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## ARTICLE

# Adverse psychological outcomes following colposcopy and related procedures: a systematic review

Mairead O'Connor<sup>1,\*</sup>, Pamela Gallagher<sup>2</sup>, Jo Waller<sup>3</sup>, Cara Martin<sup>4</sup>, J.J. O'Leary<sup>4</sup>, and L. Sharp<sup>1</sup>, on behalf of the Irish Cervical Screening Research Consortium (CERVIVA)

<sup>1</sup> National Cancer Registry Ireland, Cork Airport Business Park, Kinsale Road, Cork, Ireland

<sup>2</sup> School of Nursing and Human Sciences, Dublin City University, Glasnevin, Dublin 9, Ireland

<sup>3</sup> Health Behaviour Research Centre, Department of Epidemiology and Public Health, University College London

<sup>4</sup> Coombe Women and Infants University Hospital, Dolphin's Barn, Dublin 8, Ireland

\* Corresponding author: Mairead O'Connor, National Cancer Registry Ireland, Building 6800, Cork Airport Business Park, Kinsale Road, Cork, Ireland; Telephone: 021-4548827; E-mail: [m.oconnor@ncri.ie](mailto:m.oconnor@ncri.ie)

## Abstract

**Background:** Although colposcopy is the leading follow-up option for women with abnormal cervical cytology, little is known about its psychological consequences.

**Objectives:** We performed a systematic review to examine: (1) what, if any, are the adverse psychological outcomes following colposcopy and related procedures; (2) what are the predictors of adverse psychological outcomes post-colposcopy; and (3) what happens to these outcomes over time.

**Search strategy:** Five electronic databases (PubMed, PsychINFO, CINAHL, Web of Science, Scopus) were searched for studies published in English during January 1986-February 2014.

**Selection criteria:** Eligible studies assessed psychological wellbeing at one or more time-points post-colposcopy.

**Data collection and analysis:** Two reviewers independently screened titles and abstracts. Full texts of potentially eligible papers were reviewed. Data were abstracted from, and a quality appraisal performed of, eligible papers.

**Main results:** 23 papers reporting 16 studies were eligible. Colposcopy and related procedures can lead to adverse psychological outcomes, particularly anxiety. Ten studies investigated predictors of adverse psychological outcomes; management type and treatment had no impact on this. Seven studies investigated temporal trends in psychological outcomes post-colposcopy; findings were mixed, especially in relation to anxiety and distress. Studies were methodologically heterogeneous.

Conclusions: Follow-up investigations and procedures for abnormal cervical cytology can cause adverse psychological outcomes among women. However, little is known about the predictors of these outcomes or how long they persist. There is a need for a more standardised approach to examining the psychological impact of colposcopy, especially longer-term outcomes.

**Keywords:** systematic review, colposcopy, screening, cervix, adverse psychological outcomes, anxiety

## Introduction

A colposcopy examination is one of the main follow-up options for women who undergo cervical screening and have an abnormal cytology result.<sup>1,2</sup> At colposcopy women may have immediate treatment or have biopsies taken and be recalled later for treatment; clinical practice varies considerably between and within countries, and is often down to the discretion of the clinician. The adverse psychological impact of an abnormal cytology result is well recognised.<sup>3,4</sup> Undergoing colposcopy can also be a distressing experience for women; numerous studies describe raised anxiety levels prior to and during the examination.<sup>5</sup> Evidence is now beginning to accrue that colposcopy and related management procedures, such as punch biopsies and large loop excision of the transformation zone (LLETZ), may be associated with major adverse psychological outcomes for some – and perhaps significant numbers of – women.<sup>6</sup> However, little is known about which types of adverse psychological outcomes are most common, what are the predictors of these adverse psychological outcomes post-colposcopy, or what is their trajectory over time.

A few reviews and overviews on the psychological impact of abnormal cytology, colposcopy and related interventions are available.<sup>7,8</sup> However, these were not systematic and, having been published more than 10 years ago, do not include more recent studies. Moreover, to our knowledge, none focused specifically on women's psychological wellbeing after (rather than before or during) colposcopy and/or related interventions. We, therefore, performed a systematic review to investigate: (1) what, if any, are the adverse psychological outcomes following colposcopy and related procedures?; (2) what are the predictors of adverse psychological outcomes post-colposcopy?; and (3) what happens to these adverse psychological outcomes over time post-colposcopy?

## Methods

### Search strategy

We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in conducting this review and preparing the manuscript.<sup>9</sup> We searched five databases (PubMed, PsychINFO, CINAHL, Web of Science and Scopus) to identify studies reporting psychological impacts of colposcopy and related procedures (henceforth referred to as “colposcopy” for brevity) published during January 1986-February 2014. Combinations of psychological, disease and intervention search terms were used (supplementary Figure S1). Psychological terms included *anxiety, depression, distress, stress, wellbeing, emotion, mental, psychological, psychosocial, psychosexual, quality of life, and emotional states*; disease terms included *cervical smear, pap smear, cytological smear, cervix, cervical, cervical intraepithelial neoplasia, CIN, cancer screening, and neoplasms*; and intervention terms included *colposcopy, conisation, ablation, cryotherapy, large loop excision of the transformation zone, LLETZ, LEEP, loop excision procedure, and laser*. Wildcards and alternative spellings were used where appropriate. Reference lists from papers of eligible studies were checked to identify any potentially eligible articles which might have been missed by the electronic searches. Figure 1 shows the number of papers identified, screened and included.

### Eligibility criteria

Full details of inclusion and exclusion criteria are presented in Table S1. To be included papers had to report on one or more adverse psychological outcome(s) at one or more time-points after colposcopy. Studies that assessed only health-related quality of life (HRQoL) or health utility, the psychological burden of HPV infection, or surrogates of psychological outcomes (such as anxiety assessed by women's need to consult medical staff of clinic for reassurance) were excluded. The assessments had to be conducted at least one day after the colposcopy; studies which assessed women immediately after the procedure and while they were still at the clinic were not eligible.

### Data extraction

Two reviewers (MOC, LS) independently screened titles and/or abstracts of records. Full text versions of papers considered potentially eligible for inclusion were read by both reviewers and their suitability for inclusion independently assessed. The reviewers then compared results and resolved any discrepancies. Data were extracted from each eligible paper on: (1) study location; (2) study design; (3) study population; (4) psychological outcomes assessed (and tools used); (5) assessment time-points; (6) main results; (7) whether the study examined predictors of adverse psychological outcomes post-colposcopy?(and, if so, the findings); and (8) whether the study assessed temporal effects in outcomes (and, if so, the findings).

### Quality appraisal

Full papers of eligible studies were critically appraised by the same two reviewers using a checklist based on established appraisal questions.<sup>10,11</sup> Each paper was assessed on 11 domains. Each domain was marked as "Yes" (Y), "No" (N), or "Partially" (P) based on the details reported in the paper (supplementary Table S2) and scored. One point was assigned for each "Yes"; 0.5 points for each "Partially" and no points for each "No". A score of  $\geq 8$  was considered good quality, 4- 7 adequate quality and  $\leq 3$  poor quality. In addition the two reviewers also independently undertook a detailed critical appraisal of the methodology and reporting for each paper.

### Statistical analysis

The study designs and methods, and the psychological outcomes assessed, were very heterogeneous so no formal statistical attempt was made to combine the findings.

## Results

### Study selection

Initial searches yielded 1385 records, 1105 of which remained after removal of duplicates. 1000 records were excluded on screening of titles/abstracts. The full text of the remaining 105 articles was assessed; following this, 23 papers reporting 16 studies were eligible for inclusion.

### Study characteristics

Of the 16 studies, four were randomised controlled trials, one was a non-randomised trial and 11 were observational studies (Table 1; abbreviated version and Table S3; full-length version). Seven studies were undertaken in the UK, two in Italy, two in The Netherlands and one each in Finland, Sweden, China, Thailand and the USA. Four stated that they included women who had cervical screening within organised programmes; this was unclear for other studies. The length of follow-up post-colposcopy ranged from 1 week to 30 months. A range of different psychological outcomes were assessed using a variety of instruments, some validated and some not. Supplementary Table S4 displays the instruments (and their abbreviations), the outcomes they measured and cut-offs used by the authors to define adverse effects. Response rates to post-colposcopy assessments were reported in eight studies and were 20%-88%. Ten studies (reported in 15 papers) investigated predictors of adverse psychological outcomes, considering a broad range of factors (e.g. age,

management received) (Table 2). Seven studies (eight papers) investigated temporal trends in adverse psychological outcomes post-colposcopy (Table 3). Twelve studies assessed psychological wellbeing at some time before colposcopy (or treatment) as well as post-colposcopy.

#### Paper quality

20 papers scored  $\geq 8$  (good quality) and three papers scored in the range 4-7 (adequate quality). No papers were considered poor quality (Supplementary Table S2). Several weaknesses were identified on the further, detailed, critical appraisal of the studies. For example, some studies used non-validated instruments to assess adverse psychological outcomes in some studies. Some assessed psychological “outcomes” prior to receipt of colposcopy and biopsy results; this could impact on women’s subsequent psychological wellbeing. For most studies the authors failed to provide any rationale for the choice of the time-points at which to assess outcomes. In those studies which assessed sexual/psychosexual functioning, the distinction between sexual and psychosexual functioning was often unclear: for example, some studies claimed they assessed psychosexual functioning but in fact, most, if not all, of the questions in the instruments were on physical aspects of sexual functioning.

#### Methodological heterogeneity

Several sources of heterogeneity between studies were evident. The timepoints for the outcome assessments varied considerably among the studies. A diverse range of instruments was used to assess the adverse psychological outcomes. The location at which women completed the assessments varied: in some studies women were mailed the instruments to complete at home; in other studies women completed the instruments while at the colposcopy clinic; in other studies again women completed instruments at home at some timepoints and at the clinic at other timepoints.

#### Adverse psychological outcomes following colposcopy

*Anxiety:* Nine studies (16 papers) reported on anxiety in women after colposcopy (or treatment) (Table 1 and Table S3). Six studies (nine papers) measured post-colposcopy state anxiety using the STAI (Spielberger State-Trait Anxiety Inventory).<sup>12-21</sup> Of these, one reported that 60% of women scored  $\geq 35$ ,<sup>14</sup> the cut-off often used to define anxiety; another that 18% of women had high anxiety (defined as  $>44$ ) at the first time-point post-colposcopy<sup>21</sup>; and a third that the mean anxiety score among women who had undergone colposcopy was higher than the norm for adult women (defined as  $>36.2$ ).<sup>20</sup> A further three studies reported prevalence of anxiety post-colposcopy using various instruments; this was 8%-29%.<sup>15,22-26</sup> In one of these studies,<sup>22-25</sup> from the UK, prevalence post-colposcopy was lower than reported among the UK general female population but in another UK study it was higher.<sup>26</sup> Three studies compared mean anxiety post-colposcopy to that among a control group; in all three, prevalence was higher in women who had had colposcopy.<sup>15,18,19,27</sup> Eight studies compared anxiety at some point before colposcopy (or treatment) with that afterwards; of these, seven reported lower anxiety at the first post-colposcopy assessment than pre-colposcopy and, in two of these, the difference was statistically significant.<sup>19,22,23</sup> In the eighth study, anxiety levels did not change before and after colposcopy.<sup>16</sup>

*Depression:* Depression post-colposcopy was reported in five studies (seven papers), assessed using different instruments (Table 1 and Table S3). Prevalence at the first assessment time-point post-colposcopy ranged from 7% to 22%.<sup>15,22-24,28</sup> In the three studies with external control groups, depression was higher among women post-colposcopy than in the control group.<sup>15,18,27</sup> Four studies compared depression pre- and post-colposcopy and in three, depression was lower at the first time-point post-colposcopy.<sup>15,19,27</sup> In the fourth study, depression was slightly higher (but not significantly higher) at the first time-point post-colposcopy compared to the pre-colposcopy assessment.<sup>23</sup>

*Distress:* Four studies (six papers) measured distress post-colposcopy, using different instruments (Table 1 and Table S3). One reported that one-third of women had procedure-related distress at the first assessment time-point.<sup>6,22</sup> Two studies used the 28-item General Health Questionnaire (GHQ)<sup>29</sup> and, in both, mean GHQ scores at the first post-colposcopy assessment were below the usual cut-off for psychiatric distress.<sup>15,30</sup> In the three studies which also conducted pre-colposcopy assessments, distress was lower at the first assessment post-colposcopy compared to pre-colposcopy.<sup>15,23,30</sup>

*Worries/fears about cancer and future fertility:* In the single available study, just over one-quarter of women were afraid of cancer and close to one-third had fears about future infertility at the first time-point post-colposcopy.<sup>19</sup> These proportions were considerably lower than the proportions reporting these fears pre-colposcopy (Table 1 and Table S3).

*Sexual/psychosexual functioning:* Seven studies (seven papers) assessed some aspect of sexual/psychosexual functioning post-colposcopy (Table 1 and Table S3). One used a validated instrument, the Female Sexual Function Index (FSFI)<sup>31</sup> and reported that the mean total FSFI score post-colposcopy was above the cut-off for female sexual disorder.<sup>32</sup>

Five studies compared pre- with post-colposcopy sexual/psychosexual functioning. Across a range of measures including sexual desire, sexual enjoyment/satisfaction, negative feelings about sex, frequency of intercourse, pain and lubrication during sex, results of the different studies were conflicting, with no consistent pattern of impact emerging.<sup>15,18,20,32,33</sup>

**Predictors of adverse psychological outcomes following colposcopy**

The 10 studies (reported in 15 papers) which investigated predictors of adverse psychological outcomes varied in the characteristics and factors examined.

*Anxiety:* Six studies (11 papers) examined whether post-colposcopy anxiety differed between subgroups (Table 2). Three studies of management received and post-colposcopy anxiety reported conflicting results; in two,<sup>17-19,23,24</sup> management received was unrelated to anxiety post-colposcopy while in the other, anxiety was lower in women treated immediately compared to those who were recalled for treatment.<sup>13,14</sup> In two studies, women with CIN2+ had higher anxiety scores than other women post-colposcopy.<sup>14,21</sup> In one study, lower socio-economic status was associated with higher anxiety levels post-colposcopy.<sup>14</sup> One study reported that women who had particularly adverse responses to their initial abnormal cytology result were at significantly greater risk of anxiety post-colposcopy,<sup>15</sup> and another found that risk was significantly higher in women with higher fears about cancer and future fertility pre-colposcopy.<sup>19</sup>

*Depression:* Three studies (six papers) assessed whether post-colposcopy depression varied between women (Table 2). In two, management received and whether or not treatment was performed were unrelated to subsequent depression levels.<sup>17,19,23,24</sup> In the other, risk of depression was significantly higher in women who had a particularly adverse response to their initial abnormal cytology test result.<sup>15</sup>

*Distress:* Two studies (three papers) investigated whether post-colposcopy distress differed between subgroups (Table 2). In one study, procedure-related distress was twice as common in women with (compared to those without) an abnormal transformation zone at colposcopy, and, in those with an abnormal transformation zone, risk of distress was raised in women with CIN2+ compared to other women. This study also found that lack of satisfaction with support following receipt of the abnormal cytology result was associated with distress six weeks post-colposcopy in women with a normal transformation zone,<sup>6</sup> while the other study reported that lack of social support and more negative life events were related to longer-term distress.<sup>34</sup>

*Worries/fears about cancer and future fertility:* No studies examined which women were at greater risk of having worries about cancer and future infertility post-colposcopy.

*Sexual/psychosexual functioning:* Four studies (four papers) examined whether particular women were at greater risk of experiencing adverse effects on their sexual or psychosexual functioning post-colposcopy (Table 2). In one study, type of treatment (LEEP or laser vaporisation) was unrelated to risk of these outcomes.<sup>35</sup> One study reported that the adverse psychosexual effects after undergoing treatment by LEEP may be worse for postmenopausal than premenopausal women,<sup>36</sup> but another found that age was unrelated to sexual/psychosexual functioning following treatment by LEEP.<sup>32</sup>

What happens to adverse psychological outcomes over time post-colposcopy?

Of the seven studies (eight papers) which examined the temporal pattern of psychological outcomes post-colposcopy, four assessed women at two time-points, one assessed women at three time-points and two assessed women at five time-points (Table 3).

*Anxiety:* Five studies (six papers) examined the temporal pattern of anxiety post-colposcopy (Table 3), with heterogeneous findings. Three studies reported lower anxiety levels (or prevalence) at the second (3 months, 8 months and 2 years, respectively for the three studies) than the first time-point (1 month for two studies and 6 months for the third study) post-colposcopy;<sup>15,18,19,21</sup> in one of these studies anxiety scores fell significantly over time.<sup>19</sup> The fourth study reported no change in mean anxiety scores between 6 months and 12 months post-colposcopy<sup>16</sup> and, in the fifth, the prevalence of anxiety increased significantly from the first (6 weeks) to the second time-point (12 months) post-colposcopy and remained stable at 18, 24 and 30 months.<sup>23</sup>

*Depression:* Three studies (three papers) investigated temporal trends in depression post-colposcopy (Table 3). Depression scores/levels did not change substantially over time in any study.

*Distress:* Four studies (four papers) measured distress over time post-colposcopy. The level of distress declined over time in three studies,<sup>15,23,30</sup> while in the other,<sup>34</sup> it rose slightly at the second time-point post-colposcopy compared to the first before declining at the third, fourth and fifth time-points (Table 3).

*Worries/fears about cancer and future fertility:* In the one available study, prevalence of cancer fears changed little between 6 months and 2 years post-colposcopy (26% and 30%, respectively). Fears about future infertility decreased over the same time (from 31% to 20%).<sup>19</sup>

*Sexual/psychosexual functioning:* The single study which described temporal patterns in sexual/psychosexual functioning found different patterns depending on the specific outcome considered (Table 3). For example, 'frequency of sex' and 'lubrication' scores increased slightly over time, 'spontaneous interest in sex' and 'orgasm' scores did not change.<sup>18</sup>

## **Discussion**

### **Main findings**

This systematic review, which included 23 papers reporting 16 separate studies, is the first to examine adverse psychological outcomes following colposcopy and related procedures. There was broad agreement among the studies that colposcopy can lead to adverse psychological outcomes for some women. Ten studies examined predictors of these outcomes. From the limited data available, management and treatment factors did not appear to affect the risk of adverse psychological outcomes, although women with CIN2+ may be at increased risk. Seven studies investigated what happens to adverse psychological outcomes over time post-colposcopy, with mixed results, particularly in relation to anxiety

and distress. Methodological heterogeneity between studies (e.g. diversity of instruments used, various different timepoints for assessment of outcomes) and weaknesses in design and reporting of individual studies made the adverse psychological outcomes difficult to quantify precisely; hence, although there are 23 papers on this topic, the exact magnitude of psychological impact specific to colposcopy (and/or related procedures) remains unknown.

#### Strengths and limitations

We followed recommended practice for conduct and reporting of systematic reviews.<sup>9</sup> Although we searched multiple databases, the possibility cannot be entirely excluded that relevant papers might have been missed. Another limitation is the absence of formal statistical combination of study results, but this was precluded by methodological heterogeneity. In addition, we did not consider 'positive' psychological outcomes (e.g. reassurance), but very few studies have reported on these.<sup>13,14</sup> Although HPV testing has been introduced in the post-treatment setting in several countries,<sup>37-39</sup> we did not consider HPV in this review largely because quantitative data has yet to emerge on whether HPV testing in this context impacts psychological wellbeing. Moreover, despite the changes in screening protocols internationally, colposcopy remains central to the management and follow-up of women with abnormal screening test results.

#### Interpretation

This review suggests that undergoing colposcopy (and related procedures) can result in adverse psychological consequences for some women. Anxiety appears to be the most prominent outcome, with several studies suggesting higher levels post-colposcopy than population norms or control groups. However, although anxiety has been investigated more extensively than any other aspect of wellbeing, uncertainties remain in part due to limitations in study design. For example, two of the eight relevant studies measured anxiety one week following colposcopy<sup>13,14,27</sup> when women who had undergone biopsy would still be waiting for results. As anxiety is a consequence of uncertainty,<sup>40</sup> it is likely that the anxiety levels in these two studies were strongly influenced by the timing of the psychological assessment. In one study<sup>13,14</sup>, women who underwent immediate treatment were compared to women who had biopsies and were recalled for treatment if necessary; the psychological assessment was conducted one-week post-colposcopy. The study found that the women who underwent immediate treatment were significantly less anxious (and less embarrassed and more relieved) than other women, suggesting that that immediate treatment for abnormal cervical cytology may avoid certain adverse psychological outcomes. However, a randomised controlled trial of the immediate treatment versus biopsy and recall found no difference in anxiety over the longer-term between the two policies.<sup>23,24</sup>

The evidence also suggests that other adverse psychological outcomes may be common post-colposcopy. For example, high proportions of women appear to experience procedure-related distress after colposcopy, but this was only measured in one study (albeit a large population-based study).<sup>6,22</sup> However, given the evidence that women can find undergoing the procedures stressful, painful and embarrassing,<sup>41-43</sup> this finding seems plausible. There is also limited evidence that women may have fears about cancer and future infertility after colposcopy. However, these findings are also from one study, which included only 100 women, meaning the estimates of prevalence of worries are rather imprecise. Still, they are consistent with emerging qualitative work which shows that women long-term distress after colposcopy is predominately related to concerns about fertility, cervical cancer and sexual intercourse.<sup>44</sup>

Another striking finding is that surprisingly few studies looked at risk factors for experiencing adverse psychological outcomes, although such information seems essential to inform the development of interventions to alleviate adverse effects. In addition, the identification of potential predictors of post-colposcopy anxiety and distress is needed to help clinicians and other medical professionals better support and monitor the more 'at-risk' women attending

colposcopy clinics. A few positive associations were reported (e.g. women with CIN2+ had higher anxiety scores than other women post-colposcopy) but most of these were seen in single (or at the most two) studies<sup>13,14,21</sup> and require confirmation. Moreover, most of the studies failed to take into account the fact that the risk factors considered may be inter-related and only reported univariate results.

Understanding the temporal trajectory of psychological wellbeing post-colposcopy is also crucial to inform the development of interventions. Overall, depression does not appear to vary greatly after colposcopy;<sup>15,19,23</sup> temporal trends in anxiety and distress were inconclusive,<sup>15,16,18,19,21,23,30,34</sup> and changes in sexual/psychosexual functioning varied depending on the specific outcome considered.<sup>18</sup> However, all of these conclusions must be viewed as preliminary given the relatively few relevant studies. Moreover, studies conducted assessments at very different time-points post-colposcopy (usually determined, as far as we can tell, pragmatically by the authors); only two conducted assessments at more than two time-points;<sup>21-23,25,34</sup> and none followed women for more than 30 months. Of particular note, no studies investigated whether the adverse psychological outcomes persisted over time for the same women or whether it was different women affected at different time-points; this is an important gap in the literature.

Although not the focus of this review, it was notable that most studies reported data which permitted the comparison of psychological wellbeing at some point pre-colposcopy and post-colposcopy. In most instances, adverse effects declined after the colposcopy. It is plausible that undergoing some form of follow-up investigation for abnormal cytology provides reassurance that may resolve some of the anxiety and uncertainty women experience following receipt of an abnormal cytology result. Moreover, it seems likely that anxiety induced by receipt of abnormal cytology results is resolved in (at least some of) those women who receive a 'normal' colposcopy result. However, recently published findings suggest that notable proportions of women with a normal colposcopy experience long-term adverse psychological outcomes.<sup>45</sup>

It was particularly noteworthy that a diverse range of instruments were used to assess psychological outcomes. Indeed some authors developed their own questionnaires despite the fact that validated instruments are available; it is unclear the extent to which these self-developed instruments were validated, or psychometric properties assessed, prior to use. In addition, there was considerable variation in the cut-offs used for some instruments, with some studies choosing arbitrary cut-offs to define/categorise women with a particular outcome. Most studies used generalised or generic measures of outcomes (e.g. STAI, HADS, MADRS-S<sup>12,46,47</sup>), rather than focussing on more specific outcomes such as fears about cancer, concerns about fertility and impact on sexual relationships which have been reported in women who have abnormal cytology tests and follow-up.<sup>3,4</sup> The exceptions to this were the study by Hellsten and colleagues<sup>19</sup> (which considered fears of cancer and future fertility) and the TOMBOLA trial,<sup>6,23</sup> which developed an instrument to measure context-specific distress (i.e. distress associated specifically with having an abnormal cytology result and undergoing follow-up).<sup>48</sup> Development of a more standardised approach to assess post-colposcopy outcomes would help both advance knowledge in this area and inform interventions.

Beyond the issue of outcome assessment, methodological heterogeneity was pronounced and makes it difficult to generalise the study findings to women who attend colposcopy clinics within organised screening programmes. Only four studies indicated clearly that study participants had participated in organised screening programmes.<sup>6,13,14,17-19,21-25</sup> Several studies took place in a single colposcopy clinic/hospital<sup>15-20,26,27,39,32,33</sup> and a few others involved multiple clinics in the same town/city;<sup>13,14,28</sup> it is possible that women attending these clinics may not be representative of the entire population attending colposcopy. In general, source populations from which participants were recruited were poorly described.

Several studies had small sample sizes; seven of 16 included  $\leq 100$  women<sup>17-19,20,27,28,32-34</sup> and only two included  $\geq 500$  participants.<sup>6,14,22-25</sup> Response/participation rates were often unclear.<sup>20,35,36</sup> In those studies that reported response rates, they varied greatly.<sup>14-16,20-26,28</sup> In addition, only a few studies provided information on non-participants (n=6).<sup>6, 13,14,23-26, ,28,30,34</sup>

## Conclusions

This review suggests that women can experience adverse psychological outcomes following colposcopy and related procedures, particularly anxiety. It has also identified significant gaps in the literature. In particular, there is uncertainty about the exact magnitude of these adverse outcomes, their duration, and the factors that may place some women at increased risk. The methodological heterogeneity in the evidence-base indicates the need for a more standardised approach. Future work might usefully focus on the identification of appropriate timepoints for assessing adverse psychological outcomes and on developing consensus on a standardised assessment tool. Psychological burden is an important cost of cervical screening and merits further investigation.

## Disclosure of interests

The authors have no conflicts of interest to declare.

## Contribution to Authorship

M O'C. search strategy, literature search and review; screened articles, data extraction and interpretation; drafting the manuscript. P.G. developed search strategy, literature search, data interpretation and critical review of manuscript. J.W. data interpretation and critical review of manuscript. L.S. obtained funding; developed search strategy, screened articles, data extraction, and critical review of the manuscript. CM, obtained funding, and critical review of the manuscript. JJO'L: obtained funding and critical review of the manuscript.

## Details of ethics approval

Not applicable

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### **Supporting Information**

Additional Supporting Information may be found in the online version of this article:

Figure S1. Search strategies for the five databases

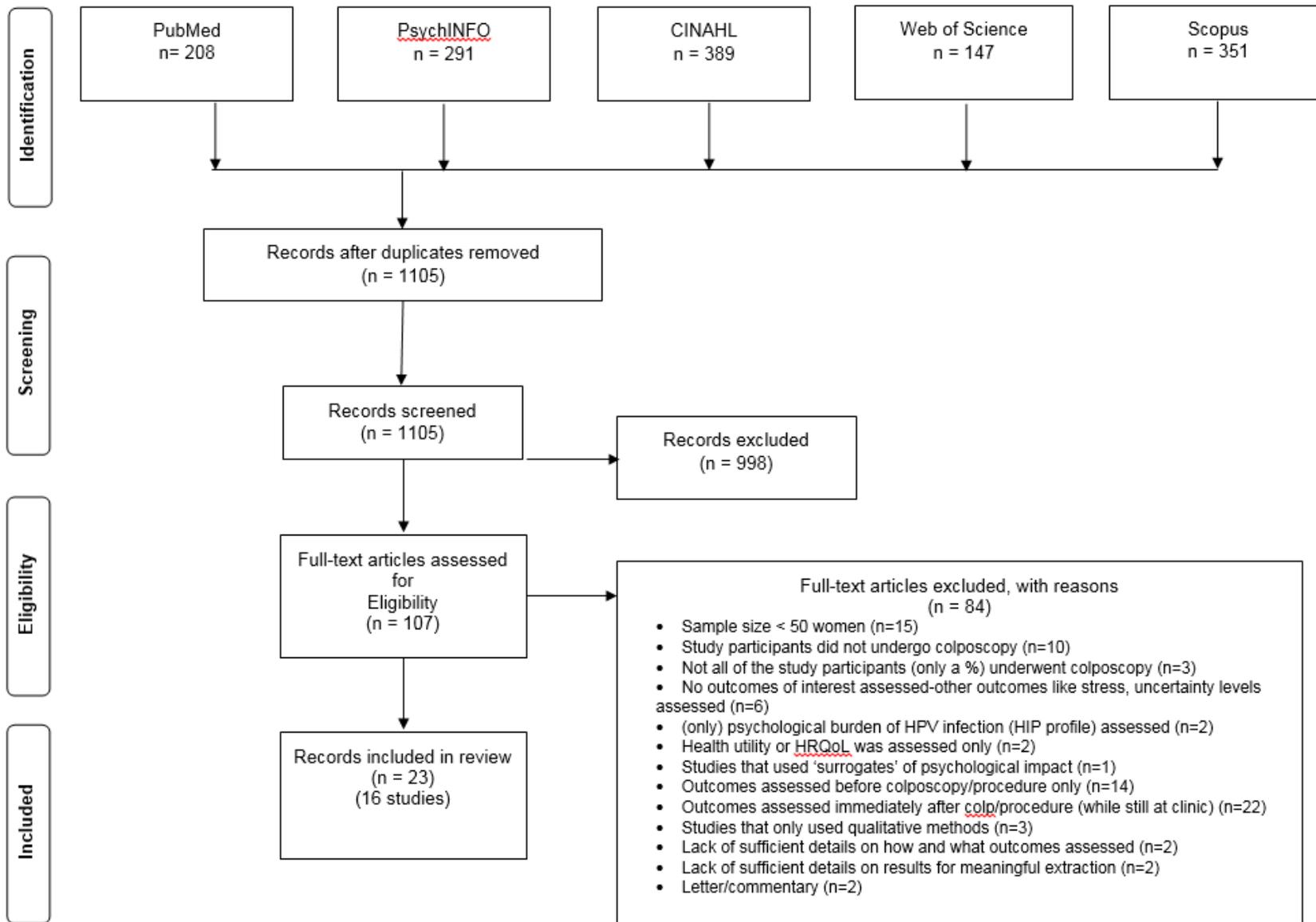
Table S1. Inclusion and exclusion criteria

Table S2. Quality appraisal of included papers

Table S3. Characteristics of included studies and papers

Table S4. Instruments (and their) abbreviations, outcomes they measured and cut-offs used by various authors

**Figure 1.** Flow diagram of study selection



**Table S1.** Inclusion and exclusion criteria

	<b>Inclusion Criteria</b>	<b>Exclusion Criteria</b>
Population	Sample size > 50 women for whom outcome data was available	Women with invasive or microinvasive cervical cancer Pregnant women HIV+ women or women with AIDS
Intervention	Women who had undergone colposcopy, or an investigation/procedure normally preceded by colposcopy (e.g. punch biopsy, LLETZ, cold coagulation)	Women who underwent other gynaecological procedures (e.g. hysteroscopy, telecolposcopy) only and did not have colposcopy. Women who underwent other gynaecological procedures and colposcopy were eligible for inclusion Women who had indications for colposcopy (i.e. abnormal cytology) but did not undergo colposcopy
Outcomes	Anxiety, depression or distress Worries/concerns/fears about fertility or cervical cancer Sexual/psychosexual functioning	Health utility (e.g. as assessed by generic preference instruments like EQ-5D), general health-related quality-of-life (e.g. as assessed by 15D HRQoL) Psychological burden of HPV infection (e.g. as assessed by HPV Impact Profile (HIP)) Surrogates of psychological outcomes (e.g. anxiety assessed by women's need to consult medical staff of clinic for reassurance)
Study design	Cross-sectional and prospective studies Control group of RCTs of colposcopy-related interventions (e.g. self-administered analgesia, information leaflets) Outcome(s) were assessed ≥1 day after colposcopy Outcome(s) were assessed outside of colposcopy clinic setting Outcome(s) were assessed by quantitative methods (e.g. surveys or interviews with structured questionnaires)	Assessment of outcome(s) involved women recalling how they had felt at some point in the past (i.e. not around the time of questionnaire/instrument completion) Outcome data collected for some or all women at a post-colposcopy clinic visit(s) Studies that only used qualitative methods (e.g. semi-structured or open interviews)
Reporting	Studies must report sufficient detail on how and what outcomes were assessed Studies must report sufficient detail on results for meaningful data extraction Full-text English language papers that report primary data and are published in peer-reviewed journals	Studies which included a sub-group of women who had colposcopies but the results of the sub-group are not reported Letters, HTAs, systematic reviews, reviews, overviews, commentaries

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**Table S2.** Quality appraisal\*of included papers (n=23)

Domains/questions**	Balasubramani et al. 2007	Orbell et al. 2004	Bell et al. 1995	Cruickshank et al. 2005	Gath et al. 1995	Gianella et al. 2012	Heinonen et al.2013	Hellsten et al. 2009	Hellsten et al. 2008a	Hellsten et al. 2008b	Howells et al. 1999	Inna et al. 2010	Kitchener et al. 2004	Korfage et al. 2014	Savard et al. 1999	Serati et al. 2010	Sharp et al. 2013a	Sharp et al. '2013b	Sharp et al. 2011	TOMBOLA Group 2009a	TOMBOLA Group 2009b	Sun et al. 2012	Tiersma et al. 2005
1. Clearly stated aims	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Participant eligibility and recruitment strategy clearly documented	P	Y	Y	Y	P	Y	P	P	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	P
3. Main features of population (and participants) and study design described	P	P	Y	Y	Y	Y	N	Y	P	Y	Y	Y	P	Y	P	Y	Y	Y	Y	Y	Y	Y	P
4. Non-responders (and non-participants) described	Y	Y	Y	Y	N	N	N	P	P	P	Y	N	Y	N	N	N	P	Y	P	P	P	N	P
5. Presence of a control group***	N	N	Y	N	Y	N	N	P	Y	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N
6. Main limitations identified	P	Y	P	P	N	Y	Y	N	N	N	N	Y	P	Y	Y	Y	Y	Y	Y	Y	Y	N	P
7. No evidence of selective reporting of results <sup>‡</sup>	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
8. Statistical methods described	P	P	Y	Y	P	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Statistical methods appropriate <sup>‡‡</sup>	Y	Y	P	P	P	Y	P	P	P	P	P	P	Y	Y	Y	P	Y	Y	Y	Y	Y	P	Y

10. Psychological outcome measures relevant, validated and described adequately	Y	Y	Y	Y	Y	P	Y	Y	P	P	P	P	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
11. Results discussed adequately†	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Total score</b>	8	9	10	9	7.5	8.5	7	8	8	8.5	8	8	9	10	8.5	8.5	9.5	10	9.5	9.5	9.5	7.5	8

\*Adapted from 'The pocket guide to critical appraisal' by Crombie,1996 and Jefferies et al. 2012

\*\*The range of possible responses to each domain/question was "Yes (Y)", "No (N)", "Partially (P)". Questions were only assigned a "Yes" (and a score of 1) if the detail necessary to fully answer the question was provided in the article; where the domain/question was dealt with to some extent, we assigned a response of "Partially" (and a score of 0.5). "No" was assigned a score of 0. \*\*\*e.g. women in general pop or women undergoing routine smear with normal result. ‡e.g. non-significant results described and discussed sufficiently. ††e.g. multivariate analysis conducted where possible and appropriate. †e.g. inconsistencies in results explained, all relevant important outcomes considered.

**Table 3.** Studies and papers that assessed what happens to these adverse psychological outcomes over time post-colposcopy

Outcome & instruments	Study/paper	Length of follow-up*	Main results
<b>Anxiety</b>			
PSE(PSE syndromes-situational anxiety and general anxiety), Leeds anxiety scale, STAI	Gath et al. 1995	8 months	<ul style="list-style-type: none"> <li>Anxiety scores on all instruments were lower at 8 months post-colposcopy than at 4 weeks post-colposcopy</li> <li>The percentages of women with situational anxiety and general anxiety were lower at 8 months than at 4 weeks post colposcopy</li> </ul>
STAI	Heinonen et al. 2013	12 months	<ul style="list-style-type: none"> <li>Mean state anxiety score did not differ at 6-months post-colposcopy (34) and 12-months post-colposcopy (34)</li> </ul>
STAI	Hellsten et al. 2008a; 2008b	24 months	<ul style="list-style-type: none"> <li>Mean state anxiety scores fell significantly (P=0.02) from 6 months to 24 months (2 years) post-colposcopy (37 vs 35), and were comparable to Swedish normative data</li> <li>Mean trait anxiety score at 2 years post-colposcopy was 35 (vs 38 at pre-colposcopy assessment)</li> </ul>
STAI-6, PCQ	Korfage et al. 2014	6 months	<ul style="list-style-type: none"> <li>14% had high anxiety levels at 3 and 6 months post-colposcopy compared to 18% at 1 month post-colposcopy. STAI scores fell significantly over time (p&lt;0.001)</li> <li>Screen-specific anxiety (PCQ) scores fell significantly over time (p&lt;0.001)</li> </ul>
HADS anxiety subscale	Sharp et al. 2011	30 months	<ul style="list-style-type: none"> <li>Prevalence of significant anxiety rose significantly (P&lt;0.001) from 8% 6 weeks post-procedure to 14% at 12-months and was 15% at 18-months, 16% at 24-months, and 14% at 30-months</li> </ul>
<b>Depression</b>			
Beck depression inventory, Leeds depression scale, PSE(PSE syndrome-somatic features of depression)	Gath et al. 1995	8 months	<ul style="list-style-type: none"> <li>Depression scores on all instruments were lower at 8 months post-colposcopy than at 4 weeks post-colposcopy</li> <li>The percentages of women with somatic features of depression was lower at 8 months post-colposcopy than at 4 weeks post-colposcopy</li> </ul>
MADRS-S	Hellsten et al. 2008b	24 months	<ul style="list-style-type: none"> <li>Mean depression scores did not change between 6-months and 2-years post-colposcopy (mean MADRS-S score 6 months post-colposcopy=7.8; mean score 2 years post-colposcopy=7.1)</li> </ul>
HADS depression subscale	Sharp et al. 2011	30 months	<ul style="list-style-type: none"> <li>Prevalence of significant depression rose slightly from 7% at 6-weeks post-procedure (7%) to 8% at 12-months, remained at that level at 18-months (8%), rose slightly at 24-months (11%) and fell slightly at 30-months (10%)</li> </ul>
<b>Distress</b>			
GHQ-28	Gath et al. 1995		<ul style="list-style-type: none"> <li>Mean total GHQ score was lower at 8 months post-colposcopy than at 4 weeks post-colposcopy (1.73 v 2.59)</li> </ul>
GHQ-28	Kitchener et al. 2004	12 months	<ul style="list-style-type: none"> <li>Mean GHQ score was lower at 12-months than at 6-months post-colposcopy (2.28 vs 2.89)</li> </ul>
POSM	Sharp et al. 2011	30 months	<ul style="list-style-type: none"> <li>The median POSM score fell from 31 at recruitment to 25 at 12-months, 24 at 18-months, 23 at 24-months, and 23 at 30-months. It fell significantly (P&lt;0.001) from 12 months post-recruitment to 18-months post-recruitment and stabilised thereafter</li> </ul>
POMS	Tiersma et al. 2005	27 months	<ul style="list-style-type: none"> <li>mean total distress score fell from baseline (diagnosis of CIN1/2) to 3-months post-diagnosis (mean distress score=29), rose slightly at 9-months (mean distress score approx 30), then declined at 15-, 24- and 30-months</li> </ul>
<b>Sexual/psychosexual functioning</b>			
Psychosexual questionnaire	Hellsten et al. 2008a	24 months	<ul style="list-style-type: none"> <li>Mean 'frequency of sex' was slightly higher at 2 years compared to 6 months post-colposcopy (3.4 v 3.3). Mean 'spontaneous interest in sex' score was the same at 2 years as it was at 6 months (2.9). Mean 'lubrication' score was slightly higher at 2 years compared to 6 months (3.4 vs 3.3). Mean 'Dyspareunia' score was slightly lower at 2 years compared to 6 months (1.0 v 1.1). Mean 'orgasm' score was the same at 2 years as it was at 6 months (2.7)**</li> <li>The mean score on the 'negative feelings' about sex subscale of the psychosexual questionnaire at 2 years was 0.8, a slight decrease from 1.0 at 6 months post-colposcopy</li> </ul>
<b>Worries/fears about cancer and future fertility</b>			
Authors own questions	Hellsten et al. 2008b	24 months	<ul style="list-style-type: none"> <li>Percentage reporting fear of cancer was slightly higher at 2 years (30%) than at 6-months (26%)</li> <li>Percentage reporting fear of future infertility fell between 6-months and 2-years (31% vs 20%)</li> </ul>

\*Length of entire follow-up (including pre-colposcopy/baseline assessments where relevant). \*\* authors did not perform analysis for comparisons between 6 months and 2 years post-colposcopy scores.

**Table S4.** Instruments (and their) abbreviations, outcomes they measured and cut-offs used by various authors

<b>Abbreviation</b>	<b>Instrument</b>	<b>Outcome(s)</b>	<b>Cut-off used to define adverse effect in included papers</b>
BDI	Beck Depression Inventory	Depression	Score of $\geq 14$ indicates mild depression(Gath et al. 1995)
EORTC-QLQ-CX24	The European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire cervical cancer module	Disease-specific and treatment-specific aspects of QoL in patients with cervical cancer Outcomes of interest are subscales (e.g. Sexual functioning, sexual activity, sexual worry, sexual enjoyment)	Authors did not use any cut-off(Sun et al. 2012)
FSFI	Female Sexual Function Index	Female sexual functioning	Authors did not use any cut-off (Serati et al. 2010)*
GHQ-28	28-Item General Health Questionnaire	Distress	A score of $>4$ indicates psychiatric caseness(Kitchener et al 2004): a score of $>5$ psychiatric morbidity(Gath et al 1995). For the purposes of this review mean/overall GHQ scores were looked at to define distress and not 'psychiatric caseness' scores
HADS	Hospital Anxiety and Depression Scale	Anxiety and depression	Score of $\geq 11$ indicates significant anxiety; score of $\geq 8$ indicates significant depression; measures clinically significant anxiety and depression(Bell et al 1995**, Cruickshank et al 2005; Sharp et al 2013a; Sharp et al., 2013b; Sharp et al., 2011; TOMBOLA Group, 2009a; TOMBOLA Group 2009b, UK )
IES	Impact of Event Scale	Procedure-related distress	Score of $\geq 9$ indicates significant distress(Sharp et al. 2013b; Sharp et al. 2011)
Leeds anxiety scale	Leeds anxiety scale	Anxiety	Score of $>6$ indicates anxiety(Gath et al. 1995)
Leeds depression scale	Leeds depression scale	Depression	Score of $> 6$ indicates depression(Gath et al. 1995)
MADRS-S	Montgomery-Åsberg Depression Rating Scale	Depression	Score of $< 12$ 'normal', 12 - 20 'mild depression', $>20$ 'moderate to severe

			depression'(Hellsten et al 2009;2008b)
PCQ	Psychological Consequences Questionnaire	Screen-specific anxiety	Authors did not use any cut-off. Overall PCQ score ranges from 0 -36; higher scores indicate more dysfunction (Korfage et al. 2014)
POMS	Profile of Mood states	Distress	Authors did not use any cut-off(Tiersma et al. 2005)
POSM	Process Outcome Specific Measure	Context-specific distress	Score of $\geq$ median score used as cut-off(Sharp et al 2013a, Sharp et al. 2011)
PSE	Present State Examination	PSE syndromes measure situational anxiety, somatic features of depression, and general anxiety	Authors measured the prevalence of these syndromes & compared to a local community sample (Gath et al. 1995)
SCID	Structured Clinical Interview for DSM-III-R	Depression	Criteria for depression according to DSM-III-R <sup>‡</sup> (Savard et al. 1999)
STAI	Spielberger State-Trait Anxiety Inventory	Anxiety	Score of >35 indicates anxiety(Balasubramani et al 2007; Orbell et al. 2004;Heinonen et al. 2013; in one study authors compared the mean scores to mean STAI score of 36.2 for normal adult women(Howells et al. 1999) <sup>‡‡</sup>
STAI-6	Six item short form Spielberger State-Trait Anxiety Inventory	Anxiety	Score of >44 was used to identify individuals who were highly anxious (Korfage et al. 2014)

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\*a score of  $\leq$  26.55 indicates female sexual disorder(Ref: Wiegel M, et al. J Sex Marital Ther. 2005;31:1-20).\*\* Bell et al 1995 used a score of  $\geq$ 11 to indicate significant depression. †Williams JBW, Gibbon M, First MB, Spitzer RL, Davies M, Borus J, Howes MJ, Kane J, Pope HG, Rounsaville B, Wittchen HU. The Structured Clinical Interview for DSM-III-R (SCID). II. Multisite test-retest reliability. Arch Gen Psychiatry 1992;49:630–6. ‡‡Gath et al 1995, Hellsten et al 2009,2008a;2008b did not use any cut-off score for measuring anxiety using the STAI but instead compared the mean STAI scores to the scores of control/reference groups.

**Figure S1.** Search strategies for the five databases

a) *PubMed*

((((((((((((anxiety[MeSH Terms] OR anxiety) OR depression[MeSH Terms]) OR depression) OR distress) OR wellbeing) OR emotion[MeSH Terms]) OR emotion\*) OR mental) OR psychological) OR psychosocial) OR psychosexual)) AND (((((((cervical smear[MeSH Terms]) OR pap smear OR cytological smear)) OR ((CIN\* OR CIN \*)) OR (cervix OR cervical)))) AND (((((((conization OR conization\*) OR (ablation\*) OR (cryotherapy) OR (large loop excision of the transformation zone) OR (LLETZ) OR (LEEP) OR (loop excision procedure\*)) OR (colposcop\*)) OR (laser)) NOT neck NOT spinal))

b) *PsychINFO*

((De "Anxiety" or De "Emotional States" or De "Stress" or De "Psychological Stress" or De "Distress") AND (De "Cervix" or De "Cancer Screening" or De "Neoplasms")) NOT cancer patients NOT children NOT childhood NOT caregiver NOT palliative NOT chemotherapy NOT prostate NOT colorectal\* NOT breast NOT lung NOT ovarian NOT pancreatic NOT neck NOT sarcoma NOT testicular

c) *CINAHL*

(MH "Cervical Smears" or MH "Cervical Intraepithelial Neoplasia") AND (MH "Colposcopy")

d) *Web of Science*

((colposcop\*) AND (cervical smear OR pap smear OR cytological smear OR cervical intraepithelial neoplasia) AND (wellbeing OR anxiety OR depression OR distress OR stress OR emotion\* OR mental OR psychological OR psychosocial OR psychosexual OR quality of life)

e) *Scopus*

((ALL(cervical smear OR cervical intraepithelial neoplasia)) AND (ALL(colposcop\*)) AND (ALL(wellbeing OR anxiety OR depression OR distress OR stress OR emotion\* OR mental OR psychological OR psychosocial OR psychosexual OR quality of life)))