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Epidemiology of porocarcinoma in England 2013–2018: a population-based registry study

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Abstract

Background Porocarcinoma (PC) is a cutaneous malignancy that differentiates towards (possibly arises from) the sweat ducts and glands. Lack of histological diagnostic markers makes clinical and pathological diagnosis complex. The limited data available suggest the incidence is increasing; however, this remains to be established in national epidemiological studies.

Objectives To report the incidence, treatment and survival of patients with PC in England from 1 January 2013 to 31 December 2018 using national cancer registry data.

Methods PC diagnoses in England during 2013–2018 were identified from the National Disease Registration Service using morphology and behaviour codes. These were registered from routinely collected pathology reports and cancer outcomes and services datasets. The 2013 European age standardized incidence rates (EASRs), Kaplan–Meier all-cause survival and log-rank test were calculated.

Results In total, 738 tumours (396 in males and 342 in females) were diagnosed. The median age at diagnosis was 82 years old (interquartile range 74–88). The most frequently affected site were lower limbs (35.4%), followed by the face (16%). The majority of the cohort received surgical excision (73.0%). The Kaplan–Meier all-cause survival was 45.4% at 5 years, which was lower than in previous studies. The EASR for the whole population was 0.25 [95% confidence interval (CI) 0.23–0.27] per 100 000 person-years (PY)]. PC incidence rates in the East of England (EASR of 0.54, 95% CI 0.47–0.63 per 100 000 PY) were three times higher than the South West (EASR of 0.14, 95% CI 0.10–0.19 per 100 000 PY) where the regional rates were the lowest.

Conclusions This study shows that there is large variation in the EASRs of PC across England. This may reflect differences in how PC is diagnosed and registered in different regions in England. These data support national assessment of the management of PC, which will inform future studies and guideline development.

What is already known about this topic?

- Porocarcinoma (PC) is a rare skin appendageal cancer with a high risk of metastasis.
- Few studies on PC epidemiology at a national level exist. The 2013 European age standardized incidence rate (EASR) has previously been estimated to be 0.13–1.9 per 100 000 person-years across different nations.
- PC is more common in the older population and often affects the lower limbs.

What does this study add?

- The Kaplan–Meier survival was 45.4% at 5 years (all cause), which was lower than in previous studies.
- The EASRs of PC in England 2013–18 was 0.31, 0.19 and 0.25 per 100 000 person-years for males, females and the whole population, respectively.
- Regional variation in PC EASRs may be because of diagnostic and coding differences or population-specific effects.

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Porocarcinoma (PC) is a rare type of skin appendageal (adnexal) cancer that differentiates towards (possibly arises from) cutaneous intraepidermal ducts of the sweat glands.[1] The high metastatic rate of PC (8–31%) sets it apart from other appendageal cancers.[2,3] PC can develop *de novo* or from benign eccrine poroma.[1]

PC incidence varies globally. The Finnish Cancer Registry reported a European age standardized rate (EASR) of 0.15 per 100 000 person-years (PY) for males and 0.10 per 100 000 PY for females between 2007 and 2017.[4] A study covering part of the East of England 2004–2013 ($n=152$ cases) reported PC EASRs of 2.4, 1.3 and 1.9 per 100 000 PY for males, females and the whole population, respectively.[5]

Even though PC can usually be distinguished from other sweat gland and duct neoplasms, it can be difficult to make the histological diagnosis. Although no definitive diagnostic immunohistochemistry profile currently exists for PC, *YAP1-NUT* gene fusions and CD117 expression have been described to aid the diagnosis.[6,7] Currently there is no agreed staging methodology for PC. Surgical excision is the most frequently utilized treatment.[8] Prognosis can be poor after surgery, with a local or regional recurrence rate of up to 35% after standard excision.[9]

This study aimed to report the incidence, treatment and survival of PC in England between 2013 and 2018. England's Rare Diseases Action Plan (2022) highlights a priority to increase awareness of rare disease and cancer among healthcare professionals to improve patient experiences and diagnoses. Providing high-quality epidemiological data on incidence, demographics and survival of patients with PC aligns with this action plan.[10]

Materials and methods

Study design, settings and participants

This is a retrospective national population-based cancer registry cohort study. Patients diagnosed with PC from 1 January 2013 to 31 December 2018 in England were identified from the NHS Digital's National Disease Registration Service (NDRS) data. International Classification of Diseases (ICD)-10 codes were used to identify tumours (Table S1; see Supporting Information).

All National Health Service (NHS) pathology laboratories are required to submit cancer pathology reports to NDRS. Pathology reports or cancer outcomes and services dataset data from multidisciplinary team meeting outcomes are combined with the patient administration system to form a cancer registration record.[11]

Thirty days before and 183 days after the diagnosis date, tumour registration records were linked to relevant surgical codes in Hospital Episode Statistics (Table S2; see Supporting Information). These codes were derived from the Office of Population Censuses and Surveys Classification of Interventions and Procedures, version 4. Diagnostic procedures included punch or incisional biopsy, curettage or shave biopsy, lymph node biopsy and biopsy not otherwise specified (NOS). Surgical treatment included excision and/or flap/graft repair, lymph node excision/dissection, amputation, Mohs micrographic surgery (MMS) and re-excision. Records were linked to mortality data from the Office for National Statistics. The event of interest was death, and the end of follow-up was 2 September 2021.

Variables

Variables extracted included diagnosis year, body site location, age, sex and ethnicity (Table S3; see Supporting Information). Deprivation quintiles data were extracted based on PC diagnosis year and calculated using Indices of Multiple Deprivation (IMD) 2015 for diagnoses made in 2013 and IMD 2019 for diagnoses made during 2014–2018.[12,13] This relative measure of deprivation, calculated at small geographical areas, used domains such as income, employment, education and crime. Postcode at diagnosis was used to group patients into seven regions based on grouped NHS regions in England.[14] Population by 5-year age bands, population at risk and PC crude counts were used to calculate EASR per 100 000 people using European Standard Population 2013.[15]

Statistical analysis

Kaplan–Meier survival, log-rank test, Poisson regression and Pearson's χ^2 test were all conducted using Stata version 17 (Stata Corporation, College Station, TX, USA). $P<0.05$ was considered statistically significant.

Results

Cohort demographics

In total, 738 patients (396 males and 342 females) were diagnosed with PC in England during 2013–2018 (Table 1). Median age at diagnosis for the whole cohort was 82 years [interquartile range (IQR) 74–88]. Median age was 80 years (IQR 72–86) in males and 84 years (IQR 74–88 years) in females. Ethnicity was unknown for 35 (5.0%) patients. Of those with available ethnicity data (703 patients), 673 (95.7%) self-reported as White. PC incidence was evenly distributed across IMD quintiles (incidence rate ratio 1.02, 95% CI 0.97–1.08).

Porocarcinoma body site distribution

The most affected sites were lower limbs (35.4%, $n=261$) followed by the face NOS (16.0%, $n=118$) (Table 1). Lower limbs included the hip and upper limbs included the shoulder. All the differences in body sites affected between males and females were statistically significant (χ^2, $P<0.05$, Figure S1; see Supporting Information). In males, 10.4% ($n=41$) of PC affected the ears compared with only 1.2% ($n=4$) in females. The scalp and neck of males (18.7%, $n=74$) were affected more than double compared with females (7.9%, $n=27$). In total, 49.1% ($n=168$) of females had PC affecting the lower limbs, compared with 23.5% ($n=93$) in males.

Porocarcinoma age-specific and annual incidence

Age-specific standardized incidence rates increased with age in both men and women across 2013–18 (Figure 1). The EASR of PC in England from 2013 to 2018 was 0.31

Table 1 Patient demographics and distribution of body sites affected of those diagnosed with porocarcinoma (PC) in England 2013–2018

Patient demographics	Males, *n* (%) (*n* = 396)	Females, *n* (%) (*n* = 342)	Overall, *n* (%) (*n* = 738)
Age at diagnosis, years			
Age, median (IQR)	80 (72–86)	84 (75–89)	82 (74–88)
< 40	6 (1.5)	4 (1.2)	10 (1.4)
40–49	9 (2.3)	8 (2.3)	17 (2.3)
50–59	18 (4.5)	13 (3.8)	31 (4.2)
60–69	49 (12.4)	29 (8.5)	78 (10.6)
70–79	105 (26.5)	73 (21.3)	178 (24.1)
80–89	158 (39.9)	132 (38.6)	290 (39.3)
≥ 90	51 (12.9)	83 (24.3)	134 (18.2)
Ethnicity			
White	361 (91.2)	312 (91.2)	673 (91.2)
Other	3 (0.8)	1 (0.3)	4 (0.5)
Asian	8 (2.0)	3 (0.9)	11 (1.5)
Black	6 (1.5)	9 (2.6)	15 (2.0)
Unknown	18 (4.5)	17 (5.0)	35 (4.7)
IMD quintile			
1 (most deprived)	49 (12.4)	70 (20.5)	119 (16.1)
2	83 (21.0)	71 (20.8)	154 (20.9)
3	94 (23.7)	75 (21.9)	169 (22.9)
4	98 (24.7)	67 (19.6)	165 (22.4)
5 (least deprived)	72 (18.2)	59 (17.3)	131 (17.8)
Body site of PC			
Ear	41 (10.4)	4 (1.2)	45 (6.1)
Eyelid	3 (0.8)	3 (0.9)	6 (0.8)
Lip (cutaneous)	0	3 (0.9)	3 (0.4)
Lower limb	93 (23.5)	168 (49.1)	261 (35.4)
Other part of face NOS	67 (16.9)	51 (14.9)	118 (16.0)
Scalp and neck	74 (18.7)	27 (7.9)	101 (13.7)
Trunk	53 (13.4)	43 (12.6)	96 (13.0)
Upper limb	57 (14.4)	36 (10.5)	93 (12.6)
Vulva NOS	0	2 (0.6)	2 (0.3)
Skin NOS	8 (2.0)	5 (1.5)	13 (1.76)

Data are *n* (%) unless specified otherwise. IMD, Indices of Multiple Deprivation; IQR, interquartile range; NOS, not otherwise specified.

[95% confidence interval (CI) 0.28–0.35] per 100 000 PY for males and 0.19 (95% CI 0.17–0.21) per 100 000 PY for females (Figure 2a). The EASR of PC in England from 2013 to 18 was 0.25 (95% CI 0.23–0.27) per 100 000 PY for the whole population (Figure 2b). The trend in EASR for the total population in England was relatively stable. (Figure 2).

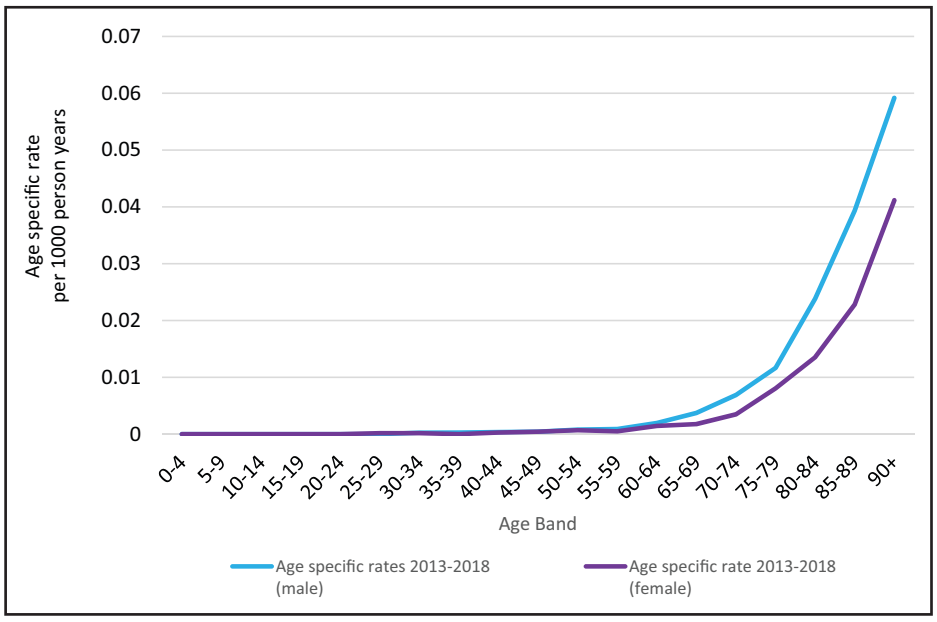


Figure 1 Age-specific incidence rate per 100 000 person-years for males and females diagnosed between 2013 and 2018 in England.

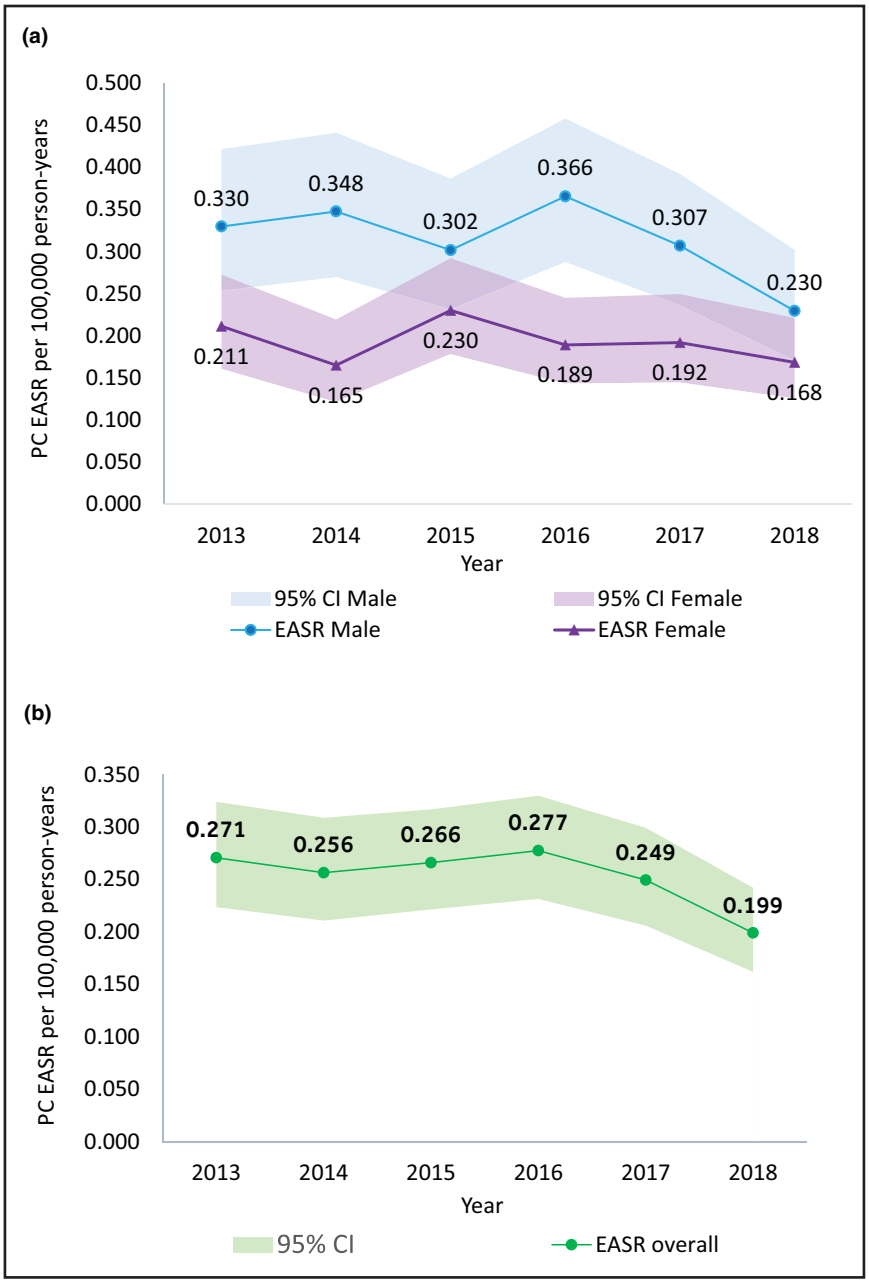


Figure 2 Trends in annual European age standardized rates (EASRs) of porocarcinoma (PC) in England 2013–2018. (a) For males and females. (b) For the whole population. Rates are presented as EASR per 100 000 person-years with 95% confidence intervals (95% CI).

Porocarcinoma regional incidence

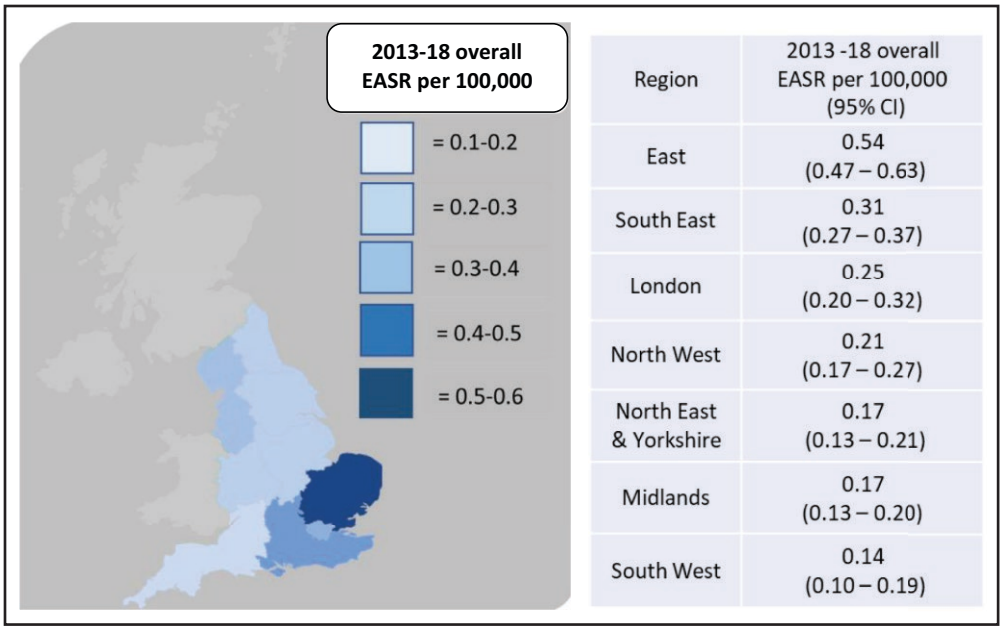
The East of England had the highest regional incidence of PC during 2013–2018 (EASR of 0.54, 95% CI 0.47–0.63 per 100 000 PY), followed by South-East of England (0.31, 95% CI 0.27–0.37 per 100 000 PY). The regional EASR was lowest in the South-West region (EASR of 0.14, 95% CI 0.10–0.19 per 100 000 PY). Other regional EASRs ranged from 0.17 to 0.31 per 100 000 PY (Figure 3).

Porocarcinoma diagnosis and treatment

In total, 624 (84.6%) patients had surgical codes associated with their tumour. Some patients received the same type of procedure or treatment more than once and others received more than one type of procedure or treatment. A total of 725 surgical codes was recorded; some patients had received both a diagnostic and a treatment procedure (Table 2). There were 84 (11.6%) patients who received surgical diagnostic procedures and 641 (88.4%) who received surgical treatment. In total, 529 (73.0.%) patients were treated by excision and/or flap/graft repair and 67 (9.2%) patients required re-excisions. There were 11 (1.5%) patients who received MMS.

Porocarcinoma survival

The median follow-up time was 39 months (IQR 24–60). At the end of follow-up, 398 (53.9%) patients had died and



Region	2013 -18 overall EASR per 100,000 (95% CI)
East	0.54 (0.47 – 0.63)
South East	0.31 (0.27 – 0.37)
London	0.25 (0.20 – 0.32)
North West	0.21 (0.17 – 0.27)
North East & Yorkshire	0.17 (0.13 – 0.21)
Midlands	0.17 (0.13 – 0.20)
South West	0.14 (0.10 – 0.19)

Figure 3 Regional variation in porocarcinoma (PC) European age standardized rates (EASRs) for 2013–2018 in England. 95% CI, 95% confidence intervals.

340 (46.1%) were alive. The Kaplan–Meier survival curves showed a similar survival pattern for males and females (Figure 4a). The median Kaplan–Meier survival time was 4.1 years (49 months) and 4.8 years (58 months) after the diagnosis of PC for males and females, respectively. The median Kaplan–Meier survival time for the whole cohort was 4.4 years (53 months) after the diagnosis of PC (Figure 4b). Survival rates for males and females were compared using the log-rank test (Figure S2; see Supporting Information). There were no significant differences between the survival times of males and females. The 1-, 3- and 5-year all-cause survival rate (Figure S3; see Supporting Information) was 87.3% (95% CI 84.6–89.5), 61.8% (95% CI 58.1–65.2) and 45.4% (95% CI 41.3–49.3).

Discussion

The epidemiology of PC is understudied; skin appendageal carcinoma data are often not included in cancer registries or not routinely reported.[16] Improvements to ICD–Oncology 3 in 2013 allowed identification of PC within NDRS.

These data represent the largest series reported to date, consisting of 738 patients. This study showed a stable trend in EASRs of PC in England 2013–2018, with an overall EASR reported as 0.25 (95% CI 0.23–0.27) per 100 000 PY. This is twice the EASR in Finland 2007–2017 (0.13 per 100 000 PY) and five times the EASR in the USA 2000–2018 (0.045 per 100 000 PY).[4,17] The most affected sites were lower limbs (35.4%, $n=261$) followed by the face (16.0%, $n=118$). A 2017 meta-analysis reported the head and neck (39.9%) and the lower extremities (33.9%) were affected the most. A reason for this disparity is that meta-analyses are subject to selection bias.[3]

The median Kaplan–Meier survival time for the whole cohort was 4.4 years (53 months) after the diagnosis of PC. Comparatively, the median expected survival for an 82-year-old UK resident male and female in 2014–2016 was 7 years (84 months) and 8 years (96 months), respectively.[18] Two recent PC epidemiology studies in the USA used Kaplan–Meier estimates to report overall all-cause 5-year survival rates of 74.8% and 68.8%.[2,19] Conversely, the all-cause 5-year survival rate of our cohort was 45.4% (95% CI 41.3–49.3). This difference may be explained by the older group of patients included in our study (median age 82 years old), compared with the US studies (median age 67 years old). Other literature on PC reported mean ages at diagnosis that varied from 67 to 76 years.[3,4,20,21]

This study used all-cause mortality data, rather than disease-specific mortality. Defining disease-specific data from the registry is complex as mortality coding is restricted to ICD-10 codes that group all nonmelanoma skin cancers (C44) together as a potential cause for death.

There was regional variation in PC incidence rates, with EASR in the East of England being three times higher than the South West where the regional rates were the lowest.

Table 2 Summary of relevant surgical diagnostic procedure and treatment codes ($n=725$) 6 months after the diagnosis of porocarcinoma

Type	*n* (%)
Surgical diagnostic procedures	
Curettage or shave biopsy	37 (5.1)
Punch or incisional biopsy	22 (3.0)
Biopsy NOS	21 (2.9)
Lymph node biopsy	4 (0.6)
Surgical treatment	
Excision and/or flap/graft repair	529 (73.0)
Re-excision	67 (9.2)
Definitive lymph node excisions/dissections	20 (2.8)
Amputation	14 (1.9)
Mohs micrographic surgery	11 (1.5)

NOS, not otherwise specified.

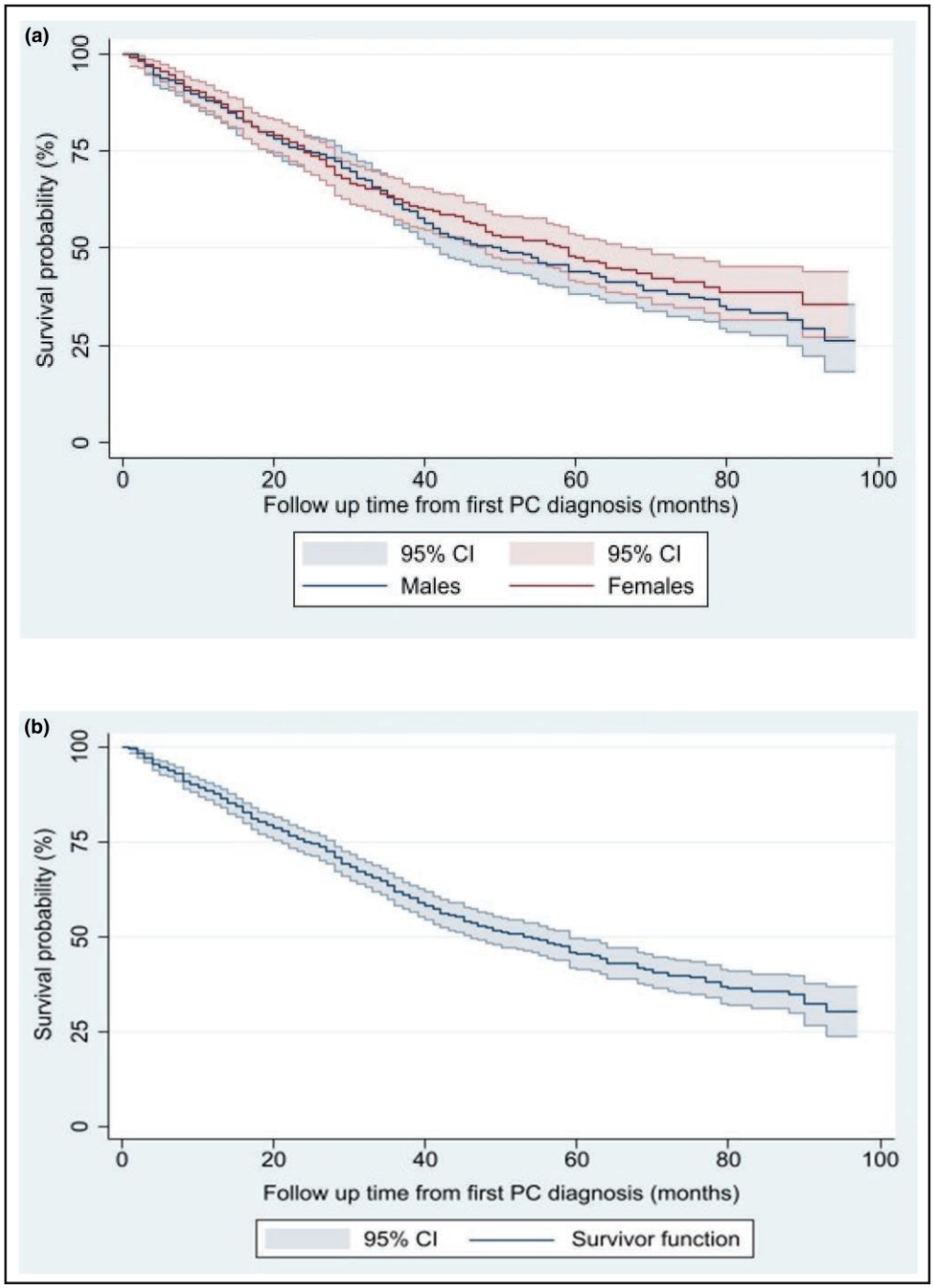


Figure 4 Kaplan–Meier survival curves for (a) males and females and (b) for the whole cohort. Figures show the survival probability as a percentage (%) with an associated 95% confidence interval (CI). PC, porocarcinoma.

This was unexpected considering the latitudinal increase in incidence often seen for skin cancer. The regional EASRs across England for basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC) has previously been shown to be highest in southern regions.[22,23]

Although there is the possibility of a true variation in regional PC incidence, higher PC incidence in the East may be because of differences in how PC is diagnosed and registered in this region. The East of England has historically been referred to as a registration data-quality beacon, with a reputation for excellence and a completeness of data that may account for higher registrations in this region. However, since the nationalization of cancer registries in 2013, this is likely to be less relevant, although regional registration practices may still differ. Additionally, a previous epidemiology PC study in 2018 covering a part of the East of England may have increased awareness in clinicians and pathologists in this region.[5]

Deprivation was not associated with PC incidence, which varies from other skin cancers such as melanoma, BCC and cSCC that are more common in those less deprived.[23,24] This may be explained by increased access to travel abroad and

thus greater ultraviolet exposure. This association between PC and ultraviolet radiation is not fully understood.[9]

The 2014–2019 CARADERM (Les CAncers RAres DERMatologiques) study found that sweat gland and duct carcinomas showed the most diagnostic discrepancy between original pathological diagnosis and expert pathological review.[25] Therefore, expert histopathological review using a regional or national model such as the CARADERM network together with use of, and research into, improved genomic and immunohistochemical diagnostic criteria for PC are likely to reduce the burden of diagnostic uncertainty for healthcare professionals and patients. The ongoing deployment of digital pathology in the NHS increases the potential for national expert histopathological review of rare cancers such as PC.

NDRS data rely upon accurate histological reporting or multidisciplinary team (MTD) discussion and so if a patient does not undergo histological confirmation of PC or MDT discussion then they may be missing from NDRS data. The inability to identify advanced disease from the registry data limits this study. Furthermore, treatment codes were not directly linked to PC tumours and relevant codes during a period of 1 month before or 6 months after the diagnosis date were instead used, which may identify procedure codes for other skin cancers during that time period.

Conclusions

This study presents, to the best of our knowledge, the first national epidemiology report of PC in England. There is large variation in the EASRs of PC across England. This may reflect differences in how PC is diagnosed and registered in different English regions. These data add to current epidemiological data and support national assessment of the management of PC, which will inform future studies and guideline development.

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Conflicts of interest

K.M. is on the *CED* editorial board. N.J.L. is on the *CED* editorial advisory board and is a trustee of the British Association of Dermatologists (BAD), a charity which owns *CED*. B.v.B. is an employee of BAD. The other authors declare they have no conflicts of interest.

Data availability

Data available within the article or its supplementary materials and further data are available on request from the authors.

Ethics statement

Ethical approval: project proposal was approved by the National Disease Registration Service (NDRS) project development steering committee. Ethical approval was not required. Informed consent: The National Disease Registries Directions 2021, Sections 254(1) and 254(6) of the 2012 Health and Social Care Act (the 2012 Act) allows the collection and processing of data on patients with cancer in England by NHS Digital and NDRS. Patients may opt out of having their confidential patient information being used for research and planning. Published data was required to meet the anonymization standard for publishing health and social care data (2013, version 1.0), including satisfying k-anonymity requirements and approval from the Caldicott Guardian.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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