Invasive cancer of the cervix: does the UK National Health Service screening programme fail due to patients' non-attendance?

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Summary

The UK National Health Service (NHS) cervical screening programme aims to prevent invasive cancer of the cervix, yet this programme fails in some women. Women diagnosed with cancer of the cervix at a colposcopy unit in the North East of England between April 1, 1997 and December 31, 2004 had cervical cytology histories classified. Thirty-seven cases were identified (median age 37 years; range 22-72 years). At six months before diagnosis, 24.3% had never undergone cytology screening (38.4% Stage IB+, 12.5% Stage IA). In addition, 59.5% of all cases were under-screened (when using criteria that included screening was 'up to date' if less than five years had elapsed between last negative test result and their diagnosis). Women in this case series failed to attend regular cervical screening, with those never attending screening more likely to present with advanced cancer.

Key words: Invasive cancer of cervix; NHS cervical screening programme; Cervical cytology.

Introduction

In the UK the National Health Service (NHS) cervical screening programme aims to reduce the incidence of and mortality from invasive cancer of the cervix by offering regular, free cervical cytology sampling to women at risk. Identifying and treating those with cervical intraepithelial neoplasia has halved the incidence and mortality of invasive cancer of the cervix in England since 1988 when the screening programme was introduced [1]. Other European cervical screening programmes have also shown a similar success. A Swedish case-control study, for example, investigating nearly all the cases of invasive cancer of the cervix between 1991 and 2001 has shown that women who adhered to screening guidelines were far less likely to develop invasive cancer (relative odds 0.21 95% confidence interval 0.16-0.28) [2].

Unfortunately despite the screening programme being highly effective in preventing cancer of the cervix, there were still 2,276 women who presented with this invasive disease in 2007 and 830 women died as a result of this cancer in 2008 [1]. It was reported in 2005 that women who failed to attend cervical cytology screening make up a disproportionately high number of cases of cancer of the cervix [3]. The most recent NHS cervical screening programme audit includes a classification of cytology histories from 6,231 women with cancer of the cervix diagnosed between April 2007 and March 2010 and 18,783 controls. It found 25.3% with Stage IB+ cases and 19.3% with Stage IA cases had no previous cytology [1]. Women with fully-invasive (Stage 1B+) cervical cancer were also less likely to have been screened regularly for the last eight years than were women in general.

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The aim of this study was to analyse attendance for cervical screening in women prior to their diagnosis of cancer of the cervix in the North East. A second aim was to determine if those with a poor screening history presented with more advanced cancer. Non-attendance for screening was reported as an important factor in the London series, but would the same be true for a population that has the second highest incidence rate for cancer of the cervix in England (age-standardised incidence rate of 10.3 per 100,000 female population between 2004-2008)? [4].

Materials and Methods

The regional colposcopy unit database was searched for patients who had attended the service with a histological diagnosis of cancer of the cervix between April 1, 1997 and December 31, 2004. For each of these cases a search was made using the National Health Authority Information System (NHAIS) to identify any previous cervical cytology tests. This database keeps a record of the date and results of each individual test along with the advised actions.

Cervical screening was offered to all women in the North East of England aged 20-64 at five yearly intervals between 1988 and 1997. From March 1997 the interval was reduced to three yearly and in October 2003 the NHS Cervical Screening Programme in England raised the age of the first invitation letter to 25 years with a three-yearly interval up to age 49 and five years thereafter to 64 years. Consequently the cases in this series were invited at variable intervals depending on their age.

Any samples that were taken in the six months prior to diagnosis were excluded from the classification process to avoid including tests that were precipitated by the presence of symptoms or were performed as an additional diagnostic aid. For simplicity, women were classified as being 'up to date' if five years or less had elapsed between the date of the last negative screening sample resulting in routine recall, and the diagnosis. It is accepted that some women would have been invited three

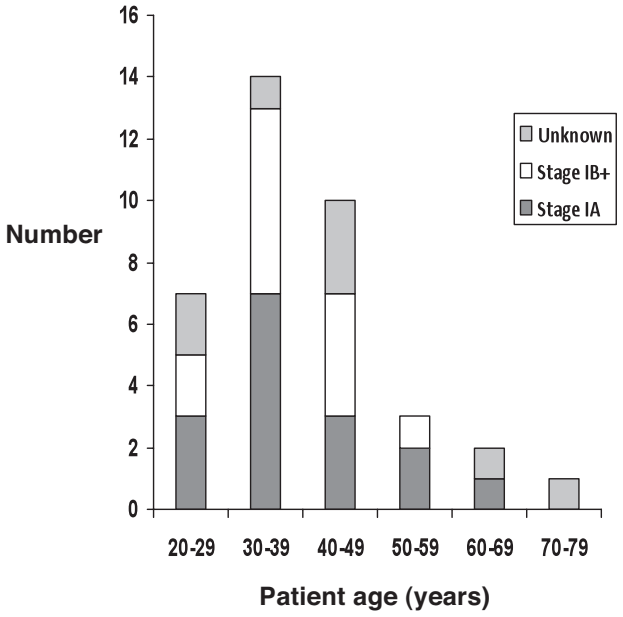

Figure 1. — Age at diagnosis of women with invasive cancer of the cervix.

yearly prior to a diagnosis and that five years is a generous allowance. For women on an early recall action code due to a previous inadequate, borderline, or mild cytology result, their screening was classified as being 'up to date' if one year and three months or less had elapsed between the date of the last screening sample and the diagnosis. For women over 65 years, their screening was 'up to date' if they had one negative test result between the ages 60 and 65 years. For women with a test indicating a need for further investigation and/or treatment at colposcopy, they were classified as being 'up to date' if they had at least one negative test result following the recommendation for colposcopy. The hospital's histology results database was searched to obtain International Federation of Gynaecology and Obstetrics (FIGO) tumour stage for the micro-invasive cancers and a minimum stage for the more advanced cases. The results were analysed for statistical significance using an exact contingency table test as described by Plackett [5].

Names, addresses, and unique identifiers such as NHS or hospital numbers were deleted and the personal identifier used was date of birth in order to anonymise the data. Research and ethics review was not required as the audit contained routinely collated data in an anonymised format.

Results

The case series included 37 women (median age 37, range 22-72). One woman had two diagnoses of invasive cancer separated by follow-up cytology samples within the time period of the study. She was included as a single case of Stage IB+. A woman aged 72 years was included as she was 61 years old when the screening programme commenced in 1988, and so would have been eligible for at least one screen before the age of 65.

Figure 1 shows the incidence of cervical cancer according to FIGO staging and age. Forty-three point three percent of cases were Stage IA, 34.2% were Stage IB+, and in 21.6% the final stage was not known. The most common histological diagnosis was squamous carcinoma reported in the majority of cases (87%). Three (8%) cases were adenocarcinoma and two (5%) were adenosquamous carcinoma.

Table 1. — *Cervical screening status at six months before diagnosis of invasive cancer of the cervix.*

Cervical screening history at six months before diagnosis	Stage IA n (%)	Stage IB+ n (%)	Unknown n (%)	Total n (%)
'Up to date'	8 (50)	2 (15.3)	5 (62.5)	15 (40.5)
Under-screened	8 (50)	11 (84.6)	3 (37.5)	22 (59.5)
Total	16 (100)	13 (100)	7 (100)	37 (100)

Table 1 shows the screening status of subjects six months or more before diagnosis - 40.5% of all cases were classified as being 'up to date' with their cervical screening examinations and 59.5% were lapsed or had never been screened. Just 15.3% of Stage IB+ cases were 'up to date' with their screening tests compared with 50% of those presenting with Stage IA cancer. The exact contingency table test for these gave a non-significant p value of 0.114.

Nine women (24.3% of all cases) had no cytology prior to the six-month exclusion period and, when divided according to FIGO Stage, 5/13 (38.4%) of Stage IB+ cases had no previous cytology compared with 2/17 (12.5%) of Stage IA cases (Figures 2 and 3). The p value of 0.19 using the exact contingency table test did not reach statistical significance. The ages at diagnosis of the women with no previous cytology were 30, 32, 37, 37, 37, 37, 40, 42, and 72 years. Of those presenting with Stage IA cancer, 43.8% had a negative sample within five years of diagnosis compared with 15.4% of Stage IB+ cases. Two women with Stage IB+ cancer were suspended from screening as they required diagnostic testing and possible treatment at colposcopy, but a negative sample was not obtained before the diagnosis was made.

Discussion

This case series confirms that women with invasive cancer of the cervix in the North East of the UK have a high rate of infrequent or non-attendance for cervical screening with 59.5% of all cases under-screened and 24.3% never screened six months or more before their diagnosis. It also shows that women with more advanced cancer are more likely never to have attended for cervical cytology (38.4% Stage IB+ cases compared with 12.5% Stage IA).

Brinkmann *et al*. published a series of 60 cases of invasive cancer of the cervix diagnosed in a London tertiary referral centre between 1988 and 1998 that coincided with the first ten years of the formal screening programme in England [3]. Fifty-five percent of these women were either non-attendees for screening or under-screened. The present local series began nine years after the introduction of the screening programme when women should have been more familiar with the screening programme and therefore more willing to participate. It is disappointing that these results show no improvement.

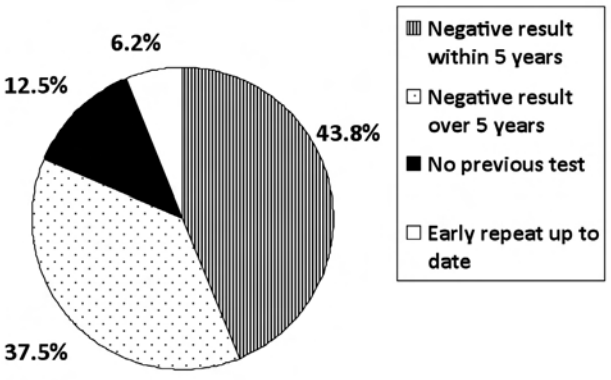

Figure 2. — Pie chart of cervical screening status at six months before diagnosis of Stage IA invasive cancer of the cervix.

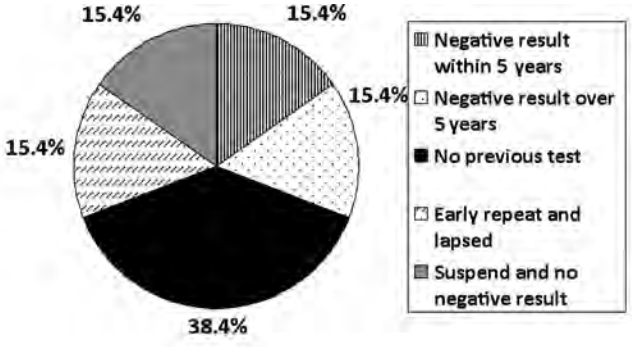

Figure 3. — Pie chart of cervical screening status at six months before diagnosis of Stage IB+ invasive cancer of the cervix.

The NHS cervical screening programme has provided a more detailed breakdown of the 2011 audit [1]. For the North East region, 23.3% of Stage IA cases and 30.8% of Stage IB+ cases were recorded as having no previous cytology, compared with 19.3% for Stage IA and 25.3% for Stage IB+ from pooled data for England. The attendance data for the recent nationwide audit (2007-2010) [1] and this local series (1997-2004) have similar methodology as both excluded cytology test results within six months of diagnosis. For the more advanced cases, the number of women with no previous cytology decreased from 38.4% to 30.8%, but for the women diagnosed with microinvasion, those without previous cytology increased from 12.5% to 23.3% between the two audit periods.

There are several weaknesses of this audit. The study would have been more informative if FIGO staging had been known for all cases. Many studies investigating cervical screening and cancer of the cervix [1, 6] include a control group of non-hysterectomised women who do not develop cancer. This type of analysis helps to identify different demographic or behavioural characteristics in those presenting with invasive cancer to age-matched women. This type of analysis was not possible for this series as cases were drawn from a specialist colposcopy unit and not primary care.

Human papilloma virus (HPV) self-sampling may be an alternative strategy for screening non-attendees of cervical screening programmes. Szarewski *et al*. found that HPV self-sampling increased participation among non-responders in a randomised trial comparing provision of self-sampling kits with a further invitation to attend for cytology testing [7]. Further studies are required to investigate the response to self-sampling in other parts of the country with different demographics to clarify whether this initiative will be successful throughout England.

Conclusion

A recent study confirmed that women with screen-detected cancers of the cervix have a far better prognosis than those presenting with symptoms [8]. This present audit also suggests that those with invasive cancers are infrequent or non-attendees of a screening programme. It is vital, therefore, that additional strategies are found to increase uptake of cervical screening across all age groups of eligible women to maximise the effectiveness of national screening programmes in preventing invasive cancer of cervix.

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