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Primary liver cancer incidence and survival in ethnic groups in England, 2001–2007

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ABSTRACT

Background: The patterns of primary liver cancer incidence and survival are not known for detailed ethnic groups within the UK. *Methods*: Data on patients resident in England diagnosed with primary liver cancer (ICD-10 C22) between 2001 and 2007 were extracted from the National Cancer Data Repository. Age-standardised incidence rate ratios (IRRs) were calculated for different ethnic groups separately for males and females, using the White ethnic groups as baselines. Overall survival was analysed using Cox regression, adjusting sequentially for age, socioeconomic deprivation and co-morbidity. *Results*: Ethnicity data were available for 75% (13,139/17,458) of primary liver cancer patients. Compared with the White male baseline, Chinese males had the highest IRR. Black African, Bangladeshi, Pakistani and Indian men also had statistically significant high IRRs. Black Caribbean men had a marginally elevated incidence rate compared with White men. In comparison with White women, Pakistani women had the highest IRR. Bangladeshi, Chinese, Black African and Indian women also had high IRRs. As observed in men, Black Caribbean women had an incidence rate closer to that of White women. Pakistani men and women, Black African women and Chinese men had statistically significantly better survival compared with their White counterparts. *Conclusion*: The variation found in the incidence of primary liver cancer, could be due to established risk factors such as hepatitis B and C infection being more prevalent among certain ethnic groups. Country of birth, age at migration and length of stay in England are likely to be important factors in this disease, and future research should examine these where possible.

1. Introduction

Primary liver cancer occurs worldwide but incidence rates vary between countries. In 2008, around 85% of cases diagnosed were in less developed regions and the highest age-standardised incidence rates were in Eastern and South-Eastern areas of Asia, and Middle and Western areas of Africa [1]. The incidence of primary liver cancer is relatively low in the UK, although it has been increasing over time [2]. Survival rates are low for patients with liver cancer [3,4] and it is the third most common cause of cancer death worldwide [1].

The most common subtypes of liver cancer are hepatocellular carcinoma and cholangiocarcinoma. The main risk factors for hepatocellular carcinoma are well established, and the importance of hepatitis B and C viruses, alcohol, tobacco and aflatoxin exposure vary in different parts of the world [5]. Hepatitis B infection is a major risk factor and is very common in China, South East Asia and Sub-Saharan Africa [5–7]. Hepatitis C virus has a low prevalence in the UK [8], however higher rates have been estimated in Pakistan and China [9]. In developed countries hepatitis C virus infection acquired via contaminated needles, and alcohol induced cirrhosis are important causes of this cancer [7]. Other factors, such as fatty liver disease, obesity and diabetes mellitus, have also been associated with primary liver cancer, although the relationship between these still require investigation [10,11]. Liver fluke infection is a particular problem in some areas of the world, most notably East Asia and Eastern Europe, and has been linked with cholangiocarcinoma [11,12].

Variations in incidence [7,13–16] and survival [17–21] have previously been shown between different ethnic groups in the US and the UK, although often examining only broader ethnic groups. This study examines primary liver cancer incidence and survival in England for more specific ethnic groups diagnosed between 2001 and 2007.

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Table 1
Characteristics table of patients diagnosed with primary liver cancer (ICD-10 C22), England, 2001–2007.

	Males		Females		Persons	
	N	%	*N*	%	*N*	%
Ethnicity						
White	7267	67.2	4606	69.3	11,873	68.0
Indian	149	1.4	74	1.1	223	1.3
Pakistani	136	1.3	74	1.1	210	1.2
Bangladeshi	54	0.5	20	0.3	74	0.4
Black Caribbean	90	0.8	51	0.8	141	0.8
Black African	104	1.0	29	0.4	133	0.8
Chinese	83	0.8	23	0.3	106	0.6
Other	275	2.5	104	1.6	379	2.2
Not known	2649	24.5	1670	25.1	4319	24.7
Age group						
<60	2403	22.2	1035	15.6	3438	19.7
60–69	2676	24.8	1216	18.3	3892	22.3
70–79	3580	33.1	2065	31.0	5645	32.3
80+	2148	19.9	2335	35.1	4483	25.7
Deprivation quintile						
1 (least deprived)	1883	17.4	1132	17.0	3015	17.3
2	1996	18.5	1253	18.8	3249	18.6
3	2114	19.6	1356	20.4	3470	19.9
4	2234	20.7	1371	20.6	3605	20.6
5 (most deprived)	2580	23.9	1539	23.1	4119	23.6
Total	10,807	100.0	6651	100.0	17,458	100.0

2. Methods

The National Cancer Data Repository contains combined data from each of the regional cancer registries on people resident in England who have been diagnosed with cancer. Information on residents of England who were diagnosed with primary liver cancer (ICD-10 code C22) between 2001 and 2007 was extracted from the National Cancer Data Repository. Records are linked to the Hospital Episode Statistics (HES) dataset, which contains self-assigned ethnicity information. Ethnicity was grouped into the following categories: White, Indian, Pakistani, Bangladeshi, Black Caribbean, Black African, Chinese, Other, and Not known.

Population data for each ethnic and age group for each year examined were from the Office for National Statistics. Data for 2001 were taken from that year's census, and population estimates were used for 2002–2007 [22]. Socioeconomic deprivation was measured using the income domain of the Indices of Deprivation 2004 [23]. The co-morbidity score used is based on episodes mentioning non-cancer diagnoses from HES occurring one year before the primary liver cancer diagnosis date [24]. The conditions are weighted according to their severity [25] and scores are generated and grouped as 0 (where no co-morbid conditions were recorded), 1, 2 or more, and Not known.

As not all patients had an ethnic group recorded, any age-standardised incidence rates calculated would be too low, as there is no corresponding population data for these patients. Therefore male and female age-standardised incidence rate ratios (IRRs) were calculated for each ethnic group, using the White groups as the baselines. Confidence intervals were calculated using the method described in Boyle and Parkin [26]. Patients diagnosed using information from death certificates only were excluded from the survival analysis as they had no additional information, such as histological verification or co-morbidity score, and their date of diagnosis was assumed to be their date of death. Overall survival was assessed using Cox regression, adjusting for age, socioeconomic deprivation and co-morbidity. Patients were followed up until 31 December 2007.

3. Results

There were 17,458 patients diagnosed with primary liver cancer in England between 2001 and 2007: 10,807 men and 6651 women. The characteristics of these patients are shown in Table 1. Female patients were older, with 35% aged 80 years or over, compared with 20% of male patients. Ethnicity information was available for 13,139 (75%) patients. The White, Indian, Pakistani, Bangladeshi, Black Caribbean, Black African and Chinese ethnic groups made up 7883 male and 4877 female patients (97% of those with a recorded ethnicity), and incidence results are presented for these groups.

Age-standardised incidence rate ratios for men are shown in Fig. 1. White men had the lowest incidence of primary liver cancer compared with men in other ethnic groups. Pakistani (IRR = 2.8, 95% confidence interval (CI) 2.1–3.7), Bangladeshi (IRR = 3.1, 95% CI 1.9–5.2), Black African (IRR = 3.3, 95% CI 2.1–5.1) and Chinese

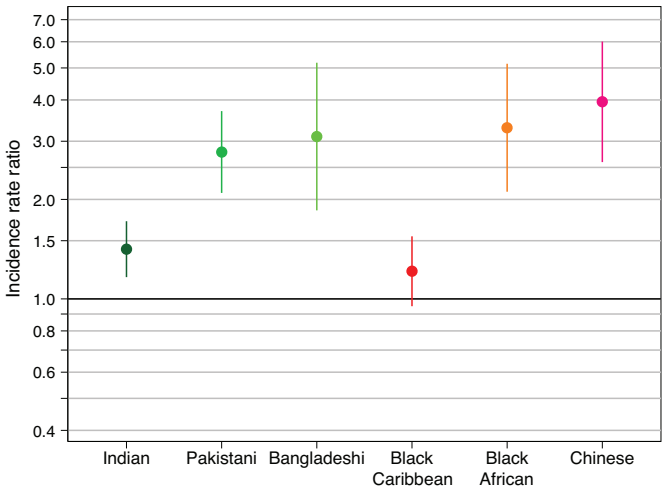

Fig. 1. Age-standardised incidence rate ratios for males diagnosed with primary liver cancer, England, 2001–2007. White men used as baseline.

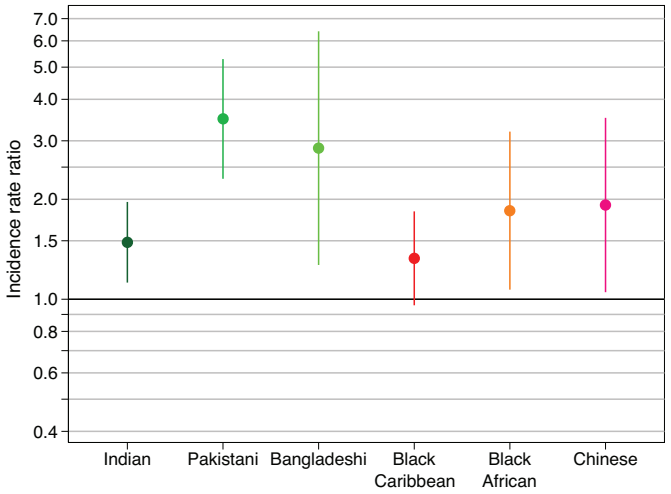

Fig. 2. Age-standardised incidence rate ratios for females diagnosed with primary liver cancer, England, 2001–2007. White women used as baseline.

(IRR = 3.9, 95% CI 2.6–6.0) men all had similarly high incidence rate ratios, while Indian (IRR = 1.4, 95% CI 1.2–1.7) and Black Caribbean (IRR = 1.2, 95% CI 1.0–1.5) men had incidence rates more similar to White men.

Fig. 2 shows the female age-standardised incidence rate ratios for different ethnic groups. A similar pattern to the male results was seen in women, with Pakistani (IRR = 3.5, 95% CI 2.3–5.3), Bangladeshi (IRR = 2.9, 95% CI 1.3–6.4), Black African (IRR = 1.8, 95% CI 1.1–3.2) and Chinese (IRR = 1.9, 95% CI 1.1–3.5) women having higher incidence rate ratios, and high incidence rates which were more similar to White women were seen for Indian (IRR = 1.5, 95% CI 1.1–2.0) and Black Caribbean (IRR = 1.3, 95% CI 1.0–1.8) women.

After excluding 1709 patients registered only from death certificates, 15,749 patients were included in the survival analysis. Table 2 shows the results for male liver cancer patients. Chinese men and those from the Other ethnic group had better survival estimates compared with White men in all of the models (fully adjusted hazard ratios (HR) = 0.65, $p < 0.01$ and HR = 0.83, $p = 0.01$, respectively). Pakistani men also had a better survival estimate, which was strengthened by adjustment for socioeconomic deprivation and unaffected by additional adjustment for co-morbidity (HR = 0.82, $p = 0.06$). Patients without a known ethnicity had worse survival than White men (HR = 1.52, $p < 0.01$).

The results for the survival analysis for women are shown in Table 3. Pakistani and Black African women had better survival than White women, and these results were materially unaffected by additional adjustment for socioeconomic deprivation and co-morbidity (HR = 0.73, $p = 0.04$ and HR = 0.59, $p = 0.03$, respectively). Again, women with no known ethnic group had worse survival than the White group (HR = 1.39, $p < 0.01$).

Men and women with primary liver cancer who lived in more deprived areas had worse survival (fully adjusted trend for both $p < 0.01$), and those with a co-morbidity score of 1 had worst survival for both sexes (male HR = 1.10, $p < 0.01$ and female HR = 1.09, $p = 0.02$).

4. Discussion

Incidence of primary liver cancer is highest in Pakistani, Bangladeshi, Black African and Chinese men and women in England. Indian men and women have incidence rates that are slightly higher than White groups, while Black Caribbean groups' rates are similar to their White counterparts. Pakistani men and

Table 2
Survival hazard ratios for male patients diagnosed with primary liver cancer, England, 2001–2007.

	Model adjusting for								
	Age			Age + deprivation			Age, deprivation + co-morbidity		
	HR	(95% CI)	p	HR	(95% CI)	p	HR	(95% CI)	p
Ethnicity									
White	1.00			1.00			1.00		
Indian	0.97	(0.80,1.18)	0.765	0.95	(0.78,1.14)	0.567	0.95	(0.78,1.15)	0.577
Pakistani	0.86	(0.70,1.05)	0.147	0.82	(0.67,1.01)	0.063	0.82	(0.67,1.01)	0.063
Bangladeshi	0.95	(0.70,1.30)	0.764	0.91	(0.67,1.24)	0.542	0.91	(0.67,1.24)	0.543
Black Caribbean	0.87	(0.68,1.12)	0.288	0.84	(0.65,1.08)	0.178	0.84	(0.65,1.08)	0.170
Black African	0.95	(0.75,1.19)	0.646	0.91	(0.72,1.15)	0.438	0.91	(0.72,1.15)	0.433
Chinese	0.66	(0.51,0.86)	0.002	0.65	(0.50,0.85)	0.002	0.65	(0.50,0.85)	0.002
Other	0.85	(0.73,0.98)	0.023	0.83	(0.71,0.95)	0.009	0.83	(0.72,0.96)	0.011
Not known	1.40	(1.33,1.48)	<0.001	1.41	(1.34,1.48)	<0.001	1.52	(1.41,1.63)	<0.001
χ^2 (8 df)		194.74			204.00			164.32	
p-Value (heterogeneity)		<0.0001			<0.0001			<0.0001	
Deprivation quintile									
1 (least deprived)				1.00			1.00		
2				1.00	(0.93,1.07)	0.954	1.00	(0.93,1.07)	0.948
3				1.08	(1.00,1.16)	0.037	1.08	(1.00,1.16)	0.041
4				1.09	(1.02,1.17)	0.017	1.09	(1.01,1.17)	0.022
5 (most deprived)				1.14	(1.06,1.22)	<0.001	1.13	(1.06,1.22)	<0.001
χ^2					18.94			18.26	
p-Trend					<0.0001			<0.0001	
Co-morbidity score									
0							1.00		
1							1.10	(1.04,1.17)	0.002
2+							1.03	(0.97,1.08)	0.341
Not known							0.90	(0.82,0.99)	0.035
χ^2 (3 df)								17.04	
p-Value (heterogeneity)								0.0007	

Table 3
Survival hazard ratios for female patients diagnosed with primary liver cancer, England, 2001–2007.

	Model adjusting for								
	Age			Age + deprivation			Age, deprivation + co-morbidity		
	HR	(95% CI)	*p*	HR	(95% CI)	*p*	HR	(95% CI)	*p*
Ethnicity									
White	1.00			1.00			1.00		
Indian	1.05	(0.80,1.38)	0.745	1.02	(0.77,1.34)	0.908	1.02	(0.77, 1.34)	0.911
Pakistani	0.76	(0.57,1.02)	0.068	0.74	(0.55,0.99)	0.041	0.73	(0.54, 0.98)	0.036
Bangladeshi	1.26	(0.77,2.07)	0.359	1.21	(0.74,1.99)	0.450	1.20	(0.73, 1.97)	0.475
Black Caribbean	0.92	(0.67,1.26)	0.601	0.88	(0.64,1.21)	0.432	0.87	(0.63, 1.20)	0.392
Black African	0.61	(0.38,0.96)	0.035	0.58	(0.37,0.93)	0.024	0.59	(0.37, 0.94)	0.025
Chinese	1.21	(0.74,1.98)	0.449	1.20	(0.73,1.97)	0.468	1.18	(0.72, 1.93)	0.510
Other	0.93	(0.74,1.17)	0.532	0.92	(0.73,1.16)	0.476	0.92	(0.73, 1.16)	0.492
Not known	1.34	(1.25,1.43)	<0.001	1.34	(1.26,1.43)	<0.001	1.39	(1.28, 1.52)	<0.001
χ^2 (8 df)		88.28			91.45			68.26	
p-Value (heterogeneity)		<0.0001			<0.0001			<0.0001	
Deprivation quintile									
1 (least deprived)				1.00			1.00		
2				1.09	(1.00,1.20)	0.058	1.09	(0.99,1.20)	0.064
3				1.16	(1.06,1.27)	0.002	1.16	(1.06,1.27)	0.002
4				1.20	(1.10,1.31)	<0.001	1.20	(1.10,1.31)	<0.001
5 (most deprived)				1.18	(1.08,1.29)	<0.001	1.18	(1.08,1.29)	<0.001
χ^2					16.50			16.08	
p-Trend					<0.0001			<0.0001	
Co-morbidity score									
0							1.00		
1							1.09	(1.02,1.18)	0.017
2+							1.04	(0.97,1.12)	0.311
Not known							0.97	(0.86,1.08)	0.559
χ^2 (3 df)								6.72	
p-Value (heterogeneity)								0.0812	

women, Black African women, Chinese men, and men from the 'Other' ethnic group had better survival compared with their White counterparts.

An earlier report that examined cancer incidence in major ethnic groups in England found that primary liver cancer incidence was around twice as high in Black men than White men [14]. In the present study, Black Caribbean and Black African men had incidence rate ratios of 1.2 and 3.3, respectively, highlighting the differences between these two ethnic groups. Results were more similar for Black women compared with White women, with rate ratios of 1.3 in Black Caribbean women and 1.7 in Black African women in the present study, and 1.7 for all Black women found previously [14]. Previously much higher incidence rates have been shown in Chinese groups in the US [7]. In California, incidence rates were three times higher in Chinese men and women than in the corresponding White groups [13], while the present study found incidence rates were around four times higher in Chinese men and twice as high in Chinese women.

The pattern of incidence in South Asians has previously been less clear. A similar incidence of liver cancer has been found in the US between a combined Indian and Pakistani group and US Whites [21], and between British Indians and British Whites in Leicester [27]. Combining South Asian groups in England, men and women were found to have incidence rates around twice as a high as their White counterparts [14]. Due to the poor survival of liver cancer patients, mortality can be used as a proxy for incidence [4]. Examining liver cancer mortality in England and Wales found higher standardised mortality ratios for first generation Indian, Pakistani and Bangladeshi men and women than the general population [28]. Bangladeshi men and women had the highest mortality, followed by Pakistani, and then Indian groups. However, when examining second generation South Asians, these groups had lower mortality than the England and Wales population. The difference between first and second generation populations highlights the possible importance of early life exposure to factors, such as hepatitis B [6,29]. Differences in hepatitis B and C infection between ethnic groups have been found within the UK [30,31].

The present study found that Pakistani men and women, and Chinese men had better survival than their White counterparts. This is similar to Goggins and Wong's [21] study that reported Indian/Pakistani and Chinese groups had better survival than the White group, although these results only reached statistical significance in the larger Chinese group. Studies in the US have examined survival in patients with hepatocellular carcinoma and intrahepatic cholangiocarcinoma separately and found that Black patients generally had worse survival than other groups [17–20]. Conversely, in the present study, Black African women had better survival than White women, and there was no statistically significant difference between the Black Caribbean and White groups. Stage of disease at diagnosis may be responsible for variation in survival among ethnic group. Some ethnic groups are intensively monitored for HBV and HCV infection resulting in earlier diagnosis and thus perhaps affecting their survival. Unfortunately, this information is not currently available in the National Cancer Data Repository, though future work examining survival should assess the impact of stage of disease where possible.

The long period of time covered by this study, and the fact that all cancer registrations in England are included, have meant that more detailed ethnic groups have been analysed. However, around a quarter of patients did not have any ethnicity information available. If these patients were from a particular ethnic group, this may have biased the results. For example, if those without ethnicity information were actually White, the incidence rate ratios for the other ethnic groups would be decreased. This

extreme assumption would misclassify some patients from other ethnic groups. Using this reclassification as a sensitivity analysis, the incidence rate ratios for Pakistani, Bangladeshi, Black African and Chinese men, and Pakistani and Bangladeshi women were still statistically significantly high (data not shown).

The availability of population estimates for different age and ethnic groups meant that the assumption that the population was unchanged since the 2001 Census was not needed. The differences between the estimated data and the original Census data are small in the older age groups, and so the results were not materially affected by using either population dataset.

This study has found variations in the incidence and survival of primary liver cancer between ethnic groups. Both clinicians and the communities affected should be aware of the higher risks in particular ethnic groups. These differences are possibly due to higher prevalence of established risk factors such as chronic hepatitis B and C viral infection in some, but not all ethnic groups. Due to the low seroprevalence of hepatitis B in the UK, country of birth, age at migration and length of stay in England are likely to be important factors in this disease, and future research should examine these where possible.

Conflict of interest statement

All authors declare that they have no conflict of interest.

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