

## Psychological impact of human papillomavirus testing in women with borderline or mildly dyskaryotic cervical smear test results: cross sectional questionnaire study

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# Primary care

## Psychological impact of human papillomavirus testing in women with borderline or mildly dyskaryotic cervical smear test results: cross sectional questionnaire study

Esther Maissi, Theresa M Marteau, Matthew Hankins, Sue Moss, Rosa Legood, Alastair Gray

### Abstract

**Objective** To describe the psychological impact on women of being tested for human papillomavirus (HPV) when smear test results are borderline or mildly dyskaryotic.

**Design** Cross sectional questionnaire study.

**Setting** Two centres participating in an English pilot study of HPV testing in women with borderline or mildly dyskaryotic smear test results.

**Participants** Women receiving borderline or mildly dyskaryotic smear test results tested for HPV and found to be HPV positive (n = 536) or HPV negative (n = 331); and women not tested for HPV with borderline or mildly dyskaryotic smear results (n = 143) or normal smear results (n = 366).

**Main outcome measures** State anxiety, distress, and concern about test result, assessed within four weeks of receipt of results.

**Results** Women with borderline or mildly dyskaryotic smear results who were HPV positive were more anxious, distressed, and concerned than the other three groups. Three variables independently predicted anxiety in HPV positive women: younger age ( $\beta = -0.11$ ,  $P = 0.03$ ), higher perceived risk of cervical cancer ( $\beta = 0.17$ ,  $P < 0.001$ ), and reporting that they did not understand the meaning of test results ( $\beta = 0.17$ ,  $P = 0.001$ ). Testing HPV negative was not reassuring: among women with abnormal smear test results, those who were HPV negative were no less anxious than those who were not tested for HPV.

**Conclusions** Informing women more effectively about the meaning of borderline or mildly dyskaryotic smear test results and HPV status, in particular about the absolute risks of cervical cancer and the prevalence of HPV infection, may avoid some anxiety for those who are HPV positive while achieving some reassurance for those who test HPV negative.

### Introduction

Human papillomavirus (HPV) is present in almost 100% of cervical cancers<sup>1</sup> and HPV positivity is associated with high grade pre-invasive lesions in women with borderline nuclear change or mild dyskaryosis. Given the relatively high rates of borderline or mildly dyskaryotic cervical smear test results, HPV testing could be used to stratify women for higher or lower risks of developing cervical cancer, and to manage them accordingly. A pilot study was mounted in England to evaluate the clinical, economic, and psychological consequences of this strategy; this paper assesses the psychological consequences.

Testing for human papillomavirus is expected to provide clearer and more effective management strategies, but there are

concerns about its potential to raise anxiety beyond the levels reported after women receive a borderline or mildly dyskaryotic smear test result.<sup>2</sup> Receiving abnormal smear test results and being referred for colposcopic examination of the cervix are associated with high anxiety levels,<sup>3-5</sup> some of which can be avoided by providing clear, salient information.<sup>6,7</sup> No data are yet available on the psychological impact of HPV testing in conjunction with cytological screening. Surveys of highly selected groups of women who have undergone HPV testing for a variety of reasons have had equivocal findings, with some showing raised levels of distress<sup>8-11</sup> and others not.<sup>12,13</sup>

Although HPV testing may raise anxiety in women who test positive, it has the potential to reassure those who test negative that their risks of developing cervical cancer, given a borderline or mildly dyskaryotic smear test result, are lower than women who with HPV infection.<sup>1</sup> This study aimed to describe the psychological impact of HPV testing in women with borderline or mildly dyskaryotic cervical smear test results and to examine the predictors of this impact.

### Methods

#### Participants

All women who had a routine cervical smear test at two of the three centres taking part in the English pilot study of liquid based cytology and HPV testing, and who received either a normal or a borderline or mildly dyskaryotic test result, were eligible for this study. They were informed about the possibility of being invited into this questionnaire based study by the letter inviting them to attend for screening. All borderline or mildly dyskaryotic smear samples were tested for human papillomavirus. After HPV testing in the pilot study, we recruited an extra group of women with borderline or mildly dyskaryotic smear test results, but no HPV testing, to assess the possible reassuring effects of receiving an HPV negative test result.

All women with borderline or mildly dyskaryotic test results over a five month period were invited to participate, as were the first 13 women each week who received a normal test result (we estimated this number was needed to achieve similar numbers in each group). When the pilot was completed, the first 42 women each week over a five week period with borderline or mildly dyskaryotic results but no HPV test results were also recruited, half from each of the two centres. In total, 2183 women were sent questionnaires within a week of the research team being informed that their smear test results had been sent to them. Up to two reminders were sent. The final sample of 1376 (63%) women comprised 366 women who had received a normal result

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and 1010 who had received a borderline or mildly dyskaryotic smear test result. In the latter group 331 were HPV negative, 536 were HPV positive, and 143 had not been tested.

### Clinical management

The box shows the written information that accompanied the test results. Clinical management varied according to test result and sometimes across centres.

*Borderline or mildly dyskaryotic test result, HPV positive*—In centre 1 all HPV positive women were referred for colposcopy. In centre 2, due to an increased workload in the colposcopy clinics, only women over 35 were referred for colposcopy. Those below 35 were invited for a repeat smear and HPV test after six months. If dyskaryosis or HPV infection persisted, these women were referred for colposcopy.

*Borderline or mildly dyskaryotic test result, HPV negative*—In both centres women were asked to attend for a repeat smear and HPV test six months later. If dyskaryosis, HPV infection, or both, was found, women were referred for colposcopy.

*Borderline or mildly dyskaryotic test result, HPV not tested*—In both centres, women with this result were asked to attend for a repeat smear test after six months. If the repeat smear showed borderline changes, mild dyskaryosis, or worse, women were referred for colposcopy.

*Normal smear test result*—Women receiving a normal result with no previous abnormal smear test results were returned to routine recall.

### Study hypotheses

Women with normal results were predicted to have anxiety scores in the normal range (mean score = 35.0), while those with borderline or mildly dyskaryotic results who were HPV negative or not tested were predicted to have raised anxiety (mean score = 38.0), with the highest levels of anxiety to be found in HPV positive women (mean score = 40.0). The formal hypotheses tested were that women with normal results would have anxiety scores significantly lower than all other groups; that women with borderline or mildly dyskaryotic smear test results who were HPV positive would have significantly higher scores than the other three groups; and that women with borderline or mildly dyskaryotic smear test results who were HPV negative would have lower anxiety scores than those who had abnormal smear test results but had not been tested for HPV.

Given a population standard deviation of 12.0, a minimum of 115 women was required in each of the four groups to detect the predicted small to medium effects ( $F = 0.16$ ),<sup>14</sup> with 80% power at the 5% level of significance. This sample size was also sufficient for pairwise comparisons to detect a mean difference of 0.37 of a standard deviation between groups, with 80% power.

### Outcome measures

*State anxiety* was assessed using the short form of the state scale of the Spielberger state-trait anxiety inventory (S-STAI-6),<sup>15</sup> prorated to give a scale range from 20 to 80. The population norm for women is 35; scores above 49 are found in patients with a diagnosis of anxiety disorder. The internal reliability of the scale in this study sample ( $n = 1288$ ) was 0.84 (Cronbach's  $\alpha$ ).

*General distress* was assessed using the 12 item general health questionnaire (range 1-12) with a clinical cutoff score of 4 ( $\alpha = 0.89$ ,  $n = 1343$ ).<sup>16</sup>

*Concern about the smear result* was assessed using two seven point rating scales (range 2-14) asking women how concerned, and how reassured, they felt about the result. Higher scores indicated more concern ( $\alpha = 0.66$ ,  $n = 1352$ ).

*Perceived risk of developing cervical cancer* was assessed using a seven point scale assessing women's perceptions of their likelihood of developing cervical cancer in the next 10 years.

### Written information provided to women with results of smear test

#### Borderline or mildly dyskaryotic test result, HPV positive

These [minor abnormalities] are not cancer. A minor abnormality means that there are small changes to the cells of your cervix. This is not unusual. Because your result showed these changes your sample was tested for the Human Papilloma Virus (HPV). HPV is a very common infection of the cervix. Most women get the virus at some point in their life. In most cases it does not need treatment and your body will clear it on its own. Some forms of the virus can cause cervical abnormalities that clear up when the virus is gone. In some women, however, the virus stays for a number of years and cervical abnormalities may develop into cancer if left untreated. HPV was found in your sample.

#### Borderline or mildly dyskaryotic test result, HPV negative

These [minor abnormalities] are not cancer. A minor abnormality means that there are small changes to the cells of your cervix, which are not unusual. Because your result showed these changes your sample was tested for the Human Papilloma Virus (HPV), which is a very common infection of the cervix. HPV was not found. This means that you are at very low risk of developing cervical cancer of the cervix.

#### Borderline or mildly dyskaryotic test result, HPV not tested

##### Centre 1

The report from the laboratory showed that the smear was mildly abnormal, which means that there are small changes to your cervix.

*Invited for repeat smear test*—These changes sometimes happen and are not cancer, and in most cases do not lead to it. It is important to give these changes a chance to return to normal by themselves without treatment. Your next test is due [date] and we will send you a reminder to make an appointment. If you would like to talk about the result, please contact your GP or the person who took the smear.

*Referred for colposcopy*—Around one woman in twelve has an abnormal smear and it is unlikely that you have cancer. However, you may need treatment, and in most cases this results in a complete cure. If you have not already received a letter inviting you for an appointment, please contact your GP or the person who took the smear to discuss the result. If further investigation is needed, it will involve an examination (colposcopy) at a hospital outpatient clinic, to determine whether any treatment is needed. The enclosed leaflet tells you more about abnormal results.

##### Centre 2

*Invited for repeat smear test*—Your recent smear test taken on [date] shows a minor change. If your test was taken at your GP surgery or local community clinic, please contact the person who took your test to discuss the result. A repeat test will be advisable on [date] and your smear taker will tell you when to make an appointment.

*Referred for colposcopy*—The result of your recent smear, taken on [date] is now available. If your test was taken at your GP surgery or local community clinic, please contact the person who took your test to discuss the result.

#### Normal smear test result

Women who have regular smears are much less likely to develop cancer of the cervix, but no screening programme can prevent every single case of cancer, so, if you develop any unusual bleeding, pain or any other symptoms that concern you, before your smear test is due, please contact your doctor.

*Understanding of smear result* was assessed by asking women to state what they believed their result meant for their current health (see table 4 for response options). The correct responses for all women is that they were very unlikely, or unlikely, to have cervical cancer.

We also recorded age, highest educational achievement, ethnic origin, and history of smear results.

### Analysis

Differences in the demographic and clinical characteristics of the groups were assessed using ANOVA and  $\chi^2$  tests. We tested the study hypotheses using ANCOVA to control for differences in age, education, centre, and smear history in the groups, with three planned linear contrasts: normal versus all abnormal borderline or mildly dyskaryotic test results; borderline or mildly dyskaryotic test results in HPV positive women versus all other groups; borderline or mildly dyskaryotic results in women who were not tested for HPV versus borderline or mildly dyskaryotic and HPV negative. We used linear trend analysis to confirm the predicted pattern of responses across the four study groups, and multiple linear regression to ascertain the best predictors of anxiety in women who received HPV positive results.

### Results

The four study groups differed in age, educational level, and whether or not this was their first smear test (table 1). We controlled for these three variables when assessing differences in emotional outcomes between the groups (table 2). In addition, we controlled for centre, although it was unrelated to any of the outcome variables in the study.

Analysis of covariance (with age, education, centre, and smear history as covariates) showed that the groups differed significantly in anxiety ( $F_{3,1218} = 4.44$ ,  $P = 0.004$ ), distress ( $F_{3,1271} = 5.37$ ,  $P = 0.001$ ), and concern ( $F_{3,1280} = 242.44$ ,  $P < 0.001$ ). Planned contrasts confirmed two of the three research hypotheses. Firstly, the group with normal test results had significantly less anxiety ( $t = 2.19$ ,  $P = 0.028$ ), distress ( $t = 2.06$ ,  $P = 0.040$ ), and concern ( $t = 24.64$ ,  $P < 0.001$ ) than the three groups with abnormal test results, taken together. Secondly, the HPV positive group had significantly higher anxiety ( $t = 3.11$ ,  $P = 0.002$ ), distress ( $t = 3.252$ ,  $P = 0.001$ ), and concern ( $t = 13.391$ ,  $P < 0.001$ ) than the other three groups taken together. The third hypothesis was not supported: women who had abnormal smear

test results who were HPV negative did not have lower anxiety ( $t = 0.064$ ,  $P = 0.949$ ), distress ( $t = 0.827$ ,  $P = 0.409$ ), or concern ( $t = 0.852$ ,  $P = 0.394$ ) than women who had abnormal smear test results but were not tested for HPV. Although this third hypothesis was not supported, a trend analysis showed a significant linear trend for all mean scores for all three outcome measures: anxiety ( $F_{1,1218} = 12.73$ ;  $P = 0.0003$ ), emotional distress ( $F_{1,1271} = 15.46$ ;  $P = 0.00009$ ), and concern ( $F_{1,1280} = 561.94$ ;  $P < 0.00001$ ) when the groups were ordered as presented in table 2, in ascending order of risk of developing cervical cancer.

All groups viewed cervical cancer as extremely serious (table 3), but they differed in their perceptions of the risk of developing it ( $F_{3,1324} = 25.51$ ;  $P < 0.0001$ ): women who were HPV positive perceived their risks as greater than all other groups (Tukey post hoc contrast tests). Perceptions of risk also followed a significant linear trend ( $F_{1,1324} = 76.08$ ;  $P < 0.0001$ ) when the groups were ordered in ascending order of actual risk.

Forty one per cent of women stated they were unaware of what HPV was. This was more common in women not tested for HPV than in those tested. In all groups, women who were familiar with HPV perceived HPV infection as important in causing cervical cancer, although those with an abnormal result who had not been tested for HPV perceived it as less important than did all other groups ( $F_{3,778} = 3.42$ ,  $P = 0.017$ ). Although most of the women tested for human papillomavirus knew what HPV was, 25% (95% confidence interval 21% to 28%) of HPV positive women stated that they did not know what it was.

The groups also differed in their understanding of their results ( $\chi^2 = 194.13$ ,  $df = 12$ ,  $P < 0.001$ ; table 4). Compared with women receiving normal results, those receiving abnormal results were less likely to think their result meant they definitely did not have, or were very unlikely to, have cervical cancer. Women with abnormal results, whether tested for HPV or not, were less likely to know what their results meant than did women receiving a normal result ( $\chi^2 = 77.96$ ,  $df = 3$ ,  $P < 0.001$ ), with 26% (22% to 29%) of those who tested HPV positive stating that they did not know what this meant for their health.

We entered all variables in the linear multiple regression, apart from perceived importance of human papillomavirus in causing cervical cancer (as 25% of women failed to respond to this item). Of these, only three variables independently predicted anxiety ( $R^2 = 0.103$ , adjusted  $R^2 = 0.084$ ,  $P < 0.001$ ): age, with younger age being associated with higher anxiety ( $\beta = -0.11$ ,

**Table 1** Demographic and clinical characteristics of women given results of cervical smear and human papillomavirus (HPV) tests. Values are numbers (percentages) unless stated otherwise

Characteristic	Normal result (n=366)	Abnormal results			Anova and $\chi^2$ tests	P value
		HPV negative (n=331)	Not tested for HPV (n=143)	HPV positive (n=536)		
Mean (SD) age (years)	40.2 (12.2)	40.5 (11.3)	35.4 (10.4)	31.6 (9.7)	F = 65.01	<0.001
College education	45 (155)	36 (112)	42 (55)	50 (258)	$\chi^2 = 17.21$	0.001
White ethnic origin	96 (352)	96 (316)	98 (129)	97 (516)	$\chi^2 = 0.99$	0.80
First smear test	8 (31)	6 (19)	8 (12)	17 (90)	$\chi^2 = 31.09$	<0.001
Previous abnormal test results	42 (155)	45 (149)	43 (61)	39 (211)	$\chi^2 = 2.80$	0.42

**Table 2** Emotional outcomes after receipt of results of smear test among women tested or not tested for human papillomavirus (HPV). Values are adjusted means (SE)

Variable	Normal result (n=366)	Abnormal result			F (P value)
		HPV negative (n=331)	Not tested for HPV (n=143)	HPV positive (n=536)	
State anxiety (S-STAI-6)	36.4 (0.7)*	37.6 (0.7)†	37.7 (1.2)†	39.6 (0.6)‡	4.44 (0.004)
Emotional distress (GHQ-12)	2.0 (0.1)*	2.1 (0.2)†	2.4 (0.3)†	2.8 (0.2)‡	5.37 (0.001)
Concern about test result	5.2 (0.1)*	8.8 (0.1)†	9.1 (0.2)†	9.7 (0.1)‡	242.46 (<0.001)

Means with the same symbols do not differ ( $P > 0.05$ ) by planned linear contrasts. Means with different symbols in a given row differed significantly.

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**Table 3** Perceptions of the threat of cervical cancer of women given different results of cervical smear and human papillomavirus (HPV) tests. Values are means (SEs) unless otherwise stated

Perception	Normal results (n=366)	Abnormal results			F (P value)
		HPV negative (n=331)	Not HPV tested (n=143)	HPV positive (n=536)	
Perceived severity (2 seven-point scales)	12.4 (0.1)*	12.3 (0.1)*	12.1 (0.2)*	12.3 (0.1)*	1.13 (0.334)
Perceived risk (seven-point scale)	3.7 (0.1)*	3.9 (0.1)*	4.1 (0.1)*	4.4 (0.1)†	25.51 (<0.0001)
% (No) unsure what HPV is	54 (199)	38 (125)	62 (89)	25 (133)	—
Perceived importance of HPV in the development of cervical cancer (by women who knew what HPV is)	5.9 (0.1)*	5.9 (0.1)*	5.3 (0.3)†	5.8 (0.1)*	3.42 (0.017)

Means with the same symbols do not differ ( $P>0.05$ ) by Tukey post hoc tests. Means with different symbols in a given row differed significantly.

**Table 4** Understanding of the meaning of smear test results of women given different results of cervical smear and human papillomavirus (HPV) tests. Values are percentages (numbers)

Statement	Normal result (n=366)	Abnormal results		
		HPV negative (n=331)	Not tested for HPV (n=143)	HPV positive (n=536)
I definitely do not have cervical cancer	31 (112)	12 (39)	15 (21)	12 (63)
I am very unlikely to have cervical cancer	39 (143)	29 (94)	19 (27)	19 (103)
I am unlikely to have cervical cancer	27 (97)	38 (125)	39 (56)	35 (187)
I am likely to have cervical cancer	0	5 (16)	8 (11)	8 (44)
I have cervical cancer	0	0	0	0
I don't know	3 (12)	16 (53)	19 (27)	26 (137)

$P=0.033$ ); perceived risk of developing cervical cancer ( $\beta=0.17$ ,  $P<0.001$ ); and reporting not knowing the meaning of the smear test result ( $\beta=0.17$ ,  $P=0.001$ ). Figures 1 and 2 show the associations between anxiety and the two strongest predictors. Two of these three variables were also predictive of distress ( $R^2=0.073$ , adjusted  $R^2=0.068$ ,  $P<0.001$ ) and concern ( $R^2=0.138$ , adjusted  $R^2=0.133$ ,  $P<0.001$ ); perceived risk of developing cervical cancer (distress  $\beta=0.20$ ,  $P<0.001$ ; concern  $\beta=0.24$ ,  $P<0.001$ ) and reporting not knowing the meaning of the result (distress  $\beta=0.15$ ,  $P<0.001$ ; concern  $\beta=0.24$ ,  $P<0.001$ ).

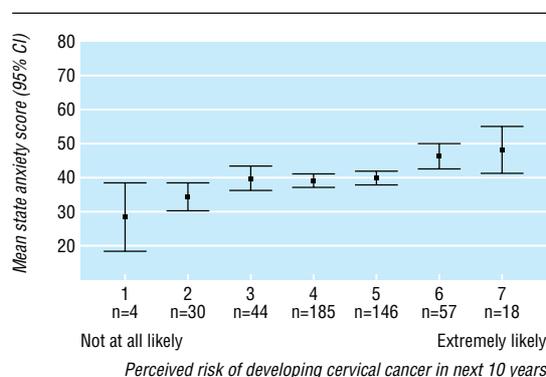
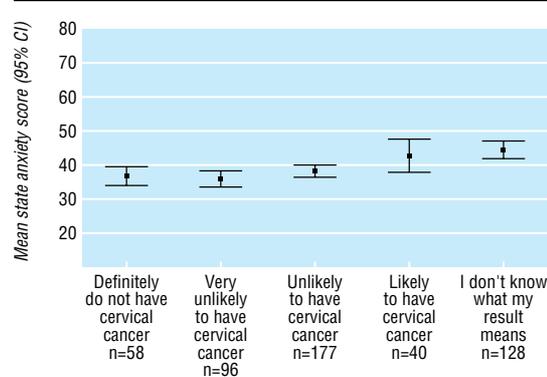
## Discussion

Informing women with borderline or mildly dyskaryotic smear test results that they are positive for HPV is associated, at least in the short term, with raised levels of state anxiety, general distress, and concern, compared with women receiving normal or cytologically abnormal smear test results. Anxiety, distress, and concern were higher when the perceived risk of developing cervical cancer was greater, and in women who reported not understanding the meaning of their test results. The mean level of

anxiety in this sample was similar to that seen in general medical and surgical patients just before surgery.<sup>17</sup> In women informed of a borderline or mildly dyskaryotic smear test result, receiving an HPV negative result was not reassuring.

Some anxiety is to be expected after receiving abnormal cervical smear test results; for some women, it may provide the necessary motivation to adhere to recommended management. However, raised anxiety can adversely affect information processing, impairing the ability to process complex information and leading to a bias towards processing threatening information.<sup>18</sup> Paradoxically, these effects can serve as barriers to processing the information that has the greatest chance of reducing anxiety. We are carrying out a six month follow up to see if these effects endure, but evidence from systematic reviews suggests that they will have dissipated.<sup>19</sup>

Women receiving borderline or mildly dyskaryotic test results know that their chances of developing cervical cancer are higher than if they had received normal results. Of concern, however, is that they seem to perceive these chances to be of a magnitude beyond that indicated by their results.<sup>20</sup> Most women thought

**Fig 1** Associations between state anxiety and perceived risk of developing cervical cancer (measured on seven point scale) in women with an abnormal smear result and positive test results for human papillomavirus**Fig 2** Associations between state anxiety and understanding of smear test results in women with an abnormal smear result and test results positive for human papillomavirus

that they were quite likely or very likely to develop cancer in the next 10 years (fig 1); this suggests a large overestimate of the true likelihood. Providing women with the absolute likelihood may diminish their perceived risks and, in turn, diminish anxiety, distress, and concern.

Perceptions of the prevalence of a health threat also affect how serious it is perceived to be, with threats perceived as more common being seen as less serious.<sup>21</sup> Women were informed that human papillomavirus is “a very common infection of the cervix,” but we do not know how they interpreted this. It is estimated that about 20% of young women and about 5% of women aged over 35 are infected at any one time.<sup>22</sup> In women with borderline or mildly dyskaryotic cervical smear test results the prevalence is higher.<sup>22</sup> Informing women of the actual prevalence of HPV infection could therefore reduce their anxiety, distress, and concern.

An appreciable number (22% (217/1003)) of women with abnormal test results stated that they did not know what their results meant. In HPV positive women, not knowing what their results meant was associated with extremely high levels of anxiety. The descriptive, cross sectional nature of the study does not allow the causal nature of this association to be established. It seems plausible, however, that not knowing what a result means, with the attendant uncertainty, could result in high levels of anxiety. Similarly, if women with negative results on HPV testing knew what this result meant in terms of the likelihood of having cervical cancer in the near future, they might feel more reassured and hence less anxious, distressed, and concerned than if they had not been tested.

Age was the least strong predictor of anxiety in women who were HPV positive, with anxiety diminishing with age. Previous research has also shown evidence of this association between ageing and reduced anxiety.<sup>23</sup>

Although many of the women receiving borderline or mildly dyskaryotic results overestimated their chances of having or developing cervical cancer, a substantial minority of women with normal results (31%) underestimated their chances, erroneously believing that they definitely do not have cervical cancer. More research is needed to evaluate how to avoid such false reassurance,<sup>24</sup> with its attendant adverse effects of delays in seeking help in the face of symptoms, and an increase in the likelihood of litigation.<sup>25</sup>

### Limitations of study

The generalisability of the results is limited by the sample. Although the response rate of 63% is good for a mailed survey,<sup>26</sup> the sample under-represents women from ethnic minority groups and women with no educational qualifications. Given the association between educational level, knowledge, and understanding of complex health information,<sup>27</sup> our study could under-represent the distress that HPV testing can cause in general population samples of women undergoing cervical screening.

### Conclusion

Studies are needed to determine, firstly, how to avoid some of the anxiety, distress, and concern caused by positive results on HPV testing and, secondly, how to provide some reassurance for women receiving negative results.

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### What is already known on this topic

Anxiety after receiving abnormal smear test results can be reduced by the provision of clear, salient information

Surveys of the psychological impact of human papillomavirus (HPV) testing carried out on highly selected samples have produced inconclusive evidence

No population based studies have evaluated the psychological impact of HPV testing in conjunction with cervical smear testing

### What this study adds

HPV positive results in women with borderline or mildly dyskaryotic smear test results are associated with anxiety, distress, and concern beyond that associated with the abnormal cytology result

Anxiety, distress, and concern are greatest in women who perceive themselves at greater risk of developing cervical cancer and who report not knowing what their results mean

Contributors: TMM, SM, and AG designed the study and together with RL designed the study questionnaire. EM collected and analysed the data. MH provided statistical advice and conducted some of the analyses. TMM and EM cowrote the first draft of the manuscript, which was read and commented on by the other four authors. TMM is guarantor.

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Competing interests: None declared.

Ethical approval: Southmead Local Research Ethics Committee (Reference No 076/01) and Northumberland and Tyne & Wear Health Authority Local Research Ethics Committee (Reference No 2001/247), which covered the laboratories that conducted the screening.

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