CRA Health

Tyrer-Cuzick FAQs

Source: www.ems-trials.org/riskevaluator/ - IBIS Breast Cancer Risk Evaluator Tool

1. v8 and v7 give higher lifetime risks than v6. Why?

There are two main reasons. Firstly, lifetime risk from v7+ runs to age 85; in v6 it was until age 80. Secondly, the population rates used have been updated to be more applicable for risk assessment of women today. Figure 1 shows how incidence has risen between 1994 and 2008-2010; Table 1 summarizes the difference between the rates used by versions 6-8. The main difference is that in 1994, women in the UK were not screened beyond age 64 (V6). The increase in rates beyond 60 mostly reflects more screening in these age groups between 2005-2010 than in 1994. Differences between UK (Thames Registry first breast cancer rates 2005-2009) and Sweden (Statistics Sweden first breast cancer rates 2006-2010) might also be explained by temporal differences in screening regimens, including that Sweden has screened later ages for longer than the UK.

Figure 1. UK Breast cancer incidence (C50, invasive) in 1994 and 2008-2010
source: www.cancerresearchuk.org

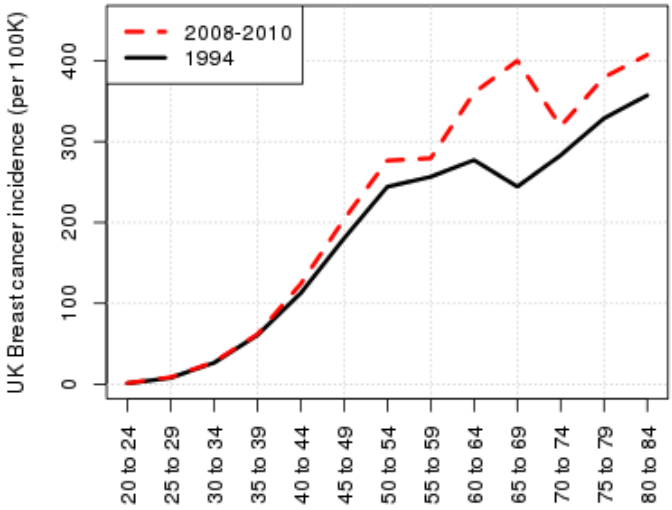

Table 1. Breast cancer rates (per year, 100K) used in the models

Age Group	v6	v7/8 (UK)	v7/8 (Sweden)
20-24	1.2	1.3	1.0
25-29	8.0	9.1	7.0
30-34	26.6	24.2	24.6
35-39	60.7	57.5	50.2
40-44	112.6	115.6	108.4
45-49	180.3	182.3	188.5
50-54	244.2	250.3	217.9
55-59	256.5	266.2	248.9
60-64	277.1	318.7	324.8
65-69	244.3	378.5	363.3
70-74	283.1	296.4	336.9
75-79	328.7	331.9	274.3
80-84	357.2	369.7	307.6

2. v8 identifies more women at high risk than v7. Why?

The main reason is that it includes more risk factors (density and SNPs). Both of these will increase the number of women accurately identified to be at high risk. If they are incorporated into the risk assessment then more women will be at high (and low) risk than when they are not used.

3. Are the rates used appropriate for the USA, or other countries?

The model uses a `period' epidemiological approach, and is calibrated to first breast cancer diagnosis rather than incidence. First breast cancer rates are not usually published. However, one way to assess whether the model is broadly in alignment is to use the SEER age-standardized incidence. Over the period 2005-2009 in the Thames cancer registry this was 119.5, and may be directly compared with the numbers published by the NCI on their website (last accessed 14th June 2013). For example, the SEER age-standardized rate between 2005-2009 in Georgia was 119.7. For comparison, the SEER age-standardized UK first cancer rate that is used in V7 is 114.7.

4. Why is competing mortality not default?

Lifetime risk including the competing mortality option gives an assessment that allows from death from other causes than breast cancer. It is not used by default for consistency: cumulative incidence is usually presented conditional on no intercurrent mortality. However, it is easy to toggle back and forth on the form by using the checkbox next to the risk assessment button.

5. What are the benign breast biopsy categories?

Table 2. Breast biopsy risk classification to use in model.
Adapted from Page and Dupont (1993), dx.doi.org/10.1007/bf00666428

No benign disease (includes no proliferation disease)
Adenosis
Apocrine change
Duct ectasia
Mild epithelial hyperplasia of usual type
Hyperplasia (not atypia) (Proliferative disease without atypia)
Hyperplasia of usual type, moderate or florid
Papilloma (probably)
Sclerosing adenosis
Atypical hyperplasia
Atypical ductal hyperplasia
Atypical lobular hyperplasia
LCIS
Lobular carcinoma in situ

The benign disease categorization shown in Table 2 is based on the classical work from Page and Dupont (1993, doi.org/10.1007/BF00666428); see also Hartmann et al (2005, www.nejm.org/doi/full/10.1056/NEJMoa044383). Fibroadenomas are considered nonproliferative unless they also contain a proliferative lesion. The 'unknown' category is for when the result from a prior biopsy is unknown.

6. Have there been any publications validating the model for risk evaluation?

Work is ongoing in a number of studies. Some articles to specifically address this issue include the following:

- Cuzick, J., Brentnall, A. R., Segal, C., Byers, H., Reuter, C., Detre, S., Lopez-Knowles, E., Sestak, I., Howell, A., Powles, T. J., Newman, W. G., Dowsett, M. To appear 2017. Impact of a panel of 88 single nucleotide polymorphisms on the risk of breast cancer in High-Risk women: Results from two randomized tamoxifen prevention trials. Journal of Clinical Oncology.
- Evans, D. G., Brentnall, A., Byers, H., Harkness, E., Stavrinos, P., Howell, A., risk study Group, F., Newman, W. G., Cuzick, J., Oct. 2016. The impact of a panel of 18 SNPs on breast cancer risk in women attending a UK familial screening clinic: a case–control study. Journal of Medical Genetics.
- Brentnall, A. R., Harkness, E. F., Astley, S. M., Donnelly, L. S., Stavrinos, P., Sampson, S., Fox, L., Sergeant, J. C., Harvie, M. N., Wilson, M., Beetles, U., Gadde, S., Lim, Y., Jain, A., Bundred, S., Barr, N., Reece, V., Howell, A., Cuzick, J., Evans, D. G., Dec. 2015. Mammographic density adds accuracy to both the Tyrer-Cuzick and gail breast cancer risk models in a prospective UK screening cohort. Breast Cancer Research 17 (1), 147+.
- Warwick, J., Birke, H., Stone, J., Warren, R. M. L., Pinney, E., Brentnall, A. R., Duffy, S. W., Howell, A., Cuzick, J., Oct. 2014. Mammographic breast density refines Tyrer-Cuzick estimates of breast cancer risk in high-risk women: findings from the placebo arm of the international breast cancer intervention study i. Breast Cancer Research 16 (5), 451+.
- Quante, A. S., A. S. Whittemore, T. Shriver, K. Strauch, and M. B. Terry (2012). Breast cancer risk assessment across the risk continuum: genetic and nongenetic risk factors contributing to differential model performance. Breast cancer research: BCR 14 (6), R144+.
- Amir, E., D. G. Evans, A. Shenton, F. Lalloo, A. Moran, C. Boggis, M. Wilson, and A. Howell (2003). Evaluation of breast cancer risk assessment packages in the family history evaluation and screening programme. Journal of medical genetics 40 (11), 807-814.