

Institution: Kingston University		
Unit of Assessment: 17 – Business and Management Studies		
Title of case study: The cost-effectiveness of protecting boys against human papillomavirus (HPV) infection		
Period when the underpinning research was undertaken: 2014 – 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Names:	Roles:	Periods employed by submitting HEI:
Giampiero Favato	Professor in Leadership and Management in Health	Sept 2010 – present
Andrea Marcellusi	Lecturer in Health Economics	Sept 2016 – present
Emannouil Noikokyris	Associate Prof in Accounting and Finance	Aug 2010 – present
Riccardo Vecchiato	Associate Prof in Strategic Management	Sept 2014 – present
Period when the claimed impact occurred: 2017 –2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Many countries introduced HPV vaccination for girls, but not boys. However, research, led by Favato, has demonstrated the cost-effectiveness of gender-neutral vaccination. This has led to:

- the introduction of gender-neutral vaccination in Italy in 2017, with 118,506 Italian boys being vaccinated and estimated savings of €71 million per year.
- a successful campaign, combining arguments for equality and cost-effectiveness, by advocacy group HPV Action to persuade the UK Government to vaccinate boys. Vaccination was expanded to include English boys (expected to prevent more than 50,00 non-cervical cancers by 2058), with Scotland and Wales following suit.
- guidance by the European Centre for Disease Prevention and Control prioritising gender neutral vaccination.

2. Underpinning research

Human papillomavirus (HPV) is a gender-neutral killer. HPV infection can induce cervical cancer in women, cancer of the penis in men, other cancers such anal, mouth and throat, and warts. HPV infection can be prevented by vaccinating individuals before they become sexually active [R1]. 80% of individuals are likely to contract a sexually transmitted virus in their lifetime. When the HPV vaccine became available in 2006, most of the National Health Services implemented a selective vaccination of 12-13-year-old girls only. This policy decision was informed by three main assumptions derived from early cost-effectiveness models:

1. Cervical cancer carries the highest economic burden of HPV-induced diseases.
2. If enough girls are vaccinated, then boys are also protected (indirectly by herd immunity).
3. Consequently, vaccinating boys is not cost-effective.

Over time, the medical community has begun to advocate for adding boys to vaccination programmes to reduce non-cervical cancers and potentially eradicate certain HPV types.

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Favato and his team of researchers in Kingston's Leadership and Management in Health Research Group decided to test the hypothesis that early cost-effectiveness studies could have under-estimated the costs of not vaccinating boys because of uncertainty in the inputs chosen to inform the economic model. Based on this premise, the outcomes of the extant literature (above) were turned into research questions, and answered:

- Is gender-neutral vaccination cost-effective?
Given policy decisions in Public Health are mostly based on cost-effectiveness, sufficient savings must be predicted before vaccination programmes are extended. The BEST II study [R2] extended a previously published transmission model [R1]. The researchers combined population dynamics, the full range of HPV-induced diseases, and the effects of having different partners over time. Following a virtual population, the study demonstrated that gender-neutral vaccination targeting the 12-year age group has an attractive cost-effectiveness profile in comparison to female-only vaccination.
- Does herd immunity effectively protect boys?
Selective vaccination of girls may suggest a high probability that one of two sexual partners is immunised, hence preventing the infection of the other and general transmission in the population. However, the findings of a systematic review [R3] indicated that none of the included studies showed due consideration of the complexities of human sexual behaviour: such as sexual mixing abroad, with someone from abroad, or with both same and opposite sex partners in a short time-period. Thus, the ecological validity of these studies, and the claimed HPV transmission effects, was undermined. The ecological bias could, even when small, result in a significant over-estimation of whether boys are protected by herd immunity. This over-estimation results in selective vaccination of girls appearing more cost-effective than it truly is. Additionally, if individual boys are not suitably protected, then the selective vaccination of girls is a gender-based inequality in public health policy.
- Is cervical cancer the highest economic burden among HPV-induced diseases?
The researchers conducted the first cost analysis based on real world data [R4] for the economic burden of HPV infection. The incidence of each diagnosis was derived from hospital discharge records and priced according to diagnosis-related group tariffs. They estimated that only 13% of the total economic burden of HPV-induced diseases was due to cervical cancer, with costs more attributable to other cervical conditions and other cancers. Oropharyngeal (throat) cancers were responsible for the highest annual burden (€215.7 million), with €187 million required to treat men.

Thus, the body of research demonstrated that a universal vaccination strategy can be cost-effective, and that there are issues of both gender inequality and cost-ineffectiveness for selective vaccination against HPV infection.

3. References to the research

R1 – Favato, G., Baio, G., Capone, A., **Marcellusi, A.**, Costa, S., Garganese, G., Picardo, M., Drummond, M., Jonsson, B., Scambia, G., Zweifel, P., Mennini, F. 'Novel health economic evaluation of a vaccination strategy to prevent HPV-related diseases: the BEST study', *Med Care.*, 50, 12, (2012). pp. 1076-85 DOI: [10.1097/MLR.0b013e318269e06d](https://doi.org/10.1097/MLR.0b013e318269e06d)

R2 – Haeussler, K., **Marcellusi, A.**, Mennini, F.S., **Favato, G.**, Picardo, M., Garganese, G., Bononi, M., Costa, S., Scambia, G., Zweifel, P., Capone, A., and Baio, G., 'Cost-effectiveness analysis of universal human papillomavirus vaccination using a dynamic Bayesian methodology: The BEST II study', *Value in Health*, 18, 8, (2015), pp 956-968. DOI: [10.1016/j.jval.2015.08.010](https://doi.org/10.1016/j.jval.2015.08.010) REF2ID: 17-67-1520

Evidence of quality of research:

- The study was supported by a research grant from Sanofi-Pasteur MSD Italia.

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- The study was cited in the Italian National Prevention Plan 2017-2019 [Annexe 1] which introduced the gender-neutral vaccination against HPV in Italy
- The study was cited by the review article advocating the nation-wide adoption of gender-neutral vaccination against HPV in Canada. DOI: [10.1016/j.ypped.2017.04.016](https://doi.org/10.1016/j.ypped.2017.04.016)

R3 – Favato, G., Easton, T., Vecchiato, R., Noikokyris, E., ‘Ecological validity of cost-effectiveness models of universal HPV vaccination: A systematic literature review.’ *Vaccine*, 35, 20, (2017), pp 2622-2632. DOI: [10.1016/j.vaccine.2017.03.093](https://doi.org/10.1016/j.vaccine.2017.03.093) REF2ID: 17-25-1476

Evidence of quality of research:

- Paper presented as Invited Speaker at the Gender Summit 9 (GS9) Conference 08–09 Nov 2016. Brussels, Belgium. <http://eprints.kingston.ac.uk/36322/1/Favato-G-36322.pdf>
- The conference paper was cited by the review article advocating the nation-wide adoption of gender-neutral vaccination against HPV in Canada.
- The study was cited in a letter advocating the adoption of gender-neutral vaccination against HPV in England published on *Lancet* 2018. DOI: [10.1016/S0140-6736\(18\)31821-X](https://doi.org/10.1016/S0140-6736(18)31821-X)

R4 – Mennini, F.S., Fabiano, G., Favato, G., Sciattella, P., Bonanni, P., Pinto, C., Marcellusi, A., ‘Economic burden of HPV9-related diseases: a real-world cost analysis from Italy’, *Eur J Health Econ*, (2019). DOI: [10.1007/s10198-019-01044-3](https://doi.org/10.1007/s10198-019-01044-3) REF2ID: 17-26-1477

4. Details of the impact

Impact on Policy, Health and Economy in Italy

On 13 January 2017, the Italian Prime Minister signed a new Levels of Care agreement for the Italian health service that made Italy the first EU country and G8 nation to adopt a nationwide gender-neutral HPV vaccination programme. The following month, the National Vaccination Plan [S1] was published. BEST [R1] was cited as evidence for proving the prevention strategy to be ‘*highly cost effective* [translation]’. BEST II [R2] was cited for its estimation of the economic impact of also vaccinating boys against HPV. With estimated cost savings of €71 million per year, the first three cohorts (188,506 boys) were vaccinated against HPV [S2].

Impact on Policy, Health and Economy in England

The government position in the UK, however, was more resistant to gender-neutral vaccination, primarily on cost-effectiveness grounds. In January 2016, Favato joined the advocacy campaign initiated in 2013 by HPV Action - a collaborative partnership of 51 patient and professional organisations in favour of gender-neutral vaccination against HPV in England. The HPV Action campaign argued that universal vaccination was a matter of gender equality, and that there was no question to answer over cost-effectiveness [S3].

Throughout 2016, HPV Action drew on the Kingston research to demonstrate the gender equality issue that men had significant lifetime risk of not being effectively protected through herd immunity [S4], with young adult males (aged 16-34) at the highest risk. For example, HPV Action decided to submit the Vaccine Paper [R3], questioning the validity of past cost-effectiveness modelling to the Scientific Secretariat to Joint Committee of Vaccination and Immunization (JCVI). In an email dated 26 April 2017, he accepted the paper and circulated it to the other Members of the JCVI committee.

In June 2016, a letter to the Secretary of State for Health from HPV Action was published in *The Times*. It formulated the ethical argument for the equal protection of both sexes for the first time. In reply, the Department of Health deferred the decision to the JCVI.

In September 2016, HPV Action had the opportunity to review the Public Health England (PHE) cost-effectiveness model in a private hearing with the JCVI. HPV Action invited Favato to the hearing and then commissioned Kingston to provide a critical review of the model. The researchers concluded that the modelling around sexual behaviours was inadequate, as it failed to include more diverse and extensive sexual mixing behaviours. This inflated the effect

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of herd immunity and the economic value of girls-only vaccination. The letter from HPV Action to JCVI made note of *'Favato's work on the cost-effectiveness of HPV vaccination'* and in the general compilation of their materials and criticisms [S5].

In July 2017, JCVI opened a consultation among stakeholders to receive feedback on an interim statement on extending HPV vaccination to adolescent boys. The concerns of HPV Action (detailed above) also were noted. The HPV Action response to the consultation discussed the modelling work of JCVI and their concerns relating to sexual behaviour, cost-savings and epidemiology; as well as additional equality issues.

A JCVI meeting in October 2017 highlighted the contribution of HPV Action in critiquing the models for cost-effectiveness. The final JCVI statement, released in 2018 after further modifications to models, found *'gender-neutral vaccination highly cost-effective at what is likely to be a realistic vaccine price and, 'that vaccination is efficacious in preventing ...other HPV related cancers'*, and recognised *'reasons of equality ...and the arguments regarding the individual level protection'* [S6]. They referred the equality decision to the Department of Health, where the Equality and Human Rights Commission supported gender-neutral vaccination.

On 24 July 2018, Public Health Minister Steve Brine announced that boys aged 12-13 in England would receive the HPV vaccine. He was *'delighted that we will now be protecting even more people from this devastating disease by extending the vaccines to boys'*. Dr Mary Ramsay, Head of Immunisations at PHE said the change *'offers us the opportunity to make HPV-related diseases a thing of the past'* [S7]. Similar announcements followed from the health ministers of Scotland and Wales. The NHS expanded the HPV vaccination to include all boys in year 8 in England from September 2019. PHE claims the programme may prevent more than 50,000 non-cervical cancers by 2058.

Reflecting on the successful campaign, Peter Baker, Campaign director at HPV Action, wrote of the importance of 'articles and conference presentations' in making the case to influential field leaders and politicians. Mention was given to *'Kingston University Business School, who comprehensively critiqued the JCVI's approach to cost-effectiveness modelling'* [S8]. The partnership is on-going, as demonstrated by HPV action's meeting with JCVI before a meeting in February 2020 to successfully ensure the continuation of the vaccination of boys, regardless of an ONS recommendation otherwise.

Following the approval in Italy and England, gender-neutral HPV vaccination has been approved in Wales, Scotland, Northern Ireland, Serbia, Croatia, Czech Republic, Denmark, Sweden, Germany and the Netherlands. By 2020, 50.1% of the EU population (before Brexit) will be covered by universal vaccination against HPV [S3].

Impact on Policy and Health in other EU countries

In July 2019, Favato was invited to participate in the development of the European Cancer Organisation (ECCO) 2019 European Cancer Summit resolution on eliminating HPV in Europe by 2030. The resolution was passed in September 2019 [S9]. According to the new ECCO guidelines, by 2025 all European country cancer plans should include actions towards achieving population-based and gender-neutral HPV vaccination. The European Centre for Disease Prevention and Control (ECDC) held a public consultation for further guidance. The ECDC accepted Favato's comments and made subsequent edits to their guidance. In 2020, ECDC released guidance on HPV vaccination in EU countries, with a focus on boys and shifting the priority of vaccination to gender-neutral national programmes [S10].

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5. Sources to corroborate the impact

- S1** – Abridged Italian National Immunisation Plan 2017-2019 (in Italian)
- S2** – [Vaccination coverage at 12/31/2017 for HPV](#), Italian Ministry of Health (in Italian)
- S3** – ‘Jabs for the boys: how the Campaign for gender-neutral HPV Vaccination was won in the UK’, Int J Men’s Com Soc Health, Vol 2, 1, (2019). DOI: [10.22374/ijmsch.v2i1.18](#).
- S4** – First presentation at HPV Action Board Meeting on March 8th, 2016.
DOI: [10.7490/f1000research.1113391.1](#)
- S5** – Letter from HPV Action to Professor Pollard, Chair of JCVI, January 2017
- S6** – Statement on HPV vaccination, JCVI. July 2018.
- S7** – [British Government announces HPV vaccination of boys](#), July 2018
- S8** – ‘[HPV vaccination for boys: how the case was won](#)’, Baker P, 2018
- S9** – [ECCO Resolution on HPV-Related Cancer Elimination](#)
- S10** – [ECDC Guidance on HPV Vaccinations in EU Countries](#)