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## Background

Female *BRCA1/2* mutation carriers have higher risk of breast and ovarian cancer in their lifetime, compared to general population. Due to the cumulative risk up to 40% and poor clinical outcome of ovarian cancer, risk-reducing salpingo-oophorectomy (RRSO) is suggested as preventive strategies in several guidelines. RRSO also showed improvement in survival outcome and efficacy of lowering risk of breast cancer. Although RRSO is generally recommended to the carriers with *BRCA1* mutation at 35-40 years of age, and those with *BRCA2* mutation at 40-45 years of age after accomplishment of childbearing, many carriers are still hesitating to receive risk-reducing procedure for ovaries and fallopian tubes unaffected by cancer. In Korea, germline genetic testing, RRSO, and contralateral prophylactic mastectomy (CPM) have been supported by national health insurance (NHI) since 2012, 2012, and 2017, respectively. Considering increase in the number of genetic testing, we also need to review and analyze the RRSO status in Korean *BRCA1/2* mutation carriers.

## Methods and Materials

In April 2014, Yonsei Cancer Center established the hereditary cancer clinic in Cancer Prevention Center and started a multidisciplinary care. We have tested *BRCA1/2* germline mutation according to the testing criteria determined by Korean Health Insurance Review and Assessment (HIRA) Service.

Table 1. Criteria for *BRCA1/2* germline mutation testing in Korea

Criteria for <i>BRCA1/2</i> germline mutation testing in Korea	
<b>BRCA1/2 mutation test</b>	
▪ The <b>breast cancer</b> patient with at least one <b>relatives</b> with breast/ ovarian/ pancreatic/ metastatic prostate cancer in the third degree;	
▪ The patient with <b>breast cancer</b> diagnosed <b>before age 40</b>	
▪ The patient with <b>triple negative breast cancer</b> diagnosed <b>before age 60</b>	
▪ The patient with <b>bilateral breast cancer</b>	
▪ The patient with <b>breast cancer and ovarian cancer</b>	
▪ The patient with <b>breast cancer and pancreatic cancer</b>	
▪ <b>Men with breast cancer</b>	
▪ The patient with <b>epithelial ovarian cancer</b> (including fallopian tubal, primary peritoneal cancer, except for pure mucinous carcinoma)	

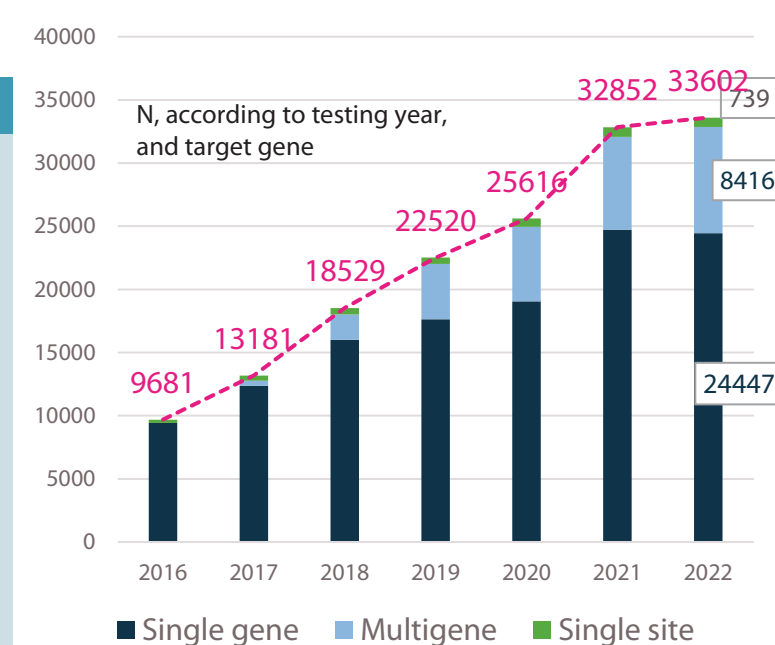


Fig 1. Number of testing hereditary cancer genes in Korea (by HIRA Bigdata open portal)

In this study, we analyzed 693 carriers with *BRCA1* or *BRCA2* germline mutation diagnosed between 2013 and 2022. We evaluated the proportion of RRSO uptake related to genetic and clinical factors.

## Key points

Germline genetic mutation was identified in *BRCA1* gene for 349 carriers, and in *BRCA2* for 344 carriers. The median age identified of mutation was 49.9 years (range, 18-83), and 663 (95.2%) were women.

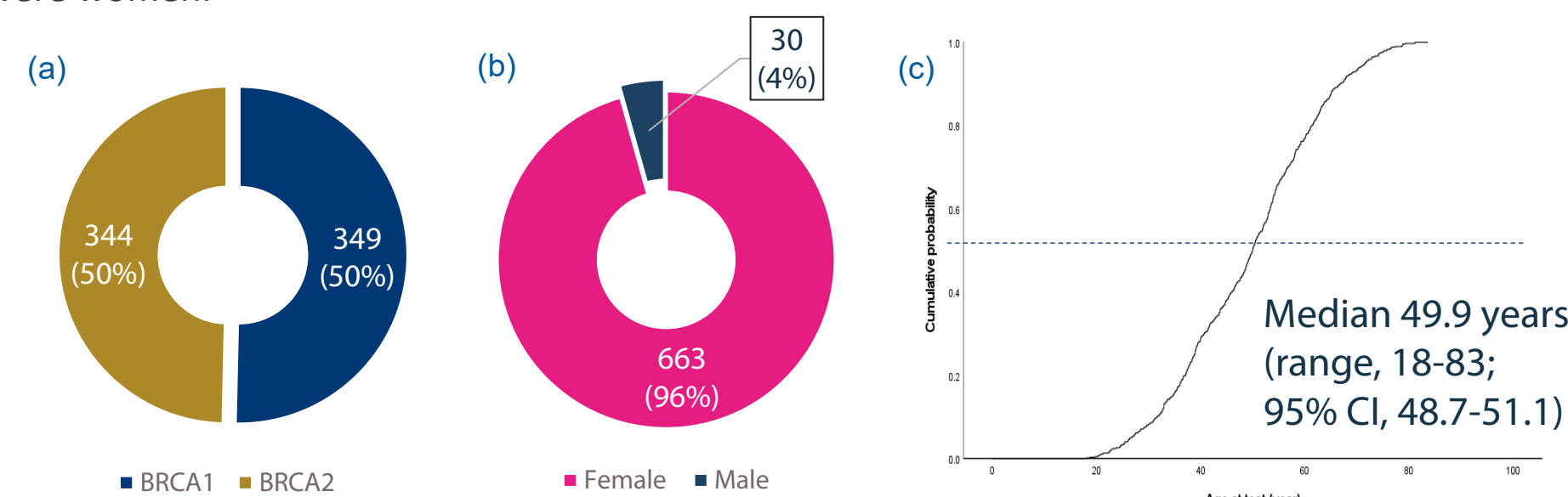


Fig 2. Clinical characteristics of the patients; (a) mutation type (b) sex (c) age at identification of mutation

There were 374 patients with breast cancer; they were diagnosed with breast cancer at median 42.5 years of age. *BRCA1* mutation carriers tended to be diagnosed of breast cancer earlier than *BRCA2* mutation carriers. (40.6 vs. 44.4 years,  $P=0.002$ )

Meanwhile, 254 patients were diagnosed with ovarian cancer at median 54.5 years of age. The age of diagnosis of ovarian cancer was also earlier in *BRCA1* mutation carriers than in *BRCA2* mutation carriers (52.8 vs. 57.9 years,  $P=0.010$ )

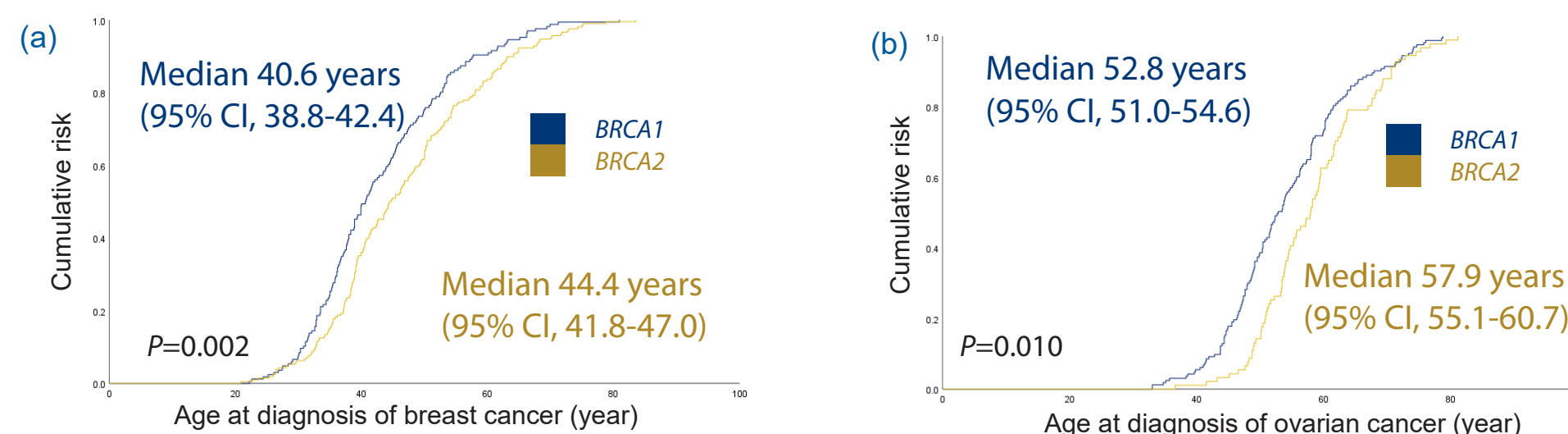


Fig 3. Cumulative breast (a) and ovarian (b) cancer risk of the carriers according to *BRCA1/2* mutation

## Conclusions

RRSO uptake tended to increase among the carriers with *BRCA1/2* mutation and indication for RRSO in Korea. Psychosocial and clinical support for decision making of preventive strategies and postmenopausal status will be necessary for the candidates.

Among 694 carriers, 153 (22.0%) received RRSO during study period. 139 patients were already diagnosed with breast cancer, and 72 patients were also received CPM.

The median age of RRSO uptake was 45.4 years in *BRCA1* mutation carriers, and 50.7 years in *BRCA2* mutation carriers; which were later than those suggested in clinical guidelines.

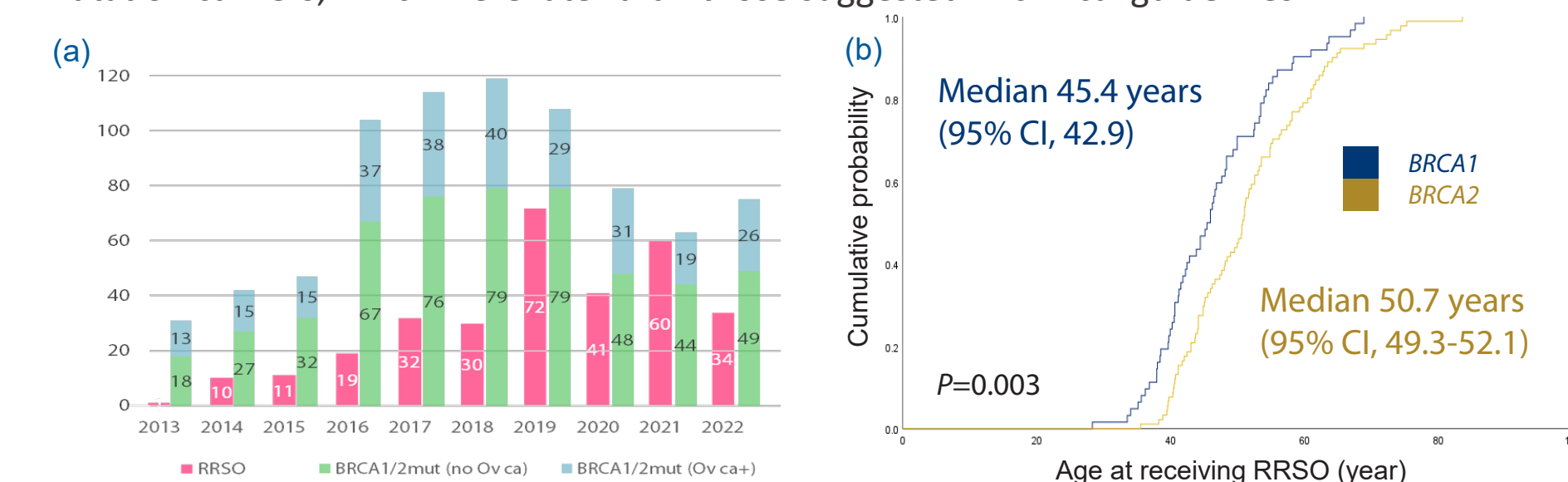


Fig 4. (a) Number of identification of *BRCA1/2* mutation and receiving RRSO according to the year; (b) Cumulative probability of RRSO uptake the carriers according to *BRCA1/2* mutation

In addition, limited to the potential candidate of RRSO (except for male, young age, and already diagnosed of ovarian cancer), proportion of RRSO uptake was 57.1% in 2013-2017, and 62.7% in 2018-2022. Especially in 2022, 79% of all candidates received RRSO until Mar 2023.

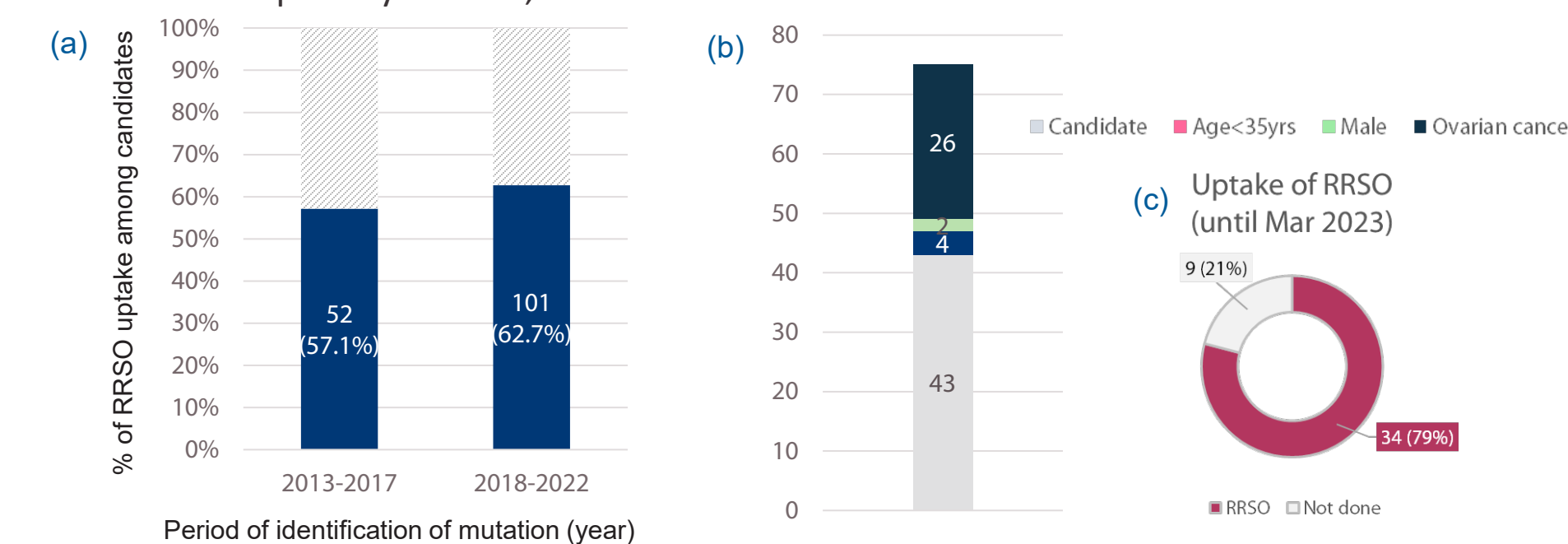


Fig 5. (a) the proportion of RRSO uptake among potential candidate (except for male, young age\*, and already diagnosed with ovarian cancer); (b) In 2022, proportion of indication or exclusion criteria or RRSO among carriers; (c) Until Mar 2023, proportion of uptake of RRSO among the candidates identified in 2022. \*Age < 35years for *BRCA1* mutation carriers; <40 years for *BRCA2* mutation carriers