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Increased incidence of renal parenchymal carcinoma in the Northern and Yorkshire region of England, 1978–1997

R Tate[a], R. Iddenden[a], P. Harnden[b], E. Morris[c], C. Craigs[a], C. Bennett[a,*], C. Brook[a], R.A. Haward[a,c], D. Forman[a,c]

[a]*Northern and Yorkshire Cancer Registry and Information Service, Arthington House, Hospital Lane, Leeds LS16 6QB, UK*
[b]*Cancer Research UK Clinical Centre and Department of Histopathology, St James's University Hospital, Beckett Street, Leeds LS9 7TF, UK*
[c]*Unit of Epidemiology and Health Services Research, The Medical School, University of Leeds, 30-32 Hyde Terrace, Leeds LS2 9LN, UK*

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Abstract

Kidney cancer remains relatively rare, but incidence and mortality rates are reported to be rising steadily across the world. To determine if such increases were occurring in the UK, we examined the rates of incidence and mortality in different histological subtypes of kidney cancer in the Northern and Yorkshire region of England. Details of all 8741 cases diagnosed between 1978 and 1997 were extracted from the population-based Northern and Yorkshire Cancer Registry. For all types of tumour, both incidence and mortality rates increased over the study period. Overall age-standardised incidence rates increased by 86% for renal parenchymal carcinoma (RPC) (80% for males, 90% for females) from 2.8 to 5.2 cases per 100 000 (3.8–6.8 male, 2.0–3.8 female). There were incidence increases in all age groups, all Carstairs index groups and in both urban and rural populations. Although increased incidental detection of kidney tumours by improved investigational techniques may account for some of this rise, we believe it unlikely that it accounts for all of the increase observed. Potential aetiological causes for the increased rates include hypertension, smoking, a diet lacking fruit and vegetables, analgesic use and, particularly, obesity.

Keywords: Kidney neoplasms; Incidence; Mortality; Epidemiology; Cancer registries

1. Introduction

In 1997, kidney cancer accounted for approximately 3% of all male and 2% of all female cancers diagnosed in the UK. This makes it the 11th and 16th most common cancer site among men and women, respectively [1]. Although it is relatively uncommon, steady rises in both incidence and mortality rates have been reported across the world [2]. In the UK between 1986 and 1997, the average annual percentage increase in age-standardised incidence was 2.6% for males and 3.2% for females [1]. It is not entirely clear, however, whether this documented increase is due to a genuine rise in the incidence of the disease, or whether it is attributable to early, 'incidental' detection because of the wider application of imaging in diagnostic investigation [3,4].

Primary tumours of the kidney arise either from the renal parenchyma or the renal pelvis, the latter consisting mostly of transitional cell carcinomas (TCC). Renal parenchymal carcinomas (RPC) are the most common, representing approximately 80% of all primary kidney tumours [5]. RPC can be subdivided into different histological subtypes, but the majority are renal cell carcinomas (over 70%) or papillary renal carcinomas (15%). Some authors [6,7] have suggested that the incidence rates of RPCs are likely to rise in the future, with female incidence rates possibly exceeding males, whereas TCC rates are predicted to stabilise.

This paper analyses the incidence and mortality patterns of kidney cancer, and in particular RPC, from 1978 to 1997 in the Northern and Yorkshire region of England.

* Corresponding author. Tel.: +44-113-392-4179; fax: +44-113-392-4178.
E-mail address: cathy.bennett@nycris.leedsth.nhs.uk (C. Bennett).

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2. Patients and methods

2.1. Sources of data

Kidney cancer incidence data were derived from the Northern and Yorkshire Cancer Registry and Information Services (NYCRIS) population-based database from 1978 to 1997. Each patient was assigned a Carstairs score, a measure of social deprivation based on census characteristics of the area of residence. The Carstairs and Morris [8] coding was obtained from the Small Area Health Statistics Unit at Imperial College School of Medicine, London. Urban/rural classifications of residential areas were obtained from the Manchester Information & Associated Services (MIMAS) Service at Manchester University's Computing Department. Both of these classification schemes are based on census enumeration districts, which were linked to patient-based individual address postcodes.

Mortality data are supplied annually to NYCRIS from the Office for National Statistics, and are not broken down into tumour sub-site. Treatment data were available for all Yorkshire patients, but were not recorded for Northern patients prior to 1998.

2.2. Classification

In all cases, the primary tumour site was classified as C64 (International Classification of Diseases (ICD)-10 kidney). Thirty-two rare histological tumour types (each type with less than 10 cases in the entire sample) were excluded from further analysis. Wilms' tumours, which occur only in children, were also excluded.

2.3. Statistical methods

The study sample was divided into four 5-year time periods by the date of diagnosis: 1978–1982, 1983–1987, 1988–1992, and 1993–1997. Age-standardised incidence and mortality rates were calculated using the direct method against the European standard population [9]. Age-specific incidence rates (age-adjusted within age categories) were also examined, with rates calculated for age groups less than 50 years, 50–64 year-olds, 65–74 year-olds, and greater than 74 years age groups. All statistical analyses were performed using STATA 6.0 (Stata Corporation, TX, USA).

2.4. Carstairs deprivation score

The Carstairs deprivation score is an unweighted combination of four standardised census variables; male unemployment, no car, overcrowded housing and low social class. Group 1 is the most affluent and Group 5 is the most deprived. The census variables used were standardised to the population of Great Britain.

2.5. Urban–rural classification

This was a bi-polar classification based upon the definition of an Urban Area such that the area of urban land should extend for 20 ha or more, have a minimum population of approximately 1000 persons, and have four or more 1991 Census Enumeration Districts (EDs) [10].

3. Results

A total of 9011 kidney cancer cases were extracted from the NYCRIS database. After excluding the rare histologies and Wilms' tumours, 8741 cases (males $n=5184$, 59%; females $n=3556$, 41%) remained for analysis. RPC constituted 68% ($n=5908$) of these, with TCC a further 7% ($n=625$). Cases without histological confirmation of RPC or TCC constituted the remaining 25% ($n=2208$). Analysis of mortality rates was based on 5885 deaths in the same time period.

3.1. Overall incidence and mortality

Both incidence and mortality rates increased over the entire period from 1978 to 1997 (Fig. 1). Age-standardised incidence rates for males increased by 60% from 5.86 to 9.39 per 100 000, while the incidence rates for females increased by 66% over the time period, from 3.11 to 5.15 per 100 000 (Table 1). Age-standardised mortality rates over the same time period showed a proportionately lower increase for both males and females. Mortality rates for males increased by 30% from 4.40 per 100 000 (95% Confidence Interval (CI) 4.1–4.7) to 5.71 (95% CI 5.3–6.1). Mortality rates for females increased by 43%, from 2.08 per 100 000 (95% CI 1.9–2.3) to 2.98 (95% CI 2.8–3.2).

3.2. Overall incidence by histological type and gender

Overall age-standardised incidence rates increased by 86% for RPC over the study period from 2.8 to 5.2 cases per 100 000. The age-standardised rates for RPC for males increased by 80% from 3.79 (95% CI 3.5–4.1) to 6.83 (95% CI 6.4–7.2) cases per 100 000, while females showed the greater increase, increasing by 89% from 2.03 (95% CI 1.8–2.2) to 3.84 (95% CI 3.6–4.1) per 100 000 (Fig. 2).

The age-standardised incidence rates for TCC also increased over the study period. For both sexes, the rates approximately doubled over this time, from 0.34 (95% CI 0.25–0.42) to 0.68 (95% CI 0.56–0.81) per 100 000 in males and from 0.19 (95% CI 0.13–0.25) to 0.37 (95% CI 0.29–0.46) per 100 000 in females. How-

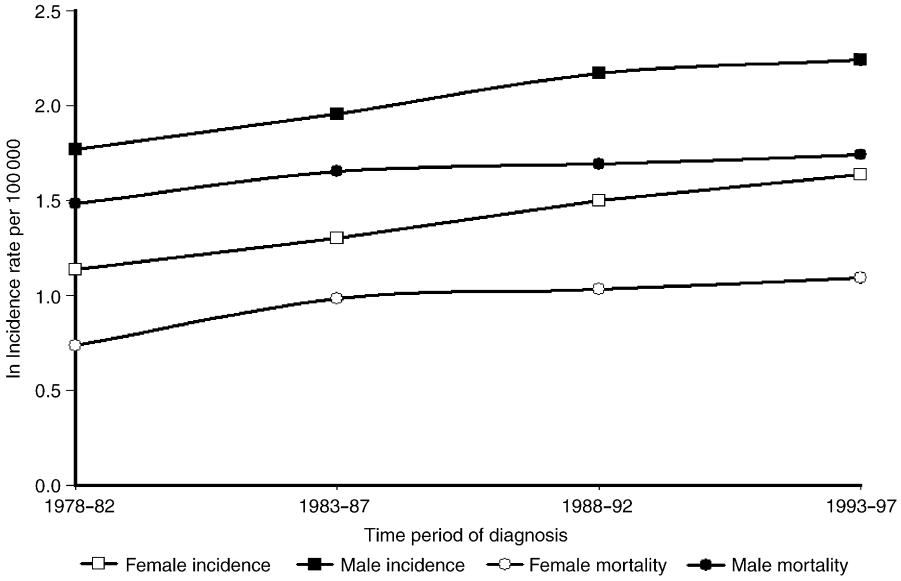

Fig. 1. Age-standardised ln incidence and ln mortality rates per 100 000 by year and gender.

Table 1
Age-standardised incidence rates (including 95% Confidence Intervals (CIs)), by age and gender

Year	Males		Females	
	Number	Rate per 100 000 (95% CIs)	Number	Rate per 100 000 (95% CIs)
1978–1982	931	5.86 (5.47–6.24)	654	3.11 (2.86–3.36)
1983–1987	1160	7.07 (6.66–7.49)	782	3.68 (3.41–3.96)
1988–1992	1456	8.76 (8.30–9.22)	961	4.49 (4.19–4.80)
1993–1997	1637	9.39 (8.93–9.86)	1159	5.15 (4.84–5.47)

ever, the number of cases still remains very small (96 cases between 1978 and 1982 and 209 cases between 1993–1997).

In contrast, the age-standardised incidence rates of unspecified or without histological confirmation cases increased only slightly over the same time period for both sexes, from 1.63 (95% CI 1.43–1.83) to 1.87 (95% CI 1.66–2.07) for males and from 0.86 (95% CI 0.73–0.98) to 0.93 (95% CI 0.81–1.06) for females. As a result the overall percentage of cases without histological confirmation has decreased from 31% in 1978–1982

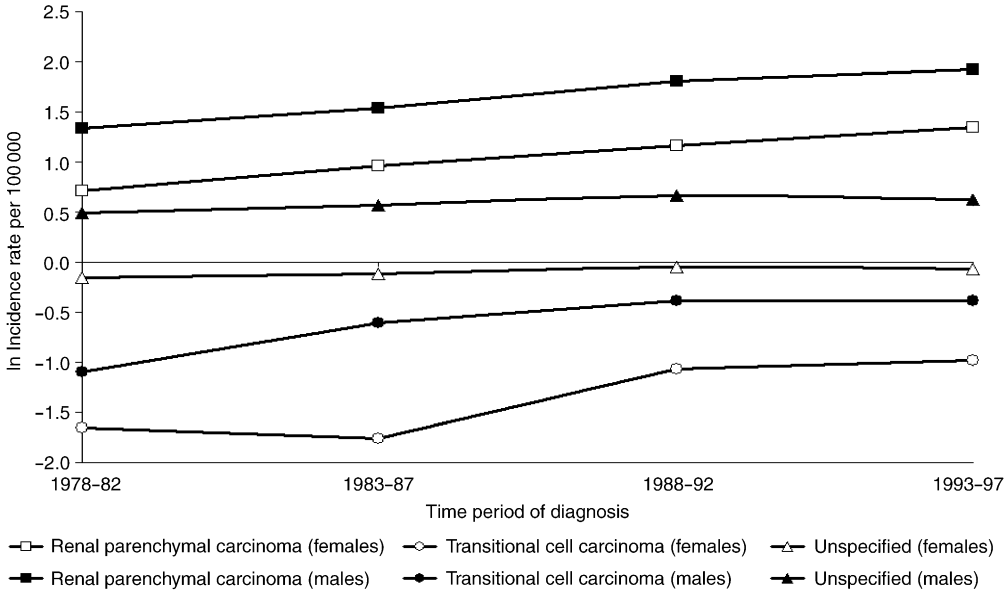

Fig. 2. Age-standardised ln incidence per 100 000 by histological type, gender and year.

Table 2
Number and percentage of cases without histological confirmation of RPC or TCC, separated according to age and year of diagnosis

Age group (years)	<50		50–64		65–74		75+		Total	
	Number	%	Number	%	Number	%	Number	%	Number	%
1978–1982	21	15	112	20	179	33	174	50	486	31
1983–1987	27	13	127	19	183	30	199	44	536	28
1988–1992	23	9	114	15	185	24	262	42	584	24
1993–1997	27	9	97	12	190	21	288	36	602	22
Total	98	11	450	16	737	26	923	42	2208	25

to 22% in 1993–1997 (Table 2). This percentage decrease is consistent across all of the age groups. These cases were excluded from the subsequent analyses.

Rates of histological confirmation could be expected to be directly related to surgical rates. Treatment rates were available across the whole time period for patients managed in Yorkshire only. In this group, there were more surgical operations in all of the age groups, particularly in those aged 50–74 years (Table 3). The overall increase was from 52% in 1978 to 1982 to 61% in 1993 to 1997.

The following analyses were performed on RPCs only.

3.3. Trends in RPC incidence by age

The age-specific incidence rates (Fig. 3) illustrate the pattern of increases in the different age groups. The largest increase was in the 75 years and over group, where the incidence more than doubled over the study period, from 8.63 to 19.82 per 100 000.

In the 65–74 years age group, the incidence rates almost doubled over the study period from 10.75 to 21.09 per 100 000. The 50–64 years and the under 50 years age groups also saw similar increments in incidence over the study period, although the rates for the latter remained very low. These rates increased from 7.24 to 12.38 and 0.53 to 1.10 per 100 000, respectively.

3.4. Trends in RPC by deprivation score

The initial time period, 1978–1982, showed a divergent pattern of incidence between the most affluent and least affluent (most deprived) quintiles, with the most deprived quintiles having an age-standardised incidence rate of 3.28 per 100 000 compared with 2.48 per 100 000 in the least deprived (most affluent). The overall trend for all deprivation groups was an increase in incidence over the study time (Fig. 4).

Table 3
Surgical rate by age and year of diagnosis (for Yorkshire only)

Age group (years)	<50		50–64		65–74		75+		Total	
	Number	%	Number	%	Number	%	Number	%	Number	%
1978–1982	54	72	174	62	149	52	56	29	433	52
1983–1987	79	72	237	62	175	54	104	38	595	55
1988–1992	123	83	318	74	245	61	116	34	802	61
1993–1997	139	79	364	77	326	67	143	32	972	61
Total	395	78	1093	70	895	60	419	33	2802	58

The overall percentage increase between 1978–1982 and 1993–1997 varies between deprivation quintiles (Table 4). In the most recent time period, 1993–1997, there was no significant ordering of quintiles in relation to deprivation.

3.5. Trends in RPC incidence by urban–rural status

The age-standardised incidence rates for both the urban and rural populations of the region increased over the study period (Fig. 5). These increases were seen in both males and females. A larger increase was observed in the urban population, for both sexes.

Amongst males, age-standardised incidence rose by 83% between 1978–1982 and 1993–1997 from 3.79 to 6.92 per 100 000 in the urban population (SRR 1.83, 95% CI 1.7–2.0). This compared with a 63% increase, from 3.79 to 6.6 cases per 100 000 among rural males for the same time period (SRR 1.62, 95% CI 1.2–2.2).

Amongst urban females, there has been a linear increase over the four time periods from 2.05 (in 1978–1982) to 3.92 (in 1993–1997) cases per 100 000 (SRR 1.91, 95% CI 1.7–2.2). Rural female incidence was increasing at a similar rate until 1988–1992, after which a small decline was observed but there was an overall increase over the study period from 1.87 to 3.16 per 100 000 (SRR 1.69, 95% CI 1.1–2.5). It should be noted that less than 10% of cases are from the rural population, so the numbers are very small, particularly for females. This will make these estimates more unstable than those for the urban females.

4. Discussion

We have found an overall increase in the incidence of kidney cancer and, in keeping with previous reports [11], incidence in males was approximately twice that in females. We also found, as have others [3,6,7,12], that the rate of increasing incidence was higher in females than males.

A major criticism of our work is that in some of our analyses we excluded all patients without a histological confirmation of their cancer (although it should perhaps be noted that those analyses involving all patients produced results consistent with those using only histologically-confirmed patients). Unlike other cancer types and because of its highly characteristic appearance, imaging alone usually enables a diagnosis of kidney cancer, and treatment is often administered without resorting to a confirmatory biopsy. However, a review of image-

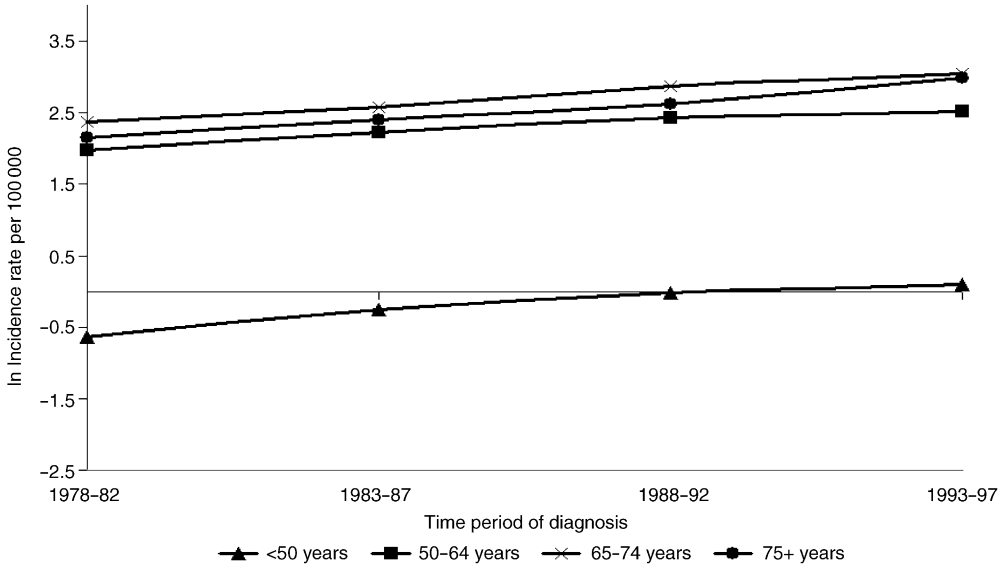

Fig. 3. Age-specific ln incidence rates by year of diagnosis.

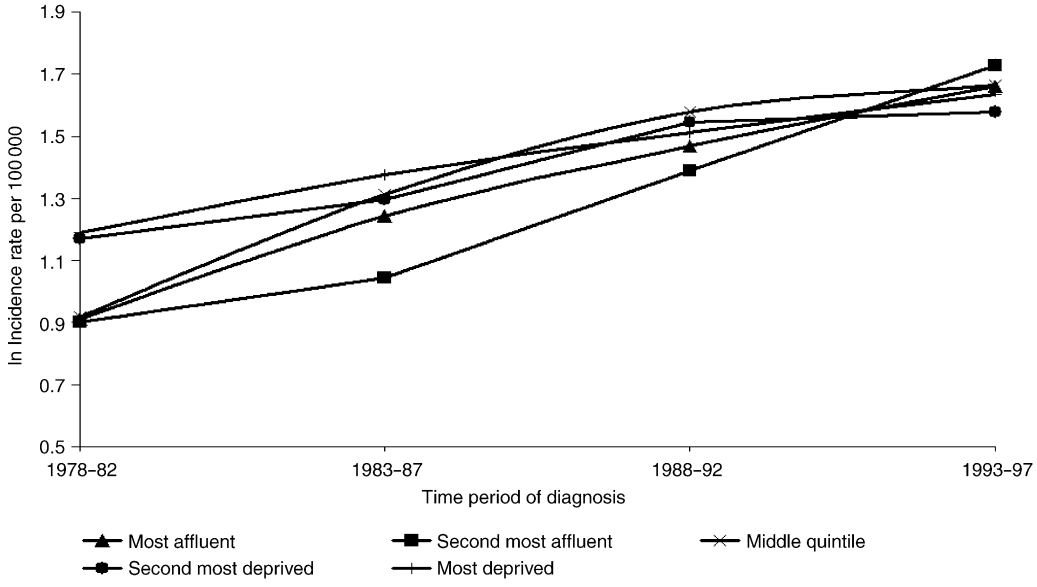

Fig. 4. Age-standardised ln incidence rates by deprivation score and year of diagnosis.

Table 4
Age-standardised incidence rates (including 95% Confidence Intervals) and overall percentage increase, by deprivation quintile

Age group	Most affluent	Second most affluent	Middle quintile	Second most deprived	Most deprived
1978–1982	2.48 (2.07–2.90)	2.46 (2.09–2.84)	2.50 (2.13–2.87)	3.22 (2.80–3.65)	3.28 (2.88–3.69)
1983–1987	3.46 (2.97–3.96)	2.84 (2.40–3.24)	3.72 (3.26–4.18)	3.65 (3.20–4.10)	3.96 (3.52–4.41)
1988–1992	4.35 (3.79–4.90)	4.01 (3.53–4.49)	4.85 (4.32–5.37)	4.69 (4.20–5.19)	4.54 (4.06–5.01)
1993–1997	5.26 (4.66–5.86)	5.63 (5.70–6.19)	5.28 (4.75–5.82)	4.85 (4.35–5.35)	5.12 (4.63–5.62)
Overall% increase	112%	128%	111%	51%	56%

guided biopsies of indeterminate renal masses demonstrated that whilst the diagnosis of malignancy was made in 62% of patients, over two-thirds of these cases were actually non-renal parenchymal tumours [13]. In our study, we have no way of determining what proportion of patients without a histological diagnosis had typical appearances on imaging and, therefore, what proportion had indeterminate masses. As there is evidence to suggest that many such cases may represent other cancer types, we have only included in our

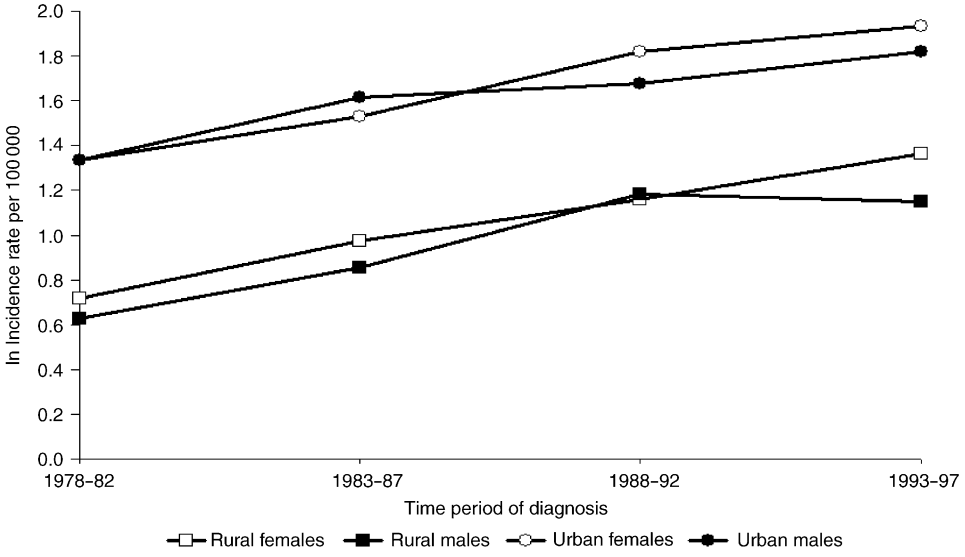

Fig. 5. Age-standardised ln incidence rates for both urban and rural populations.

analysis patients with a histological confirmation of RPC.

During the study period, histological confirmation rates improved slightly from 69% in 1978–1982 to 78% in 1993–1997 (Table 2). Although this may account for some of the observed increase in the incidence of RPC, the increase in incidence of RPC exceeded the rate of increase of pathological ascertainment of diagnosis. As such, we do not believe our observed incidence to be entirely attributable to this effect. This argument is supported by reference to other studies that have documented increasing incidences with stable histological confirmation rates of over 90% [6].

We also considered the possibility that the upward trend in incidence was related to the recent more widespread use of ultrasonography and other investigational techniques which, since the 1970s, have led to the more frequent detection of asymptomatic tumours [3,4]. For example, in a series of 400 patients studied by Patard and colleagues, 151 or 38% of these had been diagnosed incidentally [14] whilst a study looking at such cancers incidentally detected at autopsy found 51 cases across a series of 7970 (0.64%) [15]. Since women with gynaecological or gall bladder symptoms may undergo abdominal investigations more commonly than men, this could partly explain the observed higher increase in incidence in females. However, mortality rates for kidney cancer have also risen. If the observed rise in incidence rates had been due solely to incidentally-detected tumours and as incidentally-detected tumours appear to have a better prognosis [3], we should have seen a concurrent improvement in survival rates. This improvement was not apparent.

Likewise, some studies suggest that incidentally-detected RPCs are of a lower stage, with a smaller percentage of metastases, than those producing symptoms [16,17]. They should, therefore, be more amenable to surgery. Our surgical rates increased by 9% overall (although the increase was more marked in the younger age groups) and, as this was still considerably less than the 86% increase in incidence of RPC we, again, conclude that the change in incidence is not due entirely to the incidental detection of kidney cancers. Furthermore, any impact of new diagnostic technologies on incidence rates would, anyway, only result in a transitory effect.

Previous studies have shown that incidental tumours were more commonly detected in the older age groups [16,18]. Although the incidence increase was higher in the oldest age group in our study, we found quite large increases across all age groups. Again, this supports our argument against incidentally-detected tumours.

For these reasons, we believe our observed increase in incidence to be a real effect. This is in agreement with other recent studies, particularly Mathew and colleagues [2] who have shown that rates are rising collectively across Europe, with the exception of Scandinavia where substantial increases were only seen in Finland.

The data presented here relating to incidence in comparison to social deprivation [17] and urbanisation [19,20] are also in agreement with other published data. We found no strong association between socio-economic status and the incidence of RPC, but an increased rate in all five socio-economic groups. We found a similar differential among urban and rural populations, and also increasing incidence among urban populations. This differential remains even though the rural population was found to be more affluent (due to a relatively prosperous farming community and growth in business people living outside cities and commuting to work), indicating that socio-economic factors are operating independently from the urban factors.

The evidence presented here, in addition to that in the literature, suggests that RPC is set to become a major

cancer of affluent societies unless its aetiology is determined and preventative measures are taken [21]. Consistently identified risk factors for the disease include smoking, obesity, hypertension, and a lack of fruit and vegetables in the diet [22–28].

Whilst smoking is a risk factor for the disease, the current decrease in per capita cigarette consumption in the UK means this factor is unlikely to account for our observed rise in incidence.

In contrast, the rate of another potential contributory factor, obesity, does correlate more intimately to our observed increase in incidence [29]. In the UK, levels of obesity have tripled in the past 20 years with 21% of women and 17% of men now classed as clinically obese [30]. Likewise, in the US it has been observed that obesity has increased in both sexes and across all age groups [23].

Less consistently identified risk factors include analgesic use, hypertension [24,31,32] and the medications used to treat hypertension [25]. These factors may also have played a role in the increased levels of incidence observed.

To date, there is, however, insufficient evidence that any of these risk factors could account entirely for our observed 86% increase in incidence.

Although the data on which this study was based were incomplete in that 25% of cases had to be excluded because of the lack of histological confirmation of RPC, some preliminary conclusions may be drawn. Increased incidence in RPC in Northern and Yorkshire from 1978 to 1997 may have resulted from a combination of improved techniques for detection and changing lifestyles. More studies are needed to elucidate the mechanisms by which smoking, obesity, hypertension and the effect of a sedentary lifestyle may increase the risk of RPC, and to separate the effect of these factors from the increase in incidentally-found tumours.

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