63)
NIH—AARP (USA)	135/157	1·69 (1·04–2·74)
Other (Canada, USA)	48/107	1·14 (0·47–2·79)
All North America	**555/1162**	**1·35 (1·11–1·65)**
All prospective studies	**2751/5429**	**1·37 (1·27–1·48)**
Retrospective studies		
Europe		
Negri/Franceschi/La Vecchia (Italy)	32/1107	1·97 (1·04–3·75)
Riman (Sweden)	145/468	1·29 (0·96–1·74)
Other (Denmark, Germany, Greece, Poland)	57/272	0·86 (0·51–1·44)
All Europe	**234/1847**	**1·25 (0·99–1·59)**
North America		
Rosenberg (USA)	51/377	1·21 (0·75–1·96)
Pike/Wu (USA)	149/131	1·02 (0·64–1·63)
Goodman/Wu (USA)	173/185	0·60 (0·38–0·94)
SHARE (USA)	97/270	0·98 (0·63–1·52)
Newcomb (USA)	113/174	1·18 (0·81–1·72)
HOPE (USA)	121/207	0·91 (0·60–1·40)
Other (Canada, USA)	260/1050	1·11 (0·84–1·48)
All North America	**964/2394**	**1·01 (0·87–1·17)**
Elsewhere		
Green/Purdie (Australia)	49/385	0·84 (0·46–1·52)
AOCS (Australia)	289/487	0·93 (0·69–1·25)
Other (China, Israel)	2/29	Insufficient data
All elsewhere	**340/901**	**0·90 (0·69–1·18)**
All retrospective studies	**1538/5142**	**1·04 (0·93–1·16)**

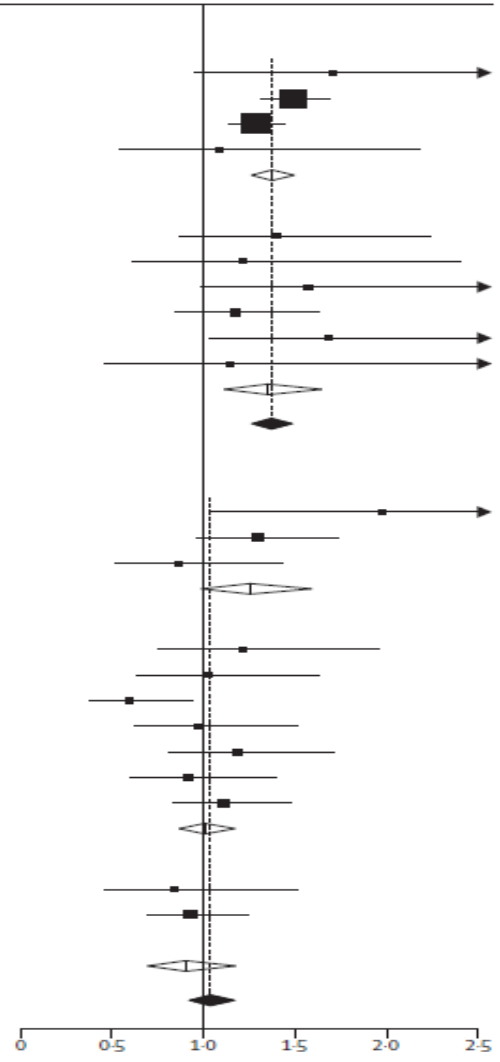

***Figure 3*: Study-specific results for the relative risk of ovarian cancer for current-or-recent users versus never-users of hormone therapy**
For study-specific details and references, see appendix pp 7–10. Dotted lines represent totals for all prospective studies and, separately, for all retrospective studies. Study-specific results are arranged by study design and region; results are given for individual studies with the most statistical information (ie, with variance of log relative risk <0·03). Results for the remaining studies are grouped together here (and given separately for every study in appendix p 14). In comparisons of relative risks in prospective versus retrospective studies, overall heterogeneity p<0·0001; for European studies, heterogeneity p=0·4; and for North American studies, heterogeneity p=0·002. In a comparison of relative risks in prospective studies, Europe versus North American heterogeneity p=0·9; for retrospective studies, Europe versus North American heterogeneity p=0·04. References provided in the appendix. *Risk relative to never-users of hormone therapy, stratified by age at diagnosis, study, and body-mass index, and adjusted for age at menopause, hysterectomy, oral contraceptive use, and parity.

Relativni rizik raka jajnika ovisno o trajanju korištenja
Sadašnje *vs* bivše korisnice

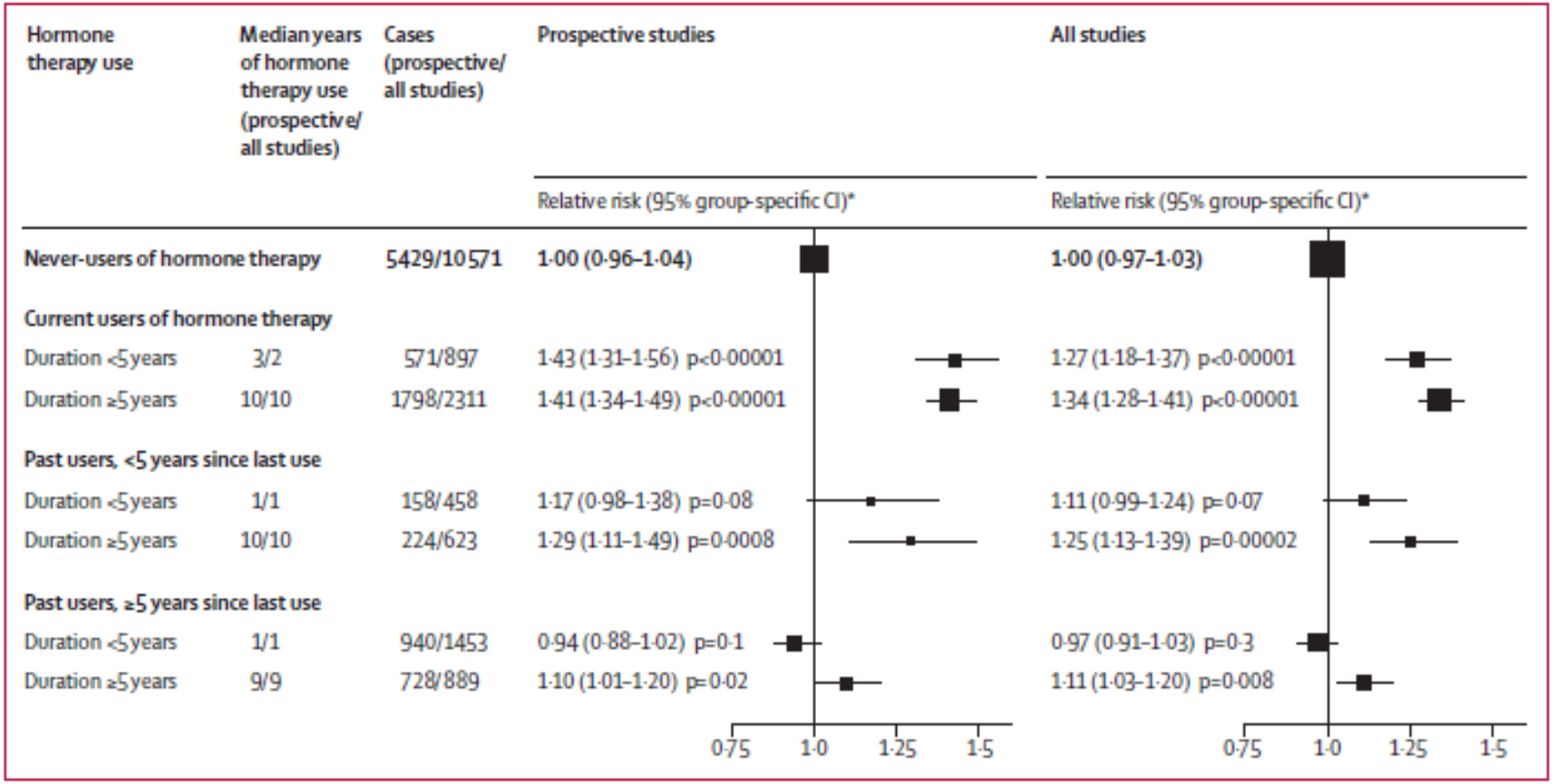

***Figure 2*: Relative risk of ovarian cancer by duration of use in current and past users of hormone therapy**

*Risk relative to never-users of hormone therapy, stratified by age at diagnosis, study, and body-mass index, and adjusted for age at menopause, hysterectomy, oral contraceptive use, and parity. p values are two-sided and include the effects of the group-specific variance in never-users.

Relativni rizik raka jajnika
Histološki subtipovi sadašnje *vs* nekorisnice HNL-a

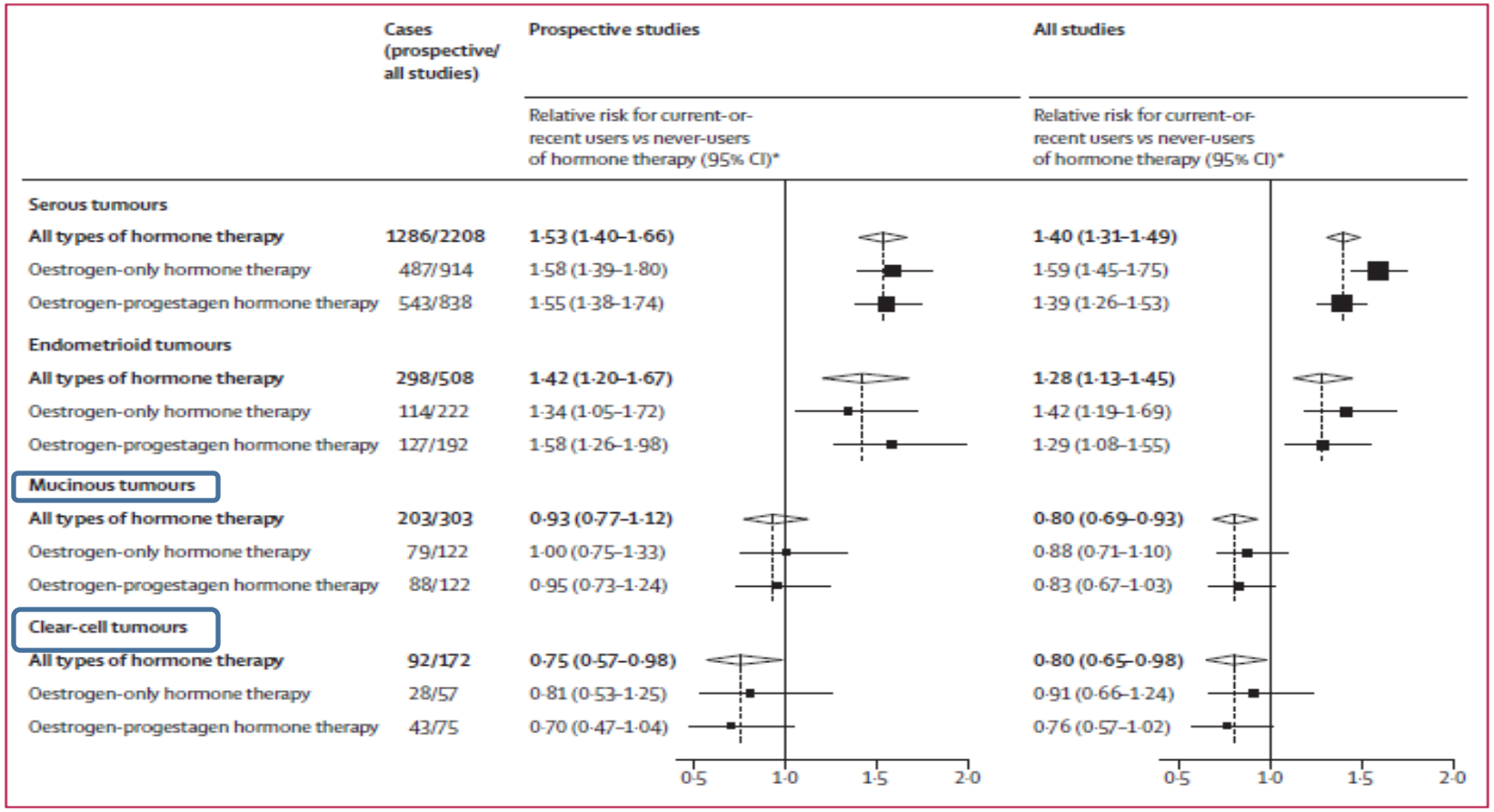

Figure 4: **Relative risk of the four most common subtypes of ovarian cancer in current-or-recent users versus never-users of hormone therapy**
Numbers do not add to totals, because some hormone therapy users were classified as using other or unknown types of hormone therapy and some epithelial tumours are classified as mixed types, other type, or type not specified. *Risks relative to never-users of hormone therapy, stratified by age at diagnosis, study, and body-mass index, and adjusted for age at menopause, hysterectomy, oral contraceptive use, and parity.

Procjena dodatne incidencije raka jajnika u Velikoj Britaniji
5 / 10 godina korištenja HNL-a

	5 year incidence of ovarian cancer per 1000 never-users of hormone therapy	Absolute 5 year excess incidence per 1000 users with 5 years of hormone therapy use	Absolute 5 year excess incidence per 1000 users with 10 years of hormone therapy use
Age 50–54 years	1·2	0·52	0·52
Age 55–59 years	1·6	0·37	0·67
Age 60–64 years	2·1	0·10	0·61
Excess incidence	..	0·99 per 1000; 1 in 1000 users	1·80 per 1000; 1 in 600 users
Excess deaths	..	0·6 per 1000; 1 in 1700 users	1·2 per 1000; 1 in 800 users

Methods and sources of data are provided in appendix p 11.

Table: **Estimated excess incidence of ovarian cancer in England associated with 5 years and with 10 years of hormone therapy use, starting at age 50 years**

Nedostaci studije

- Nema korelacije s dozom primjenjenog HNL-a
- Oralna *vs* neoralna primjena HNL-a
- Sekvencijska *vs* kontinuirana progesteronska terapija
- Nema korelacije prema BMI, prethodne primjene OHK ili dobi menopauze
- Inkorektni izračun relativnog i apsolutnog rizika – revidirani apsolutni rizik 1 extra slučaj/1 000 žena/5 godina (ispod kapaciteta predikcije meta analiza opservacijskih studija)

Ovarian cancer and hormone replacement therapy in the Million Women Study

*Million Women Study Collaborators**

Summary

Background Ovarian cancer is the fourth most common cancer in women in the UK, with about 6700 developing the malignancy and 4600 dying from it every year. However, there is limited information about the risk of ovarian cancer associated with the use of hormone replacement therapy (HRT).

Methods 948 576 postmenopausal women from the UK Million Women Study who did not have previous cancer or bilateral oophorectomy were followed-up for an average of 5·3 years for incident ovarian cancer and 6·9 years for death. Information on HRT use was obtained at recruitment and updated where possible. Relative risks for ovarian cancer were calculated, stratified by age and hysterectomy status, and adjusted by area of residence, socioeconomic group, time since menopause, parity, body-mass index, alcohol consumption, and use of oral contraceptives.

Findings When they last reported HRT use, 287 143 women (30%) were current users and 186 751 (20%) were past users. During follow-up, 2273 incident ovarian cancers and 1591 deaths from the malignancy were recorded. Current users were significantly more likely to develop and die from ovarian cancer than never users (relative risk 1·20 [95% CI 1·09–1·32; p=0·0002] for incident disease and 1·23 [1·09–1·38; p=0·0006] for death). For current users of HRT, incidence of ovarian cancer increased with increasing duration of use, but did not differ significantly by type of preparation used, its constituents, or mode of administration. Risks associated with HRT varied significantly according to tumour histology (p<0·0001), and in women with epithelial tumours the relative risk for current versus never use of HRT was greater for serous than for mucinous, endometroid, or clear cell tumours (1·53 [1·31–1·79], 0·72 [0·52–1·00], 1·05 [0·77–1·43], or 0·77 [0·48–1·23], respectively). Past users of HRT were not at an increased risk of ovarian cancer (0·98 [0·88–1·11] and 0·97 [0·84–1·11], respectively, for incident and fatal disease). Over 5 years, the standardised incidence rates for ovarian cancer in current and never users of HRT were 2·6 (2·4–2·9) and 2·2 (2·1–2·3) per 1000, respectively—ie, one extra ovarian cancer in roughly 2500 users; death rates were 1·6 (1·4–1·8) and 1·3 (1·2–1·4) per 1000, respectively—ie, one extra ovarian cancer death in roughly 3300 users.

Interpretation Women who use HRT are at an increased risk of both incident and fatal ovarian cancer. Since 1991, use of HRT has resulted in some 1300 additional ovarian cancers and 1000 additional deaths from the malignancy in the UK.

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See **Comment** page 1667

*Listed at end of report

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Million women's study – rak jajnika

	HRT use			Total (n=948 576)
	Never (n=474 682)	Past (n=186 751)	Current (n=287 143)	
Characteristics				
Mean age at entry (SD)	57·9 (4·9)	57·0 (4·3)	56·1 (4·1)	57·2 (4·6)
Upper third of socioeconomic group (n, %)	151 426 (32·1%)	63 477 (34·3%)	100 143 (35·1%)	315 046 (33·4%)
Mean parity (SD)	2·1 (1·3)	2·2 (1·2)	2·1 (1·2)	2·2 (1·3)
Past use of oral contraceptives (n, %)	223 316 (47·4%)	115 935 (62·6%)	188 452 (66·2%)	527 703 (56·1%)
Mean, body-mass index, kg/m^2 (n)	25·9 (4·9)	25·9 (4·5)	25·1 (4·3)	25·7 (4·6)
Strenuous physical activity >once/week (n, %)	171 134 (37·6%)	71 584 (39·6%)	112 731 (40·5%)	355 449 (38·9%)
Mean alcohol intake, g/day (SD)	5·4 (7·1)	6·4 (7·6)	6·9 (7·9)	6·1 (7·5)
Current smoker (n, %)	87 312 (19·6%)	35 615 (20·2%)	57 242 (21·0%)	180 169 (20·2%)
Hysterectomy (n, %)	61 470 (13·0%)	38 004 (20·4%)	81 978 (28·6%)	181 452 (19·1%)
Follow-up for ovarian cancer				
Woman-years of follow-up for incidence (1000s)	2515·0	943·8	1532·7	4991·5
Number of incident ovarian cancers	1142	391	740	2273
Woman-years of follow-up for death (1000s)	3285·0	1255·2	1977·7	6517·9
Number of ovarian cancer deaths	819	275	497	1591

Table: **Characteristics of the study population according to last reported use of HRT**

Lancet 2007; 369: 1703–10
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April 19, 2007
DOI:10.1016/S0140-6736(07)60534-0
See **Comment** page 1667
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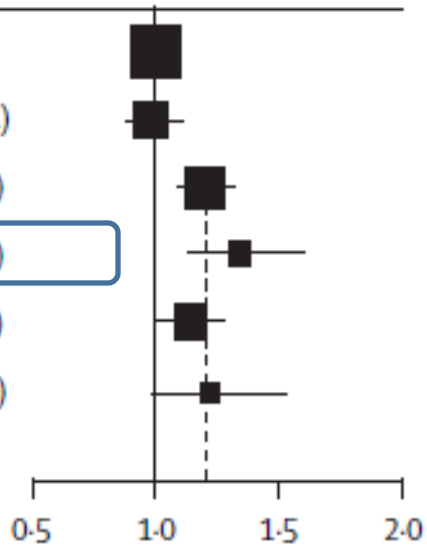
Relativni rizik incidencije raka jajnika ovisno o korištenju HNL-a

Last reported HRT use	Years of HRT use*	Cases/ population (1000s)	Relative risk (95% CI)
Never users	..	1142/474·7	1·00
Past users	3·3	391/186·8	0·98 (0·88–1·11)
All current users	7·7	740/287·1	1·20 (1·09–1·32)
Oestrogen-only	9·2	242/85·9	1·34 (1·13–1·60)
Oestrogen+progestagen	6·9	414/169·3	1·14 (1·01–1·28)
Other	7·0	84/31·9	1·22 (0·98–1·53)



948 576 korisnica
1/2500 novih slučajeva raka jajnika
1/3300 smrtni ishod od OC

Figure 1: **Relative risk of incident ovarian cancer, by use of HRT**

Relative risks are for HRT users compared with never-users, stratified by age and hysterectomy status, and adjusted by region of residence, socioeconomic group, time since menopause, parity, body-mass index, alcohol consumption, and use of oral contraceptives. *Estimated average duration of use of HRT among cases at the time of diagnosis of ovarian cancer.

Relativni rizik raka jajnika
Sadašnje *vs* nekorisnice HNL-a ovisno o tipu HNL-a

Last reported HRT use	Years of HRT use*	Cases/ population (1000s)	Relative risk (95% CI)
All current users	7·7	740/287·1	1·20 (1·09–1·32)
Duration of use			
<5 years	3·8	210/89·3	1·05 (0·90–1·23)
5–9 years	7·3	309/113·7	1·24 (1·09–1·41)
≥10 years	12·3	198/75·2	1·31 (1·12–1·53)
Oestrogen-only			
By duration			
<5 years	4·0	40/20·3	0·89 (0·64–1·25)
≥5 years	10·3	196/62·5	1·53 (1·27–1·84)
By constituent			
Equine oestrogen	9·4	108/36·4	1·38 (1·10–1·73)
Oestradiol	8·6	116/43·5	1·33 (1·07–1·64)
By mode of administration			
Oral	9·1	149/51·3	1·37 (1·12–1·68)
Transdermal	8·8	75/28·5	1·28 (0·99–1·64)
Oestrogen+progestagen			
By duration			
<5 years	3·8	141/58·7	1·09 (0·91–1·30)
≥5 years	8·6	263/106·1	1·17 (1·02–1·34)
By constituent			
(levo) Norgestrel	7·2	160/62·3	1·13 (0·95–1·33)
Norethisterone	6·6	172/67·2	1·22 (1·04–1·44)
Medroxyprogesterone acetate	7·2	69/34·4	0·99 (0·77–1·26)
By regimen			
Continuous	6·8	162/71·1	1·13 (0·95–1·33)
Sequential	6·9	234/92·4	1·14 (0·98–1·32)

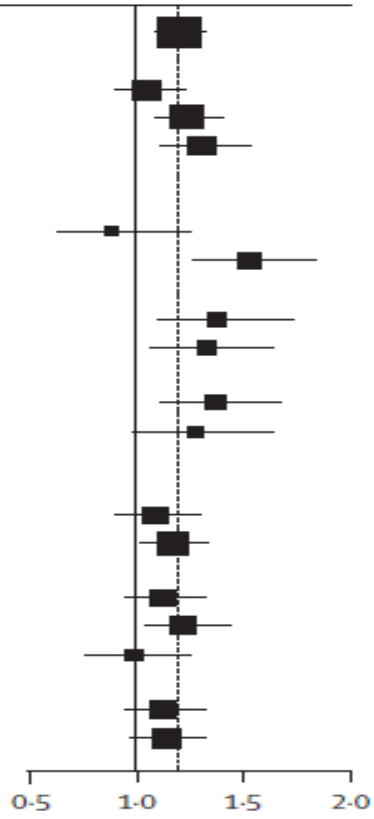


Figure 2: **Relative risk of incident ovarian cancer in current compared with never users of HRT, by pattern of use of HRT**

Relative risks are for HRT users compared with never-users, stratified by age and hysterectomy status, and adjusted by region of residence, socioeconomic group, time since menopause, parity, body-mass index, alcohol consumption, and use of oral contraceptives. * Estimated duration of use of HRT among cases at time of diagnosis of ovarian cancer.

Rizik raka jajnika s obzirom na različite karakteristike
Sadašnje *vs* nekorisnice HNL-a

Characteristics of participants	Years of HRT use*	Cases/ population (1000s)	Relative risk (current vs never; 95% CI)
All women	7·7	740/287·1	1·20 (1·09–1·32)
Age at entry			
<60 years	6·8	462/201·1	1·10 (0·97–1·25)
≥60 years	9·2	278/86·0	1·33 (1·15–1·55)
Socioeconomic status			
High	7·7	329/119·8	1·26 (1·08–1·46)
Low	7·7	406/165·0	1·14 (1·00–1·30)
Number of children			
<2	7·6	223/69·0	1·25 (1·05–1·49)
≥2	7·7	516/217·6	1·17 (1·04–1·32)
Previous use of oral contraceptives			
No	8·0	327/96·2	1·23 (1·07–1·41)
Yes	7·5	410/188·5	1·15 (1·00–1·33)
Body-mass index			
<25	7·8	350/143·5	1·14 (0·99–1·33)
25–29	7·5	260/93·4	1·28 (1·08–1·51)
≥30	7·9	94/37·6	1·11 (0·86–1·43)
Strenuous physical activity			
None/once a week	7·5	427/165·6	1·17 (1·03–1·33)
More than once a week	7·9	293/112·7	1·22 (1·04–1·43)
Alcohol consumption			
≤10g/day	7·7	571/220·9	1·17 (1·05–1·31)
>10g/day	7·6	169/66·2	1·29 (1·03–1·61)
Current smoker			
Yes	7·6	119/57·2	1·14 (0·89–1·46)
No	7·7	587/215·0	1·20 (1·08–1·34)
Hysterectomy			
Yes	9·3	244/82·0	1·47 (1·18–1·83)
No	6·9	496/205·2	1·12 (1·00–1·25)

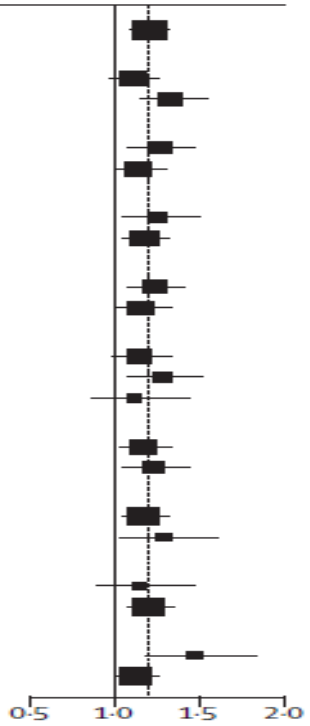


Figure 3: **Relative risk of ovarian cancer in current compared with never users of HRT, by various characteristics of the study participants**

Relative risks are for HRT users compared with never-users, stratified by age and hysterectomy status, and adjusted by region of residence, socioeconomic group, time since menopause, parity, body-mass index, alcohol consumption, and use of oral contraceptives, where appropriate. Totals are not always the same because of missing values.
*Estimated duration of use of HRT among cases at time of diagnosis of ovarian cancer.

Relativni rizik raka jajnika prema histološkim subtipovima
Sadašnje *vs* nekorisnice HNL-a

Tumour type	Years of HRT use*	Number of cases in current users/ never users	Relative risk (95% CI)
All malignant tumours	7·7	740/1142	1·20 (1·09–1·32)
All epithelial tumours	7·5	715/1068	1·24 (1·12–1·37)
Serous	7·6	304/380	1·53 (1·31–1·79)
Mucinous	7·1	56/134	0·72 (0·52–1·00)
Endometroid	7·5	72/114	1·05 (0·77–1·43)
Clear cell	6·8	25/61	0·77 (0·48–1·23)
Mixed/other/NOS	7·5	258/379	1·34 (1·13–1·58)
All non-epithelial tumours	9·8	8/19	0·52 (0·22–1·22)
Malignant tumour, NOS	8·1	17/55	0·51 (0·29–0·90)

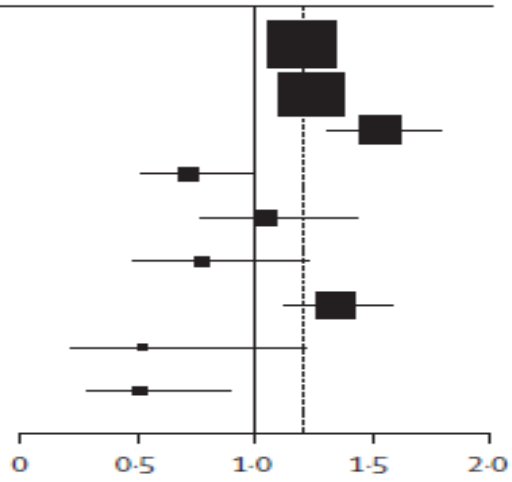


Figure 4: **Relative risk of various histological types of ovarian cancer in current users of HRT compared with never users**

Relative risks are for HRT users compared with never-users, stratified by age and hysterectomy status, and adjusted by region of residence, socioeconomic group, time since menopause, parity, body-mass index, alcohol consumption, and use of oral contraceptives, where appropriate. Totals are not always the same because of missing values. NOS=not otherwise specified. *Estimated duration of use of HRT among cases at time of diagnosis of ovarian cancer.

Relativni rizik smrtnog ishoda raka jajnika ovisno o korištenju i tipu HNL-a

Last reported HRT use	Number of deaths	Relative risk (95% CI)
Never users	819	1·00
Past users	275	0·97 (0·84–1·11)
All current users	497	1·23 (1·09–1·38)
Oestrogen-only	167	1·48 (1·20–1·81)
Oestrogen+progestagen	276	1·15 (1·00–1·33)
Other	54	1·14 (0·87–1·51)

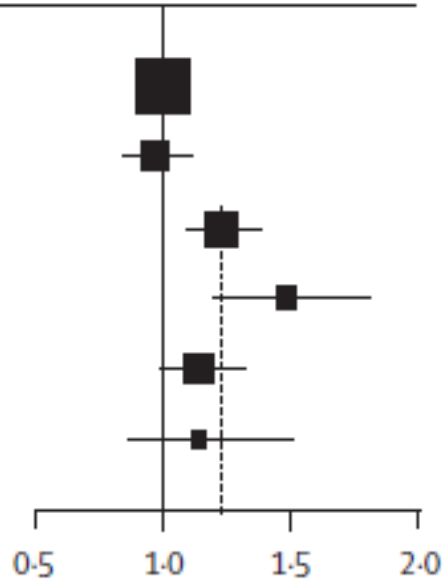


Figure 5: **Relative risk of death from ovarian cancer, by use of HRT**

Relative risks are for HRT users compared with never-users, stratified by age and hysterectomy status, and adjusted by region of residence, socioeconomic group, time since menopause, parity, body-mass index, alcohol consumption, and use of oral contraceptives.

Meta analiza publiciranih rezultata
RR raka jajnika sadašnje korisnice vs nekorisnice

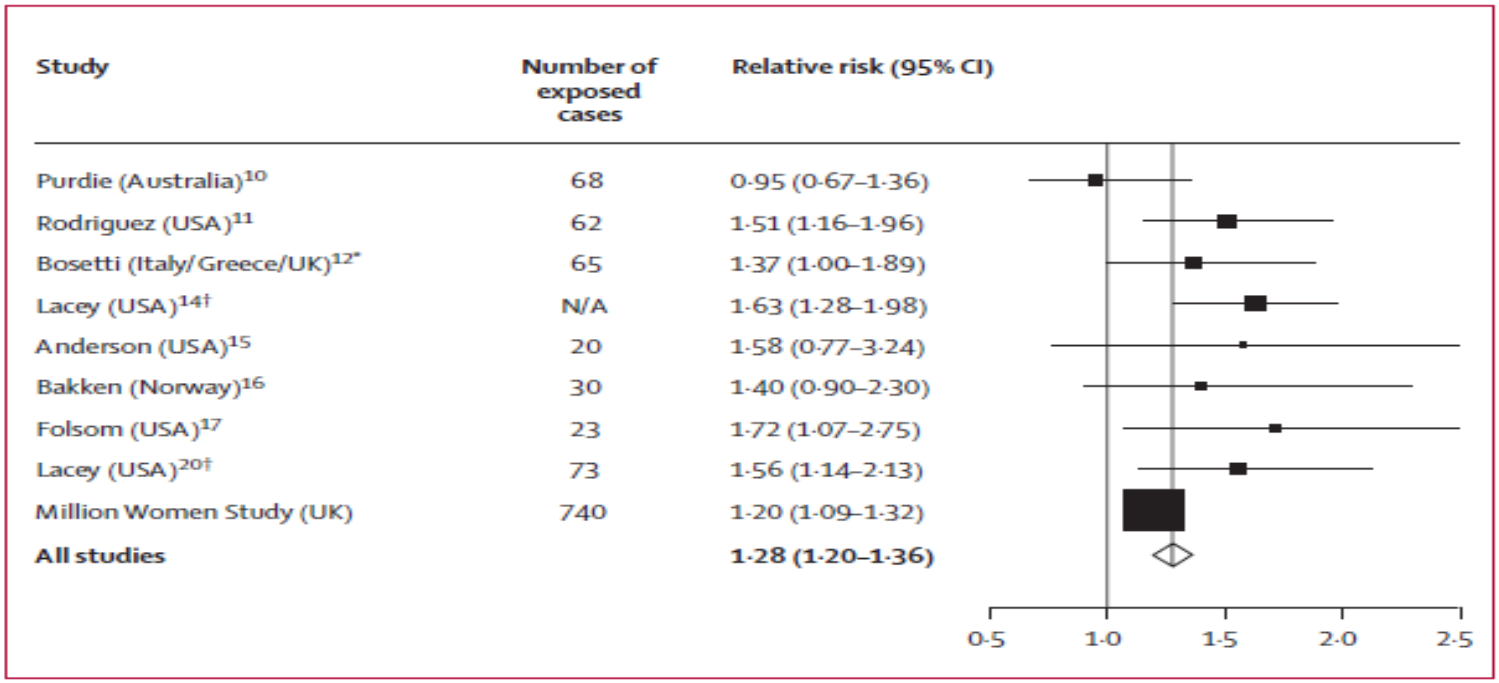
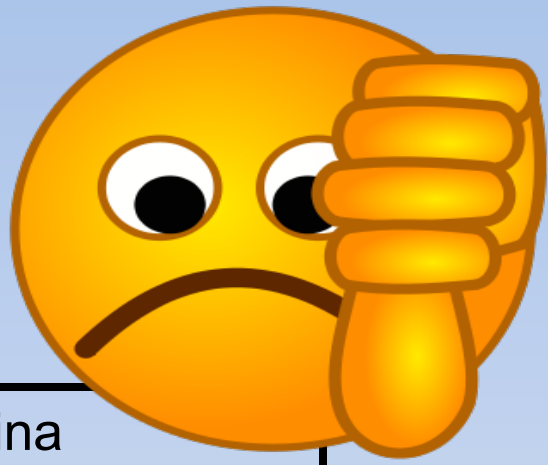


Figure 7: **Meta-analysis of published results on the relative risk of ovarian cancer in current users of HRT compared with never users**

*Current users and those who ceased less than 10 years previously. †Relative risk calculated from values quoted for subgroups of current users and those who ceased use less than 2 years previously. N/A=not available.

- Studije s malim uzorkom
- Prosječno korištenje HNL-a različito
- Bez usporedbe prema tipu i trajanju korištenja HNL-a

Nedostaci studije



- Klinički irelevantno – 4/10 000 korisnica više od 5 godina
- Manji rizik nego povezanost s debljinom, izostankom tjelovježbe, pušenje, nuliparitet, konzumacija alkohola

Neves E Castro et al. Gynecol Endocrinol 2007; 23: 410-13.

- Prosječna životna dob 57.2
- IMS –RR 1.2 minimalni klinički značaj – nedvojbeno statistička značajnost s velikim brojem ispitanica
- Apsolutni rizik 1 dodatni slučaj/ 2500 žena, mortalitet 1/3300 korisnica HNL-a više od 5 godina

International Menopause Society
MENOPAUSE
Episode 4

Is menopausal hormone therapy (HRT) safe?

WHO, EU i US smjernice
Ne spominju rizik raka jajnika

CLIMACTERIC 2013;16:203–204

Global Consensus Statement on Menopausal Hormone Therapy

T. J. de Villiers, M. L. S. Gass*, C. J. Haines†, J. E. Hall‡, R. A. Lobo**, D. D. Pierroz†† and M. Rees‡‡

MediClinic Panorama and Department of Obstetrics and Gynecology, Stellenbosch University, Cape Town, South Africa; *Department of Surgery, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University School of Medicine, Cleveland, OH, USA; †Department of Obstetrics and Gynecology, The Chinese University of Hong Kong, Prince of Wales Hospital Shatin, New Territories, Hong Kong SAR; ‡Department of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA; **Department of Obstetrics and Gynecology, Columbia University, New York, NY, USA; ††University of Geneva, Switzerland; ‡‡Reader Emeritus, University of Oxford, UK

The following Consensus Statement is endorsed by The American Society for Reproductive Medicine, The Asia Pacific Menopause Federation, The Endocrine Society, The European Menopause and Andropause Society, The International Menopause Society, The International Osteoporosis Foundation and The North American Menopause Society.

The 2013 British Menopause Society & Women's Health Concern recommendations on hormone replacement therapy

Nick Panay , Haitham Hamoda , Roopen Arya and Michael Savvas ; on behalf of The British Menopause Society and Women's Health Concern

Menopause International 19(2) 59–68

•Published data on the role of HRT and risk of ovarian cancer are conflicting

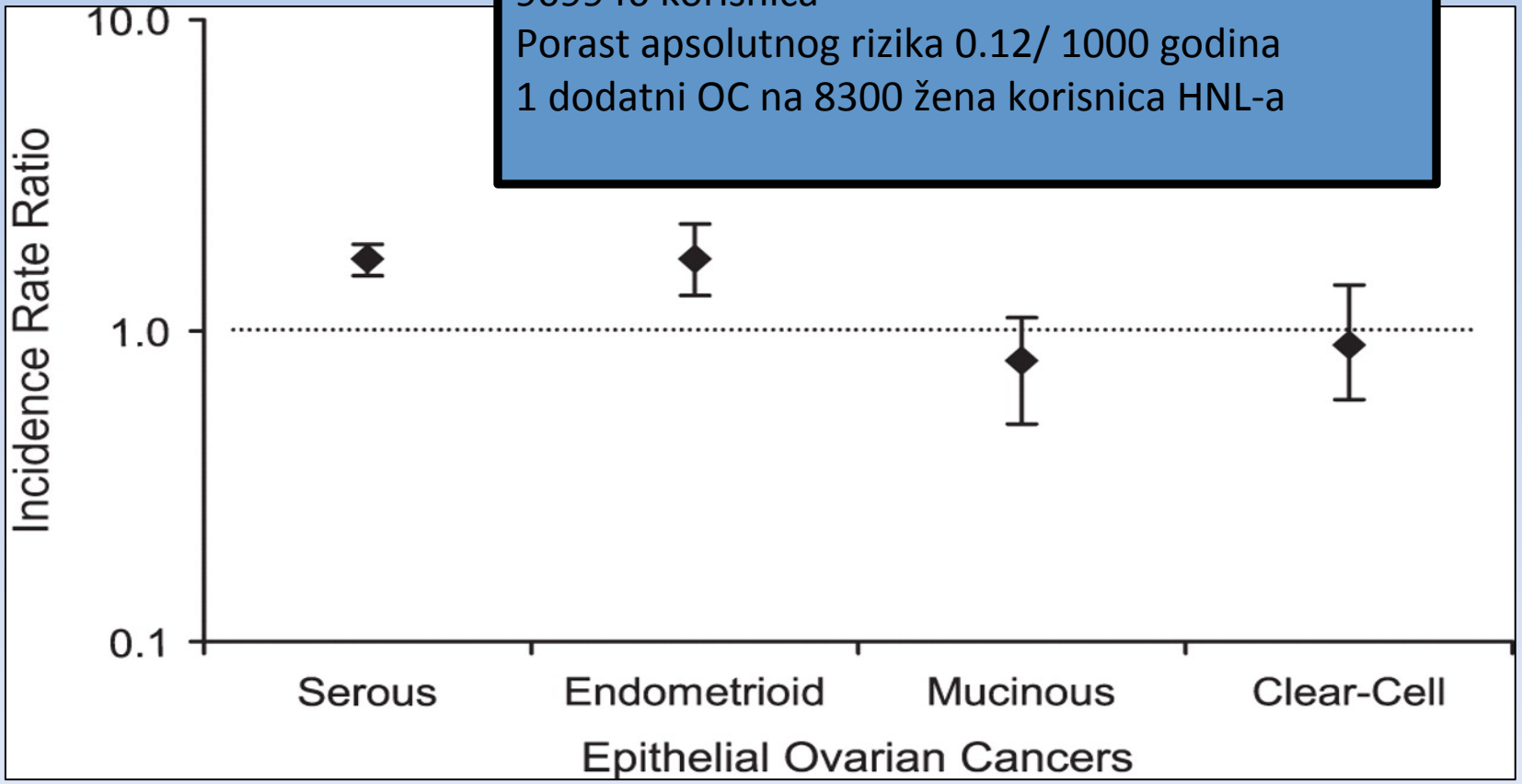
Updated IMS recommendations on postmenopausal hormone therapy and preventive strategies for midlife health

D. W. Sturdee and A. Pines on behalf of the International Menopause Society Writing Group Writing Group: D. F. Archer, R. J. Baber, D. Barlow, M. H. Birkha¨user, M. Brincat, L. Cardozo, T. J. de Villiers, M. Gambacciani, A. A. Gompel, V. W. Henderson, C. Kluft, R. A. Lobo, A. H. MacLennan, J. Marsden, R. E. Nappi, N. Panay, J. H. Pickar, D. Robinson, J. Simon, R. L. Sitruk-Ware and J. C. Stevenson

CLIMACTERIC 2011;14:302–320

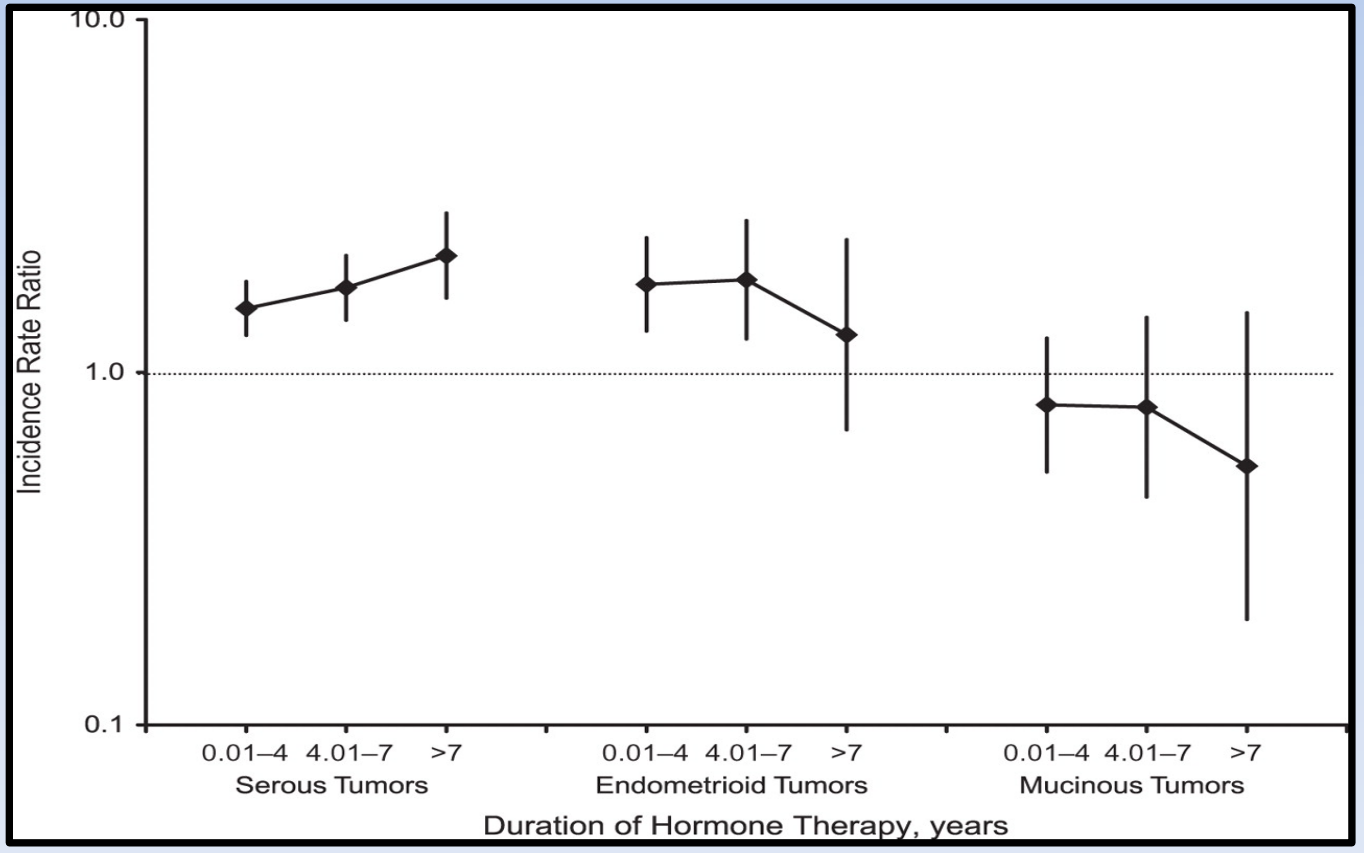
Incidencija RR epitelnih zloćudnih tumora jajnika u sadašnjih korisnica
Danish Sex Hormone Register Study, 1995–2005.

909946 korisnica
Porast apsolutnog rizika 0.12/ 1000 godina
1 dodatni OC na 8300 žena korisnica HNL-a



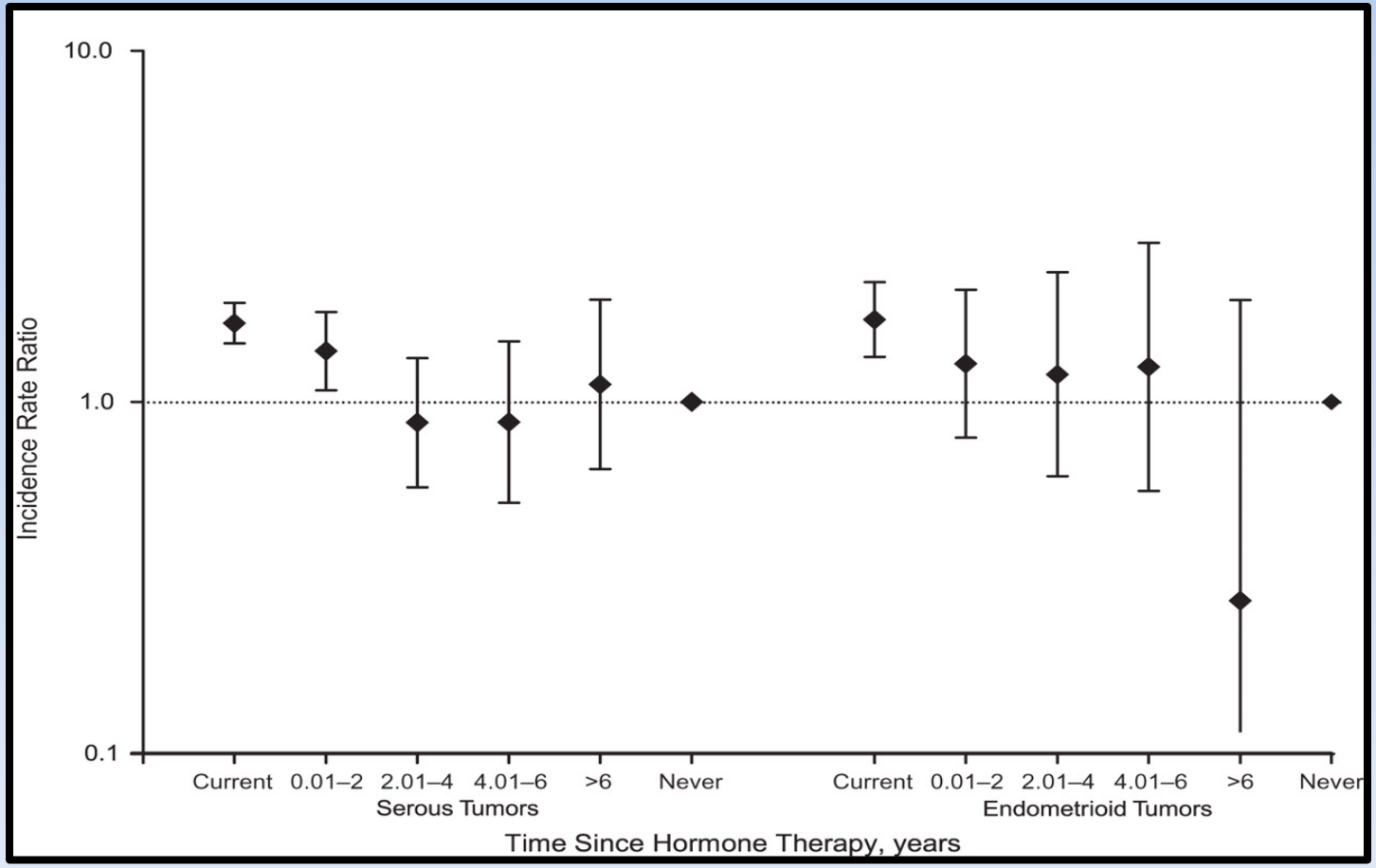
Lina Steinrud Mørch et al. Am. J. Epidemiol. 2012;175:1234-1242

Incidencija RR zloćudnih epitelnih tumora jajnika i trajanje primjene HNL-a Danish Sex Hormone Register Study, 1995–2005.



Lina Steinrud Mørch et al. Am. J. Epidemiol. 2012;175:1234-1242

RR seroznog i endometrioidnog zloćudnog tumora jajnika i vrijeme proteklo od korištenja HNL-a
Danish Sex Hormone Register Study, 1995–2005.

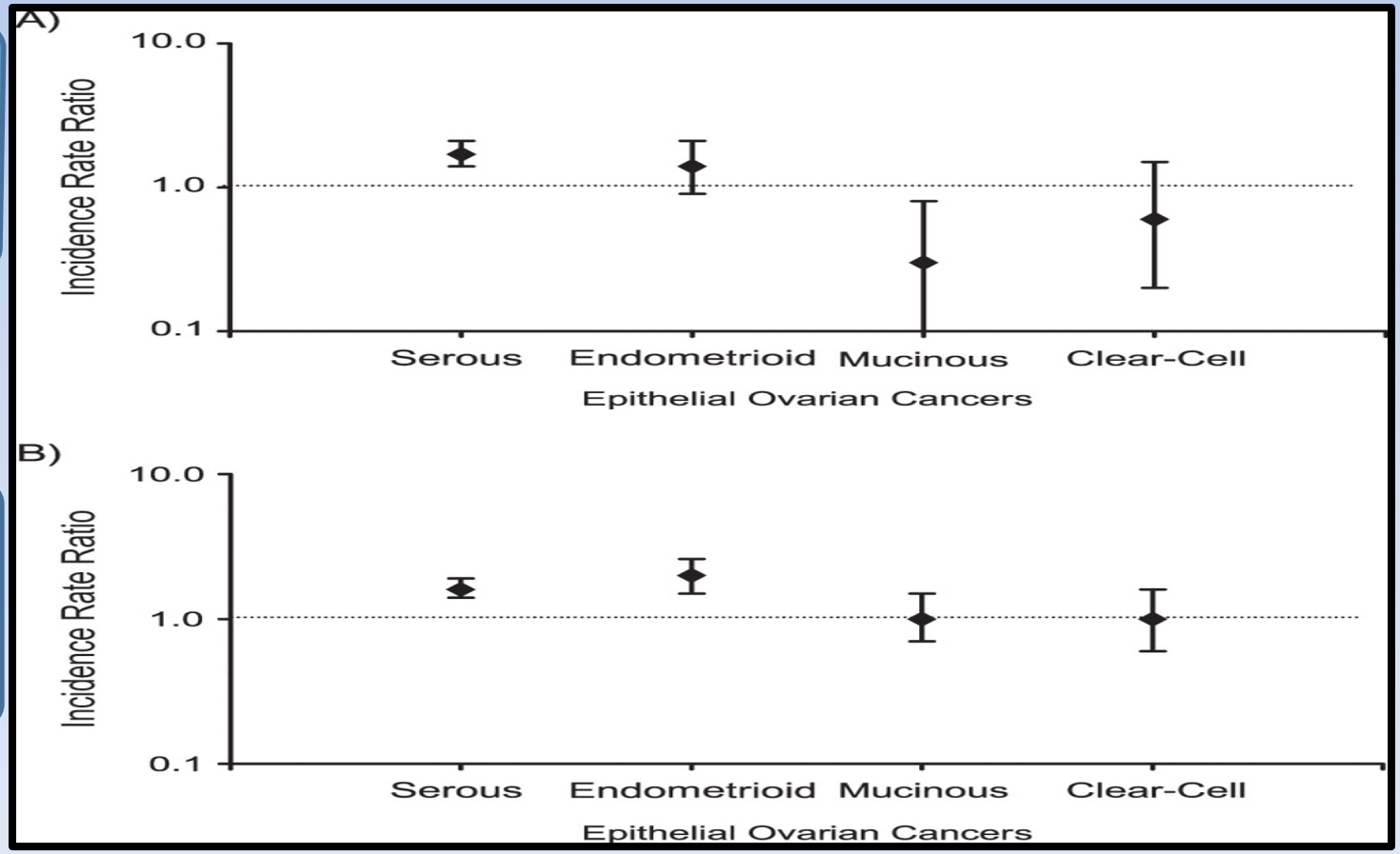


Lina Steinrud Mørch et al. Am. J. Epidemiol. 2012;175:1234-1242

RR epitelnih zloćudnih tumora jajnika i HNL
Danish Sex Hormone Register Study, 1995–2005.

Estrogen HNL

E + P HNL



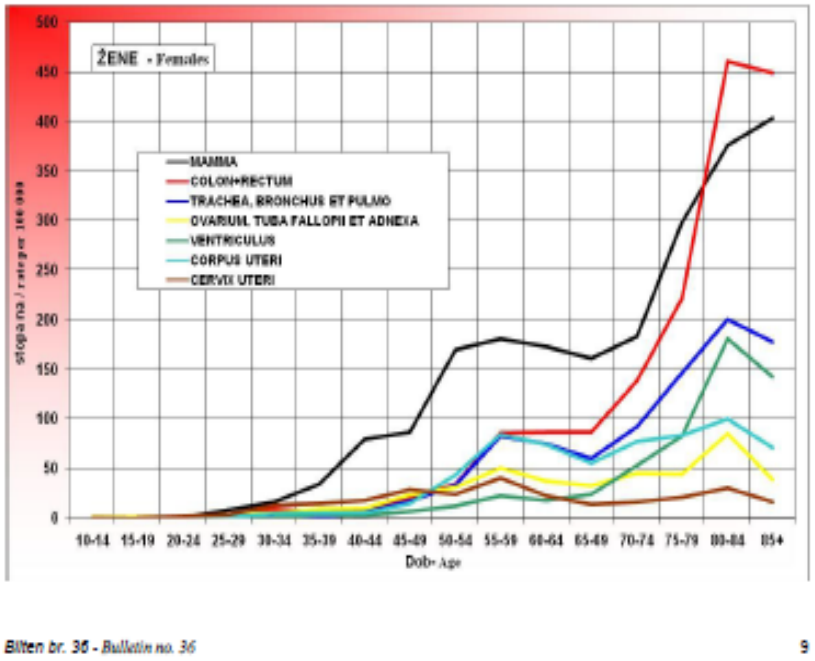
Lina Steinrud Mørch et al. Am. J. Epidemiol. 2012;175:1234-1242

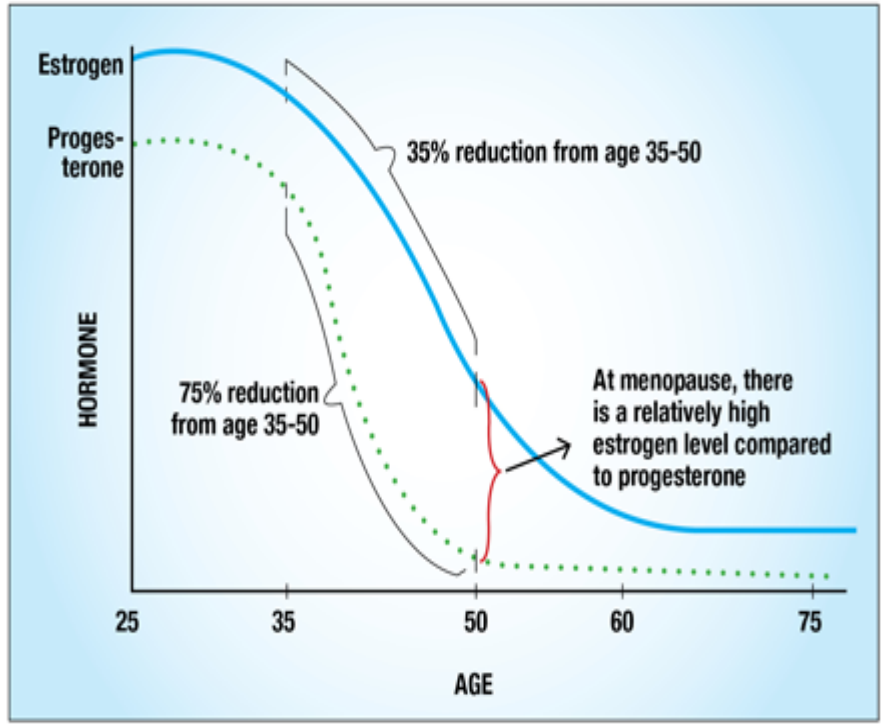
Nedostaci
Danish Sex Hormone Register Study, 1995–2005.

- Dob
- Korištenje OHK
- Žene s anamnezom zloćudne bolesti
- Tjelesna aktivnost i rak jajnika
- Bez podataka o prethodnim operacijama (histerektomija i adneksektomija) u starijih žena
- Nema podataka o izloženosti HNL-u prije uključenja u studiju
- Način primjene lokalni vs transdermalni vs oralni HNL i rizik raka jajnika
- U meta analizi nema pristupa podacima zbog pravnog aspekta podacima studije

Rak jajnika

Incidencija raste s životnom dobi





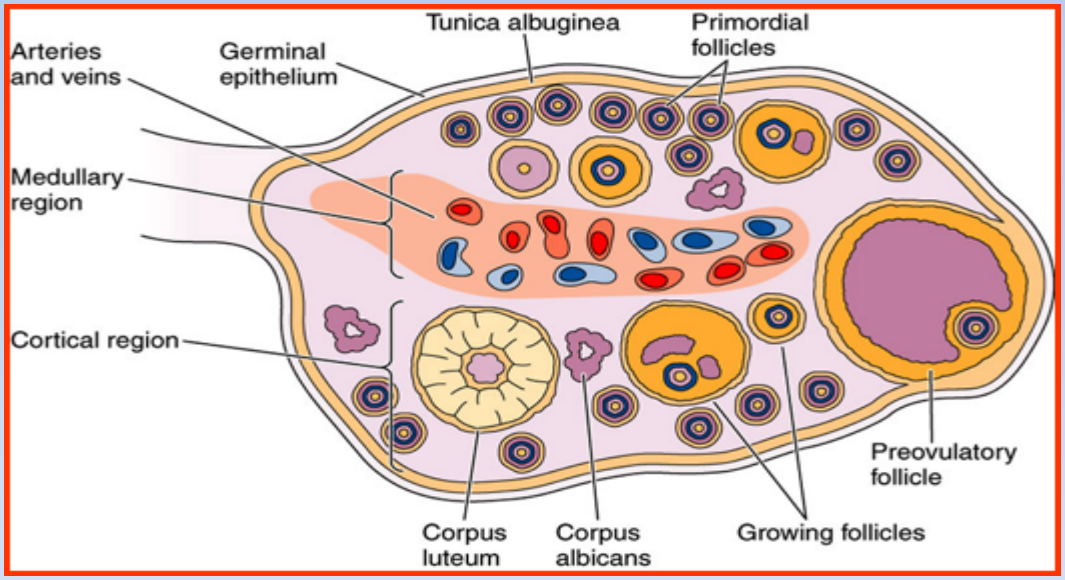
Hrvatski zavod za javno zdravstvo, Zagreb 2013, bilten 36.

Brojni etiološki faktori

nasljedni

upalni

geografski



reproduktivni

hormonski

kirurški

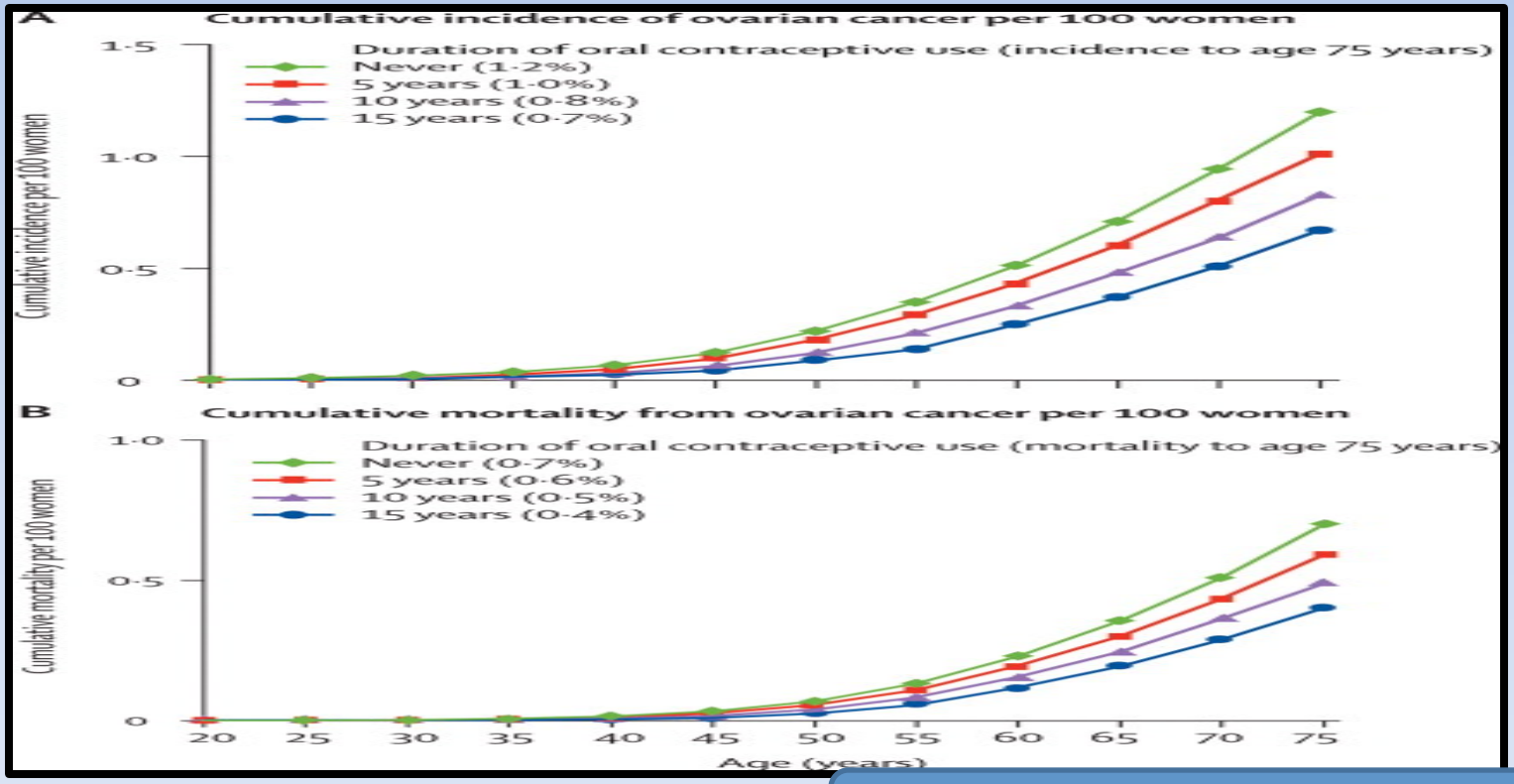
- hormonska kontracepcija , paritet, dojenje – zaštitnici jajnika
- podvezivanje jajovoda, histerektomija ?

OHK – deplecija stem cells – dugotrajni protektivni učinak
HNL – preegzistentni Ca ili prekancerozna promjena – sadašnje korisnice – zašto je potrebno 5 godina izloženosti da se generira značajan RR

•E2 blokira rane dogadjaje, a promovira kasnije korake u karcinogenezi

akcelerira rast postojećeg tumora

Apsolutni rizik raka jajnika za žene ovisno o trajanju korištenja oralne hormonske kontracepcije



A. Kumulativna incidencija raka jajnika / 100 žena
B. Kumulativni mortalitet od raka jajnika / 100 žena

OHK smanjuje rizik seroznog, endometrioidnog i clear cell karcinoma, a ne mucinoznog

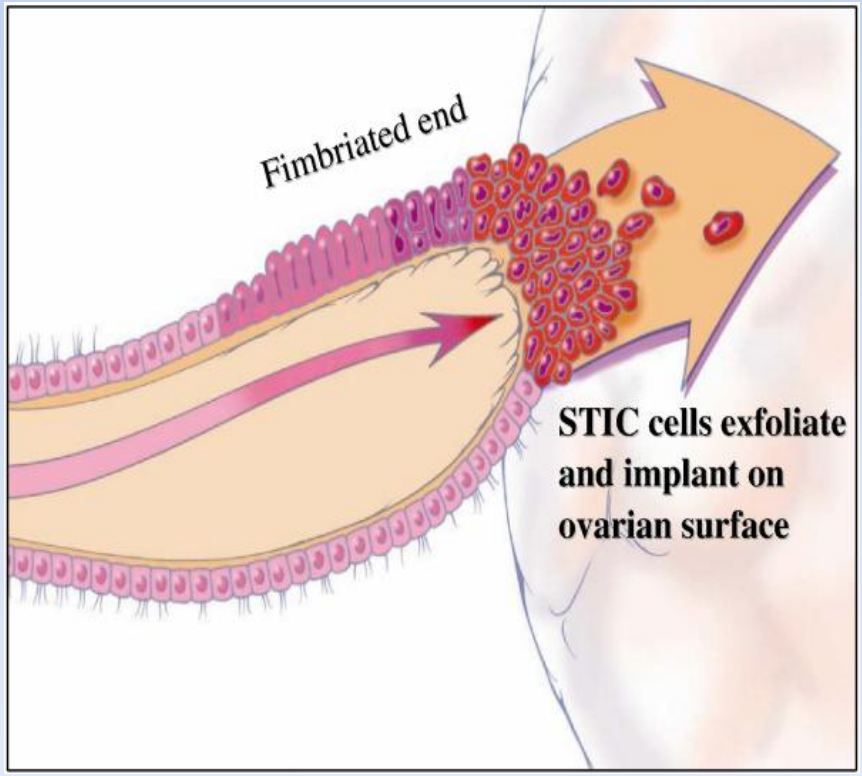
• **Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23 257 women with ovarian cancer and 87 303 controls**

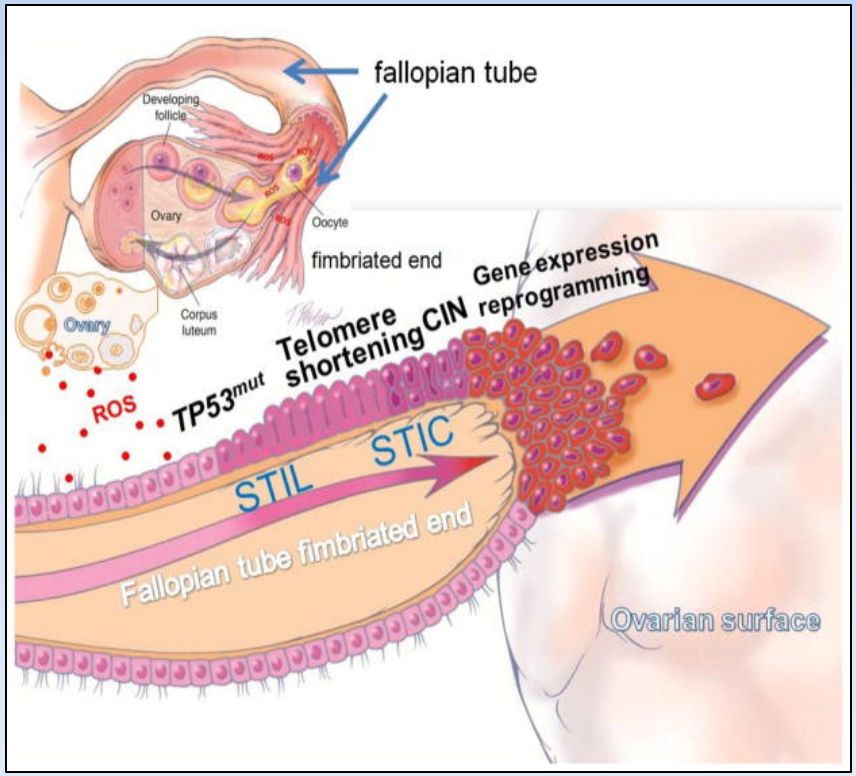
null, Volume 371, Issue 9609, 2008, 303–314
Collaborative Group on Epidemiological Studies of Ovarian Cancer http://dx.doi.org/10.1016/S0140-6736(08)60167-1

Nova paradigma – ekstraovarijsko porijeklo epitelnih zloćudnih tumora jajnika

hipoteza neprestanih ovulacija
gonadotropinska hipoteza
hipoteza zdjelične kontaminacije

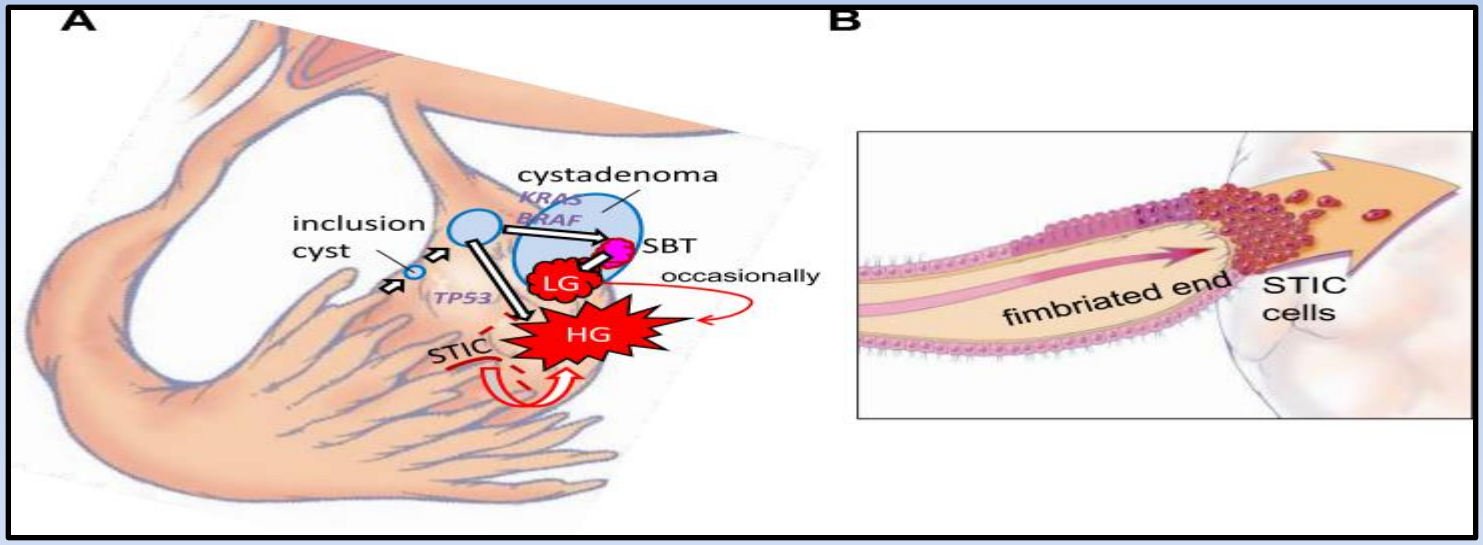
DUALISTIČKI MODEL OVARIJSKE KARCINOGENEZE





Kurman RJ[1], Shih IeM. Hum Pathol. 2011 Jul;42(7):918-31. doi: 0.1016/ j.humpath.2011.03.003.

DUALISTIČKI MODEL OVARIJSKE KARCINOGENEZE
Serozni epitelni karcinom jajnika



•Normalni epitel fimbrija jajovoda
•Implantacija na jajnik – inkluzijske ciste

Mutacija *KRAS/BRAF/ ERRB2* or *TP53*

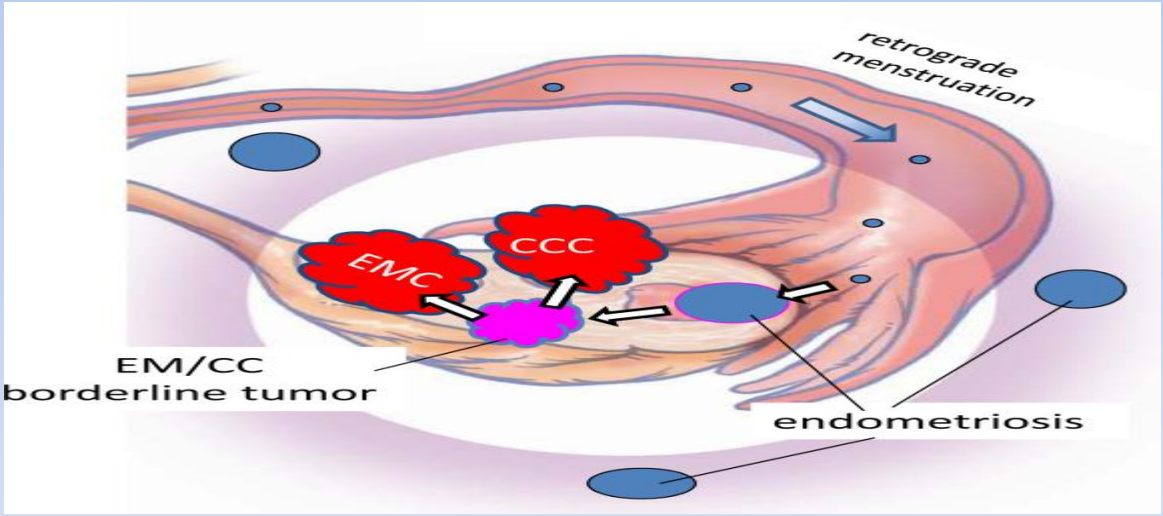
Low grade

High grade

•Eksfolijacija zloćudnih stanica seroznog tubarnog intraepitelnog karcinoma
•Implantacija STIC-a na jajnik

Kurman RJ[1], Shih IeM. Hum Pathol. 2011 Jul;42(7):918-31. doi: 0.1016/j.humpath.2011.03.003.

Razvoj low-grade endometrioidnog i clear cell karcinoma



- Retrogradna menstruacija
- Implantacija endometrijskog tkiva na površinu jajnika
- Endometriotična cista
- Low grade endometrioidni tumori jajnika

Kurman RJ[1], Shih IeM. Hum Pathol. 2011 Jul;42(7):918-31. doi: 0.1016/j.humpath.2011.03.003.

Zaključak

• WHO, EU, USA (WHI) smjernice za HNL – ne spominju rizik raka jajnika

• UK smjernice (očito će biti revidirane) – rizik može biti povećan s dugotrajnom primjenom HNL-a

• HNL ne uzrokuje rak jajnika

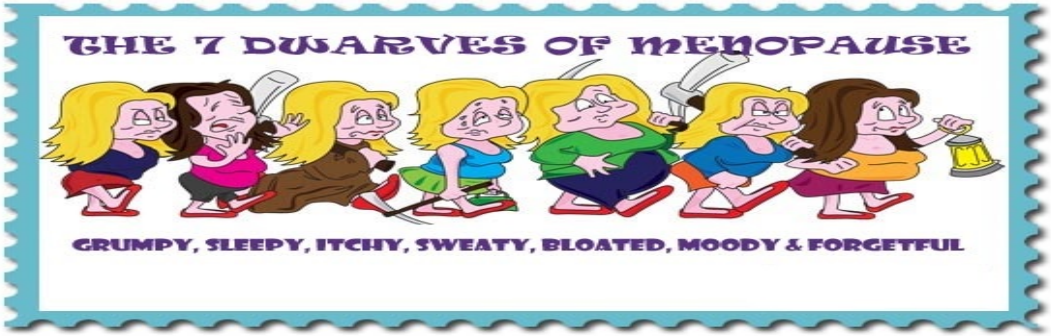
• rak jajnika multifaktorijalna bolest – nekorištenje HNL-a neće smanjiti ili prevenirati razvoj raka jajnika

• rani početak primjene do 5 godina –dobrobit nadmašuje potencijalne rizike

• Individualizirani pristup primjeni HNL-a


Forever 18


MINE
USED TO BE AN
EAGLE TOO


THE 7 DWARVES OF MENOPAUSE
GRUMPY, SLEEPY, ITCHY, SWEATY, BLOATED, MOODY & FORGETFUL

HVALA NA PAŽNJI !