

**The impact of HPV testing on women's responses to
the EQ-5D questionnaire within the English cervical
screening programme**

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ABSTRACT

Aim

The NHS Cervical Screening Programme is considering human papillomavirus (HPV) testing alongside cytological screening. However, recent evidence suggests that HPV testing has a psychological impact, although raised levels of concern appear to have no significant impact on the women's HRQoL. We aim to explore in depth the sensitivity of EQ-5D and its dimensions taking account of age and screening results.

Methods

In the ARTISTIC Trial in Greater Manchester 24,510 women were randomly allocated to receive both their cytology and HPV results (revealed arm), or their cytology result only (concealed arm). Thus they formed 2 concealed arm groups - cytology normal and cytology abnormal; and 4 revealed arm groups - both cytology and HPV results normal/abnormal; cytology abnormal, HPV result normal; and cytology normal, HPV abnormal. In a postal survey, participants completed the EQ-5D (as well as the GHQ and STAI instruments).

Results

2512 (69.4%) out of 3622 questionnaires were returned with the EQ-5D completed. The outcomes for the five dimensions of the EQ-5D showed significant differences in Mobility, Usual Activity and Anxiety/depression, with more women reporting higher levels of anxiety/depression in the HPV positive groups. However, there were no statistically significant differences in utility scores between groups: mean score of 0.859 (SD=0.200). Multiple regression models examined the role of demographic variables (age, education), cytology and HPV test results, on utility scores and adjust for their impact in order to detect the true impact of HPV testing.

Conclusions

Our analyses could not demonstrate that HPV testing affected utility scores measured using the EQ-5D instrument, although there were indications that women who were Normal/HPV+ were more likely to report some anxiety/depression compared to women with normal smears who tested negative.

Introduction

The NHS cervical screening programme, set up in 1988, has been responsible for a significant fall in the incidence and death rate from cervical cancer in the United Kingdom. (1) Screening has been offered to women up to the age of 64 at three to five-yearly intervals and each year over 4 million cervical smears are taken and examined for cytological evidence of changes occurring in the cells of the cervix. (2) The screening programme relies on women attending their general practice or family planning clinic where trained nurses or doctors use the Papanicolaou technique to obtain a smear. Slides with the cell samples are transported to cytology laboratories for examination, and letters containing the results are sent to the women and their doctors.

Epidemiological research established in the 1990s that human papillomaviruses (HPV), most frequently HPV 16, are the primary cause of cervical intraepithelial neoplasia (CIN) (3) and they are present in 99% of cervical cancers. (4) A test for detecting the presence of HPV in the DNA of cervical cells was developed with the potential of being used for mass screening. Non-randomised studies have shown that HPV DNA testing was more sensitive than cytology for detecting CIN, and the International Agency for Research on Cancer has now concluded that testing for HPV as a primary screening strategy could reduce the incidence of CIN and mortality. (5)

Human papillomaviruses found in the cervix are sexually transmitted infections and the viruses are widely prevalent in the general population, especially among younger women. Infected women are asymptomatic and there is no treatment available. In many women, the virus clears after a few months; in other women, the virus persists, or they are re-infected, and these are the women considered to be most at risk of developing CIN. So while HPV testing is particularly sensitive, it lacks specificity and large numbers of women may test positive in the absence of clinically significant cytological abnormality.

Previous work found that conventional cervical screening was associated with a significant psychological morbidity when women were asked to attend for a repeat smear because the initial smear was inadequate for cytological examination. (6) The women were sensitive to the possibility they might develop cancer eventually. The liquid based cytology (LBC) technique for taking cervical smears, which is now being introduced in the NHS cervical screening programme, should greatly reduce laboratory rates for inadequate slides. (7) So researchers are focusing their attention now on the psychological impact of HPV testing alongside cytological screening.

In north London, McCaffery and colleagues (8) surveyed women with normal cytology results who had been tested at the same time for HPV and found that those who tested positive for HPV were significantly more anxious than those who were HPV negative, as measured by the short form of Spielberger's State Trait Anxiety Inventory (STAI). Elsewhere in England, Maissi and colleagues (9) used the same instrument with women whose smear cytology showed borderline changes or mild dyskaryosis and, likewise, observed higher levels of anxiety among those who were HPV positive. Similar levels of anxiety were recorded among women who tested HPV negative and women who were not HPV tested. STAI assesses a subject's feelings at this moment in time, unlike the General Health Questionnaire (GHQ), another widely used psychological instrument, which assesses health in general over the past few weeks. (10)

In order to evaluate the role of HPV testing in primary cervical screening, a randomised trial (the ARTISTIC Trial) is being conducted within the routine NHS cervical programme in Greater Manchester. This trial will compare outcomes in women whose HPV test result is concealed with those in whom it is revealed and acted upon. A total of 24,510 eligible women with satisfactory cytology and HPV results were enrolled (18,386 revealed and 6,124 concealed). The psychological impact of receiving the screening results was assessed in a postal survey of samples of eligible women using the GHQ and STAI instruments. The postal questionnaires also incorporated the EuroQol EQ-5D instrument used regularly in economic evaluations for measuring the health-related quality of life (HRQoL) of individuals. (11) The instrument, which applies to the subjects' health state, is in two main parts: the first covers five dimensions (mobility, self-care, usual activities, pain and discomfort, and anxiety and depression) with three statements listed for each dimension. A tariff is derived from the answers to the statements. The second part consists of a visual analogue scale (VAS) calibrated from 0 to 100, on which the subjects' indicate how good or bad their health is. Supplementary questions cover certain demographic items.

The EQ-5D instrument has been used infrequently in studies of cervical screening; an exception is the Maissi study (see above) in which the instrument was incorporated in psychological questionnaires sent to women after receiving their results (baseline) and six months later. (12) Participants included two groups of women receiving abnormal smear test results and were found to be either HPV positive or HPV negative; and two groups not tested for HPV and either received abnormal smear test results or normal smear test results.

No significant difference in HRQoL valuations was observed between four study groups at one or six months. The researchers concluded that the raised levels of concern recorded using other instruments at baseline may not have had a significant impact on the women's

HRQoL or, alternatively, the EQ-5D may not have been sufficiently sensitive to detect the impact.

The psychological survey for the ARTISTIC Trial has provided an opportunity to explore the sensitivity of the EQ-5D instrument in assessing the psychological states of women undergoing screening. The objective of this paper is to assess whether the EQ-5D instrument detects anxiety/depression in women whose screening results are positive for cytology, or HPV, or for both types of tests.

Methods

Between July 2001 and October 2003, women aged 20 –64 years attending for routine cervical screening in four health authorities in Greater Manchester were invited to participate in the ARTISTIC Trial. The trial is, therefore, a population-based study and representative of women in a heavily populated British conurbation. All women who signed a consent form had a smear collected using the LBC technique and the smear sample was tested for HPV. They were randomly allocated, three to one, to receive their HPV result (the revealed arm) or not learn the result (the concealed arm). The Patient Information Leaflet distributed to the women when first recruited explained that they might be selected to complete a survey questionnaire if they decided to participate in the trial. The North West Multicentre Research Ethics Committee approved the psychological survey.

The psychological postal survey was begun in June 2002, when all women newly entered in the Trial were sent a questionnaire booklet. The women formed six groups:

- Concealed arm:
 - cytology normal;
 - cytology abnormal;
- Revealed arm:
 - both cytology and HPV results normal;
 - cytology abnormal, HPV result normal;
 - cytology normal, HPV abnormal;
 - both cytology and HPV results abnormal.

‘Abnormal cytology’ groups included women with mild dyskaryosis/borderline smear results. The booklets were posted from the Trial Office 10-14 days after the women’s results notification letters were sent out. Fourteen days later a reminder letter was sent to the non-responders, followed up by a second reminder letter and booklet if necessary. The survey

continued until the numbers of respondents required in each group for sufficient statistical power (powered for the GHQ instrument) were fulfilled or, for the smallest groups, until the recruitment period ended.

Data from the questionnaires were entered in an Excel® file by research nurses. The statistical analyses of the responses to the EQ-5D instrument were performed using SPSS v. 13. Comparison of continuous data was made by ANOVA, Bonferroni post hoc (for pairwise comparisons of group means), and for categorical variables, Chi-square analysis was used. A *p* value of <0.05 was considered significant.

Results

Response rates

3622 questionnaires were sent to women. Of these 2512 (69.4%) questionnaires were returned with the EQ-5D completed. Response rates were similar by trial arm: 68.4% for the concealed and 69.7% for the revealed arm. (See Table 1.)

Utility scores were calculated for 604 women in the concealed arm, mean age (SD) 39.65 (11.62) years; and 1908 women in the revealed arm, mean age 39.23(11.84) years. Women with abnormal smear were younger than the women with normal smear in the concealed arm, while in the revealed arm women with HPV negative tests were on average 5 years older than those who were HPV positive ($p < 0.001$). The subgroup of women with positive test results and abnormal smear were the youngest, as shown in Table 1.

Table. 1 Response rate to questionnaire and background characteristics.

Questionnaires	Concealed arm		Revealed arm				Total
	Normal smear	Abnormal smear	Normal HPV -	Abnormal HPV -	Normal HPV +	Abnormal HPV +	
Sent , n	631	252	1341	422	663	313	3622
Mean age	39.62	35.98	40.41	40.06	36.31	30.22	38.29
(SD)	(12.10)	(10.47)	(11.78)	(10.46)	(11.95)	(8.76)	(11.78)
EQ-5D completed, <i>n</i> (%)	444 (70.4)	160 (63.5)	988 (73.7)	291 (69.0)	433 (65.3)	196 (62.2)	2512 (69.4)
Mean age	40.18	36.95	40.78	40.33	36.56	30.87	38.88
(SD)	(11.83)	(10.04)	(11.61)	(10.06)	(11.79)	(9.03)	(11.58)
Education after min school leaving age	63.7%	69.4%	60.3%	61.0%	64.8%	78.1%	63.7%
Degree or equivalent prof education	41.5%	45.9%	38.4%	39.5%	37.7%	44.3%	39.9%
Current smoker	24.4%	26.5%	26.6%	25.2%	27.8%	20.6%	25.8%

EQ-5D Questionnaire findings

There were no statistically significant differences between the utility scores of the 6 groups. (See Table 2.)

Table 2. Utility scores by subgroup.

Utility score	Concealed arm*		Revealed arm*				Total
	Normal smear	Abnormal smear	Normal HPV -	Abnormal HPV -	Normal HPV +	Abnormal HPV +	
Mean	0.867	0.855	0.856	0.852	0.863	0.857	0.859
(SD)	0.193	0.177	0.214	0.199	0.186	0.197	0.200

* - ANOVA - NS; Bonferroni post hoc – NS for all pairwise comparisons

Figure 1 is a graphical presentation of the mean outcomes for the five dimensions of the EQ-5D and the mean (SD) values are summarised in Table 3. Significant differences were observed for three of the five dimensions: Mobility, Usual Activity and Anxiety/depression. In the anxiety/depression dimension the mean outcome was greater in the Normal/HPV+ve (Revealed) group compared with the Normal/HPV-ve(Revealed) group ($p=0.031$).

Figure 1. Mean outcomes for the EQ-5D dimensions.

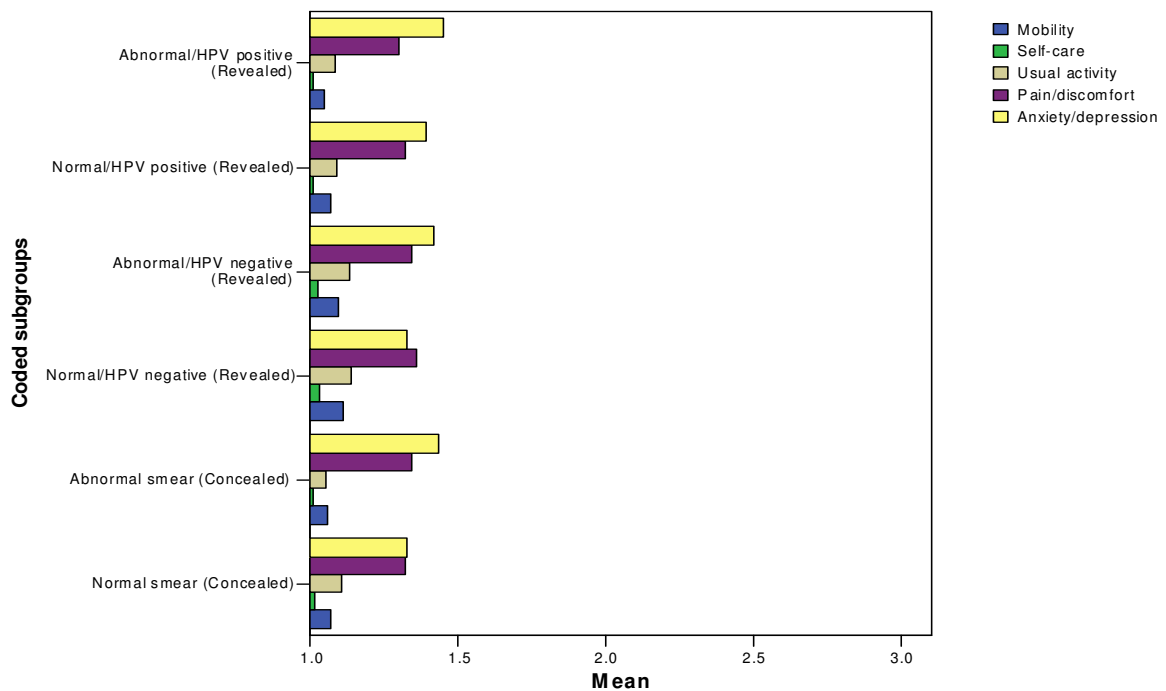


Table 3. Mean (SD) outcomes of EQ-5D dimensions.

Subgroups		Mobility	Self-care	Usual activity	Pain/discomfort	Anxiety/depression
Normal smear (Concealed)	Mean	1.07	1.01	1.11	1.32	1.33
	SD	0.255	0.116	0.329	0.523	0.524
Abnormal smear (Concealed)	Mean	1.06	1.01	1.05	1.34	1.44
	SD	0.231	0.079	0.219	0.487	0.601
Normal/ HPV negative (Revealed)	Mean	1.11	1.03	1.14	1.36	1.33
	SD	0.315	0.169	0.363	0.542	0.519
Abnormal/ HPV negative (Revealed)	Mean	1.09	1.02	1.13	1.34	1.42
	SD	0.291	0.175	0.348	0.510	0.560
Normal/ HPV positive (Revealed)	Mean	1.07	1.01	1.09	1.32	1.39
	SD	0.250	0.096	0.298	0.511	0.543
Abnormal/ HPV positive (Revealed)	Mean	1.05	1.01	1.08	1.30	1.45
	SD	0.210	0.101	0.275	0.511	0.566
Total	Mean	1.09	1.02	1.11	1.34	1.37
	SD	0.280	0.141	0.331	0.524	0.540
ANOVA		F=3.534 P=0.003	F=1.721 P=0.126	F=3.249 P=0.006	F=0.711 P=0.615	F=3.765 P=0.002

Frequency distribution (profile) of the EQ-5D descriptive system is reported in Table 4. Differences in responses between groups were significant in the Mobility ($\chi^2=17.590$, $p=0.004$) and Anxiety/Depression ($\chi^2=22.476$, $p=0.013$) dimensions.

Table 4. Frequency distribution (profile) of the EQ-5D descriptive system.

EQ-5D Profile	Concealed arm		Revealed arm			
	Normal smear	Abnormal smear	Normal/ HPV -	Abnormal/ HPV -	Normal/ HPV +	Abnormal/ HPV +
Mobility						
no problem (%)	93.0	94.4	88.9	90.7	93.3	95.4
some problems (%)	7.0	5.6	11.1	9.3	6.7	4.6
confined to bed (%)	0	0	0	0	0	0
Self-care*						
no problem (%)	98.6	99.4	97.4	97.9	99.1	99.0
some problems (%)	1.4	0.6	2.5	1.7	0.9	1.0
unable to (%)	0	0	0.1	0.3	0	0
Usual Activities*						
no problem (%)	90.1	95.0	86.7	87.3	91.0	91.8
some problems (%)	9.2	5.0	12.7	12.4	8.8	8.2
unable to (%)	0.7	0	0.6	0.3	0.2	0
Pain/Discomfort*						
none (%)	70.5	66.9	67.2	67.7	69.8	72.8
moderate (%)	26.8	32.5	29.6	30.6	28.1	24.6
extreme (%)	2.7	0.6	3.1	1.7	2.1	2.6
Anxiety/Depression						
none (%)	70.2	61.9	69.7	61.7	63.4	58.7
moderate (%)	27.1	32.5	27.9	34.8	33.8	37.8
extreme (%)	2.7	5.6	2.4	3.4	2.8	3.6

* - χ^2 NS

In the revealed arm the proportion of women who reported no anxiety/depression in the Normal/HPV -ve group was significantly greater compared with the Normal/HPV +ve group ($\chi^2 = 5.359$, $p = 0.021$).

The EQ VAS provided the women's assessment of their health state. Unlike utility scores, VAS scores varied across subgroups, with the highest score reported in the 'Normal smear' subgroup of the concealed arm.

Table 5. EQ VAS score

EQ VAS score (%)	Concealed arm		Revealed arm			
	Normal smear	Abnormal smear	Normal/HPV -	Abnormal/HPV -	Normal/HPV +	Abnormal/HPV +
Mean *	77.9	73.3	76.7	74.4	75.6	76.4
SD	15.5	18.5	17.3	18.1	15.7	16.1

* Concealed only: $F = 8.779$, $p = 0.003$; Revealed only: $F = 1.519$, $p = 0.208$

Impact of HPV testing on women as detected by EQ-5D

The smear results of the women who received a questionnaire ranged from 'normal' to 'mild' changes. The presence of borderline or mild changes in the cells typically is not accompanied by any symptoms, thus it is very unlikely that they may be related to changes in any of the 'physical' EQ-5D dimensions compared with women with 'normal' cervix. However, being screened and receiving results that are not 'normal' and would require further investigations may have an impact on the 'anxiety/depression' dimension of EQ-5D.

Direct comparison of mean utility scores between groups and within arms did not produce any significant differences. However, the breakdown of results by dimensions proved otherwise. (See Table 3 and Table 4). Also, women in the Normal/HPV positive group were younger than the women in the Normal/HPV negative group in the revealed arm and any changes in anxiety/depression could have been offset by the overall better health in general as reported in the four physical dimensions. Differences in utility scores of these two groups were not statistically significant even when women were compared by age group as follows: 21 to 30 years old, 31 to 40, 41 to 50, 51 to 60, and 61 years and above.

Multiple regression models (method: Stepwise, weighted by age group) were constructed to examine the role of demographic variables (age, education), cytology and HPV test results, on utility scores. Results of the analyses suggest that although age and education were relatively good predictors, the goodness-of-fit of the models was still not satisfactory (See Appendix).

Changes in the ‘anxiety/depression’ dimension of EQ-5D

Since the purpose of this study was to assess whether the EQ-5D instrument detects anxiety/depression in women whose screening results were positive for LBC, or HPV or for both types of tests, we analysed the data after resetting the other four dimensions to level 1. Utility scores were then calculated for each group based on differences in the anxiety/depression dimension only.

Table 6. ‘Adjusted’ utility scores.

Utility score	Concealed arm		Revealed arm				Total
	Normal smear	Abnormal smear	Normal HPV -	Abnormal HPV –	Normal HPV +	Abnormal HPV +	
Mean	0.943	0.917	0.941	0.926	0.930	0.920	0.935
(SD)	0.111	0.142	0.112	0.121	0.117	0.124	0.117

Concealed only: F= 5.285, p=0.022;

Revealed only: F= 2.915, p=0.033; Bonferroni post-hoc: NS

These results suggest that there may be statistically significant differences between the utility scores of women in each arm. As expected, women with normal results (normal smear in the concealed arm and normal smear and HPV negative in the revealed arm), had the highest mean scores, while abnormalities were associated with lower scores.

Comparisons of ‘adjusted’ scores between Normal/HPV- and Normal/HPV+ women within age groups, remained non-significant. For example, in the 31-40 years age range the utility score was higher in the Normal/HPV+ group, but after the adjustment the opposite was observed, although neither of the differences were statistically significant. (See Table 7)

Table 7. Utility scores and adjusted scores in the 31-40 years group (revealed arm).

Subgroups		Utility score	Adjusted utility score
Normal/HPV negative (Revealed)	Mean	.87873	.94604
	N	296	296
	Std. Deviation	.203815	.110064
Normal/HPV positive (Revealed)	Mean	.89342	.93610
	N	141	141
	Std. Deviation	.168932	.121461
Total	Mean	.88347	.94283
	N	437	437
	Std. Deviation	.193177	.113821

Unblinded comparisons

Women in the concealed arm underwent both LBC and HPV tests, but the HPV test result was not revealed to them and had no impact on their management. Because of the random allocation of women to the trial arms we could assume that women with similar test results were also comparable in other key characteristics. Thus, such group comparisons would be the most appropriate when assessing the potential impact of HPV testing on women.

We compared women in either arm who were Normal/HPV +ve or Normal/HPV –ve.. The results from the unblinded comparisons are summarised in Table 8.

Table 8. Tests for significance of differences between groups.

Utility score Mean (SD)		Revealed arm	
		Normal/HPV – 0.856 (0.214)	Normal/HPV + 0.863 (0.186)
Concealed arm	Normal/HPV – 0.873 (0.185)	Age - NS Education, Smoking - χ^2 NS No anxiety: χ^2 NS Utility score - NS	Age – p<0.001 Education, Smoking - χ^2 NS No anxiety: $\chi^2=5.454$, p=0.020 Utility score – NS
	Normal/HPV + 0.851 (0.218)	Age – p=0.029 Education, Smoking - χ^2 NS No anxiety: χ^2 NS Utility score - NS	Age - NS Education, Smoking - χ^2 NS No anxiety: χ^2 NS Utility score – NS

Similarly to table 7, table 9 compares utility scores in the 31-40 age group. Differences between groups were not significant.

Table 9. Utility scores and adjusted scores in the 31-40 years group (concealed arm).

Subgroups		Utility score	Adjusted utility score
Normal smear (Concealed) HPV-ve	Mean	.88648	.93465
	N	101	101
	Std. Deviation	.173873	.126064
Normal smear (Concealed) HPV+ve	Mean	.90081	.95496
	N	27	27
	Std. Deviation	.166937	.070729
Total	Mean	.88950	.93894
	N	128	128
	Std. Deviation	.171884	.116648

Discussion

In this paper we report the findings from the EQ-5D questionnaire completed by women taking part in the ARTISTIC trial. This instrument was one of several that were used to assess the psycho-social impact of HPV testing on women taking part in the routine cervical screening programme in England. Utility scores were calculated as they were needed for the purposes of the CUA alongside ARTISTIC.

Previously published utilities cover the invasive stages of cervical cancer, while little is known of the impact of HPV testing on women whose smear results are normal. Previous studies have suggested that HPV testing affected the levels of anxiety/depression, but these changes were not picked up by EQ-5D for women with mild and borderline cytology changes both at baseline and follow-up (9, 12).

The HPV infection is quite common; it can last for up to 12 months, and may not clear even after that period of time. Since its psychological impact has been demonstrated, it is reasonable to account for that in an economic model. HPV testing may have effect on women either by reassuring them of the very low risk of developing cancer (negative test), or by indicating increased risk of the disease when the test is positive.

There are two questions – 1/ Does an HPV +ve result affect the utility of a woman with a normal smear, and 2/ Is EQ-5D an appropriate instrument to detect such changes, should they happen? In this study, we did not detect any differences in the utility scores of the subgroups of screened women. However, further analyses showed that EQ-5D seemed to have detected differences in the anxiety/depression dimension in women with abnormal results, but those differences were lost, or maybe cancelled, by the other dimensions when utility scores were calculated. The reason could be in the incidence and prevalence of the

HPV infection in different age groups. Younger women on average have better health than older women, but are more likely to have the HPV infection compared with older women. As a result, women in the Normal/HPV positive group were younger than the women in the Normal/HPV negative group in the revealed arm and any changes in anxiety/depression could have been offset by the overall better health in general as reported in the four physical dimensions. Separating women in age groups resulted yet again in similar utility scores. One reason may be, that women of similar age, who were in better health, might be more sexually active and more likely to get infected with HPV. So, the EQ-5D instrument would once again fail to uncover any impact of HPV infection on utility scores.

All these analyses are based on the premises that women are fully aware of the causal relationship between HPV and cervical cancer. Although all women had been informed about it at the enrolment phase of the trial, we have no evidence of their actual awareness at the time they received their results and filled in the questionnaire.

Further research is needed to elicit utilities of screened women in various health states. Such research will feed into the assessment of screening programmes with various approaches to the use of HPV testing and will shed light on the usefulness of EQ-5D in the context of screening for diseases.

(Next step: We also intend to compare our findings to the other instruments completed by women together with the EQ-5D questionnaire.)

All comments and suggestions on how to improve this paper are most welcome. Thank you!

References

1. Peto J, Gilham C, Deacon J, Taylor C, Evans C, Binns W, et al. Cervical HPV infection and neoplasia in a large population-based prospective study: the Manchester cohort. *Br J Cancer* 2004;91(5):942-53.
2. Patnick J. Review of recommendations on cervical cancer screening in the European Union. *Minerva Ginecol* 2003;55(4):293-5.
3. International Agency for Research on Cancer. Human papillomaviruses. IARC Monographs on the evaluation of carcinogenic risks to humans 1995;64.
4. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol* 1999;189(1):12-9.
5. IARC Working Group on the Evaluation of Cancer-Preventive Strategies. Cervix cancer screening, IARC Handbooks of cancer prevention, Vol.10. Lyon: IARC; 2005.
6. Bell S, Porter M, Kitchener H, Fraser C, Fisher P, Mann E. Psychological response to cervical screening. *Prev Med* 1995;24(6):610-6.
7. Dowie R, Stoykova B, Crawford D, Desai M, Mather J, Morgan K, et al. Liquid-based cytology can improve efficiency of cervical smear readers: evidence from timing surveys in two NHS cytology laboratories. *Cytopathology* 2006;17(2):65-72.
8. McCaffery K, Waller J, Forrest S, Cadman L, Szarewski A, Wardle J. Testing positive for human papillomavirus in routine cervical screening: examination of psychosocial impact. *BJOG* 2004;111(12):1437-43.
9. Maissi E, Marteau TM, Hankins M, Moss S, Legood R, Gray A. Psychological impact of human papillomavirus testing in women with borderline or mildly dyskaryotic cervical smear test results: cross sectional questionnaire study. *BMJ* 2004;328(7451):1293.
10. Bridges KW, Goldberg DP. The validation of the GHQ-28 and the use of the MMSE in neurological in-patients. *Br J Psychiatry* 1986;148:548-53.
11. Brooks R. EuroQol: the current state of play. *Health Policy* 1996;37(1):53-72.
12. Maissi E, Marteau TM, Hankins M, Moss S, Legood R, Gray A. The psychological impact of human papillomavirus testing in women with borderline or mildly dyskaryotic cervical smear test results: 6-month follow-up. *Br J Cancer* 2005;92(6):990-4.

APPENDIX

Regression

Variables Entered/Removed^{a,b,c}

Model	Variables Entered	Variables Removed	Method
1	DEGREE	.	Stepwise (Criteria: Probability-of-F-to-enter <= .050, Probability-of-F-to-remove >= .100).
2	Age	.	Stepwise (Criteria: Probability-of-F-to-enter <= .050, Probability-of-F-to-remove >= .100).
3	EDUCATION	.	Stepwise (Criteria: Probability-of-F-to-enter <= .050, Probability-of-F-to-remove >= .100).

- a. Dependent Variable: Utility score
- b. Weighted Least Squares Regression - Weighted by Age group
- c. Models are based only on cases for which Utility value is available = YES

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
	Utility value is available = YES (Selected)			
1	.177 ^a	.031	.031	.318999
2	.209 ^b	.044	.043	.316993
3	.222 ^c	.050	.048	.316113

- a. Predictors: (Constant), DEGREE
- b. Predictors: (Constant), DEGREE, Age
- c. Predictors: (Constant), DEGREE, Age, EDUCATION

ANOVA^{d,e,f}

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	8.094	1	8.094	79.540	.000 ^a
	Residual	250.635	2463	.102		
	Total	258.729	2464			
2	Regression	11.336	2	5.668	56.408	.000 ^b
	Residual	247.393	2462	.100		
	Total	258.729	2464			
3	Regression	12.807	3	4.269	42.722	.000 ^c
	Residual	245.922	2461	.100		
	Total	258.729	2464			

a. Predictors: (Constant), DEGREE

b. Predictors: (Constant), DEGREE, Age

c. Predictors: (Constant), DEGREE, Age, EDUCATION

d. Dependent Variable: Utility score

e. Weighted Least Squares Regression - Weighted by Age group

f. Selecting only cases for which Utility value is available = YES

Coefficients^{a,b,c}

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B		Correlations			Collinearity Statistics		
		B	Std. Error	Beta			Lower Bound	Upper Bound	Zero-order	Partial	Part	Tolerance	VIF	
1	(Constant)	.821	.005		159.767	.000	.811	.831						
	DEGREE	.076	.008	.177	8.919	.000	.059	.092	.177	.177	.177	1.000	1.000	
2	(Constant)	.915	.017		52.974	.000	.881	.949						
	DEGREE	.069	.009	.162	8.120	.000	.052	.086	.177	.162	.160	.982	1.019	
	Age of woman at date of Qs	-.002	.000	-.113	-5.680	.000	-.003	-.001	-.135	-.114	-.112	.982	1.019	
3	(Constant)	.889	.018		48.058	.000	.853	.925						
	DEGREE	.048	.010	.113	4.793	.000	.029	.068	.177	.096	.094	.697	1.435	
	Age of woman at date of Qs	-.002	.000	-.099	-4.914	.000	-.003	-.001	-.135	-.099	-.097	.950	1.053	
	EDUCATIO	.038	.010	.092	3.837	.000	.019	.058	.176	.077	.075	.674	1.483	

a. Dependent Variable: Utility score

b. Weighted Least Squares Regression - Weighted by Age group

c. Selecting only cases for which Utility value is available = YES

Excluded Variables^{d,e}

Model	Beta In	t	Sig.	Partial Correlation	Collinearity Statistics			
					Tolerance	VIF	Minimum Tolerance	
1	Age	-.113 ^a	-5.680	.000	-.114	.982	1.019	.982
	Smear Result	-.003 ^a	-.150	.881	-.003	.997	1.003	.997
	HPV Result	-.016 ^a	-.810	.418	-.016	1.000	1.000	1.000
	EDUCATION	.113 ^a	4.775	.000	.096	.697	1.435	.697
2	Smear Result	-.020 ^b	-.979	.328	-.020	.977	1.024	.961
	HPV Result	-.023 ^b	-1.148	.251	-.023	.996	1.004	.978
	EDUCATION	.092 ^b	3.837	.000	.077	.674	1.483	.674
3	Smear Result	-.022 ^c	-1.087	.277	-.022	.976	1.025	.674
	HPV Result	-.022 ^c	-1.106	.269	-.022	.996	1.004	.674

a. Predictors in the Model: (Constant), DEGREE

b. Predictors in the Model: (Constant), DEGREE, Age

c. Predictors in the Model: (Constant), DEGREE, Age, EDUCATION

d. Dependent Variable: Utility score

e. Weighted Least Squares Regression - Weighted by Age group

Collinearity Diagnostics^{a,b,c}

Model	Dimension	Eigenvalue	Condition Index	Variance Proportions			
				(Constant)	DEGREE	Age	EDUCATIO N
1	1	1.606	1.000	.20	.20		
	2	.394	2.018	.80	.80		
2	1	2.441	1.000	.01	.06	.01	
	2	.530	2.146	.01	.88	.02	
	3	.029	9.114	.98	.06	.97	
3	1	3.182	1.000	.00	.03	.00	.02
	2	.571	2.360	.01	.39	.02	.04
	3	.220	3.804	.00	.58	.01	.84
	4	.027	10.886	.98	.00	.96	.10

a. Dependent Variable: Utility score

b. Weighted Least Squares Regression - Weighted by Age group

c. Selecting only cases for which Utility value is available = YES