Regional variations of Basal cell carcinoma incidence in the UK using THIN database (2004–2010)

Running title: BCC incidence in the UK population

A. Musah[1], J.E. Gibson[1], J. Leonardi-Bee[1], M.R. Cave[2], E.L. Ander[2], F. Bath-Hextall[3]

[1]Division of Epidemiology and Public Health, Clinical Sciences Building (Phase 2), University of Nottingham, Nottingham NG5 1PB, UK

[2]British Geological Survey, Environmental Science Centre, Nottingham NG12 5GG, UK

[3]Centre of Evidence Based Dermatology, King's Meadow Campus, University of Nottingham, Nottingham NG7 2NR, UK

Conflicts of interest: None declared

What is already known about this topic?

- Incidence rate of BCC in the UK is high compared with other types of nonmelanoma skin cancers.
- Risk factors include exposure to UV through sunlight or tanning beds, age and ethnicity.
- Incidence in the younger population is rising, although incidence increases after 40 years of age.
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What does this study add?

- These findings provide novel estimates for regional incidence rates across the UK.
- They provide novel estimates for levels of socioeconomic deprivation in UK.

Corresponding author: Anwar Musah

Room C109, Division of Epidemiology and Public Health,

Clinical Sciences Building (Phase 2), Nottingham City Hospital Campus,

University of Nottingham, Nottingham, NG5 1PB, UK

Telephone: +44 (0)115 823 1382;

Email address: mcxam23@nottingham.ac.uk

Abstract

Background Basal cell carcinoma (BCC) is one the most common type of nonmelanoma skin cancer affecting the Caucasian population; however, little is known about how the incidence varies across regions in the UK.

Methods Data from 2004 to 2010 was obtained from The Health Improvement Network (THIN database). European and World Age-standardised incidence rates (EASRs and WASRs, respectively) were obtained for country-level estimates and levels of socioeconomic deprivation, whilst Strategic Health Authority-level estimates were directly age-sex

standardised to UK standard population. Incidence rate ratios (IRR) were estimated using multivariable Poisson regression models.

Results The overall EASR and WASR of BCC in the UK was 98.6 per 100,000 person-years and 66.9 per 100,000 person-years, respectively. Regional-level incidence rates indicated a significant geographical variation in the distribution of BCC, which was more pronounced in the southern parts of the country; South East Coast had the highest BCC rate followed by South Central, Wales and South West. Incidence rates were substantially higher in the least deprived groups and we observed a trend of decreasing incidence with increasing levels of deprivation ($p < 0.001$). Finally, in terms of age groups, the largest annual increase was observed among those aged 30 to 49 years.

Conclusions BCC is an increasing health problem in the UK; the southern regions of UK and those in the least deprived groups had a higher incidence of BCC. Our finding indicates the increased incidence of BCC for younger age groups below 49 years.

Basal cell carcinoma (BCC), a form of non-melanoma skin cancer (NMSC) is the most common malignant neoplasm found in humans and the incidence is increasing in the US, Canada, Australia and most European countries.[1–5] Risk factors include exposure to UV through sunlight or tanning beds,[6–8] advancement of age,[9] gender,[9,10] skin type (i.e. fair, white or freckled skin),[9,11–13] history of skin cancer,[14] and some environmental and occupational factors.[15]

The incidence of BCC in the UK is increasing at an unprecedented rate. The overall incidence of NMSC is estimated to be well over 100,000 cases per year, with BCC accounting for 75% of cases, squamous cell carcinoma (SCC) for 20% and other rare skin cancer types (i.e.

Merkel cell carcinoma, Kaposi's sarcoma and T-cell lymphoma of the skin) for 5%.[16] Recent studies have shown that whilst the incidence of BCC varies geographically in the UK[1,17], rapidly increasing incidence has been observed in many areas. For instance, in West Glamorgan (Wales) the incidence rate increased by 60% between 1988 and 1998.[18] Similarly, in England, the incidence of BCC in North Humberside tripled over the 13 year period from 1978 to 1991.[1,19] Scotland and Northern Ireland have lower incidence of BCC relative to England and Wales, however, within the past two decades the incidence of BCC among men has risen approximately by 16% in Scotland and 18% in Northern Ireland.[20,21] The elderly population contributes substantially to the disease burden, with risk of BCC increasing after 40 years of age, however, we are now seeing an increased incidence in younger people and in particular those of ≤30 years of age.[22]

Socioeconomic status and deprivation are also known to modify the risk of BCC. Some studies suggest that BCC appears to be more common in those belonging to higher social class[13,23,24]. However such associations are not well understood and the distribution of BCC in terms of levels socioeconomic deprivation in the UK population is unknown.

We therefore used data from a UK-wide database of primary care medical records to derive contemporary regional breakdowns of the incidence of BCC in UK. We present novel incidence rate estimates stratified by level of socioeconomic deprivation in the UK and additional analyses examining whether BCC incidence has continued to increase in recent years, particularly in the younger age groups.

Materials and Methods

Study design and data source

We conducted a large population-based study using data from The Health Improvement Network (THIN). THIN is a large database comprised of anonymised primary care electronic medical records of more than 10 million patients from across all regions of the UK. The information contained within THIN includes details on all diagnoses made by or reported to the general practitioner, as well as other additional health information relevant to primary care. THIN is recognised for its completeness and accuracy of data recording, and has been validated for its suitability for use in medical research,[25] including specific validation of diagnoses of BCC.[26] In addition, a range of socio-demographic indicators are available in THIN, including quintiles of Townsend Deprivation Index[27] in each patient's postcode of residence.

Study population

The medical histories and deprivation indicators of all adults with a first recorded diagnosis of BCC between January 1st, 2004 and December 31st, 2010, were extracted from THIN. Subjects diagnosed with Basal cell nevus syndrome (or Gorlin's syndrome), organoid naevi or other genetic syndromes were excluded from the study. Patient ages were categorised into 10-year bands (18–29, 30–39, 40–49, 50–64, 65–79 and 80+ years). Patients were categorised into thirteen regional based (in England) on the Strategic Health Authority (SHA) or devolved government administration (Wales, Scotland and Northern Ireland) to which each patient's primary care practice belongs as follows: North East, North West, Yorkshire and Humber, East Midlands, West Midlands, East of England, London, South East Coast, South

Central, South West, Wales, Scotland and Northern Ireland. This is the only spatially referenced data available from the anonymised patient records.

Statistical analysis

The primary outcome measures were incidence rates (IR) of BCC in the whole UK, in its constituent countries and principalities, and each English SHA region. We also estimated the incidence of BCC across quintiles of socioeconomic deprivation groups. IRs were calculated as the number of patients receiving their first diagnosis of BCC divided by the total number of person-years at risk. Diagnoses within the first year of registration with a participating primary care practice were excluded as such recordings can relate to prevalent, rather than incident, events (being an artefact of back-entry of records from a previous practitioner). Second or subsequent diagnoses were also excluded as these are difficult to differentiate from recurrences and follow-up consultations in primary care records. Population denominators were mid-year (1st July) total numbers of persons registered for at least one year at a primary care practice enrolled in THIN. IRs are presented as rates per 100,000 person-years. We derived estimates for European and World Age-Standardised incidence Rates (EASRs and WASRs, respectively) using the direct standardisation method to allow direct comparisons between country-level incidence rates (i.e. UK, England, Scotland, Northern Ireland and Wales) with other populations.[28] IRs of BCC at a regional level were directly age-sex standardised to the UK standard population.[29]

Poisson multivariable regression model was used to examine the effects of all factors (i.e. calendar year of diagnosis, socioeconomic deprivation and regions) on the incidence of BCC adjusted for sex and age groups. Stratified Poisson multivariable analyses were used to determine whether associations between all factors and the incidence of BCC were modified

by sex, while controlling for age groups. For secondary analyses, we further used stratified models by age groups to assess calendar years as a continuous variable in order to determine the average change (per year) in incidence of BCC. Incidence rate ratios (IRR) were estimated with 95% confidence intervals (CI). All statistical analyses were carried out using STATA version 12 (STATA Corporation, College Station, TX, USA).

Results

There were 38,121 incident cases of BCC were identified from 546 general practices in the THIN database. Mean age was 64 years (standard deviation, SD 13 years) with slightly more men (52.4%) diagnosed with a BCC.

Incidence rates of BCC at country and regional level

The crude IR of BCC between 2004 and 2010 in our THIN database was 171.9 per 100,000 person-years (95% CI: 170.1–173.6). The crude IR of BCC was higher among men (183.1 per 100,000 person-years; 95% CI: 180.5–185.6) than women (161.0 per 100,000 person-years; 95% CI: 158.7–163.4) (Table 1). When comparing the overall figures between 2004 and 2010, we found that there was an increase from 154.0 per 100,000 person-years to 182.0 per 100,000 person-years. Our Poisson multivariable regression model show that the overall significant 16% increase in incidence in 2010 as compared to 2004 (IRR 1.16, 95% CI: 1.11–1.20), which equates to an average increase of 2.5% per year (95% CI: 1.9% – 3.0%; *p* for trend = 0.001) (Table 2).

Comparatively, at a country-level, Wales has significantly the highest overall crude rate of BCC (IR 196.4, 95% CI: 189.2–203.8) followed by England (IR 178.5, 95% CI: 176.5–

180.5). We observed the incidences were low in Scotland (IR 128.7, 95% CI: 124.6–133.0) and Northern Ireland (IR 131.6, 95% CI: 123.3–140.3) (Table 1), and from the 95% confidence intervals, there is no significant difference in the incidence of BCC between Scotland and Northern Ireland.

We observed important geographical variations in the distribution of BCC (Figure 1). The age-sex standardised incidence rate of BCC in South East Coast, South West, South Central and Wales are significantly higher than other regions of the UK (Table 3). Our models show that the incidence of BCC were significantly lower in West Midlands (IRR 0.92, 95% CI: 0.88–0.97), Northern Ireland (IRR 0.92, 95% CI: 0.85–0.98) and Scotland (IRR 0.87, 95% CI: 0.83–0.91) than in London (the referent). Conversely, we found that the incidence of BCC was significantly higher in South East Coast (IRR 1.28, 95% CI: 1.22–1.34), Wales (IRR 1.23, 95% CI: 1.16–1.29), South Central (IRR 1.21, 95% CI: 1.15–1.27), South West (IRR 1.15, 95% CI: 1.09–1.21) than in London. Our results show no substantial sex-specific difference in the incidence of BCC in any regions.

Trends in BCC over time by age group

Models were stratified by age groups to determine the effects of calendar years on the incidence of BCC. Our results show a small average increase of 0.4% per year in the age group of 18–29 years, however, this failed to reach statistical significance (95% CI: -8.0% to 9.3%; $p = 0.91$). In particular, the largest average increase in incidence was observed for those in 30–39 years (3.9% per year, 95% CI: 0.2% to 7.7%; $p = 0.04$) and 40–49 (4.0% per year, 95% CI: 2.0% to 6.1%; $p < 0.001$) age groups (Figure 2).

Incidence rates by socioeconomic deprivation

The crude incidence of BCC was significantly highest for those living in areas with the lower levels of deprivation, with estimates of 222.5 per 100,000 person-years (95% CI: 218.5–226.5) and 203.2 per 100,000 person-years (95% CI: 199.1–207.3) for those in the 1st quintile (least deprived) and 2nd quintile, respectively (Table 4). We observed that the incidence of BCC was lowest for those living in the most deprived areas (IR 110.6, 95% CI: 106.8–114.7).

Using our models, there appeared to be a linear effect of decreasing incidence of BCC with increasing levels of deprivation (*p* for trend < 0.001). We found that those living in the least deprived areas were 50% significantly more likely to have a BCC than those with the highest levels of deprivation (IRR 1.50, 95% CI: 1.44–1.56). Our models also show substantial difference in magnitude of the incidence of BCC between men and women, where the incidence rate was higher in men than in women.

Discussion

Our results indicate that the incidence rate of BCC is increasing in the general population, in particular amongst those aged 30 to 49 years. It shows that Wales and the southern parts of England have the highest recorded rates of skin BCC. For socioeconomic deprivation, incidence of BCC was consistently higher in the least deprived groups. Based on our estimates (i.e. EASRs), they show that approximately 61,500 new cases of BCC are diagnosed annually in the UK population. Previous reports using EASRs have estimated that 53,000 cases of BCC were reported yearly using a cohort between 1996 and 2003,[17] comparatively; this represents an overall increase of 16% in diagnosis rates in the past decade.

This study has several strengths; to our knowledge, it uses the largest sample size of incident cases of BCC compared to previous research conducted in the UK.[13,17–21,23] Due to our large sample size means that our findings are unlikely to be due by chance. Also, the data was obtained from a national database and prospectively recorded by GPs, thus excluding the possibility of recording or recall bias in both our exposure and outcome. The major limitation is our inability to account for important factors such as history of sun exposure during childhood and adolescence (i.e. frequency of sunburns and overseas holidays),[30,31] latitudinal position (i.e. proximity to the equator),[9,32] settings of occupation (i.e. indoor, mixed or outdoor)[33] and skin type (i.e. fair, white or freckled skin)[13]. In addition, we were unable to classify adults according to subtypes of BCC (i.e. superficial, nodular or infiltrative).

Our results for country-level incidence rates were consistent with previous studies showing escalating rates in England, Northern Ireland, Scotland and Wales.[18–21] The most likely explanation for the rise in incidence may be linked to previous behaviour with regards to sun exposure during childhood or adolescence. Exposure to UV radiation during this stage plays a significant role in the future development of BCC. Previous studies have shown that subjects to have reported to travel frequently and spend more than 4 or 5 weeks (per year) at the beach before the age of 20 years were more likely to have developed the skin malignancy in their adulthood.[30,31] Although we were unable to account for this factor, history of sun exposure through frequent holidays to sunnier places has been a strong predictor for BCC. Another likely explanation may be possibly due to UK's aging population. BCC is highly prevalent in the older age groups; in our cohort, the number of cases diagnosed with the skin malignancy was consistently high among those aged 50+ years.

We found a significant increase among those aged 30–39 and 40–49 years. A previous study has shown similar findings, where the annual increase in incidence was estimated to be approximately 3.9% and 5.2% for 30–39 and 40–49 years, respectively, although these estimates did not reach statistical significance.[17] Interestingly, we found an increase among those aged 18–29 years is increasing, although our models showed no statistical significance. The incidence of BCC in this particular age group have risen to approximately 5.2 per 100,000 person-year in 2009 (Figure 2), which is consistent with escalating rates observed by others.[22]

We observed especially high incidence in areas of South East Coast, South Central, South West and Wales. Compared to London, we found there were significant increases in the risk of developing BCC in these areas. This observation may be linked to several environment factors. The most prominent is the latitudinal position of a location.[9,32] Areas in proximity to the equator, but situated in the temperate zone usually experience prolonged duration of sunlight in the summer season. In the UK, the hours of sunshine normally last longer in the south than the northern regions of UK, especially during the summer season, the southern parts of England and Wales are usually known to receive the greatest hours of annual sunshine.[34]

Our findings for socioeconomic deprivation showed that the incidence was high among the least deprived groups, and that the risks for BCC tends to decrease as the level of deprivation increased. Our results are consistent with previous studies conducted in the UK and Netherlands.[13,24] It is interesting to note the wide difference in incidence of BCC between the least and most deprived groups which may be an indication that socioeconomic status or deprivation is risk factor for BCC. This observation may be linked to higher levels of income

for frequent holidays overseas to sunnier places, thereby exposing the skin to sunlight, or having available funds for pursuing other lifestyle habits which are risk factors for BCC, for instance, the frequent use of tanning beds[8–10] or consumption of alcohol.[35] Interestingly, we also observed that the incidences differ substantially between sexes, perhaps, this may possibly be due to differences in behaviour in terms of sun exposure, clothing habits and tanning behaviour.[13,24]

BCC is an increasingly important health problem in the UK, with extremely high levels observed in the least deprived groups, and in the southern parts of the UK. Due to the multi-factorial nature of BCC, further work is warranted to identify causes, as well as, investigate the detailed reasons of these findings. Our results demonstrate that the incidence of BCC will continue to rise much higher in all age bands if it remains unchecked, which will have a significant impact on the workload and costs for health services. Better strategies are required to inform the public of the risk factors associated with the skin malignancy, as well as, which preventive measures can be implemented to avoid future development of BCC.

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Table 1: Crude and sex-specific age-standardised incidence rates of Basal cell carcinoma in UK and countries, THIN database (2004–2010)

	Men (*n*)	Women (*n*)	Overall (*N*)
United Kingdom			
Crude	183.1 (19,960)	161.0 (18,161)	171.9 (38,121)
EASR[a]	112.2	88.1	98.6
WASR[b]	74.8	60.7	66.9
England			
Crude	189.9 (16,079)	167.5 (14,671)	178.5 (30,750)
EASR	114.9	91.4	101.5
WASR	76.6	63.1	69.0
Northern Ireland			
Crude	144.7 (502)	119.3 (439)	131.6 (941)
EASR	99.6	67.5	81.6
WASR	66.2	45.2	54.6
Scotland			
Crude	137.9 (1,904)	119.8 (1,704)	128.7 (3,608)
EASR	89.3	65.6	75.9
WASR	59.1	44.7	51.1
Wales			
Crude	208.1 (1,475)	185.0 (1,347)	196.4 (2,822)
EASR	128.7	103.1	114.4
WASR	86.4	71.3	78.1

[a]EASR, European age-standardised rate.
[b]WASR, World age-standardised rate.

Table 2: Overall and sex-specific incidence rate ratio (IRR) estimates showing associations between incidence of BCC and risk factors.

	Men[a]		Women[a]		Overall[b]	
	IRR	(95% CI)[c]	IRR	(95% CI)	IRR	(95% CI)
Years						
2004	1		1		1	
2005	1.07	(1.02 – 1.14)	1.00	(0.94 – 1.06)	1.04	(0.99 – 1.08)
2006	1.10	(1.04 – 1.16)	1.07	(1.07 – 1.13)	1.09	(1.04 – 1.13)
2007	1.14	(1.08 – 1.21)	1.16	(1.10 – 1.23)	1.15	(1.10 – 1.20)
2008	1.16	(1.10 – 1.22)	1.16	(1.10 – 1.23)	1.16	(1.12 – 1.20)
2009	1.15	(1.09 – 1.22)	1.13	(1.07 – 1.20)	1.15	(1.10 – 1.19)
2010	1.12	(1.06 – 1.18)	1.21	(1.14 – 1.27)	1.16	(1.12 – 1.21)
Annual increase	1.8%	(1.1% – 2.5%)	3.2%	(2.5% – 4.0%)	2.5%	(1.9% – 3.0%)
(*p* for trend)	$p = 0.003$		$p = 0.008$		$p < 0.001$	
Socioeconomic deprivation[d]						
5th (Most deprived)	1		1		1	
4th	1.13	(1.06 – 1.20)	1.01	(0.95 – 1.08)	1.07	(1.02 – 1.12)
3rd	1.28	(1.21 – 1.36)	1.13	(1.07 – 1.20)	1.21	(1.16 – 1.26)
2nd	1.47	(1.39 – 1.56)	1.26	(1.19 – 1.33)	1.37	(1.31 – 1.43)
1st (Least deprived)	1.62	(1.53 – 1.72)	1.36	(1.28 – 1.44)	1.50	(1.44 – 1.56)
Unknown	1.22	(1.11 – 1.35)	1.12	(1.01 – 1.23)	1.17	(1.09 – 1.25)
(*p* for trend)	$p < 0.001$		$p < 0.001$		$p < 0.001$	
Regions						
London	1		1		1	
Scotland	0.91	(0.85 – 0.98)	0.82	(0.76 – 0.88)	0.87	(0.83 – 0.91)
Northern Ireland	0.99	(0.89 – 1.10)	0.84	(0.76 – 0.94)	0.92	(0.85 – 0.98)
West Midlands	0.93	(0.87 – 1.00)	0.92	(0.85 – 0.99)	0.92	(0.88 – 0.97)
North West	0.98	(0.91 – 1.05)	0.93	(0.87 – 1.00)	0.96	(0.91 – 1.01)
Yorkshire & Humber	1.04	(0.96 – 1.15)	0.98	(0.89 – 1.08)	1.01	(0.95 – 1.08)
East Midlands	1.02	(0.93 – 1.11)	1.02	(0.93 – 1.12)	1.02	(0.96 – 1.09)
North East	1.08	(0.97 – 1.19)	1.03	(0.93 – 1.14)	1.05	(0.98 – 1.13)
East of England	1.05	(0.98 – 1.13)	1.02	(0.95 – 1.10)	1.04	(0.98 – 1.09)
Wales	1.25	(1.17 – 1.35)	1.19	(1.11 – 1.29)	1.23	(1.16 – 1.29)
South Central	1.24	(1.16 – 1.32)	1.18	(1.10 – 1.26)	1.21	(1.15 – 1.27)
South West	1.19	(1.12 – 1.28)	1.10	(1.03 – 1.18)	1.15	(1.09 – 1.21)
South East Coast	1.30	(1.21 – 1.39)	1.27	(1.18 – 1.36)	1.28	(1.22 – 1.34)

[a]Models were stratified by sex, includes all covariates and adjusted for age groups: i.e. 18–29, 30–39, 40–49, 50–64, 65–79 and 80+ years.
[b]Overall model includes all covariates and adjusted for sex and age bands: i.e. 18–29, 30–39, 40–49, 50–64, 65–79 and 80+ years.
[c]IRR, incidence rate ratio; CI, 95% confidence interval.
[d]Quintiles of Townsend deprivation index.

Table 3: Regional-level estimates for sex-specific and age-sex standardised incidence rates of Basal cell carcinoma in UK, THIN database (2004–2010)

Regions	Age-sex standardised rate[a] Overall (N)	Sex-specific age standardised rate[b] Men (n)	Women (n)
Scotland	127.9	139.5 (1,904)	116.8 (1,704)
Northern Ireland	138.4	155.4 (502)	122.2 (439)
London	144.0	148.6 (1,432)	139.6 (1,415)
West Midlands	144.1	152.2 (1,537)	136.3 (1,422)
North West	146.5	156.6 (1,785)	136.8 (1,627)
Yorkshire & Humber	151.4	163.3 (686)	140.0 (618)
North East	156.0	165.2 (539)	147.2 (503)
East Midlands	158.6	166.4 (776)	151.2 (718)
East of England	161.1	170.7 (1,457)	151.8 (1,325)
South West	180.2	196.2 (2,438)	165.0 (2,123)
Wales	185.7	197.6 (1,475)	174.4 (1,347)
South Central	193.5	208.7 (2,998)	178.9 (2,645)
South East Coast	202.7	215.0 (2,431)	191.0 (2,275)

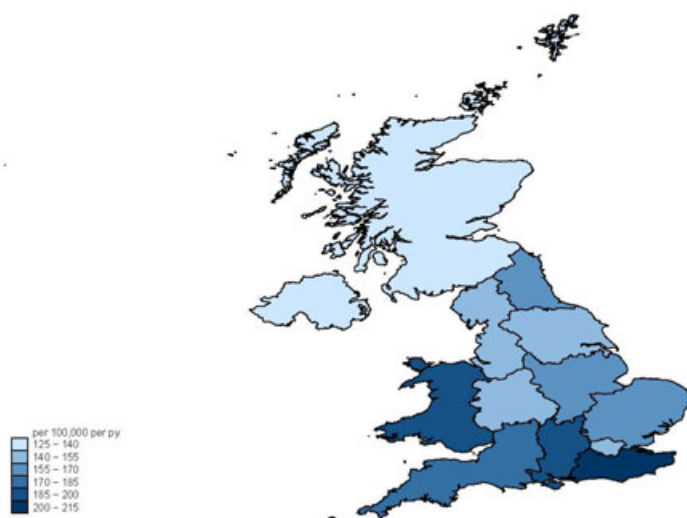[a]Estimates are directly age-sex standardised using UK as the standard population.
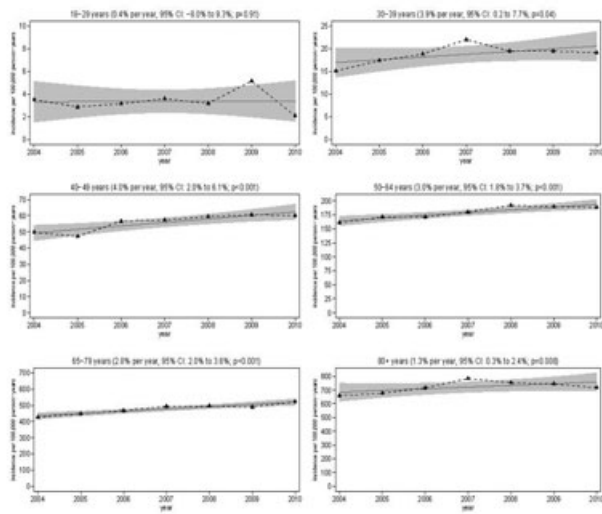[b]Sex-specific estimates are directly age-standardised using the UK as the standard population.

Table 4: Crude and sex-specific age-standardised incidence rates of Basal cell carcinoma in the UK, by quintiles of Townsend deprivation index (THIN database 2004–2010)

(a) Deprivation index	1	2	3	4	5	Unknown
Overall						
Crude	222.5 (12,070)	203.2 (9,575)	162.1 (7,175)	131.7 (5,173)	110.7 (3,013)	115.6 (1,115)
EASR[a]	120.2	106.9	92.2	79.4	70.6	–
WASR[b]	82.1	72.7	62.4	53.5	47.2	–
Men						
Crude	246.7 (6,602)	220.8 (5,097)	169.7 (3,677)	134.3 (2,583)	106.0 (1,441)	119.0 (560)
EASR	137.5	122.0	104.7	90.4	77.4	–
WASR	92.3	81.5	69.6	59.7	50.9	–
Women						
Crude	198.9 (5,468)	186.2 (4,478)	154.7 (3,498)	129.2 (2,590)	115.3 (1,572)	112.4 (555)
EASR	105.7	94.9	83.1	71.9	66.2	–
WASR	73.2	65.7	57.1	49.2	44.7	–

[a]EASR, European age-standardised rate.
[b]WASR, World age-standardised rate.

per 100,000 per py
125 – 140
140 – 155
155 – 170
170 – 185
185 – 200
200 – 215

(NB: The scales on the y¯axis vary)