SHORT REPORT

HPV vaccine acceptability in HIV-infected and HIV negative men who have sex with men (MSM) in Ireland

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ABSTRACT

Background Men who have sex with men (MSM), particularly HIV-infected MSM are disproportionately affected by HPV infection and associated disease. The HPV vaccine has potential to greatly reduce the burden of HPV-associated disease including anal cancer in MSM. The efficacy of the HPV vaccine is dependent on high levels of vaccine uptake. The aim of this study was to examine HPV vaccine acceptability and factors influencing vaccine acceptability in MSM in Ireland. **Methods** A self-administered survey was distributed to HIV-infected and HIV negative MSM examining HPV vaccine acceptability and factors associated with vaccine acceptability. Logistic regression was used to identify key variables and predictors of HPV vaccine acceptability. **Results** 302 MSM participated in the study. Acceptability of HPV vaccine was 31% (unconditional), 51% (conditional on stated efficacy and a cost of €300), 65% (conditional on stated efficacy and a cost of €100) and 78% (conditional on stated efficacy and no cost). Cost was negatively associated with HPV vaccine acceptability ($p < 0.01$) while knowledge of HPV vaccine efficacy was significantly associated with vaccine acceptability, even in the context of associated cost ($p < 0.01$). **Conclusions** Acceptability of HPV vaccine in MSM in Ireland is high based on no cost vaccine and on stated vaccine efficacy (78%). Cost is negatively associated with vaccine acceptability. Understanding levels of knowledge of HPV infection, HPV associated disease and attitudes toward HPV vaccination are important as they will contribute to HPV vaccine acceptability among MSM and will help guide effective preventive programs.

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Background

HPV is the most common sexually transmitted infection (STI) worldwide.¹ It is causally associated with cervical cancer, penile cancer, vulval cancer, oropharyngeal cancer and anal cancer.²

The prevalence of HPV infection is greater in MSM, particularly in HIV-infected MSM compared to the general population.^{3,4,5} The reported incidence of anal cancer in MSM is up to 35 cases per 100,000⁶ and up to 131 cases per 100,000 in HIV-infected MSM.⁷

The quadrivalent HPV vaccine (HPV-4v) (GardasilTM, Merck and Co., Inc.) is highly efficacious in preventing infection with HPV vaccine types 6/11/16/18, related external genital lesions, and anal intraepithelial neoplasia (AIN) in males and females.^{8,9} The 9-valent HPV vaccine (HPV-9v) (Gardasil 9TM, Merck and Co., Inc.), has recently been approved for the same indications, offering additional protection against HPV types 31, 33, 45, 52, and 58.¹⁰

While gender neutral vaccination programs offer the best preventive opportunities, such programs are unlikely to be implemented where levels of female vaccination coverage are high due to lack of cost-effectiveness evidence.¹¹ HPV vaccination of boys and male adolescents is not yet recommended in Ireland or in the majority of European countries that provide HPV vaccination for girls through national immunization programs due to lack of cost effectiveness data.

High levels of female vaccination coverage have been shown to decrease genital warts in both females and unvaccinated heterosexual males through herd immunity, however no protection has been observed in MSM.¹² Targeted vaccination of MSM has been shown to be cost-effective up to and beyond the age of 26 years.^{13,14,15}

Emerging evidence suggests that HPV-4v may provide additional benefits in older sexually experienced MSM who have previous exposure to HPV by reducing high grade anal lesions (HGAIN) progression and recurrence among MSM.¹⁶ The HPV-4v has also shown to be effective for the prevention of anal condyloma of older MSM.¹⁷

The Joint Commission on Immunisation and Vaccination (JCVI) in the UK are reviewing the cost effectiveness of universal vaccination of boys and girls through the national immunization program as well as targeted vaccination of MSM aged 16–40 years in sexual health and HIV clinics.¹⁸

When considering the feasibility of targeted HPV vaccination, it is important to examine vaccine acceptability and factors influencing acceptability as low vaccine uptake will fail to reduce HPV-related diseases.

There is no data available on acceptability of HPV vaccine in MSM in Ireland and only two published studies examining HPV vaccine acceptability in Europe. A meta-analysis of HPV vaccine acceptability in MSM including data from North

America and Australia (where HPV vaccine is offered to boys and MSM up to the age of 26 years through national programs) found that approximately 50% of MSM would accept HPV vaccine.¹⁹

Success of targeted vaccination programs for preventing HPV associated disease such as anal cancer in MSM will greatly depend on high levels of uptake of HPV vaccine.

The aim of this study was to examine HPV vaccine acceptability and factors associated with HPV vaccine acceptability in MSM.

Results

Background characteristic

302 MSM participated in the study. Baseline characteristics are outlined in Table 1. 39% were aged 18–30 years, 79% were educated to third level or above. 77% reported unprotected anal intercourse (UAI) with a male partner, 30% reported a sexually transmitted infection (STI) in the previous 12 months while 62% reported multiple male sex partners in the previous 12 months. 156 (52%) were HIV-infected.

Knowledge and perceived severity of HPV infection

Appropriate knowledge response relating to HPV infection ranged from 16% to 58% (Table 2). 58% recognized that HPV could affect men. 22% recognized that HPV could not be treated with antibiotics. 16% recognized that HPV infection does not commonly lead to death.

24% perceived that prevalence of HPV infection in MSM in Ireland was high, 44% perceived the infectivity of HPV infection to be high, 33% believed their chance of catching HPV was high. 28% perceived that HPV infection was highly likely to damages physical health, 46% perceived that HPV was highly

Table 2. Knowledge and perceived severity of HPV infection.

Knowledge of HPV Infection	N	(%) ^a
HPV can affect men		
No	15	5
Yes*	172	58
Don't know	110	37
HPV can be treated with antibiotics		
No*	65	22
Yes	51	17
Don't know	177	60
HPV infection can commonly lead to death		
No*	48	16
Yes	64	22
Don't know	180	62
Perceived Susceptibility to HPV		
The chance of you catching HPV infection is		
Low	56	22
Moderate	112	44
High	84	33
Prevalence of HPV infection in MSM in Ireland is		
Low	52	22
Moderate	129	54
High	58	24
The infectivity of HPV is		
Low	36	15
Moderate	99	41
High	105	44
Perceived Severity of HPV Infection		
The chance of HPV infection impacting on physical health is		
Low	62	27
Moderate	113	46
High	60	28
The chance of HPV infection causing genital warts is		
Low	41	17
Moderate	87	36
High	111	46
The chance of HPV infection causing penile/anal cancer is		
Low	62	26
Moderate	113	48
High	60	26

^aProportion of respondents for each characteristic. Missing data not shown.

*Appropriate response

Table 1. Demographic and behavioral characteristics of participants (n = 302).

Background Characteristics	n	(%) ^a
Age group		
18–30	117	39
31–40	87	29
41–60	97	32
Highest education level attained		
Secondary School/equivalent or lower	60	21
College or above	223	79
Diagnosed as having a sexually transmitted infection in the past 12 months ^b		
No	209	70
Yes	90	30
Ever had unprotected anal intercourse with a male partner		
No	68	23
Yes	231	77
Number of male partners that you have had anal intercourse with in the past 12 months		
0	44	15
1	69	23
2–5	120	40
>6	67	22
HIV-positive	156	52

^aProportion of respondents for each characteristic. Missing data not shown.

^bBased on self-reporting, includes chlamydia, gonorrhoea, syphilis, genital warts and genital herpes.

likely to cause genital warts while 26% perceived that HPV was highly likely to cause penile or anal cancer.

Knowledge and perceptions relating to HPV vaccine

Appropriate knowledge response relating to HPV vaccine ranged from 21% to 56% (Table 3). 29% recognized that HPV vaccine was effective in men. 21% recognized that HPV vaccine series consisted of 3 doses. 56% recognized that it would be optimal to receive HPV vaccine at a younger age.

30% perceived that HPV vaccine would prevent genital warts while 26% perceived that HPV vaccine would prevent penile and anal cancers.

11% believed HPV vaccines were expensive. 25% believed HPV vaccine may have side-effects.

HPV vaccines acceptability

Acceptability of HPV vaccine was 31% (unconditional), 51% (conditional on stated efficacy (90% for prevention of genital warts and 75% for prevention of HPV induced cancers) and a cost of €300), 65% (conditional on stated efficacies and a

Table 3. HPV vaccine knowledge/perceived efficacy of HPV vaccine.

HPV vaccine knowledge	n	(%) ^a
An effective HPV vaccine is available for men		
No	30	11
Yes*	87	31
Don't know	167	59
The number of shots of HPV vaccine required is		
1–2	108	54
3*	64	32
4 or above	29	14
The best age to receive HPV vaccine is		
30 years or above	36	18
Below 30 years*	170	82
Perceptions relating to HPV vaccine		
The HPV vaccine is effective in preventing genital warts		
Not effective	12	4
Effective	82	30
Don't know	180	66
The HPV vaccine is effective in preventing penile and anal cancer		
Not effective	18	7
Effective	71	26
Don't know	189	68
The HPV vaccine is effective in preventing sexually transmitted infections other than genital warts		
Not effective	59	21
Effective	40	14
Don't know	178	64
The HPV vaccine is too expensive		
No	36	13
Yes	29	11
Don't know	212	77
The HPV vaccine could have side effects		
No	19	7
Yes	69	25
Don't know	189	68

^aProportion of respondents for each characteristic. Missing data not shown.

*Appropriate response

discounted cost of €100) and 78% (conditional on stated efficacies and free price) (Table 4).

Factors associated with vaccine acceptability based on stated efficacies and free vaccine

Individual factors identified as being significantly associated with HPV vaccine acceptability based on no cost vaccine on univariate analysis are reported in Table 5. There was no significant difference in HPV vaccine acceptability identified in HIV-infected MSM versus HIV negative MSM based on no cost vaccine ($p = 0.9$).

Discussion

Baseline demographic data (Table 1.) indicate that MSM who participated in this study were at high risk of HPV infection and associated disease.

Our study included HIV-infected ($n = 156$) and HIV negative ($n = 146$) MSM aged 18 to 60 years. While current guidelines recommend HPV vaccine for MSM up to the age of 26 years, emerging evidence suggests that HPV vaccine may have efficacy beyond primary prevention and thus may be of benefit in older MSM.^{16,17} In this context, investigating the

Table 4. Intention to take up HPV vaccine.

Intention to take up HPV vaccine	n	(%) ^a
Do you plan to take up HPV vaccine in the next 6 months?		
Yes	87	31
No	42	15
Don't know	152	54
Would you take the HPV vaccine if it was 90% effective in preventing genital warts, 75% effective in preventing anal cancer and cost €300 in total?		
Yes	144	51
No	48	17
Don't know	87	31
Would you take the HPV vaccine if it was 90% effective in preventing genital warts, 75% effective in preventing anal cancer at a discounted price of €100 in total?		
Yes	179	65
No	21	8
Don't know	76	28
Would you take the HPV vaccine if it was 90% effective in preventing genital warts, 75% effective in preventing anal cancer and free?		
Yes	217	78
No	3	1
Don't know	57	21

^aProportion of respondents for each characteristic. Missing data not shown.

acceptability of HPV vaccine in a group that includes MSM >26 years is of relevance.

Reported unconditional acceptability of HPV vaccine observed in our study (31%) is lower than that reported in similar international studies in MSM 47–74%.^{20,21,22} This may be due to poor knowledge relating to HPV infection, HPV associated disease and HPV vaccine in MSM in Ireland.

HPV vaccine acceptability increased from 31% (unconditional) to 51% when participants were informed of efficacy of HPV vaccine for prevention of genital warts and anal/penile cancer, even in the context of associated vaccine cost of €300. This highlights the important role of education interventions in raising awareness of HPV infection and highlighting the potential role of HPV vaccine in prevention and protection. Such interventions will be critical in ensuring the success of targeted HPV vaccine programs.

Cost was found to be significantly associated with HPV vaccine acceptability. HPV vaccine acceptability increased from 51% based on a cost of €300 for the vaccine series to 78% based on no cost vaccine ($p < 0.01$). Similar studies undertaken in MSM in Australia²³ and Hong Kong²⁴ also identified cost as a significant factor influencing HPV vaccine acceptability in MSM.

Cost effectiveness data currently supports vaccination of MSM <26 year¹³ with recent research suggesting HPV vaccine would be cost effective regardless of age in HIV-infected MSM.^{14,15} Despite these findings HPV vaccine for MSM is currently not funded through the national program in Ireland or in the majority of European countries. As cost is significantly associated with HPV vaccine acceptability provision of free HPV vaccine through national programmes will be an important factor to consider if targeted vaccination programmes are to be successful.

Table 5. Background Characteristics significantly associated with HPV vaccine acceptability (n = 277).

	P value	OR _(u)	95%CI
Demographic data			
Higher education level attained	0.01	3.01	1.57–5.749
Correct knowledge items relating to HPV infection/ vaccine			
HPV can affect men	0.01	4.87	2.62–9.05
HPV can be treated with antibiotics	0.03	2.57	1.1–5.99
Best age to receive vaccine	0.01	1.29	0.15–11.26
Perceptions regarding HPV infection/ vaccine			
The chance of HPV impacting on health is moderate/high	0.01	2.65	1.32–5.35
HPV vaccine effective preventing genital warts	0.02	2.54	1.17–5.48
HPV vaccine effective preventing anal/penile cancer	0.01	4.08	1.55–10.72
Not effective preventing other STI	0.01	3.96	1.36–11.49
HPV vaccine is expensive	0.07	6.45	0.85–49.07
Vaccine has side effects	0.01	3.67	1.5–8.97

Abbreviations: STI, Sexually Transmitted Infection, OR, Odds ratio, CI, confidence interval

Participants in our study had a poor knowledge of HPV-infection and HPV vaccination. Appropriate HPV infection and HPV vaccine knowledge response rates ranged from 16–58% (Table 2) and 32–82% (Table 3) respectively. MSM who completed the survey had a low perceived susceptibility (33%) to HPV infection despite being from a high risk group.

Less than 50% of study participants were aware that HPV could cause genital warts while only 26% were aware that HPV could cause penile or anal cancer.

Factors associated with HPV vaccine acceptability were examined based on no cost vaccine, as this would best reflect the real life scenario should a targeted HPV immunization program be introduced for MSM in Ireland.

Higher education level was significantly associated with HPV vaccine acceptability [odds ratio (OR) 3.01, 95% CI 1.57 – 5.75, $p = 0.01$] based on stated efficacy (90% effective in preventing genital warts, 75% effective in preventing anal cancer). This may represent greater understanding or insight into the stated protective effects of the vaccine in more educated individuals. Awareness campaigns and education interventions to promote HPV vaccine must use simplified material with a clear message to ensure it is easily understandable regardless of level of education so it can reach the widest audience. This will help to ensure the highest level of vaccine coverage can be achieved.

A number of individual knowledge items relating to HPV infection and HPV vaccine were significantly associated with HPV vaccine acceptability again highlighting the importance of awareness and education in promoting the HPV vaccine in MSM (Table 5). The finding that individual knowledge items relating to HPV infection increases HPV vaccine acceptability supports findings from other similar surveys.^{22–25} Educational interventions should be developed to improve knowledge of HPV infection and associated disease to optimize HPV vaccine acceptability.

Other studies of HPV vaccine acceptability have found that a recommendation from a health care provider is an important factor in acceptability of HPV vaccine. While this was not examined in our study it should be considered when education programs are being developed.²⁰

Perception that HPV vaccine will protect against genital warts, penile and anal cancers were associated with HPV vaccine acceptability on univariate analysis (Table 5). Interestingly perception that HPV vaccine may have side effects (OR 3.67,

CI) 1.50–8.97, $p = 0.01$) and that HPV vaccine is expensive (OR 6.45, CI 0.85–49.07, $p = 0.07$) and were positively associated with vaccine acceptability.

As factors reported as associated with HPV vaccine acceptability are based on the scenario of no cost vaccine, perception that market cost of the vaccine is high may attribute a value to the vaccine and represent an incentive to avail of no cost vaccine.

Acknowledgment that the HPV vaccine may have side effects (although specific side effects were not stated) was positively associated with HPV vaccine acceptability. This may indicate that despite perception of associated side effects relating to vaccine, the risk benefit profile would be such that individuals would choose to receive vaccine.

Our study has a number of limitations; convenience sampling was undertaken and results may be subject to selection bias. HIV-infected MSM are over-represented in the study as one sampling site was a HIV outpatient clinic and thus results are not generalizable to the general MSM population. Interestingly there was no significant difference in HPV vaccine acceptability between HIV-infected and HIV negative MSM based on no cost vaccine.

In addition, as this was a self-administered questionnaire not all questions were completed and missing data was not included in the analysis thus some findings must be interpreted with caution. The ordering effect was not accounted for in the survey design which may represent a bias. Information on MSM who refused to participate the study was not recorded although anecdotal reports indicate that participation rates in survey were high. Self-reported sexual behaviors are subject to recall bias. Finally, reported acceptability of a vaccine does not correlate with uptake of a vaccine. We do not know what proportion of those who indicated that they planned to receive the vaccine were subsequently vaccinated. At the time of the study none of the MSM surveyed had received the HPV vaccine.

This research provides important insights into acceptability of HPV vaccine in MSM in Ireland and adds to limited data available in this area. Given the outlined limitations it should be considered a pilot study and data should be interpreted with caution pending further research in the area.

Immunization programs providing universal HPV vaccination to HPV infection naïve individuals have the greatest potential to prevent HPV-associated disease. Such programs

are unlikely to be implemented in Ireland or in the majority of European countries in the short term given lack of cost effectiveness data. Universal vaccine programs, while offering the best preventative opportunities to those vaccinated, will have no effect on risk of HPV associated disease in current high-risk adult populations such as MSM.

Our study indicates that acceptability of HPV vaccination in MSM would be high and would be expected to increase following implementation of health education programs outlining the risks of HPV associated disease and efficacies of the HPV vaccine. Much of this education could be delivered synergistically using existing infrastructure alongside HIV prevention programs.

A growing body of evidence suggests the potential of HPV vaccine to prevent development of HPV-associated disease in older MSM.^{26,27,28} Although no therapeutic benefit of HPV vaccine has been demonstrated for the treatment of active disease present at the time of vaccination, emerging data suggests a possible benefit of HPV vaccination in the setting of previous disease.^{14,15}

Sexual health and HIV outpatient clinics are well placed to facilitate targeted/catch-up HPV vaccination for the high risk groups including HIV-infected and HIV negative MSM, particularly in the setting of similar effective models for hepatitis B vaccination.²⁹

The landscape in relation to HPV infection, prevention and associated disease is evolving rapidly. The recently available nonavalent HPV vaccine (HPV-9v) offers protection against an additional 5 oncogenic HPV types (31, 33, 45, 52, and 58) associated anal cancers in MSM.^{30,31}

Targeted HPV vaccine has potential to greatly reduce the increasing burden of HPV associated anal cancer in MSM and HIV-infected MSM in the future. Our study suggests that acceptability of HPV vaccine will be high and given the individual and population health benefits vaccine should not be withheld.

Methods

Study population

MSM aged 18 years and over were invited to complete an anonymous self-filled survey from January 2014 to April 2014. The survey was developed in partnership with researchers and community-based associations in Dublin, and was piloted among 20 participants prior to implementation. The survey was based on previous published studies examining HPV vaccine acceptability in MSM.^{22,23,24} Participants provided verbal informed consent. Recruitment was from 2 sites, a walk in sexual health clinic (The Gay Men's Health Service, GMHS) and a HIV outpatient clinic (The Department of Genitourinary medicine and Infectious Diseases, St James's Hospital, GUIDE) in Dublin Ireland. Convenience sampling was performed. Refusal to participate in the study was not recorded.

Measures

Socio-demographic information including highest education level attained, history of STI, unprotected anal intercourse (UAI) and number of male sex partners in the last year was

recorded (Table 1). Questions explored knowledge and cognitions on HPV infection and vaccine (Table 2).

Intention to take the HPV vaccine in the next 6 months and acceptability of HPV vaccine was assessed based on modified scenarios including unconditional, relating to stated HPV vaccine efficacy (HPV vaccine is 90% effective for prevention of genital warts and 75% effective for prevention of HPV induced anal/penile cancer) and vaccine cost (based on cost of €300 per vaccine series, a discounted cost of €100 per vaccine series or no cost vaccine) (Table 3).

Statistical analysis

Basic demographics were reported as totals and percentages. Missing data was excluded from analysis. To examine factors associated with HPV vaccine acceptability for no cost vaccine univariate odds ratios were calculated. Corresponding 95% confidence intervals (CI) of odds ratios were presented (Table 4). SPSS version 22.0 was used for data analysis, with *p* values of <0.05 taken as statistically significant.

Ethics approval

Ethics approval was obtained from the local research ethics committee.

Disclosure of potential conflicts of interest

No listed author has a conflict of interest to declare.

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Author contributions

All authors have contributed to the design, drafting and review of this manuscript. CS, CB, SC, OS designed, drafted and reviewed the manuscript. CS, AL, SOD, SD, MQ designed the survey tool, participated in data collection and reviewed the manuscript.

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