

# Karma TYRER-CUZICK and BOADICEA variables

Karma calculates the TYRER-CUZICK scoring and the BOADICEA (Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm) scoring based on the data Karma collects from the study participants responding to a web based questionnaire.

TYRER-CUZICK and BOADICEA calculates the individual/population risk of developing breast/ovarian cancer based on familial history and lifestyle factors.

The Tyrer-Cuzick algorithm requires following input factors (as compared to BOADICEA)

#### Similarities in accounting for risk factors

- Age
- BRCA-gene mutation
- Ovarian cancer
- Ashkenazi origin
- Family: brest (incl. bilateral) / ovarian cancer age
- Relatives: breast/ovarian cancer age

#### Differences

#### In Tyrer-Cuzick only

- RMI
- Age at menarche
- Age at first child
- Menopause (pre/peri/post)
- HRT use (previous/current/planned)
- Benign breast disease (hyperplasia, atypical hyperplasia, LCIS, unknown)
- \*Mortality of non-BC causes (competing risk)

#### In BOADICEA only

- Twin cancer status
- Pancrea/prostate cancer in family

Karma holds the following TYRER-CUZICK and BOADICEA variables.

#### TYRER-CUZICK

TYRER-CUZICK (named after its creators) is a risk model for predicting breast cancer risks for individuals and for the population in general. The model computes risk for breast cancer based on overall population risk and for individualized family history, lifestyle factors, and the probability of carrying BRCA genes and other predisposing genes. The population risk is given by national breast cancer incidence rates, e.g. Swedish, stratified by woman age. The individualized risk is given for each individual as the deviation in risk from the average woman at a certain age. If the average age for menarche is 13 in population and the woman in question had menarche at age 10, then this woman will be at higher risk of developing breast cancer due to the menarche risk factor. The risk for the individual woman is the overall population risk plus/minus the specific deviation of risk for the woman.

More details are available at https://ems-trials.org/riskevaluator/

#### General variables

#### age\_riskassessed

Age of woman at risk assessment. Healthy women and non-prevalent BC cases have their risk assessed at survey interview date. Invasive and insitu BC cases have their risk assessed at year of BC. BMI and HRT are assessed at interview date (not BC date) for the BC cases.

#### age\_interview

Age at survey interview.

#### yearofbirth

Year of birth.

#### started\_time

Time of survey interview.

# bc\_1stdiagdate

Date of first BC diagnosis.

#### bc\_prevalent

BC diagnosis prior to survey interview date.

# bc\_malign

Invasive BC diagnosis.

# Individual breast cancer risk (1.0 is 1%)

# risk\_breastcancer\_own\_1yr

Individual risk for developing breast cancer in 1 year.

# risk\_breastcancer\_own\_2yr,3yr,4yr,5yr,10yr,20yr,lifetime

Individual risk for developing breast cancer in 2-20 years or in (remaining) lifetime.

#### Breast cancer risk in population

# risk\_breastcancer\_pop\_1yr

Population risk for developing breast cancer in 1 year.

### risk\_breastcancer\_ pop \_2yr,3yr,4yr,5yr,10yr,20yr,lifetime

Population risk for developing breast cancer in 2-20 years or in (remaining) lifetime.

# Individual mutation carrier probability

### prob\_brca1\_own\_mutation

Individual probability of carrying a BRCA1 mutation.

#### prob\_brca2\_own\_mutation

Individual probability of carrying a BRCA2 mutation.

# prob\_brca\_own\_nomutation

Individual probability of not carrying any BRCA mutation.

# Mutation carrier probability in population

#### prob\_brca1\_pop\_mutation

Probability of carrying a BRCA1 mutation in population.

#### prob\_brca2\_pop\_mutation

Probability of carrying a BRCA2 mutation in population.

# prob\_brca\_pop\_nomutation

Probability of not carrying any BRCA mutation in population.

# **Risk factors in Tyrer-Cuzick score**

#### menacrche

Age at menarche.

#### parous

Parity. 0 is no liveborn children, 1 is one or more children, 2 is unkown.

# age\_1

Age at giving birth to first child.

#### menostat

Menopausal status, 0 is pre, 1 is peri, 2 is post. 3 us unknown.

#### ht

Length.

#### wt

Weight.

#### hyper

Diagnosed with any type of hyperplasia.

#### ah

Diagnosed with atypical hyperplasia.

#### **Icis**

Diagnosed with lobular cancer in-situ.

#### ovarian\_status

Diagnosed with ovarian cancer.

#### ageoc

Age at ovarian cancer diagnosis.

#### menacrche

Age at menarche.

#### ashkanazi

Ashkenazi jewish descent.

#### hrt\_use

Use of hormonal replacement therapy. 0 is no use, 1 is more than 5 years ago, 2 is less than 5 years ago, 3 is current use.

#### hrt\_type

Type of HRT used. 0 is estrogen only HRT, 1 is combined HRT tablet.

#### inuselength

Years of HRT use. Not coded in Karma.

#### hrt\_last\_use

Years since last use of HRT.

#### genetic\_test

Genetic test performed. 0 is never, 1 negative test, 2 is BRCA1, 3 is BRCA2.

#### father genetic test

Genetic test performed on father to woman. 0 is never, 1 negative test, 2 is BRCA1, 3 is BRCA2.

#### mother\_affected\_status

Mother with breast ancer. 0 is no, 1 is yes.

# mother\_ovarian\_status

Mother with ovarian ancer. 0 is no, 1 is yes.

# mother\_age

Age when mother developed BC.

# mother\_bilateral\_age

Age when mother developed bilateral BC.

# n\_sisters

Numbers of sisters.

# **System variables**

#### version

Tyrer-Cuzick algorithm version.

#### **BOADICEA**

BOADICEA (Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm) is a risk model for familial breast and ovarian cancer. The model can be used to compute age specific risks for breast and ovarian cancer and builds on family history pedigrees. The data used in BOADICEA is collected as part of the Karma web based questionnaire and will be used for estimating BRCA1/2 carrier ship in the Karma unselected population.

More details are available at https://www.canrisk.org/

#### Breast and ovarian cancer risks (0.01 is 1%)

#### risk\_breastcancer\_1yr

Risk for developing breast cancer in one year.

risk\_breastcancer\_2yr, 3yr, 4yr, 5yr, 10yr, 15yr, 20yr, 25yr

Risk for developing breast cancer in x years.

#### risk\_ovariancancer\_1yr

Risk for developing ovarian cancer in one year.

risk\_ovariancancer\_2yr, 3yr, 4yr, 5yr, 10yr, 15yr, 20yr, 25yr

Risk for developing ovarian cancer in x years.

#### age

Age at assessment.

# yearofbirth

Year of birth.

# **BRCA1/BRCA2** mutation carrier probabilities

# prob\_brca1\_mutation

Probability of carrying a BRCA1 mutation.

# prob\_brca2\_mutation

Probability of carrying a BRCA2 mutation.

# prob\_brca\_nomutation

Probability of not carrying any BRCA mutation.

# **System variables**

# interview\_end

Date of assessing the BOADICEA raw variables.