Title: Are healthcare professionals prepared to implement HPV testing? A review of psychosocial determinants of HPV test acceptability in primary cervical cancer screening

Running title: Psychosocial Determinants of HPV Testing

Ovidiu Tatar, MD, MSc^{a,j}, Kristina Wade, BSc^a, Emily McBride, MSc^b, Erika Thompson, PhD^c, Katharine J. Head, PhD^d, Samara Perez, PhD^e, Gilla K. Shapiro, PhD^f, Jo Waller, PhD^g, Gregory Zimet, PhD^h, Zeev Rosberger, PhD^{a,i}

^aLady Davis Institute for Medical Research, Jewish General Hospital Montreal, Canada

^bResearch Department of Behavioural Science and Health Institute of Epidemiology and Health Care, University College London London, United Kingdom

^cDepartment of Health Behavior and Health Systems School of Public Health University of North Texas Health Science Center Fort Worth, Texas

^dDepartment of Communication Studies IU School of Liberal Arts at IUPUI Indianapolis, Indiana

^eMont Royal Psychology Montreal, Canada

^gResearch Department of Behavioural Science and Health, Institute of Epidemiology and Health Care, University College London, United Kingdom.

^hSection of Adolescent Medicine, Indiana University School of Medicine, Indianapolis, Indiana

ⁱDepartment of Psychology, Psychiatry and Oncology, McGill University, Montreal, Canada

*jCorresponding author

Research Center-Centre Hospitalier de l'Université de Montréal (CRCHUM) Montréal, Canada ovidiu.tatar@mail.mcgill.ca

f Department of Supportive Care, Princess Margaret Cancer Centre, Toronto, Canada.

1. Abstract

- 2 **Background**. Guidelines for cervical cancer screening have been updated to include human
- 3 papillomavirus (HPV) testing, which is more sensitive compared to cytology in detecting
- 4 cervical intraepithelial neoplasia. Because of its increased sensitivity, a negative HPV test is
- 5 more re-assuring for a woman that she is at low-risk for precancerous cervical lesions than a
- 6 negative Pap test. Prompted by the inadequate translation of HPV test-based screening guidelines
- 7 into practice, we aimed to synthesize the literature regarding healthcare providers (HCPs)
- 8 knowledge, attitudes and practices related to HPV testing and the influence of psychosocial
- 9 factors on HCPs acceptability of HPV testing in primary cervical cancer screening.
- 10 Methods: We searched Medline, Embase, PsycINFO, CINAHL, Global Health, and Web of
- Science for journal articles from January 1, 1980 to July 25, 2018. A narrative synthesis of HCPs
- 12 knowledge, attitudes and practices related to HPV testing is provided. Informed by the Patient
- 13 Pathway framework, we used deductive thematic analysis to synthesize the influence of
- psychosocial factors on HCPs acceptability of HPV testing.
- 15 **Results:** The most important HCPs knowledge gaps are related to the superior sensitivity of the
- 16 HPV test and age specific guidelines recommendations for HPV testing. 30-50% of HCPs are not
- 17 compliant with guideline recommendations for HPV testing e.g., screening at shorter intervals
- than recommended. Barriers, facilitators and contradictory evidence of HCPs' acceptability of
- 19 the HPV test are grouped by category: a) factors related to the HCP; b) patient intrinsic factors;
- 20 c) factors corresponding to HCP's practice environment; d) healthcare system factors.
- 21 Conclusions: HCP's adherence to guidelines for HPV testing in cervical cancer screening is
- suboptimal and could be improved by specialty organizations ensuring consistency across
- 23 guidelines. Targeted educational interventions to address barriers of HPV test acceptability

identified in this review may facilitate the translation of HPV testing recommendations intopractice.

Keywords: HPV test; cervical cancer screening; healthcare providers; knowledge, attitudes and beliefs; HPV test acceptability; cervical cancer screening guidelines

Worldwide, approximately 530,000 women are newly diagnosed with cervical cancer

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

2627

2. Introduction

annually, and almost 266,000 will die from the disease⁽¹⁾. As long-term persistent infection with an oncogenic genotype of human papillomavirus (HPV) has been found to be a necessary risk factor for developing cervical cancer^(2, 3), recommendations for cervical screening to include the HPV DNA test together with cytology (co-testing) were issued in the US as early as 2002⁽⁴⁾. In recent years, evidence has accumulated that in the primary cervical cancer screening setting, HPV testing has superior sensitivity compared to cytology in detecting cervical intraepithelial neoplasia⁽⁵⁻⁸⁾ and that screening intervals can be extended to five years or beyond–compared to three years for cytology alone—in women with a negative HPV test⁽⁹⁻¹¹⁾. Consequently, in the last decade, recommendations of major health organizations in the US, Europe, and Australia have been updated repeatedly and currently include HPV testing-either as a stand-alone test or as cotesting—for primary cervical cancer screening of women older than 30 years (or even as low as 25 years in some jurisdictions)(12-15). In the context of continuous change in primary cervical cancer screening recommendations (for both cytology and HPV testing) related to women's age of screening initiation, age-specific screening intervals and screening discontinuation, research indicates that less than 20% of healthcare providers (HCPs i.e., family practitioners (FPs), internal medicine specialists (IMs), obstetrics-gynecologists (OB/GYNs), nurse practitioners (NPs), physician assistants (PAs))in the

US follow all age-related guideline recommendations released in 2009 or in 2012 by the American College of Obstetricians and Gynecologists (ACOG), American Cancer Society (ACS), and the United States Preventive Services Task Force (USPSTF)^(16, 17). Poor practice implementation of HPV testing guidelines have been driven by HCPs' worry that increasing screening intervals with the HPV test would put women at increased risk of pre-cancer and cancer⁽¹⁸⁾ and perception that the HPV test alone is less effective than cytology (Pap) in detecting pre-cancerous lesions⁽¹⁹⁾. HCPs are concerned that gynecologic health issues other than cervical cancer prevention could be missed if yearly examinations are not performed. Women might feel less motivated to consult a doctor annually if the cervical cancer screening interval is increased to 3 years or more by using HPV test-based screening instead of annual Pap screening^(17, 20). To our knowledge, there has been no review of psychosocial factors that influence HCPs' recommendations of the HPV test in primary screening for cervical cancer to date. This study synthesizes the literature regarding current HCPs practices and attitudes related to HPV testing and the influences of psychosocial factors on HCPs acceptability of HPV testing in primary cervical cancer screening. It is important to more comprehensively understand HCPs' concerns related to modified cervical cancer screening recommendations in order for interventions to adequately address these concerns and more effectively translate the latest guideline recommendations for HPV testing into practice to ensure optimal cervical cancer screening.

3. Materials and Methods

48

49

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64

65

66

67

68

69

70

The review was guided by the following three research questions: 1) "What are HCPs' perceptions related to HPV testing in primary screening for cervical cancer?", 2) "How is HPV testing used by HCPs in primary screening for cervical cancer?", and 3) "How do psychosocial factors influence HCPs' acceptability of HPV testing in primary screening for cervical cancer?".

We searched Medline, Embase, PsycINFO, CINAHL, Global Health, and Web of Science for journal articles between January 1, 1980 and July 25, 2018. The search strategy was developed for Medline by our research team and adapted for the other databases¹. The following eligibility criteria were applied: 1) Population: HCPs involved in *primary screening*² for cervical cancer; 2) Outcome: knowledge, attitudes, beliefs, and acceptability³ related to using HPV testing in primary cervical cancer screening; 3) Study design: empirical studies, without restrictions of study methodology; and 4) Languages: English, French, or German. References retrieved from database searches were saved in EndNote and duplicates were removed. We used a combination of keywords in EndNote to identify references related to healthcare providers and HPV test use (Figure 1). Then, we selected references in two phases: in phase one, we screened for eligible articles based on titles and abstracts, and in phase two, full text articles were retrieved and read, and the final set of eligible articles was identified. In phase two, the selection of references was performed independently by two researchers (KW and OT) and disagreements on whether an article should be retained were mediated by the senior researcher (ZR). In the second phase, we decided to exclude articles referring to HCPs not directly involved in the clinical decision of using the HPV test in primary screening (e.g., HCPs working in laboratories, students, etc). Qualitative (e.g., quotes) and quantitative (e.g., proportions, odds ratios) data from included studies were extracted and organized in an Excel spreadsheet in the following

90 factors related to HPV test acceptability. In line with the first two research questions, we provide

71

72

73

74

75

76

77

78

79

80

81

82

83

84

85

86

87

88

89

categories and were used in the data synthesis phase: knowledge, attitudes/beliefs, practice and

¹ The search strategy for Medline is available at: https://www.crd.york.ac.uk/PROSPEROFILES/78254_STRATEGY_20181017.pdf

² In primary screening, the HPV test (including HPV co-testing) is used in women with no history of cervical cytological abnormalities i.e., abnormal Pap results. The addition of the HPV DNA test to cytology (Pap test) is known as co-testing.

³ The term acceptability defined herein includes HPV test uptake (already recommended by the HCPs); and intentions or willingness to recommend the HPV test

a narrative synthesis of HCPs' knowledge, attitudes and beliefs related to the HPV test and its uptake and intentions to be used in primary screening for cervical cancer. For the third research question, we used the Patient Pathway framework⁽²¹⁾ – a conceptual model that categorizes factors with influence on the patient-HCP encounter and the level of preventive care that a patient receives—to synthesize the influence of psychosocial factors on HPV test acceptability. The Patient Pathway framework has been previously used in explaining screening mammography referral rates⁽²²⁾ and stipulates that the probability that a patient will receive screening services by clinicians is determined by factors related to the HCP, patient intrinsic factors, and characteristics specific to patients' and HCP's environment⁽²¹⁾. In our synthesis, we conceptualized environmental factors as two different entities: factors corresponding to HCP's practice environment and healthcare system factors. Informed by the Patient Pathway framework we performed deductive qualitative thematic analysis and grouped psychosocial factors into four categories: a) factors related to the HCP, b) patient intrinsic factors (from the perspective of HCPs), c) factors corresponding to HCP's practice environment and d) healthcare system factors. For each category, we synthesized evidence of factors' influence on HPV test acceptability into barriers, facilitators, and contradictory evidence (i.e., evidence for both barriers and facilitators), and presented the results in tabular form. Deductive analysis was performed by OT and supervised by ZR.

4. Results

91

92

93

94

95

96

97

98

99

100

101

102

103

104

105

106

107

108

109

110

111

112

113

In Figure 1 we present the study selection diagram. In total, we retained 32 studies, four used qualitative (23-26) and 28 used quantitative methodology^(2, 16-20, 27-47). Included studies covered HCPs opinions from five continents: Europe (i.e., UK⁽⁴⁷⁾, Germany⁽³⁸⁾ and Italy⁽³⁹⁾), North America (i.e., Canada^(24, 26, 35) and the US^(2, 16-20, 23, 29-31, 34, 36, 40-44, 46)), Africa (i.e., Cameroon⁽²⁸⁾)

and Nigeria⁽²⁵⁾), Asia (i.e., China⁽²⁷⁾, Jordan⁽⁴⁵⁾, South Korea⁽³³⁾ and Thailand⁽³⁷⁾) and Oceania (i.e., Australia⁽³²⁾). Details of each included study can be found in Appendix A.

116

117

118

119

120

121

122

123

124

125

126

127

128

129

130

131

132

133

134

135

114

115

4.1 Knowledge

While HCPs were found to have up-to-date knowledge related to the prevalence of HPV infection and the causal relationship between persistent infection with high-risk HPV and cervical cancer, gaps in knowledge were identified as fewer than 50% of HCPs in Hong Kong knew that infection can occur in the absence of identifiable sexual risk factors and that HPV genotypes associated with cervical cancer differ from those associated with genital warts⁽²⁷⁾. As expected, HCPs' knowledge about HPV and HPV testing increased over time after 2006 when the first HPV vaccine was approved which represented a turning point in cervical cancer prevention. While in 2006, 10% of US physicians were not even aware that an HPV test was already available⁽³⁶⁾, data from 2011 showed that 47% of physicians and nurses in Cameroon knew that the HPV test can be used for cervical cancer screening⁽²⁸⁾. In the UK, Patel et al (2016) found increased HPV test knowledge among nurses (>70% correct answers) who participated in regular screening education sessions; their knowledge gaps were related to the sample collection procedure for HPV testing and reassurance offered by a negative HPV test result for low-risk of cervical lesions (47). Surprisingly, despite recommendations of specialty organizations in the US, Europe and Australia to include HPV testing in primary screening for cervical cancer⁽¹²⁻¹⁵⁾, HPV test knowledge among HCPs remains insufficient, highlighting a lack of understanding of the

indications for HPV testing and implications of a positive result. Thus, more than half of HCPs

in Hong Kong (in 2010) and Italy (in 2015) were unaware that HPV testing (including cotesting) is more sensitive than cytology in detecting high-grade cervical intraepithelial neoplasias^(27, 48), that the HPV test is not generally recommended in primary screening of women younger than 30^(27, 48), that a negative HPV test (without cytology), in Italy, allows extension of the cervical cancer screening interval to five years⁽⁴⁸⁾, and that no recommendations have been issued for more frequent HPV testing for cervical cancer in women diagnosed with genital warts⁽²⁷⁾. In the US, Teoh et al. (2015) found that only 5.7% of HCPs were knowledgeable about *all* age specific cervical cancer guidelines updated in 2012 by the ACS, ASCCP and ASCP⁴ but 83.7% of respondents knew that in women 30-65 years the recommended screening interval for co-testing (combined Pap and HPV test) increased from 3 to 5 years⁽⁴⁰⁾.

Among OB/GYNs in Italy, correlates of higher HPV test knowledge in primary screening for cervical cancer were found to be related to: HCPs perceiving their cervical cancer screening knowledge to be good to excellent (OR = 1.46; CI: 1.12-1.91), higher number of hours worked (OR = 1.02; CI: 1.01-1.03), and knowledge that the Pap test is not recommended annually⁽⁴⁸⁾.

4.2 Attitudes and beliefs

HCP's attitudes and beliefs were grouped into five sub-categories: acceptability of guidelines, beliefs about test efficacy, communication of results to patients, HPV self-sampling and point of care testing, and beliefs about screening intervals.

4.2.1 Acceptability of guidelines

Irwin et al. (2006) and Boone et al. (2014) found that half of US HCPs in their study considered cervical cancer screening guidelines valuable^(16, 36) while 35% of all HCPs do not

⁴ ACS: American Cancer Society; ASCCP: American Society for Colposcopy and Cervical Pathology; ASCP: American Society for Clinical Pathology;

consider current guidelines clinically reliable and appropriate (including 59% of obstetrics-gynecologists (OB/GYNs), 28% of family practitioners (FPs), 38% of nurse practitioners (NPs) and physician assistants (PAs), and 26% of internal medicine specialists (IMs))⁽¹⁶⁾. While over 90% of OB/GYNs in Italy⁽⁴⁸⁾ and over 80% of colposcopists in Canada⁽³⁵⁾ were comfortable with recommendations endorsing HPV testing in primary screening for cervical cancer and believed that guidelines released by scientific associations and national and international agencies are very useful in cervical cancer prevention, 41% of OB/GYNs in Italy suggested that cervical cancer screening should be done annually (against recommendations), irrespective of the test used⁽⁴⁸⁾.

4.2.2 Beliefs about test efficacy

Approximately 85% of HCPs in the US perceived liquid-based cytology as the most effective test for reducing cervical cancer mortality, followed by co-testing (64-82%) and Pap (~50%)^(29, 30, 34, 43). Despite the fact that over 70% of HCPs (OB/GYNs, IMs and FPs) in the US agree that the HPV test alone represents an effective screening modality⁽¹⁹⁾, it was generally perceived to be less effective than Pap^(19, 38), co-testing⁽¹⁹⁾, or colposcopy⁽³⁸⁾. Among Italian OB/GYNs, Caglioti et al. (2017) found that the preferred cervical cancer screening test in women ≥30 years was Pap (~39%) (followed by an HPV test in case of an abnormal Pap test); about 28% of OB/GYNs preferred the HPV test (with triage using the Pap test in case of a positive HPV-DNA test) or cotesting⁽⁴⁸⁾. In contradiction with recommendations for cervical cancer screening, ~41% of OB/GYNs preferred the HPV test alone to screen women aged <30 years⁽⁴⁸⁾. In less developed healthcare systems, OB/GYNs believe that introducing HPV testing into antenatal care would be an innovation due to its increased sensitivity in detecting precancerous lesions and could contribute to increasing screening uptake⁽²⁵⁾. Generally, over 70% of HCPs consider co-testing

easy to implement and useful in planning next steps after an abnormal Pap result and in estimating the cancer risk⁽⁴¹⁾.

4.2.3 Communication of results to patients

Lin et al. (2015) found that 75% of HCPs ordering a co-test, would engage in discussing possible results with their patients; compared to Pap positive and HPV test positive (co-test) results, HCPs were more likely to believe that Pap negative and HPV positive co-test results would be too complicated for patients to understand and could trigger patients' worries related to treatment options⁽⁴²⁾. HCPs believe that providing positive HPV test results require appropriate communication strategies to alleviate women's stigma associated with an sexually transmitted infection (STI) diagnosis⁽²⁶⁾.

4.2.4 HPV self-sampling and point of care testing

HPV testing on self-collected cervical samples (i.e., self-sampling) represents an alternative to physician collected samples and is performed by using a specially designed self-sampling devices which are commercially available in many countries. Interviews with HCPs revealed that discussing the self-collection option with under-screened women is probably more important than offering them alternative diagnostic procedures (i.e., cytology versus HPV testing)⁽²⁶⁾. Trope et al (2009) found high perceived benefits and increased preference among field-oriented HCPs (compared to hospital-oriented) for a new hypothetical protocol that includes HPV self-sampling at home for women living in villages, followed by visual inspection with acetic acid (VIA) in HPV positive women; this protocol would represent an alternative to performing VIA in all women⁽³⁷⁾. In the US Affiliated Pacific Islands, more than 30% of HCPs felt that a point-of-care HPV test (which can identify high-risk HPV types faster than the standard HPV test,

allowing for therapeutic measures to be taken on the same day) would be better than the conventional HPV test⁽³⁴⁾.

4.2.5 Beliefs about screening intervals

202

203

204

205

206

207

208

209

210

211

212

213

214

215

216

217

218

219

220

221

222

Encouragingly, Regier et al. (2013) found a significant increase over time in the proportion of colposcopists who openly advocate for HPV testing as the primary tool in cervical cancer screening (19% increase from 2010 to 2011, CI: 0.01–0.38); colposcopists' confidence that their personal attitudes would affect family practitioners' attitudes toward primary HPV testing increased by 13% from 2010 to 2011 (CI: 0.01–0.30)⁽³⁵⁾. Most HCPs showed positive attitudes towards extending the screening interval in women ≥30 years with normal co-test results; providers who recommended a three year interval after a normal co-test, reported more often that extending routine screening to three years would be good (80%), easy (67%) and beneficial (68%) compared to providers who recommended annual screening after a normal co-test (p < .05)⁽¹⁸⁾. Roland et al. (2013) found that after normal co-test results, ~24% of HCPs perceived extending the screening interval in women ≥30 years as being harmful, difficult or bad⁽²⁰⁾. In 2010 and 2011, 40% and 53% of colposcopists, respectively, felt that four years between HPV tests was too long⁽³⁵⁾. Benard et al. (2016) found that educational interventions (grand rounds, academic detailing sessions, etc.) significantly increased the odds of HCPs reporting that extending the screening interval for women with a normal co-test result to three years would be good (OR 6.45, p = 0.038), easy (OR = 5.18, p = 0.032), beneficial (OR = 8.53, p = 0.034), and that it would not cause patients to lose contact with the medical system (OR = 9.80, p = $0.044)^{(41)}$.

4.3 Practice and intentions

224	In Table 1, we present a synopsis of the applicable cervical screening recommendations used
225	by each author in relation to the year of data collection as shown in the far right-hand column.
226	Against recommendations for age-specific practices, 31-43% of HCPs would prematurely initiate
227	cervical screening before age 21 with either cytology or co-testing ^(16, 17) . For women in the age
228	range 21-29, practitioners generally over-screened by performing annual Pap tests (74% of
229	OB/GYNs) ⁽¹⁷⁾ , 35-85% of HCPs (lowest proportion among OB/GYNs) inappropriately screened
230	with the co-test ^(36, 40, 44, 46) and recommended it yearly or every three years (13-42% of
231	OB/GYNs, FPs, IMs, NPs, PAs) ^(16, 44) . Cooper et al. (2017) found that for women less than 25
232	years old, approximately 24% of OB/GYNs and 43-61% of FPs and IMs would incorrectly
233	recommend the HPV test alone ⁽⁴⁶⁾ . In women aged 30-65 years, reported co-testing use is highly
234	variable: 28-80% among HCPs in the US $^{(17,19,20,30,36,40)}$ and 28% among OB/GYNs in Italy $^{(39)}$.
235	In the US, 23-43% of HCPs stated they do not conduct an HPV test at all in women 30-65 years
236	old ^(17, 30) . In women aged 30 to 65 years, with a normal Pap result and negative HPV test results,
237	over-screening remained an issue as 25-48% of HCPs (higher among OB/GYN than FP)
238	perform/would perform co-testing every three years instead of the recommended five years (16, 40,
239	^{46, 48)} or even at one or two year intervals (20-55% of physicians) ^(19, 30, 41, 46, 48) . After a negative
240	HPV test, 44% of Italian OB/GYNs comply with European guidelines and recommend the next
241	HPV test after five years ⁽⁴⁸⁾ . In women ≥30 years old, most OB/GYNs (78-84%), and to a lesser
242	extent IMs and FPs (45-64%) prefer to use the Pap test in primary screening, with triage using
243	HPV testing in case of a positive Pap ^(30, 48) . Remarkably, Perkins et al. (2013) found that 53% of
244	OB/GYN still perform annual Pap in women older than 30 years ⁽¹⁷⁾ . After age 65, 14-50% of

providers continue to recommend ongoing screening^(16, 17, 40) and ~11% continue to use cotesting^(16, 40).

HCPs reported low to medium intentions (34-60%) to change their screening practices from annual cytology to extended three or five yearly co-testing in women aged >25 years^(32, 33) or > 30 years old women⁽⁴³⁾, if new recommendations were about to be released. Intentions of HCPs to recommend HPV self-sampling varied between 32-78%, if the test were proven to have high sensitivity, specificity, cost-effectiveness and were acceptable by the patient^(31, 34).

4.4 Influence of psychosocial factors on HCPs acceptability of HPV testing

In Table 2 we present (informed by the Patient Pathway framework) the influence of factors on HPV test acceptability grouped into: 1) factors related to the HCP, 2) patient intrinsic factors, 3) factors corresponding to HCP's practice environment and 4) healthcare system factors.

5. Discussion

In the present review, we included published articles of qualitative and quantitative methodology to provide the most comprehensive synthesis of psychosocial factors (i.e., knowledge, attitudes and behaviors) associated with HCPs acceptability of HPV testing in primary cervical cancer screening.

Surprisingly, we found that 30-50% of HCPs did not follow age-specific guideline recommendations for HPV testing and that over-screening (e.g., screening at shorter intervals than recommended by guidelines) with the HPV test and/or cytology represents a widespread practice. In the context of HPV-based testing, over-screening (e.g., beginning of screening before 25 years, yearly testing in women aged 30-65) could inflict psychological distress on women receiving a positive HPV test result, has no clinical relevance since most HPV infections are cleared by the immunological system, and requires unnecessary medical costs. Insufficient

knowledge of cervical cancer screening guidelines (40) and HPV test knowledge gaps (e.g., higher sensitivity of the HPV test compared to cytology (Pap) in detecting high-grade cervical intraepithelial neoplasia and/or a negative HPV test allowing the extension of screening intervals to 5 years or beyond)^(27, 39) could explain low HCPs' compliance with guidelines. While educational interventions were found to positively influence HCPs attitudes towards HPV testbased cancer screening guidelines (i.e., considering extending the screening interval after a normal co-test as being good, easy and beneficial)⁽⁴¹⁾, these changing attitudes might not translate into implementation of guidelines. For example, Caglioti et al. (2017) found that ~40% of HCPs who viewed screening guidelines as useful still considered that screening should be done annually, independent of the test used⁽³⁹⁾. On the other end of the spectrum are HCPs who consider current guidelines clinically unreliable and inappropriate (~ 35% of HCPs)⁽¹⁶⁾ and who might be reluctant to change their practice; this could be the case, especially if screening guidelines in their jurisdiction/health system/organization do not incorporate HPV testing^(26, 36, 36) ⁴⁰⁾, their administration and/or colleagues discourage the use of HPV test-based screening^(2, 20, 36) or they feel at risk for liability when adopting extended screening intervals and cervical dysplasia is missed⁽²⁰⁾. The inconsistent translation of HPV test-based screening guidelines into practice may likely be complicated by the multiple changes in recommendations (guidelines) since 2001 by different national and international specialty organizations that were often out of synch related to the optimal age of screening debut, age specific screening intervals and discontinuation of screening (see Table 1). For example, the contradictory influence of HCPs specialty on HPV test acceptability could be explained by the discrepancies in HPV test recommendations by different organizations, as HCPs have the option to either follow the recommendations issued by their

268

269

270

271

272

273

274

275

276

277

278

279

280

281

282

283

284

285

286

287

288

289

professional organization or those issued by other national or international authorities (which may be slightly different). An important barrier towards adopting extended screening intervals with the HPV test (i.e., not sooner than every 3 years) is represented by the long-standing annual Pap screening practice, which is no longer recommended by any organization. For women, the annual Pap screening could represent a culturally-embedded and difficult to dismantle expectation while for physicians it could be associated with economic incentives for continuing annual gynecologic follow-ups. This conclusion is further explained in that HCPs (notably, OB/GYNs) are worried that longer screening intervals would put patients at increased risk for cancer (with potential risk of HCP liability), would then result in higher rates of pre-cancer (18) and/or would negatively influence adherence to other annual examinations (e.g., pelvic examination) or screening tests (17, 20).

Among high-income countries, HPV testing is being increasingly incorporated into cervical screening programs. Organized, HPV test-based screening programs (that replace cytology) are in various stages of implementation in Australia^(15,49), the Netherlands^(49,50), Sweden⁽⁴⁹⁾ and Italy⁽⁴⁹⁾ while the United Kingdom⁽⁵¹⁾ and Norway⁽⁴⁹⁾ will begin in 2019 and New Zealand⁽⁵²⁾ will follow in 2021. The overview of barriers and facilitators provided in our synthesis is especially useful for understanding HPV test acceptability in opportunistic cervical cancer screening environments where adherence to the latest screening recommendations is highly dependent on HCPs opinions—as opposed to organized programs where screening follows a predetermined strategy—and could assist policy makers in planning and implementation of HPV test-based cervical cancer screening programs in new jurisdictions. Given the successful results of national HPV vaccination programs, it is highly likely that national HPV screening programs would be equally successful.

Another major innovation with potential to increase acceptability and lower cost is HPV testing on self-collected cervical samples (self-sampling). Self-sampling "represents a new advance in cancer control that is unequivocally empowering to women" (53) as it can effectively reach, in both organized and opportunistic cervical cancer screening environments, underscreened (and often marginalised) women in which about half of all invasive cervical cancers are diagnosed⁽⁵³⁾. Despite a slightly lower sensitivity and specificity in detecting cervical intraepithelial neoplasia (CIN2 and CIN3) of HPV testing on self-samples than of HPV testing on a clinician-taken sample^(54, 55), Nelson et al. (2017) found that 97% of women found selfsampling to be generally acceptable, 65% would prefer self-sampling over clinician-based sampling for HPV testing and considered self-sampling less embarrassing, respecting privacy and easy to use⁽⁵⁶⁾. In our review, we found that HCPs viewed self-sampling as a facilitator of HPV testing as it alleviates women's concerns about privacy and body discomfort during Pap examination, has the potential to reach women in underserved locations and reduces the burden of women's return to the medical system^(23, 24). Strategies to increase HCPs recommendations for self-sampling should take into consideration HCPs worries that self-sampling could be associated with missed opportunities to address other health issues and that women's decreased health literacy represents a barrier to an efficient screening, mostly due to poor quality of the self-collected sample (23, 31). We found the Patient Pathway Framework useful to synthesize factors that influence HCPs acceptability of the HPV test into following categories: a) HCP specific, b) patient-specific, c) HCP practice specific and d) healthcare system specific. Importantly, we found an overlap between patient-specific psychosocial factors related to HPV test acceptability and the results of our previous systematic review of factors that influence women's acceptability of HPV testing in

314

315

316

317

318

319

320

321

322

323

324

325

326

327

328

329

330

331

332

333

334

335

primary screening for cervical cancer⁽⁵⁷⁾. These overlapping patient-specific factors merit special consideration as they can act as barriers in the uptake of HPV testing and include: women's negative attitudes toward increasing the screening interval, negative emotions and perceptions related to HPV testing (e.g., shame and anxiety linked to testing for a sexually transmitted infection), women's low health literacy (i.e., decreased HPV test knowledge and insufficient use of health information channels), risky health behaviors (e.g., smoking), low socioeconomic status and non-white ethnicity⁽⁵⁷⁾. Given these additional barriers, it becomes exceedingly important to recognize that while guidelines, policy changes and training for HCPs to assure improved HPV screening implementation, we must also make equally strong interventions in gauging, guiding and educating all women successfully in kind and in synchrony. Failure to engage, consult and inform women's needs in the immense task of changing 70 years of cervical screening practices can lead to confusion and resistance, as has occurred recently in Australia. Systematic and informed policy decisions must be made with all stakeholders involved. Our study has a number of limitations. The synthesis of HCPs' practice and intentions to use the HPV test is based mostly on studies conducted in the US (13 out of 16) and cannot be reliably generalised to HCPs recommendation habits in other countries. The heterogeneity in healthcare settings, women's accessibility and affordability of HPV testing and constantly evolving guidelines for cervical screening further limit the generalizability of our results. Most studies included in our review originated in North America (22 out of 32) and no data were included from HCPs who practice in healthcare systems where an organized HPV test-based cervical screening program exists; this affects the generalisability of our results while prompting the need for further research in other healthcare environments and geographical areas. We did

337

338

339

340

341

342

343

344

345

346

347

348

349

350

351

352

353

354

355

356

357

358

not perform a structured quality appraisal of included studies which could have introduced bias in the interpretation of barriers and facilitators of HPV test acceptability.

6. Conclusions

While major specialty organizations have included HPV testing in their recommendations for primary cervical cancer screening, the adherence of HCPs to the guidelines is suboptimal. Possible explanations include insufficient HPV test and guidelines knowledge as well as the heterogeneity of published guidelines related to HPV testing recommendations. Psychosocial barriers of HPV test acceptability can be categorized into: factors related to the HCP (e.g., concerns related to delaying screening initiation to 25 years, extending testing intervals beyond 5 years), patient intrinsic factors (e.g., stigma and anxiety related to testing for a sexually transmitted disease), factors corresponding to HCP's practice environment (e.g., HPV testing guidelines not endorsed by their healthcare organization) and healthcare system factors (e.g., opportunistic cervical cancer screening environment). Future research is needed to estimate the association between psychosocial factors and HPV test acceptability in primary screening for cervical cancer from the perspective of HCPs practicing in healthcare systems where organized HPV test-based screening has been implemented.

Acknowledgements

We would like to thank to Genevieve Gore (McGill Liaison Librarian) for her precious support with validating the search strategy.

Author Disclosure Statement

Gregory Zimet reports grants from Merck, grants from Roche, personal fees from Merck, outside the submitted work. All other authors declare that no competing financial interests exists.

REFERENCES

- 1. Bruni L, Barrionuevo-Rosas L, Albero G, et al. (2017). ICO Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World. Summary Report 27 July 2017. (July 27, 2017). http://www.hpvcentre.net/statistics/reports/XWX.pdf (accessed December 3, 2018).
- 2. Hoover K, Koumans EH, Montano D, et al. Access of Black, Hispanic, and nonprivately insured women to liquid-based cytology, human papillomavirus DNA testing, and on-site colposcopy in the United States. J Low Genit Tract Dis 2009;13:17-27.
- 3. Giuliano AR, Nyitray AG, Kreimer AR, et al. EUROGIN 2014 roadmap: differences in human papillomavirus infection natural history, transmission and human papillomavirus-related cancer incidence by gender and anatomic site of infection. Int J Cancer 2015;136:2752-2760.
- 4. Saslow D, Runowicz CD, Solomon D, et al. American Cancer Society guideline for the early detection of cervical neoplasia and cancer. CA Cancer J Clin 2002;52:342-362.
- 5. Bulkmans NW, Berkhof J, Rozendaal L, et al. Human papillomavirus DNA testing for the detection of cervical intraepithelial neoplasia grade 3 and cancer: 5-year follow-up of a randomised controlled implementation trial. Lancet 2007;370:1764-1772.
- 6. Naucler P, Ryd W, Tornberg S, et al. Human papillomavirus and Papanicolaou tests to screen for cervical cancer. The New England journal of medicine 2007;357:1589-1597.
- 7. Ronco G, Giorgi-Rossi P, Carozzi F, et al. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial. Lancet Oncol 2010;11:249-257.

- 8. Anttila A, Kotaniemi-Talonen L, Leinonen M, et al. Rate of cervical cancer, severe intraepithelial neoplasia, and adenocarcinoma in situ in primary HPV DNA screening with cytology triage: randomised study within organised screening programme. BMJ 2010;340:c1804.
- 9. Crosbie EJ, Einstein MH, Franceschi S, et al. Human papillomavirus and cervical cancer. Lancet 2013;382:889-899.
- 10. Franco EL, Mahmud SM, Tota J, et al. The expected impact of HPV vaccination on the accuracy of cervical cancer screening: the need for a paradigm change. Arch Med Res 2009;40:478-485.
- 11. Ronco G, Dillner J, Elfstrom KM, et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. Lancet 2014;383:524-532.
- 12. Huh WK, Ault KA, Chelmow D, et al. Use of primary high-risk human papillomavirus testing for cervical cancer screening: interim clinical guidance. Gynecol Oncol 2015;136:178-182.
- 13. U.S. Preventive Services Task Force. (2018). Final Recommendation Statement. Cervical Cancer: Screening. (August, 2018).

https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/cervical-cancer-screening2 (accessed December 3, 2018).

14. von Karsa L, Arbyn M, De Vuyst H, et al. European guidelines for quality assurance in cervical cancer screening. Summary of the supplements on HPV screening and vaccination. Papillomavirus Research 2015;1:22-31.

- 15. Australian Government Department of Health. (2017). National Cervical Screening Program. http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/cervical-screening-1 (accessed December 3, 2018).
- 16. Boone E, Lewis L, Karp M. Discontent and Confusion: Primary Care Providers' Opinions and Understanding of Current Cervical Cancer Screening Recommendations. J Womens Health (Larchmt) 2016;25:255-262.
- 17. Perkins RB, Anderson BL, Gorin SS, et al. Challenges in cervical cancer prevention: a survey of U.S. obstetrician-gynecologists. Am J Prev Med 2013;45:175-181.
- 18. Roland KB, Greek A, Hawkins NA, et al. Provider beliefs associated with cervical cancer screening interval recommendations: A pilot study in Federally Qualified Health Centers. Prev Med Rep 2015;2:444-447.
- 19. Cooper CP, Saraiya M. Perceived effectiveness of HPV test as a primary screening modality among US providers. Prev Med 2015;78:33-37.
- 20. Roland KB, Benard VB, Greek A, et al. Primary care provider practices and beliefs related to cervical cancer screening with the HPV test in Federally Qualified Health Centers. Prev Med 2013;57:419-425.
- 21. Pommerenke FA, Dietrich A. Improving and maintaining preventive services. Part 1: Applying the patient path model. J Fam Pract 1992;34:86-91.
- 22. Haggerty J, Tamblyn R, Abrahamowicz M, et al. Screening mammography referral rates for women ages 50 to 69 years by recently-licensed family physicians: physician and practice environment correlates. Prev Med 1999;29:391-404.

- 23. Katz ML, Zimmermann BJ, Moore D, et al. Perspectives from health-care providers and women about completing human papillomavirus (HPV) self-testing at home. Women Health 2017;57:1161-1177.
- 24. Wakewich P, Wood B, Davey C, et al. Colonial legacy and the experience of First Nations women in cervical cancer screening: a Canadian multi-community study. Crit Public Health 2016;26:368-380.
- 25. Filade TE, Dareng EO, Olawande T, et al. Attitude to Human Papillomavirus

 Deoxyribonucleic Acid-Based Cervical Cancer Screening in Antenatal Care in Nigeria: A

 Qualitative Study. Front Public Health 2017;5:226.
- 26. Wood B, Russell VL, El-Khatib Z, et al. "They Should Be Asking Us": A Qualitative Decisional Needs Assessment for Women Considering Cervical Cancer Screening. Glob Qual Nurs Res 2018;5:2333393618783632.
- 27. Kwan TT, Lo SS, Tam KF, et al. Assessment of knowledge and stigmatizing attitudes related to human papillomavirus among Hong Kong Chinese healthcare providers. Int J Gynaecol Obstet 2012;116:52-56.
- 28. McCarey C, Pirek D, Tebeu PM, et al. Awareness of HPV and cervical cancer prevention among Cameroonian healthcare workers. BMC Womens Health 2011;11:45.
- 29. Benard VB, Saraiya MS, Soman A, et al. Cancer screening practices among physicians in the national breast and cervical cancer early detection program. J Womens Health (Larchmt) 2011;20:1479-1484.
- 30. Saraiya M, Berkowitz Z, Yabroff KR, et al. Cervical cancer screening with both human papillomavirus and Papanicolaou testing vs Papanicolaou testing alone: what screening intervals are physicians recommending? Arch Intern Med 2010;170:977-985.

- 31. Mao C, Kulasingam SL, Whitham HK, et al. Clinician and Patient Acceptability of Self-Collected Human Papillomavirus Testing for Cervical Cancer Screening. J Womens Health (Larchmt) 2017;26:609-615.
- 32. Yap D, Liang X, Garland SM, et al. Clinicians' attitude towards changes in Australian National Cervical Screening Program. J Clin Virol 2016;76 Suppl 1:S81-S87.
- 33. Chung HH, Kim JW, Kang SB. Cost is a barrier to widespread use of liquid-based cytology for cervical cancer screening in Korea. J Korean Med Sci 2006;21:1054-1059.
- 34. Townsend JS, Stormo AR, Roland KB, et al. Current cervical cancer screening knowledge, awareness, and practices among U.S. affiliated pacific island providers: opportunities and challenges. Oncologist 2014;19:383-393.
- 35. Regier DA, van der Hoek K, Ogilvie G, et al. Exploring Colposcopists' Attitudes Towards Use of HPV Testing as a Primary Screening Tool for Cervical Cancer in British Columbia. J Obstet Gynaecol Can 2013;35:657-663.
- 36. Jain N, Irwin KL, Montano D, et al. Family Physicians' Knowledge of Genital Human Papillomavirus (HPV) Infection and HPV-related Conditions, United States, 2004. Fam Med 2006;38:483-489.
- 37. Trope LA, Chumworathayi B, Blumenthal PD. Preventing cervical cancer: stakeholder attitudes toward CareHPV-focused screening programs in Roi-et Province, Thailand. Int J Gynecol Cancer 2009;19:1432-1438.
- 38. Kuitto K, Pickel S, Jahn D. Ansichten und Erfahrungswerte über die Praxis der Früherkennungs- und Präventionsmaßnahmen von Gebärmutterhalskrebs. Prävention und Gesundheitsförderung 2010;5:38-45.

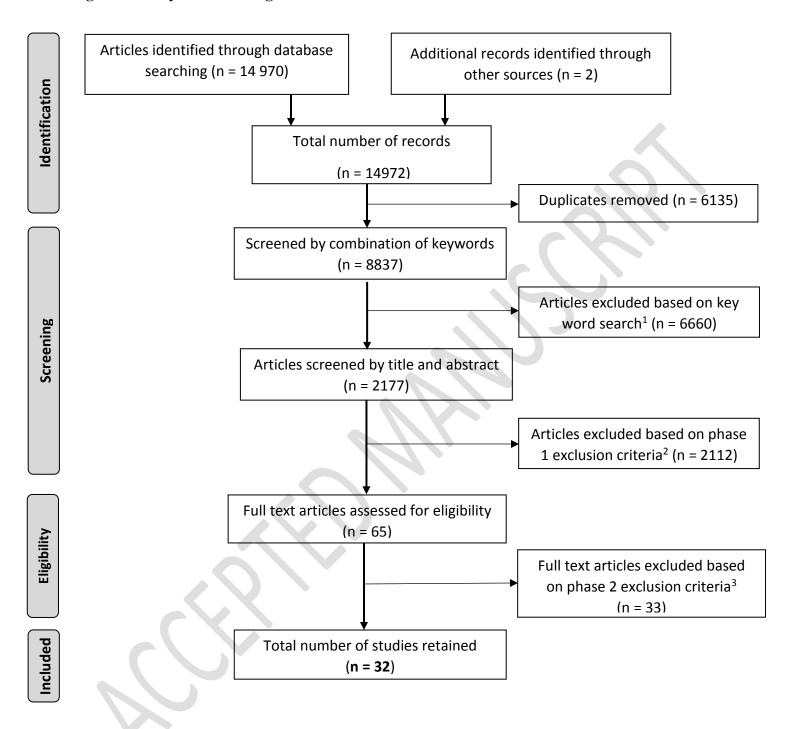
- 39. Caglioti C, Pileggi C, Nobile CG, et al. Gynecologists and human papillomavirus DNA testing: exploring knowledge, attitudes, and practice in Italy. Eur J Cancer Prev 2017;26:249-256.
- 40. Teoh DG, Marriott AE, Isaksson Vogel R, et al. Adherence to the 2012 national cervical cancer screening guidelines: a pilot study. Am J Obstet Gynecol 2015;212:62 e61-69.
- 41. Benard VB, Greek A, Roland KB, et al. Change in Provider Beliefs Regarding Cervical Cancer Screening Intervals After an Educational Intervention. J Womens Health (Larchmt) 2016;25:422-427.
- 42. Lin L, Benard VB, Greek A, et al. Communication practices about HPV testing among providers in Federally Qualified Health Centers. Prev Med Rep 2015;2:436-439.
- 43. Saint M, Gildengorin G, Sawaya GF. Current cervical neoplasia screening practices of obstetrician/gynecologists in the US. Am J Obstet Gynecol 2005;192:414-421.
- 44. Corbelli J, Borrero S, Bonnema R, et al. Differences among primary care physicians' adherence to 2009 ACOG guidelines for cervical cancer screening. J Womens Health (Larchmt) 2014;23:397-403.
- 45. Lataifeh I, Amarin Z, Khader Y. A survey of the knowledge and attitude of Jordanian obstetricians and gynaecologists to cervical cancer screening. J Obstet Gynaecol 2009;29:757-760.
- 46. Cooper CP, Saraiya M. Primary HPV testing recommendations of US providers, 2015. Prev Med 2017;105:372-377.
- 47. Patel H, Austin-Smith K, Sherman SM, et al. Knowledge, attitudes and awareness of the human papillomavirus amongst primary care practice nurses: an evaluation of current training in England. J Public Health (Oxf) 2017;39:601-608.

- 48. Caglioti C, Pileggi C, Nobile CG, et al. Gynecologists and human papillomavirus DNA testing: exploring knowledge, attitudes, and practice in Italy. European Journal of Cancer Prevention 2017;26:249-256.
- 49. Wentzensen N, Arbyn M, Berkhof J, et al. Eurogin 2016 Roadmap: how HPV knowledge is changing screening practice. Int J Cancer 2017;140:2192-2200.
- 50. National Institute for Public Health and the Environment. (2018). Cervical screening programme. (2018). https://www.rivm.nl/en/Topics/C/Cervical_cancer_screening_programme (accessed December 3, 2018).
- 51. Stubbs R. (2016). HPV primary screening in the cervical screening programme. (April 13, 2016). https://phescreening.blog.gov.uk/2016/04/13/hpv-primary-screening-in-the-cervical-screening-programme/ (accessed December 3, 2018).
- 52. National Screening Unit. (2017). Updated Guidelines for Cervical Screening in New Zealand. (October 26, 2017). https://www.nsu.govt.nz/health-professionals/national-cervical-screening-programme/hpv-primary-screening (accessed December 3, 2018).
- 53. Franco EL. Self-sampling for cervical cancer screening: Empowering women to lead a paradigm change in cancer control. Curr Oncol 2018;25:e1-e3.
- 54. Arbyn M, Verdoodt F, Snijders PJ, et al. Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis. Lancet Oncol 2014;15:172-183.
- 55. Arbyn M, Smith SB, Temin S, et al. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. BMJ 2018;363:k4823.

56. Nelson EJ, Maynard BR, Loux T, et al. The acceptability of self-sampled screening for HPV DNA: a systematic review and meta-analysis. Sex Transm Infect 2017;93:56-61.

57. Tatar O, Thompson E, Naz A, et al. Factors associated with human papillomavirus (HPV) test acceptability in primary screening for cervical cancer: A mixed methods research synthesis. Prev Med 2018;116:40-50.

Figure 1. Study selection diagram



¹Key word search terms: physician* (any field) OR doctor* (any field) OR provider*(any field) OR HPV test*(any field)

²Phase 1 exclusion criteria for titles and abstracts: 1) not population of interest (i.e. healthcare providers involved in primary screening), 2) not outcomes of interest (psychosocial factors, intentions, correlates of acceptability), 3) not empirical studies, 4) no abstract 5) not HPV testing in primary screening for cervical cancer, 6) Only knowledge of risk factors for cervical cancer, 7) Only HPV knowledge, 8) only Pap related, 9) Only HPV vaccine related

³Phase 2 exclusion criteria for full text articles: Phase 1 exclusion criteria AND full text not in English, French or German AND study population comprise only HCPs not involved in making decisions related to HPV test use (e.g., laboratory workers, students). HCP, health care provider; HPV, human papillomavirus

Year of screening recommendation	Screening Initiation /Recommending organization	Age 21-29/Recommending organization	Age 30 to age of discontinuation/Recommending organization	Discontinuation/Recom mending organization	Author and year of data collection
2001-2003	Cytology within 3 years of sexual activity or at age 21 (ACS, ACOG) OR at sexual activity debut or 20y/KSOG	Annual (conventional cytology) or every 2 years (liquid cytology) (ACS, ACOG) OR annual cytology (KSOG)	30-70y, in women who have had 3 consecutive negative cytology results the recommended screening interval with cytology was 2 to 3 years (ACS, ACOG) OR HPV co-testing no sooner than every 3 years (ACS-preliminary recommendation) FOR annual cytology (KSOG) OR biannual cytology (KMHW)	>70y, in women with adequate prior screening** (ACS, ACOG)	Irwin (2004) Saraiya (2006- 2007) Chung (2005) Saint (2003)
2009	21y, with cytology only (ACOG, USPTF, ACS)	Cytology only, every 2 years (ACOG, USPTF, ACS)	30-65y, cytology every 3 years OR co-testing every 3 years (ACOG, USPTF, ACS)	>70y, in women with adequate prior screening (ACOG, USPTF, ACS)	Perkins (2011) Corbelli (2012) ¶ Roland (2009- 2010) Benard (2009-2010) Townsend (2011)
2012	21y with cytology only (ACOG, ACS, USPTF, ASCCP, ASCP) OR 18 years/ (RANZCOG)	Cytology only, every 3 years (ACOG, ACS, USPTF, ASCCP, ASCP) OR cytology every 2 years/ (RANZCOG)	30-65y, cytology every 3 years OR co-testing every 5 years (ACOG, ACS, USPTF, ASCCP, ASCP) OR cytology every 2 years (RANZCOG)	>65y, in women with adequate prior screening** (ACOG, ACS, USPTF, ASCCP, ASCP) OR >69y, (RANZCOG)	Boone (2014) Teoh (2013) Cooper (2012) § Yap (2014) Mao (2013- 2014)
2015-2016	21y with cytology only (ACOG, ACS, USPTF, ASCCP, ASCP) OR 20-30y (EGQACCS- 2008)	Cytology every 3 years (ACOG, ACS, USPTF, ASCCP, ASCP) OR cytology every 3-5 years/ (EGQACCS-2008) OR HPV test alone every 3 years for women >25y (SGO, ASCCP*, ACOG)	30-65y, cytology every 3 years OR co-testing every 5 years (ACOG, ACS, USPTF, ASCCP, ASCP) OR cytology every 3-5 years (EGQACCS 2008) OR HPV test alone no sooner than every 3 years (SGO, ASCCP*, ACOG) OR HPV testing alone (not co-testing), no sooner than every 5 years (EGQACCS-2015)	>65y, in women with adequate prior screening** (ACOG, ACS, USPTF, ASCCP, ASCP) OR >60-65y, in women with adequate prior screening (EGQACCS- 2008, 2015)	Cooper (2015) Caglioti (2015)

Table 1. Cervical cancer screening recommendations for included quantitative studies over time

Note: ACS: American Cancer Society; ACOG: American College of Obstetricians and Gynecologists; ASCCP: American Society for Colposcopy and Cervical Pathology; ASCP: American Society for Clinical Pathology; EGQACCS: European guidelines for quality assurance in cervical cancer screening(14, 49); KSOG: Korean Society of Obstetrics and Gynecology; KMHW: Korean Ministry of Health and Welfare; RANZCOG: The Royal Australian and New Zealand College of Obstetricians and Gynaecologists(50); SGO: Society of Gynecologic Oncology; USPTF: United States Preventive Services Task Force; * Interim Guidance Report issued by SGO and ASCCP(12); ** Adequate prior screening can be defined as three consecutive negative cytology results or two consecutive negative co-test results within the previous 10 years, with the most recent test performed within the past 5 years(51); ¶ data collected before 2012 guidelines change; § For screening practice only the 2012 data was used; ACS, ACOG and USPTF guidelines were issue shortly before the survey was distributed; ¥ Saslow et al. (2002) American Cancer Society Guideline for the Early Detection of Cervical Neoplasia and Cancer(4)

Table 2. Barriers and Facilitators of Healthcare Providers Acceptability of the HPV Test in Primary Screening for Cervical Cancer

Factors related to the HCP								
Barriers	Facilitators	Contradictory evidence						
Concern that cervical cancer could be missed if screening initiation with the HPV test is delayed to 25 y ⁽³²⁾	Higher HPV and HPV test knowledge (e.g., higher sensitivity of the HPV test in detecting precancerous lesions) ^(36, 39)	Consider screening guidelines valuable/HCPs are influenced by guidelines ^(32, 36, 46)						
• Belief that women > 30 y would fear that cervical cancer could be missed by extending the co-test screening interval from 1 to 3 years ⁽²⁰⁾	 Less perceived need of information on cervical cancer screening⁽³⁹⁾ Knowledge that the Pap test is not 	• Influence from patients (i.e., patients either reject extended screening intervals or want to know their HPV infection status) ^(20, 36, 40, 46)						
Concern that increasing screening intervals beyond 1 year with the co-test would put women at increased risk of pre-cancer and cancer (18) Public follows and a street and cancer (18)	 recommended annually⁽³⁹⁾ Educational interventions increase acceptability of an interval of 3 years for co-testing⁽⁴¹⁾ 	Influence from administration and colleagues who discourage use of co-testing						
Belief that annual exams and other screening tests could be missed if Pap is not offered and the screening interval after a normal co-test is increased to 3 years ^(17, 20)	 Increased cervical cancer knowledge (e.g., cervical changes in young women are usually low grade and have a high rate of regression) was associated with higher acceptability to start 	 and extending screening intervals to 3 years⁽²⁰⁾ Concerns that integration of HPV testing in antenatal care could be associated with 						
 Belief that using self-sampling could be associated with missed opportunities to address other health issues⁽³¹⁾ 	 screening at 25y⁽³²⁾ Respecting guidelines for extended interval screening for the Pap test (i.e., 3 years instead of 	 pregnancy loss⁽²⁵⁾ Specialty: higher HPV test acceptability in OB/GYN than FP^(2, 19, 36) or IM^(19, 36, 44) or 						
 Beliefs that delaying screening debut to 25y and increasing screening intervals are strategies to reduce government costs⁽³²⁾ 	 annually)⁽³⁰⁾ Perception that extending the screening interval for co-testing is promoted by professional 	opposite effect ^(32, 46) . Compared to IM, acceptability in FP was higher ⁽⁴⁴⁾ or lower ⁽⁴⁶⁾ • Volume of cytology examinations: higher						
Belief that discussing the association between a STI and cervical cancer could have negative emotional effect on women and would be time consuming ⁽³⁶⁾	journals, professional specialty organizations and national health organizations ⁽¹⁸⁾ • Use of self-sampling method ⁽²⁴⁾ • Higher acceptability of co-testing at 3 years	Pap volume increase HPV test acceptability ⁽³⁰⁾ . Increased volume of liquid cytology increase ⁽³⁶⁾ or decrease HPV test acceptability ⁽³⁰⁾ . \geq 45 screenings/month						
 Insufficient knowledge of cervical cancer screening guidelines⁽⁴⁰⁾ Age > 40 and > 10 years of practice concerned about women's ability to use self-sampling⁽³¹⁾ 	interval (instead of yearly) in HCPs who consider yearly pelvic examination less useful ⁽³⁰⁾ • Higher acceptability among Asian and Hispanic	associated with lower HPV test acceptability for women ≥30y ⁽⁴⁶⁾ • Gender: Lower acceptability in male HCP ^(2, 17, 36, 44) or opposite effect ⁽⁴⁶⁾						
	individuals ⁽⁴⁶⁾	E.F						

Table 2 (continued). Barriers and Facilitators of Healthcare Providers Acceptability of the HPV Test in Primary Screening for Cervical Cancer

	Patient intrinsic factors							
I	Barriers		Facilitators	Contradictory evidence				
 self-sampling^(31, 39) Stigma associated with about increased cervital increase perception of procedure^(23, 35) Irregular Pap testing barriers for extending women ≥ 30y⁽²⁰⁾ Decreased health little self-sampling^(23, 31) High risk for cervical cytological abnormal act as barrier to delay and increasing screen 	th testing for a STI, worry ical cancer screening interval, of cancer risk, fear of history and smoking are g screening intervals in racy is a barrier for using l cancer (e.g., history of lities, immunocompromised) ying screening debut to 25 y ning intervals in women	•	Concerns about privacy and body discomfort during Pap examination are viewed as facilitators of self-sampling ^(23, 24) Exclusive same-sex relationship is a facilitator for delaying screening debut to 25y ⁽³²⁾	HPV vaccination status ^(32, 46)				
history of STI and se								

Table 2 (continued). Barriers and Facilitators of Healthcare Providers Acceptability of the HPV Test in Primary Screening for Cervical Cancer

Factors corresponding to HCP's practice environment							
Barriers	Facilitators	Contradictory evidence					
 Public outpatient setting (versus public hospital)⁽³⁹⁾ Rural/military practice (versus suburban/urban)⁽¹⁷⁾ HPV testing guidelines not endorsed by HCP's healthcare organization^(36, 40) HPV test not offered by their laboratory⁽³⁶⁾ Caring for ≥ 25% black population⁽²⁾ Lower proportion (<75%) of privately insured patients^(2, 36, 40) 	 Private and nonsolo (i.e., single specialty group) practice^(2, 36) Northeastern (versus Southern) US gynecologists⁽¹⁷⁾ Electronic medical system usage⁽³⁰⁾ 	Timely access (on-site) to colposcopy ⁽³⁶⁾					
	Healthcare system factors						
Barriers	Facilitators	Contradictory evidence					
 Opportunistic cervical cancer screening environment (e.g., postponing screening debut to 25y and extending screening intervals could facilitate women to lose contact with the medical system, higher HCP's perceived risk of liability for extended screening intervals)^(20, 32) Screening guidelines in their jurisdiction (e.g., province) do not incorporate HPV testing⁽²⁶⁾ Poor designed self-sampling information materials for women⁽²³⁾ 	Use of personal communication of self- sampling results to underscreened patients creates education opportunities and promotes women to return to the medical system ⁽²³⁾	Cost of screening for the patient: extended screening intervals decrease cost and could act as facilitator (Roland, 2013), if the HPV test is not reimbursed HCP may not communicate the option (26, 36, 40)					

Note: Contradictory evidence includes factors for which evidence for both barriers and facilitators was found

Appendix A. Summary of included studies

Author and year of publication	Country	Title	Aim/Objectives	Participants	Data collection method	Year of data collection
Benard V.B. et al., 2011	USA	Cancer Screening Practices Among Physicians in the National Breast and Cervical Cancer Early Detection Program	To describe the demographic and practice characteristics of participating and non-participating physicians to the National Breast and Cervical Cancer Early Detection Program, as well as their beliefs, adoption of new screening technologies, and recommendations for breast and cervical cancer screening.	886 physicians (FP, IM, GP, OB/GYN)	Cross- sectional survey	2006- 2007
Benard V.B. et al., 2016	USA	Change in Provider Beliefs Regarding Cervical Cancer Screening Intervals After an Educational Intervention	The study objective was to assess changes in provider attitudes and beliefs to extending screening intervals among low-income women by using an educational intervention to promote recommended screening practices i.e., lengthening the screening interval to 3 years	84 HCPs at baseline and 52 HCPs at follow-up	Survey (baseline and 12 months' follow-up)	2009- 2010
Boone E. et al., 2016	USA	Discontent and Confusion: Primary Care Providers' Opinions and Understanding of Current Cervical Cancer Screening Recommendations	To elucidate causes of non- adherence of primary care providers to primary screening for cervical cancer guidelines released in 2012 by ACOG, ACS, and USPSTF	1268 HCPs (OB/GYN, FP, IM, NP and PA)	Cross- sectional survey	2014

Author and year of publication	Country	Title	Aim/Objectives	Participants	Data collection method	Year of data collection
Cagliotti C. et al., 2017	Italy	Gynecologists and human papillomavirus DNA testing: exploring knowledge, attitudes, and practice in Italy	To examine the knowledge, attitudes, and practice of OB/GYN related to the use of HPV DNA testing in primary screening for cervical cancer	582 OB/GYN	Cross- sectional survey	2015
Chung H.H. et al., 2006	South Korea	Cost is a Barrier to Widespread Use of Liquid-Based Cytology for Cervical Cancer Screening in Korea	This study aimed to document current cervical cancer screening practices of OB/GYN in South Korea	254 OB/GYN	Cross- sectional survey	2005
Cooper C.P. et al., 2015	USA	Perceived effectiveness of HPV test as a primary screening modality among US providers	To explore HCPs perceptions of the effectiveness of the HPV test in population-based screening for cervical cancer	1040 HCPs in 2009 (189 IM, 494 FP, 141 NP and 216 OB/GYN) and 1039 HCPs in 2012 (205 IM, 435 FP, 155 NP and 244 OB/GYN)	Cross- sectional survey	2009 and 2012
Cooper C.P. et al., 2017	USA	Primary HPV testing recommendations of US providers, 2015	To examine physicians' HPV testing recommendations	843 HCPs (FP, IM and OB/GYN)	Cross- sectional survey	2015
Corbelli J. et al., 2014	USA	Differences Among Primary Care Physicians' Adherence to 2009 ACOG Guidelines for Cervical Cancer Screening	To assess the compliance of HCPs with 2009 ACOG guidelines for cervical cancer screening	316 HCPs (IM, IM- Pediatricians, FP, OB/GYN)	Cross- sectional survey	2012
Filade T. E. et al., 2017	Nigeria	Attitude to Human Papillomavirus Deoxyribonucleic Acid-Based Cervical Cancer Screening in Antenatal Care in Nigeria: A Qualitative Study	To explore the attitude of HCPs and pregnant women toward the hypothetical introduction of HPV DNA testing into routine antenatal care	82 pregnant women (focus groups) and 13 HCPs (OB/GYN and midwifes)	9 focus groups and 13 in-depth interviews	2015- 2016

Author and year of publication	Country	Title	Aim/Objectives	Participants	Data collection method	Year of data collection
Hoover K. et al., 2009	USA	Access of Black, Hispanic, and nonprivately insured women to liquid-based cytology, human papillomavirus DNA testing, and on-site colposcopy in the United States	To determine if patients' sociodemographics was associated with HCPs use of liquid-based cytology, HPV testing, and on-site colposcopy	2981 HCPs (OB/GYN, nurse midwifes, FP, adolescent medicine physicians, IM, NP, PA)	Cross- sectional survey	2004
Irwin K. et al., 2006	USA	Cervical cancer screening, abnormal cytology management, and counseling practices in the United States	To assess HCPs knowledge and practices related to HPV testing as an adjunct to cytology and for colposcopic triage for ASCUS cytology results	2,980 HCPs (463 OB/GYN, 622 nurse midwifes, 333 FP, 293 Adolescent Medicine, 220IM, 591 NP, 458 PA)	Cross- sectional survey	2004
Jain N. et al., 2006	USA	Family Physicians' Knowledge of Genital Human Papillomavirus (HPV) Infection and HPV-related Conditions, United States, 2004	To assess the relationship between family physicians' knowledge about HPV, HPV test and delivered counseling messages when collecting samples for cytology and managing anogenital warts	368 FP	Cross- sectional survey	2004
Katz M.L. et al., 2017	USA	Perspectives from health-care providers and women about completing human papillomavirus (HPV) self-testing at home	To explore among women and HCPs the perceived acceptability, barriers and facilitators of HPV self-testing	Focus groups with 28 HCPs (1 physicians, 16 nurses, 8 NP and 3 medical assistants) and nurses) and focus groups/interviews with 15 women	Focus groups and in-depth interviews	2014- 2015
Kuitto K. et al., 2010	Germany	Perspectives on and experiences with early detection and preventive measures against cervical cancer. Results of an expert survey among physicians	To gain knowledge about prevention measures against cervical cancer i.e., cervical cancer screening and HPV vaccination in daily practice	112 physicians (OB/GYN, pediatricians, FP, public health)	Cross- sectional survey	2008- 2009

Author and year of publication	Country	Title	Aim/Objectives	Participants	Data collection method	Year of data collection
		in Mecklenburg–Western Pomerania				
Kwan T.C. et al., 2012	China	Assessment of knowledge and stigmatizing attitudes related to human papillomavirus among Hong Kong Chinese healthcare providers	To assess knowledge and attitudes related HPV and HPV testing among HCPs in Hong Kong	137 HCPs (37 physicians and 100 nurses including smear-taking trainees)	Cross- sectional survey	2010
Lataifeh I. et al., 2009	Jordan	A survey of the knowledge and attitude of Jordanian obstetricians and gynaecologists to cervical cancer screening	To assess knowledge and attitudes towards cervical screening	392 OB/GYN	Cross- sectional survey	Not reported
Lin L. et al., 2015	USA	Communication practices about HPV testing among providers in Federally Qualified Health Centers	To assess HCPs perceptions of their communication practices about the HPV co-test, and the risks and benefits of discussing co-test results with patients	98 HCPs (OB/GYN, FP or NP)	Cross- sectional survey	2009- 2010
Mao C. et al., 2017	USA	Clinician and Patient Acceptability of Self-Collected Human Papillomavirus Testing for Cervical Cancer Screening	To evaluate clinician and patient attitudes related to home self-collected HPV testing for cervical cancer screening	1769 women and 118 HCPs (OB/GYN, IM, FP, midwifes, NP, women's health specialist)	Cross- sectional survey	2012- women and 2013- 2014- HCPs
McCarey C. et al., 2011	Cameroon	Awareness of HPV and cervical cancer prevention among Cameroonian healthcare workers	To assess knowledge and awareness of cervical cancer prevention among HCPs	401 HCPs (GP, Pediatrics, OB/GYN, nurse- midwifes, nursing- midwifery students and medical students)	Cross- sectional survey	2009

Author and year of publication	Country	Title	Aim/Objectives	Participants	Data collection method	Year of data collection
Patel H. et al., 2017	UK	Knowledge, attitudes and awareness of the human papillomavirus amongst primary care practice nurses: an evaluation of current training in England	To evaluate the effectiveness of HPV education and to determine the level of HPV knowledge in nurses involved in cervical smear sampling	94 practice nurses	Cross- sectional survey	2015
Perkins R.B. et al., 2013	USA	Challenges in Cervical Cancer Prevention A Survey of U.S. Obstetrician-Gynecologists	To examine attitudes, practice, and barriers related to HPV vaccination and the 2009 ACOG cervical cancer screening guidelines among OB/GYN	366 OB/GYN	Cross- sectional survey	2011- 2012
Regier D.A. et al., 2013	Canada	Exploring Colposcopists' Attitudes Towards Use of HPV Testing as a Primary Screening Tool for Cervical Cancer in British Columbia	To explore colposcopists' attitudes regarding HPV testing in primary cervical cancer screening	35 colposcopists in 2010 and 46 in 2011	Cross- sectional surveys	2010 and 2011
Roland K.B. et al., 2013	USA	Primary care provider practices and beliefs related to cervical cancer screening with the HPV test in Federally Qualified Health Centers	To assess HCPs practices, attitudes and beliefs related to primary screening in cervical cancer with HPV co-testing and extending screening intervals	98 HCPs (65 physicians, 20 NP, 6 nurse midwife, 7 PA), specialty: 35 FP, 8 IM, 52 OB/GYN, 1 Pediatrics	Cross- sectional survey	2009- 2010
Roland K.B. et al., 2015	USA	Provider beliefs associated with cervical cancer screening interval recommendations: A pilot study in Federally Qualified Health Centers	To examine HCPs characteristics and attitudes and beliefs associated with their cervical cancer screening interval recommendations.	82 HCPs (55 physicians, 17 NP, 10 other), specialty: 29 FP, 46 OB/GYN, 7 other	Cross- sectional survey	2009- 2010

Author and year of publication	Country	Title	Aim/Objectives	Participants	Data collection method	Year of data collection
Saint M. et al., 2005	USA	Current cervical neoplasia screening practices of obstetrician/ gynecologists in the US	To determine the cervical cancer screening practices of obstetrician/ gynecologists in the US related to the ACS 2002 guidelines	185 OB/GYN	Cross- sectional survey	2003
Saraiya M. et al., 2010	USA	Cervical Cancer Screening With Both Human Papillomavirus and Papanicolaou Testing vs Papanicolaou Testing Alone	To assess practices of primary care physicians related to cervical cancer screening, including their recommendations of extended screening intervals with Pap and/or HPV cotesting	950 HCPs (408 GP/FP, 224 IM, 318 OB/GYN)	Cross- sectional survey	2006- 2007
Teoh D.G.K. et al., 2015	USA	Adherence to the 2012 national cervical cancer screening guidelines: a pilot study	To evaluate HCPs knowledge, practices, and attitudes/beliefs related to the 2012 cervical cancer screening guidelines	124 HCPs (86 physicians, 12 PA, 19 NP, 18 other) specialty: 31 OB/GYN, 27 IM, 52 FP, 19 midwifery, 6- other)	Cross- sectional survey	2013
Townsend J.S. et al., 2014	USA	Current Cervical Cancer Screening Knowledge, Awareness, and Practices Among U.S. Affiliated Pacific Island Providers: Opportunities and Challenges	To assess HCPs cervical cancer-related knowledge, screening practices, barriers of cervical cancer screening and awareness of HPV testing	72 HCPs (29 physicians, 35 nurses or midwifes, 1 PA, 7 other)	Cross- sectional survey	2011
Trope L.A. et al., 2009	Thailand	Preventing Cervical Cancer Stakeholder Attitudes Toward CareHPV-Focused Screening Programs in Roi-et Province, Thailand	To rank HCPs opinions about 5 cervical screening protocols in terms of benefits for reducing cervical cancer and protocol preference	88 HCPs (48 nurses, 4 colposcopists 16 medical directors and 20 health officers)	Cross- sectional survey	2007- 2008

Author and year of publication	Country	Title	Aim/Objectives	Participants	Data collection method	Year of data collection
Wakewich P. et al., 2016	Canada	Colonial legacy and the experience of First Nations women in cervical cancer screening: a Canadian multicommunity study	To, elicit women's and HCPs opinions about sexual health, preventive health services and HPV self-sampling as an alternative to Pap testing in screening for cervical cancer	16 HCP (nurses, health managers/directors, community health representatives and elders) and 69 community females	Interviews (HCPs) and 8 focus groups (women)	2011- 2012
Wood B. et al., 2018	Canada	"They Should Be Asking Us": A Qualitative Decisional Needs Assessment for Women Considering Cervical Cancer Screening	To examine women's shared decision-making needs in evaluating cervical cancer screening options	7 women, 3 HCPs (2 nurses and 1 GP) and 2 health system managers	Semi- structured interviews	2016
Yap D. et al., 2016	Australia	Clinicians' attitude towards changes in Australian National Cervical Screening Program	To understand HCPs acceptability, barriers and facilitators of using HPV testing starting at 25 years of age, every 5 years in primary screening for cervical cancer	956 HCPs (571 OB/GYN, 260 GP and 124 trainee)	Cross- sectional survey	2014