

The risk of breast cancer associated with specific mutation of BRCA1 and BRCA2 among Korean population

Boyoung Park^{1,2}, Seung Hyun Ma^{2,3}, Sung-won Kim^{4,5}, Sei-Hyun Ahn⁶,
Min Hyuk Lee⁷, Sue K. Park^{2,3}, Korean Breast Cancer Society

¹ National Cancer Control Institute, National Cancer Center, Goyang, Korea

²Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, Korea

³Cancer Research Institute, Seoul National University, Seoul, Korea

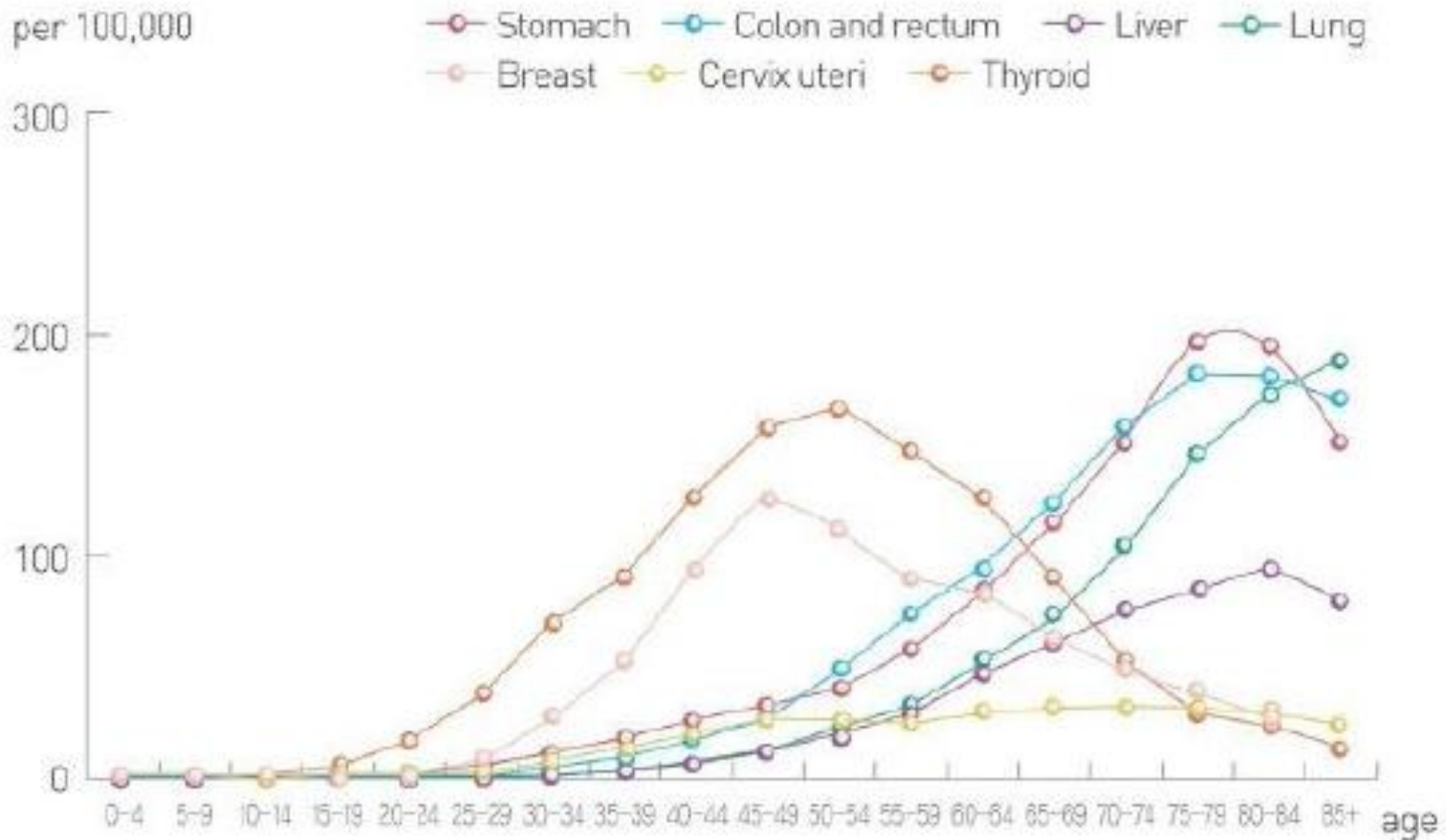
⁴Department of Surgery, Seoul National University College of Medicine, Seoul, Korea

⁵Department of Surgery, Seoul National University Bundang Hospital, Seongnam, Korea

⁶Department of Surgery, University of Ulsan and Asan Medical Center, Seoul, Korea

⁷Department of Surgery, College of Medicine, Soonchunhyang University Seoul, Korea

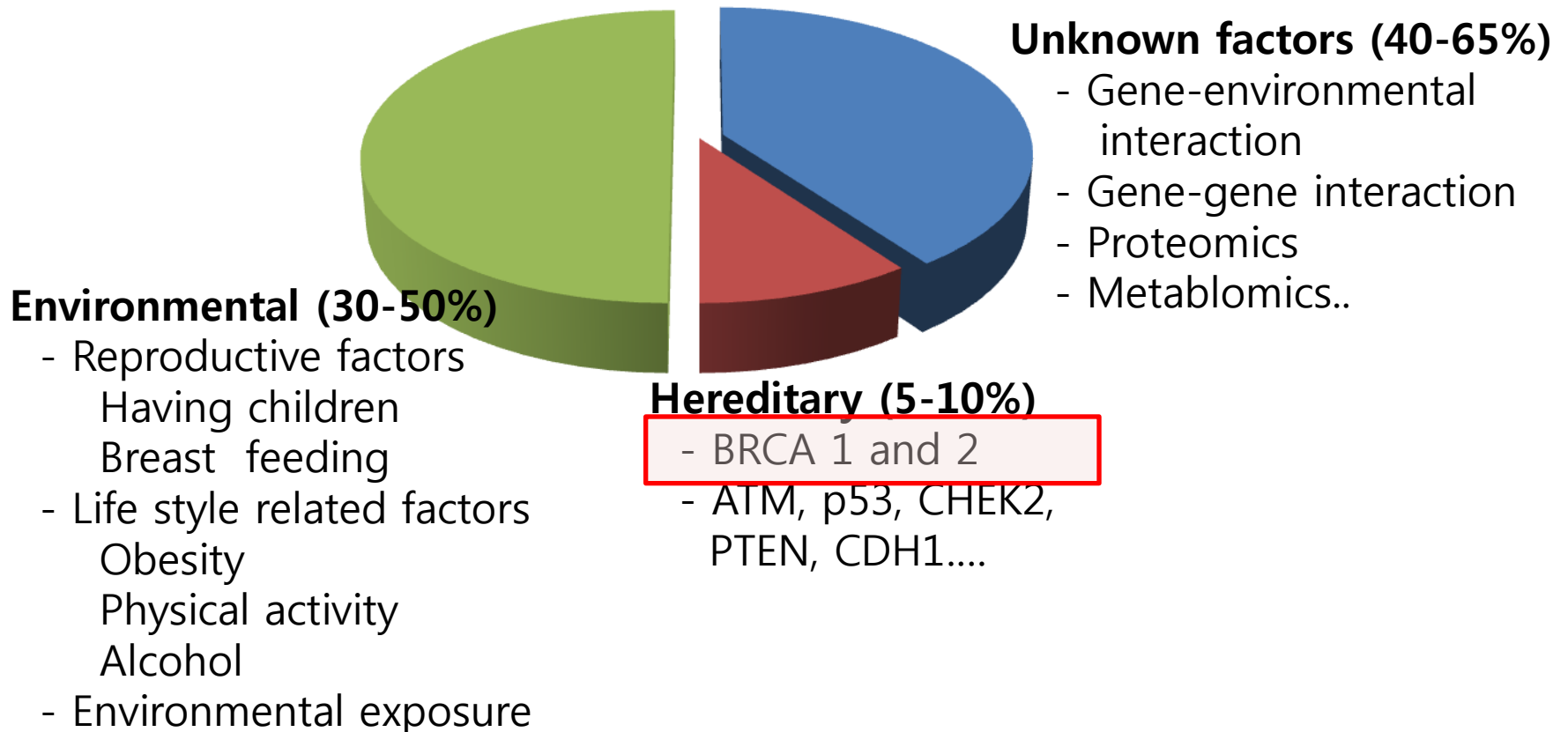
Background/Purposes



Source: Ministry of Health & Welfare. The Korea Central Cancer Registry, 2010

Background/Purposes

• Etiology of Breast Cancer



Background/Purposes

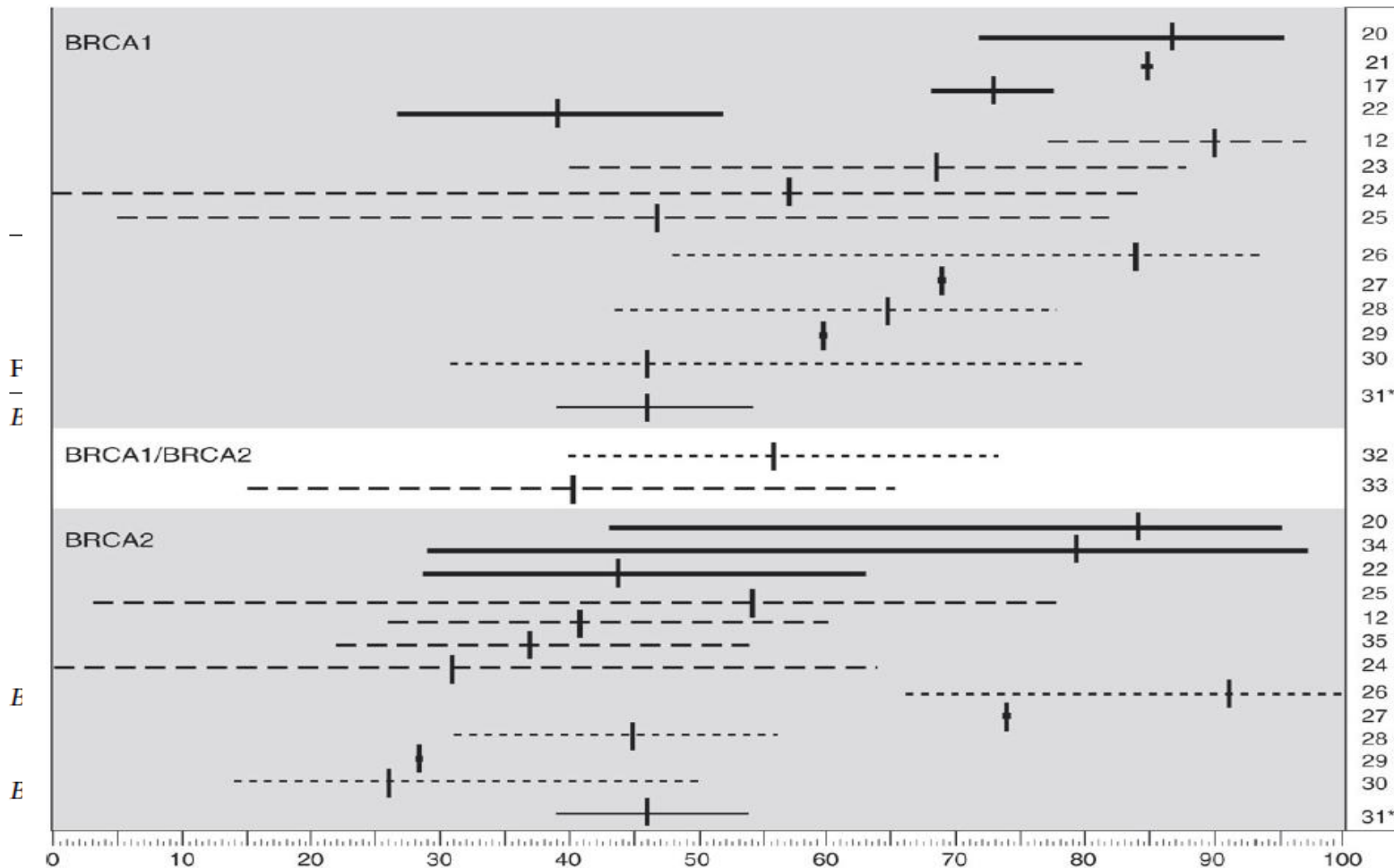
- **Methods for calculating penetrance**

	Multiple-case families	Population based	Hospital based
Index case	Family with multiple family members	Without regard to family history	Volunteer case proband
Risk estimation	Higher risk	Lower risk	Lower risk
Weakness	Not reflect the average risks in all carriers in the population	Partial participation Lack of precision	Lack of precision

- The most robust method: follow up the cohort of BRCA mutation carriers prospectively
 - Yearly breast cancer risk: 2.5%

Background/Purposes

- Breast cancer risk due to mutations in BRCA1/2



————+———— 95% Confidence intervals (where provided) with point estimates
 ————— Multiple-case, linkage and clinic-based ascertainment
 - - - - - Population-based ascertainment
 ········· Affected proband, hospital-based and volunteer ascertainment
 * Mixed population-based and multiple-case ascertainment

Background/Purposes

- Previous study results of the cumulative risk of BC and OC in Korea

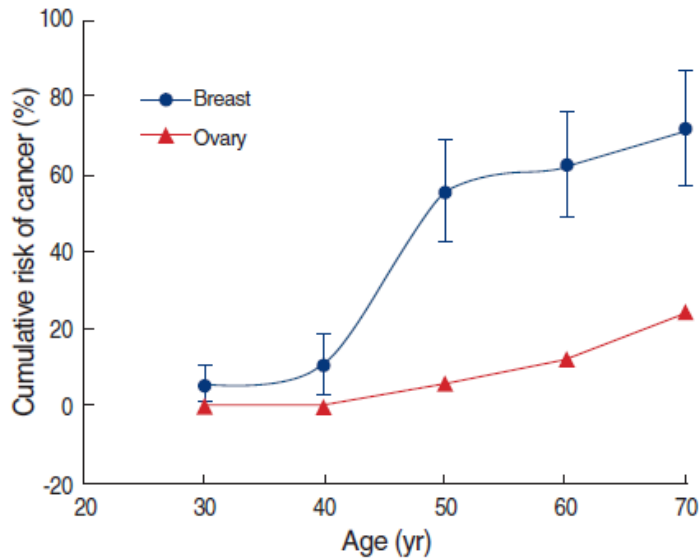


Figure 1. Cumulative risk of breast and ovary cancer till each age among family members with *BRCA1* mutation carriers.

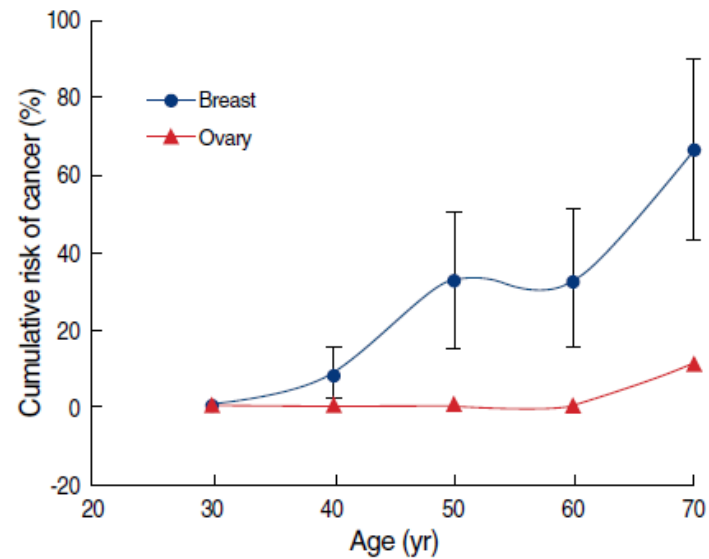


Figure 2. Cumulative risk of breast and ovary cancer till each age among family members with *BRCA2* mutation carriers.

- Purpose: To estimate the risk of breast and ovarian cancer in the women of BRCA mutation carriers

Methods

- **Study subjects**

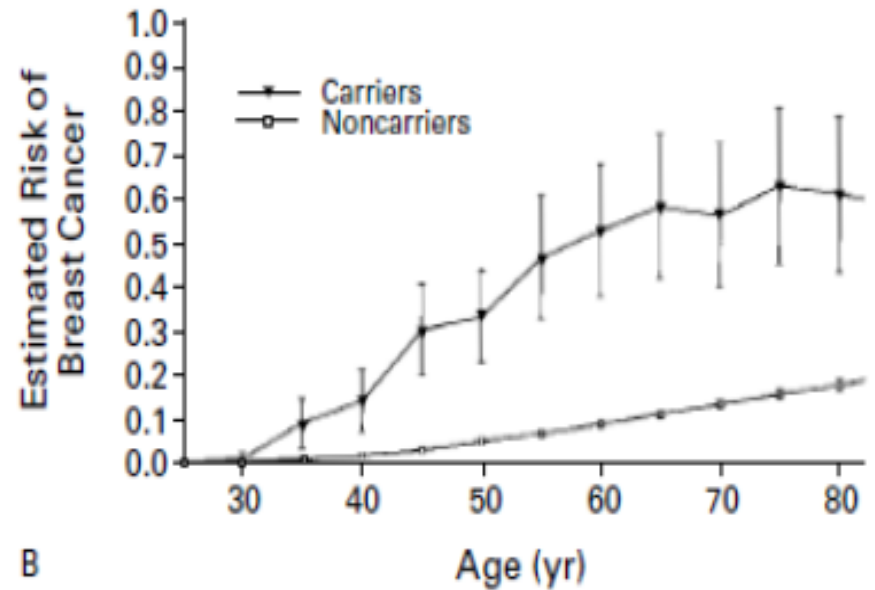
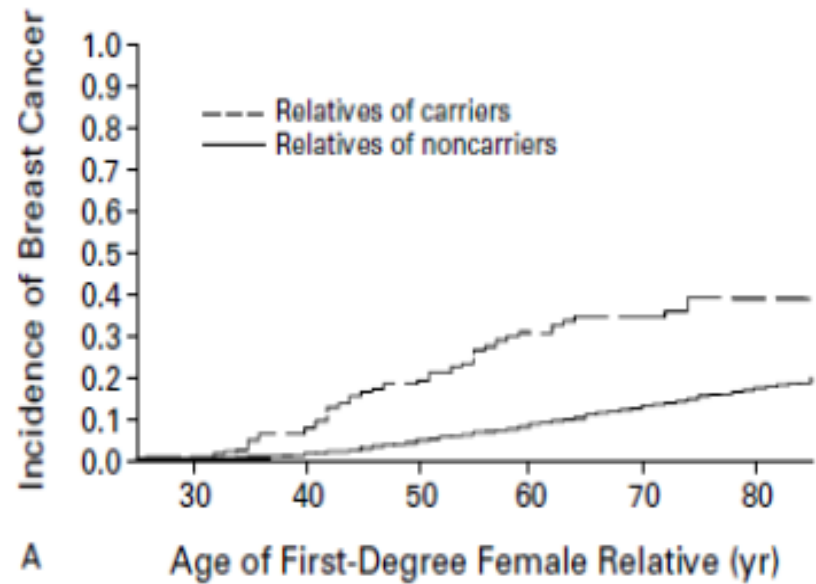
- Korean Hereditary Breast Cancer (KOHBRA) study participants
 - ✓ Nationwide study to estimate the prevalence of *BRCA1/2* mutations and ovarian cancer among a high-risk group of patients with hereditary breast cancer and their families.
 - ✓ Breast cancer patients with family history, breast cancer patients in high risk group, family members of *BRCA1/2* mutation carriers

- **Method for calculating the risk of breast/ovarian cancer**

- Kin-cohort design
- Kaplan-Meier analysis

Methods

- Kin-cohort analysis



Methods

- **Kaplan-Meier analysis**
 - follow-up information of known carriers only
- **Comparison of the Kin-cohort and Kaplan-Meier analysis**

	Kin-cohort design	Kaplan-Meier analysis
Study subject	Female first degree relatives of the patients	Female BRCA mutation carrier relatives of the affected carriers
Subject mutation status	Known/unknown	Only BRCA mutation (+)
Proband	Exclude in the analysis Both BRCA mutation (+)/(-)	Exclude in the analysis Only BRCA mutation (+)
Cumulative risk	Kaplan-Meier analysis	Kaplan-Meier analysis
Penetrance	Calculating using cumulative risk $S_1 = 2R_+ - R_-$ $S_0 = (1 + p / 1 - p)$	Same as cumulative risk

Results

- **Summary statistics for families and carriers used in predicting the mutation status**

	Full pedigrees	1st degree relatives over 10 ^{1,3}	All of the relatives with BRCA mutation test result over 20 ^{2,3}
N of families	1775	1709	251
N of subjects	40546	9772	330
Mean N of members per family	22.8	5.7	1.31
BC cases, N (%)	2629 (7.4)	502	35(10.6)
Age of BC cases, mean (SD)	43.5(11.1)	48.6(11.2)	49.4(11.0)
Bilateral BC cases, N (%)	271	37	6(17.1)
BRCA1/2 mutation test	2396	-	330 ⁴
N of BRCA1/2 mutation carrier		-	180

¹ For Kin-cohort analysis, pedigree information was considered

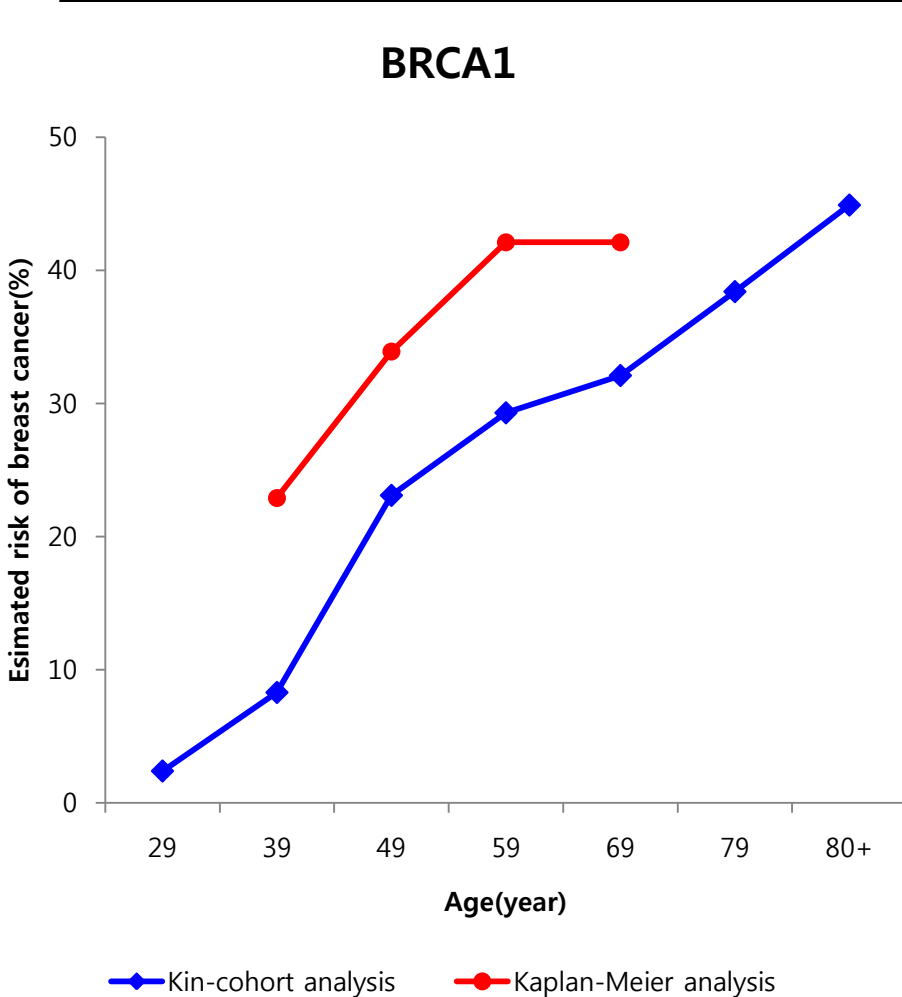
² For Kaplan-Meier analysis, information about BRCA mutation and cancer status were considered

³ Excluding probands

⁴ All the subjects had BRCA test results

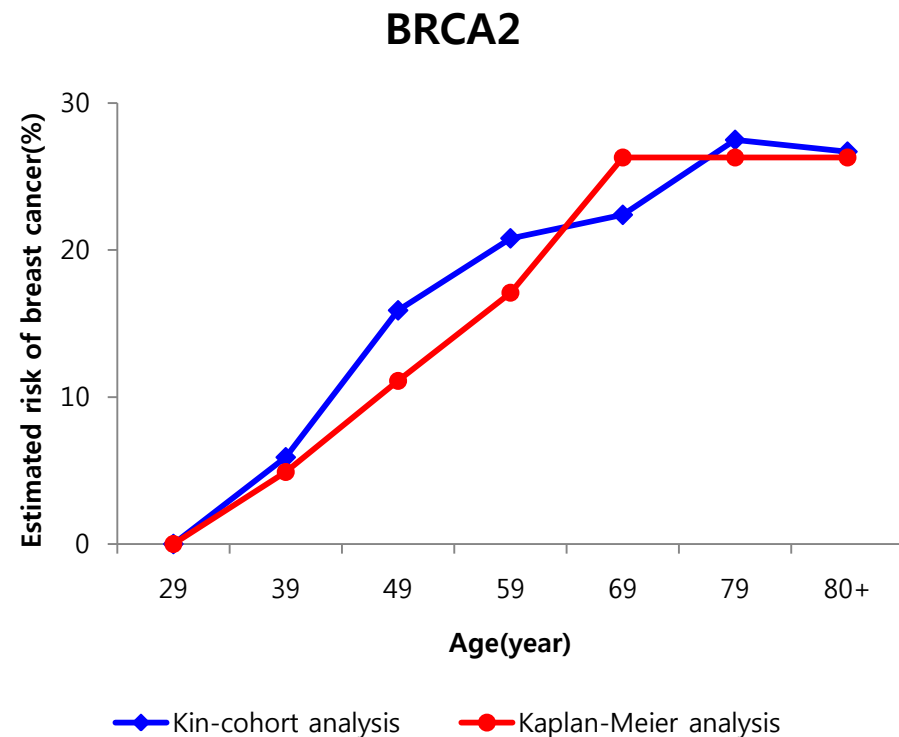
Result

- Risk of breast cancer associated with mutation of BRCA1/2



Kaplan-Meier analysis

sk	N of carriers	N of BC	Cumulative risk% (SE)

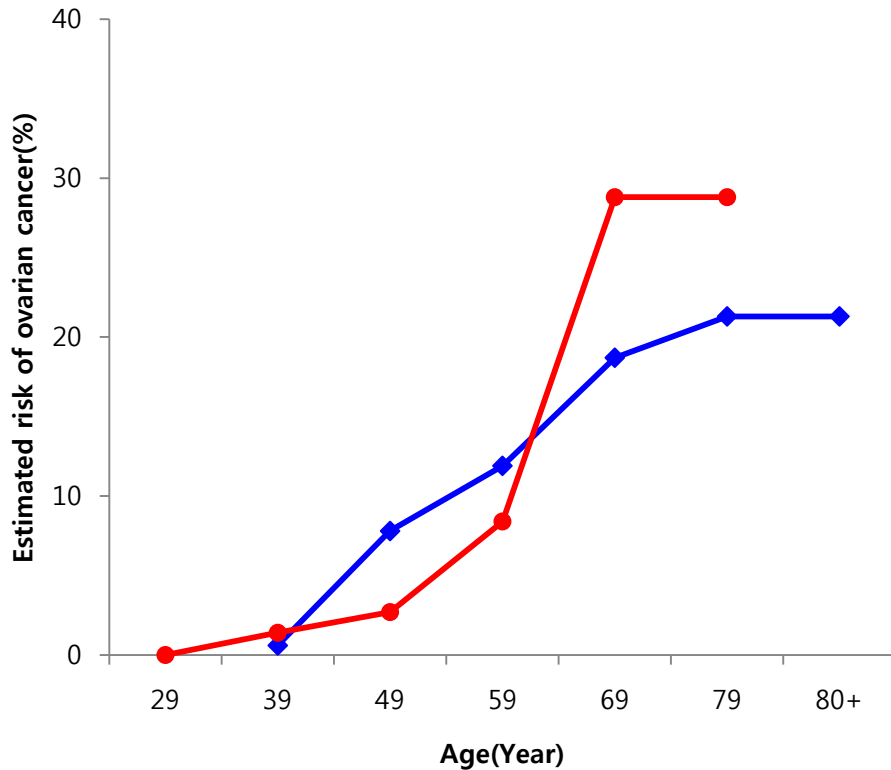


Result

- Risk of ovarian cancer associated with mutation of BRCA1/2

Kin-cohort analysis

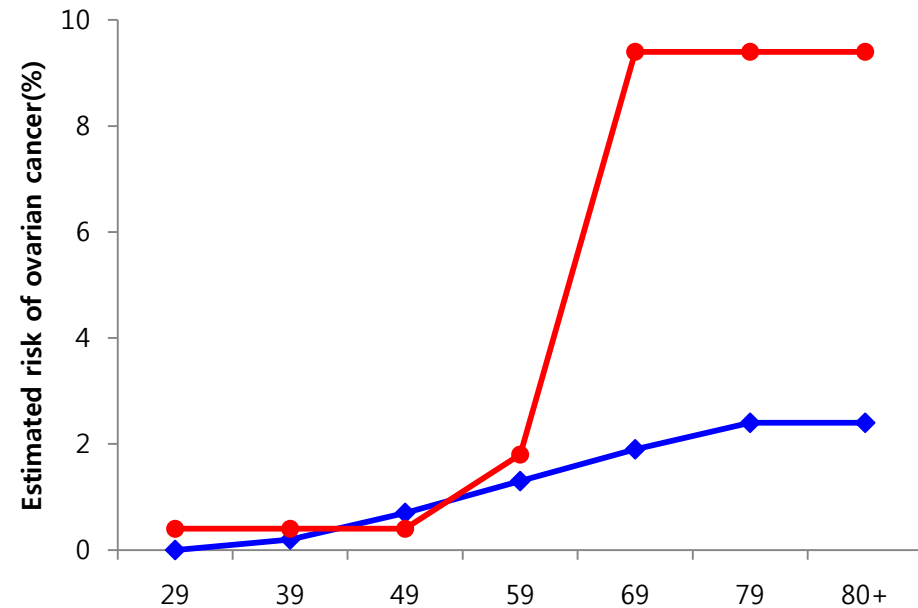
BRCA1



◆ Kin-cohort analysis ● Kaplan-Meier analysis

Kaplan-Meier analysis

risk	N of carriers	N of BC	Cumulative risk, (SE)
	157	0	0.0



◆ Kin-cohort analysis ● Kaplan-Meier analysis

Result

- Risk of contralateral breast cancer associated with mutation of BRCA1/2

Kaplan-Meier analysis			
Age	N of carriers ²	N of breast cancer	Cumulative risk,% (SE) ³
BRCA1			
<1 year ¹	124	3	2.4(1.4)
0-4 year ¹	74	6	10.3(3.3)
0-9 year ¹	35	11	38.5(7.4)
0-14 year ¹	8	3	61.6(11.5)
0-15+ year ¹	4	2	80.8(11.2)
BRCA2			
<1 year ¹	1515	115	7.6(0.7)
0-4 year ¹	738	42	12.8(1.0)
0-9 year ¹	203	26	24.0(2.2)
0-14 year ¹	48	10	39.8(4.8)
0-15+ year ¹	21	2	45.6(5.8)

¹ Time after diagnosis of primary breast cancer

² Total number of carriers at risk

³ Cumulative risk of contralateral breast cancer in family with *BRCA1/2* mutation.

Discussion

- **Limitation of the results**

	Kin-cohort design	Kaplan-Meier analysis
Study subject	First degree relatives of the participants without BC were not included → Over- or under-estimation	Relatives of the affected noncarrier were not included Carriers without family history of BC were not included → Over-estimation
Information	Unexact information of the BC incidence of the relatives	Not consider the presumed carriers

- **Strength of the results**

- Comparison of the two methods
- Relatively large sample size

THANK YOU