Ethnicity and outcome of young breast cancer patients in the United Kingdom: the POSH study

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Background: Black ethnic groups have a higher breast cancer mortality than Whites. American studies have identified variations in tumour biology and unequal health-care access as causative factors. We compared tumour pathology, treatment and outcomes in three ethnic groups in young breast cancer patients treated in the United Kingdom.

Methods: Women aged <40 years at breast cancer diagnosis were recruited to the POSH national cohort study (MREC: 00/06/69). Personal characteristics, tumour pathology and treatment data were collected at diagnosis. Follow-up data were collected annually. Overall survival (OS) and distant relapse-free survival (DRFS) were assessed using Kaplan–Meier curves, and multivariate analyses were performed using Cox regression.

Results: Ethnicity data were available for 2915 patients including 2690 (91.0%) Whites, 118 (4.0%) Blacks and 87 (2.9%) Asians. Median tumour diameter at presentation was greater in Blacks than Whites (26.0 mm vs 22.0 mm, P = 0.0103), and multifocal tumours were more frequent in both Blacks (43.4%) and Asians (37.0%) than Whites (28.9%). ER/PR/HER2-negative tumours were significantly more frequent in Blacks (26.1%) than Whites (18.6%, P = 0.043). Use of chemotherapy was similarly high in all ethnic groups (89% B vs 88.6% W vs 89.7% A). A 5-year DRFS was significantly lower in Blacks than Asians (62.8% B vs 77.0% A, P = 0.0473) or Whites (62.8% B vs 77.0% W, P = 0.0053) and a 5-year OS for Black patients, 71.1% (95% CI: 61.0–79.1%), was significantly lower than that of Whites (82.4%, 95% CI: 80.8–83.9%, W vs B: P = 0.0160). In multivariate analysis, Black ethnicity had an effect on DRFS in oestrogen receptor (ER)-positive patients that is independent of body mass index, tumour size, grade or nodal status, HR: 1.60 (95% CI: 1.03–2.47, P = 0.035).

Conclusion: Despite equal access to health care, young Black women in the United Kingdom have a significantly poorer outcome than White patients. Black ethnicity is an independent risk factor for reduced DRFS particularly in ER-positive patients.

Although the overall incidence of invasive breast cancer remains lower in Black women than White women, the risk of developing breast cancer is higher in Blacks than Whites in women aged 45 and under (Newman and Alfonso, 1997; Harding and Rosato, 1999; Ward et al, 2004; Chlebowski et al, 2005; Smigal et al, 2006; Jack et al, 2009). There is now substantial evidence that Black women with breast cancer have a poorer prognosis than non-Black patients (Joslyn and West, 2000; Jatoi et al, 2003; Carey et al, 2006;
Grann et al, 2006; Albain et al, 2009). This disparity in outcome is widening with time (Menashe et al, 2009). Whether ethnicity is an independent prognostic factor remains controversial.

Many studies have attributed the inferior outcomes in Black women to an increased incidence of adverse biological features. Blacks have an increased incidence of larger and higher-grade tumours with more lymph node involvement than Whites (Elledge et al, 1994; Dignam, 2000; Joslyn and West, 2000; Carey et al, 2006; Bowen et al, 2008). Blacks are also more likely to have ER-negative tumours than Whites, and there is an increased percentage of triple-negative (ER/PR/HER2-) and basal cell tumours in this ethnic group (Carey et al, 2006; Bauer et al, 2007). The mean age of diagnosis is lower in Blacks than Whites, and this may partially explain the increased incidence of aggressive biological features in some non-age-matched studies (El-Tamer and Wait, 1999; Newman and Alfonso, 2007).

Most studies have been confounded by other factors, with most published data derived from American populations where access to diagnostic health care and treatment is affected by economic status and may vary between different ethnic groups (Bickell et al, 2006). Lower uptake of screening and lower rates of chemotherapy use in Blacks compared with other ethnic groups have been reported, with an association between health insurance status and receipt of chemotherapy (Freedman and Yea, 2011). Variations in other social and cultural factors between ethnic groups may also promote differential outcomes (Gerend and Pai, 2008).

Published data on the effect of ethnicity on breast cancer in the United Kingdom are limited but demonstrate a similar effect of ethnicity on outcome as the American studies, (Wild et al, 2006; Bowen et al, 2008; Jack et al, 2009). In their retrospective study of 102 Black and 191 White British women, Bowen et al (2008) observed a higher frequency of grade 3 tumours, lymph node-positive disease, negative oestrogen receptor and progesterone receptor status and triple-negative tumours in Black women than White women, with significantly worse survival in Blacks than Whites for patients with small (<2.0) tumours only. The cancer registry based analysis of Jack et al (2009) also reported significantly worse overall survival in Black African women than White women after adjustment for age, stage and treatment (HR: 1.24). This variation was less marked when breast cancer specific mortality was examined (HR: 1.09).

The POSH study is a prospective observational study of patients aged less than 41 years with breast cancer, diagnosed and treated in the United Kingdom (Eccles et al, 2007). This cohort of almost 3000 patients diagnosed and treated within the 21st Century represents, to the best of our knowledge, the largest prospective study of young breast cancer patients to date. All patients were managed within the National Health Service (NHS), and therefore had equal access to diagnostic, surgical and oncology services. Screening for breast cancer is not offered to women below age 40 years in the United Kingdom, thus removing this potentially confounding factor. Here we report the pathology and treatment of these patients according to their ethnic origin and compare outcome in White, Black and Asian patients.

**PATIENTS AND METHODS**

POSH is a multicentre prospective observational cohort study of young women diagnosed with breast cancer in the United Kingdom between 2000 and 2008, (http://www.southampton.ac.uk/medicine/research/posh.page).

The detailed study protocol was published in 2007 (Eccles et al, 2007). This study received approval from the South West Multicentre Research Ethics Committee (MREC 00/6/69).

**Patients.** Female patients were recruited from 127 UK hospitals. Patients were eligible if diagnosed with invasive breast cancer between 01 January 2000 and 31 January 2008 at an age of 40 years or younger. Potential recruits were identified within 12 months of initial diagnosis. All patients received treatment according to local protocols. Written consent was obtained.

**Study variables and data sources.** Details of personal characteristics, tumour pathology, disease stage and treatment received were collected from medical records. Pathology and imaging data have been verified with copies of original reports from sites. For patients treated with neo-adjuvant chemotherapy, initial tumour diameter was derived from radiological reports. Family history and personal risk factors were collected using a questionnaire completed by participants at recruitment. Ethnicity was self-reported, and patients were subsequently categorised into ethnic and racial categories according to National Institute of Health reporting guidelines, (NIH policy on reporting race and ethnicity data: subjects in clinical research 8-2001 http://grants1.nih.gov/grants/ guide/notice-files/NOT-OD-01-053.html). Patients were categorised as Black if they reported ‘Black British’, ‘African’, ‘Black Caribbean’, ‘Caribbean’ or ‘West Indian’ ethnicity and Asian if they reported, ‘Asian’, ‘British Asian’, ‘Asian-Pakistani’ or ‘Indian subcontinent’ ethnicity.

Detailed clinical follow-up data, including date and site of disease recurrence, were obtained from medical records at 6 months, 12 months and at yearly intervals post diagnosis until death or loss to follow-up. Patients were flagged in the NHS Medical Research Information Service to facilitate automatic notification of date and cause of death. This paper presents analyses conducted on follow-up data received until 11 April 2012.

**Tumour receptor status data.** ER, PR and HER2 receptor status of primary tumours was primarily determined from routine diagnostic pathology tests. Hormone receptor levels equivalent to an Allred score of ≥3 were categorised as positive. Tissue microarray, (TMA) data from central pathology review at St. Bartholomew’s Hospital, London has been performed on 1336 randomly selected tumour samples. TMA results for ER, PR and HER2 receptor status have been used to corroborate clinical data or supplement missing data points on receptor status for these 1336 patients. BRCA1/2 mutation testing is in progress.

**Statistical analysis.** Details of the target sample size (3000) are reported in the protocol (Eccles et al, 2007). The statistical analysis was conducted according to a pre-specified plan and as recommended by STROBE (STrengthening the Reporting of Observational Studies in Epidemiology) guidelines (von Elm et al, 2007). Analyses were performed in STATA v11.2 on records with complete data (levels of missingness were reported). Summary statistics were used to describe the cohort. Where appropriate, Pearson’s chi-squared or Mann–Whitney tests were performed in order to identify whether there were any specific differences in the characteristics between ethnic categories.

Overall survival (OS) and distant relapse-free survival (DRFS) were assessed using Kaplan–Meier curves. These were defined as time from date of invasive breast cancer diagnosis to death from any cause (OS) and to distant relapse or death from breast cancer (DRFS). Patients who had not experienced an event at the time of analysis were censored at their date of last follow-up. Multivariate analyses using Cox regression were performed according to the pre-specified analysis plan to adjust for the effect of confirmed prognostic factors (tumour grade, total tumour diameter, nodal status, ER status and body mass index) on DRFS in the different ethnic groups. The proportionality assumption was assessed by inspecting the Nelson-Aalen plots and Schoenfeld residuals and was satisfied in each case.
The POSH study recruited 3095 patients across England (2695), Scotland, Wales and Northern Ireland. After excluding 139 trial participants (Figure 1), 2956 patients were included in this analysis.

Patient characteristics and presentation. Self-reported ethnicity was available for 2915 (98.6%) patients. Of these 2902 reported a single ethnic/racial category; 2690 (92.7%) were classified as White/Caucasian, 106 (3.7%) as Black, 86 (3.0%) as Asian; and 20 (0.7%) were from ‘other’ ethnic groups. Thirteen patients reported mixed ethnicity: eight Black/Caucasian, three Caribbean/White, one Caribbean/Irish and one Chinese/White. In view of the small number of mixed ethnicity patients, these patients were categorised as Black (12) or Asian (1) for the purpose of further analyses. Patients from ‘other’ ethnic groups (n = 20) were excluded from further analyses.

Table 1 demonstrates patient demographics and breast cancer risk factors in White, Black and Asian ethnic groups. Median age at diagnosis of breast cancer was significantly lower in Asians than Whites (35 years B vs 36 years W, P = 0.001) or Blacks (35 years A vs 36 years B, P = 0.0472). Median body mass index was significantly higher in Black patients than Whites (26.9 kg m⁻² B vs 24.6 kg m⁻² W, P < 0.001) and Asians (26.9 kg m⁻² B vs 24.1 kg m⁻² A, P < 0.001). The proportion of patients with at least one child was 71.6% of Whites, 69.0% of Blacks and 79.1% of Asians, with no statistically significant differences between groups. The median number of children in patients who had at least one child was significantly higher in Blacks than Whites (P = 0.011). Symptomatic presentation accounted for 98% (2900) of the trial cohort, and mode of presentation was similar in all ethnic categories.

Tumour pathology. Median total tumour diameter was significantly greater in Blacks (26.0 mm B vs 22.0 mm W, P = 0.0103), and multifocal tumours were more frequent in Blacks (43.4%) than Whites (28.9%, P = 0.002) Table 2. The median total tumour diameter for unifocal disease was significantly smaller than the median total tumour diameter of patients with multifocal disease (<0.001). There was an increased frequency of grade 3 tumours in Blacks (68.1%) compared with Whites (60.4%), and a higher proportion of Blacks had positive nodal involvement than Whites (56.1% B vs 50.8% W) but these differences were not significant. Both Blacks and Asians had a higher frequency of ER-negative tumours than Whites (37.6% B, 42.5% A, 33.5% W), but this was not statistically significant. There were no significant differences in the frequency of HER2 overexpressing tumours between ethnic groups. However, the frequency of ER/PR/HER2-negative tumours was significantly higher in Blacks (26.1%) than Whites (18.6%, P = 0.043). Data for tumour grade, histological type, nodal status, presence of metastases and ER status were missing in 0–4.6% of cases only. Data for tumour distribution, PR status and HER2 status were missing more frequently, in up to 16.1%, 20.5% and 13.7% of cases, respectively.

Treatment. Most patients 98.6% (2915) had surgical treatment (Table 3). Rates of breast conserving surgery were lower in Blacks than Whites or Asians (39.8% B vs 48.1% W vs 48.3% A). Use of chemotherapy in early breast cancer patients was similarly high in all ethnic groups (89% B vs 88.6% W vs 89.7% A), but a higher proportion of Blacks received neo-adjuvant chemotherapy than Whites or Asians (23.7% B vs 14.8% W vs 20.7% A). The numbers of patients receiving anthracycline/taxane chemotherapy were similar in each ethnic group. Missing data for trastuzumab and hormonal therapy including ovarian suppression precluded the use of chi-squared tests to compare the proportions of ethnic categories receiving these treatments.

Follow-up and survival. At the time of analysis, length of follow-up ranged from 1 month to 11 years (median 5 years). Only 72 patients (2.4%) had been lost to follow-up. Isolated local relapse...
| Characteristic | All*: n = 2956 (100.0%) | W: n = 2690 (91.0%) | B: n = 118 (4.0%) | A: n = 87 (2.9%) | P-value\(\text{ii}\) |
|----------------|-------------------------|---------------------|------------------|------------------|------------------|
| **Median (range, IQR), number of patients** | | | | | |
| Age at diagnosis, in years | 36 (18–40, 33–38), 2956 | 36 (18–40, 34–38), 2690 | 36 (18–40, 33–38), 118 | 35 (23–40, 32–37), 87 | W Vs B: P = 0.463 (NS) |
| Duration of follow-up, in months | 60.5 (14–138.1, 45.4–75.4), 2956 | 60.8 (14–138.1, 46.5–76.3), 2690 | 47.8 (8–138.1, 57.4–70.8), 118 | 56.0 (8–102.0, 38.2–71.0), 87 | — |
| Age at menarche, in years | 13 (8–18, 12–14), 2956 | 13 (8–18, 12–14), 2690 | 12 (8–17, 12–14), 118 | 13 (9–18, 12–13), 87 | W Vs B: P = 0.560 (NS) |
| Body mass index, in kg m\(^{-2}\) | 24.6 (14.7–59.5, 22.1–28.4), 2842 | 24.6 (14.7–59.5, 22.1–28.4), 2610 | 25.9 (18.9–49.1, 23.3–31.2), 113 | 24.1 (17.2–39.0, 21.3–26.5), 79 | W Vs B: P < 0.001 |
| Missing/unknown | 876 (29.6%) | 792 (29.4%) | 39 (33.1%) | 22 (25.3%) | W Vs A: P = 0.0401 |
| Age at first birth, in years | 27 (13–40, 23–30), 2080 | 27 (13–40, 23–30), 1998 | 26 (14–37, 20–30), 79 | 25 (16–36, 22–29), 65 | W Vs B: P = 0.200 (NS) |
| Number of children | 2097 (71.6%) | 1912 (71.6%) | 80 (69.0%) | 68 (79.1%) | W Vs B: P = 0.545 (NS) |
| Number without children, n(%) | 834 (28.5%) | 760 (28.4%) | 36 (31.0%) | 18 (20.9%) | W Vs A: P = 0.128 (NS) |
| Missing/unknown | 25 (0.9%) | 18 (0.7%) | 2 (1.7%) | 1 (1.2%) | W Vs A: P = 0.921 (NS) |
| Number of children – median (range, IQR), n for patients with \(\geq 1\) child | 2 (1–8, 1–2), 2097 | 2 (1–8, 1–2), 1912 | 2 (1–4, 2–3), 80 | 2 (1–5, 2–3), 68 | W Vs B: P = 0.011 |

| Number of patients (%) | | | | | |
| **Presentation:** | | | | | |
| Symptomatic | 2900 (99.6%) | 2645 (98.6%) | 116 (98.3%) | 86 (100.0%) | W Vs B: P = 0.770 (NS) |
| Screen detected | 30 (1.0%) | 26 (1.0%) | 1 (0.9%) | 0 (0%) | W Vs A: P = 0.548 (NS) |
| Other | 12 (0.4%) | 11 (0.4%) | 1 (0.9%) | 0 (0%) | B Vs A: P = 0.479 (NS) |
| Missing/unknown | 14 (0.5%) | 8 (0.3%) | 0 (0%) | 1 (1.2%) | W Vs B: P = 0.003 |

| Age at diagnosis, in years | 18 to 25 | 26 to 30 | 31 to 35 | 36 to 40 | |
|--------------------------|---------|---------|---------|---------| |
| Symptomatic | 46 (1.6%) | 269 (9.1%) | 900 (30.5%) | 1741 (58.9%) | |
| Screen detected | 39 (1.5%) | 240 (8.9%) | 810 (30.1%) | 1601 (55.9%) | |
| Other | 26 (1.0%) | 13 (11.0%) | 35 (29.7%) | 68 (57.6%) | |
| Missing/unknown | 11 (0.4%) | 1 (0.9%) | 2 (1.7%) | 1 (1.2%) | |
| Number of patients | 269 (9.1%) | 269 (9.1%) | 80 (76.3%) | 49 (76.3%) | |
| Never | 269 (9.0%) | 269 (9.0%) | 80 (67.8%) | 49 (76.3%) | |
| Use of contraceptive pill | 2958 (87.9%) | 2958 (87.9%) | 2958 (87.9%) | 2958 (87.9%) | |
| Ever | 2958 (87.9%) | 2958 (87.9%) | 2958 (87.9%) | 2958 (87.9%) | |
| Never | 358 (12.1%) | 358 (12.1%) | 358 (12.1%) | 358 (12.1%) | |
| Smoker | | | | | |
| Ever | 1455 (50.8%) | 1368 (52.4%) | 1243 (47.6%) | 16 (18.8%) | |
| Never | 1408 (49.2%) | 1234 (47.6%) | 67 (25.8%) | 69 (81.2%) | |
| Missing/unknown | 93 (3.2%) | 79 (2.9%) | 4 (3.4%) | 2 (2.3%) | |

| Menopausal status | | | | | |
| Premenopausal | 2885 (99.6%) | 2634 (99.6%) | 114 (100.0%) | 86 (98.9%) | |
| Perimenopausal | 5 (0.2%) | 4 (0.2%) | 0 (0%) | 1 (1.2%) | |
| Postmenopausal | 7 (0.2%) | 7 (0.3%) | 0 (0%) | 0 (0%) | |
| Missing/unknown | 59 (2.0%) | 45 (1.7%) | 4 (3.4%) | 0 (0%) | |

| No. of patients with first or second degree relatives with breast cancer | | | | | |
| First degree | 418 (14.7%) | 382 (14.7%) | 18 (15.8%) | 5 (6.0%) | |
| Second degree | 554 (19.4%) | 521 (20.0%) | 14 (12.3%) | 9 (10.8%) | |

| No. of relatives with breast cancer | | | | | |
| 0 | 1874 (65.8%) | 1696 (65.2%) | 82 (71.9%) | 69 (83.1%) | |
| 1 | 702 (24.6%) | 651 (25.0%) | 21 (18.4%) | 12 (14.5%) | |
| 2 | 199 (7.0%) | 189 (7.3%) | 5 (4.4%) | 1 (1.2%) | |
| > 2 | 75 (2.6%) | 67 (2.6%) | 6 (5.3%) | 4 (4.6%) | |
| Missing/unknown | 106 (3.6%) | 87 (3.2%) | 4 (3.4%) | 4 (4.6%) | |

**Abbreviations:** A = Asian; B = Black; IQR = Inter-Quartile Range; NS = not significant; W = White.

*Includes patients in an Other or Missing/unknown Ethnic group.

**P-values from Pearson’s chi-squared test between Ethnic groups and each categorical variable (excluding Other Ethnic groups and missing/unknown data); \(\text{ii}\)P-values from Mann–Whitney test between Ethnic groups and each continuous variable (excluding Other Ethnic groups and missing/unknown data).*
| Tumour characteristics | All*: n = 2956 (100.0%) | W: n = 2690 (91.0%) | B: n = 118 (4.0%) | A: n = 87 (2.9%) | P-value†† |
|------------------------|------------------------|---------------------|------------------|------------------|-----------|
| **Number of patients %** |                        |                     |                  |                  |           |
| **Histological grade** |                        |                     |                  |                  |           |
| 1                      | 163 (5.7%)             | 147 (5.6%)          | 1 (0.9%)         | 10 (11.8%)       | W vs B: P = 0.055 (NS) |
| 2                      | 972 (33.8%)            | 891 (34.0%)         | 35 (30.0%)       | 24 (28.2%)       | W vs A: P = 0.045 |
| 3                      | 1742 (60.6%)           | 1586 (60.4%)        | 77 (68.1%)       | 51 (60.0%)       | B vs A: P = 0.004 |
| **Histological type**  |                        |                     |                  |                  |           |
| Ductal                 | 2556 (87.6%)           | 2320 (87.3%)        | 101 (87.8%)      | 81 (94.2%)       | W vs B: P = 0.882 (NS) |
| Lobular                | 134 (4.6%)             | 126 (4.7%)          | 5 (4.4%)         | 1 (1.2%)         | W vs A: P = 0.026 (NS) |
| Ductal and Lobular     | 78 (2.7%)              | 74 (2.8%)           | 2 (1.7%)         | 1 (1.2%)         | B vs A: P = 0.445 (NS) |
| Not graded/missing/unknown | 39 (1.3%)            | 33 (1.2%)           | 3 (2.5%)         | 1 (1.2%)         |           |
| **Distribution of cancer** |                        |                     |                  |                  |           |
| Localised              | 1873 (70.2%)           | 1741 (71.1%)        | 56 (56.6%)       | 46 (63.0%)       | W vs B: P = 0.002 |
| Multifocal             | 797 (29.9%)            | 707 (28.9%)         | 43 (43.4%)       | 27 (37.0%)       | W vs A: P = 0.133 (NS) |
| Missing/unknown        | 286 (9.7%)             | 242 (9.0%)          | 19 (16.1%)       | 14 (16.1%)       | B vs A: P = 0.395 (NS) |
| **Pathological T stage (all patients)** |                        |                     |                  |                  |           |
| T0                     | 73 (2.5%)              | 63 (2.4%)           | 4 (3.4%)         | 3 (3.5%)         | W vs B: P < 0.001 |
| T1                     | 1411 (47.9%)           | 1300 (48.5%)        | 40 (33.9%)       | 42 (48.3%)       | W vs A: P = 0.370 (NS) |
| T2                     | 1167 (39.6%)           | 1064 (39.7%)        | 45 (38.1%)       | 36 (41.4%)       | B vs A: P = 0.014 |
| T3                     | 189 (6.4%)             | 167 (6.2%)          | 18 (15.3%)       | 2 (2.3%)         |           |
| T4                     | 6 (0.2%)               | 5 (0.2%)            | 0 (0%)           | 1 (1.2%)         |           |
| Tis                    | 21 (0.7%)              | 18 (0.7%)           | 1 (0.9%)         | 1 (1.2%)         |           |
| Tx                     | 77 (2.6%)              | 62 (2.3%)           | 10 (8.5%)        | 2 (2.3%)         |           |
| Missing/unknown        | 12 (0.4%)              | 11 (0.4%)           | 0 (0%)           | 0 (0%)           |           |
| **N stage**            |                        |                     |                  |                  |           |
| N0                     | 1417 (48.9%)           | 1302 (49.2%)        | 50 (43.9%)       | 40 (48.2%)       | W vs B: P = 0.260 (NS) |
| N1                     | 1484 (51.2%)           | 1342 (50.8%)        | 64 (56.1%)       | 43 (51.8%)       | W vs A: P = 0.850 (NS) |
| Missing/unknown        | 55 (1.9%)              | 46 (1.7%)           | 4 (3.4%)         | 4 (4.6%)         | B vs A: P = 0.547 (NS) |
| **M stage**            |                        |                     |                  |                  |           |
| M0                     | 2860 (97.5%)           | 2613 (97.6%)        | 111 (94.9%)      | 84 (96.6%)       | W vs B: P = 0.069 (NS) |
| M1                     | 74 (2.5%)              | 65 (2.4%)           | 6 (5.1%)         | 3 (3.5%)         | W vs A: P = 0.545 (NS) |
| Missing/unknown        | 22 (0.7%)              | 12 (0.5%)           | 1 (0.9%)         | 0 (0%)           | B vs A: P = 0.563 (NS) |
| **ER Status**         |                        |                     |                  |                  |           |
| Positive               | 1947 (66.1%)           | 1782 (66.5%)        | 73 (62.4%)       | 50 (57.5%)       | W vs B: P = 0.358 (NS) |
| Negative               | 997 (33.9%)            | 898 (33.5%)         | 44 (37.6%)       | 37 (42.5%)       | W vs A: P = 0.080 (NS) |
| Missing/unknown        | 12 (0.4%)              | 10 (0.4%)           | 1 (0.9%)         | 0 (0%)           | B vs A: P = 0.477 (NS) |
| **PR Status**         |                        |                     |                  |                  |           |
| Positive               | 1342 (56.5%)           | 1215 (56.8%)        | 65 (58.0%)       | 40 (50%)         | W vs B: P = 0.793 (NS) |
| Negative               | 1033 (43.5%)           | 925 (43.2%)         | 47 (42.0%)       | 40 (50%)         | W vs A: P = 0.230 (NS) |
| Missing/unknown        | 581 (19.7%)            | 550 (20.5%)         | 6 (5.1%)         | 7 (8.1%)         | B vs A: P = 0.270 (NS) |
| **HER2 Status**       |                        |                     |                  |                  |           |
| Positive               | 717 (28.1%)            | 657 (28.3%)         | 22 (20.2%)       | 22 (29.7%)       | W vs B: P = 0.065 (NS) |
| Negative               | 1839 (72.0%)           | 1664 (71.7%)        | 87 (79.8%)       | 52 (70.3%)       | W vs A: P = 0.789 (NS) |
| Missing/unknown        | 400 (13.5%)            | 369 (13.7%)         | 9 (7.6%)         | 13 (14.9%)       | B vs A: P = 0.138 (NS) |
| **TNT Status**        |                        |                     |                  |                  |           |
| TNT                    | 537 (19.0%)            | 478 (18.6%)         | 30 (26.1%)       | 19 (23.2%)       | W vs B: P = 0.043 |
| Not TNT                | 2296 (81.0%)           | 2099 (81.5%)        | 85 (73.9%)       | 63 (76.8%)       | W vs A: P = 0.291 (NS) |
| Missing/unknown        | 123 (4.2%)             | 113 (4.2%)          | 3 (2.5%)         | 5 (8.8%)         | B vs A: P = 0.641 (NS) |
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Table 2. (Continued)

|                  | All*: n = 2956 (100.0%) | W: n = 2690 (91.0%) | B: n = 118 (4.0%) | A: n = 87 (2.9%) | P-value*11 |
|------------------|------------------------|---------------------|------------------|----------------|-------------|
| Median (range, IQR), number of patients | Maximum tumour diametera in mm (all patients) | 22 (15–33, 0–199), 2763 | 193 (6.5%) | 26 (15–50, 1–110), 103 | 15 (12.7%) | 26 (15–35, 0.15–98), 80 | W vs B: P = 0.0103 |
|                  | missing/unknown, n | 952 (63.7%) | 357 (23.9%) | 186 (12.4%) | 1495 (100.0%) | 59 (2.0%) | 2 (1–5, 1–50), 1495 | 2 (1–5, 1–50), 1352 | 65 (1–4, 1–20), 43 | W vs B: P = 0.496 (NS) |
| No. of positive axillary lymph nodes recovered (all patients) | Median (IQR, range), n | 859 (63.5%) | 324 (24.0%) | 169 (12.5%) | 1352 (100.0%) | 50 (1.9%) | 2 (1–5, 1–50), 1495 | 2 (1–5, 1–50), 1352 | 65 (1–4, 1–20), 43 | W vs B: P = 0.0143 |
|                  | Missing/unknown, n | 41 (63.1%) | 14 (21.5%) | 10 (15.4%) | 65 (100.0%) | 4 (3.4%) | 2 (1–5, 1–50), 1495 | 2 (1–5, 1–50), 1352 | 65 (1–4, 1–20), 43 | W vs B: P = 0.0169 |
|                  | Total, n | 32 (74.4%) | 9 (20.9%) | 2 (4.7%) | 43 (100.0%) | 4 (4.6%) | 1 (1–5, 1–50), 1495 | 1 (1–5, 1–50), 1352 | 1 (1–4, 1–20), 43 | W vs B: P = 0.754 (NS) |
| No. of positive axillary lymph nodes recovered (all patients), n(%) | Missing/unknown, n | 9 (2.9%) | 2 (1.9%) | 4 (3.4%) | 9 (2.9%) | 4 (4.6%) | W vs A: P = 0.0940 (NS) |

Abbreviations: ER = oestrogen receptor; HER2 = human epidermal growth factor receptor 2; IQR = inter-quartile range; PR = progesterone receptor; TNT = triple negative.

*1Includes patients in an other or missing/unknown ethnic group.
*2Includes data from TMA as well as primary POSH data.
*3Includes patients with an ER negative, HER2-negative and PR-negative status.
*4Maximum tumour diameter includes ductal carcinoma in situ.
*5P-values obtained from the Pearson’s chi-squared test between ethnic groups and each categorical variable (excluding other ethnic groups and missing/unknown data).
*6P-values obtained from the Mann-Whitney test between ethnic groups and each continuous variable (excluding Other Ethnic groups missing/unknown data).

The primary aim of the POSH prospective, multicentre study is to determine whether the prognosis of patients with breast cancer is altered by inherited genetic factors. The presenting characteristics, pathology, treatment and survival of this large cohort of early-onset breast cancer patients diagnosed and treated in the first decade of this century have recently been published (Copson et al., 2013); genetic analysis of the study cohort is in progress. The POSH study cohort provides a unique opportunity to compare the outcomes of different ethnic groups in an age group that is not eligible for breast screening and in a population that receives entirely public funded health care, thus eliminating these potentially confounding socio-economic factors. We present here the clinical course of Blacks, Asians and Whites recruited to this study.

Our data confirm conclusions from retrospective studies that Blacks have a tendency towards more biologically aggressive tumours with significantly larger tumours and increased incidence of triple-negative tumours, and trends towards increased frequency of grade 3 and node-positive tumours (Elledge et al., 1994; Dignam, 2000; Joslyn and West, 2000; Carey et al., 2006; Bowen et al., 2008). Our finding of a higher incidence of multifocal tumours in Blacks than Whites is in agreement with other data (Litton et al., 2007). The incidence of multifocal disease in all ethnic groups of this cohort was higher than in some comparable series; this is likely to reflect the fact that multi-focality was defined pathologically following surgery in this study, rather than radiologically before surgery. The presence of multifocal disease was not incorporated into our multivariate analysis as both the definition of multifocality and the independent prognostic effect of this feature over and above total tumour diameter remain controversial (Coombs and Boyages, 2005).

All of our cohort were diagnosed and treated within the UK NHS according to local protocols and therefore had equal access to standard therapies. There was no difference in receipt of chemotherapy for early breast cancer between ethnic groups, unlike the data from Bickell et al (2006) who reported use of appropriate chemotherapy in only 67% of Blacks compared with 78% of Whites. The increased use of neo-adjuvant rather than adjuvant chemotherapy in Blacks in our cohort is likely to be due
to the increased frequency of larger tumours in this ethnic group. Use of anthracyline/taxane combination chemotherapy was similar in each ethnic category, in contrast to Griggs et al (2007a) who reported increased use of non-standard chemotherapy in American Blacks. There are also reports that Blacks are more likely to receive reduced dose chemotherapy and to discontinue chemotherapy prematurely (Griggs et al, 2007b; Hershman et al, 2009). Such treatment modifications could reflect higher rates of co-morbidities in Blacks compared with Whites, although Blacks do not have increased rates of neutropenic complications despite lower baseline white blood counts (Tammemagi et al, 2005; Hershman et al, 2009). We currently have insufficient data to compare chemotherapy dose density in our cohort. However, increased mortality in Blacks compared with Whites enrolled in SWOG chemotherapy

| Table 3. Treatment details                      | All*: n = 2956 (100.0%) | W: n = 2690 (91.0%) | B: n = 118 (4.0%) | A: n = 87 (2.9%) | P-value1/2 |
|------------------------------------------------|--------------------------|---------------------|------------------|-----------------|-----------|
| Number of patients (%)                           |                          |                     |                  |                 |           |
| Definitive surgery                               |                          |                     |                  |                 |           |
| Breast conserving surgery                       | 1409 (47.7%)             | 1294 (48.1%)        | 47 (39.8%)       | 42 (48.3%)      | W vs B: P < 0.001 |
| Mastectomy                                       | 1497 (50.7%)             | 1355 (50.4%)        | 64 (54.2%)       | 44 (50.6%)      | W vs A: P = 0.978 (NS) |
| Nodal surgery only                               | 9 (0.3%)                 | 6 (0.2%)            | 2 (1.7%)         | 0 (0%)          | B vs A: P = 0.255 (NS) |
| No surgery                                       | 39 (1.3%)                | 33 (1.2%)           | 5 (4.2%)         | 1 (1.2%)        |           |
| Missing/unknown                                  | 2 (0.1%)                 | 2 (0.1%)            | 0 (0%)           | 0 (0%)          |           |
| Chemotherapy timing                              |                          |                     |                  |                 |           |
| Adjuvantantracycline &/or taxane                 | 2642 (89.4%)             | 2405 (89.4%)        | 110 (93.2%)      | 80 (92.0%)      | W vs B: P = 0.239 (NS) |
| Neo-adjuvant                                     | 24 (0.8%)                | 23 (0.9%)           | 0 (0%)           | 1 (1.2%)        | W vs A: P = 0.653 (NS) |
| Palliative                                       | 54 (1.8%)                | 46 (1.7%)           | 5 (4.2%)         | 3 (3.5%)        | B vs A: P = 0.942 (NS) |
| Not applicable                                   | 290 (9.8%)               | 262 (9.7%)          | 8 (6.8%)         | 6 (6.9%)        |           |
| Adjuvant trastuzumab                             |                          |                     |                  |                 |           |
| Yes                                             | 363 (12.3%)              | 332 (12.3%)         | 9 (7.6%)         | 11 (12.6%)      |           |
| Other treatment period/missing/unknown           | 2593 (87.7%)             | 2358 (87.7%)        | 109 (92.4%)      | 76 (87.4%)      |           |
| Adjuvant radiotherapy                            |                          |                     |                  |                 |           |
| Yes                                             | 2358 (79.8%)             | 2160 (80.3%)        | 87 (73.7%)       | 67 (77.0%)      |           |
| No/missing/unknown                               | 598 (20.2%)              | 530 (19.7%)         | 31 (26.3%)       | 20 (23.0%)      |           |
| ER-positive patients only                        | All*: n = 1947 (100.0%)  | W: n = 1782 (91.5%) | B: n = 73 (3.8%) | A: n = 50 (2.6%) |
| Adjuvant hormone treatment                      |                          |                     |                  |                 |           |
| Yes                                             | 1725 (88.6%)             | 1591 (89.3%)        | 59 (80.8%)       | 42 (84.0%)      |           |
| No/missing/unknown                               | 222 (11.4%)              | 191 (10.7%)         | 14 (19.2%)       | 8 (16.0%)       |           |
| Ovarian suppression (in any treatment period) Medical (LHRH agonist) |                          |                     |                  |                 |           |
| Yes                                             | 655 (33.6%)              | 605 (34.0%)         | 21 (28.8%)       | 11 (22.0%)      |           |
| No/missing/unknown                               | 1292 (66.4%)             | 1177 (66.1%)        | 52 (71.2%)       | 39 (78.0%)      |           |
| Irradiation                                     |                          |                     |                  |                 |           |
| Yes                                             | 11 (0.6%)                | 11 (0.6%)           | 0 (0%)           | 0 (0%)          |           |
| No/missing/unknown                               | 1936 (99.4%)             | 1771 (99.4%)        | 73 (100%)        | 50 (100.0%)     |           |
| Oophorectomy                                    |                          |                     |                  |                 |           |
| Yes                                             | 324 (16.6%)              | 307 (17.2%)         | 5 (6.9%)         | 5 (10.0%)       |           |
| No/missing/unknown                               | 1623 (83.4%)             | 1475 (82.8%)        | 68 (93.2%)       | 45 (90.0%)      |           |

Abbreviations: A = Asian; B = Black; NS = not significant; W = White.
1Includes patients in an Other or Missing/unknown Ethnic group.
2Excluding any treatment for M1 disease.
3For example, CMF or anything not containing an anthracycline or taxane.
4P-values from Pearson’s chi-squared test between ethnic groups and each categorical variable (excluding other ethnic groups and missing/unknown data).
5P-values from Mann–Whitney test between ethnic groups and each continuous variable (excluding Other Ethnic groups and missing/unknown data).
The findings of a number of previous USA and UK studies (Joslyn et al., 2006; Wild et al., 2006; Jack et al., 2009; Albain et al., 2009) have demonstrated that Asian ethnicity is significantly associated with a worse outcome compared to White ethnicity. This is in agreement with other studies showing no significant difference in the outcome of Whites and Asians (Wild et al., 2006; Jack et al., 2009; Albain et al., 2009). Data on the association between Asian ethnicity and breast cancer prognosis are more limited, but our data are consistent with other studies showing no significant difference in the outcome of Whites and Asians (Wild et al., 2006). Our multivariate analyses indicate that the inferior outcomes of Blacks are not fully explained by an increased frequency of adverse

As anticipated, the major cause of death in this cohort was breast cancer. Our data show clearly that both DSFS and OS were significantly lower in Blacks than Whites. This is in agreement with the findings of a number of previous USA and UK studies (Joslyn and West, 2000; Jatoi et al., 2003; Carey et al., 2006; Grann et al., 2006; Wild et al., 2006; Jack et al., 2009; Albain et al., 2009). Data on the association between Asian ethnicity and breast cancer prognosis are more limited, but our data are consistent with other studies showing no significant difference in the outcome of Whites and Asians (Wild et al., 2006).

Abbreviations: W = White; A = Asian; B = Black; CI = confidence interval; DSFS = distant recurrence-free survival; OS = overall survival.
Table 5. Multivariate Analyses—DRFS

| Group of patients | Ethnic category | N* | HR (95% CI) | P-value | N* | HR (95% CI) | P-value |
|-------------------|----------------|----|-------------|---------|----|-------------|---------|
| All patients      | W             | 2872 | 1 (Reference cat.) | — | 2581 | 1 (Reference cat.) | — |
|                   | B             | 1.91 (1.39, 2.40) | <0.001 | 1.50 (1.06, 2.13) | 0.023 |
|                   | A             | 0.96 (0.60, 1.54) | 0.875 (NS) | 0.85 (0.48, 1.51) | 0.578 (NS) |
| ER-negative patients only | W | 974 | 1 (Reference cat.) | — | 862 | 1 (Reference cat.) | — |
|                   | B             | 1.73 (1.04, 2.87) | 0.034 | 1.31 (0.73, 2.36) | 0.369 (NS) |
|                   | A             | 0.82 (0.40, 1.65) | 0.575 (NS) | 0.76 (0.31, 1.85) | 0.546 (NS) |
| ER-positive patients only | W | 1888 | 1 (Reference cat.) | — | 1716 | 1 (Reference cat.) | — |
|                   | B             | 2.03 (1.36, 3.02) | <0.001 | 1.60 (1.03, 2.47) | 0.035 |
|                   | A             | 1.04 (0.55, 1.94) | 0.910 (NS) | 0.90 (0.42, 1.90) | 0.776 (NS) |
| Triple negative patients only | W | 524 | 1 (Reference cat.) | — | 477 | 1 (Reference cat.) | — |
|                   | B             | 1.39 (0.71, 2.73) | 0.340 (NS) | 1.18 (0.52, 2.69) | 0.693 (NS) |
|                   | A             | 0.19 (0.03, 1.33) | 0.094 (NS) | 0.28 (0.04, 2.03) | 0.209 (NS) |

Abbreviations: A = Asian; B = Black; CI = Confidence Interval; DRFS = Distant Recurrence-Free Survival; W = White.

Univariate analyses: results obtained by fitting a Cox model with ethnic grouping as the only covariate.

Multivariate analyses: results obtained by fitting a Cox model with ethnic grouping as a covariate and adjusting for body mass index, tumour grade, size and nodal status.

Number of Caucasian/White, Black and Asian patients.

Number of Caucasian/White, Black and Asian patients with complete data for body mass index, tumour grade, size and nodal status.

Unadjusted

Adjusted

Table 5. Multivariate Analyses—DRFS

| Group of patients | Ethnic category | N* | HR (95% CI) | P-value | N* | HR (95% CI) | P-value |
|-------------------|----------------|----|-------------|---------|----|-------------|---------|
| All patients      | W             | 2872 | 1 (Reference cat.) | — | 2581 | 1 (Reference cat.) | — |
|                   | B             | 1.91 (1.39, 2.40) | <0.001 | 1.50 (1.06, 2.13) | 0.023 |
|                   | A             | 0.96 (0.60, 1.54) | 0.875 (NS) | 0.85 (0.48, 1.51) | 0.578 (NS) |
| ER-negative patients only | W | 974 | 1 (Reference cat.) | — | 862 | 1 (Reference cat.) | — |
|                   | B             | 1.73 (1.04, 2.87) | 0.034 | 1.31 (0.73, 2.36) | 0.369 (NS) |
|                   | A             | 0.82 (0.40, 1.65) | 0.575 (NS) | 0.76 (0.31, 1.85) | 0.546 (NS) |
| ER-positive patients only | W | 1888 | 1 (Reference cat.) | — | 1716 | 1 (Reference cat.) | — |
|                   | B             | 2.03 (1.36, 3.02) | <0.001 | 1.60 (1.03, 2.47) | 0.035 |
|                   | A             | 1.04 (0.55, 1.94) | 0.910 (NS) | 0.90 (0.42, 1.90) | 0.776 (NS) |
| Triple negative patients only | W | 524 | 1 (Reference cat.) | — | 477 | 1 (Reference cat.) | — |
|                   | B             | 1.39 (0.71, 2.73) | 0.340 (NS) | 1.18 (0.52, 2.69) | 0.693 (NS) |
|                   | A             | 0.19 (0.03, 1.33) | 0.094 (NS) | 0.28 (0.04, 2.03) | 0.209 (NS) |

Abbreviations: A = Asian; B = Black; CI = Confidence Interval; DRFS = Distant Recurrence-Free Survival; W = White.

Univariate analyses: results obtained by fitting a Cox model with ethnic grouping as the only covariate.

Multivariate analyses: results obtained by fitting a Cox model with ethnic grouping as a covariate and adjusting for body mass index, tumour grade, size and nodal status.

Number of Caucasian/White, Black and Asian patients.

Number of Caucasian/White, Black and Asian patients with complete data for body mass index, tumour grade, size and nodal status.

Unadjusted

Adjusted

pathological features. In particular, our separate analyses of ER-positive, ER-negative and triple-negative patients confirm previous reports that the poor prognosis of Blacks is not fully explained by the increased incidence of triple-negative tumours (Albain et al., 2009), although we cannot entirely exclude other confounding biological factors. Our analysis is based on biological features obtainable from routine histopathological review; it is feasible that our results could be explained by differences in tumour gene expression profiles. An excess of luminal B tumours (a subtype of ER-positive breast cancer defined by increased proliferation, relative resistance to chemotherapy compared with other highly proliferative breast cancers, and poor outcome with endocrine therapy) in Blacks could, for example, explain our findings, (Perou et al., 2000). Alternatively, it is well established that breast cancers diagnosed during or within a year of pregnancy tend to be more aggressive than cancers in nulliparous women (reviewed by Azim et al., 2012), and it is possible that our results could be explained by a higher number of pregnancy associated tumours in Blacks than other ethnic groups. Our data set does not permit us to make direct assessments about the number of pregnancy-related cancers in our cohort, as pregnancy was assessed as a risk factor for breast cancer rather than a potential prognostic factor, and we therefore lack data on the date of second and subsequent pregnancies. However, the fact that Blacks who had already started their families by the time of their diagnosis were more likely to have a larger number of children than Whites suggests that Blacks would have spent more time being pregnant before their cancer diagnosis and could therefore have been at a higher risk of pregnancy-related breast cancer.

Although previous publications have reported persistence of ethnicity as an independent prognostic factor in both ER-negative and positive patients after adjustment for other pathological
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factors, we found this in ER-positive patients only. Albain et al (2009) also found a greater hazard ratio in Black premenopausal ER-positive patients than ER-negative patients (1.74 vs 1.29), and Hershman et al (2009) commented that their finding of no interaction between race and tumour ER status should 'not be overinterpreted' given their small sample size and the long survival of their non-age selected patients. The small number of events in our ER-negative Black patients may affect our ability to demonstrate an independent effect of ethnicity in ER-negative patients. However, our finding that Black ethnicity is particularly an independent prognostic factor particularly in young ER-positive patients could suggest that either the use or effectiveness of hormonal therapy may vary significantly between ethnic groups. Bickell et al (2006) reported significantly lower use of adjuvant hormonal therapy in Blacks (71%) than Whites (80%) in women treated in America. Unexpectedly, we also found a lower percentage of ER-positive Black patients (80.8%) treated with hormonal therapy than White patients (89.3%); however, we cannot confirm that this is a statistically significant difference owing to missing data. It has been reported that compliance with tamoxifen is significantly lower in non-Whites than Whites (Partridge et al, 2003). Reduced compliance with hormonal therapy remains a possible explanation for our observations, although we did not collect compliance data. Our finding that more oophorectomies were performed in White than Asian or Black women could reflect a higher proportion of identified BRCA mutations in our Whites than Black or Asian patients as reported elsewhere (Ademuyiwa and Olopade, 2003).

Pharmacogenetics may also have a role in ethnic populations with different genetic structure. Some CYP2D6 variants associated with 'poor metabolism' of tamoxifen are more common in Blacks than other ethnic groups (Bradford, 2002; Gaedigk et al, 2002). However, it is currently controversial whether CYP2D6 genotype directly affects breast cancer survival in patients on adjuvant tamoxifen (Abraham et al, 2010). Albain et al (2009) reported inferior outcome in Blacks compared with Whites in other 'sex-specific' cancers as well as breast cancer. This suggests that other hormonal influences could interact with genetic factors. However, studies of the association between polymorphisms of the CYP1A1 gene (involved in oestrogen metabolism) and risk of breast cancer in African-Americans have been inconclusive (Taioli et al, 1995; Bailey et al, 1998).

Many publications have examined the role of socio-economic factors in the presentation and outcome of malignancies. In a systematic review of mostly American studies, socio-economic position was found to explain part of the variation in OS between ethnic groups but did not account for differences in breast cancer survival (McKenzie and Jeffreys, 2009). Other social issues may also cause disparities in breast cancer outcome in different ethnic groups. McKenzie and Jeffreys (2009) noted that, 'although there is a lack of major systemic genetic differences between ethnic groups, there are extensive differences in lifestyle'. Their systematic review however found little evidence to indicate that smoking or alcohol use could explain the inferior survival of Blacks compared with Whites, unlike BMI which did explain some of this variation (McKenzie and Jeffreys, 2009).

Health systems such as the UK NHS are designed to provide equal access to health care; however, this does not automatically equate to equal use of health care (Forbes et al, 2011). Recent immigration is frequently associated with linguistic and cultural challenges, which may act as barriers to accessing health care. It has also been reported that Blacks are less aware of symptoms of breast cancer than other groups and are less likely to self-check (Forbes et al, 2011). Therefore, the increased average tumour size may reflect a cultural tendency to delay presentation, as all our patients were below the minimum age for breast cancer screening. However, there was no significant difference between the rates of nodal involvement in the different ethnic groups in our cohort. Details of follow-up routines were not collected in this study; however, the independent effect of ethnicity persists when limiting the analyses to hospitals treating both White and Black patients (data not shown). Clearly, our cohort contains a much smaller number of Black patients than in many of the American published series. However, the proportion of Black patients in the POSH cohort is very similar to the English population as a whole (2.9%). English cancer registry data for 2007 includes ethnicity data on only 80% of patients but indicate that 3.8% of breast cancers diagnosed in under 50 year olds were in Black women (National Cancer Intelligence Network, 2011), suggesting that our data are representative of the premenopausal English population. The average age of diagnosis is lower in Black women than Caucasians in the United Kingdom as elsewhere (Bowen et al, 2008). We cannot exclude selection bias; patients who agree to participate in clinical trials may not fully represent the general population. However, previous work indicates these patients may be more compliant with treatment than non-trial patients (Antman et al, 1985).

Categorisation of patients into broad ethnic categories on the basis of self-reported ethnicity is a simplification of a very complex picture. We have not attempted to differentiate between Blacks of African and Caribbean descent because of small patient numbers. However, previous data suggest that there is disparity in the outcome of these two groups (Wild et al, 2006). The complexities of categorising ethnicity and the controversies associated with analysing data from individuals with mixed ethnicity have been highlighted previously (Agymang et al, 2005; Aspinall, 2011); however, here we have been transparent in our management of these data. Place of birth may provide additional information about genetic ancestry (Ingleby, 2008).

Other limitations of this study include the low number of ER-negative patients in the Black and Asian groups. The target sample size of the POSH study (n = 3000) was calculated to detect a 10% difference in event rates between BRCA mutation carriers and sporadic early-onset breast cancer patients. It is likely that this study was underpowered to demonstrate an independent effect of ethnicity in ER-negative patients. Incomplete data on HER2 status reflect the time course of recruitment to this study, with routine HER2 testing largely being introduced from 2005 onwards, while missing PR data are largely accounted for by the fact that some of the recruiting hospitals did not routinely assess PR status during the study period. In addition, inconsistencies in the reporting of trastuzumab use, hormonal therapy and ovarian suppression have resulted in missing data, which has precluded a formal analysis of the use of these treatments in different ethnic groups. We have also not attempted to classify the socio-economic status of patients, as the POSH study did not collect data on income or education.

However, the POSH cohort is the first prospective study of young breast cancer patients treated within the UK NHS and, unlike previous registry based retrospective series, includes extensive data on treatment as well as pathology. This analysis of the effect of ethnicity on breast cancer outcome is strengthened by our use of a pre-specified analysis plan and STROBE reporting guidelines. Ethnicity was also directly self-reported by study participants, rather than inferred from other information, and we have been explicit in our categorisation of ethnic groups. Our data also benefits from the fact that all patients received 'modern' oncological therapies, in contrast to some historical registry studies.

We have recently published a comprehensive description of the entire POSH cohort, which confirms the poor medium term outcome of both ER-positive and ER-negative patients aged 40 years or under at the time of diagnosis (Copson et al, 2013). The cause for the poor outcome of young breast cancer patients currently remains controversial; the POSH study ultimately aims to
determine whether this is in part due to underlying inherited genetic mutations.

This publication from the POSH study provides valuable confirmation that Black ethnicity is an independent marker of poor prognosis in this young age group. Further research is clearly required to establish whether the effect of Black ethnicity is indeed more marked in ER-positive than ER-negative disease, and if so whether this is related to the use or effectiveness of Tamoxifen. In addition, there is a need to clarify the contribution of socioeconomic position, education and breast cancer awareness to outcome of early breast cancer in different ethnic groups in the United Kingdom. The fact that almost 50% of patients in all ethnic groups presented with tumours ≥ 2.0 cm does of course raise questions about the need for screening in younger women. However, as robust evidence for screening mammography in this group does not exist, and there are demonstrable differences in breast awareness between different ethnic groups then improving education and understanding of breast cancer in these populations may be effective in reducing the differences observed in tumour size in this study (Forbes et al, 2011).

CONCLUSION

We present the first prospective study of young breast cancer patients in the United Kingdom to analyse outcome data according to ethnicity. Our results confirm that Black patients have an increased risk of breast cancer recurrence than Whites despite equal access to health care including adjuvant therapies. Black ethnicity is an independent indicator of poor prognosis in young women with invasive breast cancer, suggesting that current treatment approaches may be less effective in this population. Further studies are required to investigate this in more detail and to optimise the management of this patient group.

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CONFLICT OF INTEREST

EC has received honoraria from Roche and RJC has received honoraria from GSK and Pfizer. RE has received educational support from Vista Diagnostics, Tepnel (now GenProbe), Illumina and Janssen-Cilag. The remaining authors declare no conflict of interest.

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APPENDIX

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