

2021

A research study into Human Papilloma Virus (HPV) vaccinations and cervical screening programmes used for young women in Ireland today, and their role in HPV prevention and the detection of Cervical Cancer.

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Recommended Citation

Delahunty, Ruth; Coleman, Niamh; Harrington, Amy; and Crowe, Shannon (2021) "A research study into Human Papilloma Virus (HPV) vaccinations and cervical screening programmes used for young women in Ireland today, and their role in HPV prevention and the detection of Cervical Cancer.," *International Undergraduate Journal of Health Sciences*: Vol. 1 : Iss. 2 , Article 4.
Available at: <https://sword.cit.ie/iujhs/vol1/iss2/4>

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Cover Page Footnote

The authors would like to thank Dr. Brigid Lucey and Dr. Annemarie Burns of Munster Technological University

A Research Study into Human Papilloma Virus (HPV) Vaccinations and Cervical Screening Programmes used for Young Women in Ireland Today, and Their Role in HPV Prevention and the Detection of Cervical Cancer.

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ABSTRACT

This paper aimed to research the Human Papilloma Virus (HPV) vaccine uptake which prevents cervical cancer (caused by HPV), and an evaluation of the Cervical Check system in Ireland for cervical cancer detection. Topics discussed were the preventative and detection measures for cervical cancer in Ireland. The population studied was 18–25-year-old women in Ireland. This study was conducted online, through Google forms, Facebook and the UCC surveys portal. The survey was anonymised, and the participants agreed for their data to be used for publishing in a scientific peer-reviewed research paper. A total of 776 participants were analysed using excel spreadsheets and data collation methods like histograms. In our study it was determined that 53.6% of young women in Ireland mistrust the Irish Cervical Check system in Ireland. It was found that a source of this mistrust was the lack of education and bias in news headlines surrounding the HPV cervical cancer preventative vaccine and the scandal in 2011. A total of 63.5% of our survey population did not receive the HPV vaccine because of parental influence and 79.8% of our participants would get the vaccine again in comparison to 89% who received it originally (9.2% decline in uptake). In conclusion, more education is needed to avoid poor uptake of the HPV vaccine and promote compliance with cervical smear testing in Ireland in the future to decrease the prevalence of cervical cancer in the general population..

KEYWORDS: Cervical cancer, HPV, vaccinations.

INTRODUCTION

Cervical cancer is a cancer of the cervix, and it occurs when pre-cancerous cells mutate and grow at an uncontrolled rate to form tumours (Dasari *et al.*, 2015). The presence of abnormal cells in the cervix is sometimes caused by infection with Human Papilloma Virus (HPV) (Dasari *et al.*, 2015). According to the 2020 annual report from the Irish Cancer Registry, 302 women in Ireland had cancer of the cervix (National Cancer Registry Ireland, 2020). Seven out of ten cervical cancer cases are caused by strains 16 and 18 of the Human Papillomavirus (Health Service Executive, 2019a). Since 2010, young females in the first year of secondary school have been offered the HPV vaccine and since September 2019, young males, in first year of secondary school have also been offered the vaccine (Health Service Executive, 2021). The most common vaccine used in Ireland is the Gardasil-9 vaccine. (Health Service Executive, 2021). Gardasil-9 protects against the nine types of HPV that cause genital warts, certain precancerous conditions, and cancers of the cervix, vagina, vulva, anus, and head and neck, including the oropharynx (National Cancer Institute, 2021). This vaccine is approved for use in females and males aged 9 to 45 years (National Cancer Institute, 2021). This vaccine has greatly reduced the cases of pre-

cancers of the cervix and is attributed with a decreasing prevalence of HPV in Ireland over the past decade (Bonanni, P *et al* 2015).

There are over one-hundred strains of HPV with both high and low-risk types (Braaten and Laufer, 2008). Two methods are currently used by healthcare practitioners in Ireland for the detection of cervical cancer/HPV, which both involve the extraction of cells from the lining of the cervix for the testing of cervical cancer. In the past, pap smears for the detection of cervical cancer cells were the original method. Since March 2020, the gold-standard method for detection has become pap smears for the identification of the HPV itself, rather than cancer cells. Blood testing options have seen some promising findings for detecting HPV although it is less accurate than cervical smears, however, more research is needed into the efficacy of these methods.

Since 2010 there has been controversy about the vaccine and the subsequent preventative measures offered to young women to monitor the development of cervical cancer (i.e. Pap smears). The source of this discourse was postulated to be routed in the false claims on social media that the HPV vaccine, could cause POTS (Postural Orthostatic Tachycardia Syndrome) and CRPS (complex regional pain syndrome), however, the European Medicines Agency in 2015 found no evidence that the HPV vaccine causes any of the above (Yih *et al.*, 2018). In 2010, there was a scandal involving a patient who was presented with a false negative test and was not informed of this until three years later. Further to this, she was diagnosed with terminal cervical cancer, it was then discovered that 161 other women received the same false negative result and 17 have died as a result (Carswell S, 2018).

This research project aimed to investigate the level of distrust in the Cervical Check system in Ireland, because of this scandal and learn more about the rumours and perceptions associated with the HPV vaccine according to women in Ireland aged 18-25.

MATERIALS & METHODS

Survey population

Irish females, aged 18-25 years, were surveyed to establish their perceptions of the current measures in place to prevent cervical cancer in Ireland.

Survey Design

The survey contained 23 questions on Google Forms. It was optional to choose multiple answers and skip a question entirely. Close-ended and open-ended questions were used. Several questions included the use of Likert scale to ascertain each participant's level of agreement or disagreement with a particular statement.

Survey distribution

The survey was distributed via Facebook and Instagram, and the UCC Surveys distribution service via email. UCC societies pages such as UCC Cancer Society, also shared the survey with followers via their social media pages. The survey was released on 06/03/2021 and was closed on 19/04/2021.

Data Analysis

Data were presented using Microsoft Excel, Microsoft Word, and the questionnaire platform Google Forms. The results were interpreted using graphs and tables. Invalid responses were excluded. Only participants born as female between the ages of 18-25 years were part of the data analysis. Closed-ended questions were analysed using bar charts and pie charts. Open-ended questions were divided into categories or counted to determine the consensus.

Ethics

The survey was voluntary and anonymised, the participants agreed for their data to be published in a scientific peer-reviewed research paper. Ethical approval and consent to use data collected, was obtained before conducting this research study. An information sheet about the objectives of the research was provided. All data obtained was confidential and stored in password-protected computers and will be destroyed after 5 years. Personal identifiers or IP addresses were not collected.

RESULTS

Survey population

In total, there were 921 submissions. Of these responses, 776 were valid. Of the valid responses, 95% (n=741) were Irish citizens and 5% (n=35) were not. A total of 99% (n=768) of these valid responses were cis-woman, 0.5% (n=4) were non-binary assigned female at birth and 0.5% (n=4) were transgender-men.

Regarding age, 38% (n=298) of the population were aged between 18-20 years, 53% (n=407) of the population was aged 21-23 years and the remaining 9% were 24-25-year-olds (n=71). Invalid respondents comprised of males and respondents 26 years of age and older. Of the population largely came from those with a scientific background with 52% of participants having studied a science or medical-based course.

Vaccination uptake and analysis

A total of 99% (n=767) of the population were pro-vaccination and 1% (n=9) were anti-vaccination. However, only 89% (n=694) of the population received the Human Papilloma Virus (HPV) vaccine and 11% (n=82) did not receive the HPV vaccine. The respondents who did not receive the HPV vaccine (n=86) were given possible reasons as to why they decided not be vaccinated (Figure 1). It can be observed that parental influence played the biggest role (63.5%) in their choice to receive the vaccine, followed by a lack of education (16.9%), and media influence (8.5%). Medical reasons played a minimal role in their decision (0.9%). A total of 5.9% attributed not getting the vaccine to a negative association with vaccines. GP influence and cost were minimal influences ranging from 1.8% to 2.5% of participants reasoning (Figure 1).

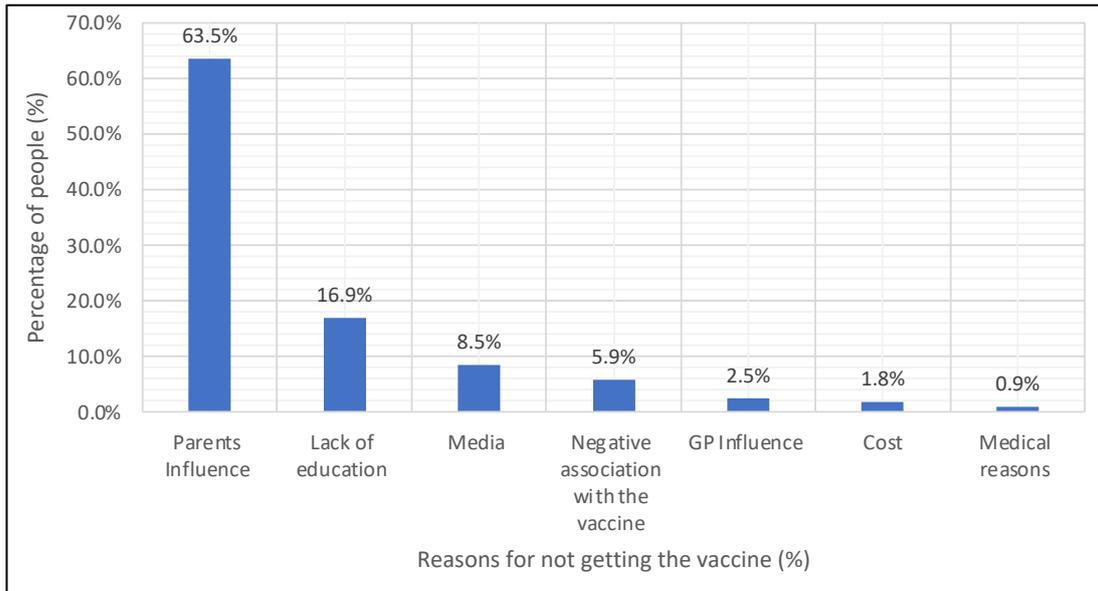


Figure 1: Analysis of the reasons that participants didn't receive the HPV vaccine.

From the full population, 79.8% of participants were very likely and only 1.5% were very unlikely to receive the vaccine if offered again for the first time, as seen in **Figure 2**. A total of 89% received the vaccine in our population, however only 79.8% would get it again.

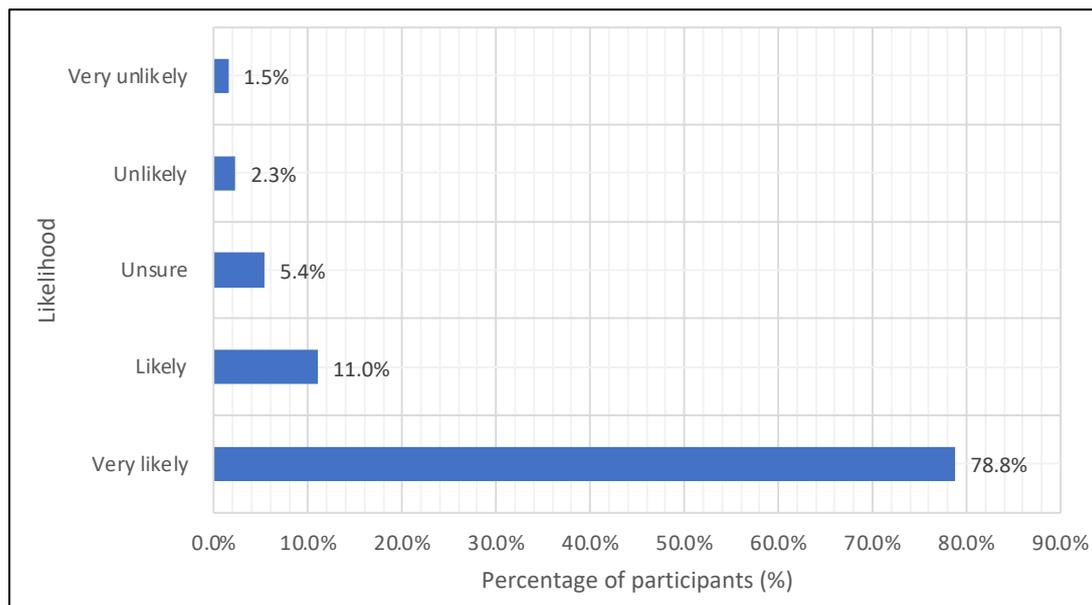


Figure 2: Analysis of percentage population (n=776) that would receive the HPV vaccine if offered again for the first time.

Analysis of side effects caused by immunisation

The participants were asked if they either a) experienced side effects themselves or b) heard of people who suffered side effects from the vaccine and if yes (n=216), and to further specify these side effects from a selection of options. As can be seen in **Figure 3**, general side effects of vaccines like fainting/dizziness/high temperature/nausea and bruising accounted for 59.7%, then narcolepsy 16.2%, Postural Orthostatic Tachycardia Syndrome 4.2%, paralysis 3.2% and fatigue 2.8%. A further 13.9% of people listed other side effects through an open-ended answer box, but these were rare and hence were accounted as 'others' on the graph.

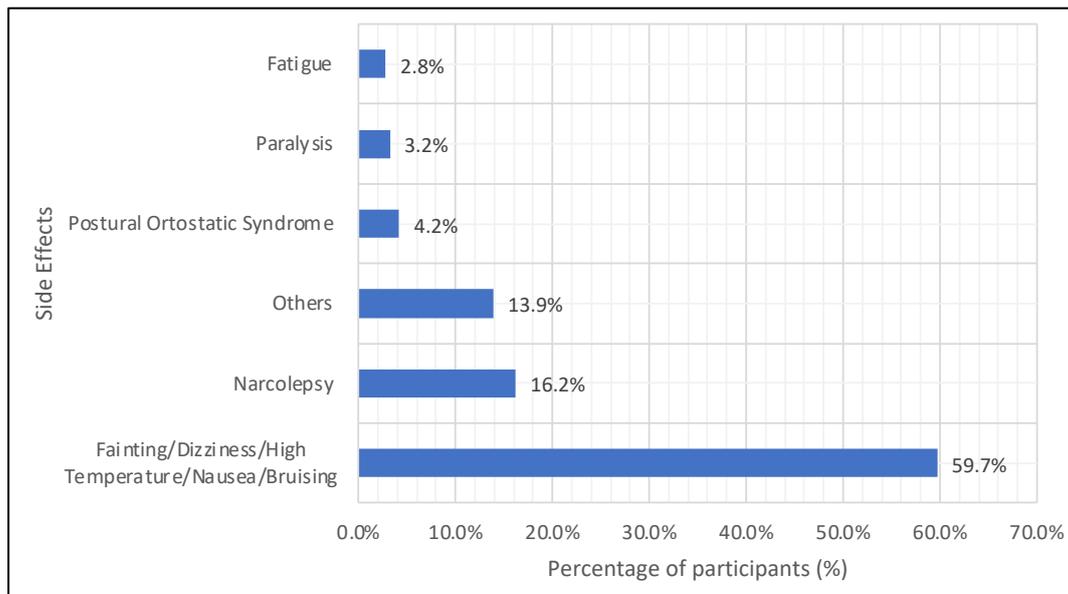


Figure 3: Side effects of the HPV vaccine that were experienced or heard about by the participants (n=216).

General Knowledge of the Population on Cervical Cancer and the HPV Vaccine

A total of 56% (n=437) of the population do not trust the Cervical Check system used in Ireland.

When receiving the vaccine, a total of 28% of people said that they received no information about the HPV vaccine, 65% said they received a pamphlet or letter and 11% said they received an informative talk. When asked if participants knew how HPV was contracted to the best of their knowledge, 70% (n=542) of people knew that HPV was transmitted sexually, 12% (n=94) said travel, skin-to-skin contact or developing it spontaneously, and 18% (n=140) of people said they didn't know. A total of 72% (n=556) did not know that 70% of people will contract HPV in their lifetime. A total of 14.2% (n=111) did not realise that even when vaccinated against HPV, women are still required to get cervical smears.

The participants were asked whether they knew that, in combination or separately, smoking and taking oral contraceptives increase cervical cancer risk. The survey found that 51% were aware of this.

Other findings

A total of 57.3% of participants said they would be very likely to get the vaccine if boys were also offered it, 28.6% were unsure and the remaining 14.1% said it would have no impact on their decision. When asked about the cost of HPV vaccination in universities, a total of 99% of students in our survey (n= 768) said that the vaccination programme currently available is unfeasible for students and 50.1% of students said reasonable prices should range from €50-199.

When the participants were asked if, when they turn twenty-five, they would avail of the Cervical Check system, 77% of participants (n=597) said they would be very likely to avail of this service, whereas 23% said they would not or were not sure whether they would avail of it. The participants were then further questioned and asked why they would not avail of this service. Of the participants, 59.7% answered fear, 46% do not know how to organise the appointment, followed by 42.1% are embarrassed and do not know what it involves.

When information relating to the poor sensitivity of the blood test method when compared to the pap smear was presented to participants, a total of 16% said they would prefer a blood test. However, 73.5% said they would use the cervical smear method (Figure 4).

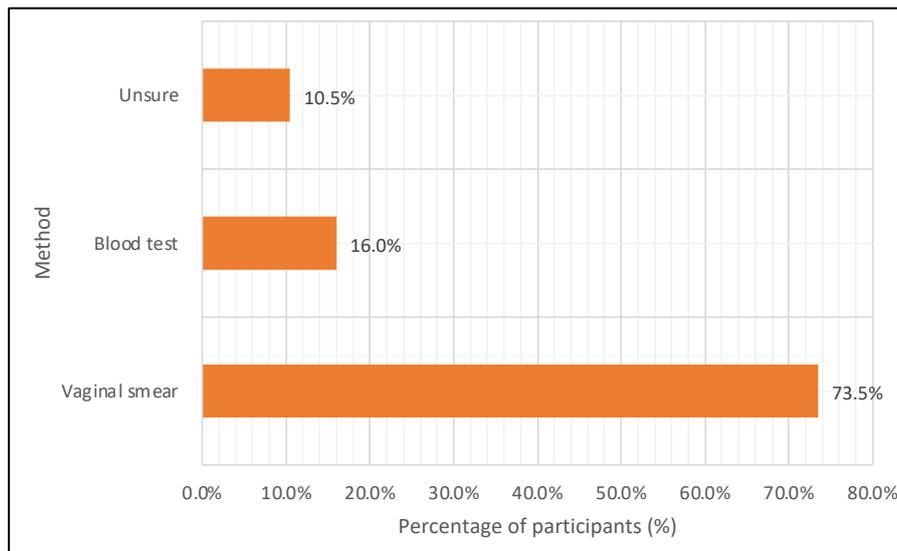


Figure 4: Preference of population for the method employed for cervical cancer screen- either vaginal smear method or blood testing.

DISCUSSION

This research project was aimed to gain insight into the perceptions of young women regarding the HPV vaccination programme and Cervical Check system in Ireland. The main measures used to prevent cervical cancer, are the HPV vaccine programme and cervical smears. Cervical Check is the national cervical cancer screening programme in Ireland.

Most cervical cancers (70%) are caused by the contraction of HPV strains 16 and 18 (Health Service Executive, 2019a). However, once HPV is contracted it can take up to 20 years to present itself as an infection (HPV infection - Side effects and causes, 2021). The virus can linger in the body for years, however it will more than likely lead to the development of antibodies against the virus which will clear it within 1-2 years (World Health Organisation, 2017). Hence, asymptomatic patients may never know that they were infected by HPV (Connor, 2018). More than 70% of people will contract HPV in their lifetime (Cervical Check, 2021). This was presented to the participants in the survey, and it was determined that 71.7% were unaware of this fact. These findings highlight how uneducated people are about HPV and highlighted the need for more education. The HPV vaccine also has strong protection against condylomas and some HPV-related cancers. However, the HPV vaccine does not give complete protection against cervical cancer, it can only help prevent infection (Cheng, Wang and Du, 2020) and 14.2% of the respondents (n=776) were unaware that regular screening is still required, even if vaccinated. From the ages of 25-60, HPV screening is completed every five years (Health Service Executive, 2019b). Screening may need to be carried out more regularly if high-risk types of human papillomavirus were detected such as HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 (The British Society for Colposcopy and Cervical Pathology, 2020).

To prevent cervical cancer a nationwide vaccination programme is in place for secondary school students. The most common vaccine in Ireland is called Gardasil-9, and it protects against the strains of HPV that cause 90% of cervical cancers (Health Service Executive, 2021). It was determined that 99% of respondents were pro-vaccination and 1% were anti-vaccination. When the participants were asked if they had received the HPV vaccine in secondary school, it was deduced that 89% had received the vaccine while 11% had not. These results were surprising and unexpected as most of the participants were pro-vaccination. It was noted that when the participants were asked if they would have received the HPV vaccine again, if it was being offered for the first time, only 79.8% said they would, compared

to 89% of people who received the vaccine in the first place (Figure 2). This disparity warrants further investigation.

The participants that did not receive the vaccine (11%), were asked what influenced their choice (Figure 1). It was determined that the dominant reason was parents' influence (63.5%). This was of course, expected, as first-year secondary school students are under eighteen and therefore require guardian approval before getting any vaccine. Media influence was 8.5% and it should be noted that, at the time, participants would have been receiving the vaccine (2009-2016), a large amount of misinformation was being presented to the public through the media regarding the HPV vaccine (Yih *et al.*, 2018). It was also deduced that 2.5% did not receive the vaccine due to their general practitioners (GPs) influence. GPs should present the relevant facts to the patient and guardians in order for them to make an educated decision. A small number of respondents (0.9%) did not receive the vaccine due to medical reasons.

All vaccinations pose a risk of mild side effects, including fainting and dizziness (Centre for Disease Control and Prevention, 2021). More than 1 in 10 people who receive the Gardasil vaccine will experience such side effects (National Health Service, 2019a). All international bodies have continually reported that the Gardasil vaccine causes no long-term side effects (Yih *et al.*, 2018). The short-term side effects of the vaccine include general mild side effects and in rare cases a severe allergic reaction (Shah *et al.*, 2019). False claims have led to a negative perception of the vaccine with many believing that Postural Orthostatic Tachycardia Syndrome (POTS), and Complex Regional Pain Syndrome (CRPS) were side effects of the vaccine (Yih *et al.*, 2018). However, the European Medicine Agency (EMA) declared that there was no evidence of this being caused directly by the vaccine and the prevalence of these symptoms didn't deviate from the expected occurrences of these symptoms in the population, without the vaccine (EMA, 2015).

It was determined from Figure 3, that the participants also experienced or heard of someone experiencing side effects like narcolepsy (16.2%), POTS (4.2%), paralysis (3.2%), dizziness (59.7%) and a further 13.9% answered 'other' and cited side effects such as insomnia and seizures. The representation of these side effects was not large enough to be accounted for in the graphical results. It was reported in 2010-2015, 958 out of 590,694 girls (0.2%) experienced a negative reaction from the HPV vaccine (MagGuill, 2017).

The HPV vaccination programme is free and offered to first-year students in secondary school (Health Service Executive, 2021). Young females, since 2010, and males since 2019, can receive the HPV vaccination (Corcoran *et al.*, 2021). Since September 2020, boys in secondary school have been offered the vaccine. A total of 57.3% of participants said they would be very likely to get the vaccine for this reason, 28.6% were unsure and the remaining 14.1% said it would have no impact on their decision (ie. a score of 0 on the Likert scale). This highlights that most women would be more likely to get the vaccine, due to this change in the vaccination programme protocol. It is not to be forgotten that HPV can cause anal-genital warts in males (Royal College of Physicians Ireland, 2018). Herd immunity is dependent on high levels of vaccination uptake in both males and females, not just females alone (Royal College of Physicians Ireland, 2018).

There are two vaccines developed to prevent HPV 16/18 related cancers (Clendinen C *et al.*, 2016). The quadrivalent HPV recombinant vaccine called Gardasil-9 and the bivalent HPV vaccine called Cervarix were developed by Merck and GlaxoSmithKline (GSK, 2019). The cost for three doses of the HPV vaccine in University College Cork student medical centre is €555 (University College Cork, 2018). A student might avail of this if they did not get the vaccine for free in secondary school. The cost in University College Dublin is €685.50 (University College Dublin, 2021). A total of 99% of students in our survey say the cost of the vaccination programme make it unfeasible for students and 50.1% of students said reasonable prices should range from €50-199. In other European countries, the timeframe in which the vaccine can be received for free is much wider, for example in Germany the vaccine is given free of charge to females between the ages of 12-17 years and, in addition to this, some statutory health insurance providers cover the complete cost of the vaccine in females aged 18-26 years old (Hense *et al.*, 2014).

The participant's knowledge was assessed on HPV, the vaccine and cervical cancer. When asked what information participants received in secondary school, 28% of people said they received no information about the HPV vaccine and this may provide possible reasons why there was a poor uptake of the vaccine. Most participants (65%) said they received a pamphlet with information, and 11% said they attended an informative talk. These findings prove that people didn't receive enough information about the vaccine.

Most of the participants, 70%, knew that HPV was transmitted sexually, 12% gave answers like travel and skin-to-skin, and 18% of people said they did not know that HPV is transmitted sexually.

Smoking and the oral contraceptive pill increase the risk of cervical cancer (Ryan *et al.*, 2018). It was deduced from the general knowledge of the population on cervical cancer and the HPV vaccine that 49% were unaware of this. This emphasises that the population are not aware of the carcinogenic effects of the pill and smoking and need better health promotion and awareness.

This is an area that encourages a lot more investment for non-profit organisations and more government funding. Possibly, if when young females are offered the HPV vaccine in secondary school for free, and if they were informed of the price of the vaccine later, this may result in higher vaccine uptake. However, public perception of the price of vaccines is misinformed, it may be forgotten the cost of regulating these vaccines, distributing them and low market prices leave the production companies with little to no profit as they are expensive (Xue *et al.*, 2020).

In January 2019, around 21,000 people underwent a cervical smear test; in January 2020 that number had fallen to 17,000 and further to this, in March 2021, 29,000 women were attending for cervical screening, which is an increase when compared to previous months (Cervical Check, 2020). Participants were surveyed about cervical smear uptake and education around the topic of the cervical check system in Ireland and the perception of the system itself. Of note, 53.6% of people do not trust the cervical check system in Ireland and would not trust their result since the scandal in 2019. Women can avail of Cervical Check when they are 25 years old, 77% of participants (n=597) said they would be very likely to avail of this service, whereas 23% said they wouldn't or weren't sure whether they would avail of it. The participants were then further questioned and asked why they would not avail of this service. Of the participants 59.7% answered fear, 46% don't know how to organise the appointment, followed by 42.1% who are embarrassed and don't know what it involves. The participants could select more than one option in this case.

Many participants were concerned that the minimum age of screening for cervical cancer is 25 and they wished for it to be lower. However, population-based screening in women under the age of 25 may lead to many women receiving unnecessary treatment for lesions that would never have developed into invasive cancer and early screening might also lead to unnecessary anxiety and upset (Cervical Check, 2021). Premature screening can cause potential risks with some treatments, including a slightly increased risk of early birth if the patient was pregnant. (Cervical Check, 2021).

The participants were asked if they would prefer another form of detection of cervical cancer that did not involve the smear test such as a blood test and they were informed that it would have decreased sensitivity compared to the cervical smear sensitivity. A total of 16% said they would prefer a blood test despite sensitivity differences (Figure 4). Further investigation into the clinical utility of blood tests is necessary and it may provide evidence that it could be combined and used as an adjunct test, with the traditional cervical smear for optimal patient outcomes. This method would provide a less intrusive and more convenient for the patient (Boltz, 2021).

As the study was distributed through the UCC Survey platform, mostly college-educated students answered the survey and approximately 52% of our population studied some form of science or medicine course. This may have led to an increased amount of scientific knowledge in our population compared to a non-scientific population surrounding HPV and cervical cancer.

In conclusion, the findings of this study suggest, education and factual scientific information on cervical cancer, are lacking amongst young women in Ireland. Knowledge of the subject would increase participation in the vaccination programme and increase the uptake of cervical smears. There is scope for new, less invasive, and less daunting methodologies to increase participation of the public to be tested for cervical cancer. In turn, this would decrease the prevalence of cervical cancer in the population. There seems to be a need for a revision of the price of the HPV vaccination programme after secondary school. There is discord and lack of trust between the Irish public and the Cervical Check system in Ireland, more research should be aimed at rebuilding this trust.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Brigid Lucey and Dr. Annemarie Burns of Munster Technological University

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