Trends in, and predictors of, anxiety and specific worries following colposcopy: a 12 month longitudinal study

Mairead O'Connor,[1] Eamonn O'Leary,[1] Jo Waller,[2] Pamela Gallagher,[3] Tom D'arcy,[4] Grainne Flannelly[5] Cara M Martin[4], Judith McRae[1], Walter Prendiville,[4] Carmel Ruttle,[4] Christine White,[6] Loretto Pilkington,[4] John J O'Leary,[4] Linda Sharp,[7] on behalf of the Irish Cervical Screening Research Consortium (CERVIVA)

[1] National Cancer Registry Ireland, Kinsale Road, Cork, Ireland

[2] Health Behaviour Research Centre, University College London, London, UK

[3] School of Nursing and Human Sciences, Dublin City University, Dublin, Ireland

[4] Coombe Women and Infants University Hospital, Dublin 8, Ireland

[5] National Maternity Hospital, Dublin 2, Ireland

[6] Trinity College Dublin, Dublin 2, Ireland

[7] Institute of Health & Society, Newcastle University, UK

Correspondence to: Mairead O'Connor, National Cancer Registry Ireland, Building 6800, Cork Airport Business Park, Kinsale Road, Cork, Ireland. Email: m.oconnor@ncri.ie

Running title: Predictors of anxiety and specific worries after colposcopy

Key words: post-colposcopy, anxiety, cancer, oncology, future fertility

Word count: 3,999

Abstract

Objective: Little is known about which women are at greatest risk of adverse psychological after-effects following colposcopy. This study examined time trends in, and identified predictors of, anxiety and specific worries over 12 months.

Methods: Women attending two hospital-based colposcopy clinics for abnormal cervical cytology were invited to complete psychosocial questionnaires at 4, 8 and 12 months following colposcopy. General anxiety and screening-specific worries (about cervical cancer, having sex and future fertility) were measured. Generalized estimating equations were used to assess associations between socio-demographic, lifestyle and clinical variables and risk of psychological outcomes.

Results: Of 584 women initially recruited, 429, 343 and 303 completed questionnaires at 4, 8 and 12 months, respectively. Screening-specific worries declined significantly over time but were still relatively high at 12 months: 23%, 39% and 18% for worries about cervical cancer, fertility and having sex, respectively. Anxiety remained stable (20%) over time. Risks of cervical cancer worry and anxiety were both almost double in women without private health insurance (cervical cancer worry: OR=1.80, 95% CI 1.25-2.61; anxiety: OR=1.84, 95% CI 1.20-2.84). Younger women (<40 years) had higher risk of fertility worries. Non-Irish women had higher risk of anxiety (OR=2.13, 95% CI 1.13-4.01).

Conclusions: Screening-specific worries declined over time but anxiety remained stable. Notable proportions of women still reported adverse outcomes 12 months following colposcopy, with predictors varying between outcomes. Women in socio-demographically vulnerable groups were at greatest risk of adverse psychological outcomes. This information could inform development of interventions to alleviate psychological distress post-colposcopy.

Introduction

Colposcopy can be a distressing experience for women and studies have shown that women have raised anxiety levels prior to, and during, the examination [1-4] Evidence is accruing that, for some women, colposcopy is also associated with adverse psychological effects afterwards [5, 6]; for example, a recent systematic review concluded that diagnosis of CIN and treatment (in which colposcopy plays an important role) is associated with negative psychological outcomes for women [7]. However, there are limitations to the current evidence-base in relation to post-colposcopy psychological wellbeing. Firstly, although several studies have suggested that women with abnormal cytology test results have quite specific concerns - for example, about cervical cancer, future fertility and having sex [8-10] - few studies have quantified these worries following colposcopy. Instead, most studies have used measures of generalised distress [11-13]. Secondly, the temporal pattern of psychological after-effects of colposcopy is unclear. In a systematic review, we found that evidence on temporal trends of anxiety and distress was limited and inconsistent; and overall, very little is known about what happens to these screening-specific concerns over time following colposcopy [14].

Thirdly, there are significant gaps in the current evidence-base on predictors of negative psychological outcomes following colposcopy [14]. From the limited data available, management and treatment factors do not appear to affect the risk of negative psychological consequences, although women with cervical intraepithelial neoplasia grade 2+ (CIN2+) may be at increased risk [5,15, 16]. Most studies considered a very limited range of potential predictors. Only one study, the UK TOMBOLA trial, has looked in detail at which subgroups of women are at higher risk. However, in this analysis, assessment of procedure-related distress took place at a short period of time (6 weeks) after women's most recent procedure [6]. Moreover, most of the available studies conducted only univariate analyses, despite the fact that potential predictors are inter-related [14]. A more comprehensive understanding of the predictors of adverse psychological outcomes might help clinicians and other medical professionals identify "at-risk" women and provide appropriate psychological support.

The current study aimed to address the gaps in this evidence-base by: (1) investigating the temporal patterns of general anxiety and specific worries following colposcopy and related

procedures (at 4, 8 and 12 months) and (2) identifying potential predictors of these adverse outcomes over this 12-month period.

Methods

Setting

The study setting was Ireland, which has a mixed public-private healthcare system. Approximately 45% of the population have private health insurance [17] and approximately 40% are entitled to free health care services under the General Medical Services (GMS) Scheme, eligibility for which is based on (low) income and/or (older) age [18]. A national cervical cancer screening programme, CervicalCheck, was implemented in 2008, offering free cervical cytology tests and follow-up, if required, to women aged 25-60 years [19]. Women typically attend their family doctor's practice for a cytology test. Women with two or more low-grade abnormal cervical cytology test results, or one high-grade result, are referred for hospital–based colposcopy in a clinic affiliated with the screening programme [19].

Participants

Women who attended two large colposcopy clinics affiliated with CervicalCheck were recruited to the study between September 2010 and July 2011. Eligible women were those who had been referred to colposcopy on the basis of an abnormal cervical cytology test result; 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 treatment) or subsequent follow-up. From hereonin, we use the term "colposcopy" for brevity to include colposcopy with or without related procedures and treatment. Women were ineligible if pregnant at the time of recruitment (i.e. at the initial colposcopy clinic appointment) or had previously had treatment for cervical abnormalities. At their clinic appointment, women were invited to take part in the study by research staff and were given a study information sheet. Those interested in participating signed consent forms and returned them to research staff. Ethical approval was obtained from the ethics committees of the Coombe Women and Infants University Hospital and the National Maternity Hospital, Dublin.

Assessment of psychological outcomes

Consenting women were invited to complete a psychosocial questionnaire which was sent by post at 4, 8 and 12 months following their initial colposcopy appointment. The outcomes of interest for this analysis were 1) generalised anxiety and 2) specific worries about cervical cancer, future fertility and having sex. Anxiety was assessed by the Hospital Anxiety and Depression Scale (HADS) [20]. The HADS was originally designed to screen for clinically significant anxiety and depression in hospital outpatient clinics, but has subsequently been validated in community settings [21]. Questions on the HADS refer to the past week; women were invited to complete the full instrument but only the seven questions forming the anxiety subscale were considered in this analysis. Specific worries about cervical cancer, future fertility and having sex were assessed using three items from the Process Outcome Specific Measure (POSM), which was developed to assess issues of concern to women being followed-up for abnormal cervical cytology [9]. These three statements have six-level Likert response options ranging from 'Strongly agree' to' Strongly disagree' and refer to the period of the previous month. For example, the statement about cervical cancer is: "In the last month I have been worried that I may have cervical cancer". The other two items have similar wording.

Assessment of potential predictors of anxiety and specific worries

Information on potential predictors of psychological outcomes was obtained from the first questionnaire, administered 4 months following the initial colposcopy appointment. This contained questions on socio-demographic characteristics and lifestyle behaviours, including age, education level, private health insurance and smoking status. Social support was assessed using one item ("About how many close friends and close relatives do you have (people you feel at ease with and can talk to about what is on your mind)?"), which was adapted from the Oslo-3 social support scale [22]. Women's satisfaction with life and general health care were assessed using items adapted from McCaffery et al. [23]. Information on clinical variables at, and following, the initial colposcopy appointment was obtained from hospital clinic records. Data extracted from clinic records were: colposcopy referral cytology, initial colposcopic impression, initial management received and initial histology results. Table 1 lists all the potential socio-

demographic and lifestyle predictors, and Table 2 the potential clinical predictors, of anxiety and specific worries available for analysis

Statistical analyses

Binary psychological outcome variables were created classifying women's surveys responses according to whether or not they were anxious, worried about cervical cancer, worried about future fertility and worried about having sex. Outcome variables were created for each assessment time point. Presence of clinically significant anxiety was defined as a HADS anxiety subscale score of ≥11 [20]. Responses to the questions on worries about cancer, fertility and sex were collapsed to produce a dichotomous variable (agree/disagree corresponding to worried/unworried) for each outcome.

Generalised Estimating Equations (GEE) were used to assess associations between socio-demographic, lifestyle, clinical variables and risk of each of the four psychological outcomes. GEE methods take into account within-subject correlations in longitudinal data and produce robust error estimates. They do not require all subjects to have completed the survey at every time point for inclusion; instead they allow for the inclusion of all surveys completed by each woman. A model was built for each of the four psychological outcomes. QIC (quasi-likelihood under the independence model criterion) statistics were used to select the best correlation structure (from among the four possible structures) for each model, with the model structure with the lowest QIC being chosen.

Univariate logistic regression was used initially to determine which potential predictors should be considered as candidate variables for inclusion in the multivariate models. Variables that were significant at the 5% level in the univariate analysis were included in the initial multivariate analysis and Wald tests used to determine which remained significant, given the presence of other independent variables. The final models only included variables that remained significant, with the exception of the time-point variable (i.e. 4, 8 or 12 months) which was included in all models regardless of significance, in order to test for a temporal trend in psychological outcomes.

Results

Characteristics of participants

Of 584 women who agreed to take part in the study: 429 (73%) completed questionnaires at 4 months following their initial colposcopy; 343 (59%) completed questionnaires at 8 months; and 303 (52%) completed questionnaires at 12 months. Women's socio-demographic, attitudinal and lifestyle characteristics at the 4-month time-point are summarised in Table 1. Women's clinical characteristics at the 4-month time-point are summarised in Table 2.

Prevalence and temporal trends of anxiety and specific worries post-colposcopy

Supplementary Figure 1 shows the prevalence of anxiety and worries about cervical cancer, future fertility and having sex at 4, 8 and 12 months following the initial colposcopy. Over the entire follow-up period, the prevalence of anxiety remained stable at around 20%, but specific worries declined significantly over time (see Supplementary Figure 1). The prevalence of worries about cervical cancer at 4, 8 and 12 months was 36%, 28% and 23%, respectively. The prevalence of worries about future fertility was 56%, 47% and 39%. In terms of having sex, 29% were worried at 4 months, 20% at 8 months and 18% at 12 months. These patterns persisted after adjustment for (other) significant predictors (Tables 3, 4, 5 and Supplementary table 2).

Predictors of anxiety over 12 months post-colposcopy

The univariate analyses of associations between socio-demographic, attitudinal, lifestyle and clinical variables and anxiety are shown in Supplementary table 1. In multivariate analysis, the following variables were significantly associated with increased risk of anxiety: nationality, private health insurance, history of depression and satisfaction with life (Table 3). The odds of anxiety were more than twice as high in women who were non-Irish compared to Irish women (multivariate OR=2.13, 95% CI 1.13 – 4.01). The likelihood of anxiety was also more than twice as high in women who had a history of depression compared to those who did not (OR=2.33, 95% CI 1.51 – 3.60). Having no private health insurance was associated with significantly higher likelihood of anxiety (OR=1.84, 95% CI 1.20 – 2.84). A higher satisfaction with life was related

to significantly lower likelihood of anxiety: with every 1 point increase in life satisfaction score, the odds of anxiety were reduced by one-third (OR=0.67, 95% CI 0.59 – 0.76).

Predictors of worries about cervical cancer over 12 months post-colposcopy

Univariate results are shown in Supplementary table 1. In addition to time point, private health insurance, smoking status, satisfaction with life and perceived severity of colposcopy examination significantly predicted worries about cervical cancer in the multivariate model (Table 4). Compared with current smokers, the odds of worries about cervical cancer were non-significantly lower in those who had never smoked (OR=0.74, 95% CI 0.48 – 1.15) and significantly lower in those who were past smokers (OR=0.52, 95% CI 0.33 – 0.80). The odds of worries about cervical cancer were raised by approximately 80% in those who had no private health insurance (multivariate OR=1.80, 95% CI 1.25 – 2.61). A higher satisfaction with life was related to significantly lower likelihood of worries about cervical cancer: with every 1 point increase in life satisfaction, the odds of worries about cervical cancer were reduced by 12% (OR=0.88, 95% CI 0.80 – 0.96). Perceived severity of the colposcopy examination was positively associated with worries about cervical cancer: with every 1 point increase in perceived severity of the colposcopy examination the odds of anxiety were increased by 84%. (OR=1.84, 95% CI 1.45 – 2.33).

Predictors of worries about future fertility over 12 months post-colposcopy

Univariate results are shown in Supplementary table 1. In multivariate analysis, the following significantly predicted worries about future fertility: age, pregnancy status and smoking status (Table 5). The odds of worries about future fertility were 82% lower in women over 40 years (OR=0.18, 95% CI 0.06 – 0.51) compared to women younger than 30 years. Women who were not pregnant had a significantly higher likelihood of worries about future fertility than women who were pregnant at the time of 4 month questionnaire (OR=4.17, 95% CI 1.61 – 10.81). Compared to current smokers, the odds of worries about future fertility were halved in those who had never smoked (OR=0.50, 95% CI 0.30 – 0.83) and in past smokers (multivariate OR=0.49, 95% CI 0.28 – 0.86); both risk estimates were significantly different from unity.

Predictors of worries about having sex over 12 months post-colposcopy

Univariate results are shown in Supplementary table 1. In multivariate analysis, the following were significant predictors of worries about having sex: age, satisfaction with life, perceived severity of the colposcopy examination and initial colposcopy histology result (Supplementary table 2). The odds of worries about having sex were almost 40% lower in women aged 30–40 years (OR=0.62, 95% CI 0.40 – 0.96), and almost 50% lower in women over 40 years (OR=0.52, 95% CI 0.33 – 0.82), compared to women younger than 30 years. Women who reported higher satisfaction with life had significantly lower risk of worries about having sex (OR=0.83, 95% CI 0.75 – 0.92). Higher perceived severity of the colposcopy examination was positively associated with worries about having sex (OR=1.57, 95% CI 1.22 – 2.03). Compared to women with CIN2+, the odds of worries about having sex was halved in women with CIN 1 (OR=0.50, 95% CI 0.30 – 0.84) and 75% lower in women without CIN (OR=0.26, 95% CI 0.14 – 0.47); both risk estimates were significantly different from unity.

Discussion

Using a powerful longitudinal design, and multivariate analyses, this study examined temporal trends in anxiety and specific worries about fertility, cancer and sex, over 12 months post-colposcopy. Anxiety remained stable while worries declined, but all four outcomes still affected notable proportions of women at 12 months post-colposcopy. The study also identified socio-demographic, attitudinal, lifestyle, and clinical factors that were significantly associated with risk of adverse psychological outcomes post-colposcopy.

Prevalence and temporal trends of anxiety and specific worries

The prevalence of anxiety post-colposcopy in our study was stable over time and similar to levels reported in two UK studies that assessed anxiety in women post-colposcopy using the HADS [24, 25]. However, it was higher than reported in the UK TOMBOLA trial [6] which followed women from approximately 6 weeks (8% had anxiety) to 30 months post-colposcopy (14% had anxiety). In that trial, all women had low-grade cytology and many had only a single test showing borderline nuclear abnormalities while in our study women with two low-grade or

one high-grade test results were eligible. This – and the fact that the two studies assessed women at different time-points - may explain the difference in prevalence of anxiety.

Data on specific post-colposcopy concerns (i.e. worries about cervical cancer, future fertility and having sex) is limited. A Swedish study [3], found the prevalence of cancer worries at 6 and 24 months post-colposcopy was 26% and 30%, respectively, compared to 36% and 28% at 4 and 8 months in our study. Prevalence of worries about future fertility was considerably higher in our study (4 months: 56%; 8 months: 47%; 12 months: 39%) than in the Swedish study (6 months: 31%; 12 months: 20%). This might be explained by the higher proportion of women aged 30 and older in our study (64% compared to 33% in [3]). Although there is a lack of empirical evidence about fertility concerns in the general population, it seems likely that these would be most prevalent among women in their 30s, as their fertility begins to decline. These findings suggest colposcopy could stimulate more concerns about future fertility among women who have a shorter time window in which to conceive (i.e. women in their 30s compared to 20s).

Prior to our study, limited data were available on prevalence of anxiety and specific worries following colposcopy. In particular, very limited data were available on temporal trends in anxiety and specific worries. Only one study, referred to earlier, assessed worries about future infertility and cancer at two-timepoints after colposcopy (~6 and 24 months) [3]. Although a number of studies have evaluated sexual/psychosexual issues post-colposcopy [14], as far as we are aware, our study is the first to investigate temporal trends in worries about having sex. Moreover, our study provides valuable data on temporal patterns of anxiety (which remained stable over the 12 month follow-up period) and worries about cervical cancer and future fertility following colposcopy. While we have shown falling worries over time, the prevalence of specific concerns at 12 months was still relatively high. These findings suggest, firstly, that women may need to be monitored longer-term for post-colposcopy worries and, secondly, that a psycho-educational intervention aimed at alleviating these longer-term concerns is required.

Predictors of anxiety and worries

The risks of worries about cervical cancer and anxiety were almost double in women who did not have private health insurance. Not having private health insurance is a marker of lower socio-

economic status in Ireland and, in the population as a whole, various markers of lower socio-economic status are associated with higher rates of mental health problems [26]; this association could explain our finding. Alternatively, it is worth noting that, in Ireland, those who have private health insurance associate it with advantages such as reassurance about timely access to healthcare and treatment [27]. Therefore, although CervicalCheck provides screening free at the point of delivery, it is possible that women with no private health insurance are more worried about getting cervical cancer because of concerns about access to cancer treatment services in the public system. Identifying women without private health insurance and better supporting them in relation to their worries during their follow-up might provide a route to alleviate some of the post-colposcopy psychological burden.

Previous studies have shown that younger women are more worried about possible consequences of abnormal cytology results on future fertility than older women [6, 10, 28]. We have extended these findings by showing that being younger (<40 years) is a significant predictor of worries about future fertility following colposcopy. Our findings suggest that younger women undergoing colposcopy may benefit from more detailed information on the actual risks of colposcopy/related procedures impacting on their fertility performance and obstetric outcomes. Evidence suggests that colposcopy alone does not impact on time to conceive [29] and that CIN treatment is associated with only a very small increased risk of preterm delivery [30]. This evidence could be communicated to women to help reassure and alleviate fertility concerns.

Women in our study who were non-Irish nationals were at increased risk of anxiety following colposcopy compared to Irish women. This echoes the large disparities observed in different healthcare settings in cervical screening uptake by ethnic backgrounds (see, for example, [31, 32]). Non-Irish women may not have English as their first language and may therefore find it difficult to understand information about colposcopy which, in turn, could increase the likelihood of anxiety following colposcopy. While the Irish cervical screening programme has produced information leaflets in 11 languages, these do not include information on women's follow-up. In addition, recent immigrants to Ireland may find it difficult to navigate the complex health system. Women from different cultural backgrounds hold different beliefs about cervical cytology tests [33]; they may also hold different beliefs about colposcopy. Development of more culturally relevant cervical screening (including follow-up) information leaflets for non-Irish

women is needed. More support generally, and assistance with patient navigation, for non-Irish women, could help reduce the risk of anxiety in these women following colposcopy.

Perceiving the colposcopy examination as serious/very serious was a significant predictor of worries about cervical cancer and having sex following colposcopy. Women's understanding of the purpose of colposcopy is poor [34, 35] and, in qualitative research, we found that women want more detailed information on what a colposcopy entails [36]. Providing more specific information, and eliciting and, where appropriate changing, women's perceptions of the colposcopy examination prior to undergoing the procedure, could help to alleviate subsequent worries.

Considering the findings overall, two striking observations emerge. Firstly, different predictors are somewhat distinctly associated with different screening-specific worries following colposcopy. For example not having private health insurance was a significant predictor of worries about cervical cancer and being younger in age (<40 years) was a significant predictor of worries about future fertility. Secondly, notwithstanding this, women who could be perceived as socio-demographically 'vulnerable' or disadvantaged were at higher risk of poor psychological outcomes. Low socio-economic status environments may stimulate disproportionate levels of negative emotions such as worry which in turn mediate the relationship between socio-economic status and health [37]. Appropriate psycho-educational interventions targeting these 'vulnerable' women could benefit their psychological wellbeing following colposcopy. For example, it may be important to reassure women with no private health insurance about cervical cancer risk. Given that women who have abnormal cytology often require at least one colposcopy, treatment, and in some cases, intensive follow-up, it is the responsibility of cervical screening programmes to identify these vulnerable women and provide them with the necessary support throughout their follow-up.

Strengths and limitations

Our study examined, for the first time in a comprehensive way, socio-demographic, attitudinal, lifestyle and clinical predictors of adverse psychological after-effects of colposcopy. We used GEE, a powerful and robust analysis method which makes use of all data points available, to

examine the temporal trends and potential predictors of post-colposcopy distress. With the exception of the UK TOMBOLA trial [38], this study is the largest to have investigated adverse psychological after-effects of colposcopy and related interventions. Although women were recruited from only two colposcopy clinics, both are affiliated with CervicalCheck and are located in hospitals with socio-economically diverse catchment areas. While there is no reason to assume that women who consented to the study are not typical of women attending colposcopy clinics throughout Ireland, we cannot be certain of this. Other limitations are: the unknown participation rate (i.e. percentage of women attending colposcopy who consented to receive questionnaires), the possibility that questionnaire responders and non-responders differed in terms of frequency of anxiety and specific worries, and the fact that we did not have information on management women received for CIN2+ after the initial colposcopic management and associated procedures.

Conclusions

Our study provides insight into the temporal trends in adverse psychological outcomes over a 12 month period following colposcopy; anxiety remained stable over time while specific worries declined. In addition, we have, for the first time, shown that different predictors are differentially associated with different screening-specific worries post-colposcopy and, in general, that women who could be perceived as socio-demographically 'vulnerable' or potentially disadvantaged are at increased risk. These findings may inform the development of support services and/or interventions to minimise risk of adverse psychological effects post-colposcopy.

Acknowledgements

This study was undertaken as part of the CERVIVA research consortium (www.cerviva.ie). The data collection for this study was funded by the Health Research Board, Ireland (HS-05-09). MOC is an ICE postdoctoral fellow funded by the Health Research Board (ICE/2011/2). We

thank the women who completed questionnaires. We are grateful to the clinicians, nurses and staff at the two colposcopy clinics for facilitating the study.

Conflict of interest

The other authors have no conflicts of interest to declare.

References

1. Marteau TM, Walker P, Giles J, Smail M. Anxieties in women undergoing colposcopy. *Br J Obstet Gynaecol* 1990;**97**:859-61.
2. 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**:462-70.
3. Hellsten C, Sjöström K, Lindqvist PG. A 2-year follow-up study of anxiety and depression in women referred for colposcopy after an abnormal cervical smear. *BJOG* 2008;**115**:212-8.
4. Tahseen S, Reid PC. Psychological distress associated with colposcopy: patients' perception. *Eur J Obstet Gynecol Reprod Biol* 2008;**139**:90-4.
5. Orbell S, Hagger M, Brown V, Tidy J. Appraisal theory and emotional sequelae of first visit to colposcopy following an abnormal cervical screening result. *Br J Health Psychol* 2004;**9**:533-55.
6. Sharp L, Cotton S, Gray N, *et al*. Long-term psychosocial impact of alternative management policies in women with low-grade abnormal cervical cytology referred for colposcopy: a randomised controlled trial. *Br J Cancer* 2011;**104:**255-64.
7. Frederiksen ME, Njor S, Lynge E, Rebolj M. Psychological effects of diagnosis and treatment of cervical intraepithelial neoplasia: a systematic review. *Sex Transm Infect* 2015;**91:**248-56.
8. Idestrom M, Milsom I, Andersson-Ellstrom A. Women's experiences of coping with a positive Pap smear: a register-based study of women with two consecutive Pap smears reported as CIN 1. *Acta Obstet Gynecol Scand* 2003;**82:**756–761.
9. Gray NM, Sharp L, Cotton SC, *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**:1153–1562.
10. Largo-Janssen T, Schijf C. What do women think about abnormal smear test results? A qualitative interview study. J Psychosom Obstet Gynecol 2005;26:141–145.
11. Gath DH, Hallam N, Mynors-Wallis L, Day A, Bond SA. Emotional reactions in women attending a UK colposcopy clinic. *J Epidemiol Comm Health* 1995;**49**:79–83.
12. Kitchener HC, Burns S, Nelson L, *et al*. A randomised controlled trial of cytological surveillance versus patient choice between surveillance and colposcopy in managing mildly abnormal cervical smears. *BJOG* 2004;**111:**63-70.
13. Tiersma ES, van der Lee ML, Garssen B, *et al*. Psychosocial factors and the course of cervical intra-epithelial neoplasia: a prospective study. *Gynecol Oncol* 2005;**97**:879-86.

14. O'Connor M, Gallagher P, Waller J, Martin C, O'Leary JJ, Sharp L. Adverse psychological outcomes 1 following colposcopy and related procedures: a systematic review. *BJOG* (accepted for publication 6th April 2015).
15. Sharp L, Cotton S, Carsin AE, *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). *Psycho-Oncology* 2013;**22**:368-80.
16. Korfage IJ, Essink-Bot ML, Westenberg SM, Helmerhorst T, Habbema JD, van Ballegooijen M. How distressing is referral to colposcopy in cervical cancer screening?: a prospective quality of life study. *Gynecol Oncol* 2014;**132**:142-8.
17. The Health Insurance Authority. Annual Report and Accounts 2013. Available from: http://www.hia.ie/sites/default/files/2013%20Annual%20Report%20and%20Accounts%20Final%20English%20Version.pdf. (Accessed March 20, 2015).
18. Health Services Executive. Primary Care Reimbursement Services: Statistical Analysis of claims and payments 2012. Available from: http://www.hse.ie/eng/staff/PCRS/PCRS_Publications/PCRSannreport12.pdf. (Accessed February 27, 2015).
19. CervicalCheck – Ireland's National Cervical Screening Programme. CervicalCheck Programme Report 2012-2013, Ireland: National Cancer Screening Service. Available from: http://www.cervicalcheck.ie/_fileupload/CervicalCheck%202012-2013(1).pdf. (Accessed March 23, 2015).
20. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**:361–370.
21. Snaith RP. The Hospital Anxiety and Depression Scale. *Health Qual Life Outcomes* 2003;**1**:29.
22. Dalgard OS, Dowrick C, Lehtinen V, *et al.* Negative life events, social support and gender difference in depression: a multinational community survey with data from the ODIN study. *Soc Psychiatry Psychiatr Epidemiol* 2006;**41**:444-51.
23. McCaffery KJ, Irwig L, Turner R, *et al.* Psychosocial outcomes of three triage methods for the management of borderline abnormal cervical smears: an open randomised trial. *BMJ* 2010;**340**:b4491.
24. Bell S, Porter M, Kitchener H, Fraser C, Fisher P, Mann E. Psychological response to cervical screening. *Prev Med* 1995;**24**:610-6.
25. Cruickshank ME, Anthony GB, Fitzmaurice A, *et al.* A randomised controlled trial to evaluate the effect of self-administered analgesia on women's experience of outpatient treatment at colposcopy. *BJOG* 2005;**112**:1652-8.

26. Barry MM, Van Lente E, Molcho M, *et al.* SLÁN 2007: Survey of Lifestyle, Attitudes and Nutrition in Ireland. Mental Health and Social Well-being Report. Available from: https://www.ucd.ie/t4cms/slan_wellbeing_report.pdf. (Accessed March 25, 2015).
27. Colombo F, Tapay N. Private Health Insurance in Ireland: A Case Study. OECD: Paris, 2004. Available from: http://www.oecd.org/ireland/29157620.pdf. (Accessed March 25, 2015).
28. Lauver DR, Baggot A, Kruse K. Women's experiences in coping with abnormal Papanicolaou results and follow-up colposcopy. *J Obstet Gynecol Neonatal Nurs* 1999;**28**:283-90.
29. Spracklen CN, Harland KK, Stegmann BJ, Saftlas AF. Cervical surgery for cervical intraepithelial neoplasia and prolonged time to conception of a live birth: a case-control study. *BJOG* 2013;**120**:960-5.
30. Castanon A, Brocklehurst P, Evans H, *et al.* Risk of preterm birth after treatment for cervical intraepithelial neoplasia among women attending colposcopy in England: retrospective-prospective cohort study. *BMJ* 2012;**345**:e5174.
31. Lu M, Moritz S, Lorenzetti D, Sykes L, Straus S, Quan H. A systematic review of interventions to increase breast and cervical cancer screening uptake among Asian women. *BMC Public Health* 2012;**12**:413.
32. Moser K, Patnick J, Beral V. Inequalities in reported use of breast and cervical screening in Great Britain: analysis of cross sectional survey data. *BMJ* 2009;**338**:b2025.
33. Johnson CE, Mues KE, Mayne SL, Kiblawi AN. Cervical cancer screening among immigrants and ethnic minorities: a systematic review using the Health Belief Model. *J Low Genit Tract Dis* 2008;**12**:232-41.
34. Sanders G, Craddock C, Wagstaff I. Factors influencing default at a hospital colposcopy clinic. *Qual Health Care* 1992;**1**:236-40.
35. Onyeka BA, Martin-Hirsch P. Information leaflets, verbal information and women's knowledge of abnormal cervical smears and colposcopy. *J Obstet Gynaecol* 2003;**23**:174-6.
36. O'Connor M, Waller J, Gallagher P, *et al.* Understanding women's differing experiences of distress following colposcopy: a qualitative interview study. *Women's Health Issues* 2015; July 17, doi: 10.1016/j.whi.2015.05.009. .
37. Gallo LC, Matthews KA. Understanding the association between socioeconomic status and physical health: do negative emotions play a role? *Psychol Bull* 2003;**129**:10-51.
38. Cotton SC, Sharp L, Little J, Duncan I, Alexander L, Cruickshank ME, et al. Trial of management of borderline and other low-grade abnormal smears (TOMBOLA): Trial design. *Contemp Clin Trials* 2006;**27**:449-71.

Table 1. Socio-demographic, attitudinal and lifestyle characteristics of participants (measured at 4 months post-colposcopy)

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 completed		
Third level (e.g. college, university)	286	67.5
Primary/secondary	138	32.5
Not stated	5	
Employment status		
Employed (working for an employer or self-employed)	306	71.7
Other*	121	28.3
Not stated	2	
Marital status		
Married/cohabiting	199	46.7
Divorced/separated/widowed	36	8.5
Single	191	44.8
Not stated	3	
Nationality		
Irish	386	90.8
Other	39	9.2
Not stated	4	
Have children		
Yes	215	50.6
No	210	49.4
Not stated	4	
Currently pregnant		
Yes*****	17	4.0
No	410	96.0
Not stated	2	
Private health insurance		
Yes	207	48.4
No	221	51.6
Not stated	1	
Smoking status		
Current smoker	140	32.8
Past smoker	134	31.4
Never smoked	153	35.8
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 satisfaction with healthcare	5.0 (1.1)****	-
Ever had an abnormal cervical cytology test result		
Yes	247	58.3
No	177	41.7
Not stated	5	
Ever had a colposcopy examination		
Yes	89	20.8
No	339	79.2
Not stated	1	
Perceived severity of 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	

*Unemployed, retired from employment, unable to work, looking after family/home or student; **Self-reported depression; ***mean is from possible Likert score of 1-10; ****mean is from possible Likert score of 1-7; *****women who were pregnant at the time of the 4-month questionnaire but not pregnant at recruitment (the initial colposcopy appointment); women who were pregnant at recruitment were not eligible to participate in the study

Table 2. Clinical characteristics of participants (measured at 4 months post-colposcopy)

Total	n	%
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
Result unavailable/colposcopy unsatisfactory	129	30.1

*Data from initial colposcopy appointment only and not subsequent colposcopy clinic visits;**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 3. Multivariate analysis of predictors of anxiety over 12 months post-colposcopy: odds ratios (OR), 95% confidence intervals (CI) and Wald test p values

Variable*	Multivariate OR	95% CI	Wald test
Timepoint post-colposcopy			
4 months	1	-	
8 months	1.17	0.88-1.55	
12 months	1.01	0.76-1.34	0.505
Nationality			
Irish	1	-	
Other	2.13	1.13-4.01	0.020
Private health insurance			
Yes	1	-	
No	1.84	1.20-2.84	0.006
History of depression†			
No	1	-	
Yes	2.33	1.51-3.60	<0.001
Satisfaction with life			
Per unit increase[a]	0.67	0.59-0.76	<0.001

*Measured at 4 months post-colposcopy. No. of observations = 996 across 416 individuals; †self-reported depression measured on the 4 month questionnaire. [a]lower score indicates lower satisfaction with life, Likert scale 1 – 10; Completely satisfied = 10; Correlation structure=Unstructured

Table 4. Multivariate analysis of predictors of worries about cervical cancer over 12 months post-colposcopy: odds ratios (OR), 95% confidence intervals (CI) and Wald test p values

Variable*	Multivariate OR	95% CI	Wald test
Timepoint post-colposcopy			
4 months	1	-	
8 months	0.63	0.47-0.83	
12 months	0.57	0.41-0.78	<0.0001
Private health insurance			
Yes	1	-	-
No	1.80	1.25-2.61	0.002
Smoking status			
Current smoker	1	-	
Past smoker	0.52	0.33-0.80	
Never smoked	0.74	0.48-1.15	0.012
Satisfaction with life			
Per unit increase[a]	0.88	0.80-0.96	0.006
Perceived severity of colposcopy exam			
Per unit increase[b]	1.84	1.45-2.33	<0.001

*Measured at 4 months post-colposcopy. No. of observations =1007 across 419 individuals; [a]Likert scale range 1-10; Completely satisfied =10; [b]higher score indicates higher perceived severity, Likert scale 1 – 4; Very serious = 4; Correlation structure = Exchangeable

Table 5. Multivariate analysis of predictors of worries about future fertility over 12 months post-colposcopy: odds ratios (OR), 95% confidence intervals (CI) and Wald test p values

Variable*	Multivariate OR	95% CI	Wald test
Timepoint post-colposcopy			
4 months	1	-	
8 months	0.63	0.45-0.88	
12 months	0.51	0.36-0.73	0.001
Age			
< 30 years	1	-	
30 – 40 years	1.26	0.81-1.96	
> 40 years	0.18	0.06-0.51	0.002
Currently pregnant**			
Yes	1	-	
No	4.17	1.61-10.81	0.003
Smoking status			
Current smoker	1	-	
Past smoker	0.49	0.28-0.86	
Never smoked	0.50	0.30-0.83	0.012

*Measured at 4 months post-colposcopy. No. of observations =599 across 301 individuals; Correlation structure = Independent; **at the time of the 4 month questionnaire.

Supplementary Table 1. Results of univariate analyses for each of the 4 outcomes: odds ratios (OR), 95% confidence intervals (CI) and p values from Chi Square tests

	Anxiety[a]		**Worried about cervical cancer[b]**		**Worried about future fertility[c]**		**Worried about having sex[d]**	
Variable								
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Time-point								
4 months	1	-	1	-	1	-	1	-
8 months	1.14	0.90-1.44	0.67	0.53-0.86	0.67	0.49-0.92	0.59	0.43-0.79
12 months	1.01	0.80-1.28	0.57	0.43-0.75	0.49	0.35-0.68	0.54	0.40-0.75
	p=0.485		p < 0.001		p < 0.001		p<0.001	
Socio-demographic, attitudinal and lifestyle variables								
Nationality								
Irish	1	-	1	-	1	-	1	-
Other	2.05	1.11-3.80	1.52	0.86-2.67	1.29	0.61-2.70	1.40	0.74-2.65
	p=0.022		p = 0.149		p=0.502		p=0.295	
Highest level of education completed								
Third level	1	-	1	-	1	-	1	-
Primary/Secondary level	1.25	0.81-1.91	1.55	1.10-2.19	0.98	0.59-1.65	1.22	0.84-1.78
	p=0.312		p=0.013		p=0.952		p=0.297	
Employment status								
Employed	1	-	1	-	1	-	1	-
Other	1.54	1.00-2.36	1.56	1.08-2.25	0.90	0.54-1.52	1.81	1.24-2.64
	p=0.049		p = 0.017		p=0.704		p=0.002	
Marital status								
Married/living with partner	1	-	1	-	1	-	1	-
Single	0.93	0.61-1.40	1.26	0.89-1.79	1.19	0.78-1.82	1.13	0.78-1.63
Separated/Widowed/Divorced	1.09	0.51-2.35	0.71	0.37-1.36	0.21	0.07-0.62	1.22	0.61-2.45
	p=0.883		p = 0.144		p=0.006		p=0.759	
Age								
< 30 years	1	-	1	-	1	-	1	-
30 - 40 years	0.92	0.58-1.44	0.79	0.53-1.18	1.03	0.66-1.60	0.69	0.45-1.04
> 40 years	0.57	0.34-0.97	0.72	0.47-1.09	0.17	0.07-0.46	0.53	0.34-0.83

	p=0.098		p = 0.258		p=0.001		p=0.018	
Have children								
Yes	1	-	1	-	1	-	1	-
No	0.88	0.59-1.32	0.67	0.48-0.94	1.82	1.17-2.83	0.99	0.70-1.42
	p=0.550		p=0.019		p=0.008		p=0.975	
Currently pregnant								
Yes	1	-	1	-	1	-	1	-
No	1.67	0.52-5.40	2.51	0.78-8.09	3.62	1.49-8.83	0.61	0.27-1.41
	p = 0.391		p = 0.122		p=0.005		p=0.249	
Medical card								
Full medical card	1	-	1	-	1	-	1	-
GP card	1.30	0.50-3.41	0.82	0.32-2.11	0.63	0.18-2.17	0.91	0.39-2.14
None	0.51	0.32-0.80	0.59	0.41-0.87	0.76	0.45-1.28	0.55	0.37-0.82
	p=0.004		p=0.025		p=0.541		p=0.010	
Private health insurance								
Yes	1	-	1	-	1	-	1	-
No	1.83	1.22-2.75	2.16	1.54-3.05	1.18	0.78-1.77	1.67	1.16-2.39
	p=0.003		p < 0.001		p=0.432		p=0.006	
Smoking status								
Current smoker	1	-	1	-	1	-	1	-
Past smoker	0.58	0.36-0.94	0.38	0.25-0.58	0.59	0.35-1.01	0.78	0.50-1.20
Never smoked	0.48	0.30-0.77	0.54	0.36-0.81	0.54	0.33-0.87	0.80	0.52-1.24
	p = 0.006		p <0.001		p=0.030		p=0.460	
History of depression								
No	1	-	1	-	1	-	1	-
Yes	3.61	2.38-5.46	1.55	1.07-2.24	1.40	0.89-2.19	1.31	0.89-1.93
	p < 0.001		p = 0.020		p=0.141		p=0.166	
Satisfaction with life								
Per unit increase*	0.66	0.59-0.74	0.88	0.80-0.97	0.91	0.80-1.03	0.86	0.78-0.95
	p < 0.001		p = 0.008		p=0.135		p=0.004	
Satisfaction with healthcare								
Per unit increase**	0.73	0.61-0.86	0.86	0.74-1.00	0.83	0.68-1.03	0.96	0.81-1.14
	p < 0.001		p=0.047		p=0.085		p=0.663	

Perceived severity of colposcopy exam								
Per unit increase***	1.28	0.97-1.68	1.85	1.48-2.32	1.18	0.90-1.53	1.73	1.35-2.20
	p = 0.083		p<0.001		p=0.228		p<0.001	
Social support: No. of close friends and relatives								
Per unit increase	0.96	0.92-1.00	0.97	0.92-1.01	0.98	0.95-1.02	0.98	0.94-1.02
	p = 0.069		p=0.149		p=0.296		p=0.299	
Ever had an abnormal cytology test result****								
Yes	1	-	1	-	1	-	1	-
No	1.07	0.71-1.60	1.39	0.99-1.96	1.25	0.82-1.89	1.24	0.87-1.78
	p = 0.748		p=0.054		p=0.298		p=0.238	
Ever had a colposcopy†								
Yes	1	-	1	-	1	-	1	-
No	0.74	0.46-1.18	0.93	0.61-1.42	0.87	0.51-1.48	0.96	0.61-1.52
	p = 0.204		p=0.735		p=0.609		p=0.874	
Clinical variables								
Referral cytology test result								
Low grade(borderline, mild)	1	-	1	-	1	-	1	-
High grade (moderate, severe)	1.22	0.77-1.92	1.44	0.98-2.12	0.84	0.48-1.47	1.57	1.05-2.33
Not available								
	p = 0.394		p=0.062		p=0.548		p=0.027	
Colposcopic impression								
Normal	1	-	1	-	1	-	1	-
Abnormal	1.14	0.73-1.77	1.75	1.16-2.63	1.39	0.89-2.17	1.74	1.13-2.69
Unsatisfactory	0.74	0.13-4.07	1.40	0.54-3.60	0.32	0.04-2.54	0.45	0.11-1.75
Not available	1.70	0.60-4.80	1.20	0.43-3.38	1.30	0.25-6.72	1.44	0.41-5.07
	p = 0.723		p=0.058		p=0.286		p=0.021	
Initial management received‡								
Colposcopy plus punch biopsies	1	-	1	-	1	-	1	-
Colposcopy only	0.95	0.60-1.49	0.94	0.62-1.43	0.93	0.58-1.47	0.73	0.47-1.13
Colposcopy plus LLETZ	1.31	0.76-2.27	1.65	1.08-2.52	1.00	0.53-1.88	1.38	0.87-2.19
	p=0.528		p=0.041		p=0.946		p=0.063	

Initial colposcopy histology result								
CIN2+	1	-	1	-	1	-	1	-
CIN 1	1.04	0.60-1.81	0.53	0.33-0.85	0.84	0.48-1.49	0.44	0.26-0.73
No CIN	0.79	0.42-1.49	0.41	0.24-0.69	0.36	0.18-0.75	0.24	0.13-0.45
Result unavailable/colposcopy unsatisfactory	0.80	0.49-1.31	0.52	0.34-0.79	0.71	0.44-1.16	0.41	0.27-0.64
	p = 0.696		p = 0.001		p=0.050		p<0.001	

[a]Correlation structure for anxiety =Unstructured. [b]Correlation structure for worried about cervical cancer=Exchangeable. [c]Correlation structure for worried about future fertility=Independent. [d]Correlation structure for worried about having sex=Exchangeable.

*range on Likert scale 1 - 10; Completely satisfied = 10. **range on Likert scale 1 - 7; Completely satisfied = 7. ***range on Likert scale 1 - 4; Very serious = 4. ****prior to taking part in the study. †prior to taking part in the study.‡ Data from initial colposcopy appointment only and not subsequent colposcopy clinic visits.

Supplementary Table 2. Multivariate analysis of predictors of worries about having sex over 12 months post-colposcopy: odds ratios (OR), 95% confidence intervals (CI) and Wald test p values

Variable*	Multivariate OR	95% CI	Wald test
Timepoint post-colposcopy			
4 months	1	-	
8 months	0.53	0.37-0.75	
12 months	0.57	0.39-0.83	0.001
Age			
< 30 years	1	-	
30 – 40 years	0.62	0.40-0.96	
> 40 years	0.52	0.33-0.82	0.012
Satisfaction with life			
Per unit increase[a]	0.83	0.75-0.92	<0.001
Perceived severity of colposcopy exam			
Per unit increase[b]	1.57	1.22-2.03	0.001
Initial colposcopy histology result			
CIN2+	1	-	
CIN1	0.50	0.30-0.84	
No CIN	0.26	0.14-0.47	
Result unavailable/colposcopy unsatisfactory	0.43	0.27-0.69	<0.001

*Measured at 4 months post-colposcopy. No. of observations =996 across 415 individuals; Correlation structure = Exchangeable; [a]Likert scale range 1-10; Completely satisfied =10; [b]higher score indicates higher perceived severity, Likert scale 1 – 4; Very serious = 4

Supplementary Figure 1. Prevalence and temporal trends of anxiety and specific worries post-colposcopy