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Review Article

Factors associated with human papillomavirus (HPV) test acceptability in primary screening for cervical cancer: A mixed methods research synthesis

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ABSTRACT

Primary screening for cervical cancer is transitioning from the longstanding Pap smear towards implementation of an HPV-DNA test, which is more sensitive than Pap cytology in detecting high-risk lesions and offers greater protection against invasive cervical carcinomas. Based on these results, many countries are recommending and implementing HPV testing-based screening programs. Understanding what factors (e.g., knowledge, attitudes) will impact on HPV test acceptability by women is crucial for ensuring adequate public health practices to optimize cervical screening uptake. We used mixed methods research synthesis to provide a categorization of the relevant factors related to HPV primary screening for cervical cancer and describe their influence on women's acceptability of HPV testing. We searched Medline, Embase, PsycINFO, CINAHL, Global Health and Web of Science for journal articles between January 1, 1980 and October 31, 2017 and retained 22 empirical articles. Our results show that while most factors associated with HPV test acceptability are included in the Health Belief Model and/or Theory of Planned Behavior (e.g., attitudes, knowledge), other important factors are not encompassed by these theoretical frameworks (e.g., health behaviors, negative emotional reactions related to HPV testing). The direction of influence of psychosocial factors on HPV test acceptability was synthesized based on 14 quantitative studies as: facilitators (e.g., high perceived HPV test benefits), barriers (e.g., negative attitudes towards increased screening intervals), contradictory evidence (e.g., sexual history) and no impact (e.g., high perceived severity of HPV infection). Further population-based studies are needed to confirm the impact of these factors on HPV-based screening acceptability.

1. Introduction

Globally, 530,000 cervical cancers cases per year are attributable to the human papillomavirus (HPV) and represent 8% of all cancers occurring worldwide (de Martel et al., 2017). The understanding of the causal connection between persistent infection with high-risk HPV types and cervical cancer (Walboomers et al., 1999; Franco et al., 2009) has led to new primary and secondary prophylaxis measures. Although primary prophylaxis of cervical cancer through HPV vaccination is considered a major achievement, secondary prophylaxis through

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screening will remain extremely important in addressing cervical cancer for decades to come because current HPV vaccines do not offer protection against all high-risk HPV types, HPV vaccine uptake is variable across the globe and the ultimate length of protection provided by vaccination is to be established yet (Paavonen et al., 2009).

Historically, the mainstay of cervical cancer screening was represented by cytology (i.e., Papanicolaou or Pap test) to screen for cervical cellular abnormalities. In recent years, HPV DNA tests (hereafter HPV test or testing) capable of identifying high-risk HPV types have been developed. Multiple studies have shown that HPV testing is more sensitive than cytology in detecting cervical intraepithelial neoplasia in primary cervical cancer screening (hereafter primary screening) (Bulkmans et al., 2007; Naucler et al., 2007; Ronco et al., 2010; Anttila et al., 2010) and has similar specificity compared to Pap testing in women aged 30 and older (Rijkaart et al., 2012). Overwhelming evidence suggests that a negative HPV test provides more reassurance to a woman that she is at low-risk for cervical lesions than a negative Pap test and supports the extension of intervals in primary screening beyond 5 years (Franco et al., 2009; Crosbie et al., 2013; Ronco et al., 2014).

This evidence has led to new recommendations that incorporate HPV testing as a primary screen for cervical cancer in women aged between 30 and 65 years, either as a stand-alone test (von Karsa et al., 2015; Huh et al., 2015; Australian Government Department of Health, 2017) or with cytology (i.e., co-testing) (The American Congress of Obstetricians and Gynecologists, 2017; The American Cancer Society medical and editorial content team, 2017; Moyer, 2012).

Misunderstandings and misconceptions related to HPV testing, fueled by lack of HPV or HPV testing knowledge (e.g., purpose of HPV testing, causal relationship between HPV and cervical cancer, natural history of HPV infection) in Australian women (Foran, 2017), lead to a petition signed by > 70,000 women against the roll out of the new primary cervical cancer screening program (HPV test every 5 years in women aged 25 to 74 years instead of Pap test every 2 years); consequently, the implementation of the program was postponed from May 1 to December 1, 2017 (Australian Government Department of Health, 2017; Williams, 2017).

No synthesis has been carried out to examine what factors' impact (e.g. facilitators, barriers) on HPV test acceptability in *primary* screening. As new guidelines have been developed and are in the process of being implemented worldwide, we aimed to provide a comprehensive description of psychosocial factors related to HPV testing and to assess their influence on HPV testing acceptability in primary screening for cervical cancer with the ultimate goal to guide interventions to promote screening.

2. Methods

We used mixed methods research synthesis (MMRS), which is a form of systematic review (Sandelowski et al., 2006; Sandelowski et al., 2012; Heyvaert et al., 2011), to answer following research questions: "What are the psychosocial factors related to HPV testing in primary screening for cervical cancer?" and "What is the influence of these factors on women's acceptability of HPV testing in primary screening for cervical cancer?". By selecting MMRS, we highlight our opinion that preventive behaviors (e.g., participating in screening) are complex and can be best understood by combining views of constructivism (subjectivity, associated with qualitative research) with views of logical empiricism (objectivity, associated with quantitative research). In integrative MMRS, findings of empirical qualitative, quantitative or mixed methods experimental or observational studies are treated as primary data that are analyzed and synthesized by using mixed methods approaches (Sandelowski et al., 2006; Sandelowski et al., 2012; Heyvaert et al., 2011) (Fig. 1). The PRISMA framework was used to guide the reporting of this review (Moher et al., 2009). The protocol was registered on International Prospective Register of Systematic Reviews (PROSPERO), registration #CRD42017078254.[1]

We searched Medline, Embase, PsycINFO, CINAHL, Global Health and Web of Science for journal articles between January 1, 1980 and October 31, 2017. The search strategy was developed for Medline by our team, validated by an experienced McGill librarian and then adapted for the other databases (Appendix A). The following eligibility criteria were applied: 1) Population: women of all ages for whom primary cervical cancer screening is recommended, 2) Outcome: psychosocial factors related to acceptability of HPV testing in *primary screening* for cervical cancer,[2] 3) Study design: empirical studies, without restrictions of study methodology, 4) Languages: English or French or German. The selection of references was performed by two researchers (OT and AN).

Records were first screened for eligibility based on titles and abstracts (phase one). Then, the full texts of retained records were retrieved and read; the final set of articles was identified based on eligibility criteria (phase 2). Disagreements in phase one and two on whether or not an article should be included were mediated by the senior researcher (ZR). For this review, we did not retain studies related to self-sampling which represents a distinct strategy to increase screening uptake and merits separate consideration. A data extraction sheet was developed in Excel and included author, title, publication date, country, objectives, study design, quantitative data collection and analysis methods, qualitative methodology, qualitative data collection methods and analysis, and number of participants. From qualitative studies, we extracted qualitative raw data without any interpretation or analysis (e.g., quotes). From quantitative studies, we extracted outcomes of acceptability (e.g. proportions, means, odds ratios).

The risk of bias in individual studies was assessed separately by two researchers (OT and ET), with the 16-item Quality Assessment Tool for Studies with Diverse Designs (QATSDD), a valid and reliable instrument developed for appraising studies in the disciplines of psychology, sociology and nursing (Sirriyeh et al., 2012). For overall scores ≤60% and > 60% we report *high* and *low* risk of bias respectively. All articles were included in the analyses, independent of their quality as we aimed to provide a comprehensive synthesis of factors.

We used a sequential exploratory (*QUAL → quan*) mixed methods design to analyze and synthesize findings of retained studies (Heyvaert et al., 2011; Creswell, 2014; Pluye and Hong, 2014). In the first phase, qualitative (*QUAL*), qualitative data from all qualitative and quantitative studies was analyzed; psychosocial factors measured in quantitative studies (e.g., anxiety, embarrassment, number of lifetime sexual partners, history of cervical screening) were treated as qualitative data (Pluye and Hong, 2014). We performed *deductive-inductive* qualitative thematic analysis to identify factors related to HPV testing. *Deductively*, we identified themes based on two frameworks widely used in health behavior research: The Health Belief Model (HBM) (Champion and Skinner, 2008) and the Theory of Planned Behavior (TPB) (Montano and Kasprzyk, 2015). *Inductively*, we developed new themes (i.e., not covered by HBM and TPB) through an iterative process, which consisted of reading the studies (and new themes) multiple times, allowing researchers to assure accurate interpretation of study results. Themes (hereinafter called factors) were further grouped into categories to enable a structured reporting of the results of the qualitative phase. The factors and categories were developed independently by two researchers (OT and ET) and then validated by the research team. The second (*quan*) phase was informed by the first, (*QUAL*) phase; for each

[1] Available at https://www.crd.york.ac.uk/prospero/.

[2] In primary screening for cervical cancer, HPV testing is used in women with no history of cervical cytological abnormalities i.e., abnormal Pap results. Because women will be in various stages of understanding the issue in terms of knowledge, attitudes and actual behavior, for the purposes of this paper we collapsed outcomes of intentions, willingness and uptake into the overarching term 'acceptability'.