Institution:
University of Cambridge

Unit of Assessment:
UoA2

Title of case study: **PREDICT: A prognostication and treatment benefit tool for early breast cancer**

1. Summary of the impact (indicative maximum 100 words)

PREDICT is a prognostication and treatment benefit tool aimed at aiding the breast cancer multi-disciplinary team in the management of women with early breast cancer. The user-friendly, web-based tool was developed in collaboration with the Cambridge Breast Unit multi-disciplinary team, the Eastern Cancer Registration and Information Centre. Implemented online, PREDICT is hosted on a NHS web-server at www.predict.nhs.uk. Since 2010 PREDICT has been used widely by clinicians throughout the UK and world-wide.

2. Underpinning research (indicative maximum 500 words)

The PREDICT model was developed in 2010 jointly by Professor Carlos Caldas (University Professor 2006-present), Professor Paul Pharoah (UOA 2: CR-UK Senior Clinical Research Fellow 1999-2009, University Reader 2009-13, University Professor 2013-present) and Dr Elizabeth Azzato (NIH/Cambridge PhD student 2008-11) in collaboration with Gordon Wishart and the Cambridge Breast Unit multi-disciplinary team.

Patients treated in the Cambridge Breast Unit are stratified for adjuvant chemotherapy according to a guideline developed in 2004. This took into account the serious adverse rate for chemotherapy and that "many physicians consider a cutoff of an additional 3% or more added benefit sufficient to justify recommending treatment". Thus, for an absolute survival benefit of < 3%, chemotherapy is not recommended, for an absolute survival benefit of 3-5% the benefits and harms are considered equivalent and discussed with the patient, for an absolute benefit of >5% chemotherapy is recommended.

Until 2010 the absolute benefits of chemotherapy were estimated using Adjuvant! Online, an online prognostic model developed over a decade ago by an American oncologist (Peter Ravdin). This is based on US data and has not been validated with UK data. Furthermore, Adjuvant! Online does not include several important prognostic variables including mode of detection and molecular biomarkers such as tumour HER2 status. Thus there was a clinical need for an equivalent model, based on and validated using UK data that was flexible and able to incorporate additional prognostic variables.

The PREDICT model was based on survival-time data on 5,700 women with early breast cancer treated between 1999 and 2003. These data were obtained through the Eastern Cancer Registration and Information Centre and used to determine the influence of key prognostic variables on survival [1]. The model was then validated using an independent data set from the West Midlands Cancer Intelligence Unit [1]. The PREDICT web interface was developed in 2010 and is hosted by the Eastern Cancer Registration and Information Centre.

In order to compare directly the performance of Adjuvant! Online and PREDICT, a second validation of PREDICT was carried out using the same data set. While both models performed well, the breast cancer specific survival calibration for PREDICT was better than that of Adjuvant! Online with similar discrimination [2].

In parallel with the PREDICT model development work, Profs Caldas and Pharoah have led a research programme investigating the molecular pathology of breast cancer in collaboration with other groups from the international Breast Cancer Association Consortium (BCAC). This research

has enabled further development of PREDICT in response to feedback from clinicians and requests for additional features in the model. In particular, there were many requests to incorporate tumour HER2 and KI67 status into the model. Results from one of the BCAC projects were used to enable the incorporation of HER2 into the model [3], with the new PREDICT model being further validated using the British Columbia data set used to validate the original model [4]. More recently, the results from another of our molecular pathology studies has informed the incorporation of tumour KI67 status into the model [5].

3. References to the research (indicative maximum of six references)

1. Wishart GC, Azzato EM, Greenberg DC, Rashbass J, Kearins O, Lawrence G, Caldas C, Pharoah PD. PREDICT: a new UK prognostic model that predicts survival following surgery for invasive breast cancer. *Breast Cancer Res.* 2010;12(1):R1.
2. Wishart GC, Bajdik CD, Azzato EM, Dicks E, Greenberg DC, Rashbass J, Caldas C, Pharoah PD. A population-based validation of the prognostic model PREDICT for early breast cancer. *Eur. J. Surg. Oncol.* 2011;37(5):411-7.
3. Blows FM, Driver KE, Schmidt MK, Broeks A, van Leeuwen FE, Wesseling J, Cheang MC, Gelmon K, Nielsen TO, Blomqvist C, Heikkila P, Heikkinen T, Nevanlinna H, Akslen LA, Begin LR, Foulkes WD, Couch FJ, Wang X, Cafourek V, Olson JE, Baglietto L, Giles GG, Severi G, McLean CA, Southey MC, Rakha E, Green AR, Ellis IO, Sherman ME, Lissowska J, Anderson WF, Cox A, Cross SS, Reed MW, Provenzano E, Dawson SJ, Dunning AM, Humphreys M, Easton DF, Garcia-Closas M, Caldas C, Pharoah PD, Huntsman D. Subtyping of breast cancer by immunohistochemistry to investigate a relationship between subtype and short and long term survival: a collaborative analysis of data for 10,159 cases from 12 studies. *PLoS Med* 2010;7(5):e1000279.
4. Wishart GC, Bajdik CD, Dicks E, Provenzano E, Schmidt MK, Sherman M, Greenberg DC, Green AR, Gelmon KA, Kosma VM, Olson JE, Beckmann MW, Winqvist R, Cross SS, Severi G, Huntsman D, Pylkas K, Ellis I, Nielsen TO, Giles G, Blomqvist C, Fasching PA, Couch FJ, Rakha E, Foulkes WD, Blows FM, Begin LR, Van't Veer LJ, Southey M, Nevanlinna H, Mannermaa A, Cox A, Cheang M, Baglietto L, Caldas C, Garcia-Closas M, Pharoah PD. PREDICT Plus: development and validation of a prognostic model for early breast cancer that includes HER2. *Br. J. Cancer* 2012;107(5):800-7.
5. Ali HR, Dawson SJ, Blows FM, Provenzano E, Leung S, Nielsen T, Pharoah PD, Caldas C. A Ki67/BCL2 index based on immunohistochemistry is highly prognostic in ER-positive breast cancer. *J. Pathol.* 2012;226(1):97-107.

4. Details of the impact (indicative maximum 750 words)

PREDICT is implemented online as a national resource with the web interface being hosted on a NHS web-server at www.predict.nhs.uk. The ~4000 monthly hits on the website indicate clearly the impact of the tool.

One of the key decisions in the management of women with early breast cancer is whether or not to offer adjuvant chemotherapy in conjunction with primary surgery and radiotherapy. The key output of PREDICT is the expected absolute reduction in mortality at five and ten years associated with adjuvant chemotherapy.

Cambridge Breast Unit (CBU)

Until 2010 the CBU estimated absolute benefits of chemotherapy were estimated using Adjuvant! Online. During 2010 and 2011 both PREDICT and Adjuvant! Online were used in parallel.

Clinical audit

The Cambridge Breast Unit carried out an audit of the first 200 patients discussed when both Adjuvant! Online and PREDICT were used by the multi-disciplinary team [6]. The chemotherapy recommendations that would have been made based on the output from each model were then compared. In 163 patients (82 per cent) the chemotherapy decision would have been the same whichever model was used, but a different recommendation would have been made for 37 patients (18 per cent), clearly demonstrating the potential for PREDICT to change clinical practice.

Change in practice
Since 2012 PREDICT has been the only model used routinely in Cambridge for all patients being discussed at the weekly multi-disciplinary team meeting. The absolute benefit of adjuvant chemotherapy estimated by PREDICT is used to guide the use of adjuvant chemotherapy according to the guideline described in section 2.

Other clinical departments in the UK

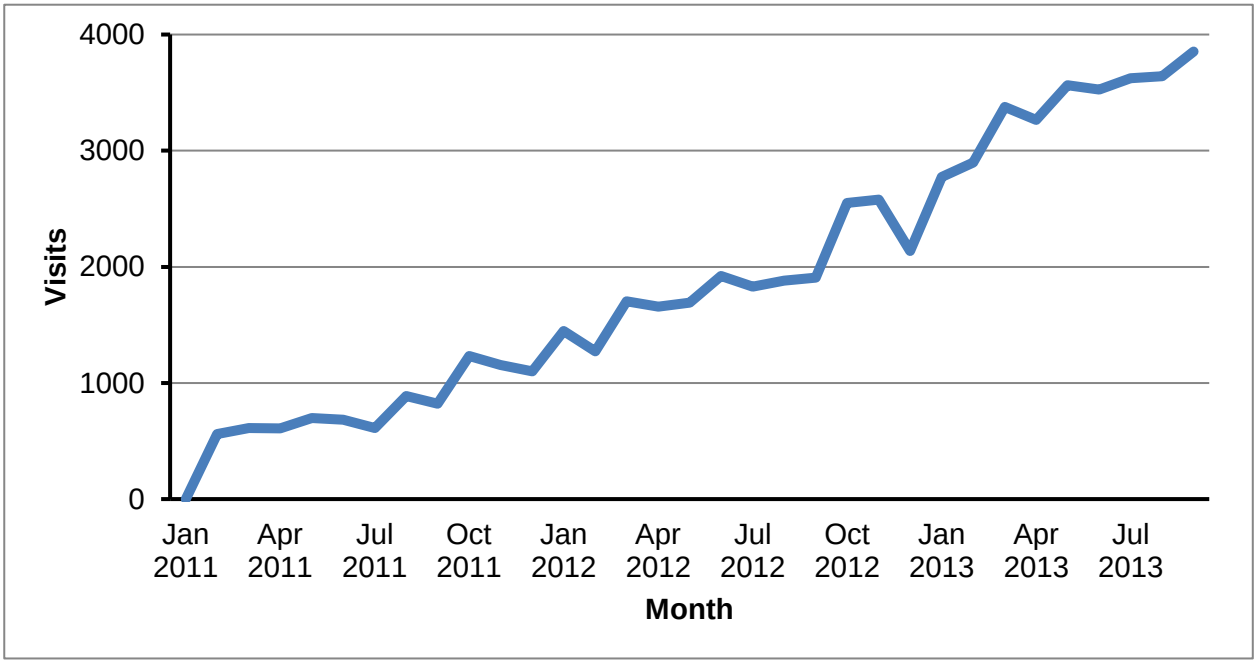
The impact of PREDICT on clinical practice is clearly demonstrated from the extensive use of the web interface (see below). We have had multiple requests from clinicians for the incorporation of additional features indicating that the model is being widely used. Personal communication indicates that PREDICT is used by the multi-disciplinary clinical teams in Belfast, Brighton, Derby, Dundee, Oxford and Sheffield, but the web usage statistics from 2012 suggest that PREDICT is being used widely across the country.

Public, Patient Partnership
PREDICT has been widely reported in regional and national media including ITV, The Times and The Daily Mail. We have clear evidence that women with breast cancer are using the tool to develop a better understanding of their own risk. This enables them to be fully informed in their discussion with their oncologists about treatment options.

Web usage data
PREDICT was designed to have a user-friendly interface to help clinicians in making clinical management decisions. Informal feedback from clinicians from both Cambridge and elsewhere has indicated that the interface is easy to use.

The number of visits to the web site each month has increased steadily since its launch in January 2011, with 3,266 visits in April 2013.

Monthly web usage statistics for the PREDICT website, Jan 2011-Jul 2013



There have been 54,600 visits to the web site with 68 per cent of the visits (37,200) being accessed from UK and ten per cent (5,800) from USA. The web site is visited from all over the UK, with London accounting for 17 per cent and Cambridge accounting for just 1 per cent of all traffic on the web site.

5. Sources to corroborate the impact (indicative maximum of 10 references)

6. Loh S-W, Rodriguez-Miguelez M, Pharoah P, Wishart G. A comparison of chemotherapy recommendations using the Predict and Adjuvant models. *Eur. J. Surg. Oncol.* 2011;37(5):S21-S22.

Press coverage: see http://www.predict.nhs.uk/press.shtml for details.

Web usage statistics from Google Analytics at https://www.google.com/analytics