

**Does the effectiveness of cervical screening vary with age? Evidence from a population-based case-control study of prospectively recorded data**

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## Abstract

**Objective:** To study the effect of cervical screening on cervical cancer incidence as a function of age with particular focus on women screened under age 25. **Design:** Population-based case-control study using prospectively recorded data on cervical screening. **Setting:** Selected centres in the UK.

**Participants:** All cases of invasive cancer diagnosed in participating centres in women (N=4,012) aged 20-69 and two controls individually matched on age and area of residency. **Main Outcome Measures:**

The OR (odds ratios) for strength of association between cervical cancer and screening at particular ages. **Results:** There is no evidence that screening women aged 22-24 reduced the incidence of cervical cancer at ages 25-29 (odds ratio 1.11, 95% confidence interval 0.83 to 1.50). Similar results were seen when cancers are restricted to squamous carcinoma and/or FIGO stage IB or worse, but the numbers are insufficient to provide narrow confidence intervals. Screening was associated with a 60% reduction of cancers in women aged 40, increasing to 80% at age 64. Screening was particularly effective in preventing advanced stage cancers. **Conclusions:** Cervical screening in women aged 20-24 has little or no impact on invasive cervical cancer rates up to age 30. Some uncertainty still exists regarding its impact on advanced stage tumours in women under age 30. By contrast, screening older women leads to a substantial reduction in cervical cancer incidence and mortality. This new evidence should help policy-makers balance screening impact on cancer rates against its harms such as over-treatment of lesions with little invasive potential.

## **Introduction**

Cervical screening is a complex process that requires careful analysis to determine the balance between its benefits and harms. For society it is important to show that screening will provide a net benefit at an affordable cost. These issues have been given prominence in the recent public controversy over screening in women aged 20-24.

Unfortunately policy makers are often forced to make decisions based on limited evidence. Such was the situation in 2003 when the screening programme in England was re-organised. One of those changes – to invite women for cervical screening at age 25 (instead of between 20 and 24) was and has remained controversial (1-6). The decision to change and standardise the age at first invitation was based, in part, on an earlier paper of ours that showed that the relative reduction in frank invasive cervical cancer associated with screening was substantially less in women aged 20-34 than it was in older women(7).

A full benefit-harms analysis is beyond the scope of this paper. Rather we aim to better define the benefits of screening at different ages.

The existing literature on this topic is limited partly because causal-inference from case-control studies is hampered by a number of biases and the possibility that factors other than those studied are driving the observed associations. Nevertheless, in the absence of randomised controlled trials addressing the particular question of interest, careful analysis of well-designed observational studies provides the best evidence on which to modify existing screening programmes. IARC's landmark meta-analysis(8) provided no details regarding the age-dependence of the results, but stated: "...age did not affect either the sensitivity of cytological screening or the distribution of the sojourn time of the disease. In particular, there was no evidence that younger women (under 35) were more at risk of developing fast growing tumours." We previously carried out a similar analysis on UK data in three age-groups: 20-39,

40-54 and 55-69. We found that the reduction in risk 3-5 years after a normal smear was greater in the older age-groups (7). Our finding was confirmed by a smaller Italian study(9) and to a lesser extent by a recent paper from Australia(10), but an important Swedish audit(11) found no evidence of screening being less effective in young women.

In this paper, we study how the association between cervical screening and a subsequent decrease in cervical cancer varies with age. This is done in a substantially enlarged dataset from the UK by estimating the odds ratios associated with screening in overlapping narrow age-bands. Additionally we concentrate on the age at which screening occurs rather than the age at which the cancers are diagnosed.

## **Materials and Methods**

### Subjects

Women diagnosed with cervical cancer were identified from histology laboratory records between January 1990 and April 2008. Collection of case-control data was done for a year at a time by local collaborators. Different centres collected cases over differing time periods depending on the availability of a collaborator. (Table S·1 provides a breakdown of cases by year of diagnosis and region of residence within the UK). Cases are women with invasive (including micro-invasive) cervical cancer. Any woman who has ever been registered with an NHS GP (and has not subsequently died or emigrated) was eligible as a control and would have had a record in the National Cervical Screening Call/Recall System. All controls were individually matched to cases based on age and place of residence: one control had the same GP as the case and a second had a different GP, but was within the same administrative area. Occasionally, only one control could be identified. The use of the same GP was to provide a crude surrogate for socio-economic status and ethnicity. The reason for selecting a

control from a different GP was to avoid overmatching as screening uptake is closely related to the GP's enthusiasm for cervical screening. Cases not in the Call/Recall System at the time of diagnosis were excluded (because such women could not be selected as controls). Control selection was done blinded to the screening information and in most cases by random selection (using a computer program). Data were collected on all selected controls so there is no selection or participation bias. Data on screening histories were abstracted from routinely recorded cervical cytology records -held on the Call/Recall System (and as such are not subject to recall bias). These records include all NHS (and many private) smears taken in the UK since 1988. After linking screening data to cases and controls by local NHS staff, the data were anonymised before being transferred to us for analysis. Details of the design have been published previously (7, 12).

After the publication of the paper in 2003 it was found that 40 of the original cases had been duplicated (i.e. the same woman was reported twice). The duplicates have now been deleted from the database; consequently the numbers of cases reported in the original article and the numbers of "prior" cases reported here are not the same. Figure 1 provides a break down of cases used throughout this paper.

### Statistical methods

The main analysis uses conditional logistic regression to estimate the association between having an adequate smear taken in a particular three-year age-band (e.g. 22-24) with cervical cancer incidence in the subsequent five-year band (e.g. 25-29). The association is expressed as the odds ratio for developing cervical cancer in the next five-year interval in those screened in a given (three-year) age-band compared to those not screened in that age-band or in the two previous years. These analyses are repeated in overlapping age-bands (e.g. screening at 22-24, 23-25, 24-26, etc). All age bands are

inclusive (i.e., 22-24 means  $\geq 22$  and  $< 25$ ). Further details (including the results of sensitivity analyses) are provided in Appendix 1.

In order to ensure that age-differences in effectiveness were not attributable to a different impact of screening on micro-invasive cancer or on adenocarcinoma, we looked at the effect of screening separately by stage and histology. Finally, we considered both all available data and only data obtained subsequent to our previous publication(7). The latter was done to examine possible trends associated with changes in screening policy and practice.

In an attempt to understand the reason for screening being less effective in young women we also looked, by age-group at the proportion of cases classified as screen-detected, prevalent, interval, never-screened or lapsed and following an abnormal smear. The intuitive description (as well the formal definition) of these categories is given in Appendix II.

Analyses were done in STATA 10 (StataCorp. 2007. *Stata Statistical Software*: Release 10. Collage Station, T: StataCorp LP).

## **Results**

### Association between screening and cervical cancer at different ages

The main results are presented graphically in Figure 2 with selected details in Table 1. They include 4,012 cases with cervical cancer (any stage, including IA) diagnosed between 1990 and 2008 (including 1,709 diagnosed since 2000), and 7889 controls. Figure 2 shows the odds ratio of cervical cancer in screened versus unscreened women as a function of age. The odds ratios are substantially below one at older ages. They, increase with decreasing age and are greater than one for those screened at age 20-22. The odds ratios relate to cancers diagnosed in a specific age band for women screened during a previous age band. For example, the estimated odds ratio of 0.26 plotted at a screening age-band of 52-54 is to be interpreted as follows: The relative risk of having cervical cancer diagnosed at

age 55-59 is approximately 0.26 in women screened at age 52-54 compared to women not screened between ages 50 and 54. These odds ratios vary from 0.18 to 0.36 between age-bands 40-42 and 62-64, corresponding to screening being associated with a reduction in the risk of cervical cancer over the subsequent 5-8 years of between 64% and 82%. In younger women the effect of screening is substantially and significantly less. Screening between the ages of 30 and 37 is associated with a reduction in the risk of cervical cancer over the next five years of between 43 and 60% (see dotted lines on Figure 2). The odds ratio for screening in the age-band 22-24 is 1.11 (95% CI 0.83 to 1.50) (Table 1). Similar estimates were obtained for screening at 20-22 and 21-23(see Figure 2). Thus screening at ages 20-24 has no detectable impact on cervical cancer rates at ages 25-29.

We also looked separately at the data on 1821 cases collected since our previous publication (figure not shown). The pattern is very similar to that for all the data. In particular, odds ratios are still close to one for women screened aged 20-25.

#### Association between screening at different ages and cervical cancer by stage and histological type of cancer

In Figure 3, we explore the sensitivity of these results to stage and/or histological type of cancer. The overall patterns are similar to those observed in Figure 2: in particular when restricted to stage IB+, the odds ratios are not significantly different from unity at young ages; as before they fall rapidly with increasing screening age between 25 and 34 years and then become fairly flat with a nadir around age 55. The odds ratios are even lower for more advanced disease, showing that advanced cancer is particularly rare in screened women. The pattern for cases with stage II or worse cancer is slightly different with a dip at age 22-24 and a second peak at age 25-28. There are only 38 cases known to have advanced cancer (stage II or worse) under age 30 so the estimated confidence intervals in Figure 3d are wide.

Despite there being over 350 cases with stage IA or worse cervical cancer (any stage) aged 25-29, there is no indication of any benefit of screening at age 22-24 (compared to those not screened at age 20-24): OR 1.11 (95% CI 0.83 to 1.50) (Table 1). Restricting analysis to stage IB+ cervical cancer makes little difference to the point estimate, but results in a wider confidence interval and allows for the possibility of a greater effect: OR=1.03 (95% CI 0.63 to 1.7) (see Figure 3b). Further restricting to stage IB+ cervical cancer aged 25-27 at diagnosis (see sensitivity analysis in Appendix 1), limits the analysis to 65 cases yielding an estimated odds ratio of 0.52 (95% CI 0.23 to 1.2).

#### Benefit associated with being screened twice by age 26

It has been argued that screening only begins to be fully effective once a woman has been screened twice and that consequently women screened aged 20-24 and again at age 25 will have a greater benefit from screening after age 25 than will those who are first screened at age 25. To study this we compared women screened both at ages 20-22 and at 23-25 with those first screened only aged 23-25. In an analysis of cancers diagnosed between ages 26.5 and 29.0 years restricted to women who were screened between ages 23 and 25 (inclusive). The odds ratio for stage IB+ cancer associated with also being screened between ages 20 and 22 (inclusive) was 0.90 (95% CI 0.38 to 2.2): For all cancers (including stage IA) the odds ratio was 1.1 (95% CI 0.62 to 2.0).

#### Screening Classification of Cases diagnosed before age 25

There were 73 cancers diagnosed between age 20 and 24 (inclusive). Of these 73 women, 5 had no previous smears, 32 were classified as screen-detected (13 on their first screen and 19 on subsequent smears), 15 as interval cancers (last smear was normal) and 21 were diagnosed following a history of abnormal smears (Table 2). In these young women, 75% of all cancers, 76% of stage IA cancers, and 81% of cancers stage IB or worse occurred despite screening. We consider cancers classified as



interval, screen detected (previously screened) and following abnormal to have occurred despite screening.

The majority of screen-detected (previously screened) cancers were micro-invasive (12 out of 19 with known stage) while most of the interval cancers were stage IB or worse (12 out of 15 with known stage) (Fisher's exact test:  $p=0.017$ ). Of the 18 stage IB+ cancers in women with a previous normal screening history, 11 (61%) occurred within 3.5 years of a negative smear.

The same classification of screening history was applied to all cases with stage IB or worse cervical cancer. The results in 10-year age groups are presented in Table 3. The proportion of women with stage IB+ cancer who have not been screened in the previous six years (never/lapsed) increases with age. Compared to cases aged 40-69, women aged 20-29 with stage IB+ cancer were far less likely to be "never screened".

## **Discussion**

### Principal findings of the study

This paper provides quantitative information about the association between screening and cervical cancer incidence as a function of age. In summarising our results we use language that assumes that the observed associations are causal. This is justified better later in the discussion. The study confirms our previous findings that cervical screening in women aged 20-34 is less effective than in older women. By studying the effect of screening in smaller age-groups, it is shown that the efficacy of screening decreases with decreasing age even within the age range 20-34.

On average participation in the UK cervical screening programme by a woman aged 35-64 reduces her risk of cervical cancer over the next five years by 60-80% and her risk of advanced cervical cancer by about 90%. The benefit of screening for women aged 25-34 is more modest. Screening in women aged 20-24 has little or no impact on cervical cancer incidence under the age of 30. This is true whether one

looks at all cancers or restricts analysis to frankly invasive (i.e. stage IB or worse) squamous carcinoma, or even to stage II or worse cancers (Figure 3). However because stage IB+ cancer is rare in young women, the confidence intervals are wide and our data do not rule out the possibility of screening in women aged 20-24 being effective in reducing stage IB+ cancer in women aged 25-27. It has also been argued that women should have their first two smears close in time in order to minimize the impact of an initial false negative smear (13). In fact our results provide no evidence for women screened aged 20-22 and then again at 23-25 being better protected than those screened only at age 23-25.

A careful review of the screening histories of cases diagnosed aged 20-24 suggests that few (if any) of them have occurred through a lack of screening. Indeed only 5 of 73 cases had not been screened in the previous six years.

#### Strengths and weaknesses of the study

We have used prospectively recorded screening data and have selected controls at random, thus eliminating both recall bias and selection bias (data were obtained for all selected controls). We believe this design to be the most appropriate given that a randomised controlled trial was not possible. Other papers have analysed trends in cancer incidence (and or mortality) before and after the introduction of screening to estimate the impact of screening in the population (14-17). Such analyses rely on comparison of observed rates with estimates of what would have happened in the absence of screening, they are subject to trends in other factors such as the quality of the cancer registry data. For women aged 20-29, who have been offered screening from the age of 20 it is not possible to reliably estimate what their rates would have been in the absence of screening.

It is always possible to criticise observational studies since women who go for screening may differ from those that do not, so that any observed effect may not be causal. However, for the observed

difference in the benefit of screening at different ages to be due to confounding, there would have to be differences in the way confounders affect the results at different ages. We know of no evidence to support such an interaction and suggest that differential benefits with age are not due to confounding, but reflect the true effects of screening. Given that we feel they are very few biases, we are comfortable saying the associations are causal, which is why we talk about the “protection” offered by screening.

This is the largest study of the impact of cervical screening on invasive cervical cancer and contains more cases than all other studies with detailed screening information combined. Some of the data presented have been published previously, but over 45% of the data are new. The results of analyses limited to the new data are qualitatively very similar to those using all the data suggesting that there have been no changes in the impact of screening in young women on cervical cancer rates despite improvements in the quality of screening in the UK.

The new analysis considers the association between screening in one age-group (e.g. 25-29) and cervical cancer in the subsequent five years (i.e. 30-34 for this example). Using this approach, the exposure is close to the usual definition of screening coverage used by many screening programmes – proportion of eligible women screened in the last 5 (or 3) years. Further, this approach more closely reflects what one could estimate by prospectively following a cohort of women. However, with a coverage interval of 3 years and a follow-up of 5 years, it could be as much as 8 years between the last screen and cancer diagnosis. Thus the benefit of regular 3 (or 5) yearly screening could be considerably greater than that implied by this model. Nevertheless the approach does attempt to measure the protection achieved with screening (which derives from the treatment initiated by a positive smear) rather than the low-risk periods associated with a negative smear.

#### Comparison with other studies

Much of the earlier literature aiming to study the protection afforded by cervical screening has not considered the possibility of different levels of protection depending on age. An important recent paper reports on the results of an audit of cervical cancer in Sweden (11). The odds ratios in that paper are similar for all age groups and they give an odds ratio of 0.42 ( $=1/2.37$ ) for the effect of three-yearly screening on cancer incidence at ages 21-29. It is important to consider the methodological differences between the analyses when interpreting these results. They consider a woman (aged 20-52) to have been screened if she had a smear between 3.5 years and 6 months prior to (the date of the case's) diagnosis. They include stage IA cancers most of which will have been screen-detected as well as screen-detected stage IB cancer. Consider a screen-detected case who has two smears 3.5 years apart. If the smear that led to diagnosis is within 6 months of diagnosis she will be classed as unscreened. A control who is screened every 3.5 years will have a chance of 86% ( $=3.0/3.5$ ) of having had a smear in the particular interval of width 3 years. Thus the inclusion of screen-detected cases introduces a considerable bias in favour of screening. Since the proportion of cancers that are stage IA or screen-detected stage IB is greater in young women, the bias is particularly strong in young women. To illustrate the point, the same analysis applied to women aged 20-29 in our study yields an odds ratio of 0.46 (0.38 to 0.56).

A case control study in New South Wales, Australia found that screening every 2 years appeared to be more protective in women over age 30 than in those aged 20-29 (10). The more favourable results for screening in women aged 20-29 in that study could be due to their controls having been selected from women who had been for screening (albeit possibly only after the date of diagnosis of the case).

### Interpretation of the results

Having designed the study to eliminate most of the biases that affect case-control studies, the observed associations are almost certainly either causal or due to confounding. The heterogeneity of

association in different age-bands within the same study argues strongly that these effects are real. One can speculate as to the biological reason for cervical screening to work better in older women.

Undoubtedly the specificity of screening is less in younger women because HPV infections are so much more common. However, this does not explain why the sensitivity of screening should be less.

We favour the explanation that, by necessity, a cancer in a 25 year old woman (infected at say 15) will have progressed from HPV infection through CIN3 faster than a cancer in a 55 year old woman (infected at perhaps 25). This means that the opportunities for detecting the small proportion of CIN3s in women in their early 20s that will progress to cancer within at most a few years are small. It is an extreme example of length-bias – most cases of CIN3 detected will be slow growing and could safely be left for several years; but the very rare cases that are progressing rapidly will most likely be missed. It has been argued that screening from aged 20 could prevent more cancers aged 25-34 than screening from age 25. Our study has very little power to detect such an effect.

Policy decisions should be based on balancing the benefits and harms of screening and need to take into account the underlying risk of cervical cancer at different ages. Such an analysis is beyond the scope of this paper. We provide more accurate estimates of the benefits of cervical screening in different age-groups which should aid policy makers in making their decisions. It has been argued that since screening undoubtedly leads to the detection of many cases of stage IA cancer in women aged 20-24 it must be doing good by preventing more advanced cancers. If this were the case, we should have found that screening at ages 20-24 leads to a reduction in stage IB+ cancers. That no such reduction was observed suggests that most of the stage IA cancers screen-detected under age 25 would still be stage IA at age 25-26 and could be picked up by screening at age 25 without adverse consequences.

This study is based on cancers diagnosed in the UK between 1990 and 2008 and smears taken within the UK from 1988 to 2008. Cervical cancer rates in women in their 20s have been relatively

high compared to other countries and abnormal cytology results have been more common in those aged 20-34 than in older women throughout this period (18, 19). We believe that the standard of smear-taking, cytology reading and fail-safe procedures for cervical screening in this study have mostly been high. Since the early-mid 1990s the UK screening programmes have put great emphasis on quality assurance and there is evidence that by the late 1990s, UK cytology was as good (or better) than anywhere in the world (20). Thus our finding that cervical screening in women aged 20-24 has at best a modest effect on the incidence of cervical cancer at ages 25-29 is almost certainly generalisable to other countries. We have no reason to believe that it would be substantially more effective elsewhere.

Any decision on when to start screening women will have to weight the benefits and harms and may depend on the local status-quo. In a setting where screening is offered to women aged 20-24 policy makers may decide to continue this policy since we have not shown that the harms exceed the benefit. By contrast, where screening is not offered to women aged 20-24, the lack of evidence of any benefit from screening in this age group dictates that the policy should not change.

#### Unanswered questions and future research

Our study does not systematically consider the harms of screening at different ages, nor do we take into account the absolute rate of cervical cancer in (screened and unscreened women of different ages).

Such a synthesis of research is necessary for rational policy making. Undoubtedly however decision making will be complicated because of the uncertainty in many of the estimates of harm and benefit.

As we have seen the confidence intervals for the impact of screening at ages 20-24 on stage II + cervical cancer are extremely wide. We have not even attempted to estimate the added impact of starting screening five years earlier on cancer at ages 30-44.

The most common harms of screening are the anxiety caused by abnormal test results and the trauma of treating CIN that would never have progressed to cancer. These can be easily estimated. It is also

possible that treatment may cause premature delivery during subsequent pregnancies. If the association observed in several studies(21, 22) is causal then screening may do serious harm, but it may simply be due to confounding. These issues require careful study.

The question of screening women aged 20-24 will decrease in importance as the cohort of women vaccinated against HPV types 16 and 18 reach their 20s. If it is questionable whether screening is worthwhile in unvaccinated women aged 20-24, there can be no doubt that the risk of cancer under age 25 in those vaccinated prior to exposure to HPV will be sufficiently low risk to make screening at such an age unjustifiable.

**Ethical review:** This project is considered service evaluation which does not require research ethics approval according to UK guidelines (NRES) (23). Permission to link cervical screening and histology (cancer registration) data has been granted by the Patient Information Advisory Group (PIAG).

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I *Peter Sasieni* declare that I participated in the design and establishment of the study, collation of data, design of the database, analysis of the data and writing of the paper and that I have seen and approved



the final version. I am also the guarantor of the study and therefore accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

I *Alejandra Castanon* declare that I participated in the collation of data, analysis of the data and writing of the paper and that I have seen and approved the final version.

I *Jack Cuzick* declare that I participated in the design and establishment of the study and writing of the paper and that I have seen and approved the final version.

#### **Summary points box**

##### **What is already known on this topic**

Cervical screening has had a substantial impact on the incidence and mortality of cervical cancer in many developed countries

Most of the benefit from cervical screening comes from the prevention of cervical cancer, but it can also lead to down-staging

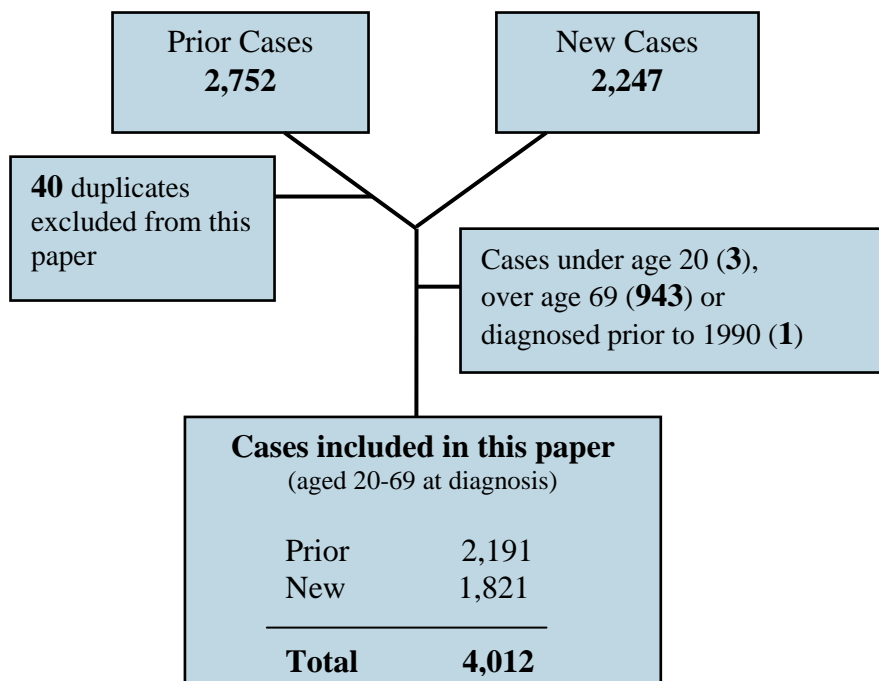
There is a suggestion that the relative protection against cervical cancer is less at ages 20-34 than it is in older women

##### **What this study adds**

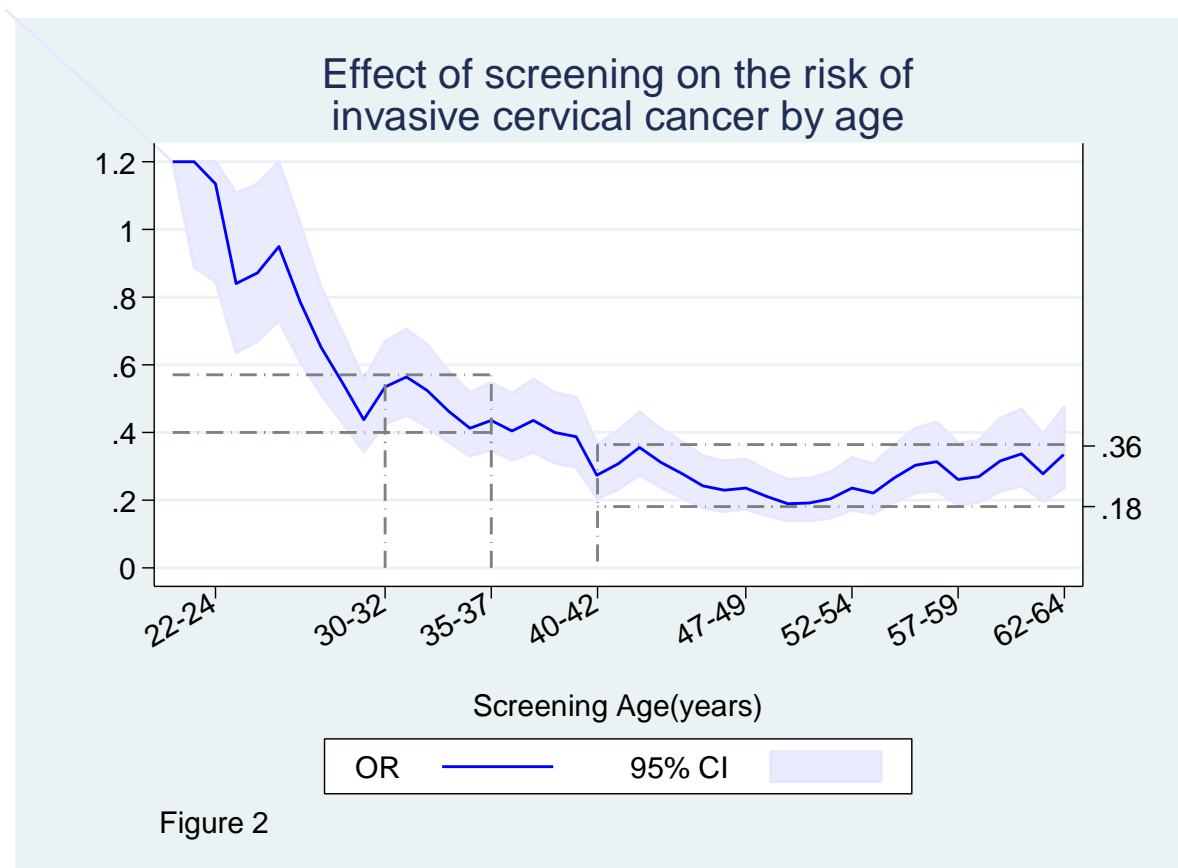
More accurate estimates of the protective effect of screening at different ages will enable policymakers to balance the benefits and harms of cervical screening with less uncertainty

New methodology for the analysis of case-control studies of screening that avoids some of the biases associated with previously used statistical methods

Cervical screening in women aged 20-24 is substantially less effective in preventing cancer (and in preventing advanced stage tumours) than is screening in older women



**Figure 1** Cases included in this paper.



**Figure 2:** Odds ratio (and 95% confidence interval) for developing (stage IA or worse) invasive cervical cancer (in the next 5 year interval) in those screened in a given (3-year) age-band compared to those not screened in that age-band (or in the 2 previous years). Odds ratios are plotted for overlapping age-bands. Dotted lines indicate the risk of developing cervical cancer, between the ages of 33-40 and between the ages of 43-65. **Note:** odds ratios and confidence intervals are truncated at 1.2. The figure is based on 4,012 cases (including 437 under age 30) and 7,889 controls.

### Effect of Stage and Histology type on the odds ratio of cervical cancer

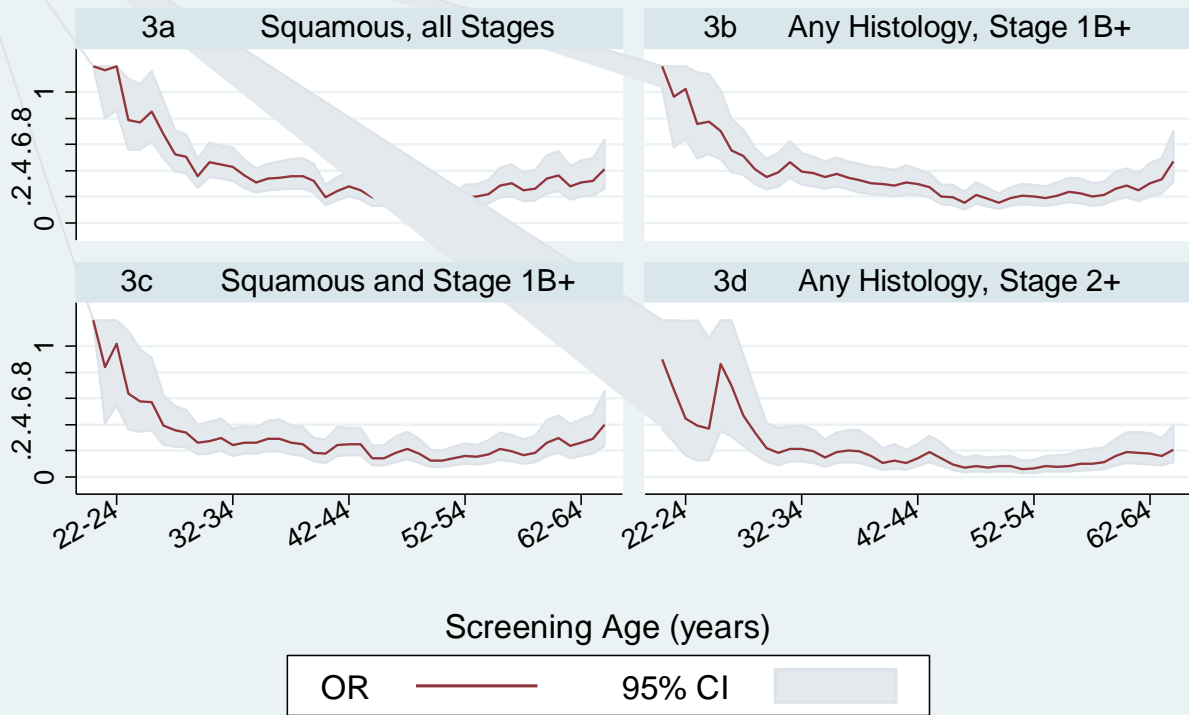


Figure 3

**Figure 3:** Effect of stage and histology type on the odds ratio of developing cervical cancer (in the next 5 year interval) given screening in the indicated age-bands. The graph is for diagnosed cancer with five years of follow-up and compares those screened in the previous 3 years with those not screened in the previous 5 years. **Note: 3a)** is based on 2,589 cases (including 303 under age 30) and 5,122 controls; **3b)** is based on 2,448 cases (including 172 under age 30) and 4,821 controls; **3c)** is based on 1,525 cases (including 107 under age 30) and 3,025 controls; **3d)** is based on 897 cases (including 38 under age 30) and 1,764 controls.

Table 1. Protective effect of screening in the past against developing cancer in the future

	Cases	Controls	OR*	95% CI
<b>Cancer diagnosed aged 25-29</b>				
Screened age 22-24	202(58%)	399(57%)	1.11	(0.83-1.50)
Screened age 20-21, but not 22-24	46(13%)	70(10%)	1.51	(0.95-2.38)
Not screened aged 20-24	103(29%)	226(33%)	1.00	
Total	<b>351(100%)</b>	<b>695(100%)</b>		
<b>Cancer diagnosed aged 35-39</b>				
Screened age 32-34	346(53%)	842(66%)	0.55	(0.44-0.69)
Screened age 30-31, but not 32-34	88(14%)	144(11%)	0.79	(0.57-1.1)
Not screened aged 30-34	214(33%)	288(23%)	1.00	
Total	<b>648(100%)</b>	<b>1274(100%)</b>		
<b>Cancer diagnosed aged 45-49</b>				
Screened age 42-44	214(45%)	583(63%)	0.37	(0.29-0.48)
Screened age 40-41, but not 42-44	55(12%)	133(14%)	0.40	(0.27-0.58)
Not screened aged 40-44	203(43%)	207(22%)	1.00	
Total	<b>472(100%)</b>	<b>923(100%)</b>		
<b>Cancer diagnosed aged 55-59</b>				
Screened age 52-54	111(33%)	389(58%)	0.26	(0.19-0.36)
Screened age 50-51, but not 52-54	32(9%)	103(15%)	0.27	(0.17-0.43)
Not screened aged 50-54	198(58%)	183(27%)	1.00	
Total	<b>341(100%)</b>	<b>675(100%)</b>		

\*Calculated by conditional logistic regression taking account of matching

Table 2. Screening history for women aged 20-24 at time of diagnosis

Screening Category	Stage			Total
	IA	IB+	Unknown	
<b>Screen detected</b>				
1 <sup>st</sup> screen	6(18%)	5(16%)	2(25%)	13(18%)
Previously screened	12(36%)	6(19%)	1(13%)	19(26%)
<b>Interval</b>	2(6%)	12(37%)	1(13%)	15(21%)
<b>Following abnormal</b>	11(33%)	8(25%)	2(25%)	21(29%)

**cytology**

<b>Never screened or lapsed</b>	2(6%)	1(3%)	2(25%)	5(7%)
<b>Total</b>	33(100%)	32(100%)	8(100%)	73(100%)

**Table 3.** Distribution of cancers stage IB or worse according to their screening classification

Screening Category	Age at Diagnosis					Total
	20-29	30-39	40-49	50-59	60-69	
<b>Screen detected</b>						
1 <sup>st</sup> screen	25(15%)	131(20%)	115(18%)	87(16%)	86(19%)	444(18%)
Previously screened	33(19%)	121(18%)	93(15%)	47(9%)	20(4%)	314(13%)
<b>Interval</b>	54(31%)	196(29%)	143(23%)	127(24%)	106(23%)	626(26%)
<b>Following abnormal cytology</b>	41(24%)	115(17%)	126(20%)	74(14%)	45(10%)	401(16%)
<b>Never screened or lapsed</b>	19(11%)	102(15%)	148(24%)	193(37%)	203(44%)	665(27%)
<b>Total</b>	172(100%)	665(100%)	625(100%)	528(100%)	460(100%)	2450(100%)

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