Emotional response to testing positive for human papillomavirus at cervical cancer screening: a mixed method systematic review with meta-analysis

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Abstract

Tens-of-millions of women every year test positive for human papillomavirus (HPV) at routine cervical screening. We performed a mixed-methods systematic review using a results-based convergent design to provide the first comprehensive overview of emotional response to testing positive for HPV (HPV+). We mapped our findings using the cognitive behavioural framework. Six electronic databases were searched from inception to 09-Nov-2019 and 33 papers were included. Random-effects meta-analyses revealed that HPV+ women with abnormal or normal cytology displayed higher short-term anxiety than those with normal results (MD on State-Trait Anxiety Inventory=7.6, 95% CI: 4.59-10.60 and MD=6.33, CI: 1.31–11.35, respectively); there were no long-term differences. Psychological distress (general/sexual/test-specific) was higher in HPV+ women with abnormal cytology in the short-term and long-term (SMD=0.68, CI: 0.32–1.03 and SMD=0.42, CI: 0.05-0.80, respectively). Testing HPV+ was also related to disgust/shame, surprise, and fear about cancer. Broadly, adverse response related to eight cognitive constructs (low control, confusion, cancer-related concerns, relationship concerns, sexual concerns, uncertainty, stigma, low trust) and six behavioural constructs (relationship problems, social impact, non-disclosure of results, idiosyncratic prevention, indirect clinical interaction, changes to sexual practice). Almost exclusive use of observational and qualitative designs limited inferences of causality and conclusions regarding clinical significance.

Keywords: Human Papillomavirus (HPV), Cervical Cancer Screening, Emotion, Mixed Methods, Meta-analysis, Psychological, Emotion, Cognitive Behavioural.

Emotional response to testing positive for human papillomavirus at cervical cancer screening: a mixed method systematic review with meta-analysis

Over 570,000 new cases of cervical cancer are diagnosed every year worldwide, virtually all caused by persistent infection with high-risk human papillomavirus (HPV), a common sexually transmitted infection (STI) (Bruni, 2019). Integration of HPV testing into cervical cancer screening is now recommended by the majority of health organisations due to its superior sensitivity for the detection of high-grade precancerous lesions compared with cytology-based testing alone (where cervical cells are microscopically examined for abnormalities) (US Preventive Services Task Force, 2018; Australian Government, 2017; vonKarsa, 2015). Using HPV as the primary (first) test in cervical screening is considered to be the gold standard in many high-income countries and means that all women who attend screening receive an HPV-positive or negative result (Cuzick et al., 2006; Kitchener et al., 2009; Kitchener et al., 2014; Rebolj et al., 2019; Ronco et al., 2014). The Netherlands and Australia were first to fully implement HPV primary screening in 2017 (Department of Public Health, 2017; Australian Government, 2017), and several high-income countries are in the planning, piloting, or early implementation stages (e.g. Sweden, Italy, UK, Norway, New Zealand) (National Screening Unit. New Zealand Government, 2017; Rebolj et al., 2019; Wentzensen et al., 2017). Other middle-and high-income countries, which have not yet switched to HPV primary screening, use HPV testing to triage borderline or low-grade abnormal cytology (Arbyn et al., 2006). Globally tens-of-millions of women every year find out they are HPV-positive at their routine cervical screen.

Over the last few decades, the psychological impact of testing positive for HPV has attracted substantial research focus with many studies assessing emotional response, e.g.

anxiety, concern about result, or worry about cancer. The rationale for research in this domain has usually been orientated towards attempts to mitigate unnecessary adverse psychological consequences (i.e. improve mental health outcomes) and to maximise screening re-attendance or help-seeking (i.e. improve behavioural outcomes). Given that cervical screening is usually a population-level intervention, assuming that HPV-diagnosis leads to even small percentages of women experiencing adverse effects, this translates to very large numbers experiencing negative psychological and/or behavioural sequelae. Hence efforts to monitor emotional response have been prioritised and commissioned through some national health bodies (Andreassen et al., 2019; Maissi et al., 2004; McBride et al., 2016). Despite research in this area however, to date, heterogeneity in local cervical screening protocols (e.g. screening tests used, order of tests) and study designs have meant that some major studies have produced mixed findings. For example, a large cross-sectional study found short-term anxiety and distress in women testing positive for HPV with abnormal cytology (Maissi et al., 2004, 2005). Qualitative research has also produced findings of anxiety, stigma, stress, and concern about sexual relationships following positive HPV results (McCaffery, Waller, Nazroo, & Wardle, 2006; Waller, McCaffery, Kitchener, Nazroo, & Wardle, 2007). However, a large randomised controlled trial which considered differences in anxiety and distress between women who were told their HPV-positive result vs. not told their result as part of routine screening practice found no overall differences (Kitchener et al., 2008). A qualitative study also reported indifference as a main theme following HPV-positive results (O'Connor et al., 2014).

In addition to mixed findings, some psychological studies have adopted methodological designs using hypothetical scenarios (Brown et al., 2007; Kwan et al., 2010; Lee et al., 2007; Waller, Marlow, & Wardle, 2009; Waller, Marlow, & Wardle, 2007). Since

these studies ask participants to imagine their emotional response to testing positive for HPV, they lack ecological validity. Other studies have combined women with oncogenic and non-oncogenic HPV types, e.g. including women with genital warts (Graziottin & Serafini, 2009), or including women receiving treatment for precancerous cervical changes (O'Connor et al., 2015; O'Connor et al., 2016). Again, this has meant that emotional response specific to testing positive for HPV at routine cervical screening has been difficult to isolate.

Further, attempts to explain emotional response to HPV have been largely atheoretical to date. One study considered the role of illness representations and emotion in women with abnormal cervical screening results (without explicit HPV diagnosis), and found that emotion was explained by independent effects of a combination of demographic, cognitive, and emotional representations (Hagger & Orbell, 2006). Leventhal's Common Sense Model (Leventhal, Phillips, & Burns, 2016) and Cognitive Behavioural Theory (Westbrook, Kennerley, & Kirk, 2011) have also been used by few studies to guide HPV-related interview or survey questions, reportedly proving useful frameworks (Maggino et al., 2007; Marlow, Wardle, Grant, & Waller, 2009). Speculatively drawing from theories and models of emotional adjustment, it is possible that appraisal and representations related to HPV diagnosis (*e.g.* sexually transmitted cause, lack of cure, perceived seriousness or control) (Folkman, Lazarus, Dunkel-Schetter, DeLongis, & Gruen, 1986; Leventhal et al., 2016), concerns about cervical screening or treatment (Phillips, Diefenbach, Kronish, Negron, & Horowitz, 2014), cultural/social norms and access to social support (Bandura, 1991), and coping or attachment style (Mikulincer & Shaver, 2008; Pietromonaco, Uchino, & Dunkel Schetter, 2013) may be important. Cognitive Behavioural Theory which underpins cognitive behavioural therapy (CBT), in particular, may act as a promising theoretical framework for provisionally mapping emotional responses and their related constructs. The CBT model

encompasses interacting dynamics between emotions, cognitions, and behaviours, and has been applied widely across health domains to identify overarching areas of importance for specific conditions (David, Cristea, & Hofmann, 2018). Whilst researchers working on psychological aspects of HPV are yet to establish a cogent theoretical framework, the CBT model may help organise relevant psychological responses and isolate areas for further concentrated theoretical developments. This is particularly relevant given that adverse emotional response to testing positive for HPV is likely linked to several other (potentially interacting) cognitive and behavioural outcomes (e.g. sexual relationships, health literacy, understanding of result). Research, however, is needed to establish which theoretical constructs are most relevant.

As it stands, there is a body of research on emotional response to HPV, but a lack of conclusive evidence which is useful for cervical screening programmes or informing theoretical advancement. Despite imminent roll-out of HPV primary screening in several countries and significant international interest, there has been no review or synthesis of the literature on emotional response. This mixed methods systematic review aimed to provide a comprehensive overview of the quantitative and qualitative literature, guided by the research questions: how do women emotionally respond to testing positive for HPV at cervical screening; and what influences emotional response to testing positive for HPV at cervical screening? Since emotions interact with, and are dependent upon, other biopsychosocial systems, the cognitive behavioural model (Westbrook et al., 2011) was also adopted to provide an overarching theoretical framework, which mapped the systematic review findings for emotional response into related themes of cognitions and behaviours. This helped formulate a preliminary working model of emotional response to HPV, in an otherwise predominantly atheoretical domain.

Method

This review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, & Altman, 2009) (See Supplementary File 1). The protocol was registered on PROSPERO on 15.08.2018 (reg: CRD42018105134).

Search Strategy

Medline, Embase, PsycINFO, CINAHL, Global Health and Web of Science were searched to retrieve articles between 01.01.1980 and 09.11.2019. The year coverage is representative of the earliest available database record until the date the last search was performed. The search concepts (HPV, cervical cancer, screening, psychological) were agreed a priori and informed by breaking down the research questions. The search strategy was developed for Medline, then validated and adapted for the other databases by an experienced librarian. Additional papers were identified by screening reference lists of included papers and searching OpenGrey (www.opengrey.eu). See Supplementary File 2 for the full list of search terms.

Design

We used a results-based convergent synthesis design, where the qualitative and quantitative evidence was analysed and presented separately, then integrated by juxtaposing the findings in a matrix table (Hong, Pluye, Bujold, & Wassef, 2017; Pluye & Hong, 2014).

For the purposes of this review, the integration synthesis was defined as refining, comparing, and contrasting emotion-focused themes across all studies. Analysis of quantitative data estimated the relevance and representativeness of emotional responses, by providing estimates of effect sizes and associations between testing HPV-positive and emotional outcomes; and analysis of qualitative data provided in-depth explanations for emotional response. See Figure 1 for an overview of this design.

--- Insert Figure 1 here ---

Eligibility

The titles, abstracts, and full-text papers generated from the searches met the following inclusion criteria:

1. Adult population (18+) diagnosed with HPV in the context of cervical cancer screening.
2. At least one emotional outcome explicitly measured, explored, or emerged.
3. Quantitative, qualitative, or mixed-methods design.
4. Article written in English, French, or German.

Studies were excluded if they:

1. Employed a hypothetical scenario design.
2. Included participants who had cervical cancer or were receiving treatment for cervical lesions.
3. Primarily focused on HPV knowledge without linking to an emotional outcome.
4. Where data on HPV-positive results could not be extracted (e.g. grouped analysis combining test result groups).

Definition of Emotion

Currently, there is no scientific consensus on an agreed definition of emotion. Popular theories, for example Plutchik's psychoevolutionary theory of emotion (Plutchik, 2001), tend to be relatively consistent in how they describe primary emotions such as sadness, fear, happiness, disgust, surprise, anticipation, trust, and anger. However, complex secondary and tertiary emotions, and their fusion with cognitions and physiological or behavioural cues, remain strongly debated across and within disciplines. Therefore, for the purposes of this review, we defined categories of emotion, and related cognitions and behaviours, based on a combination of the American Psychological Association (APA) published definitions (www.dictionary.apa.org/emotion), validated outcomes reported in papers, and the review team's interpretation in the coding and analysis stages.

Selection Process

Extracted studies were included/excluded as part of a two-step screening process based on title/abstract and full text. All titles and abstracts were screened by two reviewers (EM, OT or KW). Abstracts that passed the initial screen progressed to full-text review. Each full-text paper was independently assessed by two reviewers (EM, LR, OT) and discrepancies were resolved through independent full-text assessment from a third reviewer (JW), followed by discussion until consensus was reached. Agreement between reviewers prior to consensus was good (Kappa = 0.701). In some cases, authors of identified papers were contacted to request additional information where eligibility was not clear.

Data Extraction

Data extraction was performed independently by two reviewers using customised Excel templates (EM, OT). Each reviewer's data extractions were compared and integrated to achieve the most comprehensive version. The information extracted across papers included: title, year published, study aims, sample size (total and by results group), population, study setting, participants (age, ethnicity, marital status, and education), design, HPV and cytology results, outcome measures and analysis (where relevant), and main findings.

Data Synthesis and Meta-Analysis

The data synthesis was conducted in three stages by two reviewers independently (EM, OT) with disagreements resolved through discussion or inclusion of a third reviewer until consensus was achieved (JW or ZR) (Thomas et al., 2004).

Firstly, for quantitative studies, we assessed study designs, outcome measures, and available data for inclusion in meta-analyses. We aimed to compare emotional responses in HPV positive groups with a control group (e.g. HPV negative and/or normal cytology). Out of seventeen quantitative studies identified, six studies did not qualify for meta-analysis because their observational design did not include a comparison (control) group. A further three studies did not report data in a format suitable for inclusion in meta-analysis and corresponding authors were contacted in attempt to retrieve data; one author no longer had access to the data and two authors did not respond. Non-validated measures (e.g. single-item questions) were also excluded from meta-analyses. From the available data, we were able to perform three meta-analyses for the outcome 'state-anxiety', and two meta-analyses representing psychological distress (by analysing outcome measures of general distress, sexual distress and test-specific distress together). We split the meta-analyses by time point (result notification ≤2 months [short-term] *vs.* >2 months [long-term]) and result group (HPV positive with abnormal or normal cytology, *vs.* control). Statistical analyses were performed using Review Manager, version 5.2 (Collaboration, 2012). Random effects models were chosen to account for heterogeneity in populations and design. Unstandardised mean differences with 95% confidence intervals were reported for anxiety as the included studies used the same outcome measure (STAI (Marteau & Bekker, 1992; Spielberger, 1983)). Standardised mean differences with 95% confidence intervals were reported for psychological distress as outcome measures differed between studies. Tests of homogeneity were conducted using the I^2 statistic (Borenstein, 2009). Low heterogeneity was depicted by I^2 values of <25%, moderate heterogeneity as 50%, and high heterogeneity as >75% (Higgins, Thompson, Deeks, & Altman, 2003). Tau-squared (τ^2) was reported to indicate estimates of between-study variance. We were unable to conduct meta-analyses for other emotional

outcomes due to lack of data. See Supplementary File 3 for the raw data extracted for inclusion in meta-analyses.

Secondly, we synthesised all quantitative findings (including measures which could not be meta-analysed) by coding each measured outcome into themes of emotion, with related cognitive and behavioural themes also coded where relevant. Similarly for qualitative studies, the data were copied verbatim and thematic analysis was performed using descriptive and analytical coding to identify emotion themes, again with related cognitive and behavioural themes also coded where relevant (Thomas & Harden, 2008).

Thirdly, to integrate the findings of the two syntheses (integrated synthesis stage), we refined the themes of emotion across the quantitative and qualitative studies. A conceptual matrix was then constructed by mapping the emotion themes by study, to allow for comparisons and contrasts. Narrative overviews of the quantitative and qualitative findings for each emotion-focussed theme are presented, with meta-analysis findings integrated.

Cognitive Behavioural Framework – Mapping Interacting Systems

Following the data synthesis stage, the cognitive behavioural model was adopted to provide an overarching and preliminary theoretical framework to map the findings into constructs of emotions, with related cognitions and behaviours (Westbrook et al., 2011). This helped address our second aim related to understanding what influences emotional response to HPV. The cognitive behavioural model, which underpins cognitive behavioural therapy, was chosen because it has a strong evidence-base for explaining emotional response across psychology and health domains (Dobson, 2013; Hofmann, Asmundson, & Beck, 2013). We used the model in its simplest form as a triad, to illustrate how emotions (feelings), cognitions

(thoughts, beliefs, attitudes) and behaviours (actions) may interact to influence one another. In practice, this meant that alongside the primary thematic analysis phase, the qualitative verbatim data and quantitative outcome measures were also coded to represent constructs of cognitions and/or behaviours. These thematic constructs where then illustratively mapped onto the triad model of the cognitive behavioural framework. Two reviewers independently coded and analysed all data (EM, OT), with disagreements resolved through discussion or inclusion of a third reviewer until consensus was achieved (JW or ZR)

Quality Assessment (Risk of Bias)

The Mixed Methods Appraisal Tool v2018 (MMAT) is a critical appraisal tool that has been specially developed for performing quality assessments in mixed method systematic reviews, and was used to assess the methodological quality of the included studies and potential for bias (Hong, Gonzalez-Reyes, & Pluye, 2018). The MMAT has independent sets of quality criteria to guide judgements for qualitative studies, randomised controlled studies, non-randomised studies, observational descriptive studies, and mixed-methods studies. The quality score for each reviewed study was based on criteria specific to the study design, which included five methodological domains and was calculated as an overall percentage. Mixed-methods studies were assessed using the mixed-methods criteria as well as the separate quantitative and qualitative criteria; their quality score could not exceed the weakest component. We intended for the MMAT to be used for illustrative and descriptive purposes and did not weight findings based on quality score alone. Rather, each study was assessed independently on its merits, limitations, and overall design in the cervical screening context by two reviewers (EM, LR, OT), with discrepancies discussed and resolved with a third reviewer (JW).

Rigour

Rigour was maintained by using a comprehensive search strategy along with documentation of eligibility decisions, which ensured descriptive validity (accuracy of data) (Sandelowski, Voils, & Barroso, 2006). Interpretive validity was achieved through use of at least two independent reviewers (EM, OT, LR) in the data extraction phase to create a comprehensive database and perform of quality assessments (Thomas & Harden, 2008). Following each stage of the data synthesis, two reviewers (EM, OT) plus a third reviewer (JW, ZR) discussed the thematic findings and resolved disagreements to help maintain theoretical validity (reliability of data interpretation) (Sandelowski et al., 2006). Pragmatic validity (efficacy and transferability of findings) was improved by inclusion of study characteristic tables providing the context around the studies, allowing readers to judge the usefulness of findings (Thomas & Harden, 2008).

Results

Search results

The database searches yielded 15,792 papers, with 9,343 titles and abstracts screened after removal of duplicates. Ninety-three papers were fully screened and 33 papers, representing 32 studies, met the selection criteria. See Figure 2 for a Prisma Diagram providing an overview of the searches and selection process.

--- Insert Figure 2 here ---

Study Characteristics

Seventeen papers were quantitative studies (Alay et al. 2020; Andreassen et al., 2019; Ferenidou et al., 2012; Garces-Palacio et al., 2019; Guerra Rodriguez et al., 2019; Kitchener et al., 2008; Kwan et al., 2011; Maggino et al., 2007; Maissi et al., 2004, 2005; McBride et al., 2020; McCaffery et al., 2004; Nagele et al. (2019); Ngu et al., 2018; Wang et al., 2010; Wang, Shi, Kang, Song, & Qiao, 2011), fifteen were qualitative (Barrera-Clavijo, Wiesner-Ceballos, & Rincón-Martínez, 2015; Barreto et al., 2016; Bertram & Magnussen, 2008; Head, Imburgia, Zimet, & Shew, 2017; Kosenko, Hurley, & Harvey, 2011; Lin, Jeng, & Wang, 2011; Linde et al., 2019; McCaffery & Irwig, 2005; McCaffery et al., 2006; McCurdy et al., 2011; O'Connor et al., 2014; Perrin et al., 2006; Tiro et al., (2019); Waller, McCaffery, et al., 2007; Wyndham-West, Durand, & Santoro, 2018) and one was mixed-methods (Daley et al., 2010). A total of 12,789 women aged between 18 and 65 participated in twenty studies

(n=12,244 quantitative; n=545 qualitative), of whom 4,305 were reported as having tested positive for HPV (n=3,874 quantitative; n=431 qualitative). Seven studies were conducted in the UK, seven in the USA, six in China, two in Colombia and the remaining eleven in Australia, Austria, Brazil, Canada, Greece, Italy, Ireland, Mexico, Norway, Tanzania, and Turkey. Twenty-one studies reported level of participant education: six used samples predominately educated to tertiary-level or above, and four primary-level or below. Fourteen studies reported a predominantly white ethnicity sample, and others predominantly African and Asian. Nearly all studies recruited women through clinical settings (e.g. hospitals, primary care), except two which used public advertisements and social media. Most studies ascertained diagnosis of HPV using clinical records; however, some relied on participant self-report. Time between participants receiving their HPV result and recruitment was not reported in the majority of studies (especially qualitative); but in those which did, the time from diagnosis ranged from shortly after receiving result (notification-2 months) to 2 years after result, with two outliers reporting 4.8 and 5 years. There were also variations in the combinations of HPV-positive and cytology result groups between studies: most used HPV-positive with abnormal cytology (any grade or mixed) and some used HPV with normal cytology, HPV with atypical squamous cells of undetermined significance, or HPV alone (no cytology test).

Observational (cross-sectional, prospective longitudinal, or cohort) designs were used in most quantitative studies (thirteen out of seventeen). Four quantitative studies used a randomised controlled design (Garces-Palacio et al., 2019; Kitchener et al., 2008; Maggino et al., 2007; Ngu et al., 2018), but only one directly tested and reported differences between result groups (Kitchener et al., 2008). The same RCT study also included additional analyses on the observational findings from women in the study arm where participants were informed

about their HPV results. All quantitative studies included at least one outcome with a core emotional component and most used widely-tested, validated scales; although some used single-item or non-validated scales and the mixed-methods study measured emotion descriptively. The most common outcomes measured were state-anxiety, sexual distress, test-specific distress, general distress, depression, fear, and shame/disgust. Fourteen of the qualitative studies conducted interviews and one conducted focus groups (Barrera-Clavijo et al., 2015). All qualitative studies described at least one emotional theme, mainly related to anxiety, test-specific distress, sexual distress, surprise and confusion, fear, shame and disgust, sadness, relief, and indifference.

Summaries presenting descriptive overviews of the studies and quality appraisal scores are presented in Tables 1 and 2.

Quality Assessment

Overall, MMAT quality scores ranged from 40% to 100%. Qualitative studies scored highest for quality (median=100%, range 40 to 100%), followed by quantitative studies (median=60%, range 40 to 100%), and the mixed methods study (40%). The main reasons for quality deductions in the quantitative studies were non-complete reporting of data and not using appropriate measures; and in qualitative studies, not sufficiently substantiating result

interpretation with data. See Supplementary File 4 for a breakdown of the quality scores by study and design.

Emotional Response

We identified eight main themes of emotion which were measured or had emerged in women testing positive for HPV: anxiety; psychological distress (three types: sexual, test-specific, and general); fear; surprise; shame and disgust; sadness; positive affect; and apathy. Each of these emotions are discussed separately with an overview of the synthesised evidence. See Table 3 for a brief definition these emotions. The main findings from the primary mixed methods study (Daley et al., 2010) were integrated with the relevant quantitative and qualitative components throughout.

Tables 4 and 5 provide an overview of the main results for the quantitative and qualitative studies respectively. Supplementary File 5 provides the integration matrix of the themes measured or emerged across all studies.

Anxiety.

Quantitative (anxiety)

Ten quantitative studies measured anxiety at different time points (Alay et al., 2020; Garces-Palacio et al., 2019; Kitchener et al., 2008; Kwan et al., 2011; Maggino et al., 2007; Maissi et al., 2004, 2005; McBride et al., 2020; McCaffery et al., 2004; Ngu et al., 2018)

mostly using the state subscale from the state-trait anxiety inventory (Marteau & Bekker, 1992; Spielberger, 1983).

We were able to perform meta-analyses including seven out of eleven studies, comparing HPV-positive with abnormal cytology groups vs. control groups (normal or negative results) for both short-term anxiety (result notification ≤2 months) and long-term anxiety (>2 months). Results revealed higher short-term anxiety for women who were HPV-positive with abnormal cytology compared to the control groups across six studies (mean difference [MD] in STAI of 7.6, 95% CI: 4.59 - 10.60, $p<.001$, $\tau^2=11.11$, $I^2=85\%$); however no differences were observed for long-term anxiety across four studies (MD = 0.03 95% CI: -1.45 – 1.51, $p=0.96$, $\tau^2=0$, $I^2=0\%$). A small meta-analysis of three studies also compared HPV-positive with normal cytology groups vs. controls, which revealed higher short-term anxiety for HPV-positive with normal cytology (MD = 6.33, 95% CI: 1.31 – 11.35, $p=.01$, $\tau^2=17.55$, $I^2=91\%$). It is worth noting that although the direction of effects were consistent across studies, high levels of statistical heterogeneity were identified in significant meta-analyses ($I^2>75\%$), therefore caution is warranted in the interpretation. See figures 3a-c for the meta-analysis findings and papers included.

Four studies which measured anxiety could not be meta-analysed due to study design (e.g. no suitable control group; (Ngu et al., 2018)) or lack of published data in the necessary format for extraction (Alay et al., 2020; Andreassen et al., 2019; Maggino et al., 2007)). Consistent with the meta-analysis findings, two of these studies, where data could not be extracted, reported higher short-term anxiety in HPV-positive groups compared to controls (Alay et al., 2020; Maggino et al., 2007) but not long-term anxiety (Andreassen et al., 2019);

and one study without a suitable control group found that anxiety decreased over time (Ngu et al., 2018).

Interestingly, an RCT which considered differences in anxiety between HPV-positive women who were told (revealed) *vs.* not told (concealed) their HPV status as part of an embedded trial in routine practice, found no differences between the groups (Kitchener et al., 2008). Predictors of anxiety in HPV-positive women were also explored in one study (Maissi et al., 2004): younger age, higher perceived risk of cervical cancer, and not understanding the meaning of test results predicted higher anxiety within 4-weeks of results; but no predictive relationships were found for perceived importance of HPV and perceived severity of cervical cancer.

--- Insert Figures 3a-c here ---

Qualitative (anxiety)

Ten qualitative studies reported anxiety as a theme following HPV-positive results (Barrera-Clavijo et al., 2015; Bertram & Magnussen, 2008; Daley et al., 2010; Head et al., 2017; Kosenko et al., 2011; McCaffery & Irwig, 2005; McCaffery et al., 2006; O'Connor et al., 2014; Waller, McCaffery, et al., 2007; Wyndham-West et al., 2018). Women who were anxious often had poor understanding of their results and/or HPV, expressed uncertainty about HPV, had often received their results by letter, and reported searching for further information on the internet (Head et al., 2017; Kosenko et al., 2011; McCaffery & Irwig, 2005; McCaffery et al., 2006; Waller, McCaffery, et al., 2007). Two studies found that women who had discussed their results face-to-face with a healthcare professional were less

anxious (Barrera-Clavijo et al., 2015; McCaffery & Irwig, 2005). One study (Waller, McCaffery, et al., 2007) interviewed women after two HPV test results (12-months apart) and found that anxiety was a dominant theme shortly after a first or second HPV-positive result, but that it did not generally persist in the time between the two tests. A second HPV-positive test compared to a first one, however, was described as being more anxiety-inducing for some women.

Distress.

Three forms of psychological distress were identified across studies: test-specific distress, sexual distress, and general distress. Test-specific distress related to the psychological burden of HPV and screening test results. Sexual distress related mostly to impacts on sexual relationships, a partner, or concerns about transmission of HPV. General distress related to adverse impacts on broad everyday functioning (e.g. lack of sleep and concentration).

Quantitative (distress)

Sixteen quantitative studies included a measure of psychological distress: ten included test-specific distress (Ferenidou et al., 2012; Garces-Palacio et al., 2019; Kwan et al., 2011; Maissi et al., 2004, 2005; McBride et al., 2020; McCaffery et al., 2004; Ngu et al., 2018; Wang et al., 2010; Wang et al., 2011), eleven sexual distress (Alay et al., 2020; Ferenidou et al., 2012; Hsu, Wang, Fetzer, Cheng, & Hsu, 2018; Kitchener et al., 2008; Kwan et al., 2011; Maggino et al., 2007; Maissi et al., 2005; McCaffery et al., 2004; Nagele et al., 2019; Wang

et al., 2010; Wang et al., 2011), and six general distress (Andreassen et al., 2019; Hsu et al., 2018; Kitchener et al., 2008; Maissi et al., 2004, 2005; McBride et al., 2020). Test-specific distress was consistently higher (worse) for women testing HPV-positive with any cytology result compared to normal results up to 6-months post-result (Maissi et al., 2005), but not at 12-months post-result (Garces-Palacio et al., 2019). There were mixed quantitative findings for sexual distress and general distress. Sexual distress was found to be higher (worse) for women testing HPV-positive in five studies; however one low quality study showed no effect (Maggino et al., 2007), and another high quality found mixed findings depending on how they analysed their data (Kitchener et al., 2008). Another small study found lower sexual desire but no differences in overall sexual function between HPV-positive groups and the control (Alay et al., 2019); and a descriptive study reported that 33.3% and 43.1% of women endorsed reduced sexual interest and reduced frequency of sexual intercourse, respectively (Ferenidou et al., 2012). In terms of longer-term impact, sexual distress was found to persist at 6-months in two studies (Kwan et al., 2011; Maissi et al., 2005); one study examined the trajectory of adjustment to sexual distress over a 12-month period and found that adjustment occurred from one-to-6-months after HPV diagnosis (Hsu). Consistently, another study found no differences over a 12-month period (Nagele et al., 2019). General psychological distress (Golderberg, 1988) was found to be slightly higher (worse) in women testing HPV-positive with abnormal cytology 4-weeks after their result in two studies (Maissi et al., 2004; McBride et al., 2020). However, no differences were found 6-months later in a follow-up study (Maissi et al., 2005) or up to 12 or 24 months later in two other studies (Andreassen et al., 2019; Nagele et al., 2019). The Kitchener et al (2008) trial again had mixed findings for general distress. Among women who were told their HPV result, being HPV-positive (vs. HPV negative) was associated with slightly higher general distress 2-weeks after the result. However, when women who had been told they were HPV-positive were compared with

HPV-positive women who had not been told their HPV test result, no differences were found. Hsu et al (2018) found that adjustment to general distress occurred between 1-and-6-months after HPV diagnosis.

We performed meta-analyses to combine the available data for test-specific distress, sexual distress, and general distress, to represent an overall measure of psychological distress in both the short-term (result notification ≤2 months) and long-term (>2 months). One study (Maissi et al., 2005) measured two forms of long-term distress (general and sexual); therefore, two meta-analyses were performed including each of these variables independently, to avoid bias through double-counting in the total sample.

Results revealed higher short-term distress for HPV-positive with abnormal cytology compared to the control across six studies (Standardised Mean Difference [SMD] = 0.68, 95% CI: 0.32 – 1.03, $p<.001$, $\tau^2=0.18$, $I^2=94\%$). Similarly, higher long-term distress was also observed for HPV-positive with abnormal cytology compared to the control across six studies, irrespective of whether we included the general or sexual distress outcome in the Maissi et al (2005) study (SMD = 0.42, 95% CI: 0.05 - 0.80, $p=.03$, $\tau^2=0.19$, $I^2=92\%$ and SMD = 0.49, 95% CI: 0.19 - 0.80, $p=.001$, $\tau^2=0.12$, $I^2=88\%$, respectively). Long-term effects appeared to be limited to test-specific and sexual distress outcomes, given that the two studies which measured general distress showed no differences (Maissi et al., 2005; McBride et al., 2020). Overall, although direction of effects were relatively consistent across studies, high levels of statistical heterogeneity were identified in all the meta-analyses ($I^2>75\%$), therefore caution is advised in the interpretations. See figures 4a-c for the meta-analysis findings for psychological distress.

--- Insert Figures 4a-c here ---

Qualitative (distress)

Themes indicative of test-specific distress emerged in thirteen qualitative studies (Barrera-Clavijo et al., 2015; Barreto et al., 2016; Bertram & Magnussen, 2008; Head et al., 2017; Kosenko et al., 2011; Lin et al., 2011; McCaffery & Irwig, 2005; McCaffery et al., 2006; McCurdy et al., 2011; O'Connor et al., 2014; Perrin et al., 2006; Waller, McCaffery, et al., 2007; Wyndham-West et al., 2018). Clear adverse impacts were reported, with many women describing concerns about HPV infection and/or the meaning of their test results. A small number of women reported that test-specific distress influenced their behaviours through triggering what they believed to be preventive action (often idiosyncratic, e.g. avoiding sharing soap/towels, exercising, or eating fruit (Barreto et al., 2016; Wyndham-West et al., 2018). One study reported that test-specific distress primarily arose from concerns about abnormal cytology rather than HPV infection; however, it only included six women who were HPV-positive (O'Connor et al., 2014). The other studies reported that HPV infection had notably adverse impacts, independent of abnormal cytology. Sexual distress was also a theme in nine qualitative studies (Barrera-Clavijo et al., 2015; Barreto et al., 2016; Bertram & Magnussen, 2008; Kosenko et al., 2011; Lin et al., 2011; McCaffery et al., 2006; McCurdy et al., 2011; Perrin et al., 2006; Waller, McCaffery, et al., 2007), with HPV-positive women often describing a range of concerns about their sexual relationships, transmission of HPV, and/or impact on their partner. Some women reported anger towards their partner and arguments due to suspected infidelity, or changing their sexual behaviours (e.g. avoiding sex) as a consequence of HPV.

Fear.

Quantitative (fear)

Two studies descriptively reported that fear was a common adverse reaction to HPV diagnosis, with 82.4% and 25% of women endorsing it descriptively (Ferenidou et al., 2012; Maggino et al., 2007). Similarly, the quantitative component of the mixed-methods study reported >75% endorsed fear; however, the authors categorised their definition of fear as endorsements of "anxious" and "worried" (Daley et al., 2010). Another study found that cervical cancer worry was higher in HPV-positive women shortly after result notification, but differences disappeared at 6-months (Kwan et al., 2011); and one study reported that worry about developing cervical cancer decreased over time (Ngu et al., 2018). Similarly, during an observational period of 12 months (baseline, 6 months, 12 months) there were no significant differences in fear of disease progression (Nagele et al., 2019).

Qualitative (fear)

Fear emerged as a dominant theme in ten qualitative studies (Barrera-Clavijo et al., 2015; Barreto et al., 2016; Bertram & Magnussen, 2008; Lin et al., 2011; Linde, Rasch, Mwaiselage, & Gammeltoft, 2019; McCurdy et al., 2011; O'Connor et al., 2014; Perrin et al., 2006; Tiro et al., 2019; Waller, McCaffery, et al., 2007). Women mainly described fears related to the development of cervical cancer, their future health, and potential infertility. Other women were afraid about the impact of their result or cancer on their family, partner, and/or friends.

Disgust and shame.

Quantitative (disgust and shame)

Six quantitative studies included measures of HPV-related shame or disgust (Daley et al., 2010; Ferenidou et al., 2012; Guerra Rodriguez, Champion, Moreno Monsivais, Olivares Ornelas, & Gil Vazquez, 2019; Ngu et al., 2018; Wang et al., 2010; Wang et al., 2011): two used the 'self-image' domain within a distress measure (Mast et al., 2009); one adapted an STD-related shame scale (Cunningham, Tschann, Gurvey, Fortenberry, & Ellen, 2002); and two used non-validated measures. Shame and disgust were higher in women testing positive for HPV with abnormal cytology when compared to normal cytology (Wang et al., 2010; Wang et al., 2011), or HPV-negative with abnormal cytology (Wang et al., 2011) within 3-months of the result. Statements relating to shame and disgust were descriptively endorsed by the majority (>50%) in a descriptive study (Daley et al., 2010); and "guilt", "shame", and "stigmatisation" were endorsed by 41.1%, 21.5%, and 15.7% respectively in another study (Ferenidou et al., 2012). HPV-related shame did not change over time (up to 6-months post result) (Ngu et al., 2018), and one correlational study found that higher stigma was significantly associated with utilising fewer coping strategies and reporting less protective behaviour related to cervical cancer (Guerra Rodriguez et al., 2019).

Qualitative (disgust and shame)

Shame and/or disgust also emerged as themes in eleven qualitative studies (Barrera-Clavijo et al., 2015; Barreto et al., 2016; Bertram & Magnussen, 2008; Lin et al., 2011; McCaffery & Irwig, 2005; McCaffery et al., 2006; McCurdy et al., 2011; O'Connor et al., 2014; Perrin et al., 2006; Waller, McCaffery, et al., 2007; Wyndham-West et al., 2018). These emotions mostly centred round concerns about disclosure of results to

partner/family/friends, judgement from others, and/or the belief that negative connotations (such as sexual promiscuity) were associated with HPV, sometimes leading to reports of stigma (McCaffery et al., 2006; O'Connor et al., 2014; Wyndham-West et al., 2018). Some women described feeling ashamed and reported variations of feeling “unclean” or “dirty”. Although shame and disgust appeared to be reported across ethnic groups, these themes seemed more dominant in studies focusing on women from non-white ethnic backgrounds.

Surprise (and confusion).

Quantitative and Qualitative (surprise)

Despite surprise and/or confusion emerging as themes in ten qualitative studies (Barreto et al., 2016; Head et al., 2017; Kosenko et al., 2011; Lin et al., 2011; Linde et al., 2019; McCaffery & Irwig, 2005; Perrin et al., 2006; Tiro et al., 2019; Waller, McCaffery, et al., 2007; Wyndham-West et al., 2018), these responses were not measured using validated scales in any of the quantitative studies. One descriptive study reported that 70.1% of HPV-positive women endorsed that they felt ‘shocked’ (Daley et al., 2010). In qualitative studies, women often expressed surprise as the first emotion experienced after receiving their HPV-positive result. Many reported subsequent confusion about the meaning of HPV and how they had acquired it. Often surprise and confusion appeared to be linked with knowledge that HPV is sexually transmitted, raising questions about its source and concerns about potential infidelity (linking to sexual distress).

Sadness.

Quantitative (sadness)

One quantitative study descriptively reported that 14.9% of women who tested HPV-positive had clinically relevant depression scores; however, there was no control group to indicate population norms (Ngu et al., 2018). Another low quality study found that depressive/intrusive thoughts were slightly higher in women who tested HPV-positive compared to HPV-negative (time point not reported) (Maggino et al., 2007). A descriptive study reported that 51.7% of HPV-positive women endorsed that they felt 'depressed' (Daley et al., 2010).

Qualitative (sadness)

Only two out of eleven qualitative studies reported sadness or feelings of depression, and in both they were minor themes (Barreto et al., 2016; Waller, McCaffery, et al., 2007).

Positive Affect (relief, acceptance).

Quantitative and Qualitative (positive affect)

In the quantitative studies, positive emotional responses, as indicated by improved outcomes following an HPV-positive result, were rarely observed. The only exception was one study where sexual satisfaction was higher in HPV-positive women (Kitchener et al., 2008). 'Relief' was also endorsed by 27.4%, 'encouraged' endorsed by 35.9%, and 'in control' endorsed by 68% of HPV-positive women in a descriptive study (Daley et al., 2010). Ten qualitative studies reported positive emotions such as relief, increased trust, and

acceptance, though they were minor themes (Barrera-Clavijo et al., 2015; Head et al., 2017; Kosenko et al., 2011; Lin et al., 2011; Linde et al., 2019; McCaffery & Irwig, 2005; Perrin et al., 2006; Tiro et al., 2019; Waller, McCaffery, et al., 2007; Wyndham-West et al., 2018). Women who reported positive emotional responses to their HPV results described receiving their test results in person by a healthcare professional, consulting with a healthcare professional after results, having a supportive partner, and/or mobilising social support. Relief that the result was HPV and not cancer was a less common theme.

Apathy.

Quantitative (apathy)

One study descriptively measured apathy and found that 38% of women reported no reactive emotion to their HPV diagnosis (Maggino et al., 2007). Although the other quantitative studies did not directly measure indifference or apathy, the lack of observed differences in emotional outcomes between women receiving HPV-positive vs. negative results may be suggestive of apathetic or ambivalent responses, reported across quantitative papers under each individual emotion.

Qualitative (apathy)

Two qualitative studies reported indifference (O'Connor et al., 2014; Tiro et al., 2019), however this was either a minor theme or related more to the HPV testing procedures than response to testing HPV-positive.

Cognitive Behavioural Framework – Interacting Systems

The emotional response findings for quantitative and qualitative studies were additionally coded to identify related cognitions and behaviours, as a starting point to determine how these three factors interact. Within the eight broad emotion-focused themes, twelve cognitive constructs and ten behavioural constructs were identified (many of which are described in the results under each emotion).

Cognitions related to emotional response.

Broadly, adverse emotional response to testing positive for HPV was linked to eight negative cognitions: low perceived control, confusion, stigma, relationship concerns, sexual concerns, cancer-related concerns, lack of trust in others, and uncertainty about meaning of result or future health.

Conversely, neutral or positive emotional responses were linked with high perceived control, trust in others, and acceptance.

Behaviours related to emotional response.

Related to behaviours, six areas were linked to adverse emotional response: negative impact on relationships, negative social impact, non-disclosure of results, idiosyncratic prevention, indirect clinical interaction (e.g. results by letter), and changes in sexual behaviour. In brief, negative impact on relationships and negative social impact referred to themes such as reports of arguments with a partner or avoiding contact with others. Non-

disclosure of results represented women who expressed that they deliberately concealed their result from others. Idiosyncratic prevention referred to reports of attempts to prevent the spread of HPV through engaging in activities that are not evidence-based, such as washing toilet seats. Indirect clinical interaction referred to receiving results by methods with no personal contact such as a mailed letter, and/or not seeking advice from a healthcare professional. Changes in sexual behaviour described lower sexual activity, avoiding sex, and/or using a condom.

Conversely, four behavioural themes were linked with positive or neutral emotional response: direct clinical interactions; social support; behaviour of others; and future screening attendance. In brief, women who reported speaking to a healthcare professional after their HPV-positive result (direct clinical interactions) or their partner/family/friends (social support) expressed feeling more reassured, less anxious, relieved, and/or more accepting. Helpful behaviours of others related to partners/friends/family sourcing information on HPV or encouraging help-seeking behaviours. Attendance at a screening appointment after receiving an HPV-positive result (future screening attendance) was described by some women as providing reassurance.

According to the cognitive behavioural model, these three constructs of emotions, cognitions, and behaviours are likely to directly influence and/or interact with one another. This formulates a working model of what may influence emotional response to testing positive for HPV. See Figure 5 for an overview of emotions, cognitions, and behaviours mapped on to the cognitive behavioural framework.

--- Insert Figure 5 here ---

Discussion

This systematic review provides a comprehensive overview of emotional response to HPV diagnosis at cervical cancer screening, as well as a provisional model for understanding how emotions may interact with cognitions and behaviours using the cognitive behavioural framework. Testing positive for HPV at cervical screening appears to be most strongly associated with short-term anxiety, short and long-term psychological distress, and related to feelings of disgust and shame, surprise, and fear about cancer. There was little evidence of sadness or depression and a minority of women reported apathy or relief that they had been diagnosed with HPV rather than cancer.

Anxiety was one of the most common adverse responses reported shortly after women had received their HPV-positive result across all studies. Our meta-analyses revealed higher short-term state anxiety in women testing positive for HPV with abnormal cytology or normal cytology when compared with normal screening results (mean difference on STAI (Spielberger, 1983) of 7.6 and 6.33, respectively); though high statistical heterogeneity was observed, potentially due to differences in screening contexts and magnitudes of effect sizes (I^2 >75%). These findings are consistent with another systematic review which found elevated anxiety in women with abnormal cytology who were attending for colposcopy (a more advanced stage in the screening process) (O'Connor et al., 2016). Interestingly, when comparing our results to this review, anxiety scores observed in colposcopy patients appeared to be descriptively similar to women testing positive for HPV with abnormal cytology (mean STAI score range: 34.0 - 49.0 pre-colposcopy vs. 39.6 - 46.0 after test result). These similarities suggest that anxiety associated with an HPV-positive screening result may be

comparable to the anxiety experienced at follow-up investigative procedures (colposcopy); or may persist from the time of result to colposcopy.

Reassuringly, however, the results from our meta-analysis revealed that anxiety did not appear to persist in the long-term (> 2 months after notification), when comparing HPV-positive with abnormal cytology vs. normal/negative result groups. Also, overall, the mean anxiety scores observed across studies did not exceed thresholds for clinical significance. The anxiety scores associated with a HPV-positive result tended to be higher than expected in the general population but lower than the cut-off for clinically important anxiety. Although, it is worth noting that all quantitative studies assessed anxiety across the whole study sample without conducting subgroup analyses. From a clinical perspective, it is highly unlikely that acute adverse emotional response to HPV would be expected or detectable at the population level. It is more likely that certain groups of women would be at higher risk of clinically important anxiety (e.g. low socioeconomic status, ethnic minority groups, low health literacy) who should additionally be studied or analysed separately. Anxiety was a dominant theme in the qualitative literature which, due to the likelihood of self-selection bias in qualitative studies, supports the notion that certain groups of women may be prone to very high anxiety.

HPV positivity was also related to psychological distress in both the short-term and long-term. Our meta-analyses (which combined sexual, test-specific, and general distress) revealed higher distress in women testing HPV-positive with abnormal cytology when compared with normal/negative results, at both result notification to 2-months, and 2-months onwards. Long-term distress (> 2-months), however, seemed to be specific to sexual and test-specific distress, as the studies which measured general distress at this time point found no differences.

Experiencing distress related to sexual relationships, infidelity, and potential transmission of the virus (sexual distress) is consistent with the broader literature on emotional response to other STIs and HPV in non-screening contexts (e.g. genital warts, other cancers) (Dodd, Waller, & Marlow, 2016; Graziottin & Serafini, 2009). In this review, sexual distress appeared mostly, but not exclusively, limited to women in relationships and/or with current sexual partners in the qualitative literature, which may help explain some heterogeneity in findings. For some women, it was also reported as associated with relationship problems (e.g. arguing over suspected infidelity) and changes in sexual practice (e.g. avoiding sex).

Distress related to meaning of screening test results (test-specific distress) was very common in the qualitative literature and was often described as the successor to surprise and confusion. It was mostly linked to low HPV awareness, not understanding result meaning, confusion about the aetiology of HPV, and concerns about future health. As HPV cannot be cured and there are no clear (practical) prevention methods available (except vaccination prior to exposure), some women reported feeling that they were not in control of their health. Low perceived control appeared related to higher test-specific distress. A small number of women also reported engaging in idiosyncratic prevention methods to help treat or "contain" HPV, such as washing toilet seats or increasing physical activity. As a psychological formulation, these forms of prevention could be interpreted as behavioural attempts to gain control and reduce distress (Westbrook et al., 2011). High levels of distress about result also appeared to be closely related to fears about developing cancer which, together, intensified overall adverse emotional response.

Shame and disgust emerged as themes in the qualitative studies and a small number of women also reported feeling that there was stigma attached to HPV, which is consistent with broader STI research (Bickford, Barton, & Mandalia, 2007; Jeynes, Chung, & Challenor, 2009; Nack, 2000). In line with sexual distress and test-specific distress, shame and disgust seemed to be associated with maladaptive behaviours. Some women reported reluctance to disclose their HPV result to others and/or to seek social support from their partner, family, or peers because of feeling ashamed. To further assess the relevance of shame and disgust in the cervical screening context, future quantitative research should incorporate validated measures which include relevant behavioural impacts.

Relatively few studies measured sadness, depression, or generalised distress. In those studies which did, there was little evidence of adverse (clinically important) effects associated with any HPV-positive result. A small number of qualitative studies reported positive or neutral emotional responses, such as relief that a test result was HPV and not cancer, or indifference. However, these were not common and/or dominant responses.

Across all studies (quantitative and qualitative), adverse emotional response was mainly related to not understanding the meaning of the result, being in a relationship or having a current sexual partner, non-white ethnicity, receiving test result by letter, not discussing the result with a healthcare professional, little social support, and lower levels of education. Adverse emotional response was observed across all studies but appeared most prominent in the qualitative literature. Although fear and surprise/confusion were common themes in the qualitative studies, they were rarely measured in the quantitative studies, highlighting a gap in quantitative research which warrants further exploration. Overall, our findings suggest that receiving an HPV-positive result at cervical screening can cause

significant disturbance for some women, however, likely the minority of the population and/or certain groups.

Methodological Considerations

Importantly, this systematic review raises some relevant methodological considerations. Nearly all studies adopted cross-sectional, descriptive, and/or qualitative designs, prohibiting inferences of causality between testing positive for HPV and emotional response. The persistence of HPV infection (and the development of abnormal cells) are closely intertwined with immunological response; and there is a body of literature which suggests that psychological or social stressors can impair immune response (Fang et al., 2008; Marsland, Walsh, Lockwood, & John-Henderson, 2017; Steptoe, Hamer, & Chida, 2007). Therefore, it cannot be ruled out that HPV activation and/or persistence are functions (or sub-functions) of psychological stress (i.e. adverse emotion). Interestingly, the one large RCT study in this review which compared anxiety and general distress between women testing HPV-positive who were told (revealed) *vs.* not told (concealed) about their HPV status (Kitchener et al., 2008), found similarly elevated anxiety scores (no differences). This suggests that elevated levels of anxiety and distress may be present prior to learning HPV-positive screening results, which supports the notion that psychological stress could play a role in HPV activation/persistence. Other research suggesting that anxiety associated with HPV is usually temporary and normalises at 6-month follow-up may provide evidence against this mechanism; although it is worth noting that 41% of HPV cases clear within 6 months (Bulkmans et al., 2007), meaning effects may be confounded. Further research is

needed to test the validity of such psychobiological mechanisms and/or other potential causative pathways.

It is also worth highlighting that very few studies analysed and/or interpreted their data in terms of clinical significance, meaning it was not possible to distinguish between normal and clinically relevant emotional responses for most outcomes. Negative response to adverse information usually a temporary process constituting a normal part of human consciousness. Therefore, studies in this review which drew implicative conclusions based on between-group differences without further interpretation provided little insight distinguishable from healthy response. To progress this field of psychological research, future studies should be designed and appropriately powered to test for clinical significance rather than between-group differences alone.

Most participants were educated to secondary level or above (where it was reported) and there were relatively few studies from low-and-middle-income countries. The highest quality studies consisted of well-educated (tertiary level) white patients living in high-income-countries which used organised screening programmes. Consequently, the main findings of this review are weighted towards relatively homogenous samples and may not be directly translatable to other settings or lower-income-countries. The qualitative studies which were conducted in low-and-middle-income-countries (Brazil, Colombia, Taiwan, Tanzania) reported stronger adverse emotional impacts (Barrera-Clavijo et al., 2015; Barreto et al., 2016; Lin et al., 2011; Linde et al., 2019). Therefore, the findings reported in this review may be conservative compared to other health systems or cultural contexts.

Finally, HPV-positive results in the reviewed studies were usually accompanied by abnormal cytology. This meant that we were unable to determine the relative impact of HPV vs. abnormal cytology for many of the emotions described. However, there were some emotions which seemed inherently related to HPV, such as sexual distress and test-specific distress. Receiving both HPV and cytology results is, nevertheless, reflective of routine screening practice, meaning that the findings of this review should provide valuable and pragmatic insights into the patient experience at screening.

Limitations

Our timely systematic review benefits from the adoption of a relatively novel and rigorous mixed methods review design. Like most reviews, we have a number of limitations worth considering when interpreting the results. Firstly, although we used a comprehensive search strategy to identify papers across six major databases, our grey literature search was limited to OpenGrey and we did not contact authors or Listservs to identify additional literature. Also, given that there is no clear agreed or distinct theoretical definition for many emotions, emotion categorisations were often based on judgements and interpretations by the review team, especially where data was measured using non-validated scales or qualitative data. The meta-analyses were performed using small numbers of studies (range: 3 - 6) which can be unreliable and subject to bias, and also prohibited moderator analyses. Therefore, relevant mechanisms could not be explored and caution is warranted in the interpretations. Lastly, whilst we used the cognitive behavioural framework to map our findings, there are several other potentially more relevant theoretical models which could be used to structure emotional reactions to HPV; e.g. Williams' Affect and Health Behavioural Framework (Williams & Evans, 2014) or Leventhal's Common Sense Model of Self-Regulation

(Leventhal et al., 2016). Using alternative theoretical frameworks may have led to different formulations but we are confident that our overall conclusions are valid.

Implications for policy and practice

As HPV primary screening is being implemented around the world, our findings provide rich insight for policymakers and clinicians into women's experience of receiving HPV-positive results. In attempts to mitigate adverse response, common themes highlighted in this review (e.g. related to confusion around cancer risk or sexual transmission) could be targeted through tailored information in screening result letters or accompanying leaflets. Clinicians working in primary care and cervical screening in areas where HPV-testing is being implemented could also use this information to pre-empt or address women's questions and concerns, especially in low-and-middle-income countries where adverse emotional response may be greater. Public health or third sector organisations running campaigns on cervical cancer screening could frame their communications to target some of the key areas, e.g. to tackle stigma associated with sexually transmitted aspects. Clinical signposting and pathways could also be embedded within cancer screening programmes to provide support for some of the sub-groups highlighted, who may be at higher risk of clinically important adverse responses (e.g. women from ethnic minority backgrounds, or those with low health literacy or without access to social support).

Conclusion

Short-term anxiety, distress about test results, distress about sexual relationships, feelings of disgust and shame, surprise, and fear about cancer appear to be the most common emotional responses to testing positive for HPV. Almost exclusive use of observational and qualitative designs, however, limits conclusions regarding clinical significance and prohibits some important causal inferences. We hope this comprehensive review, paired with our provisional framework of relevant emotional, cognitive, and behavioural factors, will act as a springboard for the development of a cogent theoretical literature on this topic.

Author Contributions

EM, ZR, OT and JW conceived the study. OT, KW and ZR conducted the searches. OT, EM, LR, and JW selected eligible studies. RMM, LM and NK provided intellectual input on the review design. EM, OT, LR and JW assisted with data extraction and quality assessments. EM, OT and JW conducted the syntheses and analyses. EM drafted the paper. All authors contributed to the final version of the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Table 1

Descriptive characteristics of quantitative studies (and mixed-methods quantitative component).

Authors	Country	Total *n*	HPV+ *n*	Cytology	Population and Setting	Study Design	Time point	Quality Score
Alay et al. (2020)	Turkey	80	19 (hrHPV) 23 (hrHPV)	Normal Abnormal	≥30 years old, referred to a gynaecology outpatient clinic upon being diagnosed with an HPV infection by the community-based cervical cancer screening program.	Prospective longitudinal	Baseline (before result) and 2-months later.	60%
Andreasson et al. (2019)	Norway	487 HPV arm 521 cytology arm	175 84 53	Normal Abnormal (any grade) Abnormal (ASCUS and low grade)	Women aged 34–69 years living in one of the four implementation counties taking part the NCCSP project which trialled two methods of HPV-based screening (primary HPV vs. primary cytology testing).	Cross-sectional (embedded within a trial)	Ranging between 4-24 months after result.	100%

Daley et al. (2010)	USA	154	154	Abnormal (any grade)	18-45 years, recruited through a student health service and five parenthood planning clinics.	Mixed-methods: cross-sectional	Not reported.	40%
Ferenidou et al. (2012)	Greece	51	51	Not reported	21-68 years, recruited through a gynaecological outpatient clinic in “Aretaieion” Hospital, Athens during 2008-2009.	Cross-sectional	Not reported	60%
Garcés-Palacio et al. (2019)	Colombia	675	50	ASCUS	Women aged 20-69 years old, with a first time Atypical Squamous Cells of Undetermined Significance (ASCUS) cytology result. This study was nested within the larger trial ‘Evaluation of Strategies for Optimal Clinical Management of Women with Atypical Squamous Cells of Undetermined Significance’ (ASCUS-COL), conducted between 2011 and 2016 in the city of Medellín.	Nested within observational arm of a larger RCT.	Baseline (before result), shortly after result, and 12-months later.	40%
Guerra Rodriguez et al. (2019)	Mexico	201	201	Not reported.	Mexican women aged 18 years and older with an HPV diagnosis for at least 12 months, recruited via mass media (radio, television, and social networks).	Cross-sectional	At least 1-year after result (Mean= 1.85 years)	60%

Hsu et al. (2018)	Taiwan, China	70 45	21	Normal Abnormal	Women 20–65 years old attending a gynaecological clinic in southern Taiwan for their first follow-up visit after diagnosis.	Prospective longitudinal	One month, 6-months, and 12-months after result.	80%
Kitchener et al. (2008)	UK	604 concealed arm	105 71	Normal Abnormal (mild/borderline)	20-64 years, participated in ARTISTIC: a RCT to determine the effectiveness of HPV testing in primary cytology screening.	1. RCT	Approx. 2 weeks after result.	100%
		1904 revealed arm	417 205	Normal Abnormal (mild/borderline)		2. Cross-sectional (revealed arm).		
Kwan et al. (2012)	Hong Kong, China	299	157	ASCUS	Mean age across groups of 36.8, recruited via routine cervical screening at one of five community health clinics of the Family Planning Association of Hong Kong.	Prospective cross-sectional	Baseline (result notification) and 6 months after result.	100%
Maggino et al. (2007)	Italy	72	36	Not reported	20-45 years, during periodical check-up at obstetrics and gynaecology clinic.	RCT	Not reported.	40%

Maissi et al. (2004)	UK	1376	536	Abnormal (mild/borderline)	Mean age across groups of 37.6, recruited through the English pilot study of liquid-based cytology and HPV testing (clinics).	Cross-sectional	Within 4 weeks of result.	100%
Maissi et al. (2005)	UK	1011	369	Abnormal (mild/borderline)	Mean age across groups of 37.9, initially recruited through the English pilot study of liquid-based cytology and HPV testing (clinics).	Cross-sectional	6-months after result.	80%
McBride et al. (2020)	UK	1127	258 179 170	Normal Normal for second time at 12-months Abnormal	Women aged 24–65 who had attended screening at one of five sites piloting HPV primary screening in England, including a control group with normal cytology who were not tested for HPV.	Cross-sectional	Mailed within 1 month after result.	100%
McCaffery et al. (2004)	UK	428	46 23	Normal Abnormal or Unsatisfactory	20-61 years, attending a National Health Service well-woman clinic in central London for routine conventional cervical screening.	Cross-sectional	Within one week of results.	60%

Nagele et al. (2019)	Austria	209	82 from conservative management	Abnormal	Mean age of 37, recruited from a university-based colposcopy clinic after referral for evaluation for suspect precancerous genital lesions.	Prospective cohort	Baseline (not defined), 6-months, and 12-months.	60%
Ngu et al. (2018)	Hong Kong, China	121	121	Normal	Mean age of 47.5, recruited through clinics in another RCT on primary screening in Hong Kong (COCY study).	RCT	Not reported.	60%
Wang, Jeng et al. (2010)	Taiwan, China	249	44	Abnormal (any grade)	18-35 years, recruited through three hospitals in Taiwan.	Cross-sectional	Within 3-months of result.	60%
Wang, Shi et al. (2011)	China	2605	179	Abnormal (any grade)	18-65 years, recruited through multicentre hospitals.	Cross-sectional	Within 3-months of result.	80%

* hrHPV = high risk HPV (type 16/18) extracted from available data. ASCUS = atypical squamous cells of undetermined significance.

Table 2

Descriptive characteristics of qualitative studies (and mixed-methods qualitative component).

Authors	Country	Total *n*	HPV+ *n*	Cytology	Population and Setting	Study Design	Time point	Quality Score
Barrera-Clavijo et al. (2015)	Colombia	93	55	Not reported	30-65 years, participating in the Columbian HPV testing screening pilot.	Focus groups	Not reported	80%
Barreto et al. (2016)	Brazil	14	14	No cytology test	20-42 years, attending a Specialised Medical Care Service (SAME).	Semi-structured Interviews	Not reported	60%
Bertram et al (2007)	USA	10	Not stated	Abnormal (mixed)	18-35 years, purposive sample of demographically diverse women who attended one Women's Health outpatient clinic that typically serves a multiethnic, low- income population.	Semi-structured Interviews	Within 5 years from test result	100%

Authors	Country	Total *n*	HPV+ *n*	Cytology	Population and Setting	Study Design	Time point	Quality Score
Daley et al. (2010)	USA	52	52	Abnormal (any grade)	18-45 years, recruited through a student health service and five parenthood planning clinics.	Mixed-methods: semi-structured interviews	Not reported	40%
Head et al. (2017)	USA	30	17 5	Normal cytology Abnormal cytology	Mean age of 27.8 years, attending for two clinical visits approximately 6 weeks apart.	Semi-structured interviews	Not reported	100%
Kosenko et al. (2012)	USA	25	25	Not reported	19-56 years, recruited through advertisements posted across cities in south eastern USA and on social media.	Semi-structured interviews	Average of 4.8 years after HPV diagnosis	100%
Lin et al. (2017)	Taiwan, China	20	20	Not reported	20-60 years, recruited using purposeful sampling through a gynaecology outpatient clinic in a university-based hospital.	Semi-structured interview	Not reported	40%

Authors	Country	Total *n*	HPV+ *n*	Cytology	Population and Setting	Study Design	Time point	Quality Score
Linde et al. (2019)	Tanzania	15	15	Not reported.	Women aged 27-55 who had tested HPV-positive during a patient-initiated screening and been appointed for a follow-up screening 14 months later.	Semi-structured interviews	At least 14 months after result.	100%
McCaffery and Irwig (2005)	Australia	19	19	Abnormal (mixed)	53% <35 years and 47% >35 years, recruited through general practice, family planning clinics, and specialist gynaecologists.	Unstructured interviews	Not reported	100%
McCaffery et al. (2006)	UK	74	57	Abnormal and normal cytology	20-64 years, recruited through clinical trials of HPV testing and colposcopy clinics in Manchester and London.	Semi-structured interviews	Not reported	100%
McCurdy et al. (2011)	USA	18	18	Abnormal (mixed)	21-45 years, who attended one of three clinics open to the general public in a border city a medically underserved area in Cameron County, Texas.	Structured interviews	Not reported	100%

Authors	Country	Total *n*	HPV+ *n*	Cytology	Population and Setting	Study Design	Time point	Quality Score
O'Connor et al. (2014)	Ireland	27	6	Abnormal (mixed)	26 to 61 years, recruited via colposcopy clinics in Ireland.	Semi-structured interviews	Within 6-months from HPV test	100%
Perrin et al. (2008)	USA	52	52	Abnormal (mixed)	18 to 44 years, recruited via three clinical sites in west central Florida – two Planned Parenthood clinics and the Student Health Service clinic at the University of South Florida (Tampa campus).	Semi-structured interviews	Within 1 week of HPV result	100%
Tiro et al. (2019)	USA	46	15 (hrHPV) 31 (other HPV type)	Mixed	Mean age 55.5 years, recruited a subset of women who were randomized as part of a pragmatic trial to receive an unsolicited mailed high risk HPV self-sampling kit, returned the kit, and tested positive.	Semi-structured interviews	Not reported.	100%
Waller et al. (2007)	UK	30	30 (at baseline)	Normal cytology	Above 20 years, recruited through the ARTISTIC trial (UK clinical screening	Semi-structured interviews	Not reported after second HPV test.	100%

Authors	Country	Total *n*	HPV+ *n*	Cytology	Population and Setting	Study Design	Time point	Quality Score
					trial) 12-months after testing HPV-positive with normal cytology.			
			21 (at 12-months)	No cytology test				
Wyndham-West et al. (2018)	Canada	20	Not reported	Not reported.	20s-40 years, recruited through an HPV vaccination clinic in Toronto, Ontario.	Semi-structured interviews	Not reported	100%

* hrHPV = high risk HPV (type 16/18).

Table 3 – Brief definition of each of the emotions identified as themes.

	Brief Definition
Anxiety	State anxiety describes an emotional state often characterized by apprehension, nervousness, and/or uncertainty related to specific or future event(s) (Spielberger, 1983).
Distress	Psychological distress is a term to describe a collection of negative emotions or type of stress that results from being overwhelmed by demands or perceived threats. Distress can impact on everyday functioning related to general or specific events (APA, 2019b)
Fear	Fear is an intense basic emotion induced by perceived danger or threat(s) (APA, 2019c).
Disgust and Shame	Disgust is characterized by strong aversion to something deemed unpleasant. Shame can stem from disgust and is characterized by a highly unpleasant feeling of humiliation or distress caused by the belief (or perception that others believe) that one has been dishonourable, immodest, or indecorous (APA, 2019f)
Surprise	Surprise is described as feelings of sudden unexpectedness. It results from violations of an expectation or detection of novelty in the environment (APA, 2019g), often followed by confusion.
Sadness	Sadness and depressive mood are usually temporary emotional states usually aroused by the loss of something that is highly valued (APA, 2019e). Clinical depression shares core characteristics with sadness but differs in that it is a serious longer-term mental illness which significantly impairs everyday functioning.
Positive Affect	Positive affect is a broad and generic term for the internal feeling that occurs when a goal has been achieved, a source of a threat has been avoided, or one is satisfied with their current situation (APA, 2019d).

Apathy	Apathy is a lack of motivation or the absence or suppression of emotion, interest, or concern, and presents as a state of indifference (APA, 2019a).

Table 4

Results of quantitative studies (or mixed-methods quantitative components) included in the review.

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
Alay et al. (2020)	To assess HPV-infected women's sexual functions and anxiety levels before and after being informed about their HPV genotype (high-risk vs. low-risk) and cytology results.	Anxiety; Sexual function.	BAI (Beck, Epstein, Brown, & Steer, 1988); FSFI (Rosen et al., 2000)	Women who had high-risk HPV genotypes 16/18 with normal or abnormal cytology had significantly higher anxiety levels after being informed of their result, compared to low-risk HPV genotypes with normal cytology. Women who tested positive for high-risk HPV 16/18 had significantly less sexual desire (one domain of the FSFI) after being informed about their test result; though there were no differences in total sexual function score.	Higher anxiety after being informed of high-risk HPV result. Less sexual desire after being informed of high-risk HPV result; however, no differences in overall sexual function.	N/A
Andreasson et al. (2019)	To compare long-term anxiety and depression scores between women	Anxiety and Depression (Combined)	PHQ-4 (Kroenke, Spitzer, Williams, & Lowe, 2009)	Women with HPV-positive results and normal or abnormal cytology were no more likely to have mild vs. normal vs. moderate/severe	No effect for combined anxiety and depression at 4-24 months.	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
Note: data from the watchful waiting arm were extracted for this review.	allocated to primary HPV screening vs. primary cytology screening.			anxiety and depression scores, compared with normal cytology at 4-24 months post-result.		
Daley et al. (2010)	To assess the emotional impact and behavioural consequences following HPV diagnosis among women who had received abnormal Pap test results.	Stigma; Fear; Self-blame; Powerlessness ; Anger; Additional emotion items; Additional attitudinal items.	Non-validated single item questions in each of the categories.	Majority (%) endorsed 'agree' or 'strongly agree' for domains that the authors categorised as: stigma; fear; self-blame; anger; several additional emotion and attitudinal items.	N/A	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
Ferenidou et al. (2012)	To demonstrate the impact of HPV diagnosis on sexual function and mental health of Greek women.	Anxiety, physical distress, guilt, anger, shame, self-confidence, stigma, fear, sexual impact and sexual function.	Non-validated single item questions, except for sexual function which used a sexual dysfunction symptom checklist.	Majority (%) endorsed that they experienced anxiety (76.5%) after HPV diagnosis as well as fear regarding health in the future (82.4%). Nearly half of the women endorsed guilt (41.1%) and anger (43.1%). A minority endorsed distress, shame, reduction in self-esteem and stigmatization (all < 22%). Reduced sexual interest (33.3%) and frequency of sexual intercourse (43.1%) were also endorsed by some.	N/A	N/A
Garcés-Palacio et al. (2019)	To assess the psychosocial impact of HPV testing, colposcopy, and Pap-smear, as triage strategies after a Pap-	Self-esteem; Anxiety; Psychosocial burden of HPV.	Rosenberg Scale (Rosenberg, 1989); STAI (Spielberger, 1983);	Women testing positive for HPV with ASCUS had higher anxiety and psychosocial burden scores shortly after their result, compared with HPV-negative women with ASCUS; however, there were no differences at 12-months. Self-	Higher anxiety and psychosocial burden shortly after result but not 12-months later. No effect for self-esteem.	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
	smear with atypical squamous cells of undetermined significance (ASCUS), and evaluate the psychosocial impact based on the results of the strategies.		HPV-Impact Profile (HIP) (Mast et al., 2009).	esteem scores did not differ shortly after result or at 12-months.		
Guerra Rodriguez et al. (2019)	To assess correlative factors that facilitate and inhibit transition to cervical cancer protective behaviour among women with HPV.	Stigma related to coping with HPV diagnosis, and cervical cancer protective behaviour.	HIV Stigma Scale adapted (Berger, Ferrans, & Lashley, 2001); Brief COPE adapted – Spanish version (Vargas-Manzanares,	Higher levels of stigma were significantly correlated with utilising fewer coping strategies ($r = -0.278$, $p<.01$) and less protective behaviour ($r = -0.163$, $p<.05$).	N/A	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
			Herrera-Olaya, Rodríguez-García, & Sepúlveda-Carrillo, 2010); Non-validated measure measuring stable sexual partner defined by condom sue, cervical cytology control, and protective communication in sexual health.			

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
Hsu et al. (2018)	To examine the psychosocial adjustment trajectory, focusing on psychological distress, sexual relationships and health care information, when receiving a positive diagnosis of HPV.	Sexual distress; Psychosocial adjustment to psychological distress and sexual relationships.	PEAPS-Q (Bennetts et al., 1995); PAIS-SR psychological distress domain and sexual relationship domain – Chinese version. (Li, Rew, & Hwang, 2012)	A trajectory of psychosocial adjustment in psychological distress and sexual relationships occur from one to 6 months after HPV diagnosis. Initial emotional distress was associated with changes in adjustment. Psychosocial adjustment to HPV was worse at 1 month compared with 6 and 12 months after diagnosis.	N/A	Current sexual activity; Presence of genital warts; Greater emotional distress at baseline.
Kitchener et al. (2008)	To assess the psychosocial impact of HPV testing as an adjunct to cytology in	Anxiety (state and trait); General psychological distress;	STAI-40 (Spielberger, 1983)	Women who knew they were HPV+ with mildly abnormal or normal cytology displayed no differences in anxiety or distress, when compared with those who did not know they were HPV+. Sexual satisfaction was lower in	1. RCT: no effect for anxiety or general distress; higher sexual distress for those with normal cytology only.	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
	routine primary cervical screening.	Sexual satisfaction.	GHQ-28 (Golderberg, 1988) Sexual Rating Scale (Fedor-Freybergh, 1977)	those who knew they were HPV+ with normal cytology, compared to those who did not know; but there were no differences for HPV+ with abnormal cytology who knew vs. did not know. Women who knew they were HPV+ with normal cytology had higher state anxiety and distress, compared to those who knew they were HPV- with normal cytology. Sexual satisfaction was higher in HPV-positive groups.	2. Cross-sectional revealed arm: higher state anxiety and general distress; lower sexual distress.	
Kwan et al. (2011)	To assess the psychological burden of testing positive for high-risk human papillomavirus (HPV) on Chinese women	Anxiety (state); Cervical cancer worry; Psychosocial burden of	S-STAI-6 (Marteau & Bekker, 1992); Adapted Breast Cancer Worry Scale (Hay,	At result notification (baseline), regardless of whether women reported knowing their HPV result, the HPV+ group with abnormal cells had significantly higher state anxiety, cervical cancer worry, and HPV-impact score, compared to the HPV- with abnormal cells group.	1. Regardless of whether women knew their HPV result, higher anxiety, fear about cervical cancer, and test-specific	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
	with atypical squamous cells of undetermined significance (ASCUS).	HPV (test-specific distress).	Buckley, & Ostroff, 2005); HPV-Impact Profile (HIP) (Mast et al., 2009)	Sub-analyses on women who reported knowing vs. not knowing their HPV result at notification (baseline), revealed no differences in anxiety, cancer worry, relationship, and sexual satisfaction between HPV+ and HPV-; however, those who knew their HPV+ result had higher HIP-impact scores (psychosocial burden/sexual distress). Irrespective of HPV result, all outcome scores decreased over time. At 6-months post-result, there were no significant differences between groups for anxiety and cervical cancer worry. However, HPV-impact score (psychosocial burden/sexual distress) remained higher for the HPV+ group.	distress at result notification (baseline). 2. When women knew their HPV result, higher test-specific distress. No effect on anxiety, cancer worry, relationship and sexual satisfaction. No effect for anxiety and fear about cancer at 6-months. Higher sexual distress at 6-months.	

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
Maggino et al. (2007)	To evaluate the impact of the communication of an HPV diagnosis on the cognitive-behavioural aspect, emotional experiences, psychic-physical well-being, and psychosexual sphere.	Anxiety (state and trait); Psycho-physiological reactions; Fears; Depressive thoughts; Intrusive thoughts and compulsive behaviours; Quality of life; Sexual Functioning.	Cognitive Behavioural Assessment (CBA 2.0) (Bertolotti, Zotti, Michielin, Vidotto, & Sanavio, 1990) SAT-P (Majani et al., 1999) BISF-W (Mazer, Leiblum, & Rosen, 2000)	Most frequent emotional reactions to HPV were fear (25%), anxiety (17%). 38% endorsed no emotional reaction. Higher state anxiety and intrusive thoughts and compulsive behaviours in HPV+ group compared to no HPV. No differences in quality of life or sexual functioning.	Higher state anxiety.	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
Maissi et al. (2004)	To describe the psychological impact on women of being tested for HPV when smear test results are borderline or mildly dyskaryotic.	Anxiety (state); General psychological distress; Concern about result.	S-STAI-6 (Marteau & Bekker, 1992) GHQ-12 (Golderberg, 1988) Non-validated 2-item questionnaire (concern)	Higher state anxiety, distress, and concern in HPV+ group compared to other test result groups.	Higher anxiety, general distress, and test-specific distress.	Younger age (β=-0.11), higher perceived risk of cancer (β=0.17) and reporting not understanding results (β=0.17) predicted higher anxiety. No effect found for other demographic factors, awareness/ importance of HPV, and perceived severity of cancer.
Maissi et al. (2005)	To describe the psychological impact on women of being	Anxiety (state); General	S-STAI-6 (Marteau & Bekker, 1992)	No differences in state anxiety and general distress at 6 months.	No differences for anxiety and distress.	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
	tested for HPV when smear test results are borderline or mildly dyskaryotic at 6 month follow-up.	psychological distress; Concern about result; Sexual health worries.	GHQ-12 (Golderberg, 1988) Non-validated 2-item questionnaire (concern) PEAPS-Q (Bennetts et al., 1995)	Concern about result and sexual health worries higher in HPV+ group compared to other test result groups at 6-months.	Higher concern about result and sexual distress	
McBride et al (2020)	To examine short-term anxiety and distress in women receiving different results following routine HPV primary testing at cervical screening.	Anxiety (state); General Psychological distress; Concern about result;	S-STAI-6 (Marteau & Bekker, 1992); GHQ-12 (Golderberg, 1988);	Anxiety was significantly higher in women testing HPV-positive with either normal cytology or abnormal cytology, compared with the control group (normal cytology). Distress was slightly higher in women who tested HPV-positive with abnormal cytology, compared with the control group. There were also increased	Higher anxiety shortly after HPV-positive with normal cytology (for first time) or abnormal cytology.	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
		Reassurance by result; Worry about cancer.	Non-validated questions assessing concern, reassurance, and worry.	odds of very high anxiety (STAI score >49) in women who tested HPV-positive with normal or abnormal cytology compared to the control group. This pattern of results was only observed among women receiving their first HPV-positive result, not among women found to have persistent HPV at 12-month follow-up. Odds of concern and worry were higher, and reassurance lower, in HPV-positive groups compared to HPV-negative and normal cytology groups.	General distress higher only for HPV-positive and abnormal cytology. Higher concern and worry, and lower reassurance.	
McCaffery et al. (2004)	To examine the psychosocial impact of testing positive for high risk HPV among women attending	Anxiety (state); Screening/test-specific distress; Feelings	S-STAI-6 (Marteau & Bekker, 1992) CSQ (Wardle, 1995)	Higher anxiety and test-specific distress in HPV+ with normal cytology, compared with HPV- with normal cytology. No differences in anxiety and test-specific distress for HPV+ with abnormal or	Higher anxiety, test-specific distress, and sexual distress.	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
	primary cervical screening.	towards sexual partner.	Non-validated 3-item questionnaire (feelings towards sexual partner).	unsatisfactory cytology, compared to HPV- with same cytology result. HPV+ had worse feelings towards sexual partner, regardless of cytology result.		
Nagele et al. (2019)	To examine the impact of different treatment strategies - surgical treatment or watchful waiting- on sexual activity, psychosocial distress, and fear of progression in women with HPV-associated premalignant genital lesions.	Fear of Progression; Sexual distress.	FoP-Q (Herschbach et al., 2005); CDDQ sexual & reproductive consequences subscale (Shinn et al., 2004).	During an observational period of 12 months (baseline, 6 months, 12 months) there were no significant differences in fear of progression or sexual distress.	No effect over 12-months.	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
Ngu et al. (2018)	To compare the effect of two educational interventions on the psychosocial wellbeing. *Note: descriptive pre-intervention data and data from the leaflet (control) arm were extracted for this review.*	Anxiety and Depression; Cervical cancer worry; Screening-related anxiety; HPV-related shame.	HADS (Zigmond & Snaith, 1983) CSQ (Wardle, 1995) Adapted Breast Cancer Worry Scale (Custers et al., 2014) Adapted STD-related shame questionnaire (Cunningham et al., 2002)	Before randomisation to leaflet vs. counselling, 38.0% and 14.9% of women had clinical relevant anxiety and depression scores respectively. Anxiety and cervical cancer worry were slightly lowered after receiving information in the form of a leaflet, but there were no differences in depression scores. Anxiety and cervical cancer worry decreased over time. There were no differences in HPV-related shame over time.	N/A	N/A
Wang, Jeng et al. (2010)	To describe the psychological impact of HPV.	Psychosocial burden of HPV (test-	HPV-Impact Profile (HIP) (Mast et al., 2009)	Higher HPV-impact score in HPV+ with abnormal cytology compared to normal cytology.	Higher test-specific and sexual distress	N/A

Authors	Psychological Aim	Relevant Outcome(s)	Measure(s)	Main relevant findings	Direction of effect for emotion in HPV+	Predictors of adverse emotion in HPV+
		specific distress).				
Wang, Shi et al. (2011)	To assess the psychological burden of Chinese women with different HPV-related diseases.	Psychosocial burden of HPV (test-specific distress).	HPV-Impact Profile (HIP) (Mast et al., 2009)	Higher HPV-impact score in HPV+ with abnormal cytology compared to normal cytology. HIP domains “sexual impact”, “self-image”, and “control/life impact” had the highest scores. HPV+ with abnormal cytology showed sustained burden at 30 days, compared to HPV- with abnormal cytology which decreased.	Higher test-specific and sexual distress.	Psychosocial burden higher for women living in urban areas compared to rural.

Table 5

Results of qualitative studies (or mixed-methods qualitative components) included in the review.

Authors	Aim	Main themes relating to emotional outcomes
Barrera-Clavijo et al. (2016)	To evaluate the effect of communication and education strategies designed for women aged 30–65 years who participated in the comparative HPV testing and cervical cancer screening study as an alternative technique to cervical cytology.	Anxiety, fear of cancer, and fatalism in HPV-positive women. Also, blame towards partner. Face-to-face discussion with a health care professional reduced anxiety for many women.
Barreto et al. (2016)	To understand the feelings of women infected with HPV.	Fear, sadness, and shame in HPV+ women.
Bertram et al (2007)	To describe the experience of women with abnormal Papanicolaou (Pap) smears with a particular focus on their informational needs.	Initial anxiety at disclosure. Stigma associated with a sexually transmitted disease (STD) and a dearth of information available for male partners were problematic and influenced decisions about disclosure of human papillomavirus (HPV) infection to current or future partners.
Daley et al. (2010)		Fear, self-blame, stigma, powerlessness, anger.

Authors	Aim	Main themes relating to emotional outcomes
	To assess the emotional impact and behavioural consequences following HPV diagnosis among women who had received abnormal Pap test results.	
Head et al. (2017)	Evaluate understanding of test results (Pap and HPV)	Confusion and anxiety in HPV+ women.
Kosenko et al. (2012)	To determine the sources of uncertainty experienced by women living with HPV	Seven sources of uncertainty: meaning of diagnosis; potential for disease progression; source of the infection; disclosure; sex and reproduction; and the HPV vaccine.
Lin et al. (2017)	To determine the psychological response of HPV infected women and their responses in terms of cognition, emotions, and behaviour.	Primarily fear, worry and suspicion. Also, disgust, shock, denial, disgust, guilt, and self-blame.
Linde et al. (2019)	To understand causes of attendance and non-attendance to a follow-up cervical cancer screening among HPV-positive women.	Fear of cancer, confusion, and relief that HPV was not cancer.

Authors	Aim	Main themes relating to emotional outcomes
McCaffery and Irwig (2005)	To explore women's understanding of HPV, their information needs and experience of HPV infection using a method grounded in women's experience	Anxiety and negative psychological response moderated by uncertainty about HPV, clinical communication, and mode of delivery of result. Anxiety most associated with receiving the test result by letter and searching the internet for further information.
McCaffery, Waller et al. (2006)	To examine the social and psychological impact of HPV testing in the context of cervical cancer screening.	Stigma, anxiety, stress, concern about sexual relationships, and worry about disclosure. Psychological burden related to relationship status and history, social and cultural norms, and understanding of key features of HPV.
McCurdy et al. (2011)	To examine Hispanic women's responses to learning they were HPV+, their decisions to disclose their HPV+ status, and their own and others' reactions to their disclosure.	All expressed surprise and fear; some expressed issues with disclosure. Higher concern expressed in single, unattached women under 28 years.
O'Connor et al. (2014)	To explore emotional responses and predictors of negative reactions among women undergoing HPV tests in routine clinical practice.	Adverse emotional response (shame, embarrassment, stigma, regret, self-blame, anxiety, worry) linked to HPV infection rather than testing. Negative emotional response primarily influenced by concerns about abnormal cytology or diagnosis of CIN. Also, to a lesser extent, by HPV knowledge, awareness of HPV being sexually transmitted, awareness of HPV prevalence, and HPV information needs.

Authors	Aim	Main themes relating to emotional outcomes
Perrin et al. (2008)	To explore women's reactions to HPV diagnosis.	Emotions related primarily to stigma, fear, self-blame, powerlessness, and anger.
Tiro et al. (2019)	To explore patient perspectives after a positive HPV self-sampling result.	Two main relevant emotional themes: intense affect after receiving positive results (e.g. fear of cancer and shock); and confusion about purpose and meaning of HPV testing. Also, relief after speaking to a healthcare professional and apathy (indifference).
Waller et al. (2007)	To examine the way in which anxiety and concern transitioned over the course of the 12 months between two HPV tests; to explore the impact of a second HPV result on disclosure behaviour; and to explore women's choice of management of persistent HPV infection.	Adverse emotional impact (anxiety, shock, confusion, distress) reported initially for first test result. However, this did not generally last in the year between the two test results. The emotional impact of a second positive HPV result 12-months later was greater for many women, sometimes causing them to disclose their result and seek support.
Wyndham-West et al. (2018)	To determine experiences surrounding HPV infections and pre-cancer.	Anxiety, shame, stigma, ‘containment’ of the infection (prevention), disclosure and social impact.

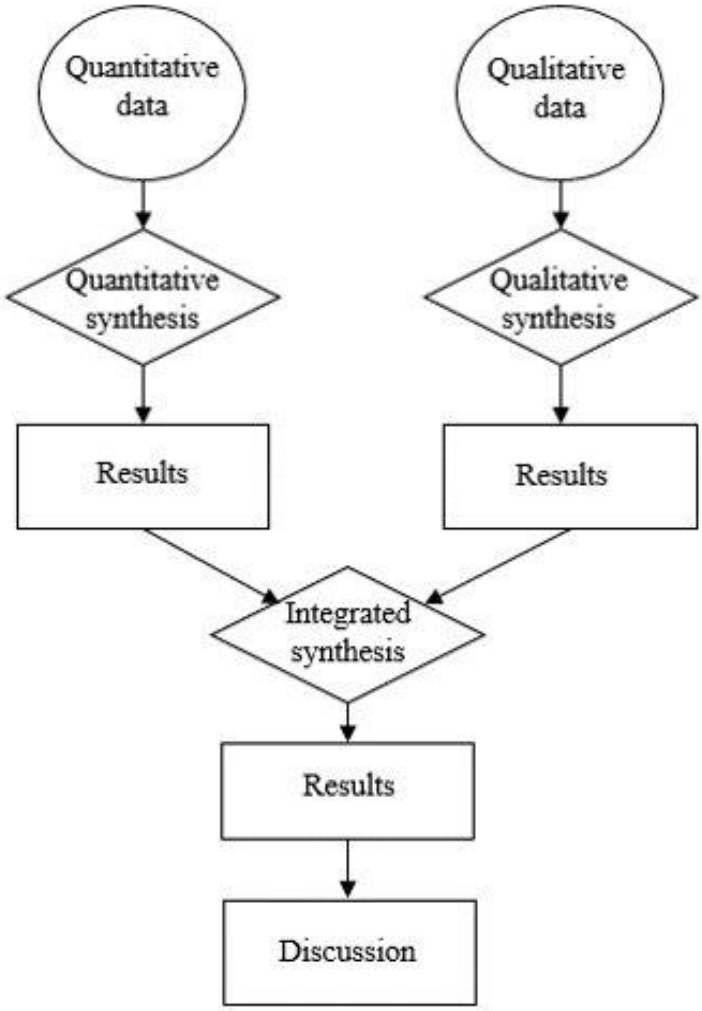

Figure 1. Overview of the results-based convergent synthesis design.

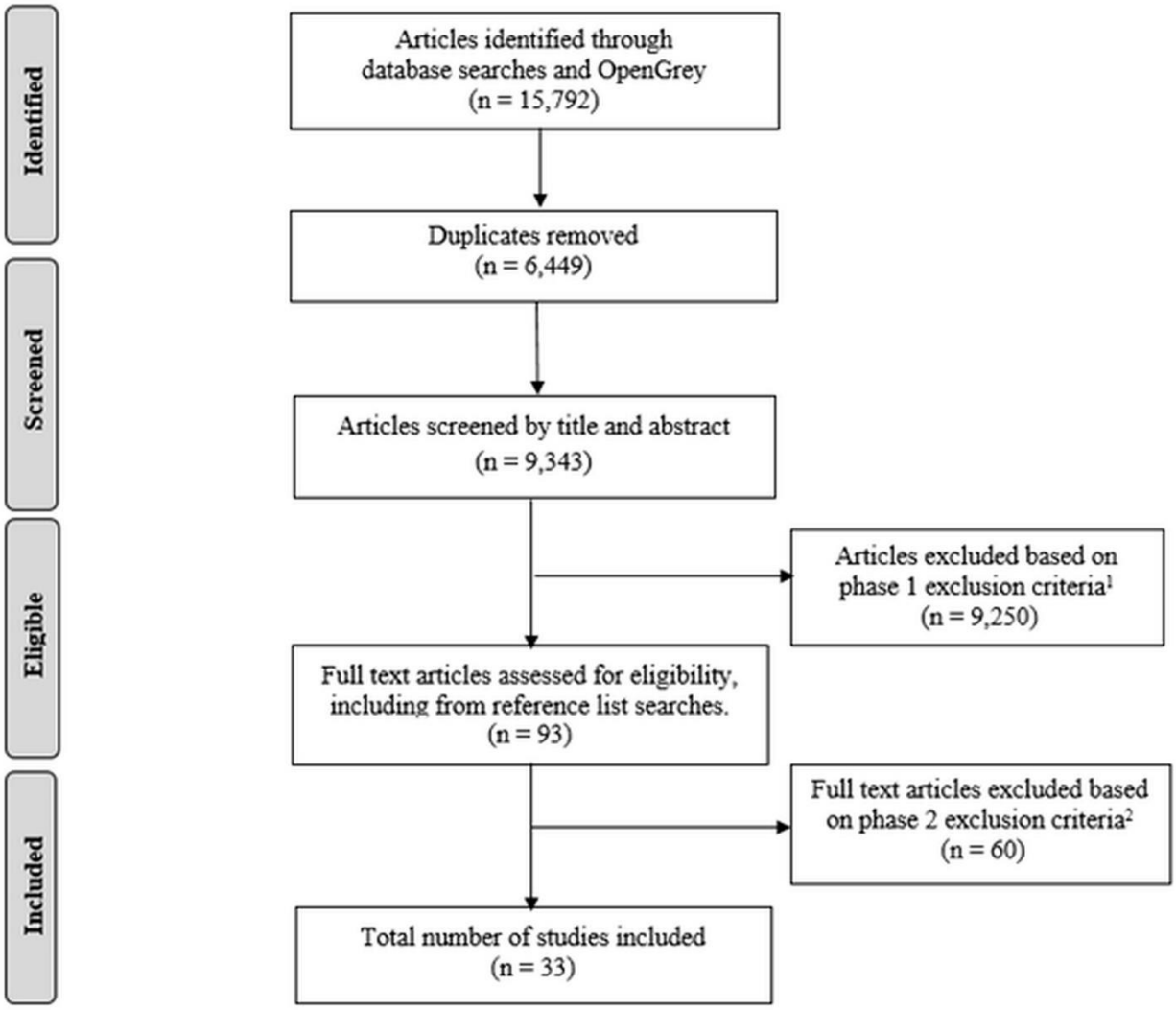

Figure 2. Prisma Flowchart: overview of searches and selection process.

[1]Phase 1 exclusion reasons for titles and abstracts: 1) not population of interest; 2) not outcomes of interest (e.g. HPV attitudes or knowledge without emotional outcome); 3) not empirical study; 4) no abstract; 5) HPV not in the context of cancer screening; 6) no clinical diagnosis of HPV (e.g. hypothetical scenario design); 7) only HPV vaccine related.
[2]Phase 2 exclusion criteria described in the eligibility section used for full text articles.

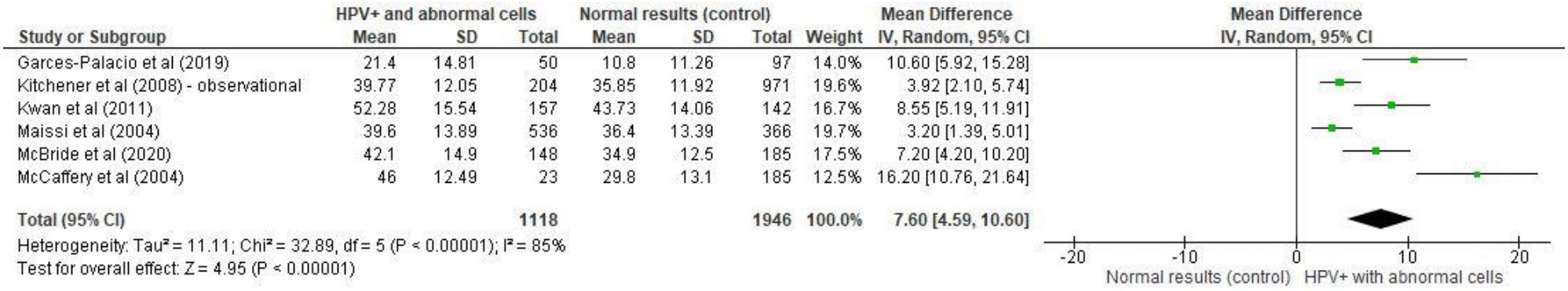

Figure 3a – Forest plot comparing short-term anxiety (result notification ≤ 2 months) between those testing positive for HPV with abnormal cytology and control groups (HPV-negative and/or normal cytology groups).

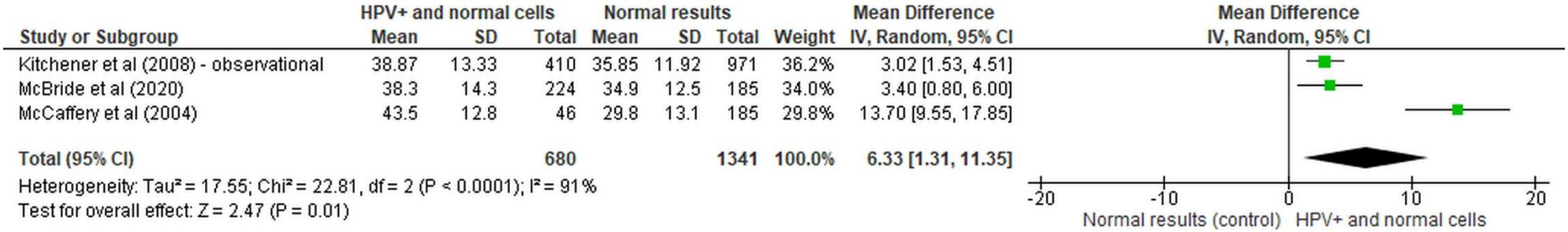

Figure 3b – Forest plot comparing short-term anxiety (result notification ≤ 2 months) between those testing positive for HPV with normal cytology and control groups (HPV-negative and/or normal cytology groups).

Study or Subgroup	HPV+ with abnormal cells Mean	SD	Total	Normal results (control) Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Garces-Palacio et al (2019)	16.5	16.62	12	12.7	10.64	25	2.1%	3.80 [-6.49, 14.09]
Kwan et al (2011)	37.39	12.28	157	37.27	11.08	142	31.3%	0.12 [-2.53, 2.77]
Maissi et al (2005)	36.7	13.44	369	36.8	13.58	288	50.5%	-0.10 [-2.18, 1.98]
McBride et al (2020)	36.8	13.1	157	37	12.1	60	16.2%	-0.20 [-3.88, 3.48]
Total (95% CI)			**695**			**515**	**100.0%**	**0.03 [-1.45, 1.51]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.55$, df = 3 (P = 0.91); $I^2 = 0\%$
Test for overall effect: Z = 0.04 (P = 0.96)

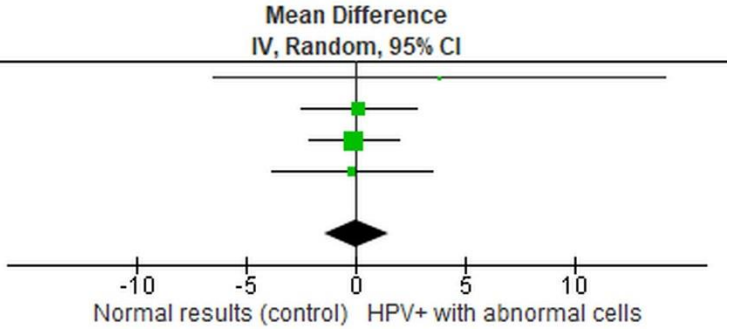

Figure 3c – Forest plot comparing long-term anxiety (>2 months) between those testing positive for HPV with abnormal cytology and control groups (HPV-negative and/or normal cytology groups).

Study or Subgroup	HPV+ and abnormal cells Mean	SD	Total	Normal results (control) Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Garces-Palacio et al (2019)	35.9	19.91	50	23.2	15.1	97	15.7%	0.75 [0.40, 1.10]
Kitchener et al (2008) - observational	4.57	5.44	201	3.31	5.18	972	17.9%	0.24 [0.09, 0.39]
Kwan et al (2011)	36.56	18.04	157	26.52	16.33	142	17.2%	0.58 [0.35, 0.81]
Maissi et al (2004)	2.8	4.63	536	2	1.91	366	18.1%	0.21 [0.08, 0.35]
McBride et al (2020)	3.3	3.8	167	2.3	3.3	204	17.5%	0.28 [0.08, 0.49]
McCaffery et al (2004)	17	2.31	23	8.9	3.45	185	13.6%	2.41 [1.92, 2.90]
Total (95% CI)			**1134**			**1966**	**100.0%**	**0.68 [0.32, 1.03]**

Heterogeneity: $Tau^2 = 0.18$; $Chi^2 = 82.45$, df = 5 ($P < 0.00001$); $I^2 = 94\%$
Test for overall effect: $Z = 3.75$ ($P = 0.0002$)

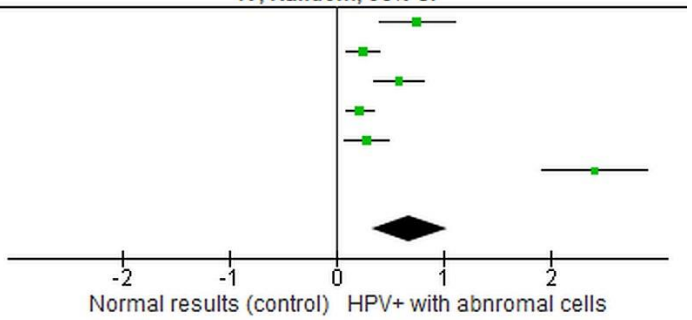

Figure 4a – Forest plot comparing short-term distress (result notification ≤ 2 months) between those testing positive for HPV with abnormal cytology and control groups (HPV-negative and/or normal cytology groups).

Study or Subgroup	HPV+ with abnormal cells Mean	SD	Total	Normal results (control) Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Garces-Palacio et al (2019)	22	12.3	12	19.5	13.02	25	11.7%	0.19 [-0.50, 0.88]
Kwan et al (2011)	30.25	18.17	157	24.36	16.21	142	18.1%	0.34 [0.11, 0.57]
Maissi et al (2005)	2.3	3.84	369	2	3.39	288	18.8%	0.08 [-0.07, 0.24]
McBride et al (2020)	2.5	3.2	177	2.5	3.7	65	17.4%	0.00 [-0.28, 0.28]
Wang, Jeng et al (2010)	48.8	20.83	44	28.2	20.83	51	15.5%	0.98 [0.55, 1.41]
Wang, Shi et al (2010)	45.8	13.56	179	33.1	13.71	504	18.6%	0.93 [0.75, 1.11]
Total (95% CI)			**938**			**1075**	**100.0%**	**0.42 [0.05, 0.80]**

Heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 65.61$, df = 5 ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: $Z = 2.21$ ($P = 0.03$)

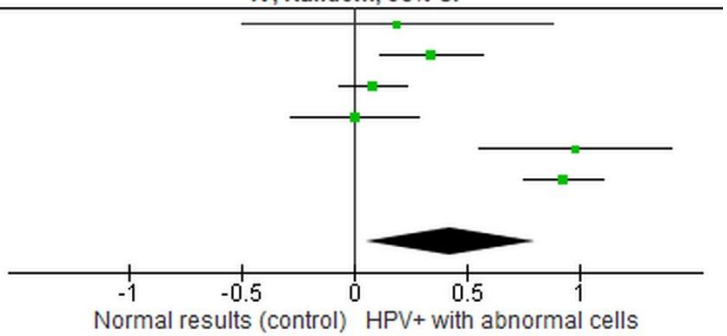

Figure 4b – Forest plot comparing long-term distress (>2 months) between those testing positive for HPV with normal cytology and control groups (HPV-negative and/or normal cytology groups), using the Maissi et al. (2005) general distress measure.

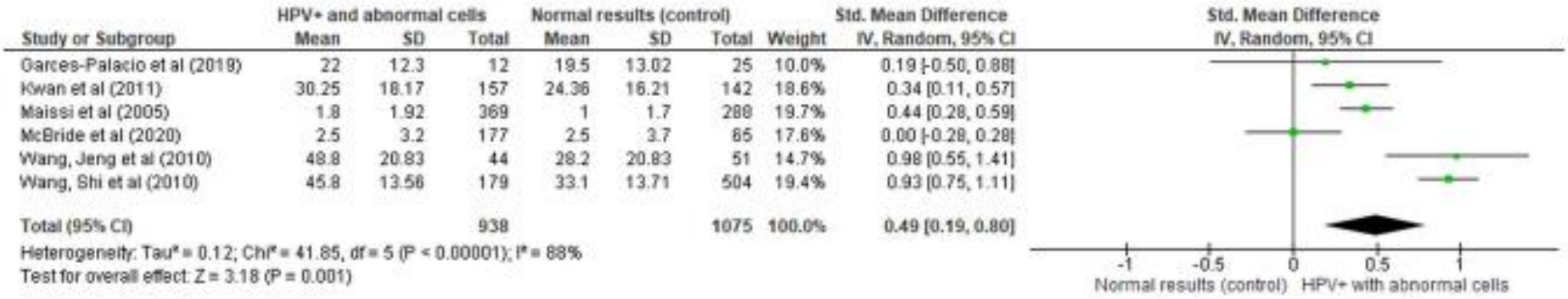

Figure 4c -. Forest plot comparing long-term distress (>2 months) between those testing positive for HPV with abnormal cytology and control groups (HPV-negative and/or normal cytology groups), using the Maissi et al. (2005) sexual distress measure.

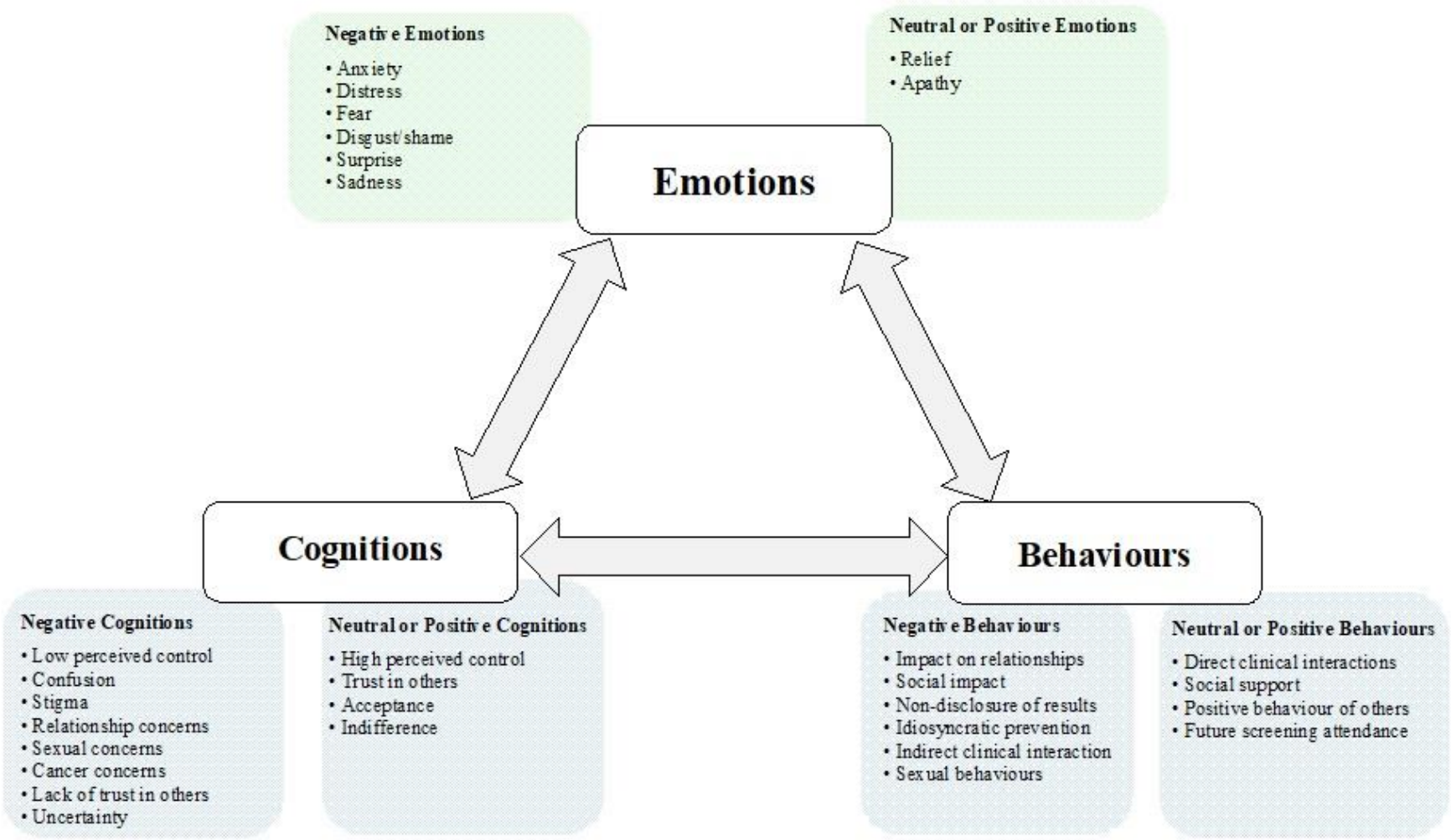

Figure 5. Emotional response to testing positive for HPV from all studies (quantitative, qualitative, mixed-methods) mapped on to a cognitive behavioural framework