REAL-WORLD VALIDATION OF ONCOTYPE DX® IN NODE NEGATIVE BREAST CANCER: A COMPARATIVE ANALYSIS WITH TAILORx

Ryan Rodgerson**(1,2)**, Mina Youssef(1,2)
University of East Anglia, Norwich, UK(1); Norfolk and Norwich University Hospital, Norwich, UK(2)

N = 397 Events = 24 Kaplan-Meier by RS: p = 0.24

Background & Objectives

- The 21-gene recurrence score (RS) guides adjuvant therapy decisions in ER+/HER2- early breast cancer.
- TAILORx[1] showed many node-negative patients with intermediate RS can safely avoid chemotherapy, particularly older patients.
- Most real-world validation comes from US datasets; UK/NHS evidence remains limited
- How RS performs in unselected NHS node-negative patients, and how closely outcomes align with TAILORx[1], is unclear, especially for younger women and intermediate scores.

Aim:

- To validate the prognostic performance of the 21-gene RS in node-negative ER+/HER2– breast cancer in routine NHS practice and compare observed outcomes with TAILORx benchmarks.

Objectives:

- Describe RS distribution, treatment patterns and event rates in node-negative patients.
- Assess associations between RS, overall and recurrence-free outcomes, and breast cancer-specific mortality.
- Benchmark observed recurrence events against TAILORx RS/age groups (A–E).

Methods

Design & setting

- Retrospective single-centre NHS cohort (Norfolk & Norwich University Hospital), ER+/HER2– early breast cancer tested with Oncotype DX®, 2015–2024.
- Node-negative (N0) patients analysed as a predefined subgroup (n = 397; total cohort n = 789)

RS Bands and TAILORx Groups

- RS 0–10 (Low), 11–25 (Intermediate), ≥26 (High), aligned with TAILORx[1] thresholds.
- Additional TAILORx[1] A–E groupings by age and RS to derive expected event counts (e.g. Group B: ≤50y, RS 11–15).

Data sources and Outcomes

- Exact Sciences dataset linked with ICE, MDT/clinic letters, Somerset Cancer Register and EDT to capture tumour features, treatment, recurrence and mortality.
- Outcomes: overall survival (OS), recurrence-free survival (RFS), breast cancer-specific mortality (BCSM); events = recurrence (local/distant) or breast cancer-related death.

Analysis

- Kaplan–Meier curves with log-rank tests and multivariable Cox regression adjusted for age, grade, T stage, treatment, etc.
- TAILORx[1] comparison: expected event counts derived from trial rates scaled to cohort size/follow-up; observed vs expected tested by χ^2 (Group B p = 0.021).

Follow-up

- Median follow-up: ~39 months
- Follow-up censored at last verified clinical contact, recurrence, or death.

Event Definitions

- RFS event = local, regional, or distant recurrence.
- BCSM event = death attributed to breast cancer (from MDT and registry coding).

Figure 1. **Node-Negative Patients by Oncotype DX Risk Group**

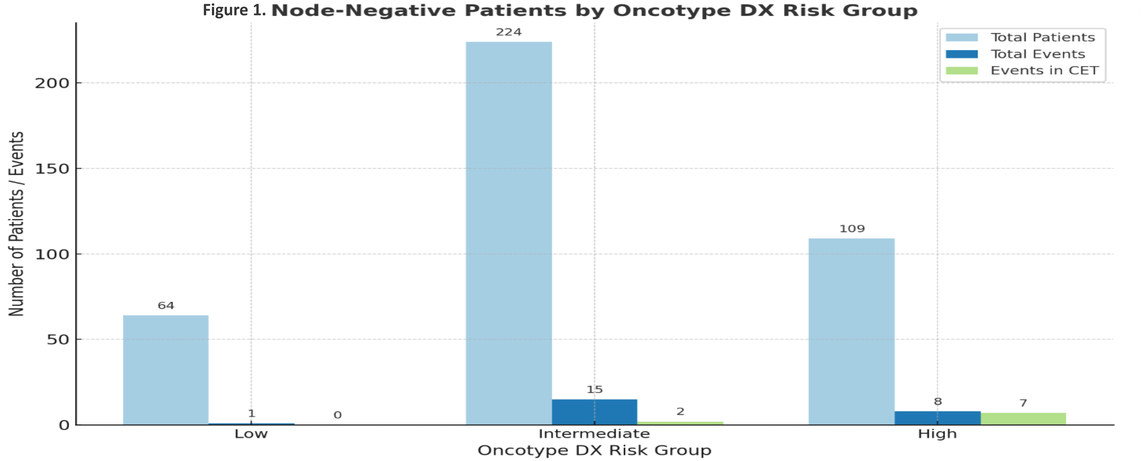
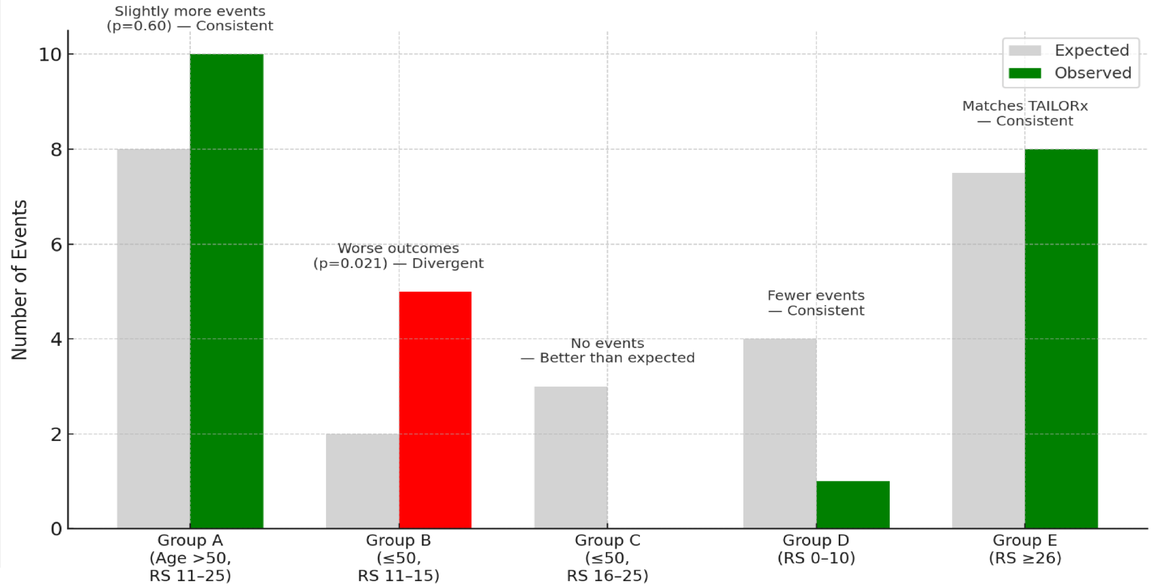


Figure 2. Observed vs Expected Events Compared to TAILORx (Grouped by Age + RS)



Results (n = 397)

Cohort & RS distribution

- Low RS 16.1% (n = 64), Intermediate 56.4% (n = 224), High 27.5% (n = 109).
- 24 events occurred in N0 patients, mainly distant recurrences or BCSM (Breast cancer-specific mortality)

Events by RS band (Figure 1)

- Low RS: 1/64 event (local recurrence in an ET-only patient); no deaths; no chemotherapy used.
- Intermediate RS: 15/224 events (6 breast-cancer deaths); 10 patients (4.5%) received CET; most events occurred in ET-only patients.
- High RS: 8/109 events; 51 patients (46.8%) received CET; 7/8 events occurred in CET recipients (likely reflecting higher baseline risk).

Cox regression

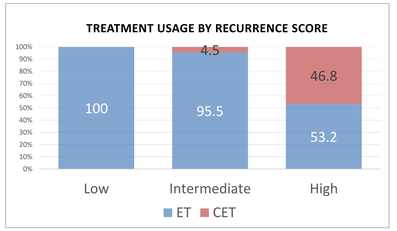
- After multivariable adjustment, **intermediate RS vs low**: aHR 9.31 (95% CI 1.16–74.80), *p* = 0.036.
- **High RS vs low**: aHR 7.59 (0.67–86.07), *p* = 0.102 (directionally similar but under-powered).
- **CET vs ET**: aHR 4.25 (1.12–16.16), *p* = 0.034 interpreted as **confounding by indication**, since CET was preferentially given to higher-risk patients.

Comparison to TAILORx[1] (Figure 2 - Observed vs Expected)

- Low-risk node-negative outcomes aligned closely with TAILORx; recurrence was rare (1 event).

Re-grouping by TAILORx[1] A–E showed:

- Groups A, D, E: observed events ≈ expected.
- **Group C** (RS 21–25, ≤50y) had **no events**, suggesting excellent outcomes.
- **Group B (≤50y, RS 11–15)** had **significantly more events than expected** (p = 0.021), indicating worse outcomes than TAILORx predicted and highlighting a potentially under-treated subgroup.



Predictor / Comparison	HR	95% CI	p-value
Intermediate RS vs low (adjusted)	9.31	1.16 - 74.80	0.036
CET vs ET (adjusted)	4.25	1.12 - 16.16	0.034
High RS vs low (adjusted)	7.59	0.67 - 86.07	0.102

Conclusions

- In this NHS node-negative cohort, **low RS patients had excellent outcomes** with endocrine therapy alone, mirroring TAILORx and supporting chemotherapy avoidance in this group.
- Most **events clustered in the intermediate-risk group**, which carried a significantly higher adjusted hazard versus low RS despite predominantly ET-only treatment.
- High-RS patients were more likely to receive CET, but small numbers limited precision; hazards were directionally higher, consistent with biological risk.
- Observed outcomes were broadly concordant with TAILORx, but **younger women with RS 11–15 (Group B)** had **worse-than-expected recurrence rates**, suggesting that TAILORx thresholds may underestimate risk in some UK real-world patients.

Clinical implications (NHS practice)

- RS is prognostically useful in N0 disease and can safely support ET-only strategies in low-risk patients.
- Intermediate scores, especially in younger women, should trigger **closer MDT review**, integration with clinical tools (e.g. PREDICT/RSClin) and careful discussion of potential chemotherapy benefit.
- Larger UK cohorts are needed to refine thresholds, validate RS-guided decisions, and understand age-specific risk in routine NHS care.

Contact: R.rodgerson@uea.ac.uk
Secondary email: rgrodgerson@gmail.com

1. Sparano, J.A. *et al.* (2018) 'Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer', *New England Journal of Medicine*, 379(2), pp. 111–121. Available at: https://doi.org/10.1056/NEJMoa1804710.