Physical after-effects of colposcopy and related procedures and their inter-relationship with psychological distress: a longitudinal survey

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Abstract

Objectives To estimate prevalence of post-colposcopy physical after-effects and investigate associations between these and subsequent psychological distress.

Design Longitudinal survey.

Setting Two hospital-based colposcopy clinics.

Population Women with abnormal cytology who underwent colposcopy (+/- related procedures).

Methods Questionnaires were mailed to women 4-, 8- and 12-months post-colposcopy. Details of physical after-effects (pain, bleeding and discharge) experienced post-colposcopy were collected at 4-months. Colposcopy-specific distress was measured using the Process Outcome Specific Measure at all time-points. Linear mixed effects regression was used to identify associations between physical after-effects and distress over 12-months, adjusting for socio-demographic and clinical variables.

Main outcome measures Prevalence of post-colposcopy physical after-effects. Associations between presence of any physical after-effects, awareness of after-effects and number of after-effects and distress.

Results 584 women were recruited (response rate=73%, 59% and 52% at 4, 8 and 12-months, respectively). 82% of women reported one or more physical after-effect(s). Multiple physical after-effects were common (two after-effects=25%; three after-effects=25%). Psychological distress scores declined significantly over time. In adjusted analyses, women who experienced all three physical after-effects had on average a 4.58 (95% CI 1.10 to 8.05) higher distress scored than those who experienced no after-effects. Women who were unaware of the possibility of experiencing after-effects scored significantly higher for distress during follow-up.

Conclusions Prevalence of physical after-effects of colposcopy and related procedures is high. The novel findings of inter-relationships between awareness of the possibility of after-effects, and experiencing multiple after-effects, and post-colposcopy distress may be relevant to the development of interventions to alleviate post-colposcopy distress.

Keywords Longitudinal survey, colposcopy, post-colposcopy distress, physical after-effects.

Tweetable abstract Experiencing multiple physical after-effects of colposcopy is associated with psychological distress.

Introduction

For cervical screening to be effective, women who have a positive screening test (irrespective of whether the initial test is cytological- or HPV-based) require follow-up. Hospital-based colposcopy examinations are a cornerstone of follow-up and likely to remain so under the newer screening protocols. Colposcopy is a very common procedure; for example, each year almost 200,000 women in England and 16,000 in Ireland are referred for colposcopy.[1,2]

Undergoing colposcopy and related treatment procedures (e.g. large loop excision of the transformation zone (LLETZ)) can be distressing and studies have shown that women may have raised anxiety levels prior to, during, and after a colposcopy.[3-7] While there is considerable evidence for psychological morbidity among women undergoing colposcopy, data on post-colposcopy physical after-effects (e.g. pain or bleeding) reported by women is relatively scarce. Nonetheless, the data that is available suggests that high proportions of women experience physical after-effects. For example, in a study of 108 women, 68% reported experiencing pain after a LLETZ,[8] while in another study of 751 women, 79% of those who had punch biopsies, and 87% of those who had a LLETZ, reported bleeding afterwards.[9] Emerging findings tentatively suggest that the physical and psychological consequences of colposcopy and related procedures may be linked. In recent qualitative work among women who had had colposcopy and/or related procedures, we found that having had physical after-effects that impacted on their lives was related to women experiencing long-term psychological distress.[10] Similarly, a quantitative study found that women who reported pain or bleeding post-colposcopy had increased risk of psychological distress,[6] but that study was cross-sectional so the direction of the association was uncertain.

In a 12-month longitudinal study of women attending colposcopy, we investigated prevalence of physical after-effects following colposcopy and related procedures and associations between experiencing physical after-effects and subsequent psychological distress. We further investigated whether women's awareness of the possibility of physical after-effects was related to subsequent distress.

Methods

Setting

The study was conducted in Ireland, which has a mixed public-private healthcare system. CervicalCheck, the national cervical screening programme was implemented in 2008, offering free cervical cytology tests and follow-up, if required, to women aged 25-60 years. Women with two or more low-grade abnormal cervical cytology test results, or one high-grade result, are referred for colposcopy in a clinic affiliated with the screening programme located in one of 15 maternity hospitals throughout Ireland.[1]

Study participants and recruitment

Women who attended CervicalCheck colposcopy clinics at two large Dublin hospitals were recruited to the study between September 2010 and July 2011. To be eligible, women had to have been referred to colposcopy on the basis of an abnormal cervical cytology test result, in the context of routine screening. They were eligible irrespective of the management they received at their initial clinic appointment (i.e. colposcopy only, punch biopsies, loop excision, or another form of intervention or treatment) or subsequent follow-up. Women who had previously had treatment for cervical abnormalities, or who were pregnant at the time of recruitment (i.e. at the initial colposcopy clinic appointment) were ineligible. At their clinic appointment, women were invited to take part in the study by research staff and were given a study information sheet. Women willing to participate in the study signed a consent form and returned it to research staff. Consenting women were invited to complete a questionnaire which was sent by post at 4, 8 and 12 months following their initial colposcopy appointment.

Ethical approval was obtained from the ethics committees of the Coombe Women and Infants University Hospital and the National Maternity Hospital, Dublin.

Assessment of physical after-effects of colposcopy and related procedures

Physical after-effects were assessed at 4 month follow-up using a questionnaire designed to measure three physical after-effects of colposcopy and related procedures - pain, bleeding and discharge- developed in the UK TOMBOLA trial.[9] Women were also asked whether they had been aware that they might experience physical after-effects. Table S1 displays the questions asked and response options.

Assessment of post-colposcopy psychological distress

Psychological distress was measured at three time points: 4, 8 and 12 months post-colposcopy. It was assessed using the Process Outcome Specific Measure (POSM), which was developed specifically to evaluate issues of concern to women being followed-up for abnormal cervical cytology.[11] The POSM contains 14 items, 7 of which can be combined into a measure of distress (Table S2;[12]). Six of these seven items have six-level Likert response options ranging from 'Strongly agree' to' Strongly disagree'. The remaining item has seven response options ranging from 'Strongly for the better' to 'Strongly for the worse'. Women were asked to indicate the extent to which each statement applied 'in the last month'. The raw score for each of the seven questions was multiplied by 100 and divided by the maximum possible raw score for that question. Item responses for each question were thus standardised to be scored out of 100. The overall distress score was obtained by calculating the arithmetic mean of the seven standardised item scores. The higher the overall score, the greater the psychological distress/burden.

Co-variates

Information on potential confounders of the relationship between physical after-effects and psychological distress was obtained from the questionnaire administered at the 4 month time-point and from women's clinic records. Questions on socio-demographic characteristics, lifestyle behaviours and attitudes, and healthcare-related history were included in the questionnaire. Data extracted from clinic records were: colposcopy referral cytology, initial colposcopic impression, initial management received and initial histology result. Table 1 and Table S3 list the co-variates available.

Statistical analyses

Stata (version 13) was used for analysis. Characteristics of respondents were summarised using descriptive statistics. Summary statistics for any, number of, and each type of, physical after-effect were calculated. T-tests were used to determine if the distress score at each time point differed between: (i) those with any versus no after-effects; and (ii) those with and without each type of after-effect. Similarly, summary statistics and t-tests were also computed for awareness of the possibility of physical after-effects. At each follow-up time point, a test for trend was calculated to assess if the distress score increased with increasing number of physical after-effects.

Since our primary aim was to determine whether presence of any physical after-effects (and/or awareness of after-effects) was associated with psychological distress, we created a binary variable which was 0 if no physical after-effects were experienced and 1 if one or more (of pain/bleeding/discharge) was experienced. In order to account for the longitudinal nature of the outcome psychological distress, we employed a linear mixed effects model, with unstructured covariance. This allowed women who have a distress score at least one follow-up time-point to be included in the analysis, with any missing data assumed to be missing at random. Initially, fixed effects for follow-up time and experience of physical after-effect(s) were included in the model. To investigate whether there were differences in the pattern of distress over time between those with and without any after-effects, an interaction between follow-up time and the binary physical after-effects variable was tested. We then included the variable awareness of physical after-effects and also tested for an interaction between follow-up time and awareness of physical after-effects.

In order to choose the final multivariable model, we started with a saturated model consisting of the physical after-effect (any/none) variable and all candidate co-variates. Using a stepwise backward approach we eliminated variables if the p-value for inclusion was greater than 0.1 (Wald test), taking care to avoid multicollinearity between co-variates. The main explanatory variable – any physical after-effects - was kept in the model regardless of its p-value. As a check of the model, we fitted models with random intercepts only and random intercepts and slopes; we

concluded that these more complex models were not required and have reported the findings from the final fixed effects multivariable model.

To determine whether *number* of physical after-effects predicted distress, we ran a multivariable model in a similar manner replacing the binary physical after-effects variable with a 4-level variable representing the number of physical after-effects experienced. As above we checked whether the variable awareness of after effects should be included in this model.

To explore whether the association between physical after-effects and distress varied by *type* of physical after-effect, we conducted a sensitivity analysis in which we re-ran the final multivariable model three times, each time replacing the any physical after-effects variable with a binary variable representing any pain or bleeding or discharge. As above we checked whether the variable awareness of after effects should be included in this model. We did not fit these three different after-effects simultaneously as they were highly correlated.

Results

Characteristics of respondents

429 of the 584 women recruited to the study completed the 4 month questionnaire (73%), 343 (59%) completed the questionnaire at 8 months; and 303 (52%) completed the questionnaire at 12 months. Table 1 displays selected socio-demographic characteristics and clinical variables for the 429 who completed the 4-month questionnaire. The additional socio-demographic, lifestyle behaviours and attitudes, and health-care related history variables are displayed in Table S3.

Prevalence of physical after-effects

Overall, 82% of women experienced at least one physical after-effect, with a quarter (25%) experiencing all three physical after-effects (Figure 1). In terms of individual after-effects, 68% reported experiencing bleeding, 58% experienced pain, and 39% experienced discharge. The majority (86%) of respondents were aware of the possibility of having after-effects following their colposcopy.

Unadjusted associations between physical after-effects and post-colposcopy psychological distress, by follow-up time point

The mean distress score at 4 months was 46.6 (of a possible 100), reducing by approximately 2 points at each subsequent follow-up time point (Table 2). The distress score was significantly higher for those with at least one physical after effect (v. none) at each time point. This result was mirrored for each of the individual after-effects, pain, bleeding and discharge (Table 2). At each time point, there was a statistically significant trend of higher distress with increasing number of after-effects ($p \leq 0.001$).

At all three time points, women who were not aware of the possibility of physical side-effects had higher distress scores than women aware of this possibility; this difference was statistically significant at the 4 and 8 month time points.

Regression results

Any physical after-effects

In the multivariable analysis with any vs. no physical after-effects as the main explanatory variable of interest, having any physical after-effect was associated with a higher distress score over the entire follow-up period (2.11; 95% CI -0.76 to 4.97; Table 3; with full multivariable results shown in Table S4), but this was not statistically significant (Wald test p-value 0.15; Table 3). In the same model, not being aware of the possibility of physical after-effects was significantly associated with higher distress score (on average 3.99 points higher) during follow-up (Wald test p-value 0.02; Table 3).

There was no significant interaction between distress score and whether or not a physical after-effect (any vs. none) was experienced over the follow-up period. In addition, there was no evidence of an interaction between awareness of physical after-effects and distress score over time.

Number of physical after-effects

In the multivariable analysis, number of physical after-effects was significantly associated with a higher distress score during follow-up (Wald test p-value 0.03, Table 3).There was also a

significant linear trend (p=0.004). In women with two physical after-effects, follow-up related distress was on average 2.20 (95% CI -0.97 to 5.38) points higher than for women who experienced none (Table 3); follow-up related distress was on average 4.58 (95% CI 1.10 to 8.05) points higher in women who experienced all three physical after-effects than in women who experienced none (Table 3). In a linear test for trend, a one unit increase in the number of physical after effects was associated with a 1.6 increase in psychological distress score, p = 0.004. Not being aware of the possibility of physical after-effects was significantly associated with on average a 4.25 (95% CI 0.93 to 7.57) higher distress score (Wald test p-value 0.01).

Sensitivity analysis: type of physical after-effect

In our sensitivity analysis, the effect size for association with (a higher) distress score was similar for each physical after-effect. In women who experienced pain, follow-up related distress was on average 2.32 (95% CI 0.01 to 4.62) points higher than for women who experienced none. Follow-up related distress was on average 2.40 (95% CI -0.06 to 4.86) points higher in women who experienced bleeding than in women who experienced none and was 2.30 (95% 0.02 to 4.57) points on average higher in women who experienced distress than in women who experienced no discharge (Table 3).

Discussion

Main findings

Our study has highlighted the burden of physical after-effects of colposcopy/treatment on women. The prevalence of physical after-effects following these types of procedures is high; four in every five women reported experiencing one or more after-effect. We also found, in longitudinal analyses, associations between physical after-effects and psychological distress following colposcopy. While there was no statistically significant difference in distress between women who experienced any physical after-effect and those who experienced none - over the entire 12 month follow-up period, women who experienced all three physical after-effects had significantly higher distress levels than women who did not (after adjusting for covariates). In addition having no awareness of the possibility of physical after-effects was significantly related to higher distress post-colposcopy in unadjusted and adjusted analyses.

Strengths and limitations

The major strengths of this study were the longitudinal design and the fact it was nested in clinics affiliated with the screening programme, so reflects real-world clinical practice. In terms of possible limitations, physical after-effects were measured at 4 months post-colposcopy and there may be some inaccuracy in recall. While we found increased distress in women with multiple after-effects, we did not have sufficiently large sample size to be able to identify whether any particular combinations of after-effects were responsible for the association. While we found statistically significant differences in the average POSM scores at each time point, further work is needed to determine whether these differences would represent a clinically meaningful difference in psychosocial wellbeing. We do not know the characteristics of non-responders (those who consented to taking part but did not respond to questionnaires). Therefore, we cannot exclude the possibility that responders and non-responders differed in terms of socio-demographic characteristics, physical after-effects or distress. Among women who responded to the 4-month questionnaire, those who also responded at 12-months had a lower mean distress score than women who did not respond at 12-months; this suggests that women who dropped out of the study were more likely to be distressed and that we may have under-estimated the true mean distress score Although women in our study would have received information leaflets

which contained some (limited) information about possible after-effects, we do not know anything about the verbal information clinic staff may have given women during their consultations about the possibility of experiencing physical after-effects, and whether/how this might have impacted on experiences.

Interpretation

The high proportions of women experiencing physical after-effects in our study are a cause for concern. Other evidence on the burden of physical after-effects of colposcopy and related procedures is scarce with most studies conducted more than 10 years ago and focused mainly on after-effects of LLETZ.[13-15] In these studies, LLETZ appears to be strong a predictor a greater physical after-effect burden. In the current study, only 18% of women underwent LLETZ treatments, yet the percentages of women overall who reported bleeding and pain was 70% and 60%, respectively. These figures are much higher than those reported (using the same instrument) in the TOMBOLA trial (pain 37%, bleeding 46%).[9] This may be due to the fact that, in the current study, approximately 75% of women were managed by colposcopy with punch biopsies or treatment compared to less than half (46%) of the women in TOMBOLA. In recent years the proportion of women with an abnormal transformation zone who have undergone diagnostic biopsies at colposcopy clinics in Ireland has increased steadily from 87.8% in 2010/2011[16] to 95.4% in 2014/2015.[1] The high proportions of physical after-effects observed in our study suggests that diagnostic biopsies can incur significant physical-after-effects for women and this needs to be considered when managing women referred to colposcopy.

Our study also found, for the first time in a longitudinal analysis, that there is a positive association between number of physical-after-effects experienced and post-colposcopy distress. Similar findings have been reported in studies of other health-related conditions. In one follow-up study among women with recurrent breast cancer, those who experienced multiple symptoms were at increased risk of distress.[17] In another study among women who had completed breast cancer treatment, greater physical side-effects predicted greater distress. [18] It may be that having one side-effect of cancer treatment (or any procedure) is anticipated by individuals and perceived as normal but worry, and hence distress, intensifies when multiple after-effects are experienced. Another explanation may relate to the representations women hold of their ‘condition’ (abnormal

cervical cytology) and their management experiences.[19] Women in our study who perceived their multiple physical after-effects as serious may have been more likely to be worried about them (and therefore have post-colposcopy distress) than those who did not have multiple physical after-effects –this is somewhat alluded to in a study of women who were treated for breast cancer, In that study, patients who viewed their illness as having serious consequences reported worse physical and mental health than those who did not .[20] Interestingly, the magnitude of the association between physical after-effects and distress in our study was similar, irrespective of the type of physical after-effect experienced. Our findings suggest more emphasis on the possibility of experiencing multiple physical after-effects in pre-colposcopy and post-colposcopy counselling may be required to minimise distress.

We have shown in a recent qualitative study that some women can have negative sensory experiences of colposcopy and related procedures (which can lead to post-colposcopy distress) and that factors contributing to women having a negative sensory procedure included sensory expectations of the procedure(s) and lack of preparatory sensory information (i.e. how the procedures may feel).[10] Similar to this, in the current study women who were unaware of the possibility of experiencing physical after-effects had greater post-colposcopy distress during follow-up than women who were aware they could experience some physical after-effects. Physical after-effects of procedures such as colposcopy, punch biopsies, and LLETZ are for the main part unavoidable. However, increasing awareness that such side-effects can occur is in principle, modifiable and raising women's awareness that physical after-effects are common and "normal" may serve to ameliorate post-colposcopy psychological wellbeing.

Our findings highlight the importance of preparing women for the possibility of experiencing (perhaps multiple) physical after-effects through counselling pre-colposcopy and the provision of appropriate procedure-related information on physical after-effects (e.g. via screening programme information materials). The novel findings of inter-relationships between awareness of the possibility of after-effects and experiencing multiple physical after-effects, and post-colposcopy distress may be relevant to the development of interventions to ease post-colposcopy distress. In particular, our findings highlight that, among women who experience multiple physical after-effects, targeted intervention measures to alleviate post-colposcopy distress are needed.

Conclusion

The prevalence of physical after-effects of colposcopy and related procedures is high. Our findings of inter-relationships between awareness of the possibility of after-effects, and experiencing multiple physical after-effects, and post-colposcopy distress may be useful for the development and targeting of interventions to alleviate post-colposcopy distress.

Disclosure of interests

None declared.

Contribution to authorship

MO'C, JMcR and LS conceived the study. LS, CMM and JOL obtained funding for the study. MO'C and JMcR was in charge of overall project coordination and data management and coordination of data collection. CR, CW and LP recruited participants at the colposcopy clinics. KOB conducted data analysis. MO'C drafted the manuscript. MO'C, KOB, JW, PG and LS contributed to interpretation of study results. TD, GF and WP provided access to potential study participants. KOB, JW, PG, TD, GF, CMM, JMcR, WP, CW, CR, LP, JJOL and LS reviewed the drafts. All authors approved the final version of the article.

Details of ethics approval

This study was approved by the research ethics committee of the Coombe Women and Infants University Hospital, Dublin (reference number: 21-2006; approved 27 April 2010) and the research ethics committee of the National Maternity Hospital, Dublin (approved 26 October 2010).

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References

1. CervicalCheck – Ireland's National Cervical Screening Programme. CervicalCheck Programme Report 2014-2015, Ireland: The National Cervical Screening Programme. Available from: http://www.cervicalcheck.ie/_fileupload/ProgrammeReports/CS-PR-PM-20%20CervicalCheck%20Programme%20Report%202014-2015.pdf. (Accessed December 10, 2016).

2. NHS National Statistics. Health and Social Care Information Centre. Cervical screening programme, England: statistics for 2014 to 2015. Available from: http://content.digital.nhs.uk/catalogue/PUB18932/nhs-cervical-stat-eng-2014-15-rep.pdf. Accessed November 12, 2016)

3. Bonevski B, Sanson-Fisher R, Girgis A, Perkins J. Women's experiences of having a colposcopic examination: self-reported satisfaction with care, perceived needs and consequences. *J Obstet Gynaecol* 1998;18:462–470.

4. Howells RE, Dunn PD, Isasi T, Chenoy R, Calvert E, Jones PW, et al. Is the provision of information leaflets before colposcopy beneficial? A prospective randomised study. *Br J Obstet Gynaecol* 1999;106:528-34.

5. Tahseen S, Reid PC. Psychological distress associated with colposcopy: patients' perception. *Eur J Obstet Gynecol Reprod Biol* 2008;139:90–94.

6. Sharp L, Cotton S, Carsin AE, Gray N, Thornton A, Cruickshank M, et al. Factors associated with psychological distress following colposcopy among women with low-grade abnormal cervical cytology: a prospective study within the Trial Of Management of Borderline and Other Low-grade Abnormal smears (TOMBOLA). Psychooncology 2013;22:368-80.

7. O'Connor M, O'Leary E, Waller J, Gallagher P, D'arcy T, Flannelly G, et al. Trends in, and predictors of, anxiety and specific worries following colposcopy: a 12-month longitudinal study. *Psychooncology* 2016;25:597-604.

8. Williams J, Jess C, Johnson N. Bleeding, discharge, pain and dysmenorrhoea after large loop excision of the transformation zone (LLETZ). *J Obstet Gynaecol* 2004;24:167-8.

9. TOMBOLA (Trial Of Management of Borderline and Other Low-grade Abnormal smears) Group, Sharp L, Cotton S, Cochran C, Gray N, Little J, et al. After-effects reported by women following colposcopy, cervical biopsies and LLETZ: results from the TOMBOLA trial. *BJOG* 2009;116:1506-14.

10. O'Connor M, Waller J, Gallagher P, Martin CM, O'Leary JJ, D'Arcy T, et al. Understanding Women's Differing Experiences of Distress after Colposcopy: A Qualitative Interview Study. *Womens Health Issues* 2015;25:528-34.

11. Gray NM, Sharp L, Cotton SC, Avis M, Philips Z, Russell I, et al. Developing a questionnaire to measure the psychosocial impact of an abnormal cervical smear result and its subsequent management: the TOMBOLA (Trial Of Management of Borderline and Other Low-grade Abnormal smears) trial. *Qual Life Res* 2005;14:1553–62.

12. Rothnie K, Cotton SC, Fielding S, Gray NM, Little J, Cruickshank ME, et al. Measuring the psychosocial burden in women with low-grade abnormal cervical cytology in the TOMBOLA trial: psychometric properties of the Process and Outcome Specific Measure (POSM). *Health Qual Life Outcomes* 2014; 12:154.

13. Lopes A, Beynon G, Robertson G, Daras V, Monaghan JM. Short term morbidity following large loop excision of the cervical transformation zone. *J Obstet Gynaecol* 1994;14:197–9.

14. Paraskevaidis E, Davidson EJ, Koliopoulos G, Alamanos Y, Lolis E, Martin-Hirsch P. Bleeding after loop electrosurgical excision procedure performed in either the follicular or luteal phase of the menstrual cycle: a randomized trial. *Obstet Gynecol* 2002;99:997–1000.

15. Dunn T, Killoran K, Wolf D. Complications of outpatient LLETZ procedures. *J Reprod Med* 2004;49:76–8.

16. CervicalCheck – Ireland's National Cervical Screening Programme. CervicalCheck Programme Report 2010-2011, Ireland: The National Cervical Screening Programme. Available from: http://www.cervicalcheck.ie/_fileupload/ProgrammeReports/CS-PR-PM-16%20CervicalCheck%20programme%20report%20Sep%202010%20-%20Aug%202011.pdf

17. Kenne Sarenmalm E1, Ohlén J, Odén A, Gaston-Johansson F. Experience and predictors of symptoms, distress and health-related quality of life over time in postmenopausal women with recurrent breast cancer. *Psychooncology* 2008;17:497-505.

18. Jim HS, Andrykowski MA, Munster PN, Jacobsen PB. Physical symptoms/side effects during breast cancer treatment predict posttreatment distress. *Ann Behav Med* 2007;34:200-8.

19. Leventhal H, Meyer D, Nerenz D. The common sense model of illness danger. In: Rachman S editor. Medical Psychology. Vol. 2. New York: Pergamon Press; 1980. pp. 7–30.

20. Rozema H, Völlink T, Lechner L. The role of illness representations in coping and health of patients treated for breast cancer. *Psychooncology* 2009;18:849-57.

Table 1. Selected socio-demographic characteristics and clinical variables*

Total	*n*	%
Age		
< 30 years	153	36.0
30 – 40 years	146	34.4
> 40 years	126	29.6
Not stated	4	
Highest level of education attained		
Third level (e.g. college, university)	286	67.5
Primary/secondary	138	32.5
Not stated	5	
Marital status		
Married/cohabiting	199	46.7
Divorced/separated/widowed	36	8.5
Single	191	44.8
Not stated	3	
Have children		
Yes	215	50.6
No	210	49.4
Not stated	4	
Private health insurance		
Yes	207	48.4
No	221	51.6
Not stated	1	
Referral cytology test result		
Low grade (borderline/mild)	329	76.7
High grade (moderate/severe)	95	22.1
Not available	5	1.2
Colposcopic impression		
Normal	114	26.6
Abnormal	293	68.3
Unsatisfactory	8	1.9
Not available	14	3.3
Initial management received		
Colposcopy only	110	25.8
Colposcopy plus punch biopsies**	241	56.4
Colposcopy plus LLETZ***	76	17.8
Not available	2	
Histology result at/following initial colposcopy		
No CIN	65	15.2
CIN 1	90	21.0
CIN 2+	145	33.8
No result/result unavailable/colposcopy unsatisfactory	129	30.1

*Measured at 4 months post-colposcopy; **Women had 1 or more biopsies taken with their colposcopy, with further procedures dependant on biopsy findings;***Women had colposcopy and were managed by immediate treatment (LLETZ; Large Loop Excision of the Transformation Zone)

Table 2. Prevalence of physical after-effects (number (%)), mean distress scores (with standard deviations (SD)) and p values for associations between physical after-effects and distress at 4, 8 and 12 months post-colposcopy

Total	**Sample characteristics at 4 months Number (%)**	**Mean (SD) distress score at 4 months (*n* =402)**	**Mean (SD) distress score at 8 months (*n* = 331)**	**Mean (SD) distress score at 12 months (*n* = 294)**
Overall distress				
Whole sample	402 (100%)	46.6 (14.7)	44.2 (13.5)	42.2 (13.9)
Any physical after-effect				
Yes	324 (82%)	47.4 (14.7)	44.8 (13.7)	43.2 (13.8)
No	73 (18%)	43.0 (14.1)	39.5 (12.5	37.6 (12.6)
p value*		0.019	0.005	0.006
Number of physical after-effects				
0	73 (18%)	43.0 (14.1)	39.5 (12.5)	37.6 (12.6)
1	81 (20%)	44.5 (13.6)	41.4 (14.6)	39.7 (13.1)
2	140 (35%)	46.8 (14.4)	44.7 (12.7)	42.7 (12.7)
3	103 (26%)	50.5 (15.4)	47.8 (13.8)	47.3 (15.2)
p-value**		0.001	<0.001	<0.001
Pain				
Yes	248 (59%)	48.1 (15.0)	45.8 (13.4)	44.2 (13.9)
No	173 (41%)	44.4 (13.9)	40.9 (13.5)	39.5 (12.9)
p value*		0.012	0.002	0.004
Bleeding				
Yes	290 (69%)	47.7 (14.4)	45.1 (13.2)	43.6 (13.6)
No	132 (31%)	43.8 (14.8)	40.5 (14.1)	38.8 (13.2)
p value *		0.012	0.006	0.003
Discharge				
Yes	167 (40%)	49.2 (15.6)	46.6 (14.5)	45.5 (15.1)
No	253 (60%)	44.9 (13.8)	42.0 (12.8)	40.3 (12.7)
p value *		0.004	0.004	0.003
Awareness of the possibility of experiencing after-effects				
Yes	370 (86%)	46.0 (14.4)	43.1 (13.1)	41.6 (13.6)
No	55 (13%)	50.8 (16.2)	48.7 (16.4)	45.1 (13.9)
p value *		0.033	0.014	0.173

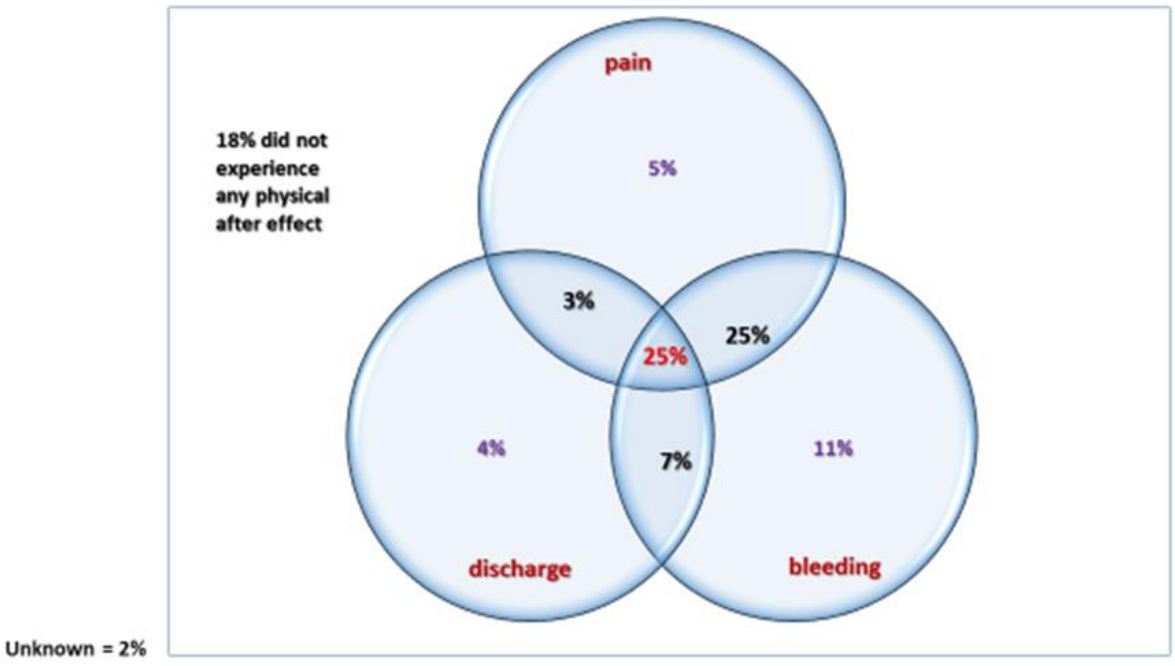
*t-test, **test for trend.

Table 3. Multivariable mixed effects model results for associations between after-effects and distress and sensitivity analysis results (to test whether distress varied by type of physical after-effect –pain, bleeding or discharge)

			Distress score*	
	Adjusted mean**	**Estimate**	**95% CI**	**p value*****
Any physical after-effects				
None	42.7 (40.2, 45.2)	Ref		
Any (vs none)	44.8 (43.6, 46.0)	2.11	(-0.76, 4.97)	0.149
Number of physical after-effects******				
0	42.5 (40.0, 45.0)	Ref		
1	42.8 (40.5, 45.1)	0.32	(-3.05, 3.68)	
2	44.7 (42.8, 46.5)	2.20	(-0.97, 5.38)	
3	47.0 (44.8, 49.2)	4.58	(1.10, 8.05)	0.030
Pain				
No	43.1 (41.4, 44.8)	Ref		
Yes	45.4 (43.9, 46.8)	2.32	(0.01, 4.62)	0.049
Bleeding				
No	42.8 (40.8, 44.7)	Ref		
Yes	45.2 (43.8, 46.4)	2.40	(-0.06, 4.86)	0.056
Discharge				
No	43.5 (42.2, 44.9)	Ref		
Yes	45.8 (44.0, 47.6)	2.30	(0.02, 4.57)	0.048
Awareness of the possibility of experiencing after-effects*******				
Yes	43.9 (42.8, 45.0)	Ref		
No	47.9 (44.8, 51.0)	4.00	(0.66, 7.32)	0.019

* All models adjusted for timepoint, awareness of possibility of physical after-effects, initial colposcopy histology result, age, smoking status, perceived severity of colposcopy exam, satisfaction with healthcare and whether or not the woman had had colposcopy prior to taking part in the current study. **Predicted margins with 95% confidence interval, from multivariable models. ***Wald test p-values. ****The test for linear trend was significant (p=0.004). *****Estimate from the primary model, with main variable of interest physical after effects (any v. none).

Figure 1. Percentages of women with none, one, two or three after-effects*



*Of 429 women, physical after-effects assessed in the 4-month questionnaire only.

Table S1. Questions (and response options) on physical after-effects of colposcopy and related procedures measured 4 months following women's initial colposcopy

1a. Did you have any discomfort/pain following your appointment?

Yes 1 No 2

If No, please go to question 2a

(1b) If Yes, How long did the discomfort/pain last?

_____ **DAYS**

(1c) If Yes, At its worst, was your discomfort/pain?

Very mild	Mild	Moderate	Severe	Very severe
1	2	3	4	5

2a. Did you have any bleeding following your appointment?

Yes 1 No 2

If No, please go to question 3a

(2b) If Yes, How long did the bleeding last?

_____ DAYS

(2c) If Yes, At its worst, was your bleeding?

Very light (spotting)	Light	Moderate	Heavy	Very heavy
1	2	3	4	5

3a. Did you have any unpleasant discharge following your appointment?

Yes 1 No 2

If No, please go to question 4

(3b) If Yes, How long did the discharge last?

_____ DAYS

(3c) If Yes, At its worst, was your discharge?

Very light	Light	Moderate	Heavy	Very heavy
1	2	3	4	5

4. Were you aware that you might have some after-effects following your appointment?

Yes 1 No 2

5. Overall were your after-effects?

I didn't have any after-effects	Same as I expected	Worse than I expected	Not as bad as I expected
1	2	3	4

Table S2. POSM items used to develop an overall POSM score

POSM item* (abbreviated)	Response options						
Feel well enough informed about my follow-up	Strongly agree	Moderately agree	Slightly agree	Slightly disagree	Moderately disagree		Strongly disagree
Worried about my general health	Strongly agree	Moderately agree	Slightly agree	Slightly disagree	Moderately disagree		Strongly disagree
Way I feel about myself has changed	Strongly for the better	Moderately for the better	Slightly for the better	Neither for the better nor worse	Slightly for the worse	Moderately for the worse	Strongly for the worse
Worried that my next smear will show changes to the cells	Strongly agree	Moderately agree	Slightly agree	Slightly disagree	Moderately disagree		Strongly disagree
Worried that I may have cervical cancer	Strongly agree	Moderately agree	Slightly agree	Slightly disagree	Moderately disagree		Strongly disagree
Worried about having sex	Strongly agree	Moderately agree	Slightly agree	Slightly disagree	Moderately disagree		Strongly disagree
Satisfied with support I have had from other people	Strongly agree	Moderately agree	Slightly agree	Slightly disagree	Moderately disagree		Strongly disagree

POSM, Process Outcome Specific Measure

Table S3. Socio-demographic characteristics (continued), lifestyle behaviours and attitudes, and health-care related history*

Total	*n*	%
Employment status		
In work (working for an employer or self-employed)	306	71.7
Other**	121	28.3
Not stated	2	
Nationality		
Irish	386	90.8
Other	39	9.2
Not stated	4	
Currently pregnant		
Yes***	17	4.0
No	410	96.0
Not stated	2	
Smoking status		
Current smoker	140	32.8
Never smoked	153	35.8
Past smoker	134	31.4
Not stated	2	
History of depression**		
Yes	123	28.9
No	303	71.1
Not stated	3	
Social support: No. of close friends and relatives		
Mean	7.4 (5.7)	-
Satisfaction with life		
Mean (SD) satisfaction with life	7.3 (1.8)*****	-
Satisfaction with healthcare		
Mean (SD) satisfaction with healthcare	5.0 (1.1)[1]	-
Ever had an abnormal cervical cytology test result[2]		
Yes	247	58.3
No	177	41.7
Not stated	5	
Ever had a colposcopy examination[3]		
Yes	89	20.8
No	339	79.2
Not stated	1	
Perceived severity of a colposcopy exam		
Not at all serious	25	5.9
Slightly serious	210	49.2
Serious	149	34.9
Very serious	43	10.1
Not stated	2	

*Measured at 4 months post-colposcopy;**Unemployed, retired from employment, unable to work, looking after family/home or student; *** women who were pregnant at the time of the 4-month questionnaire but not pregnant at recruitment (the initial colposcopy appointment);****Self-reported depression;*****mean is from possible Likert score of 1-10; [1]mean is from possible Likert score of 1-7; [2]Prior to the one the woman had at study recruitment; [3]Prior to taking part in the study

Table S4. Multivariable mixed effects model for association between distress score and experiencing none v any physical after-effects

	Adjusted mean*	Distress score Estimate	95% CI	p value**
Any physical after-effects				
None	42.7 (40.2, 45.2)	Ref		
Any (v none)	44.8 (43.6, 46.0)	2.11	(-0.76, 4.97)	0.149
Awareness of physical after-effects				
Yes	43.9 (42.8, 45.0)	Ref		
No	47.9 (44.7, 51.0)	3.99	(0.66, 7.32)	0.019
Timepoint	45.8 (44.5, 47.0)	-1.60	(-2.34, -0.85)	<0.001
Initial Colposcopy Histology result				
No CIN	41.9 (39.1, 44.6)	Ref		
CIN 1	44.7 (42.4, 47.1)	2.89	(-0.69, 6.48)	
CIN 2+	47.5 (45.5, 49.5)	5.65	(2.26, 9.04)	
No result/result unavailable/colposcopy unsatisfactory	42.0 (40.0, 44.1)	0.17	(-3.23, 3.58)	<0.001
Perceived severity of colposcopy exam				
Not serious	35.6 (31.1, 40.2)	Ref		
Slightly serious	42.5 (41.0, 44.0)	6.89	(2.08, 11.69)	
Serious	46.7 (44.9, 48.5)	11.10	(6.17, 16.02)	
Very serious	50.8 (47.3, 54.2)	15.16	(9.37, 20.95)	<0.001
Ever had a colposcopy* **				
Yes	43.5 (42.3, 44.7)	Ref		
No	47.9 (45.6, 50.3)	-4.45	(-7.13, -1.76)	0.001
Satisfaction with healthcare				
Per unit increase****	44.4 (43.4, 45.5)	-2.46	(-3.49, -1.44)	<0.001
Smoking status				
Current smoker	46.5 (44.5, 48.4)	Ref		
Never smoked	44.9 (43.1, 46.7)	-1.51	(-4.21, 1.19)	
Past smoker	41.8 (39.9, 43.7)	-4.70	(-7.46, -1.95)	0.003
Age				
< 30 years	47.1 (45.3, 48.9)	Ref		
30 - 40 years	44.1 (42.3, 45.9)	-3.01	(-5.58, -0.45)	
≥ 40 years	41.8 (39.8, 43.7)	-5.35	(-8.03, -2.67)	<0.001

*predicted margins with 95% confidence intervals, from multivariable models;**Wald test p value; ***Prior to the one the woman had at study recruitment; ****Likert scale range 1-7; Completely satisfied = 7.