Changes in risk factors of breast cancer and its effect on breast cancer risk in Korean females

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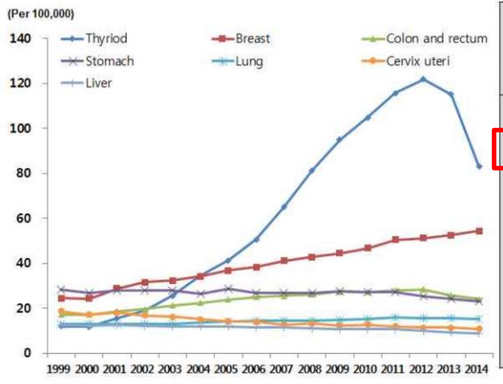
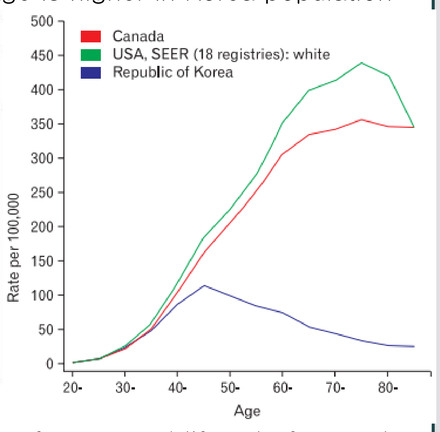
BACKGROUND

- Female breast cancer incidence has shown continuously increasing trend in Korea population and unlike Western population, breast cancer incidence at younger age is higher in Korea population



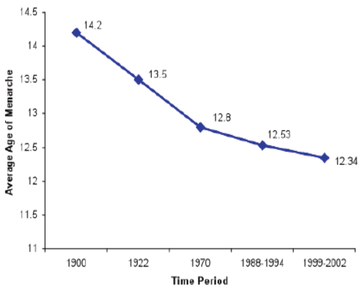
Cancer	Trend1		Trend2	
	Year	Annual rate of change (%)	Year	Annual rate of change (%)
Thyroid	1999-2011	22.3*	2011-2014	-11.7*
Breast	1999-2005	7.5*	2005-2014	4.5*
Colon and rectum	1999-2011	4.5*	2011-2014	-6.5*
Stomach	1999-2011	-0.3	2011-2014	-5.4*
Lung	1999-2011	1.9*	2011-2014	-0.5
Cervix uteri	1999-2014	-3.7*		
Liver	1999-2011	-1.4*	2011-2014	-6.0*

* P < .05

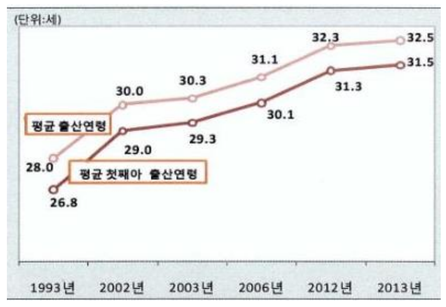


- Several major risk factors of breast cancer including reproductive factors and lifestyle factors has been changed rapidly

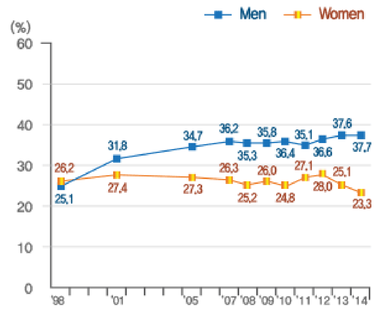
Age at menarche



Age of delivery



Obesity



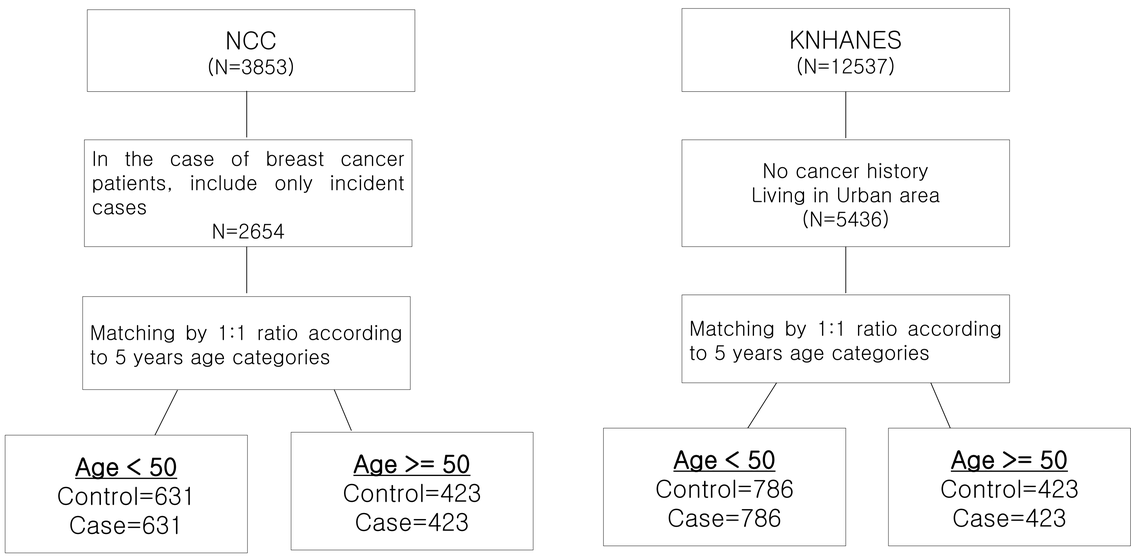
- Considering that an odds ratio (OR), is a relative term based on a distribution of a risk factor in two groups, previous OR for breast cancer might be changed as the changes of the distribution of major risk factors.

PURPOSE OF THIS STUDY

- To compare the effects of known risk factors and theirs strength of the association between previously published Korean breast cancer case-control study results which was conducted in late 1990s and early 2000s and newly constructing case-control study results
- To compare the strength of the association between hospital base case-control study and hospital base case- population base control study to measure the amount of selection bias related with control selection

PARTICIPANTS and METHODS

- **Data and Study population**
  - Hospital base case-control study
    - Breast cancer patients recruited from NCC between 2012.4~2017.3
    - Health examinee controls recruited from NCC between 2012.4~2016.9
  - Hospital based case- population base controls study
    - Breast cancer patients recruited from NCC between 2012.4~2017.3
    - 2013~2015 Korea National Health and Nutrition Examination Survey
  - Separate datasets by the two age groups, less than 50 and above 50 and handling each datasets considering different risk factors etiology before and after menopause
  - Cases and controls were matched by 5-year age group (Hospital base case-control study) and residence area and 5-year age group (Hospital based case- population base controls study)



- **Assessment**
  - By structured questionnaire
    - Female related : age at menarche, age at menopause, pregnancy, age at first pregnancy, duration of breast feeding, oral contraceptive usage
    - Confounders: age, region(only for KNHANES), educational levels(only for KNHANES).
    - Other demographic and socioeconomic characteristics: Body Mass Index (BMI), family history of breast cancer

RESULTS

- Effects of known risk factors and theirs strength of the association between hospital base case-control study and hospital base case- population base control study and a previous study Park et al.
- Use multivariate logistic regression and bootstrapping 3000times to obtain robust results

Age<50 years	NCC			KNHANES			Previous study (Park et al,2013)
	N(Control vs Case)	OR	P-value	N(Control vs Case)	OR	P-value	OR
Family history of breast cancer							
No	562 (89.3%)	530 (84.1%)	1	Not included in KNHANES questionnnare			1
Yes	63 (9.9%)	84 (13.3%)	1.38 (1.25-1.49)	0.05			1.12 (0.81-1.56)
Age at Menarche (years)							
<13	136 (21.5%)	149 (23.6%)	1.47 (1.13-2.10)	0.15	212 (26.9%)	200 (25.4%)	2.30 (1.69-3.01)	0.03	1.87 (1.37-2.54)
13-16	470 (74.5%)	466 (74%)	1.53 (1.16-2.13)	0.13	536 (68.1%)	568 (72.3%)	2.99 (2.20-3.97)	<0.001	1.44 (1.17-1.76)
>=17	20 (3.1%)	11 (1.8%)	1		37 (4.8%)	13 (1.7%)	1		1
Menopause							
Premenopausal	471 (74.7%)	569 (90.4%)	1.11 (1.01-1.25)	0.69	739 (94.1%)	715 (91%)	0.54 (0.39-0.69)	0.02	1.74 (1.42-2.14)
Postmenopausal	54 (8.6%)	51 (8.1%)	1		46 (5.9%)	60 (7.6%)	1		1
Age at first full-term pregnancy (years)							
Nullipara	68 (10.8%)	122 (19.3%)	2.12 (1.81-2.47)	0.01	104 (13.3%)	164 (20.9%)	2.40 (1.86-2.98)	<0.001	1.08 (0.8-1.45)
<24	45 (7.2%)	33 (5.2%)	1		91 (11.5%)	37 (4.7%)	1		1
24-30	359 (56.9%)	316 (50.1%)	1.33 (1.20-1.52)	0.38	469 (59.7%)	382 (48.6%)	1.22 (1.01-1.44)	0.1	1.16 (0.97-1.39)
>=31	89 (14.2%)	144 (22.8%)	2.23 (1.95-2.54)	0.01	120 (15.3%)	183 (23.3%)	2.13 (1.64-2.61)	<0.001	1.25 (0.93-1.69)
Duration of Breast feeding (months)							
Never	64 (10.2%)	114 (18%)	1.40 (1.28-1.55)	0.06	81 (10.3%)	154 (19.6%)	2.36 (1.96-3.01)	0.05	0.93 (0.77-1.12)
0-6	272 (43.2%)	276 (43.8%)	1.00 (0.93-1.09)	0.74	341 (43.3%)	334 (42.5%)	1.26 (1.12-1.43)	<0.001	1.25 (1.01-1.53)
>6	232 (36.8%)	229 (36.3%)	1		363 (46.2%)	285 (36.3%)	1		1
Oral contraceptive usage							
Never	492 (78.2%)	549 (87.1%)	1		708 (90%)	685 (87.2%)	1		1
Ever	116 (18.5%)	76 (12%)	0.59 (0.54-0.66)	<0.001	78 (9.9%)	94 (12%)	1.37 (1.10-1.72)	0.05	1.24 (0.91-1.69)
Exercise							
<once/week	280 (44.5%)	389 (61.8%)	2.77 (2.58-2.99)	<0.001	268 (34.1%)	488 (62.1%)	6.28 (5.50-7.05)	<0.001	1.33 (1.12-1.59)
>=once/week	295 (46.9%)	121 (19.1%)	1		518 (65.8%)	154 (19.6%)	1		1

Age>=50 years	NCC			KNHANES			Previous study (Park et al, 20013)
	N(Control vs Case)	OR	P-value	N(Control vs Case)	OR	P-value	OR
Family history of breast cancer							
No	376 (89%)	335 (79.2%)	1	Not included in KNHANES questionnnare			1
Yes	32 (7.6%)	79 (18.7%)	2.91 (2.32-3.57)	<0.001			2.01 (1.28-3.13)
Age at Menarche (years)							
<13	33 (7.7%)	23 (5.4%)	0.97 (0.76-1.32)	0.36	39 (9.1%)	23 (5.4%)	1.19 (0.81-1.67)	0.75	2.4 (1.38-4.19)
13-16	325 (76.8%)	342 (80.9%)	1.09 (0.9-1.27)	0.41	302 (71.4%)	342 (80.9%)	1.95 (1.53-2.48)	<0.001	1.53 (1.29-1.81)
>=17	61 (14.5%)	52 (12.3%)	1		78 (18.4%)	52 (12.3%)	1		1
Age at menopause (years)							
Premenopausal	20 (4.6%)	109 (25.8%)	3.76 (2.97-4.69)	<0.001	71 (16.9%)	109 (25.8%)	1.18 (0.82-1.74)	0.73	2.50 (1.78-3.51)
<44	35 (8.2%)	36 (8.5%)	1		38 (9%)	36 (8.5%)	1		1
45-49	103 (24.3%)	76 (18%)	0.62 (0.5-0.75)	0.1	115 (27.1%)	76 (18%)	0.52 (0.37-0.73)	0.04	1.34 (0.99-1.83)
50-54	167 (39.6%)	162 (38.3%)	0.80 (0.63-0.97)	0.44	175 (41.4%)	162 (38.3%)	0.76 (0.54-1.06)	0.06	1.36 (1.01-1.82)
>=55	26 (6.1%)	32 (7.6%)	0.87 (0.59-1.19)	0.68	21 (4.9%)	32 (7.6%)	1.16 (0.71-1.90)	0.87	1.62 (1.09-2.39)
Pregnancy							
Nullipara	6 (1.4%)	18 (4.3%)	2.18 (1.61-3.18)	0.07	8 (1.9%)	18 (4.3%)	2.74 (1.39-6.07)	0.05	1.88 (1.24-2.84)
Para	405 (95.6%)	399 (94.3%)	1		412 (97.5%)	399 (94.3%)	1		1
Body mass index							
<25	329 (77.8%)	290 (68.6%)	1		284 (67.1%)	290 (68.6%)	1		1
25-29.9	70 (16.6%)	102 (24.1%)	1.92 (1.64-2.23)	0.01	117 (27.6%)	102 (24.1%)	0.86 (0.71-1.07)	<0.001	1.16 (0.97-1.38)
>=30	15 (3.5%)	16 (3.8%)	0.83 (0.63-1.16)	0.63	21 (5.1%)	16 (3.8%)	0.40 (0.29-0.56)	0.01	2.28 (1.49-3.48)
Oral contraceptive usage							
Never	327 (77.4%)	356 (84.2%)	1		350 (82.7%)	356 (84.2%)	1		1
Ever	82 (19.3%)	61 (14.4%)	0.77 (0.67-0.89)	0.12	71 (16.7%)	61 (14.4%)	0.89 (0.69-1.11)	0.44	1.52 (1.12-2.06)
Exercise							
<once/week	139(32.9%)	248(58.6%)	4.46 (4.00-5.24)	<0.001	129(30.6%)	248(58.6%)	6.39 (5.18-8.05)	<0.001	1.84 (1.50-2.27)
>=once/week	255 (60.2%)	94 (22.2%)	1		292 (69%)	94 (22.2%)	1		1

CONCLUSIONS

- In general, the direction and magnitude ORs of selected breast cancer risk factors were comparable with the previous results in NCC cases-controls, except for oral contraceptive use which showed reverse association or non-significant association.
- Some variables related to pregnancy, like age of first delivery, duration of breast feeding show higher odds ratio than odds ratio of previous study. This can be related to change of lifestyles.
- When the ORs were compared between two types of controls, the magnitude ORs were higher in population base control
  - Expected selection bias of hospital base controls would be minimal and population base controls may show higher selection bias
  - In case-control study, source of cases and controls should be same to avoid biased results
- There may be better model by adjusting cut offs of explanatory variables or selecting new variables, cause some variables reflect change of lifestyles and were not significant (Ex: age at menopause)

Acknowledgement

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