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ORIGINAL ARTICLE

Title: Rising incidence of anal cancer in England 1990-2010; a population-based study

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ABSTRACT

Aim: Although anal cancer is a relatively rare disease, its incidence has been reported to be increasing in several different countries across the world. This study aimed to investigate changes in incidence rates over time in England.

Methods: 13,940 individuals with a primary diagnosis of anal cancer between 1990 and 2010 were identified in the cancer registry component of the English National Cancer Data Repository. Tumours were grouped (using their ICD-0 morphology codes) into squamous cell carcinomas, basaloid and cloacogenic carcinomas, adenocarcinomas and other cancer types. Secular trends in incidence over this time period were then investigated overall and in relation to morphology, age and sex.

Results: In males there was a 69% increase in squamous cell anal carcinomas over the study period with their incidence rate rising from 0.43 per 100,000 population in 1990-1994 to 0.73 in 2006-2010. The increase in women was even greater as the rate per 100,000 population rose by 126% from 0.50 in 1990-1994 to 1.13 in 2006-2010.

Conclusion: This study shows that between 1990 and 2010 the incidence of anal cancer in England significantly increased. This effect was particularly marked in women.

INTRODUCTION

Although anal cancer is a relatively rare disease, numerous international reports have shown its incidence is increasing.[1-7] These rising incidence rates are thought to be due to an increase in the number of anal squamous cell carcinomas (the predominant form of the disease) for which the major risk factor is infection with the human papilloma virus (HPV). Little is known about trends in the incidence of anal cancer in England so this study aimed to investigate trends across the country by quantifying age-standardised and age-specific rates in relation to sex and age between 1990 and 2010.

METHODS

Information was extracted from the cancer registry data component of the National Cancer Data Repository (NCDR) on every individual diagnosed with a primary anal cancer (International Classification of Diseases Version 10 code C21) in England between 1990 and 2010. The tumours of this population were then categorised into either squamous cell carcinomas, basaloid and cloacogenic carcinomas, adenocarcinomas or other cancers based on their ICD-O morphology codes.[8]

Mid-year population estimates were obtained from the Office of National Statistics[9] and used to calculate five-year moving average age-standardised incidence rates by direct standardisation to the European Standard population. Age-specific incidence rates for males and females of anal cancer squamous cell tumours for four specific time periods (1990-1994, 1995-1999, 2000-2004 and 2005-2009) were also investigated. .

RESULTS

Between 1990 and 2010, 13,940 individuals were diagnosed with anal cancer in England. Table 1 shows the percentage distribution of anal cancers across the different morphology sub-types of the disease and illustrates that squamous cell carcinomas were the most common form of the cancer. The morphological distribution of tumours between males and females was, however, significantly different with a greater proportion of women having squamous cell carcinomas and men having a high proportion of adenocarcinomas ($P<0.01$).

Trends in age-standardised incidence rates both overall and for each morphological type of the disease for males are shown in Figure 1A. There was little change in the incidence of anal adenocarcinomas and basaloid or cloacogenic tumours over the study period but, in contrast, there was a 69% increase in squamous cell tumours with their incidence rate rising from 0.43 per 100,000 population in 1990-1994 to 0.73 in 2006-2010.

Amongst females there was, again, little change in the age-standardised incidence rate of adenocarcinomas, basaloid or cloacogenic tumours over time (Figure 1B). There was, however, a major increase in the incidence rate of squamous cell tumours. The rate per 100,000 population rose from 0.50 in 1990-1994 to 1.13 in 2006-2010 amounting to a 126% increase.

Figures 2A and B show the age-specific incidence rates by sex of squamous tumours over four consecutive time periods. They demonstrate an increase in incidence over time for both males and females but with rates increasing predominantly in those of middle and old age and being particularly marked in women.

DISCUSSION

This study shows that whilst, in comparison to other large bowel tumours, anal cancer remains relatively rare in England, its incidence is significantly increasing. Over the twenty year time period of this study the rates of the most common form of the disease (squamous cell carcinomas) have increased by 69% in men and 126% in women. Age-specific analyses by sex indicate that the incidence of the disease is increasing in both men and women, but particularly in women in middle and older age groups. The disease also occurred significantly more frequently in those who resided in more socio-economically deprived areas.

These findings are consistent with the anal cancer incidence trends reported from many other countries worldwide as, although not universal,[6] major increases in incidence have been observed in Denmark,[5;10] the United States of America,[3;4] Scotland,[2] Sweden,[7] and Australia[6]. This study confirms these increases in incidence in one of the largest whole populations studied. What is driving the increase in the incidence of anal cancer is not clear. Although both smoking[11;12] and immunosuppression[11;11;13;14] are associated with the disease, the strongest risk factor for squamous cell tumours is infection with the human papilloma virus (HPV).[11;15-17] The rising incidence of anal cancer could be anticipated, therefore, to be associated with the increasing exposure to this virus and, as sexual behaviours[11;18] such as a history of multiple sexual partners, anorectal intercourse and sexually transmitted infections (especially human immuno-deficiency virus (HIV)) all predispose individuals to a greater risk of HPV infection, this may explain the higher rates observed in these populations.

Anorectal intercourse is associated with a greater risk of the disease so it is, perhaps, not surprising that some studies have shown an elevated risk of the disease in homosexual men. The National Survey of Sexual Attitudes and Lifestyle however indicates that a much greater proportion of females participate in anal intercourse than males.[19] This may, therefore, contribute to the greater incidence rates observed in women.

In 2008 a national HPV vaccination programme was introduced for girls aged 12 and 13 across the UK[20] and, although this could be anticipated to lead to a reduction in incidence of anal cancers in the future, given the age of the population affected by the disease the impact of the programme will take many decades to have an effect. No such screening programme has been implemented for males and whilst heterosexual men may be offered some 'herd immunity' via the current vaccination scheme, men who have sex with men would receive no such benefit. As a result, the increasing incidence rates of anal cancer in men could be anticipated to rise still further. This further strengthens the arguments for introducing HPV immunisation in boys as has occurred now in Australia.[21]

The increasing incidence in older patients observed in this study is an important observation with significant service implications. The curative treatment of squamous type anal cancers involves a relatively intensive schedule of concurrent chemotherapy with mitomycin C, 5 fluorouracil and a course of 50.4Gy of radiotherapy over five and a half weeks.[22] Many elderly patients have poorer performance status and significant co-morbidities that may limit their suitability for standard treatment or result in them experiencing greater toxicity. Similarly, in those patients who have residual or recurrent disease the option of radical salvage surgery carries a considerable morbidity, particularly with increasing age. Whilst there is evidence of the efficacy of lower dose chemoradiotherapy in small case series,[23;24] further work is required to determine the optimum treatment schedule for the growing elderly population who may be considered unsuitable for standard therapy.

In addition, the major increases in incidence observed across England have implications for the NHS. Current guidance recommends that anal cancer should be managed in specialist centres with sufficient anal cancer workloads to ensure optimal expertise and management.[25] With the significant increase in incidence of the disease it would appear likely that the workloads of these units will also increase. Ensuring that these centres are adequately resourced to deal with the new cases will be important.

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TABLES

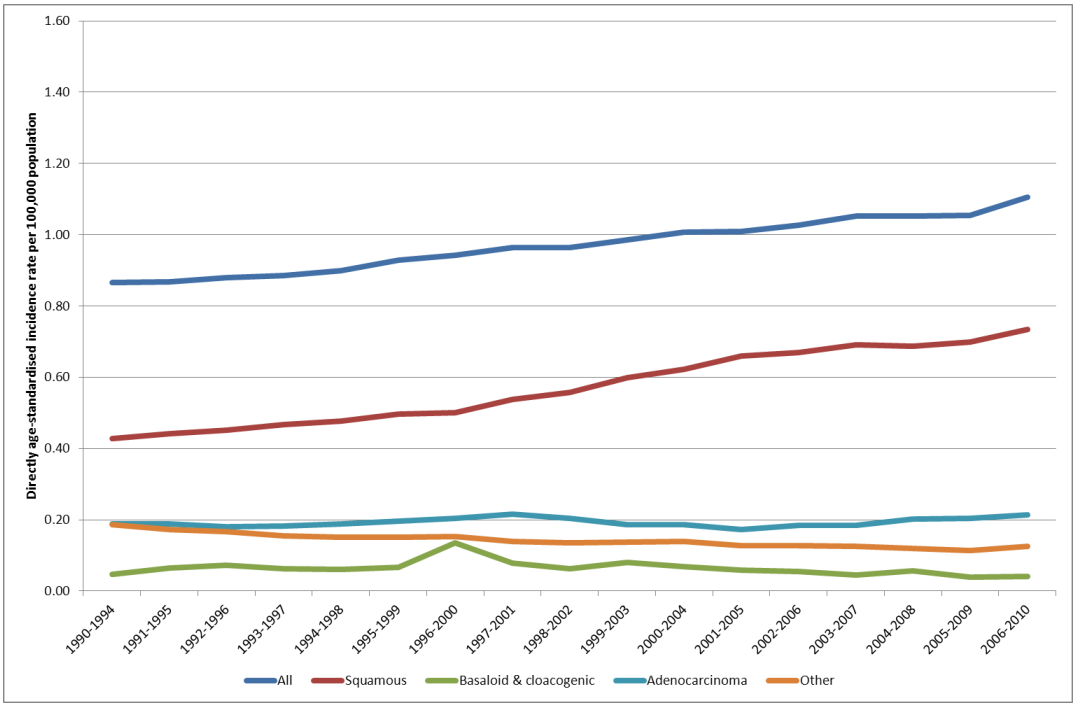
Table 1: Histological type of anal cancer in relation to sex (England 1990-2010)

Histological type	Males		Females		Total	
	n	%	n	%	n	%
Squamous cell carcinoma	3,235	58.4	5,248	62.5	8,483	60.9
Basaloid & cloacogenic carcinomas	327	5.9	792	9.4	1,119	8.0
Adenocarcinoma	1,145	20.7	1,228	14.6	2,373	17.0
Other	836	15.1	1,127	13.4	1,963	14.1
Total	5,543	100.0	8,395	100.0	13,938	100.0

FIGURES

Figure 1: Age standardised incidence rates of anal cancer by major histological type (five-year average) across England 1990-2010

A. Males



B. Females

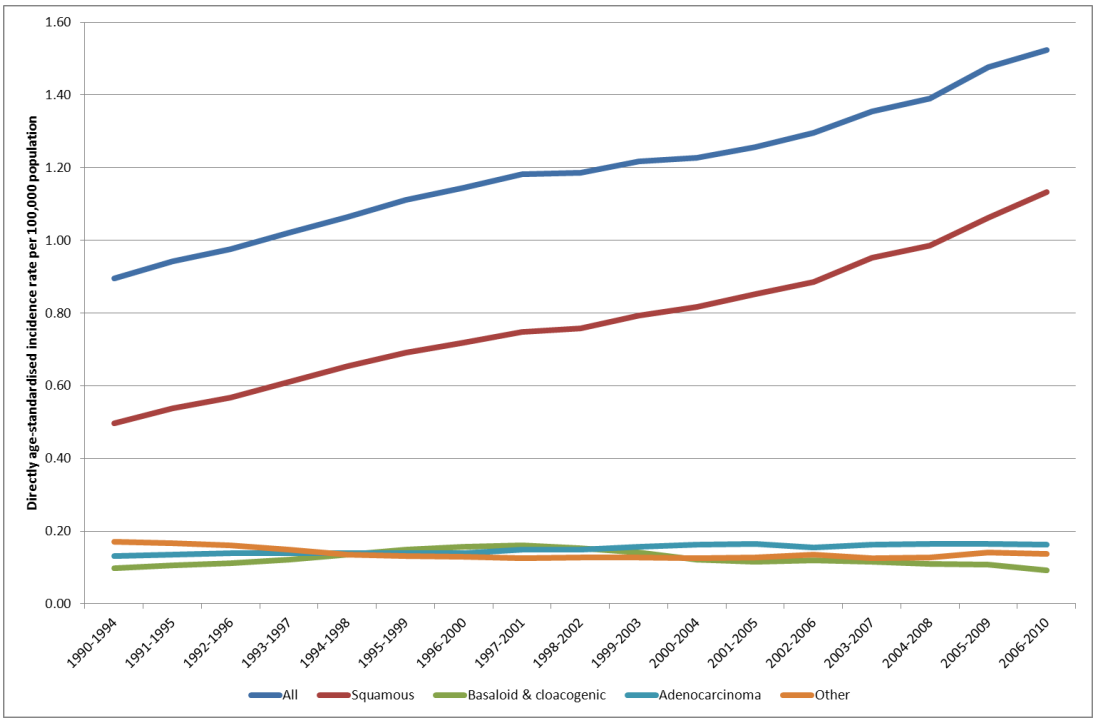
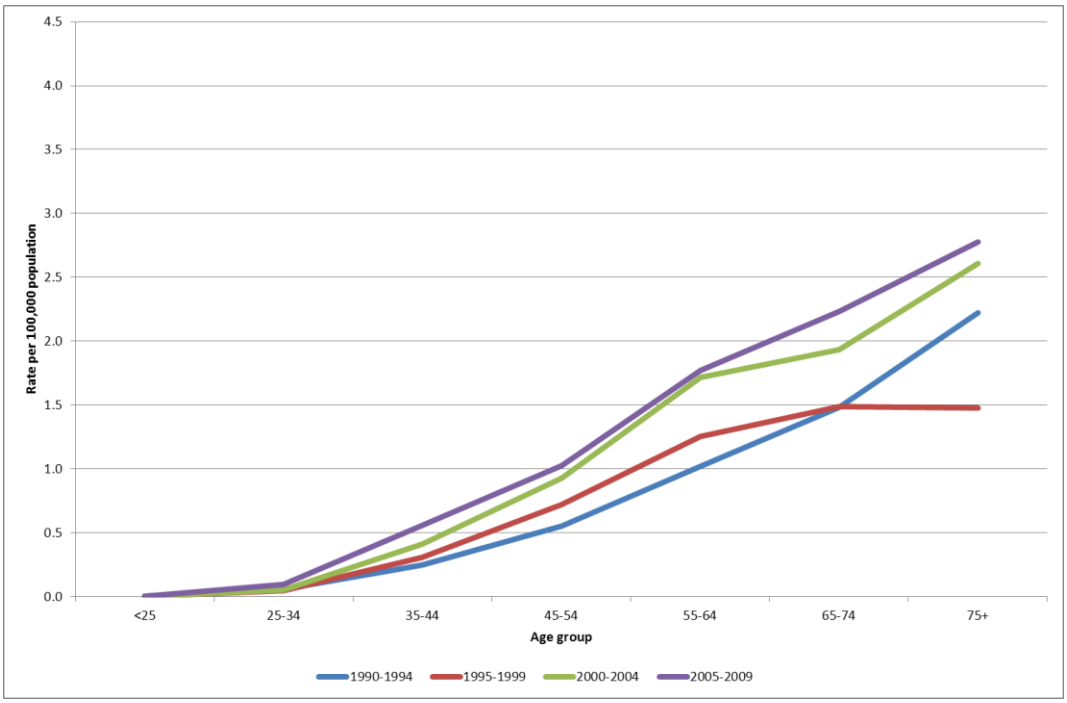


Figure 2: Age-specific incidence rates of squamous cell anal carcinomas by period of diagnosis 1990 – 2009

A. Males



B. Females