Mother's preferences and willingness to pay for human papillomavirus vaccination for their daughters: a discrete choice experiment in Hong Kong

Abstract

Objective: To determine the preference of mothers in Hong Kong and their willingness-to-pay (WTP) for human papillomavirus (HPV) vaccination for their daughters.

Method: A discrete choice experiment survey with a two-alternative study design was developed. Data was collected from pediatric specialist outpatient clinics from 482 mothers with daughters aged 8-17 years old. Preferences of the four attributes of HPV vaccines (protection against cervical cancer, protection duration, side-effects, and out-of-pocket costs) were evaluated. The marginal and overall WTP were estimated using multinomial logistic regression. A subgroup analysis was conducted to explore the impact of socio-economic factors on mothers' WTP.

Results: Side-effects were considered the most important attributes of the decision to receive or not receive the vaccine followed by protection against cervical cancer, protection duration, and out-of-pocket cost. All attributes were statistically significant factors determining the preference of and WTP for the vaccine. Maximum WTP for ideal vaccines developed using the best technology was HK$12,526 (US$1,606). The estimated WTP for vaccines currently available was HK$1,620 (US$208), significantly lower than current market price. Those who have a high monthly household income (>HK$50,000) had a greater maximum WTP and WTP for current vaccines than those with a lower household income.

Conclusions: This study provides new data on how features of the HPV vaccine are viewed and valued by mothers by determining their perception of ideal or improved and current vaccine technologies. These findings could contribute to future policies on the improvement of HPV vaccine and be useful for immunization service in Hong Kong.

Keywords: vaccination; HPV; willingness-to-pay; discrete choice experiment;

Manuscript Text

Introduction

Cervical cancer was the eighth most common cancer among females in Hong Kong in 2014, accounting for about 3.3% of all new cancer cases in females(1). In the most recent cancer registry conducted in Hong Kong, there were 472 cases of cervical cancer diagnosed in 2014 with an age-standardised incidence rate of 8.1 per 100,000 in the population. In the past two decades, burden of the disease is relatively higher compared to other developed countries(2), although both the incidence and mortality rates of cervical cancer show a decreasing trend(1).

To further reduce the burden of cervical cancer, cervical cancer screening program was organised and launched in 2004(3) and two preventive vaccines were introduced and became available for females in the community as of 2006(4). The two commercially-available vaccines offer about 70% protection against various strains of the human papillomavirus (HPV)(5), which causes cervical carcinoma(6). However, HPV vaccines have yet to be integrated into the government's immunisation schedule in Hong Kong(7). Instead, people voluntarily seek the vaccine in private clinics with the administration rate for adolescent girls was as low as 2.4% in 2008 and 9.1% in 2012 due to lack of HPV vaccination program currently organised(4, 8). However, including the HPV vaccination for girls aged from 12 years old and upwards is considered a cost-effective option compared to only offering cervical cancer screening (9, 10).

The success of the HPV vaccination program largely depends on the attitude of local stakeholders towards the risks and benefits of the vaccination (11-13). For the purpose of policy decision-making and improving health services, it is important to understand the various factors that may affect consumer's demand and their decision towards administering the vaccine. Factors associated with decision-making not only includes the results of economic evaluation but also other considerations such as consumer's demand and preference. With regards to the HPV vaccination, mothers who are highly involved in the decision to vaccinate or not vaccinate their daughters aged under 18 years old(14, 15) were therefore regarded as the critical consumer of the HPV vaccination. This study adopted a discrete choice experiment (DCE) to determine consumer preference of the HPV vaccine attributes and their willingness-to-pay (WTP) for the vaccine in Hong Kong. Similar studies have been conducted in other countries (16-20), however given that consumer preference may be subject to cultural differences, the applicability of research from overseas to the local community may be limited. The aim of this study is to

investigate the effect of consumers' choices and behaviour in Hong Kong when contemplating the attributes of the HPV vaccination, to determine local consumers' preference towards the vaccine and measure their demand in terms of WTP, as well as identify gaps in promoting this vaccination. It is anticipated that this study will provide useful information on immunization services in Hong Kong to help create local HPV vaccination policies in a more effective and economically-sustainable way.

Methods

A cross-sectional survey was conducted in two local public hospitals where a stratified sampling approach was adopted to recruit mothers as subjects who match the inclusion criteria in paediatric specialist outpatient clinics in the Princess Margaret Hospital (PMH), Kowloon, and Queen Mary Hospital (QMH), Hong Kong Island.

Target population

Given that the decision to vaccinate girls aged 8-17 would largely be determined by their mothers[14, 15], mothers in the paediatric clinics are regarded as the consumers in this study, as was the case in similar studies conducted overseas[16, 19]. As such, fathers or any other carers of the girls were not considered in this survey.

Study Design

Attributes and levels identification

The relevant attributes and levels for DCE have been identified through literature review with reference to attributes used in the HPV vaccine DCE studies conducted in the US, Canada, the Netherlands and Vietnam [16-19] and interviews with relevant local experts, consisting of two paediatricians and two non-paediatric medical practitioners, who are involved in policy-making and are clinical experts in the fields of vaccinations and infectious diseases. A pilot of these attributes was conducted in October 2012 when our research team interviewed eight paediatricians and eight mothers who matched the inclusion criteria to identify the most important attributes to be included in the DCE survey. The results of this pilot data (***Table 1***) indicate the top four attributes: 'Protection against cervical cancer', 'Protection duration', 'Side effects', and 'out-of-pocket cost'. Each attribute was assigned four levels to give the participants

a range of the best and worst levels to construct the experimental design. All levels of each shortlisted attribute were selected based on the overseas DCE studies (16-18). The 'Protection duration' and 'out-of-pocket cost' levels were expressed in years and dollars respectively. The 'Protection against cervical cancer' level was expressed in a percentage and presented in terms of an absolute risk reduction that was mainly used for the description of risk information in the DCE survey(21). The 'Side effects' level concerns the potential side-effects following administration of the HPV vaccination and is expressed as a frequency. Therefore, the identification of attributes and their relevant levels were justified and supported by literature review, and expert and respondent input from pilot data. The complete list of attributes and corresponding levels is listed in *Appendix 1*.

Discrete choice experiment design

To avoid impractically-large sample sizes, the complete set of combinations of all attribute levels corresponding to a full factorial design (4*4*4*4=256 hypothetical vaccine profiles) was not used in this experiment. Rather, an orthogonal design (ORTHOPLAN procedure, IBM SPSS Statistics for Windows, Version 22.0) was used to produce 16 hypothetical vaccine profiles (see *Appendix 2)* allowing the main effects to be estimated.

In our experimental design, each choice set contained three options: two vaccine profiles and one "opt-out" option (i.e. no vaccination) (see *Appendix 2*). Two vaccine profiles were chosen from 16 vaccine profiles without any replacement to form eight choice sets. All eight choice sets were established from achieving four desirable properties(22) of orthogonality (i.e. the independence between attributes), a balanced level (i.e. the same frequencies among levels of attributes), a minimum overlap of levels for each attribute in each choice set, and a utility balance (i.e. the options in each choice set have similar probabilities of being chosen).

Respondent fatigue, cognitive feasibility and statistical efficiency were the properties considered. The maximum number of choice sets for respondents was limited to eight (23, 24). All respondents completed eight choice sets to minimize respondent fatigue. In our DCE design, we included nine choice sets in total with the first choice set to be used as an assessment of the respondents' rationality. This single choice set was formed by dominated profile pairs (all the levels of one vaccine profile dominated by the levels of a different one) to test the rationality of the choices made. For example, based on assumption that the respondents prefer a more-effective but a lower-cost vaccine, respondents were expected to reject one vaccine that was

considered worse than another. Respondents who contradicted this assumption of rationality were excluded from the analysis.

Data collection

The survey included questions on socio-demographics, and aspects of health and vaccine experiences as identified from the literature. A list of these items is outlined in ***Appendix 3***. Trained research assistants screened the eligibility of participants identified in the paediatric specialist outpatient clinics in PMH and QMH between June 2014 and May 2015. The purpose of the study was explained to all participants and written consent was obtained. Each participant was presented with a choice to be surveyed in Traditional Chinese or English using an online platform (SurveyMonkey Inc, Palo Alto, California, USA, more information is available at www.surveymonkey.com). The survey was conducted using a portable electronic device on either a laptop or tablet. The research assistant accompanied each participant from commencement to completion of the survey with assistance on any queries they may have. Participants who refused to give consent were excluded from the study.

Sample Size Calculation

According to Orme's rule of thumb formula(25), at least 125 participants are required for a two-alternative experimental design (the alternatives of two vaccines and "no vaccination" did not have varying attributes). The experimental design consisted of eight questions, each one examined by the participants, and the maximum number of levels for any one attribute was four. At least 63 mothers with a low and high household income are required to enhance the representativeness of the sample taken.

Statistical Analysis

The DCE choices were analysed by a multinomial logistic regression model, which regressed the response to the choice question (i.e. vaccine 1, vaccine 2, or no vaccination) of the vaccine attributes and levels (see ***Table 1***). For 'no vaccination' which is defined as the opt-out option, the levels of all attributes were all set to zero. It is assumed that there is a linearity in the levels of each attribute and there is no interaction between the attributes. Utility was expressed in terms of WTP using the preference weights from the logit model. By adopting the linear assumption, the marginal utility would increase by the preference weight value with each percentage change

of protection and side effects or each year change for protection duration. Therefore, the WTP could be determined by taking the ratio of the preference weight of the attribute to the preference weight of out-of-pocket cost. The marginal WTP, which represents the monetary value that the participant is willing to pay for per unit for the attribute, is calculated by multiplying the preference weight of the attribute with changes in levels per unit (i.e. % for protection against cervical cancer and side effects or year for protection duration) as shown in ***Equation 1***.

Equation 1: $\text{Marginal WTP} = \dfrac{\text{Preference Weight}_{\text{attribute}} \times \text{DLevel}_{\text{attribute}}}{\text{Preference Weight}_{\text{out-of-pocket cost}}}$

To calculate the total WTP for a specific vaccine profile, the marginal WTP for each attribute could be added together as follows:

Equation 2:

$\text{Total WTP} = \text{Marginal WTP}_{\text{protection}} + \text{Marginal WTP}_{\text{protection duration}} + \text{Marginal WTP}_{\text{side effects}}$

The maximum WTP for development of the vaccine using ideal technology was calculated by incorporating 100% protection, lifetime protection duration, and 0% side effects into ***Equation 2***. Furthermore, the WTP for vaccines currently available is calculated by substituting the difference between the attribute levels of having the vaccination and not having the vaccination at all (70% protection against cervical cancer, 10-year protection duration and 10% of side effects), which were generally obtained from related clinical literature (26-29).

Log-likelihood, Akaike information criterion (AIC), Bayesian information criterion (BIC) and Nagelkerke's Pseudo R-square were reported to inform the goodness-of-fit of our regression models (30). Regression coefficients estimate for each attribute with their corresponding 95% confidence intervals and the WTP were reported. A subgroup analysis was conducted by different groups of education levels (Primary 1 to 6 for those aged between 6-11 years old, junior secondary year 1 to 3 for those aged between 12-14 years old, senior secondary year 4 to 6 for those aged between 15-17 years old, tertiary leading to non-degrees and tertiary leading to degrees) and monthly household income (<HK$10,000; HK10,000-20,000; HK$20,001-30,000; HK$30,001-50,000; HK$50,001-100,000; and >HK$10,000). The relative importance of different attributes of the HPV vaccination was compared to similar studies conducted in the US, Vietnam and Thailand (16, 19, 20). All statistical analyses were conducted using the Statistical Analysis System (SAS) version 9.3.

Results

Socio-demographic profiles and HPV perceptions

A total of 482 mothers (equalling a response rate of 79.1%) were interviewed with 181 and 301 complete responses from PMH and QMH respectively. The percentage of mothers who declined to participate the study was 20.9% with the main reasons for refusal given as not enough time or not interested in the study. *Table 2* shows the respondents' characteristics and experiences in relation to HPV or the HPV vaccine. The respondents have a mean age of 42.9 years old, more than half were born in Hong Kong and majority were educated to secondary level or higher. Less than half of the respondents had monthly household income more than HK$30,000. In general, respondents were familiar with the vaccine. More than three-quarters of the mothers had previously heard about the HPV vaccines and were concerned about their daughters' risk of HPV infection and cervical cancer. However, more than half of mothers believed the vaccines are somewhat / very unsafe and some of them refused their daughter to be administered. More than 95% declared that either sex education or abstinence should be taught at school.

Preferences and WTP for HPV vaccines of all respondents

The frequency of mothers' choices under different scenarios is shown in *Table 3*. In the first scenario, the rationality test, 99.4% of mothers made the more reasonable choice of higher protection effectiveness, longer protection duration and lower probability of side effects. In the actual DCE of the two to nine scenario, 58.3%-86.3% of mothers chose one of the two vaccines by leveraging the health benefit, risks and costs.

With all the attributes treated as continuous variables in the regression, larger preference weights indicate a more-preferred vaccine attribute. For a specific attribute, a positive coefficient indicates that the corresponding attribute increases positivity and a higher level of this attribute is preferred. This also implies that higher level of this attribute is associated with a higher WTP as well as the increased likelihood to purchase. Conversely, a negative coefficient indicates that the attribute generates negativity and so lower levels are preferred. *Table 4* shows the mothers' preferences estimated from the statistical model. All the

attributes have significant impact on utility (p<0.001). The most important attribute is side effects, followed by protection against cervical cancer and the duration of protection.

The marginal WTP for each attribute and the overall WTP for the vaccine are reported in **Table 5**. For each attribute, zero was used as the reference group for the corresponding marginal estimation of WTP. Vaccine effectiveness, defined as the cervical cancer protection rate, is highly valued with largest WTP margin of HK$5,431. Mothers are similarly willing to pay for lifetime protection (HK$3,545) and the greatest side-effect reduction from 14 to 0 to the amount of 100 (HK$3,550). The maximum WTP for vaccinations developed using ideal and the best technology is HK$12,526. It essentially reflects mothers' perceived benefits and the great demand of eliminating their daughter's risk of cervical cancer. The WTP for vaccines currently on the market is HK$1,620, which is relatively lower than the current market price (HK$4,500 for full-course consisting of 3 injections).

Preferences and WTP for HPV vaccines among different socio-economic groups

To further explore the impact of socio-economic factors on mothers' preferences and the WTP HPV vaccines, we conducted subgroup analyses on different levels of household income and education using the same statistical model. Estimated preference weights by education and income groups are given in more detail in **Appendix 4 and 5**. All the attributes showed a similar significant (P<0.05) impact on the utilities across all income and education groups, except the out-of-pocket cost attribute for primary education level. Preference weights and ranking of attributes were consistent with the overall analysis, the most important attributes being considered as side effects, followed by protection against cervical cancer and protection duration.

Mothers' WTP for HPV vaccines among different education levels and income groups are accordingly illustrated in **Figure 1**. In general, the maximum WTP and WTP for current vaccines are positively correlated with education level. However, the maximum WTP for the full vaccine course peaks at non-degree tertiary level to the amount of HK$16,053 while the WTP for vaccines currently offered peaks at degree tertiary level to the amount of HK$1,942. It is also noted at a primary education level, the value of the WTP for current vaccines is in the negatives

(-HK$462) due to the greater negative impact of the marginal WTP of side effects when considering the whole picture.

Interestingly, in the stratified analysis for different income groups, both the maximum WTP and WTP for vaccines currently offered were higher for those with a household income level greater than HK$50,000 (see *Figure 1*). Lower income groups with a household income of <HK$10,000 and HK$10,001-20,000 show similar trends. The income group with a monthly household income of HK$30,001-50,000 is willing to pay the least for both the ideal or currently-offered vaccine for the prevention of cervical cancer. Mothers with a monthly household income of >HK$100,000 are the only one subgroup of the population who are willing to pay (HK$5,885) more than the current market price for vaccines currently offered.

Discussion

Cervical cancer is one of most deadly and yet preventable cancers. However, the burden of the disease is relatively higher than other health areas as at present there is no universal organized screening or vaccination program in Hong Kong(1). Currently, the HPV vaccination among teenage girls is largely opportunistic and the reported administration rate is continuously low (4, 8). Understanding the factors that determine the administration of the HPV vaccine is crucial for designing a more-effective vaccine-promotion program and for re-evaluating current immunisation policies. It is particularly important in the light of the recently-available and newly-developed 9-valent vaccine(31). As far as we are aware, this is the first local study using a quantitative approach and systemic analysis to reveal consumers' preferences and the WTP in relation to HPV vaccines in Hong Kong. Our study suggests that the effectiveness of cervical cancer protection, the protection duration, side effects and out-of-pocket costs are all significant factors in the determination of whether to administer the HPV vaccine. However, preferences and WTP are culture-specific and subject to socio-economic status as indicated by education level and household income.

Findings from this DCE survey demonstrates that 'protection effectiveness' and 'protection duration' were significant attributes when making the decision of whether to administer the HPV vaccination in line with the previous studies(16-19). In contrast to the commonly-recognised most important attribute as 'protection effectiveness' in the US(16), the Netherlands(17), Vietnam(19) and Thailand(20), mothers in Hong Kong considered 'side effects' as a priority

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when making the decision about the vaccine. This may be attributed to the differences in culture, ethnicity and education levels in medical decision-making(32). For example, our sample group from Hong Kong appear to be more conservative on sexual health issues (such as believing abstinence should be taught in schools, a rate of 96.7% vs. 21.6%) and less educated (tertiary level education or above, a rate of 27.5% vs. 39.7%) when compared with mothers in the US.(16).

Our survey has determined that 80% of mothers have previously heard of the HPV vaccines and the demand and conceived health benefits/risks from HPV vaccines are high as indicated by the maximum WTP. In the main and subgroup analyses, mothers' maximum WTP was consistently beyond the market price for the currently-available vaccine regardless of their education and income levels. The value of the HPV vaccination might reflect the fear of cervical cancer, in part contributed by health education and marketing for HPV vaccinations and cervical cancer prevention from diverse sectors in the recent years(33). On the other hand, the overall WTP for vaccines currently offered is still lower than the market price. Subsidised or part-payment from the government should be considered for to help meet the demand for the HPV vaccination, similar to that of the Childhood Influenza Vaccination Subsidy Scheme(34) which encourages parents of children aged between 6 months and 6 years to let their children receive influenza vaccinations in private clinics. Nevertheless, the WTP for current vaccines (HK$1,620) is likely to be underestimated due to its 70% effectiveness against cervical cancer, 10-year protection duration and 10% of all side effects based on literature. With the launch of the 9-valent HPV vaccine and a longer follow-up period being offered, the WTP for vaccines is expected to increase, and subsequently, the effectiveness and protection duration will also increase.

As expected, social disparity in Hong Kong is evident and the WTP of mothers varies depending on their monthly household incomes. However, it may be inappropriate to generalise the overall WTP to all consumers across Hong Kong when determining vaccination policy. Interestingly, instead of a positive correlation, mothers with monthly household income of >$50,000 had a greater maximum WTP and WTP for vaccines currently being offered than mothers with an income of $50,000 or less. Mothers belonging to the monthly income group of HK$20,001-30,000 were willing to pay the least for either the vaccines currently offered or those created using ideal and improved technology to prevent cervical cancer. Despite the majority of factors related to the respondents' socioeconomic status and knowledge of cervical cancer being collected (including household income, educational level, employment status and past

experience with cervical cancer/screening/vaccines), mothers' insurance status was one of the most important socioeconomic factors that would impact their decision. Although Hong Kong has a well-established healthcare system and a high coverage for public healthcare services, reimbursement of private healthcare services from employment-based or self-financed commercial health insurance companies is common practice. Further studies could collect information on the status of insurance which may be an important factor affecting the WTP of respondents.

Limitations

Several limitations are worth mentioning. Firstly, although this is a stated-preference survey, it may also be argued that true preferences are not revealed as the decisions made are only hypothetical. However, we tried to maximize the validity of preferences by providing alternative options within the nine choice sets. Secondly, all choice sets considered a limited number of attributes based on the reviewed literature and pilot study. Other attributes, especially for the protection against genital warts, may also reflect other preferences. Nevertheless, we included eight candidate attributes based on the best relevant literature available and selected the most important four attributes from the preferences of medical practitioners and mother at the pilot stage of the study. Our approach also reflects local stakeholders' preferences and was efficient and practical for the DCE design and questionnaire (35). Thirdly, this study examined preferences among mothers who were seeking medical care for their children in paediatric specialist outpatient clinics in two public hospitals. This survey does not include preferences of the WTP for HPV vaccines among mothers who choose not to seek medical care for their children at that time or from among mothers take their children to private healthcare institutions. Thus, a selection and response bias from the convenient sampling method cannot be avoided and the general applicability of the findings of this study to Hong Kong as a whole must be cautiously interpreted. Fourthly, in the multinomial logistic regression, we treated all variables as continuous with a linear distribution and no interaction between attributes. Respondents' demographic characteristics and past experience of HPV/HPV vaccines were not adjusted in the model. Instead, we performed a stratified analysis based on income and the level of education that casts a light on the impact of social-economic factors of respondents' preferences and their willingness to allow their daughters to receive the vaccine.

Conclusion

This study reveals that the demand and conceived health benefits of the HPV vaccines are high among mothers in Hong Kong with daughters of 8-17 years of age. They consider the side-effects as the most important attribute, followed by the effectiveness of protection, protection duration and out-of-pocket cost. Despite the high demand, the willingness-to-pay for vaccinations currently offered on the market is still lower than the market price and varies among different socio-economic groups.

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Figure Legend

Figure 1. Willingness-to-pay for HPV vaccines by mothers' education level (upper) and by monthly household income (lower).