

Output:

All specific objectives were reached and for the scientific community B-CAST has delivered >50 peer-reviewed publications together with <u>BCAC</u> / <u>Netherlands Cancer Institute</u> to date, and several others are in the pipeline. Selected important results related to the five objectives of B-CAST are outline below:

The first objective was to define the influence of risk factors, including reproductive history, lifestyle, mammographic breast density (referred to onwards as non-genetic) and germline genetic variation, on breast cancer overall and by subtypes characterized by clinical and molecular markers. We showed that non-genetic breast cancer risk factors act independently of genetic risk factors, which is highly important for the development of breast cancer risk models, and prediction tools. We also showed that genetic and non-genetic factors have differential associations with oestrogen-receptor positive and negative tumours.

The second objective was to define the influence of risk factors and tumour subtypes on clinical prognosis. We showed that non-genetic risk factors that affect survival, e.g. time since pregnancy, body mass index, act similarly among tumour subtypes.

The third objective was to develop and validate breast cancer risk and prognostication models for breast cancer, overall and by subtypes, informed by knowledge acquired under above objectives. We worked on the development of three risk modules (BOADICEA, iCARE, KARMA) and one prognostication model (PREDICT); most important was the validation of the updated BOADICEA model.

The fourth objective was to implement these models into online tools for risk prediction and prognostication; and make them available in multiple countries/languages. The BOADICEA model was implemented in the CanRisk tool (https://canrisk.org/). We successful CE marked CanRisk, making it the only CE marked breast cancer risk tool available in the public domain. We translated CanRisk in Spanish, German, French, and Dutch; Italian and Portuguese versions will be made available soon. For breast cancer prognostication, the PREDICT model (now with an extended endocrine therapy option) is also available in the public domain in English, French and Spanish; a Dutch version will be made available soon (https://breast.predict.nhs.uk/). Both models are used extensively worldwide.

The fifth object was to raise awareness, i.e. promote the development and integration of personalized breast cancer prevention within national public health programmes. For the public and policy makers, we published two policy and a workshop report (Personalising Breast Cancer Prevention – bridging the gap between research and policy (2020); Personalised prevention in breast cancer - the policy landscape (2017); Personalising prevention for breast cancer (2019). We also published an explainer and animation on breast cancer risk models and tools targeting a wider scientific and lay audience 'What is a breast risk models and what is a breast cancer tool?' and a blog on 'Are we ready for earlier breast cancer screening?'.

We disseminated our results in open symposia such as a kick-off meeting in September 2015 and the closing symposium 'Breast Cancer Risk and Prognostication - Germline and Tumour Genetics' in February 2021. Both events were delivered together with BRIDGES; the online closing symposium was very well received and attended by ~200 participants each day consisting of both established and junior researchers from Europe, UK, USA and other countries. We also co-organized the ENVISION Meeting in 2020 together with other Horizon2020 projects working on breast cancer. This led to the position statement 'Personalised early detection and prevention of breast cancer: ENVISION Network Consensus Statement' in Nature Reviews Clinical Oncology.

B-CAST was featured together with BRIDGES in the Impact Series which is an open access science magazine disseminating valuable scientific research to key stakeholders in science and society. The workshop report was covered by CORDIS and translated in 6 languages <u>CORDIS News</u> and our paper on BOADICEA - the comprehensive risk prediction model, received national and international <u>media coverage</u>.