

**THE ROLE OF HUMAN PAPILLOMAVIRUS VACCINES IN
REDUCING THE RISK OF CERVICAL CANCER IN IRELAND -
A HEALTH TECHNOLOGY ASSESSMENT**



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TECHNICAL APPENDIX 3

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APPENDIX 3

TECHNICAL DESCRIPTION OF THE MODEL

The agent-based model used for simulating sexual networks and the transmission of HPV in Ireland is programmed in Netlogo.* It simulates a population of 25,000 individuals and their sexual relations as a network, where individuals / agents constitute the network nodes and relationships are represented as network links. The agents' sexual behaviours are based on rules which take the properties of the individual agent into account.

Variables

The model operates with a number of variables; some of them related to the entire population (global variables), and some variables specific to the agents (agent variables). Table 1 lists the most important variables.

* Netlogo: <http://ccl.northwestern.edu/netlogo>. Center for Connected Learning and Computer-Based Modeling. Northwestern University, Evanston, IL.

Table 1. Important model variables

Variable	Default value	Comment
<u>Global Variables</u>		
Time	Time step = 1 month	
CIN progression probabilities	See Table 2	
CIN regressions probabilities	See Table 2	
Risk of HPV-16 infection per act	0.3	Differences in risk corresponds to differences in prevalence**
Risk of HPV-18 infection per act	0.13	
HPV-16 duration	Exponential distribution with mean = 14 months	
HPV-18 duration		
<u>Agent Variables</u>		
Age	10-79	
Sex	Female/Male	
Partner-preference	88%: 1; 12%: 2	Preference for number of concurrent partners
Intercourse Frequency	$((a+bx)/(1+cx+dx^2))^*$ $(a/1+b*EXP(-c*age))$	See Figure 2
Relation duration		
Infected-with-16?	Time of infection	
Infected-with-18?	Time of infection	
Vaccinated against HPV-16	Yes/No	
Vaccinated against HPV-18	Yes/No	
CIN1-3 status	Yes/No	
Conisation	Time	

*Rational function attributing intercourse frequency per month as a function of a random number between 0 and 100. Results are frequencies varying between 0 and 12 (Figure 1). The function is applied to 95% of the model population while the remaining 5% are assigned frequencies between 20 and 31 in order to allow for high-risk behaviour.

** Elbasha E, Dasbach E, Insinga R. Model for assessing human papillomavirus vaccination strategies. Emerg Infect Dis 2007; 13:28-41.

All individuals are allocated a preference for a number of concurrent partners. Eighty eight percent are given a preference for one partner and 12 percent are given a preference for two concurrent partners during the course of a month. This is a preference they try to achieve and is dependent on whether they can find available partners. The values are derived through calibration of the model.

Table 2. Transition probabilities from HPV infection to various stages of cell changes.

Stage	Transition probability
From HPV to CIN1	0.017 per month
From CIN1 to CIN2	0.300 per year
From CIN2 to CIN3	0.780 per year
From CIN3 to cervical cancer	0.140 per year
From CIN1 to HPV	0.329 per year
From CIN2 to CIN1	0.100 per year
From CIN3 to CIN2	0.020 per year

Model dynamics

The agents act according to specific rules which are coded in the model. The most important rules in the model control the forming and ending of relations.

Figure 1. Distribution of intercourse-frequencies.

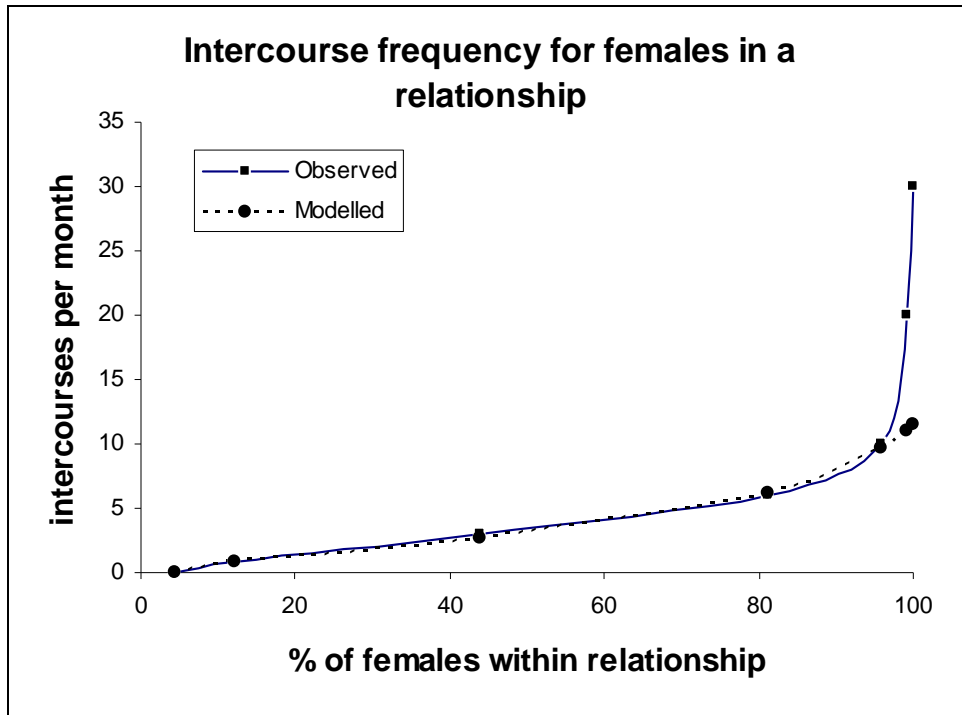


Figure 2. Duration of relations. Logistic function dependent on age of the agent.



Stochasticity

The model operates with stochastic processes driven by a pseudo-random number generator (RNG) based on the Mersenne Twister algorithm. The most important stochastic processes involves the procedure for infecting agents with HPV, the procedures controlling the risk of progressing from HPV through different levels of CIN, the code for having agents choose a partner and the procedure for picking the agents to vaccinate.

The RNG is controlled by seeding values. Each scenario presented in the report is run 30 times where the seed value is varied from 1 to 30. The mean HPV prevalence's of the 30 runs, and the variance of this value is reported as the model output.

By controlling the random numbers, scenarios can be compared to each other, and differences in the results that exceed the 'internal' variance of each result can be attributed to changes in model code. An example is the results of the baseline scenario compared to scenario 1: the impact of a vaccination strategy is obvious, and clearly not caused by stochastic fluctuations in the model. However, comparing scenario 2 and 3, one would expect the increased vaccination coverage of scenario 3 to cause a greater reduction in the HPV prevalence than was observed. However, because of the number of simulations, there is still some residual uncertainty about the exact size of the change in LYG attributable to each scenario.

The model simulates the interaction patterns among a population of 25,000 individuals.