NHSCSP AUDIT OF INVASIVE CERVICAL CANCER: NATIONAL REPORT 2009-2012

June 2013

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PREFACE

Since April 2007, the regional Quality Assurance Reference Centres (QARCs) in England have adopted a standardised protocol for capturing screening data on all cases of cervical cancer. The data are aggregated in a national database for the purpose of audit, with the aim of monitoring and improving the service.

The first national audit report analysing these data appeared in July 2011, and covered cases of invasive cervical cancer diagnosed between April 2007 and March 2010. The second national audit report updated the data presented in the first, extended the period under scrutiny to March 2011, and covered both cytology and histology review data. This, the third national report, includes cases diagnosed between April 2009 and March 2012, presenting data on the most recently diagnosed cases only. We have therefore prioritised timeliness over data completeness, and readers should take note of the caveats attached to this approach.

The data in this report are influenced by two wider changes. Firstly, data from April 2010 reflect a new policy (issued back in 2003, but implemented more recently) raising the age at which women are first invited for screening from 20 to 25. Since almost 50% of women are now screened for the first time within a few months of their 25th birthday, a small peak of screen-detected cancers at age 25 is observable. Secondly, the so-called 'Jade Goody effect' can be seen in the results, which show an increase in both cervical cytology testing and cancer diagnosis in late 2008 and early 2009, in the wake of the publicity surrounding the reality star's diagnosis of cervical cancer (August 2008) and untimely death from the disease (March 2009).

Finally, a word about the future. The ways in which the cervical screening programmes collect audit data, and the accuracy of those data, continue to improve. New audit guidelines, which will make the process more efficient and less time-consuming, were implemented in 2012 and will be reflected in the 2014 annual publication.

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EXECUTIVE SUMMARY

The NHS Cervical Screening Programme (NHS CSP) in England provides high-quality cervical screening to a target population of about 14 million women. The NHS CSP is highly effective in preventing cervical cancer, and still more effective in preventing death from the disease.

- The NHS CSP audit comprises 10,920 women with confirmed diagnoses of cervical cancer (an estimated 90% of all cervical cancers diagnosed between January 2007 and December 2010 in England).
- This report focuses on 6,508 women who had a confirmed diagnosis of cervical cancer between April 2009 and March 2012. They are compared to 12,841 women without cervical cancer.
- The proportion of missing staging data continues to decrease (from 13.3% in last year's publication to 10.5%).
- The age at which cervical cancer is diagnosed in England has changed radically in the last 40 years:
    - In 1977, the observed rate per 100,000 observed in women aged 25-29 was 9.5 and in those age 30-34 it was 15.3, whereas by 1997 it had risen to 11.1 and 15.4 respectively. By 2010, the rate per 100,000 women aged 25-29 was 17.4, and 17.7 for women aged 30-34. Reasons for this change most likely include increases in underlying risk factors for cervical cancer (such as rates of SITs and smoking) and improvements in histopathological reporting of early stage cancer.
    - The opposite is observed for incidence in women age 50-64: in 1977 they had rates of over 32 per 100,000, by in 1997 the rates were 13.4 per 100,000 and in 2010 rates were under 10. The decrease in rates in this age group is a direct result of screening: women are diagnosed and treated for pre cancerous disease preventing the development of cancer.
    - Rates in women aged 20-24 have hardly changed over the years they were 2.5 in 1977, 2.8 in 1997 and 2.6 in 2010. Cervical cancer is rare in this age group (1.9% of cases in this audit) and screening is less effective. Now that women are no longer invited for screening till age 25 we expect rates to decrease in this age group, because some of the screen detected cancers at age 24 will now be screen detected at age 25. In fact a decrease in the proportion of cancers diagnosed in this age group is already apparent for the audit year 2011-2012 (Appendix C, Table 2) and a change in the stage at which cancers are diagnosed can also be seen (Section 4, Figure 4).
- Almost half (47%) of all the cases diagnosed in women aged 25-49 are micro-invasive cancers (stage 1A). 34% are stage 1B. However, in women aged 50 to 64, 50% of cancers are stage 2 or worse.
- Over 70% of stage 1A1 cancers were treated conservatively (by cone biopsy, loop excision or trachelectomy). In comparison, only 47% of stage 1A2 cases were treated conservatively.
- Since October 2009, a quarter of all women diagnosed between the ages of 25 and 34 were diagnosed at the age of 25. Between April 2007 and September 2009, just 8% of women within this same age range were diagnosed at 25. Sending women their first invitation to cervical screening at the age of 25 instead of 20 has therefore resulted in an increase in diagnoses of early stage cancer (1A) at age 25. However, there is no

evidence to suggest that women who attend screening for the first time at the age of 25 have an increased risk of being diagnosed with stage 1B or worse cervical cancer.

- Despite improvements in histopathological reporting, women diagnosed with squamous carcinoma are more likely to be diagnosed when the cancer is at an early stage (40% of all squamous carcinoma was stage 1A) when compared to those diagnosed with adenocarcinoma (25% were diagnosed as stage 1A).
- The percentage of women with no cytology test (other than up to six months prior to diagnosis) is 27.4% for stage 1A cancer and 26.3% for stage 1B+ compared to only 13.3% in the population controls (Appendix C, Table 14). The proportion of women with no cytology test up to six months before diagnosis has increased substantially in those age 25-34 since October 2009 in both cases and controls (Figure 9).
- Nearly a third (21670/6508) women with cervical cancer did not have a cytology test indicating referral to colposcopy. At the other extreme 3% of cases had more than one referral to colposcopy (with at least two negative tests in between referrals) before diagnosis.
- Focusing on women with one referral to colposcopy before diagnosis and at least one colposcopy appointment recorded, we found the 77% are diagnosed within 4 months of the referring cytology. However 11% have a delay of 2 or more years between referral and diagnosis.
- Women with an interval of 2 years or more between referral and diagnosis are less likely to have been referred to colposcopy on a severe or worse cytological result and they are more likely to be diagnosed with stage 2 or worse cancer when compared to those with an interval of less than 2 years. Fortunately these women account for only 7% of all cancers in the audit.

1. CONTEXT

1.1 The burden of cervical cancer in England

Cervical cancer is a malignant neoplasm of the cervix uteri. In 2010, 2,305 cases were registered in England, with an incidence rate of 8.7 per 100,000 women (calculated using corresponding mid-year resident population).[1] The highest incidence was among women aged 30–34 (17.7 per 100,000 women), followed by women aged 25–29 (17.4 per 100,000 women). The cervical cancer age-standardised incidence rate (world) for England in 2010 was 6.9 per 100,000, in 1975 it was 11.0[2] and for sub-Saharan Africa it was 31.7 per 100,000 in 2008.[3] Thus it is reasonable to suggest that, in the absence of cervical screening, the age standardised incidence rate (world) would be between 11 and 32 cases per 100,000 women.

Mortality from cervical cancer is substantially lower than incidence, with 830 deaths reported in 2009.[4] Age-standardised relative survival for patients diagnosed from 2005 to 2009 was 83.6% at 1 year and 66.6% at 5 years.[5]

1.2 Epidemiology of HPV and cervical cancer

Human papillomavirus (HPV) is a common, sexually transmitted infection. A small proportion of women who are infected with high-risk forms of this virus can go on to develop cervical cancer.

There is consistent evidence from across the world that high-risk HPV (HR-HPV) infection is a necessary cause of cervical cancer, and optimal testing systems have identified the virus in all invasive specimens.[6] HR-HPV is implicated in both squamous cell carcinoma (SCC) and adenocarcinoma (ADC), as well in over 95% cases of cervical intraepithelial neoplasia grade 3 (CIN3), which can subsequently develop into cancer.

Cofactors that appear to increase the risk of developing cervical cancer in HPV-infected women include the use of oral contraceptives, smoking, high parity, unidentified genetic factors (possibly related to immunity), and previous exposure to other sexually transmitted diseases, such as *Chlamydia trachomatis* and herpes virus type 2. Women exposed to human immunodeficiency virus (HIV) are at elevated risk of HPV infection, HPV persistence, and cervical cancer.

Cervical screening and treatment of high-grade CIN have the potential to prevent the development of cervical cancer in HPV-infected women, and screening programmes have therefore had a substantial impact on cervical cancer incidence in many countries.[7]

1.3 Cervical screening

Cervical screening is not a test for cancer, but a means of preventing it. The English cervical screening programme uses cervical cytology and HPV testing to detect abnormalities which could lead to cancer if left untreated. Early treatment can prevent the development of almost 100% of cervical cancers.[7]

Though cervical screening sometimes does not detect an abnormality before the onset of cancer, it increases the chance of detecting asymptomatic disease at an early stage, which means that treatment is more straightforward and more likely to be successful. Virtually all micro-invasive (stage 1A) cancers are diagnosed by screening; these can often be treated with fertility-sparing surgery[8], and can usually be cured (5 year survival >98%).

The cytological screening test involves the collection, staining, and microscopic examination of cells from the cervix. Between 1988 and 2003, conventional smears were used to screen women: samples were taken from around the cervix and wiped onto a glass slide, which was then sent to the laboratory for examination. Between 2003 and 2008, a new way of preparing samples, known as liquid-based cytology (LBC) was introduced nationwide. Here, cells are brushed from the neck of the womb and placed into a small vial of preservative fluid. This is then sent to the laboratory, where a glass slide is prepared. The introduction of LBC has decreased the proportion of samples that are inadequate for evaluation, producing more representative specimens with less of the distracting background material that was found in conventional smears.[9]

1.4 HR-HPV DNA testing

There are over 100 types of HPV, most of which do not cause significant disease in humans. However, around 15 types of HPV have been implicated in cervical cancer, notably types 16 and 18, which together give rise to some 70% of all cases. Research has shown that women with no evidence of HR-HPV infection are extremely unlikely to have concurrent precursor disease or cervical cancer, or to develop either for the following 6 years. [10]

HR-HPV testing detects high-risk forms of HPV. Over the last few years, different uses for such tests have been under evaluation in England:

- to triage women whose cytology shows borderline changes or low-grade dyskaryosis, so that only those who are positive for HR-HPV are sent for further investigation.
- as a 'test of cure', to reduce the duration of surveillance following treatment for CIN by safely returning women to routine recall at an earlier date.
- to replace cytology as the primary screening test.

As of April 2012, HR-HPV testing was introduced in England for triage and test of cure, following successful use at six sentinel sites within the NHSCSP.

1.5 Eligible age range and intervals for screening within the NHSCSP

The NHSCSP aims to reduce the incidence of, and mortality from, invasive cervical cancer. It does this by regularly screening all women at risk, so that abnormalities that might otherwise develop into invasive cancer can be identified and treated.

Cervical screening was introduced in England in the mid-1960s. By the mid-1980s, many women were undergoing regular cervical cytology, but there was concern that those at greatest risk were not being tested, and that those who had positive results were not being effectively followed up and treated. In response, the NHSCSP was established in 1988, after the Department of Health introduced quality standards for screening services and instructed all health authorities to introduce computerised 'call and recall' systems to manage invitations and results.

Between 1988 and 2003, women were invited for cervical screening at least every five years (and not more frequently than once every three years) from the age of 20 to the age of 64. In October 2003, it was announced that women would receive their first invitation five years later, at the age of 25, and that the interval between screening episodes would be three years up to the age of 49. Thereafter, women would be recalled every five years until the age of 64 (Table A). This remains current policy.

However, while this alteration was announced in 2003, it was designed to take effect from the date of a woman's next screening invitation. This meant that a woman screened prior to 2003 at the age of 20 had already been allocated a three-year recall, and could therefore have been invited again in 2006, despite the fact that she was still not 25. Similarly, a 61-year old women screened in 2003 could have been invited again three years later if her screening due date had been entered on the call and recall system before the change in policy. Moreover, in some parts of England, the policy change to a minimum age of 25 was not implemented until October 2005. It was therefore not until November 2010 that routine invitations to those aged 20-24 ceased.

Today, all women between the ages of 25 and 64 are eligible for free cervical screening. However, because first invitations are sent out a few months before a woman's 25th birthday, some women will still be screened at the age of 24. Cervical screening is not offered to women who have no cervix, or to those who have made an informed choice to opt out of the programme.

Table A Cervical screening intervals since October 2003

Age group (years)	Frequency of screening
25	First invitation.
25–49	Every 3 years.
50–64	Every 5 years.
65+	Routine screening for women who have not been screened since the age of 50, or who have had recent abnormal test results.

1.5.1 NHAIS

All women aged between 25 and 64 and registered with a GP in England are eligible for cervical screening, including migrants. The process of calling and recalling women for screening is managed by a computer database called the National Health Authority Information System, or NHAIS (also known as 'the Exeter system'). NHAIS manages the invitation process, keeps a record of test results, and, if all is well, recalls the woman for her next routine appointment in three or five years, depending on her age.

The programme screens almost four million women in England each year. In total, almost four and a half million samples per annum are examined by pathology laboratories (some women have more than one test, for clinical reasons or because a sample has proven to be inadequate).

While no cervical screening test can be 100% effective, cervical screening programmes greatly reduce the incidence of this cancer in the screened population. Since the establishment of the NHSCSP, the number of cervical cancer diagnoses has halved from 16 per 100,000 women in 1988 to 8 per 100,000 women in 2005, despite increasing rates of HPV infection. Another measure of the programme's effectiveness is its coverage, defined as the percentage of women in the target age group (25–64) who have been adequately screened in the last five years. In 2011/2012, screening coverage of eligible women was 78.6%.[11]

1.6 Cervical screening and HPV vaccination

Two prophylactic HPV vaccines are known to be effective at preventing both persistent HR-HPV infection, and the high-grade cellular abnormality (CIN3) that it can cause. In September 2008, a national HR-HPV immunisation programme was introduced to vaccinate girls against HPV 16 and 18. It covers young women aged 12–13, but also includes a catch-up programme for those born between 1990 and 1995.

Despite this vaccination programme, the NHSCSP will continue to play an important role in the fight against cervical cancer. It will screen those women who have not been vaccinated, and it will also play a role in monitoring the vaccinated population because they are at risk of carrying non-vaccine HPV types and because vaccination in women that are already infected can fail. The role of the screening programme in these women can be better defined once clearer data are available about the cross-protection given by the vaccine for other HPV types, and the duration of the protection provided. Interim studies are needed to explore the impact of HPV vaccination, and to determine the best course of action for the cervical screening programme in future.

A woman's HPV vaccination status should be recorded on the call and recall computer system, so that her future screening interval can be determined. Unfortunately, the completeness with which this information is recorded is very variable, though ongoing work aims to simplify the process and improve the completeness and accuracy of the data.

2. AUDIT OF INVASIVE CERVICAL CANCERS

2.1 Introduction

Unfortunately, despite the effectiveness of population-based screening, women continue to develop cervical cancer. The reasons for this were recognised before the NHSCSP was established in 1988, and have been taken into account in previous recommendations emerging from this audit.[12]

Five-year cervical screening coverage has been around 80% since 1993, so the majority of cancers in England are probably occurring in women who have been screened at some point in their lives. Monitoring incidence and mortality rates in this population can determine whether the programme is achieving its objectives. It does not give a complete picture, however; nor does it indicate the effectiveness of the screening programme under optimal conditions.

2.2 Purpose of the audit

The purpose of the NHSCSP audit of invasive cervical cancer (hereafter, 'the audit') is to monitor the effectiveness of the cervical screening programme, to identify areas of good practice and indicate where improvements might be made, and to monitor cases where the programme fails to prevent cervical cancer. The audit can also monitor whether alterations to the programme (for example, changes to the screening technologies employed, to the age range over which women are called for testing, and to the frequency of screening at different ages) are affecting the incidence of cervical cancer in the screened population.

All cervical cancers are included in this audit, irrespective of their clinical stage, or the age of the woman at the time of diagnosis. The audit thus provides an early indicator of the pattern of disease incidence, using cases which have not necessarily been fully abstracted by the cancer registries. It allows the proportion of screen-detected cases to be determined, and explains why some cases occurred (e.g. diagnoses of cervical cancer in previously unscreened women, or cases that result from a failure of colposcopic treatment).

Monitoring the effectiveness of the NHSCSP requires accurate data about the incidence of, prognosis for, and mortality from cervical cancer. Additionally, these data need to be linked to individual-level information about screening uptake and outcome. In order to obtain consistently reported information for this purpose, all parties in the NHSCSP were asked to follow the same national protocol for auditing cases of invasive cervical cancer.[11]

2.3 Audit Protocol

Although there are minor differences in the procedure employed by different regions, the broad principles of the audit, including the allocation of key roles, are the same nationwide. These were first outlined in the document *Audit of Invasive Cervical Cancers (*NHSCSP publication no 28)[12] and subsequently updated in April 2012[13] A further update was introduced in April 2013[14]. These guidelines are currently being incorporated into an updated version of NHSCSP publication no 28, which will be published shortly.

The NHSCSP Audit Management Group is the steering committee for the audit. Based on its data and findings, the Group approves updates and makes recommendations.

In brief, when a case of histologically confirmed invasive cervical cancer has been identified, the clinician treating the woman must ensure that the Hospital-Based Programme

Coordinator (HBPC) and the regional Quality Assurance Reference Centre (QARC) are informed. This will initiate a cascade of audit activities. The role of the HBPC is to organise audit activities locally (i.e. within each Trust). The role of the QARC is to ensure that local cytology, histology, and colposcopy review processes are coordinated according to the national audit protocol, and to liaise with Cancer Registries to ascertain that the information captured includes a record of the diagnostic status of each cancer case (though the extent of this cooperation varies between regions). The QARC also assembles all the data for a region, ready for national collation.

2.3.1 Ethical approval

Anonymised data are routinely collected for women who have developed cervical cancer (known as 'cases') and for women of the same age who have not (known as 'controls'). Since collection of these data is regarded as part of the NHSCSP's service evaluation, the process is exempt from research ethics review by the National Research Ethics Service.[15]

2.3.2 Selection of controls

To permit rigorous evaluation of the programme, cases of cervical cancer are compared to controls of the same age. Controls are identified using bespoke software within NHAIS.

All controls are registered with a GP in the same administrative district as the case, and women who are known to have had a hysterectomy are excluded. Additionally, controls fall into the following groups, based on their similarity with cases:

- GP controls, from the same group practice as the case.
- District controls, who share the same first half of a postcode with the case, but who are registered with a different GP.
- Screened controls, who underwent cytological tests over roughly the same period as the case (used where the case may have been diagnosed as a result of screening).
- Abnormal controls, who received an abnormal cytology test report during roughly the same period as the case.

Each case is assigned two population controls (one GP control and one district control). In addition, some cases are assigned controls to match the woman's screening history. This allows the audit of both cases that are detected by screening (known as 'screen-detected cancers'), and cases where a woman received an abnormal screening result and was referred to a colposcopist some time before her actual diagnosis (see section 4.1).

Population controls are used to study the importance of coverage and the efficacy of the screening programme. Screened controls are used to explore the impact of the screening interval on the incidence of screen-detected cancers. Abnormal controls are used to compare the way in which cases and controls are managed by the screening programme after a cytological test is reported as abnormal.

2.3.3 Databases and other data sources

The audit is designed to collect data from a number of sources on a woman's age, stage, and call and recall status, as well as on her cytology, colposcopy, and histology results. Information on a woman's screening invitations and results, and laboratory data on her

cytology, are drawn from NHAIS via Open Exeter.* Coordination between the HBPC and the QARCs is needed to obtain all other records, due to variability in the availability of data and level of access to the different databases. Colposcopy clinics are contacted for records of all appointments (e.g. information on patient attendance, details of the examiner, data on the colposcopic impression, account of any procedures performed). Histology results are also collated to produce a fuller picture, and to facilitate slide review.

An audit database has been created to aggregate all data collected by regional QARCs for epidemiological analysis.

2.3.3.1 Essential fields

To generate a minimum dataset, information about each case of cervical cancer is entered into the database via a number of essential fields (see Appendix A).

2.3.3.2 Cytology screening history

Before 2003, cytology samples took the form of conventional smears, but between 2004 and 2008, laboratories converted to liquid-based cytology (LBC). To reflect the use of both technologies during the audit period, this document refers to cytology 'tests' or 'samples', not to 'smears'.

Details of every recorded cytology test for both cases and controls were downloaded from NHAIS. The dataset included a large number of privately-taken samples, as well as information on all NHSCSP tests. The following information was obtained:

- the date on which the test was taken.
- the result of the test.
- the action code resulting from the test.

(The action code is the national code used to define the woman's recall type, the type of notifications required, and the period of time between recalls. It determines the management action for each woman in the light of her latest test result, and records any additional clinical input).

Additionally, from April 2012, the following information is included in the NHAIS download:

- the interval between tests.
- the date in which the woman's next test is due.
- the HR-HPV test result (where was an HR-HPV test was performed).
- the reason a woman postponed screening (where appropriate).
- the reason a woman was ceased from screening (where appropriate).

The following additional information is collected from NHAIS for cases:

- date of birth.
- date of cancer diagnosis.
- the FIGO stage of the tumour.
- histology of the tumour.
- treatment received (now an essential field).
- the woman's score according to an Index of Multiple Deprivation (now an essential field).

* Open Exeter is a portal that allows bodies such as NHS trusts, GP practices, and laboratories to access the Exeter (NHAIS) system.

For controls, date of birth and Index of Multiple Deprivation score were collected.

2.3.3.3 Colposcopy

Colposcopy data were obtained for cases, including:

- date of appointment.
- attendance at appointment.
- whether the examination was satisfactory.
- information on any surgical procedure(s) performed.

Non-essential additional fields included:

- colposcopic impression.
- pathological diagnosis.
- whether the woman was pregnant.
- time to next follow-up appointment.

Colposcopy review guidelines and data collection forms were rolled out in April 2013. Results from this review should provide insight into colposcopic management in women who go on to be diagnosed with cervical cancer.

2.3.3.4 Cytology and histology reviews

Audit guidelines covering the period of this report mandate that when a case of cervical cancer is confirmed, all cytology samples and histology specimens obtained over the 10 years preceding diagnosis, including those that led to diagnosis, must be reviewed. The primary purpose of this slide review is educational, and collated national results from this exercise, with detailed analysis and commentary, have been published separately.[16] While some of these data are summarized here, those interested in obtaining a more detailed picture should refer to the published document.

Data obtained from the review process include:

- date of the original sample or specimen.
- date of the review.
- type of reviewer (screener, checker, advanced practitioner, consultant).
- original sample or specimen result.
- result of the review/consensus.

Following the implementation of revised guidelines in April 2012, fewer slides need to be reviewed and, in the case of cytology, fewer reviews per slide as required. This will result in a significant reduction in workload, as diagnostic biopsies, which currently form 78% of histology reviews (4,780 out of 6,122 reviews) will not form part of future audits. The introduction of the new audit guidelines was followed by a 3 month period (April to June 2012) where reviews of cytology and histology samples from women diagnosed with cervical cancer as part of audit were suspended. As a result, the number of reviews submitted for this publication has barely changed from last year and the new data is insufficient to present on its own. Therefore, no review results will be presented this year; however a full report on the first year of the new guidelines will be presented in next year's report. For details on the review results please refer to the Audit report for 2007-2010.

2.3.3.5 GP notes

Following a recent review by the West Midlands QARC, the Evaluation Committee has agreed that, in most cases, it is not possible systematically to collect useful information from this source. Consequently, information derived from GP notes is no longer required as part of this audit.

However, it may be of interest to collect information from GP notes where a woman's screening history is unclear. This may yield additional information on her symptoms (if the cancer is symptomatic), and may also explain any non-attendance at appointments (e.g. where there is evidence of pregnancy, travel, co-morbidity, or private treatment). There are currently several other projects exploring the possibility of obtaining information from GP notes. The Evaluation Committee will evaluate the results from these projects and assess whether there is a feasible way to obtain data from this source before revising the audit protocol.

2.3.3.6 HR-HPV tests

HR-HPV DNA is currently being introduced nationally as part of the NHSCSP, following evaluation at three pilot and six Sentinel Sites. It is used for two purposes:

1. To triage of women with low-grade or borderline cytology reports. Where HR-HPV is found, these women are referred immediately to colposcopy, but where women are HR-HPV-negative, they are returned to routine (three- or five-yearly) recall.
2. As a 'test of cure' for women who have been treated for cervical intraepithelial neoplasia (CIN). If a cytology test, taken six months after treatment, is reported as normal, borderline, or low-grade, an HR-HPV test is performed. Women who are HR-HPV-negative are returned to routine recall, but those who are HR-HPV-positive are referred to colposcopy. (Women with high-grade cytology six months after treatment are referred immediately to colposcopy, without this additional HR-HPV test).

HR-HPV test results are currently recorded on NHAIS and have been added to the list of essential fields.

2.3.3.7 Index of Multiple Deprivation

The Office of the Deputy Prime Minister produces the English Indices of Deprivation, from which the Index of Multiple Deprivation, utilized by this audit, is derived.*

For the purpose of this exercise, the index of deprivation has been divided into deciles, from the most deprived (0) to the least (9). The Index of Multiple Deprivation score is derived from each woman's postcode. To facilitate the collection of this field, the woman's home postcode is now captured as part of the NHAIS download and converted automatically by the audit database into a deciles. Only the deprivation deciles are collected nationally.

However, because this data field is currently not essential, it has not been reported consistently across QARCs. The data received to date, while quite revealing, are therefore incomplete (see Appendix B, Table 1a). Since 2012 this field is essential and more detailed analysis will be possible in future.

* For more information see https://www.gov.uk/government/publications/english-indices-of-deprivation-2010-technical-report.

2.3.4 Data aggregation

Names, addresses, and unique identifiers (such as NHS numbers) are deleted before data are transferred to the national audit database. The only data that might be considered "person-identifiable" received by the audit is date of birth. However, since there are 750 women in England between the ages of 20 and 65 with any given date of birth, this information is considered insufficient to identify a particular individual, effectively making the data anonymous.

3. DATA COMPLETENESS AND LIMITATIONS

The findings presented in this report should be approached in light of the available information's varying degree of completeness (see Appendix B). The difficulties involved in ensuring the completeness of essential data fields are described below.

It is rare for data to be reported as missing, but missing data should be distinguished from incompleteness of record. Missing data may be unavailable (e.g. where a death certificate, which does not provide information about cancer staging, has been used), or may not yet have been recorded as part of the audit. For this reason, the term 'none recorded' has been used to cover both scenarios, although reference is also made to 'missing values'.

Other cases may be subject to reporting delays, having been submitted to the audit before all essential fields could be completed. In these instances, missing fields are updated as and when data become available, with the result that complete information may not be received for some months after the case has been registered. An additional challenge, which can create further delay, is the need to coordinate between the various aspects of the audit process when a case of cervical cancer is diagnosed. In future, as the completeness of the audit for each case will be monitored, it will be possible to distinguish between data that are not available (after reasonable efforts have been made to collect them) and data that have not yet been collected (see Appendix B).

3.1 Cancers and population controls

Cases of cervical cancer are identified by NHS hospital staff (primarily via gynae-oncology), and confirmed by histology. A small proportion of cancers will be missed by the audit, and a very small proportion will be excluded because the patients are not registered with an NHS GP. Table D (Section 4.1) illustrates the limited extent of this problem, comparing the number of registrations for cervical cancer in a given calendar year with the number of cases picked up by the audit over the same period of time.

Controls are selected randomly (subject to matching) from women registered with an NHS GP. All those selected are included in the audit.

3.2 Dealing with missing values

Cases reported by the MB1 series (Cancer registration statistics in England) between 2008 and 2010 were compared to those recorded in the audit for the same period by age at diagnosis to explore whether missing values (in particular those for FIGO stage) are related to the age at which the cancer is diagnosed or the FIGO stage at diagnosis. The aim was to ascertain whether there is a subset of women for whom a delay in the inclusion of the cancer in the audit is more likely (see Table C). The number of cases in the audit for 208-2010 is 92% of the number of cervical cancer registrations in England over the same three years. However, the data are more likely to include cases diagnosed in women between the ages of 25 and 64 (96% of all registered cancers), than in women over the age of 65 (74% of registered cancers).

We also assessed the completeness of the data for FIGO stage by comparing the distribution of staged cancers diagnosed between April 2008 and March 2009 across four audit years (Table D). Women with a cancer of unknown stage and those whose case was not registered into the audit straight away were more likely to have been diagnosed with stage 2 or worse cancer. For instance, looking at cancers diagnosed in April 2008 to March

2009, 23% of those registered by October 2009 were stage 2 or worse, but by October 2012 30% were stage 2 or worse.

In previous reports, we assumed that data for FIGO staging was missing at random. In recent audits, this has led to an overestimation of the proportion of stage 1A cancers and an underestimation of the proportion of stage 2+ cancers. This bias applies to figures that present stage distribution over time. However, results shown in Table E (Section 4.1) suggest that, in recent years, cancers have been registered into the audit in a timelier manner. If this trend continues, the bias in the stage distribution should diminish year on year.

For this report we have used a more complicated model that takes into account the differential delays in obtaining stage[1].

3.3 Cytology

Since data for cytological tests are downloaded directly from NHAIS, completeness is assumed for all cases and controls. This is because cytological test results are recorded for all women who participate in the NHSCSP, and for some of those who are tested privately. The audit does not attempt to capture screening events that take place outside the UK.

3.4 Colposcopy

The quality and completeness of the colposcopic data are variable. This is principally because there is no central database to act as a repository for this information (indeed, most colposcopy records were not computerised until 2001). It is therefore difficult to determine where a woman attended for colposcopy, particularly if she visited more than one clinic.

The best indicator of whether a woman is likely to have had colposcopy is the presence of a 'suspend' code in her cytology record (see Table 19). Similarly, a record from the histology laboratory would suggest that a sample was taken at colposcopy. However, neither the cytology nor the histology record provides conclusive information regarding colposcopic examination.

3.5 Histology

The quality and completeness of the data on histology in this audit are also variable, as there is no national link between histology laboratories. The proportion of histological samples reviewed in the audit is based on the total number of samples recorded in the database, rather than the total number of histological samples taken within the NHSCSP.

3.6 HR-HPV DNA

Data on HR-HPV testing are now being collected directly from NHAIS in conjunction with the cytology data. We expect to be able to report on this in coming years.

3.7 Treatment

[1] For each QARC, a multinomial logistic regression model was fitted with outcome 'stage at diagnosis' and explanatory variables age group, treatment type and year of diagnosis. Using the results of this model, the probability of each stage category was then predicted for each individual with missing stage

Data on treatment are obtained by the HBPC from patient notes or from the meeting notes of the multidisciplinary team (MDT). These fields tend to be provided as data become available, which may mean that the information is missing for a few months after cases are first entered in the audit. Obtaining treatment data can be especially challenging where women are diagnosed in one centre and treated in another.

There has been some confusion over the use of the category 'none' to report treatment. The intended meaning is that the treating hospital has given only palliative care, but at least one QARC interpreted the category as 'no treatment was reported'. Additionally, some HBPCs used 'none' when micro-invasive cancers were treated solely with the diagnostic LLETZ/cone biopsy. While efforts have been made to correct this miscommunication for the future, some cases classified as 'none' in the audit may, in fact, have received treatment. From 2011 onwards, we are able to distinguish between 'palliative care' and 'no treatment'.

Table B Cancers reported nationally compared to those reported in the Audit between January 2008 and December 2010.

Total cases reported	<20	20-24	25-29	30-34	35-39	40-44	45-49	50-55	55-59	60-64	65-69	70-74	75-79	80-84	85 and over	Total	Aged 25-64
MB1 series 2008/10	2	147	963	980	1,006	841	609	465	432	418	300	319	306	294	304	7,386	5,714
Audit 2008/10	1	143	997	969	992	829	580	401	376	362	264	242	227	217	178	6,778	5,506
Proportion	50.0%	97.3%	103.5%	98.9%	98.6%	98.6%	95.2%	86.2%	87.0%	86.6%	88.0%	75.9%	74.2%	73.8%	58.6%	91.8%	96.4%
Difference	1	4	-34	11	14	12	29	64	56	56	36	77	79	77	126	608	208

Table C Cancers in women aged 20-64 diagnosed between April 2008 and March 2009

Data received as of	Observed stage by year of audit data							Proportion of those with stage recorded		
	1A	**1B**	**2**	**3+**	**1B+**	**None recorded**	**Total**	**% 1A**	**%1B**	**%2+**
Oct-09	463	380	130	109	67	419	**1,568**	40.30%	36.70%	23.10%
Oct-10	646	598	239	201	82	398	**2,164**	36.60%	36.50%	26.90%
Oct-11	665	651	275	241	90	283	**2,205**	34.60%	36.50%	28.90%
Oct-12	669	659	295	259	93	277	**2,252**	33.90%	35.90%	30.20%

4. ANALYSIS AND COMMENTARY

This section analyses and discusses the audit's key findings. Detailed data tables are presented in Appendix C.

4.1 Invasive cervical cancer

Over the period 2007–2012, 10,920 cases of invasive cervical cancer and 21,581 controls were included in the audit. Table D (see also Table B, section 3.2) provides a broad assessment of the audit's coverage, comparing the number of cases of invasive cervical cancer included in each audit year (corresponding to the financial year) with the number reported nationally in each calendar year. Although some cases included in the audit are not included in Cancer Registry data, and vice versa, the number of cancers reported to registries is only around 9% greater than the number included here. Updated estimates from the Office for National Statistics (ONS) report 2,766 diagnoses of invasive cervical cancer during 2009 and 2,346 during 2010, whereas the audit comprises 2,452 cases during 2009-10 and 2,087 during 2010-11.[17] All QARCs are working to minimise these discrepancies and to make both data sources more directly comparable.

Table D also presents a recent history of the number of cervical cancers included in each audit year. We have included this to illustrate the amount of new data received each year. Compared to national registrations, 72% of cancers diagnosed between April 2009 and March 2010 had been reported into the audit by October 2010, rising to 85% by October 2011 and 89% by October 2012. By comparison, 80% of cancers diagnosed between April 2010 and March 2011 had been reported into the audit by October 2011 and 89% by October 2012. These numbers suggest that data are being entered into the audit in an increasingly timely manner.

However, there is a trade-off between presenting data in a timely manner and the completeness of that same data. We have emphasized timeliness, and this year's report includes a great deal of detail on when we receive the data and how this timing affects our estimates of FIGO stage and age at diagnosis (see Section 3.1). Additionally, we focus only on the most recently diagnosed cervical cancers by restricting the data in this report to 6,508 cases diagnosed between April 2009 and March 2012 and their 12,841 controls (see table E). However where relevant, we have used all cancers reported to the audit.

Table D Number of cases of cervical cancer included in this report compared with those reported nationally

Audit Year	Calendar year	Cases included in 2010 report	Cases included in 2011 report	No of cases in this Audit report	Cancer Registrations£
2007-2008	2007	2,089	2,136	2,158	2337
2008-2009	2008	2,164	2,205	2,254	2409
2009-2010	2009	1,978	2,349	2,452	2766
2010-2011	2010	0	1,876	2,087	2346
2011-2012	2011	0	0	1,969	2511
Total				**10,920**	**12369**

£ Source: We have used updated number of registrations from Table 8 of the Office for National Statistics MB1 publication 42 (2011). As with the audit, ONS receive notification of a few extra cancers after they have published their yearly statistics.

Most cases submitted to the audit have at least two age-matched population controls (GP and district). However, for a small number of cases (23), only one of these controls was identified (see Table E), while 76 cases were submitted with no population control. For a defined subset of cases, up to two further controls were selected, resulting in 3,084 screened controls and 3,784 abnormal controls (see section 2.4.3.1.)

Table E Number of cases of invasive cervical cancer and controls submitted to the 2009–2012 audit by QARC region[a]

QARC	Case	Two Population Controls (GP and District)	One Population Control (GP or District)	No Population Controls
East of England	618	617	0	1
East Midlands	660	652	6	2
London	622	544	6	72
North East	425	424	1	0
Yorkshire	763	760	3	0
North West	831	829	2	0
South Central	495	494	1	0
South East Coast	510	509	1	0
South West	762	761	1	0
West Midlands	822	819	2	1
Total	**6508**	**6409**	**23**	**76**

*Cancers diagnosed 01/04/09 to 31/03/2012

4.2 Age at which invasive cervical cancer is diagnosed

Figure 1 shows the percentage distribution of cases of cervical cancer by age in the 2009–2012 audit, compared to the numbers reported nationally for 2007-2010. The peak number of cases is observed in the 25–29 year old age group (1,037 or 15.9%), followed closely by cases in women aged 30-34 (888 or 13.6%), and aged 35-39 (819 or 12.6%). Nationally, the peak incidence is observed in those aged 35-39, followed by those aged 30-34. The underreporting of cases to the audit increases with the age of diagnosis, so that we are missing more cases for women over the age of 65 than for those under age 65.

82% of all cases of invasive cervical cancer in this audit fell within the age group eligible for cervical screening (25-64 years, see Table 3, Appendix C). In 2010, women in this age group made up 78% of all cervical cancer registrations in England. As a proportion of all cancers, invasive cervical cancer at FIGO stage 2 or worse was more likely to be diagnosed in women over the age of 50 than in those under 50, with stage 1A disease becoming increasingly infrequent with age. By contrast, between the ages of 25 and 49, the majority of women diagnosed with cervical cancer were found to have stage 1A or 1B disease (see Table 6a, Appendix C).

The difference in the stage at diagnosis by age is even more apparent when looking at rates of cervical cancer (Figure 2). We used the observed rates of cervical cancer by age group reported in the MB1 series in 2010 and applied the FIGO stage distribution observed in the audit dataset. The age at which cervical cancer is diagnosed in England has changed radically in the last 40 years. For example in 1977 the rate per 100,000 observed in women aged 25-29 was 9.5 and in those age 30-34 was 15.3, by 1997 these had increased to 11.1 and 15.4 respectively.[2] In 2010 the rate in women aged 25-29 was 17.4 and 17.7 in women aged 30-34. Reasons for this dramatic change in cancer rates include increases in

underlying risk factors for cervical cancer (such as rates of SITs and smoking) and improvements in histopathological reporting of early stage cancer.

The opposite is observed for incidence in women age 50-64: in 1977 they had rates of over 32 per 100,000, in 1997 the rates were 13.4 per 100,00 and by 2010 rates were under 10 per 100,000 women.[2] We believe that changes in cancer rates in this age group are a direct result of cervical screening. Indeed the effect screening has had on all age groups can be seen by the reduction of over 70% in mortality from the disease due to prevention of cervical cancer and earlier stage at diagnosis.

Rates in women aged 20-24 have hardly changed over the years, they were 2.5 in 1977, 2.8 in 1997 and 2.6 in 2010.[2] Cervical cancer is rare in this age group (1.9% of cases in this audit) and screening is less effective in this age group when compared to older women.

We are keen to identify any changes in the FIGO stage of cancers diagnosed aged 25-29 as a result of the change in screening policy. It is too early to show any results in this report, but we continue to monitor the situation and will report on any changes in subsequent reports.

4.3 FIGO stage of invasive cervical cancers

Table F shows the observed number of cervical cancer cases by FIGO stage for each QARC region. FIGO stage information is missing for 9.33% of cases and clinical staging was not possible for 1.14% of women, therefore no staging data is available for 10.5% of cases (see Appendix B, Table 1b). The distinction between cases with missing stage data and cases where clinical staging was not possible is a recent one. It is difficult to determine the true proportion of cancers where staging is not possible, but we could speculate that it is similar to the proportion with missing histological data on type, i.e. 3.5% of cases (see Table 8, Appendix C).

The proportion of cases with missing stage has been reduced by a third since the first audit report was published (from 17% to 11% in this report), but we now know that those cancers where the FIGO stage is unknown tend to turn out to be higher stage than those with known stage. Therefore, we estimate that had all the cancers been staged, 35% of cancers in the audit would be stage 1A, 32% stage 1B, and 33% stage 2 or worse (Table G).

In 1,293 out of 2,167 cases of 1A cancer, further details were provided, and these suggest that 92% are 1A1 and only 8% 1A2 (see Table 4, Appendix C). 89% of women with stage 1A1 cancer were aged between 25 and 49, while only 1.3% were over the age of 65. Similarly in 949 out of 1896 cases of 1B cancer, further details were provided, and these suggest that 88% are 1B1 and 12% are 1B2.

Figure 3 shows the percentage distribution of invasive cervical cancer by FIGO stage and by age group in those women with a known FIGO stage. As the age of women increases, the proportion of cases diagnosed as FIGO stage 1A decreases, and the proportion of women diagnosed at FIGO stage 2+ increases. Stage 1A cancer is often screen-detected, and treatment generally has fewer side effects and is more likely to be curative. The large proportion of cervical cancer cases diagnosed at stage 1A (particularly those at stage 1A1) in women under the age of 50 can be regarded as a benefit of the screening programme. The exception is women aged <25. As fewer women under the age of 25 attend screening due to the raising of the lower age limit for the programme, the likelihood of screen-detected cancer in this group decreases. Therefore, it is mostly those women who are investigated because of symptoms who are likely to be diagnosed at this age.

Figure 4 shows the estimated percentage distribution of cervical cancer cases by FIGO stage, year of diagnosis, and age. Estimates for the last two years of data included in the audit are dotted, as this more recent data is less complete and we are less certain of the accuracy of the results. The effect of raising the age at which women are first invited for screening from 20 to 25 can be clearly seen from 2009 onwards.

65% of women in the audit were diagnosed between the age of 25 and 49. 46% of these women are diagnosed with stage 1A cancer and a further 36% with stage 1B cancer. The 'Jade Goody effect' (a rise in the number of younger women attending cervical screening appointments following the diagnosis and untimely death of the reality TV star) can also be seen in an increase in the number of stage 1A cancers diagnosed in this age group in 2009.

Women over the age of 50 at diagnosis, and particularly those diagnosed after the age of 65, are more likely to be diagnosed with advanced stage cancer than younger women. There has been no discernible change in the stage distribution for these women since the audit began in 2007.

Figure 1 FIGO stage of cervical cancer cases: estimated percentage distribution, by age

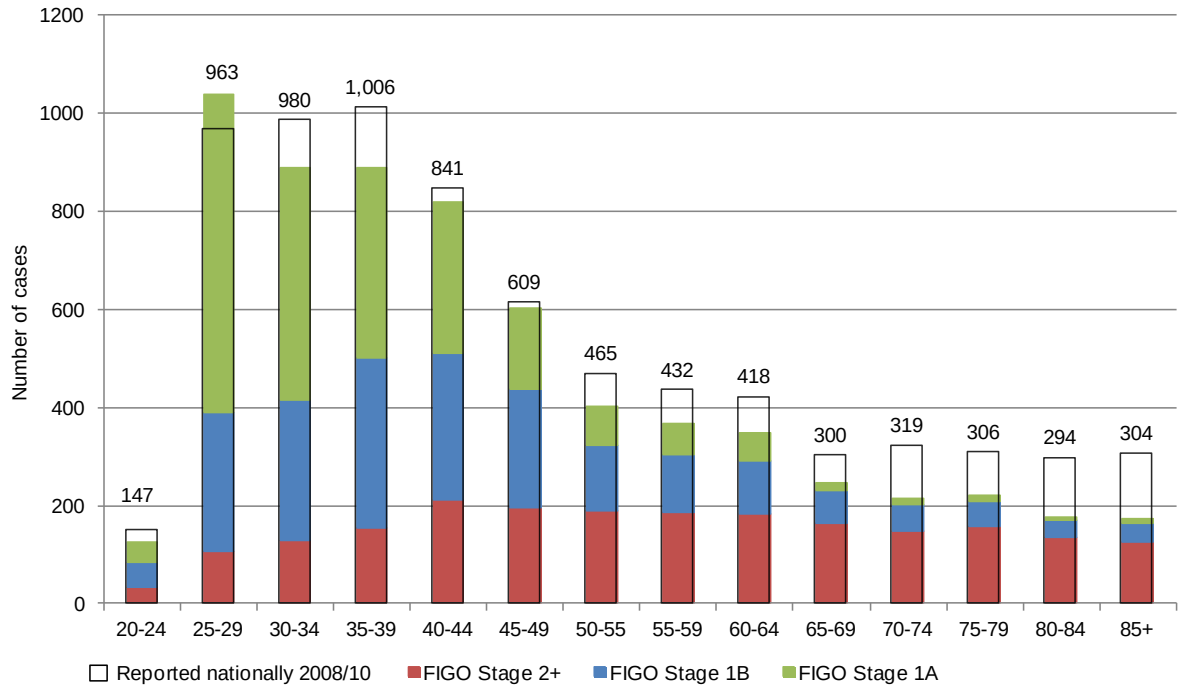


Figure 2 Observed 2010 rates per 100,000 women: by FIGO stage of cervical cancer cases and age

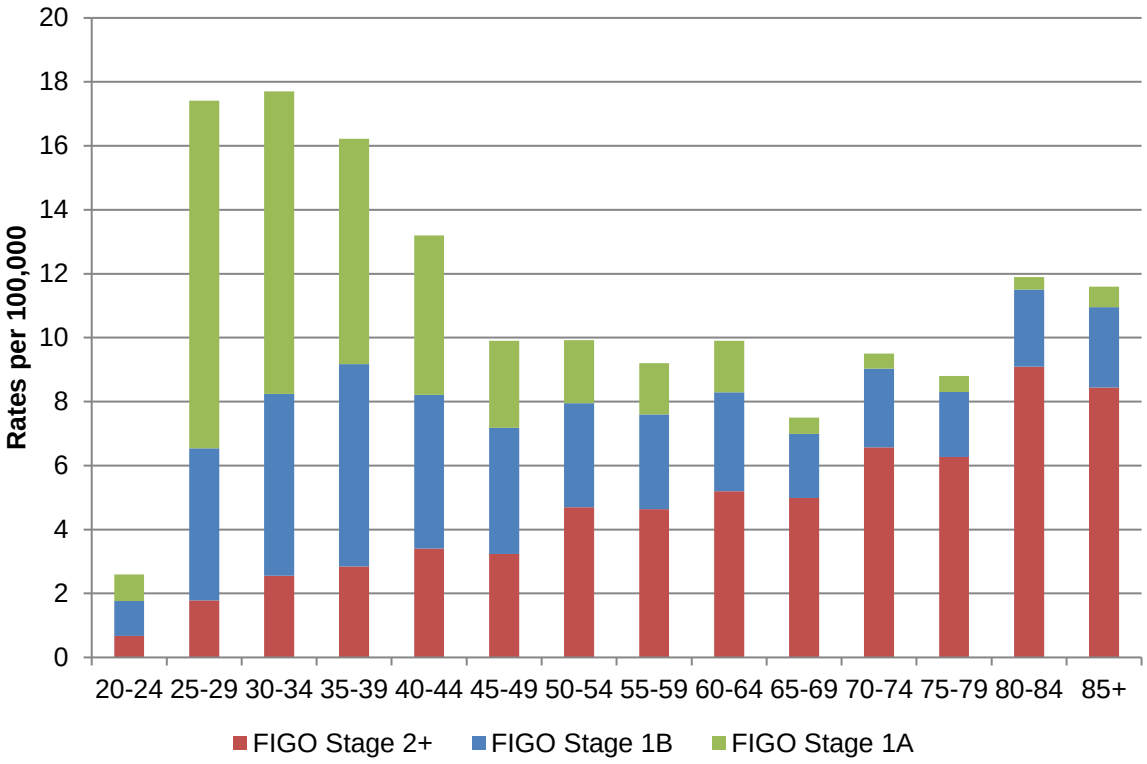


Figure 3 FIGO stage of cervical cancer cases: percentage distribution, by age-group

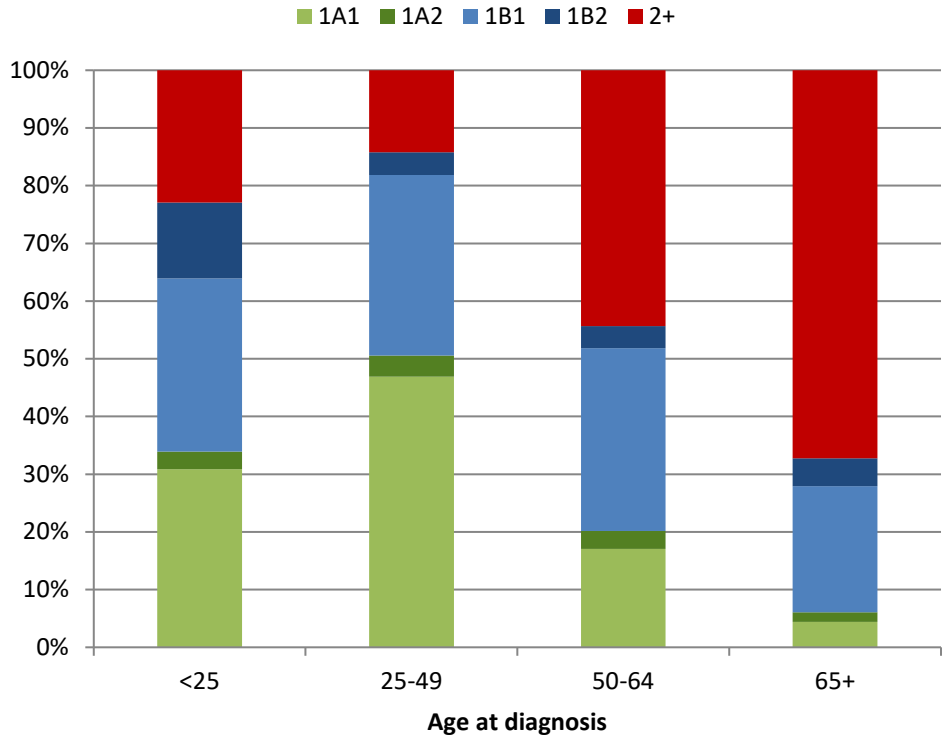


Figure 4 FIGO stage of cervical cancers cases: estimated percentage distribution by financial year

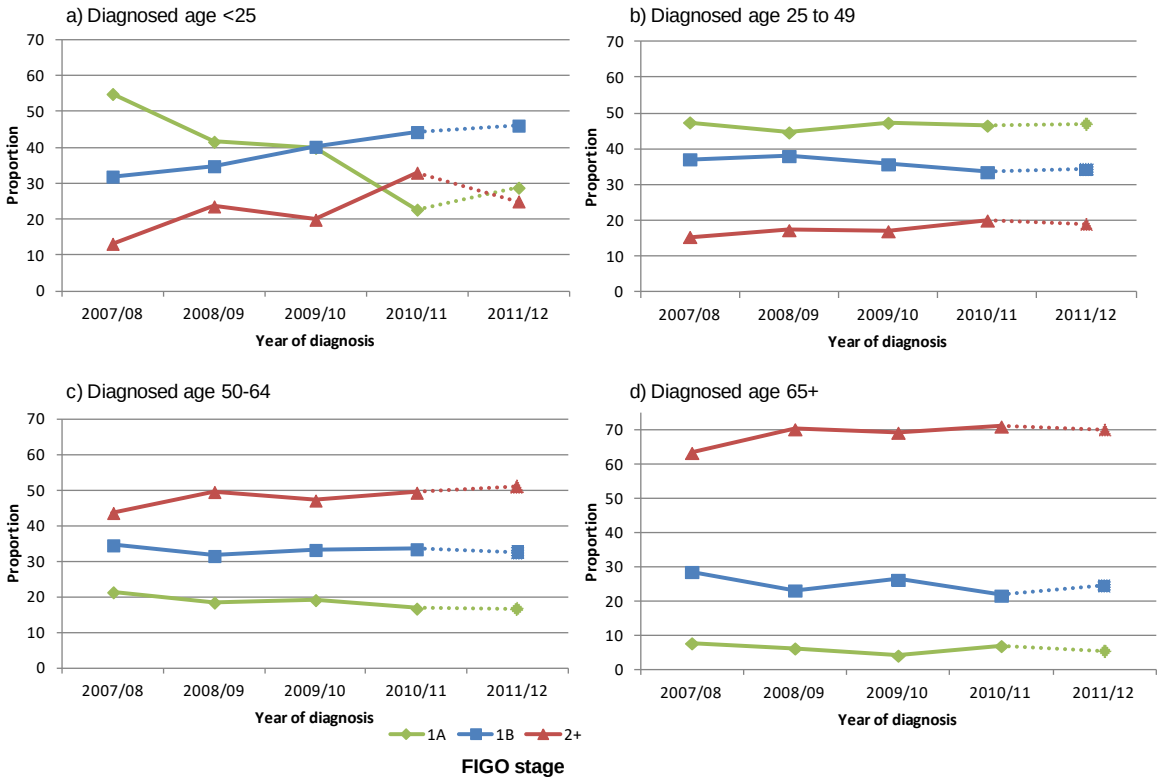


Table F Number of cervical cancer cases by FIGO stage in 2009-2012 audit, by QARC region

QARC Region	1A		1B		2+		1B(NOS)*		None recorded		Total	
East of England	196	32%	205	33%	170	28%	4	1%	43	7%	618	100%
East Midlands	241	37%	197	30%	111	17%	2	0%	109	17%	660	100%
London	202	32%	162	26%	182	29%	52	8%	24	4%	622	100%
North East	139	33%	124	29%	51	12%	73	17%	38	9%	425	100%
Yorkshire and the Humber	318	42%	184	24%	67	9%	28	4%	166	22%	763	100%
North West	259	31%	252	30%	103	12%	89	11%	128	15%	831	100%
South Central	178	36%	153	31%	134	27%	1	0%	29	6%	495	100%
South East Coast	180	35%	164	32%	116	23%	12	2%	38	7%	510	100%
South West	239	31%	239	31%	235	31%	28	4%	21	3%	762	100%
West Midlands	215	26%	216	26%	306	37%	0	0%	85	10%	822	100%
Total	**2,167**	**33%**	**1,896**	**29%**	**1,475**	**23%**	**289**	**4%**	**681**	**10.5%**	**6,508**	**100%**

* Cases reported as 1B(NOS) (are known to be stage 1B or worse but detailed stage is not known)

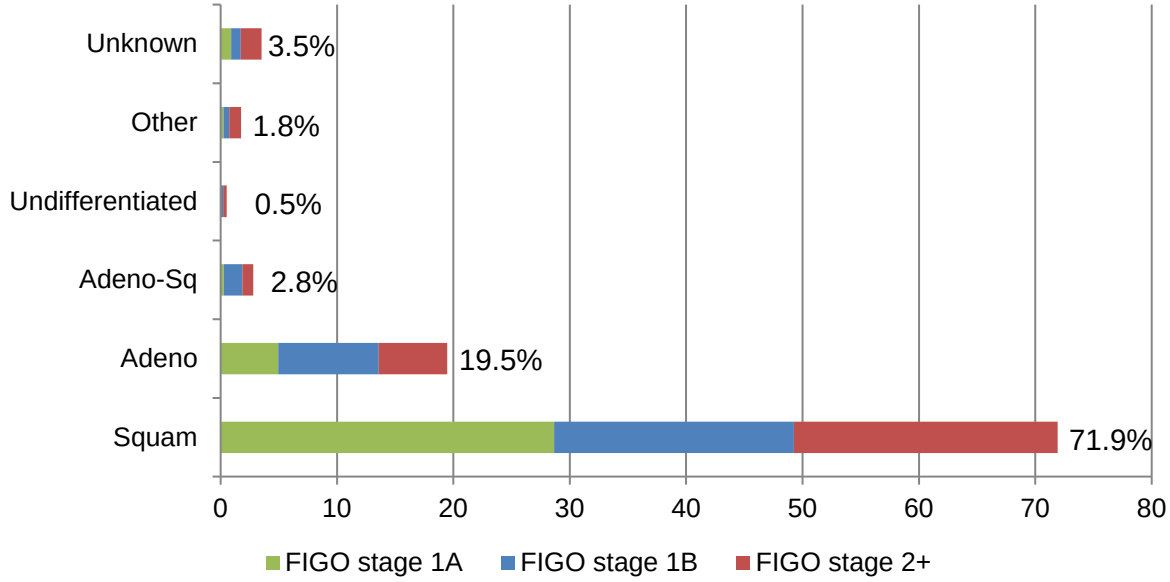
Table G Estimated percent distribution of cervical cancer cases by FIGO stage in 2009-2012 audit, by QARC region

QARC Region	1A	1B	2+	Total
East of England	32%	37%	31%	100%
East Midlands	38%	32%	30%	100%
London	35%	27%	38%	100%
North East	36%	34%	29%	100%
Yorkshire and the Humber	45%	30%	25%	100%
North West	33%	37%	30%	100%
South Central	36%	32%	31%	100%
South East Coast	37%	35%	28%	100%
South West	32%	33%	35%	100%
West Midlands	27%	28%	45%	100%
Total	**35%**	**32%**	**33%**	**100%**

4.4 Histology of invasive cervical cancers

Figure 5 shows the distribution of invasive cervical cancer cases by histological type. Most of the cases of cervical cancer show squamous histology (72%), while 20% are adenocarcinomas. Adenosquamous types are significantly rarer. Squamous carcinoma is more likely to be diagnosed as stage 1A cancer than the other histological types: 40% were stage 1A compared to 25% of adenocarcinoma and 9% of adenosquamous cases. Over half of the cases with undifferentiated or other histological types were diagnosed as stage 2 or worse.

Figure 5 Percentage of cervical cancer cases, by histology



4.5 Treatment of invasive cervical cancers

Figure 6 shows the distribution of treatment for cervical cancers, according to age (see also Table 12). The most aggressive treatment employed in each case has been captured. Treatment was recorded in 4,394 cases (68%) (Table 11), and out of those, the most common treatment was cone biopsy/loop excision/trachelectomy (32.6%), followed by simple or radical hysterectomy (25.6%), and radiotherapy plus chemotherapy ± hysterectomy (25.2%). Only 2.4% of those treated by cone biopsy/loop excision/trachelectomy had a trachelectomy. 4% of treatments were recorded as 'none'.

Filtering the results by age reveals that for women aged 50 to 64, the most common treatment was chemotherapy plus radiotherapy ± hysterectomy (42%), followed by hysterectomy alone (27%). By contrast, 45% of women under 50 had fertility-sparing treatment (cone biospy/loop excision or trachelectomy) with only 29% undergoing a hysterectomy (simple or radical). For those aged 65 to 79, chemotherapy plus radiotherapy ± hysterectomy (41%) was the most common treatment, followed by radiotherapy ± hysterectomy (24%). However, 14% of women in this age group reportedly received no treatment, other than perhaps palliative care. Given the substantially poorer relative survival of elderly cervical cancer patients nationally,[18] this appears to warrant further investigation. It should be borne in mind, however, that some regions may have recorded 'no treatment' because they were unable to find a record of treatment, rather than because the patient was not treated (see section 3.7).

Figure 6 Percentage treatment of cervical cancer cases, by age at diagnosis

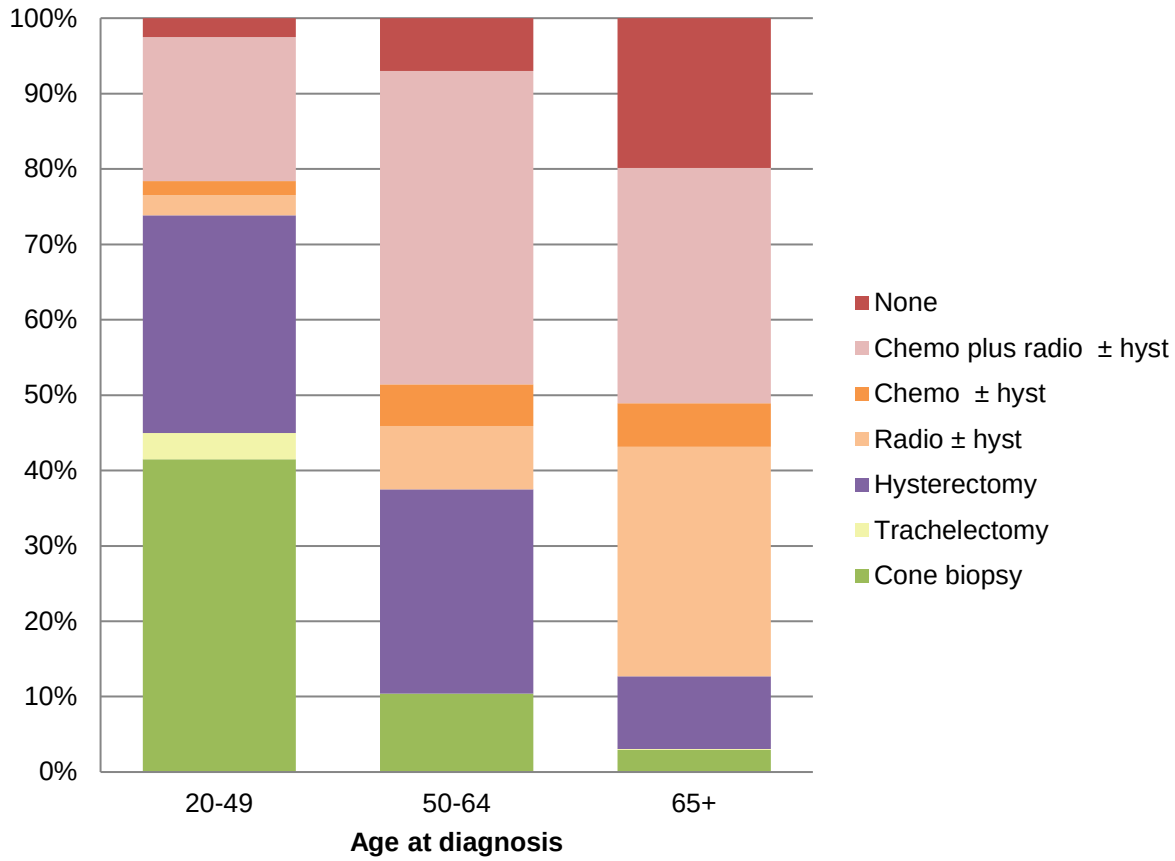
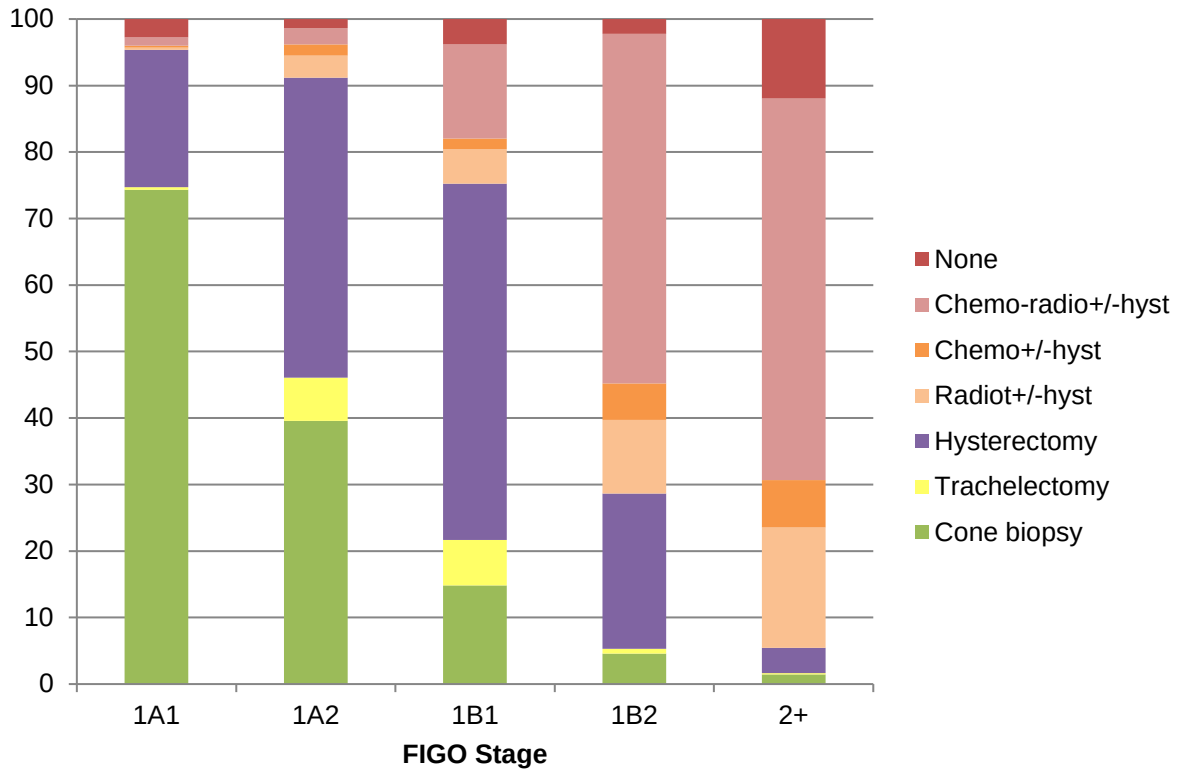


Figure 7 shows the distribution of treatment for invasive cervical cancer by stage of disease. The graph reveals that the majority of women diagnosed with FIGO stage 1A1 cancer received cone biopsy/loop excision (74%), whereas those with stage 1A2 are more likely to have non-fertility preserving treatment (52%). Women with stage 1B1 cancer were most likely to have had a simple or radical hysterectomy (54%), whereas those with stage 1B2 were more likely to have chemotherapy plus radiotherapy ± hysterectomy (53%). The majority of those with stage 2 or worse (57%) cancer received chemotherapy plus radiotherapy ± hysterectomy. Note that a very small proportion (1%) of cancers diagnosed at stage 1A1 are recorded as having been treated with chemotherapy plus radiotherapy ± hysterectomy. Similarly, 1% of stage 2 or worse cancers are recorded as having a cone biopsy. These are clearly misclassifications of stage and/or treatment which we are endeavouring to correct for the future.

Figure 7 Percentage treatment of cervical cancer cases by FIGO stage



4.6 Cervical screening history (cases compared with controls)

4.6.1 Proportion of women never screened

Figure 8 shows the proportion of cases and controls with no recorded screening history up to six months prior to diagnosis in women aged 25 or older. 681 cases are excluded because no information on stage was available. The data show that controls were generally more likely than cases to have attended screening previously. Note that we have excluded 46 women aged 65 or over with FIGO stage 1A cancer because the lack of routine screening for women in this age group means that it is unlikely that these cancers were screen-detected. Instead, this small number of cancers (46 out of 1033 in women aged over 65) may represent rare instances of incidental cancer diagnosis.

The proportion of women with invasive cervical cancer and no cytology tests (other than within 6 months of diagnosis) has remained constant for all age groups since the audit started, except for women aged 25–34. Figure 9 shows the proportion of cases and controls aged 25-34 by screening history over two time periods (April 2007-September 2009 and October 2009-March 2012). The data reveal that the proportion of women whose screening history is up to date has not changed over time, whereas the proportion of women with no screening history before diagnosis (those who have 'never' been screened) has almost doubled and the number of women who are lapsed attenders has decreased. This change is due to the fact that a large proportion of women are now being diagnosed as a result of their first smear at age 25 (25% of all cases diagnosed between October 2009 and March 2012 aged 25-34 had their first smear at age 25, compared to 8% before October 2009).

Table H presents the odds ratios of developing cancer for women who have never been screened, compared to those who attend screening as recommended, by diagnosis period.

The risk of being diagnosed with cervical cancer is significantly increased for women who have never been screened across all age groups, compared with that for women who have attended regularly. For cancers diagnosed in women over the age of 35 there is no difference in the odds ratio between the two diagnosis periods (April 2007-September 2009 and October 2009-March 2012). However, for women aged 25-34, the odds ratio of being diagnosed with stage 1A cancer among those who had not previously been screened compared to those that attend regularly was much greater after September 2009. This difference in the odds ratio was not observed for stage 1B or worse cancers.

The results presented in this section suggest an increase in the number of women diagnosed aged 25-34 with stage 1A cancer and no previous screening history most likely due to the fact that women get invited for screening at the age of 25. Although the proportion of women with no prior screening history has increased since October 2009 among those diagnosed with stage 1B cancer, the results do not suggest that that odds of developing 1B or worse cancer among women who have not been previously screened compared to those screened regularly has changed between periods.

It should be noted that we cannot yet assess the full impact of the change in policy until all the women diagnosed with cancer age 25-34 are invited for screening at age 25. Currently all women aged 28-34 were invited from age 20.

Figure 8 Proportion of women with no screening test (other than those taken within six months of diagnosis), by FIGO stage and age.

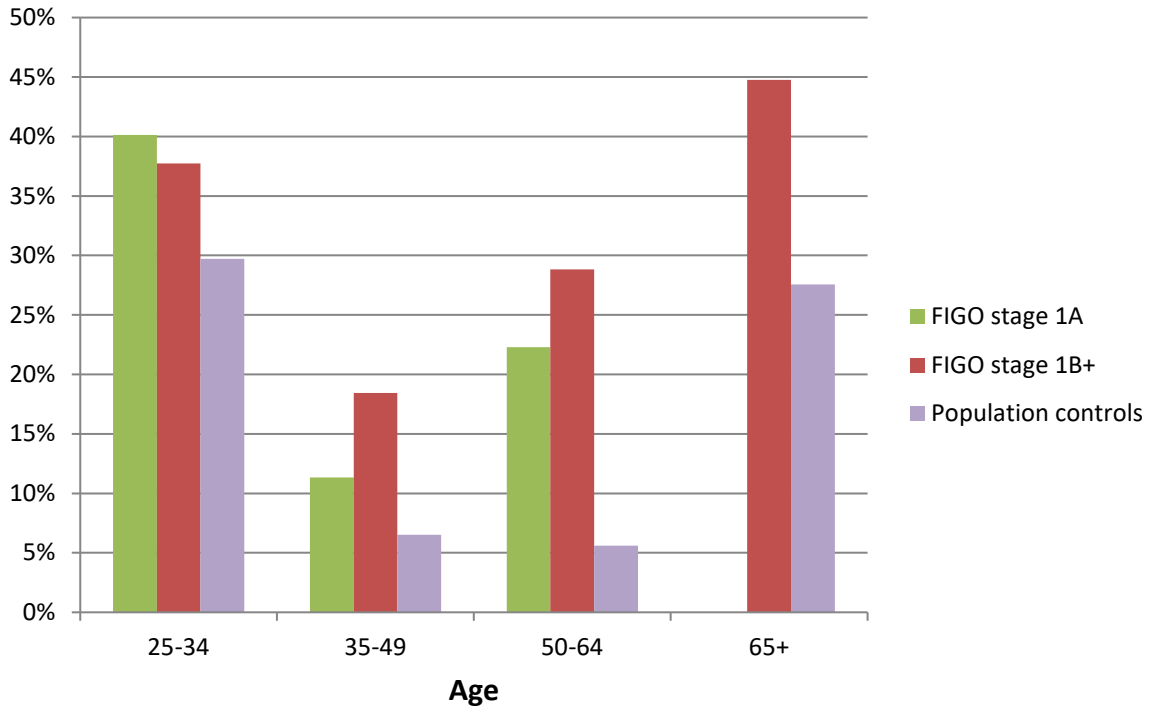


Figure 9 Screening history of women diagnosed aged 25-34 and their controls, by FIGO stage and diagnosis period.

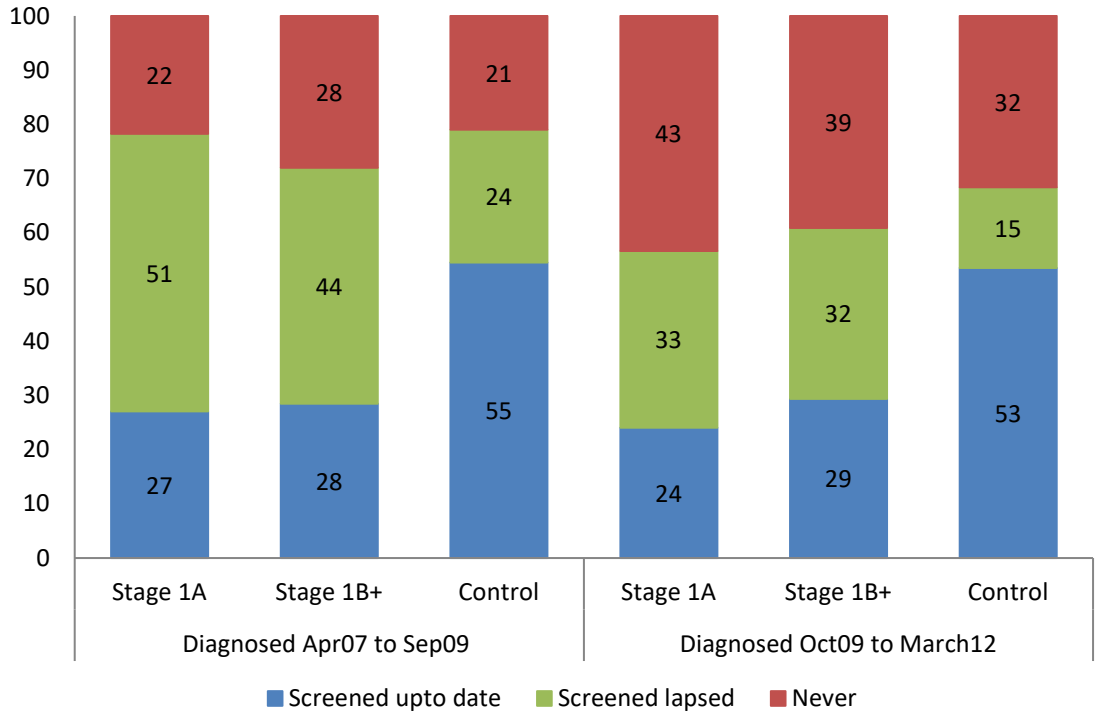


Table H Odds ratio of cervical cancer diagnosis in women with no history of cervical screening compared to those attending screening as recommended (i.e. every 3 or 5 years), by diagnosis period

Age	FIGO stage	Diagnosed April 2007 to September 2009		Diagnosed October 2009 to March 2012	
		OR	95% CI	OR	95% CI
25-34	1A	1.96	(1.52-2.53)	3.42	(2.68-4.35)
	1B+	2.95	(2.25-3.87)	2.59	(1.98-3.40)
35-49	1A	4.17	(2.91-5.97)	4.24	(2.89-6.23)
	1B+	7.46	(5.64-9.87)	8.25	(6.18-11.01)
50-64	1A	5.33	(2.76-10.27)	6.02	(2.94-12.35)
	1B+	12.93	(9.10-18.38)	13.51	(9.45-19.33)

4.7 Colposcopy

Collecting colposcopy data for this audit has been challenging, and the variability of the available information has made interpretation still more difficult. However, data on colposcopic history are of particular importance where there is an interval of four months or more between cytology results that indicate referral and subsequent diagnosis. This is because the interval indicates either a delay in administering the diagnostic procedure (attributable to the woman or her service provider), or the recurrence of a previously-treated cervical abnormality.

Out of the 6508 cervical cancer cases in the audit, 31% (1,985) do not have a cytology test indicating referral to colposcopy. 175 of the 4523 (69%) women with at least one referral to colposcopy before diagnosis had the referring cytology on the same date as a colposcopy or on the date of diagnosis. These women were considered not to have been referred before diagnosis, because the data suggest that the cytology was taken at colposcopy and therefore it does not represent a screening opportunity.

The majority of women in the dataset 64% (4,133) have one cytology test indicating referral to colposcopy, 3.2% have more than one referral to colposcopy[2] (assumed to be in long term follow-up for previous cervical abnormality) and 33% (2,152) have no referrals to colposcopy. A summary of those referred to colposcopy can be found in Table 19.

Of those with one referral to colposcopy: 77.6% were referred on a severe or worse cytology, 9.4% on a moderate, 4.8% on a mild, 7.4% on a borderline, 0.5% on a negative and 0.3% on an inadequate test.

No colposcopy information was available for 37% of women with one referral to colposcopy and the completeness of the colposcopy data we do have is uncertain. We found a higher proportion of women with no recorded colposcopy were referred two or more years before diagnosis (16%) when compared to those for whom we do have colposcopy information (11%). However the proportion diagnosed within 4 months was the same (76% vs. 77%) and no difference between the groups was observed in terms of the result of their referring cytology; suggesting this is purely a data capture issue. Therefore we will only present detailed results for women with at least one colposcopic appointment recorded in the dataset (n=2,606).

A summary of the intervals between referral and diagnosis, referral and colposcopy and colposcopy to diagnosis in women with one referral recorded is presented in Table I. Overall the majority (77%) of women with one referral to colposcopy are diagnosed within 4 months of the abnormal cytology; however 11% have a delay in diagnosis of 2 years or more.

Among those with a recorded colposcopy appointment before diagnosis (n=2606), the longer the interval between referral and diagnosis the less likely it is that the woman was referred with a severe or worse test (see Figure 10). Furthermore when the referral to colposcopy occurred 2 or more years before diagnosis the cancer is less likely to be diagnosed as FIGO stage 1A and much more likely to be diagnosed as FIGO stage 2 or worse (see Figure 11).

To assess the colposcopy history of those women for whom a delay in diagnosis is suspected we will focus on those women with a delay of more than 4 months between referral and diagnosis, they represent 23% (605/2606) of all women for whom we have colposcopy. Colposcopy history for women with a diagnosis more than 4 months after

[2] A new referral episode is only counted when a woman has at least two negative cytology tests between tests with an action code of suspend

referral by the time from referral to diagnosis is presented in Table J. The first thing to note about the table is the proportion of women for whom we only have a colposcopy within 2 months of diagnosis. For 32% of the women in this table the only colposcopy appointment recorded is the one where the diagnosis of cancer was made. Information on the colposcopy where the diagnosis was made is relatively easy to obtain. As the time between diagnosis and colposcopy increases it becomes harder to obtain information about the colposcopy visit. Indeed 40% of those diagnosed more than 2 years after referral only have a colposcopy within 2 months of diagnosis. We are unable to say in such cases whether there was a lack of failsafe (i.e. the women did not attend), colposcopy failure (i.e. the woman attended earlier and was discharged without treatment) or whether it was treatment failure.

Most of the women (41%) for whom the delay in diagnosis was less than a year after referral have had an appointment where a punch biopsy revealed CIN2 or worse and 5% were treated at least once before diagnosis. However when the delay is between 12 and 23 months we see that 24% either did not have a punch biopsy on their first colposcopy or the results of the punch biopsy was normal and 16% were treated (unsuccessfully) on the first colposcopy. A further 20% were diagnosed with CIN2 or worse on a punch biopsy, but their diagnosis was still delayed over a year.

The data are insufficient to identify exactly what lead to the delay in diagnosis. However it is clear that having a delay of two or more years between suspected abnormalities on your cervical test and diagnosis may have an impact on the stage at which your cancer is diagnosed. However there is also evidence that these cancers may be harder to identify, as the referral cytology was less likely to be severe. We do not have the data to further ascertain whether the delays are in the patients themselves or provider delays. Fortunately delays in diagnosis of two years or more represent a small proportion of all cases of cervical cancer, approximately 7% (i.e. 11% of those with one referral to colposcopy (4133) = 455, 455/6508= 6.9%).

Table I Summary of the intervals between referral and diagnosis, referral and colposcopy and colposcopy to diagnosis in women with one cytology indicating referral to colposcopy and at least one colposcopy recorded in the dataset

	Women with one cytology indicating referral to colposcopy and a recorded colposcopy[1]					
	Time from referral to diagnosis[2]		Time from referral to first colposcopy		Time from first colposcopy to diagnosis	
	N	%	N	%	N	%
0-3.99 months	2001	77%	2336	90%	2279	88%
4-6.99 months	123	5%	50	2%	35	1%
7-11.99 months	102	4%	33	1%	74	3%
12-23.99 months	99	4%	26	1%	76	3%
24+ months	281	11%	161	6%	138	5%
Total	2606	100%	2606	100%	2602	100%

[1]There was no colposcopy appointment recorded for 1524 (37%) women
[2]Note that very similar proportions were observed among women with at least one referral to colposcopy but no recorded colposcopy with the exception of a larger proportion of women (16%) being diagnosed more than 2 years after referral.

Figure 10 Result of the referring cytology by time from diagnosis, in those with a recorded colposcopy

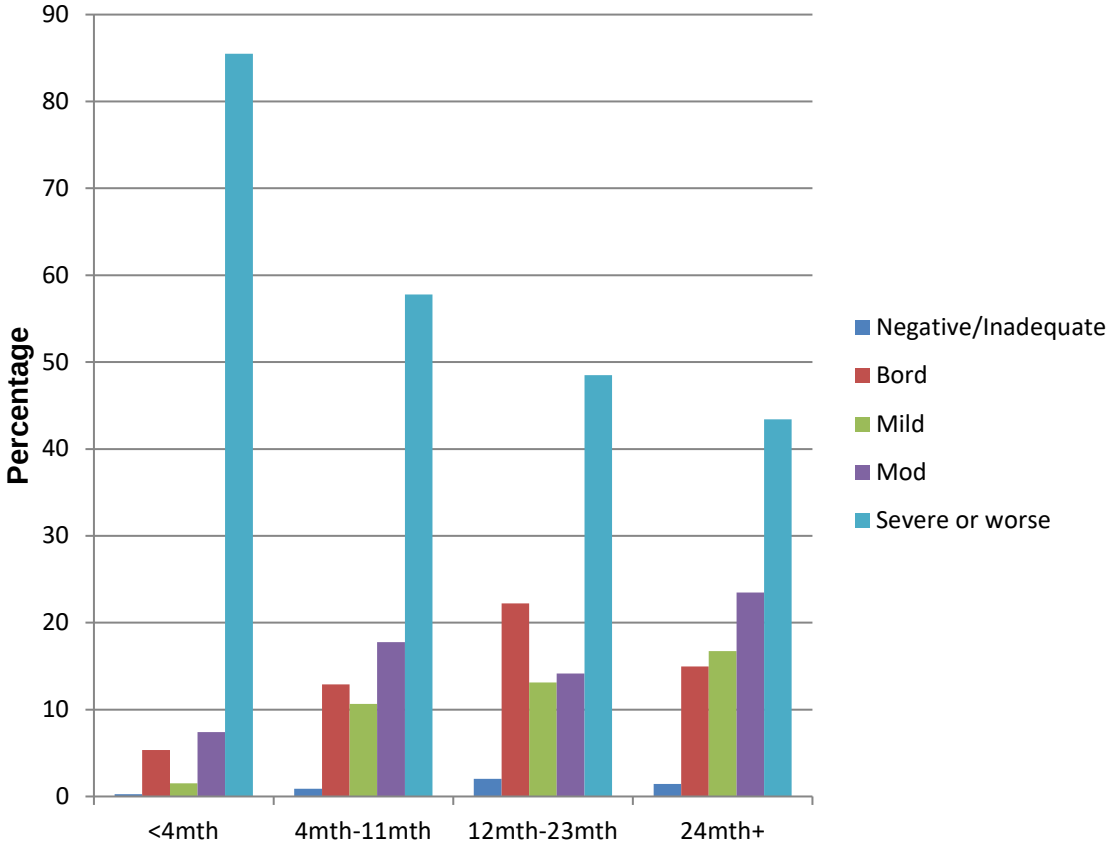


Figure 11 FIGO stage by time from the first recorded cytology indicating referral to colposcopy and diagnosis

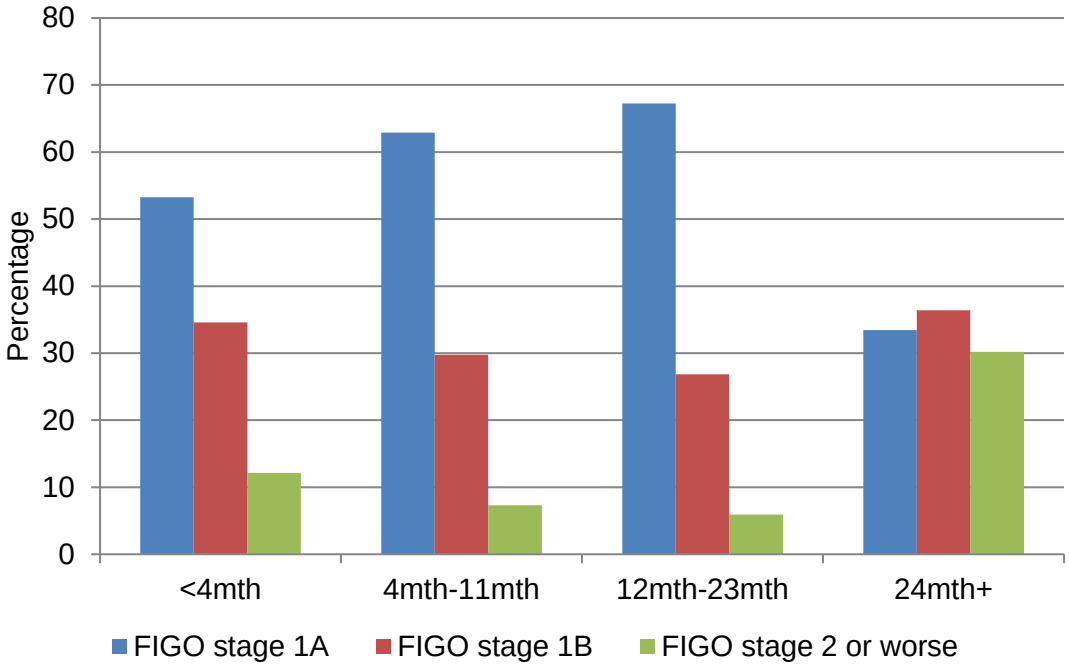


Table J Colposcopy history in women with a diagnosis more than 4 months after referral, by time from referral to diagnosis

	4-11mth		12-23mth		24mth or more		Total	
	N	%	N	%	N	%	N	%
No record (except within 2 months of diagnosis)	43	35%	37	18%	111	40%	191	32%
DNA	6	5%	13	6%	18	6%	37	6%
Colp normal/No biopsy on first colposcopy after referral	11	9%	48	24%	43	15%	102	17%
Punch biopsy (or unknown procedure) with a diagnosis of								
<CIN2	6	5%	30	15%	35	12%	71	12%
CIN2+	51	41%	41	20%	32	11%	124	20%
Treatment	6	5%	32	16%	42	15%	80	13%
Total	**123**	**100%**	**201**	**100%**	**281**	**100%**	**605**	**100%**

5. FUTURE DEVELOPMENTS/ ONGOING WORK

Results from this audit are presented to the Advisory Group, and changes will be implemented as part of the screening programme where appropriate.

This audit forms the basis for a number of peer-reviewed articles. The following manuscripts are either under peer review or have very recently been accepted for publication and should be widely available over the next few months: (i) harms and benefits of screening from age 20 when compared to screening from age 25, (ii) the degree of protection offered by screening women who are over the age of 65, (iii) How much could primary human papillomavirus testing reduce cervical cancer incidence and morbidity (J Med Screen) and (iv) characteristics and screening history of women diagnosed with cervical cancer age 20-29 (BJC).

Over the next 12 months we will use the data to analyse: (i) the impact of the 'Jade Goody effect' on the diagnosis of cervical cancer within the screening programme, (ii) comparison of different screening history classifications and (iii) the risk of developing cervical cancer following a cytology test taken as part of the screening programme.

The audit management group have updated the audit guidelines in order to make the review process more efficient and to enhance its educational focus. It is too soon to report on the outcomes of these changes but we continue to monitor the situation. The colposcopy review process will continue to be improved as part of future audit protocol documents.

In the longer term, the audit database will be integrated into the new national cancer registry for England, which will increase capacity to store and manage information on each registration. This will enable screening history to be related to mortality allowing us to study survival.

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GLOSSARY

Action code	This field (downloaded as part of the screening history from NHAIS) denotes the action to be taken in response to the result of each cytology test. The codes are: A. Routine screening/call and recall. H. Result recorded, but no change in current action code. (This code is normally used when privately-taken cytology tests are entered into the system). R. Early recall at an interval specified by the laboratory. S. Suspend recall pending referral.
Cases	Women diagnosed with invasive cervical cancer in England.
Controls	Women who have not been diagnosed with cervical cancer, who are registered with a GP in England. They are matched by age and place of residence with a case.
Cervical Screening Evaluation Group /Audit Management Group	The group charged with evaluating developments in the NHS Cervical Screening Programme. The CSEG oversaw the NHS CSP national audit until February 2011, when an Audit Management Group was established, consisting of a subgroup of individuals from the Evaluation Group. The new Audit Management Group is charged with coordinating the development of audit protocols, and with gathering and disseminating recommendations for best practice
Confidence Interval	Confidence interval is a term used in inferential statistics that measures the probability that a population parameter will fall between two set values. The confidence interval can take any number of probabilities, with the most common being 95% or 99%.
Exeter call and recall system	The system used to invite women for screening. Since 1988, it has stored screening records for all women registered with a GP
FIGO stage	The cancer staging classification developed by the International Federation of Gynaecological Oncologists (I, IA, IA1, IA2, IB, IB1, IB2,III, IIIA, IIIA, IV, IVA, IVB).
Hospital Based Programme Coordinators (HBPC)	The named individual within each NHS trust who is responsible for collating cases of invasive cervical cancer and initiating the audit process.
Quality Assurance Reference Centres (QARC)	The nine Quality Assurance Reference Centres (QARCs) in England are responsible for the quality of the screening programme in their area. With the exception of the North East and Yorkshire and The Humber QARCs, each covers one region of the country.

APPENDIX A: ESSENTIAL FIELDS

SECTION A & A1	**Personal details**	NHS number (to be held locally) Date of birth For cases only: Date of diagnosis Stage of tumour (FIGO) Histology Treatment Index of Multiple Deprivation
SECTION B	**Cytology**	Reason for no cytology Date test was taken Result of cytology test HPV result
SECTION C	**Colposcopy**	For cases only: Number of colposcopic appointments Date of colposcopy Attendance type Colposcopist Surgical procedure
SECTION C2	**Colposcopy review**	All fields should be completed
SECTION D1	**Histology cancer diagnosis**	For cases only: Date of specimen Type of specimen Pathological diagnosis FIGO stage
SECTION D2	**Specimen history**	Date of specimen Type of specimen Pathological diagnosis Excision status
SECTION E Cytology Review of cases	**E1. Original slide**	Slide ID Cytology type Date of original test Original test result
	E2. Review results	Reviewed location Review result Original result NFR (no further review)
SECTION F Histology Review of cases	**F1. Original specimen**	Specimen ID Date of original specimen Pathological diagnosis Evidence of TZ sampling
	F2. Review results	Reviewed at Review pathological diagnosis Excision status

APPENDIX B: COMPLETION OF DATA (ESSENTIAL FIELDS)

NHS Number is not received nationally

B-1 Proportion of essential data collected for cases in **Section A. Personal and cancer details**

		Section A: Essential fields							
		Date of Birth		Date of Diagnosis		Stage*		Histology*	
QARC Region	**Case**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
East of England	618	618	100	618	100	580	93.9	617	99.8
East Midlands	660	660	100	660	100	552	83.6	630	95.5
London	622	622	100	622	100	598	96.1	605	97.3
North East	425	425	100	425	100	387	91.1	419	98.6
Yorkshire and the Humber	763	763	100	763	100	598	78.4	717	94.0
North West	831	831	100	831	100	703	84.6	829	99.8
South Central	495	495	100	495	100	471	95.2	472	95.4
South East Coast	510	510	100	510	100	477	93.5	468	91.8
South West	762	762	100	762	100	751	98.6	760	99.7
West Midlands	822	822	100	822	100	784	95.4	819	99.6
Total	**6508**	**6508**	**100**	**6508**	**100**	**5901**	**90.7**	**6336**	**97.4**

*Cases where data collection is complete and stage is missing are considered to be staged as a reasonable amount of effort has been made to collect the data. Incomplete cases with a stage recorded as X (or missing) are considered not to have stage. Please refer to section 6 for full details regarding missing data

B-1a Proportion of non-essential data collected for cases in **Section A. Personal and cancer details**

		Section A: Non-essential fields								
		Treatment (in those with known tx, **excluding** those reported as none*)		Treatment (in those with tx recorded **including** those recorded as none)		Index of Multiple Deprivation			Index of Multiple Deprivation	
QARC Region	**Case**	n	%	n	%	n	%	**All Controls**	n	%
East of England	618	474	76.7	496	80.3	602	97.4	1234	139	11.3
East Midlands	660	461	69.8	474	71.8	0	0.0	1310	0	0.0
London	622	373	60.0	434	69.8	90	14.5	1094	328	30.0
North East	425	118	27.8	120	28.2	424	99.8	849	48	5.7
Yorkshire and the Humber	763	301	39.4	306	40.1	732	95.9	1523	130	8.5
North West	831	231	27.8	259	31.2	709	85.3	1660	352	21.2
South Central	495	434	87.7	462	93.3	493	99.6	989	967	97.8
South East Coast	510	387	75.9	401	78.6	492	96.5	1019	956	93.8
South West	762	632	82.9	659	86.5	748	98.2	1523	1503	98.7
West Midlands	822	735	89.4	783	95.3	814	99.0	1640	0	0.0
Total	**6508**	**4146**	**63.7**	**4394**	**67.5**	**5104**	**78.4**	**12841**	**4423**	**34.4**

*Where treatment was recorded as "None" we assume it means "none other than palliative care". Attempts have been made to clarify this issue and there is now a category for palliative care; however some misclassification may still remain and therefore they are excluded from this column

B-1b Proportion of cases with FIGO stage reported as none available, none recorded,* or '1B+' (1B or worse), by QARC region, age, and audit year

QARC Region	None recorded	None available	1B+ (NOS)	Total
East of England	6.2	0.8	0.7	618
East Midlands	16.4	0.2	0.3	660
London	3.9	0.0	8.4	622
North East	8.9	0.0	17.2	425
Yorkshire and the Humber	21.6	0.1	3.7	763
North West	15.4	0.0	10.7	831
South Central	4.9	1.0	0.2	495
South East Coast	7.5	0.0	2.4	510
South West	1.4	1.3	3.7	762
West Midlands	4.6	5.7	0.0	822
Age				
<25	10.2	0.8	3.2	127
25-49	7.5	0.3	3.5	4,232
50-64	10.5	1.5	6.2	1,116
65+	15.4	4.3	6.8	1,033
Audit Year				
2009-2010	8.5	1.1	4.2	2452
2010-2011	8.9	1.3	5.0	2,087
2011-2012	10.8	1.1	4.1	1,969
Total	**9.3**	**1.1**	**4.4**	**6508**

*where stage is reported as none available instead of none recorded a reasonable amount of effort has been made to find the stage, but none has been available. This is derived from cases recorded as "Audit complete" which means that no further details are being sought for these women. The option to report cases as "none available" has only been available to all QARCs since April 2012.

B-2 Proportion of data collected for cases in **Section B. Cytology**

Section B: Cytology								
			Completeness of data among recorded cytology tests					
			Date test was taken		Result of Test		Action Code	
QARC Region	Case	Total No. of tests on cases[a]	n	%	n	%	n	%
East of England	618	2,633	2,633	100	2,633	100	2,633	100
East Midlands	660	2,957	2,957	100	2,957	100	2,957	100
London	622	1,443	1,443	100	1,443	100	1,443	100
North East	425	1,675	1,675	100	1,675	100	1,672	100
Yorkshire and the Humber	763	3,230	3,230	100	3,230	100	3,226	99.9
North West	831	3,646	3,646	100	3,646	100	3,642	99.9
South Central	495	2,292	2,292	100	2,292	100	2,281	99.5
South East Coast	510	2,242	2,242	100	2,242	100	2,240	99.9
South West	762	2,995	2,995	100	2,995	100	2,995	100
West Midlands	822	3,506	3,506	100	3,506	100	3,505	100
Total	**6508**	**26,619**	**26,619**	**100**	**26,619**	**100**	**26594**	**99.9**[b]

[a] Cytology tests known to the Audit and taken before diagnosis

[b] Cytology data obtained directly from Open Exeter should have all three data fields complete. Missing data, we believe, is the result of inclusion into the audit of cytology tests taken before the programme started in 1988 and a few slides that were found in the laboratory, but not recorded on Exeter. These tests will not have “Action Code” as this field is generated by Exeter.

B-3 Proportion of data collected for cases in **Section C: Colposcopy**

	Section C: Colposcopy									
	No. of cases with an Action Code of suspend	No. of cases with a suspend and a colposcopy		Additional cases with a colp but no suspend (n)	No. of Colp appts	Date of colp		Satisfactory exam or DNA		Colposcopic procedure
QARC Region		n	%		n	n	%	n	%	n
East of England	421	312	74.1	39	516	516	100	515	100	479
East Midlands	456	204	44.7	23	368	368	100	368	100	331
London[1]	445	439	98.7	166	847	847	100	0	0	360
North East	305	129	42.3	18	214	214	100	214	100	200
Yorkshire and the Humber	570	239	41.9	33	418	418	100	418	100	364
North West	600	262	43.7	27	474	474	100	474	100	423
South Central	346	278	80.3	26	490	490	100	490	100	447
South East Coast	372	266	71.5	19	516	516	100	516	100	440
South West	487	386	79.3	45	751	751	100	751	100	676
West Midlands	521	328	63.0	34	601	601	100	601	100	567
Total	**4523**	**2843**	**62.9**	**430**	**5195**	**5195**	**100**	**4347**	**83.7**	**4287**

[1] London reports the diagnostic sample for every cancer, this has been taken as a colposcopy appointment making the results look complete. However cases very rarely have any other colposcopy recorded

APPENDIX CI: LIST OF DATA TABLES

APPENDIX CII: DATA TABLES

Table 1. Number of cases of invasive cervical cancer, 2009-2012, by audit year and QARC*

	Year					
QARC Region	**2007-2008**	**2008-2009**	**2009-2010**	**2010-2011**	**2011-2012**	**T**
East of England	182	217	217	211	190	1
East Midlands	200	195	233	219	208	1
London	237	231	278	212	132	1
North East	134	160	170	125	130	
Yorkshire and the Humber	268	244	271	236	256	1
North West	314	298	324	271	236	1
South Central	170	164	187	162	146	
South East Coast	145	158	195	160	155	
South West	262	288	285	249	228	1
West Midlands	246	299	292	242	288	1
Total	**2158**	**2254**	**2452**	**2087**	**1969**	**1**

*Audit year between 1 April and the 31 March

Table 2. Number and percentage of invasive cervical cancer in 2009-2012 audit in five-year age groups, by year of diagnosis

Audit Year[1]	<20[2]	20-24	25-29	30-34	35-39	40-44	45-49	50-55	55-59	60-64	65-69	70-74	75-79	80+
2009-2010	0	52	392	367	358	299	211	138	127	121	89	90	74	134
2010-2011	0	45	320	270	279	252	193	142	125	120	91	64	70	116
2011-2012	1	29	325	251	250	268	197	122	115	106	67	59	78	101
Total	**1**	**126**	**1037**	**888**	**887**	**819**	**601**	**402**	**367**	**347**	**247**	**213**	**222**	**351**
Percent														
2009-2010	0.0	2.1	16.0	15.0	14.6	12.2	8.6	5.6	5.2	4.9	3.6	3.7	3.0	5.5
2010-2011	0.0	2.2	15.3	12.9	13.4	12.1	9.2	6.8	6.0	5.7	4.4	3.1	3.4	5.6
2011-2012	0.1	1.5	16.5	12.7	12.7	13.6	10.0	6.2	5.8	5.4	3.4	3.0	4.0	5.1
Total	**0.0**	**1.9**	**15.9**	**13.6**	**13.6**	**12.6**	**9.2**	**6.2**	**5.6**	**5.3**	**3.8**	**3.3**	**3.4**	**5.4**

[1]Audit year runs 1 April to 31 March

[2] Case 19.5 yrs old

Table 3. Number and percentage of invasive cervical cancer cases in 2009-2012 audit for each QARC region, by age

QARC Region	<25	25-49	50-64	65+	Total
East of England	10	379	126	103	618
East Midlands	17	460	86	97	660
London	14	403	118	87	622
North East	10	277	80	58	425
Yorkshire and the Humber	13	526	129	95	763
North West	22	552	131	126	831
South Central	6	331	78	80	495
South East Coast	9	343	90	68	510
South West	18	464	125	155	762
West Midlands	8	497	153	164	822
Total	**127**	**4232**	**1116**	**1033**	**6508**
Percent					
East of England	1.6	61.3	20.4	16.7	100
East Midlands	2.6	69.7	13.0	14.7	100
London	2.3	64.8	19.0	14.0	100
North East	2.4	65.2	18.8	13.6	100
Yorkshire and the Humber	1.7	68.9	16.9	12.5	100
North West	2.6	66.4	15.8	15.2	100
South Central	1.2	66.9	15.8	16.2	100
South East Coast	1.8	67.3	17.6	13.3	100
South West	2.4	60.9	16.4	20.3	100
West Midlands	1.0	60.5	18.6	20.0	100
Total	**2.0**	**65.0**	**17.1**	**15.9**	**100**

*Table 4. Number and percentage of invasive cervical cancer cases in 2009-2012 audit, by FIGO Stage**

FIGO Stage	Number	Percentage
1A NOS	874	13.4
1A1	1,186	18.2
1A2	107	1.6
1B+ NOS	289	4.4
1B NOS	947	14.6
1B1	834	12.8
1B2	115	1.8
2 NOS	40	0.6
2A	124	1.9
2B	606	9.3
3 NOS	67	1.0
3A	60	0.9
3B	249	3.8
4 NOS	142	2.2
4A	91	1.4
4B	96	1.5
None available	69	1.1
None recorded	612	9.4
Total	**6508**	**100**

*NOS= not otherwise specified (or not further specified)

Table 5. Number of invasive cervical cancer cases in 2009-2012 audit for each QARC region, by FIGO stage

QARC Region	1A	1B	2	3	4	1B+	None recorded	Total
East of England	196	205	86	44	40	4	43	618
East Midlands	241	197	61	25	25	2	109	660
London	202	162	94	51	37	52	24	622
North East	139	124	30	12	9	73	38	425
Yorkshire and the Humber	318	184	31	21	15	28	166	763
North West	259	252	50	31	22	89	128	831
South Central	178	153	61	39	34	1	29	495
South East Coast	180	164	66	28	22	12	38	510
South West	239	239	123	56	56	28	21	762
West Midlands	215	216	168	69	69	0	85	822
Total	**2167**	**1896**	**770**	**376**	**329**	**289**	**681**	**6508**

Table 5a. FIGO stage of invasive cervical cancer cases in 2009-2012: estimated percent distribution, by QARC region

QARC Region	1A	1B	2+	Total
East of England	32.5%	36.9%	30.6%	100
East Midlands	38.0%	32.0%	30.0%	100
London	35.0%	27.2%	37.8%	100
North East	36.3%	34.2%	29.5%	100
Yorkshire and the Humber	44.8%	30.1%	25.1%	100
North West	33.3%	36.9%	29.9%	100
South Central	36.4%	32.1%	31.5%	100
South East Coast	36.9%	35.3%	27.8%	100
South West	32.4%	32.8%	34.8%	100
West Midlands	26.9%	28.2%	44.9%	100
England	**35.0%**	**32.4%**	**32.6%**	**100**

Table 6. Number of invasive cervical cancer cases in 2009-2012 audit, by age and FIGO stage

Age	1A	1B	2	3	4	1B+(NOS)	None Recorded	Total
<25	37	47	16	6	3	4	14	127
25-49	1,900	1,322	337	116	81	146	330	4232
50-64	184	324	202	107	96	69	134	1116
65+	46	203	215	147	149	70	203	1033
Total	**2167**	**1896**	**770**	**376**	**329**	**289**	**681**	**6508**

Table 6a. FIGO stage of invasive cervical cancer cases in 2009–2012 audit: estimated percentage distribution, by age-group

Age	1A	1B	2	Total	Total
<25	31.8	42.3	25.8	100	127
25-49	46.8	34.3	18.8	100	4232
50-64	17.9	32.2	49.9	100	1116
65+	5.4	23.8	70.8	100	1033
All ages	**35.0**	**32.4**	**32.6**	**100**	**6508**

Table 7. Number of invasive cervical cancer cases in 2009-2012 audit, by FIGO stage and year of diagnosis

Year	1A	1B	2	3	4	1B+(NOS)	None Recorded	Total
2009-2010	826	735	284	147	121	103	236	2,452
2010-2011	674	586	285	126	99	105	212	2,087
2011-2012	667	575	201	103	109	81	233	1,969
Total	**2167**	**1896**	**770**	**376**	**329**	**289**	**681**	**6508**

Table 7a. FIGO stage of invasive cervical cancer cases: estimated percentage distribution, by year of diagnosis

Year	1A	1B	2	Total
2009-2010	35.8	33.6	30.7	100
2010-2011	33.9	31.4	34.7	100
2011-2012	35.2	32.1	32.7	100
Total	**35.0**	**32.4**	**32.6**	**100**

Table 8. Number and percentage of invasive cervical cancer cases in 2009-2012 audit, by histology

Year	Squamous	Adenocarcinoma	Adeno-Squamous	Undifferentiated	Other	None recorded
2009-2010	1,748	492	72	15	35	90
2010-2011	1,518	384	58	6	46	75
2011-2012	1,415	390	53	13	34	64
Total	**4681**	**1266**	**183**	**34**	**115**	**229**
Percent						
2009-2010	71.3	20.1	2.9	0.6	1.4	3.7
2010-2011	72.7	18.4	2.8	0.3	2.2	3.6
2011-2012	71.9	19.8	2.7	0.7	1.7	3.3
Total	**71.9**	**19.5**	**2.8**	**0.5**	**1.8**	**3.5**

Table 9. Number and percentage of invasive cervical cancer cases in 2009-2012 audit, by age at diagnosis and histology

Age	Squamous	Adenocarcinoma	Adeno-Squamous	Other (incl undifferentiated)	None recorded	Total
<25	92	21	4	8	2	127
25-49	3074	838	121	68	131	4232
50-64	795	227	33	24	37	1116
65+	720	180	25	49	59	1033
Total	**4681**	**1266**	**183**	**149**	**229**	**6508**
Percent						
<25	72.4	16.5	3.1	6.3	1.6	100
25-49	72.6	19.8	2.9	1.6	3.1	100
50-64	71.2	20.3	3.0	2.2	3.3	100
65+	69.7	17.4	2.4	4.7	5.7	100
All ages	**71.9**	**19.5**	**2.8**	**2.3**	**3.5**	**100**

Table 10. Percentage of invasive cervical cancer cases in 2009-2012 audit, by FIGO Stage and histology

Stage	Squamous	Adenocarcinoma	Adeno-Squamous	Other (incl undifferentiated)	None recorded	Total
1A	38.3	23.4	7.7	8.7	21.4	33.3
1B+	52.9	65.2	84.2	70.5	41.9	56.2
None recorded	8.7	11.4	8.2	20.8	36.7	10.5
Total	**100**	**100**	**100**	**100**	**100**	**100**

Table 11. Number of invasive cervical cancer in 2009-2012 audit for each QARC region, by treatment

QARC Region	None	Cone biopsy/ Loop excision	Trachalectomy	Simple hysterectomy	Radical hysterectomy	Hysterectomy/Radio therapy	Hysterectomy/chem otherapy	Hysterectomy/Radio /Chemo	Radiotherapy	Chemotherapy	Radiothearpy/ Chemotherapy	Palliative care	Other	None recorded	Total
East of England	22	150	20	31	97	5	4	13	21	12	120	1	0	122	618
East Midlands	13	137	5	50	105	4	1	7	36	12	104	0	0	186	660
London	61	80	16	36	68	5	2	3	37	15	96	0	15	188	622
North East	2	38	2	8	33	1	0	1	7	3	25	0	0	305	425
Yorkshire and the Humber	5	113	3	21	54	7	0	5	18	7	73	0	0	457	763
North West	28	129	4	14	37	2	1	2	16	2	24	0	0	572	831
South Central	28	179	8	21	72	10	4	11	21	11	96	1	0	33	495
South East Coast	14	172	6	30	74	3	0	10	22	10	60	0	0	109	510
South West	27	177	20	46	135	9	1	18	51	17	158	0	0	103	762
West Midlands	48	154	20	142	51	10	6	46	58	27	215	6	0	39	822
Total	**248**	**1329**	**104**	**399**	**726**	**56**	**19**	**116**	**287**	**116**	**971**	**8**	**15**	**2114**	**6508**

Table 11a. Percentage of invasive cervical cancer cases in 2009–2012 audit for each QARC region, by treatment

QARC Region	None	Cone biopsy/ Loop excision	Trachalectomy	Simple hysterectomy	Radical hysterectomy	Hysterectomy/Radiotherapy	Hysterectomy/chemotherapy	Hysterectomy/Radio/ Chemo	Radiotherapy	Chemotherapy	Radiothearpy/ Chemotherapy	Palliative care	Other	None recorded	Total
East of England	3.6	24.3	3.2	5.0	15.7	0.8	0.6	2.1	3.4	1.9	19.4	0.2	0.0	19.7	100
East Midlands	2.0	20.8	0.8	7.6	15.9	0.6	0.2	1.1	5.5	1.8	15.8	0.0	0.0	28.2	100
London	9.8	12.9	2.6	5.8	10.9	0.8	0.3	0.5	5.9	2.4	15.4	0.0	2.4	30.2	100
North East	0.5	8.9	0.5	1.9	7.8	0.2	0.0	0.2	1.6	0.7	5.9	0.0	0.0	71.8	100
Yorkshire and the Humber	0.7	14.8	0.4	2.8	7.1	0.9	0.0	0.7	2.4	0.9	9.6	0.0	0.0	59.9	100
North West	3.4	15.5	0.5	1.7	4.5	0.2	0.1	0.2	1.9	0.2	2.9	0.0	0.0	68.8	100
South Central	5.7	36.2	1.6	4.2	14.5	2.0	0.8	2.2	4.2	2.2	19.4	0.2	0.0	6.7	100
South East Coast	2.7	33.7	1.2	5.9	14.5	0.6	0.0	2.0	4.3	2.0	11.8	0.0	0.0	21.4	100
South West	3.5	23.2	2.6	6.0	17.7	1.2	0.1	2.4	6.7	2.2	20.7	0.0	0.0	13.5	100
West Midlands	5.8	18.7	2.4	17.3	6.2	1.2	0.7	5.6	7.1	3.3	26.2	0.7	0.0	4.7	100
Total	**3.8**	**20.4**	**1.6**	**6.1**	**11.2**	**0.9**	**0.3**	**1.8**	**4.4**	**1.8**	**14.9**	**0.1**	**0.2**	**32.5**	**100**

Table 12. Number and percentage of invasive cervical cancer cases in 2009–2012 audit, by age at diagnosis and treatment

Treatment	<50	50-64	65-79	80+	Total
None(palliative)	73	53	60	70	256
Cone biopsy/ Loop excision	1231	79	13	6	1329
Trachelectomy	103	0	0	1	104
Hysterectomy only (simple or radical)	856	206	47	16	1125
Radiotherapy (+/- hysterectomy)	80	64	103	96	343
Chemotherapy (+/- hysterectomy)	55	42	32	6	135
Chemo-radiotherapy (+/- hysterectomy)	567	316	180	24	1087
Not recorded (Other)	1394	356	247	132	2129
Total	**4359**	**1116**	**682**	**351**	**6508**
Percent					
None(palliative)	1.7	4.7	8.8	19.9	3.9
Cone biopsy/ Loop excision	28.2	7.1	1.9	1.7	20.4
Trachelectomy	2.4	0.0	0.0	0.3	1.6
Hysterectomy only (simple or radical)	19.6	18.5	6.9	4.6	17.3
Radiotherapy (+/- hysterectomy)	1.8	5.7	15.1	27.4	5.3
Chemotherapy (+/- hysterectomy)	1.3	3.8	4.7	1.7	2.1
Chemo-radiotherapy (+/- hysterectomy)	13.0	28.3	26.4	6.8	16.7
Not recorded (Other)	32.0	31.9	36.2	37.6	32.7
Total	**100**	**100**	**100**	**100**	**100**

Table 13. Number of invasive cervical cancer cases in 2009-2012 audit, by FIGO Stage and treatment

Treatment	1A	1B	2	3	4	1B+(NOS)	None recorded	Total
None(palliative)	34	39	24	35	62	18	44	256
Cone biopsy/ Loop excision	1078	180	12	1	5	10	43	1329
Trachelectomy	14	83	3	0	0	2	2	104
Hysterectomy	343	680	36	10	3	17	36	1125
Radiotherapy (+/- hyst)	8	78	91	71	56	8	31	343
Chemotherapy (+/- hyst)	6	28	27	25	35	4	10	135
Radiotherapy/Chemotherapy (+/- hyst)	20	260	444	172	99	33	59	1087
Not recorded(Other)	664	548	133	62	69	197	456	2129
Total	**2167**	**1896**	**770**	**376**	**329**	**289**	**681**	**6508**

Table 13a. FIGO stage of invasive cervical cancer cases: estimated percentage distribution in 2009–2012 audit, by treatment

Treatment	1A	1B	2	Total
None(palliative)	13.8	20.4	65.7	100
Cone biopsy/ Loop excision	83.3	15.0	1.8	100
Trachelectomy	13.5	83.7	2.9	100
Hysterectomy	31.5	63.6	5.0	100
Radiotherapy (+/- hyst)	2.5	24.3	73.2	100
Chemotherapy (+/- hyst)	4.6	21.8	73.6	100
Radiotherapy/Chemotherapy (+/- hyst)	1.9	25.6	72.5	100
Not recorded (Other)	34.4	31.3	34.3	100
Total	**35.0**	**32.4**	**32.6**	**100**

Table 14. Cervical screening status of invasive cervical cancer cases and controls aged 25-64, up to six months prior to diagnosis (percentages)

Cervical screening status up to six months prior to diagnosis	Population Controls		Cases Stage 1A		Cases Stage 1B+		Cases Stage not recorded	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
No cytology test (except within 6 months of diagnosis)	1,379	13.3	570	27.4	735	26.3	128	27.6
Last smear routine and								
Up to date	6,305	60.9	405	19.4	678	24.2	125	26.9
Lapsed	1,702	16.4	567	27.2	790	28.2	121	26.1
Last smear early repeat								
Up to date	455	4.4	152	7.3	141	5.0	21	4.5
Lapsed	369	3.6	144	6.9	245	8.8	34	7.3
Last smear suspend (not followed by any negative(s))	76	0.7	231	11.1	190	6.8	32	6.9
Last smear suspend (followed by at least one negative)	73	0.7	15	0.7	21	0.8	3	0.6
Total	**10,359**	**100**	**2084**	**100**	**2800**	**100**	**464**	**100**

We have used the action code provided by Exeter to determine whether the last cytology test lead to a routine recall, early recall or suspend from the recall programme. After a routine recall interval we consider the screening to be up to date when the diagnosis occurred within 3.5 years (or 5.5 years for older women) from the routine cytology test. After an action code of early repeat we consider the screening to be up to date when the diagnosis occurred within 1.25 years (or .25 years if the test was inadequate) of the early repeat test. When the last test (six month before diagnosis) was suspend and was followed by at least one negative test, women were up to date if the diagnosis was made within 1.5 years of the test leading to the suspend code. Those that were suspended more than 6 months before diagnosis and are not followed by any negative tests are considered to be lapsed.

Table 15. Cervical screening status of invasive cervical cancer cases and controls up to six months prior to diagnosis (numbers and percentages), by age

Cervical screening status up to six months prior to diagnosis	All Cases					Controls				
	20-24	**25-49**	**50-64**	**65-79**	**80+**	**20-24**	**20-49**	**50-64**	**65-79**	**80+**
No cytology test (except within six months of diagnosis)	114	1,125	308	238	217	393	1,260	119	177	387
Last smear routine and										
Up to date	4	888	320	271	114	22	4,711	1,594	957	295
Lapsed	1	1,217	261	99	5	9	1,338	364	158	5
Last smear early repeat and										
Up to date	4	275	39	6	6	6	415	40	4	5
Lapsed	0	328	95	50	8	1	313	56	42	9
Last smear suspend*	3	399	93	18	1	1	130	19	4	2
Total	**126**	**4,232**	**1,116**	**682**	**351**	**432**	**8,167**	**2,192**	**1,342**	**703**
Percent										
No cytology test (except within six months of diagnosis)	90.5	26.6	27.6	34.9	61.8	91.0	15.4	5.4	13.2	55.0
Last smear routine and										
Up to date	3.2	21.0	28.7	39.7	32.5	5.1	57.7	72.7	71.3	42.0
Lapsed	0.8	28.8	23.4	14.5	1.4	2.1	16.4	16.6	11.8	0.7
Last smear early repeat and										
Up to date	3.2	6.5	3.5	0.9	1.7	1.4	5.1	1.8	0.3	0.7
Lapsed	0.0	7.8	8.5	7.3	2.3	0.2	3.8	2.6	3.1	1.3
Last smear suspend*	2.4	9.4	8.3	2.6	0.3	0.2	1.6	0.9	0.3	0.3
Total	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

* The categories "last smear suspend (not followed by any negative)" and "last smear suspend (followed by al least one negative)" found in table 14 are combined due to small numbers

Table 16. Number and percentage of population controls (GP plus district controls) screened in the 3-5 year interval preceding the date of diagnosis of their matched case, by age

Age		Total	Not screened in previous interval	Screened once in previous interval	Screened twice in previous interval	Screened ≥3 times in previous interval
20-24		437	394	32	5	6
25-29		1880	735	966	87	92
30-34		1730	552	977	94	107
35-39		1745	505	1074	93	73
40-44		1629	424	1078	60	67
45-49		1183	334	779	37	33
50-54		798	152	381	226	39
55-59		724	180	487	37	20
60-64		670	188	452	20	10
65-69		482	112	285	74	11
70-74		419	105	203	88	23
75-79		441	144	184	98	15
80+		703	404	212	75	12
Total		12841	4229	7110	994	508
Percent	National Coverage reported in 2011/12*	Coverage (>=1 test in interval)	%	%	%	%
20-24	3.6	9.8†	90.2	7.3	1.1	1.4
25-29	63.0	60.9	39.1	51.4	4.6	4.9
30-34	72.7	68.1	31.9	56.5	5.4	6.2
35-39	76.1	71.1	28.9	61.5	5.3	4.2
40-44	78.1	74.0	26.0	66.2	3.7	4.1
45-49	78.3	71.8	28.2	65.8	3.1	2.8
50-54	82.8	81.0	19.0	47.7	28.3	4.9
55-59	76.6	75.1	24.9	67.3	5.1	2.8
60-64	72.7	71.9	28.1	67.5	3.0	1.5
65-69	-	76.8	23.2	59.1	15.4	2.3
70-74	-	74.9	25.1	48.4	21.0	5.5
75-79	-	67.3	32.7	41.7	22.2	3.4
80+	-	42.5	57.5	30.2	10.7	1.7
Total			**32.9**	**55.4**	**7.7**	**4.0**

* Source: NHS Cervical Screening Programme in England in 2011-11. **Note:** we have used the 3 yearly coverage for women aged 20-49 and the 5 yearly coverage for women aged 50-64 using table 2 (see reference 9)

† Note: 71.8% of controls aged 20-24 are aged 24, only 4.5% are aged 20 or 21. Thus this age group is a reflection of the age at which their matched cases were diagnosed and not of the distribution of women aged 20-24 nationally. This explains the difference in coverage nationally and in the audit.

Table 16a. Number and percentage of population controls (GP plus district controls) screened in the 3-5 year interval preceding the date of diagnosis of their matched case (aged 25-64), by QARC region

QARC	Total	Not screened in previous interval	Screened once in previous interval	Screened twice in previous interval	Screened ≥3 times in previous interval
East of England	989	250	623	70	46
East Midlands	1054	292	662	50	50
London	909	304	501	67	37
North East	690	203	410	48	29
Yorkshire and the Humber	1277	387	774	70	46
North West	1352	405	790	92	65
South Central	812	250	468	65	29
South East Coast	848	269	497	49	33
South West	1159	330	710	71	48
West Midlands	1269	380	759	72	58
Total	**10359**	**3070**	**6194**	**654**	**441**
Percent	**Coverage** (>=1 test in interval)				
East of England	74.7	25.3	63.0	7.1	4.7
East Midlands	72.3	27.7	62.8	4.7	4.7
London	66.6	33.4	55.1	7.4	4.1
North East	70.6	29.4	59.4	7.0	4.2
Yorkshire and the Humber	69.7	30.3	60.6	5.5	3.6
North West	70.0	30.0	58.4	6.8	4.8
South Central	69.2	30.8	57.6	8.0	3.6
South East Coast	68.3	31.7	58.6	5.8	3.9
South West	71.5	28.5	61.3	6.1	4.1
West Midlands	70.1	29.9	59.8	5.7	4.6
Total		**29.6**	**59.8**	**6.3**	**4.3**

Table 17. Time to previous cytology among screened controls

	Time to previous screen						
Age	**<2.75 yrs**	**2.75-3.5 yrs**	**3.5-4.75 yrs**	**4.75-5.5 yrs**	**5.5-9.5 yrs**	**No previous cytology within 9.5 years**	**Total**
25-29	13	105	32	20	42	385	597
30-34	11	162	70	27	52	101	423
35-39	15	164	53	23	51	55	361
40-44	8	178	38	20	32	24	300
45-49	7	122	28	5	20	10	192
50-54	6	50	16	5	10	11	98
55-59	2	4	3	58	13	5	85
60-64	0	4	9	41	6	12	72
Total	**62**	**789**	**249**	**199**	**226**	**603**	**2128**
Percent							
25-29	2.2	17.6	5.4	3.4	7.0	64.5	100
30-34	2.6	38.3	16.5	6.4	12.3	23.9	100
35-39	4.2	45.4	14.7	6.4	14.1	15.2	100
40-44	2.7	59.3	12.7	6.7	10.7	8.0	100
45-49	3.6	63.5	14.6	2.6	10.4	5.2	100
50-54	6.1	51.0	16.3	5.1	10.2	11.2	100
55-59	2.4	4.7	3.5	68.2	15.3	5.9	100
60-64	0.0	5.6	12.5	56.9	8.3	16.7	100
Total	**2.9**	**37.1**	**11.7**	**9.4**	**10.6**	**28.3**	**100**

Table 17a. Time to previous cytology test among potentially screen-detected cases of cervical cancer and their screened controls*

	Time to previous screen													
Age	**<3.5 yrs**		**3.5-4.75 yrs**		**4.75-5.5 yrs**		**5.5-9.5 yrs**		**No previous cytology within 9.5 yrs**		**Total**		**<5.5 yrs**	
	Cases	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**
25-34	226	291	96	102	43	47	121	94	546	486	1032	1020	365	440
35-49	296	464	88	119	38	48	131	103	298	89	851	853	422	631
50-64	28	66	17	28	54	104	24	29	130	28	253	255	99	198
Total	**550**	**821**	**201**	**249**	**135**	**199**	**276**	**226**	**974**	**603**	**2136**	**2128**	**886**	**1269**
Percent														
	Cases	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**
25-34	21.9	28.5	9.3	10.0	4.2	4.6	11.7	9.2	52.9	47.6	100	100	35.4	43.1
35-49	34.8	54.4	10.3	14.0	4.5	5.6	15.4	12.1	35.0	10.4	100	100	49.6	74.0
50-64	11.1	25.9	6.7	11.0	21.3	40.8	9.5	11.4	51.4	11.0	100	100	39.1	77.6
Total	**25.7**	**38.6**	**9.4**	**11.7**	**6.3**	**9.4**	**12.9**	**10.6**	**45.6**	**28.3**	**100**	**100**	**41.5**	**59.6**

*A potentially screen-detected case is one in which cytology results are consistent with screen detection; there is no national record of whether the cytology was in response to screening or to symptoms

Table 18. Maximum interval between cytology tests (over the previous 8 years) among cases with FIGO stage 1B+ and their population controls

	Maximum Interval between cytology tests											
Age	**<3.5 yrs**		**3.5-4.75 yrs**		**4.75-5.5 yrs**		**5.5-7yrs**		**>7 yrs or no cytology**		**Total**	
	Cases	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**
28-34	92	344	112	249	54	111	63	151	246	268	567	1123
35-49	251	1058	225	626	86	213	139	250	596	400	1297	2547
50-64	87	354	106	481	99	301	48	151	458	264	798	1551
Total	**430**	**1756**	**443**	**1356**	**239**	**625**	**250**	**552**	**1300**	**932**	**2662**	**5221**
Percent												
28-34	16.2	30.6	19.8	22.2	9.5	9.9	11.1	13.4	43.4	23.9	100	100
35-49	19.4	41.5	17.3	24.6	6.6	8.4	10.7	9.8	46.0	15.7	100	100
50-64	10.9	22.8	13.3	31.0	12.4	19.4	6.0	9.7	57.4	17.0	100	100
Total	**16.2**	**33.6**	**16.6**	**26.0**	**9.0**	**12.0**	**9.4**	**10.6**	**48.8**	**17.9**	**100**	**100**

Table 19. Number and percentage of invasive cervical cancer cases in 2009-2012 audit with colposcopic appointment recorded, by QARC region

QARC region	Number of cases	Cases with a recorded colposcopy		Cases with an action code "suspend"		Cases with a "suspend" code >4 months before diagnosis		Cases with "Suspend" >4 months before diagnosis + colposcopy		Cases with "Suspend" >4 months before diagnosis + colposcopy (excluding colposcopy within 2 months of diagnosis)	
		n	%	n	%	n	%	n	%	n	%
East of England	618	351	56.8	421	68.1	104	16.8	73	70.2	49	47.1
East Midlands	660	227	34.4	456	69.1	119	18.0	61	51.3	31	26.1
London	622	605	97.3	445	71.5	126	20.3	125	99.2	60	47.6
North East	425	147	34.6	305	71.8	56	13.2	23	41.1	17	30.4
Yorkshire and the Humber	763	272	35.6	570	74.7	145	19.0	68	46.9	40	27.6
North West	831	289	34.8	600	72.2	193	23.2	80	41.5	52	26.9
South Central	495	304	61.4	346	69.9	76	15.4	63	82.9	47	61.8
South East Coast	510	285	55.9	372	72.9	91	17.8	59	64.8	43	47.3
South West	762	431	56.6	487	63.9	140	18.4	105	75.0	76	54.3
West Midlands	822	362	44.0	521	63.4	149	18.1	86	57.7	60	40.3
Total	**6508**	**3273**	**50.3**	**4523**	**69.5**	**1199**	**18.4**	**743**	**62.0**	**475**	**39.6**

Table 20. Original cytology result by review result[1]

Original result	Review Result																	
	Negative		Inadequate		Borderline		Low-grade (mild)		Low-grade (Mod)		High-grade (severe)		?Invasive		?Glandular		Total	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Negative	2,800	51.1	506	9.2	997	18.2	135	2.5	181	3.3	572	10.4	29	0.5	260	4.7	5,480	100
Inadequate	58	8.2	417	59.1	93	13.2	15	2.1	12	1.7	72	10.2	11	1.6	27	3.8	705	100
Borderline	22	2.3	10	1.0	424	43.4	69	7.1	64	6.6	234	24.0	20	2.0	134	13.7	977	100
Low-grade (mild)	4	1.1	1	0.3	35	9.5	152	41.3	78	21.2	88	23.9	5	1.4	5	1.4	368	100
High-grade (moderate)	1	0.2	0	0.0	6	1.5	4	1.0	138	33.9	229	56.3	19	4.7	10	2.5	407	100
High-grade (severe)	9	0.4	3	0.1	5	0.2	0	0.0	9	0.4	1,788	85.1	204	9.7	84	4.0	2,102	100
?Invasive	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	41	6.1	621	91.9	12	1.8	676	100
?Glandular	2	0.4	0	0.0	3	0.6	0	0.0	0	0.0	30	5.7	13	2.5	479	90.9	527	100
Total	2,897	25.8	937	8.3	1,563	13.9	375	3.3	483	4.3	3,054	27.2	922	8.2	1,011	9.0	11,242	100

[1] Updated version of Table 1 in Castanon et al[14]