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

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18

19 *Running title:* Physical after-effects of colposcopy and distress

20

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23

24 **Abstract**

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

27 **Design** Longitudinal survey.

28 **Setting** Two hospital-based colposcopy clinics.

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

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

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

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

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

51

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

53

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

56

57 **Introduction**

58 For cervical screening to be effective, women who have a positive screening test (irrespective of
59 whether the initial test is cytological- or HPV-based) require follow-up. Hospital-based
60 colposcopy examinations are a cornerstone of follow-up and likely to remain so under the newer
61 screening protocols. Colposcopy is a very common procedure; for example, each year almost
62 200,000 women in England and 16,000 in Ireland are referred for colposcopy.^{1,2}

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

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

84

85

86 **Methods**

87 **Setting**

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

94 **Study participants and recruitment**

95 Women who attended CervicalCheck colposcopy clinics at two large Dublin hospitals were
96 recruited to the study between September 2010 and July 2011. To be eligible, women had to
97 have been referred to colposcopy on the basis of an abnormal cervical cytology test result, in the
98 context of routine screening. They were eligible irrespective of the management they received at
99 their initial clinic appointment (i.e. colposcopy only, punch biopsies, loop excision, or another
100 form of intervention or treatment) or subsequent follow-up. Women who had previously had
101 treatment for cervical abnormalities, or who were pregnant at the time of recruitment (i.e. at the
102 initial colposcopy clinic appointment) were ineligible. At their clinic appointment, women were
103 invited to take part in the study by research staff and were given a study information sheet.
104 Women willing to participate in the study signed a consent form and returned it to research staff.
105 Consenting women were invited to complete a questionnaire which was sent by post at 4, 8 and
106 12 months following their initial colposcopy appointment.

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

109

110

111 **Assessment of physical after-effects of colposcopy and related procedures**

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

117

118 **Assessment of post-colposcopy psychological distress**

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

131 **Co-variates**

132 Information on potential confounders of the relationship between physical after-effects and
133 psychological distress was obtained from the questionnaire administered at the 4 month time-
134 point and from women's clinic records. Questions on socio-demographic characteristics, lifestyle
135 behaviours and attitudes, and healthcare-related history were included in the questionnaire. Data
136 extracted from clinic records were: colposcopy referral cytology, initial colposcopic impression,

137 | initial management received and initial histology result. Table 1 [and Table S3](#) lists the co-
138 variates available.

139 **Statistical analyses**

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

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

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

166 of the model, we fitted models with random intercepts only and random intercepts and slopes; we
167 concluded that these more complex models were not required and have reported the findings
168 from the final fixed effects multivariable model.

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

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

179 **Results**

180 **Characteristics of respondents**

181 429 of the 584 women recruited to the study completed the 4 month questionnaire (73%), 343
182 (59%) completed the questionnaire at 8 months; and 303 (52%) completed the questionnaire at
183 12 months. Table 1 displays ~~the women's selected~~ socio-demographic characteristics, ~~lifestyle~~
184 ~~behaviours and attitudes, health care related history~~ and clinical variables for the 429 who
185 completed the 4-month questionnaire. The additional socio-demographic characteristics, lifestyle
186 behaviours and attitudes, and health-care related history variables are displayed in Table S3.

187

188 **Prevalence of physical after-effects**

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

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

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

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

205 **Regression results**

206 *Any physical after-effects*

207 In the multivariable analysis with any vs. no physical after-effects as the main explanatory
208 variable of interest, having any physical after-effect was associated with a higher distress score
209 over the entire follow-up period (2.11; 95% CI -0.76 to 4.97; Table 3; with full multivariable
210 results shown in Table S43), but this was not statistically significant (Wald test p-value 0.15;
211 Table 3). In the same model, not being aware of the possibility of physical after-effects was
212 significantly associated with higher distress score (on average 3.99 points higher) during follow-
213 up (Wald test p-value 0.02; Table 3).

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

218 *Number of physical after-effects*

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

221 significant linear trend ($p=0.004$). In women with two physical after-effects, follow-up related
222 distress was on average 2.20 (95% CI -0.97 to 5.38) points higher than for women who
223 experienced none (Table 3); follow-up related distress was on average 4.58 (95% CI 1.10 to
224 8.05) points higher in women who experienced all three physical after-effects than in women
225 who experienced none (Table 3). In a linear test for trend, a one unit increase in the number of
226 physical after effects was associated with a 1.6 increase in psychological distress score, $p =$
227 0.004. Not being aware of the possibility of physical after-effects was significantly associated
228 with on average a 4.25 (95% CI 0.93 to 7.57) higher distress score (Wald test p -value 0.01).

229 *Sensitivity analysis: type of physical after-effect*

230 In our sensitivity analysis, the effect size for association with (a higher) distress score was
231 similar for each physical after-effect. In women who experienced pain, follow-up related distress
232 was on average 2.32 (95% CI 0.01 to 4.62) points higher than for women who experienced none.
233 Follow-up related distress was on average 2.40 (95% CI -0.06 to 4.86) points higher in women
234 who experienced bleeding than in women who experienced none and was 2.30 (95% 0.02 to
235 4.57) points on average higher in women who experienced distress than in women who
236 experienced no discharge (Table 3).

237

238

239 **Discussion**

240 **Main findings**

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

251 **Strengths and limitations**

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

267 | mean distress score- Although women in our study would have received information leaflets
268 | ~~(either at the clinic or by post prior to their appointment)~~ which contained some (limited)
269 | information about possible after-effects, we do not know anything about the verbal information
270 | ~~clinicians and other~~ clinic staff may have given women during their consultations about the
271 | possibility of experiencing physical after-effects, and whether/how this might have impacted on
272 | experiences ~~and distress~~.

273 | **Interpretation**

274 | The high proportions of women experiencing physical after-effects in our study are a cause for
275 | concern. Other evidence on the burden of physical after-effects of colposcopy and related
276 | procedures is scarce with most studies conducted more than 10 years ago and focused mainly on
277 | after-effects of LLETZ.¹³⁻¹⁵ In these studies, LLETZ appears to be strong a predictor a greater
278 | physical after-effect burden. In the current study, only 18% of women underwent LLETZ
279 | treatments, yet the percentages of women overall who reported bleeding and pain was 70% and
280 | 60%, respectively. These figures are much higher than those reported (using the same
281 | instrument) in the ~~UK~~ TOMBOLA trial (pain 37%, bleeding 46%, ~~discharge 34%~~).⁹ This may be
282 | due to the fact that, in the current study, approximately 75% of women were managed by
283 | colposcopy with punch biopsies or treatment compared to less than half (46%) of the women in
284 | TOMBOLA. In recent years the ~~number of~~ proportion of women with an abnormal
285 | transformation zone who have undergone diagnostic biopsies at colposcopy clinics in Ireland has
286 | increased steadily over time from 87.8% in 2010/2011¹⁶ to 95.4% in 2014/2015.¹ ~~This increase~~
287 | ~~is mostly likely due to the change in CervicalCheck's quality assurance standards in 2014 to a~~
288 | ~~lower threshold for diagnostic biopsy performance in >90% of cases where the transformation~~
289 | ~~zone is documented as abnormal at colposcopy. Prior to 2014, the performance target for~~
290 | ~~diagnostic biopsies within CervicalCheck was >95%.¹⁶~~ The higher ~~er~~ proportions of physical after-
291 | effects observed in our study suggests that diagnostic biopsies can incur significant physical-
292 | after-effects for women and this needs to be considered when managing women referred to
293 | colposcopy for their abnormal cervical cytology.

294 | Our study also found, for the first time in a longitudinal analysis, that there is a positive
295 | association between number of physical-after-effects experienced and post-colposcopy distress.

296 Similar findings have been reported in studies of other health-related conditions. In one follow-
297 up study among women with recurrent breast cancer, those who experienced multiple ~~and~~
298 ~~concurrent~~ symptoms were at increased risk of ~~psychological~~ distress.¹⁷ In another study among
299 women who had completed breast cancer treatment, greater physical side-effects predicted
300 greater distress.¹⁸ It may be that having one side-effect of ~~cancer or~~ cancer treatment (or any
301 ~~medical~~ procedure) is anticipated by individuals and perceived as ~~relatively~~ normal but worry,
302 and hence distress, intensifies when multiple after-effects are experienced. Another ~~possible~~
303 explanation may relate to the representations women hold of their ‘condition’ (abnormal cervical
304 cytology) and their management experiences.¹⁹ Women in our study who perceived their multiple
305 physical after-effects as serious may have been more likely to be worried about them (and
306 therefore have post-colposcopy distress) than those who did not have multiple physical after-
307 effects –this is somewhat alluded to in a study of women who were treated for breast cancer, In
308 that study, patients who viewed their illness as ~~having a condition with~~ serious ~~symptoms and~~
309 consequences ~~were found to reported~~ worse physical and mental health than those who did not.²⁰
310 Interestingly, the magnitude of the association between physical after-effects and distress in our
311 study was similar, irrespective of the type of physical after-effect experienced. Our findings
312 suggest more emphasis on the possibility of experiencing multiple physical after-effects in pre-
313 colposcopy and post-colposcopy counselling may be required to ~~help~~ minimise distress.

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

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

376 **Conclusion**

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

381

382

383

384 **Disclosure of interests**

385 None declared.

386 **Contribution to authorship**

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

394 **Details of ethics approval**

395 This study was approved by the research ethics committee of the Coombe Women and Infants
396 University Hospital, Dublin (reference number: 21-2006; approved 27 April 2010) and the
397 research ethics committee of the National Maternity Hospital, Dublin (approved 26 October
398 2010).

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407

408

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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 1. Selected socio-demographic characteristics and clinical variables*

Total	<i>n</i>	%
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)

	Adjusted mean**	Estimate	Distress score* 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).