Modeling the consequences of regional heterogeneity in human papillomavirus (HPV) vaccination uptake on transmission in Switzerland

Supporting Information - Text S1

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Contents

1 Basic reproduction number

The basic reproduction number, R_0, can be calculated using the next-generation matrix method as described by Diekmann et al. [1, 2]. As we did not consider sex-specific differences in sexual behavior or the natural history of HPV-16, and assumed that the sexual behavior of individuals is the same across all cantons, we can simplify the model into a single population with two different sexual activity groups. The transmission matrix F can then be given by

$$F = \begin{bmatrix} \beta c_l \rho_{ll} n_l / n_l & \beta c_l \rho_{lh} n_l / n_h \\ \beta c_h \rho_{hl} n_h / n_l & \beta c_h \rho_{hh} n_h / n_h \end{bmatrix}, \tag{1}$$

whereas the transition matrix V is given by

$$V = \begin{bmatrix} \gamma + \mu + m n_h & -m n_l \\ -m n_l & \gamma + \mu + m n_l \end{bmatrix}. \tag{2}$$

R_0 is defined as the dominant eigenvalue of the next-generation matrix $G = FV^{-1}$. Since we consider a heterosexual population, the sex-specific value of the basic reproduction number is given by R_0^2.

2 Alternative models

In order to compare the modeled prevalence of HPV-16 in Switzerland and Britain, we parameterized the transmission model with data from the third British National Survey of Sexual Attitudes and Lifestyles 3 (Natsal-3) [3]. To this end, we estimated the sexual partner change rates for the same two sexual activity groups (Table S3). For better comparison between Switzerland and Britain, we forced the size of the sexual activity groups to be the same between the two countries (see Table 1). The estimated heterosexual partner change rates for both sexual activity groups in Britain are higher than in Switzerland. Hence, the modeled pre-vaccination prevalence of HPV-16 for a given per partnership transmission probability is higher for the British model than the Swiss model (Fig. S3). The per partnership transmission probability is a highly model-specific parameter with considerable uncertainty. Two different modeling studies estimated the transmission probability at 0.72 (95% posterior interval: [0.29 - 1.00]) [4] and 0.80 (95% posterior interval: [0.60, 0.99]) [5]. For our subsequent analyses, we chose a transmission probability of 0.80, as estimated by Bogaards et al. [5], because it results in realistic HPV-16 prevalences for Britain and Switzerland.

3 HPV-16 dynamics: Vaccination coverage and prevalence

We compared the functional relationship between the vaccination coverage and the expected reduction in HPV-16 prevalence from our model with data from a systematic review [6]. In the model described in the main text, we assumed that women can only become vaccinated before they enter the population of 18–24 year olds. For a given proportion of women that become vaccinated p, it typically takes a number of years until the proportion of vaccinated women across the 18–24 year age band approaches the same value. In order to compare our model results with the data, we did a modification in how vaccination is modeled and assumed that all 18–24 year old susceptible women can become vaccinated at rate p per year. We then considered the proportion of women that are vaccinated at a given time point as the effective vaccination coverage. The modeled reduction in HPV-16 prevalence 2–4 years after onset of vaccination is in good agreement with the reported data from several studies that covered a time span of 1–4 years (Fig. S2).

4 Additional figures

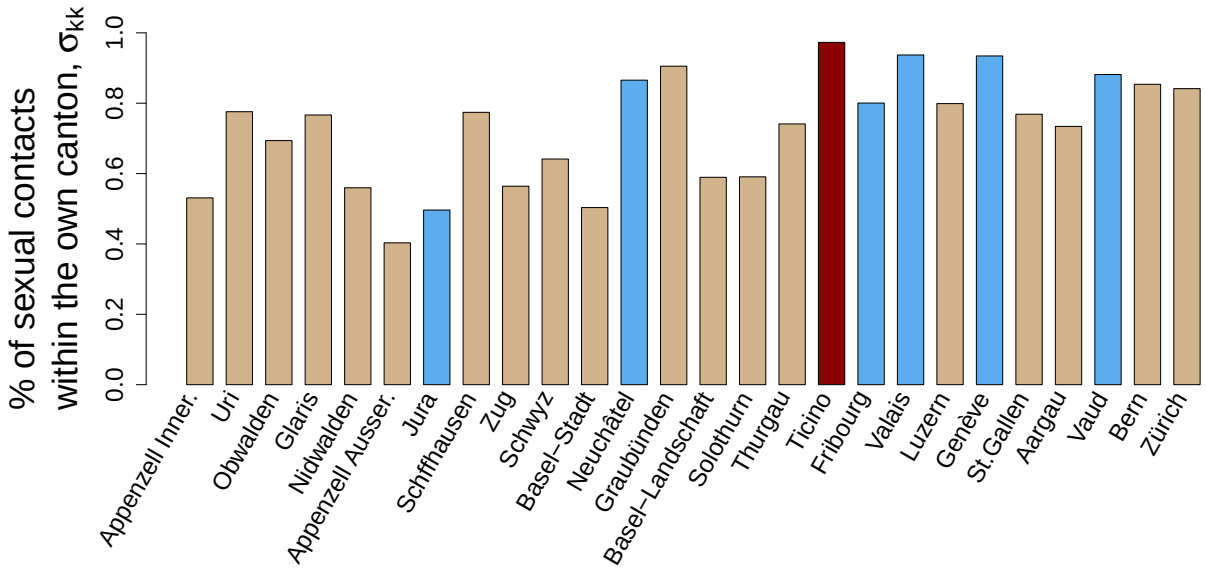

Figure S1. Proportion of intra-cantonal contacts (σ_{kk}) for the mobility-informed sexual mixing scenario. The weighted average across all cantons was set to 0.8. Cantons with a French-, German- or Italian-speaking majority are indicated in blue, beige and red, respectively. Cantons are ranked by increasing population size.

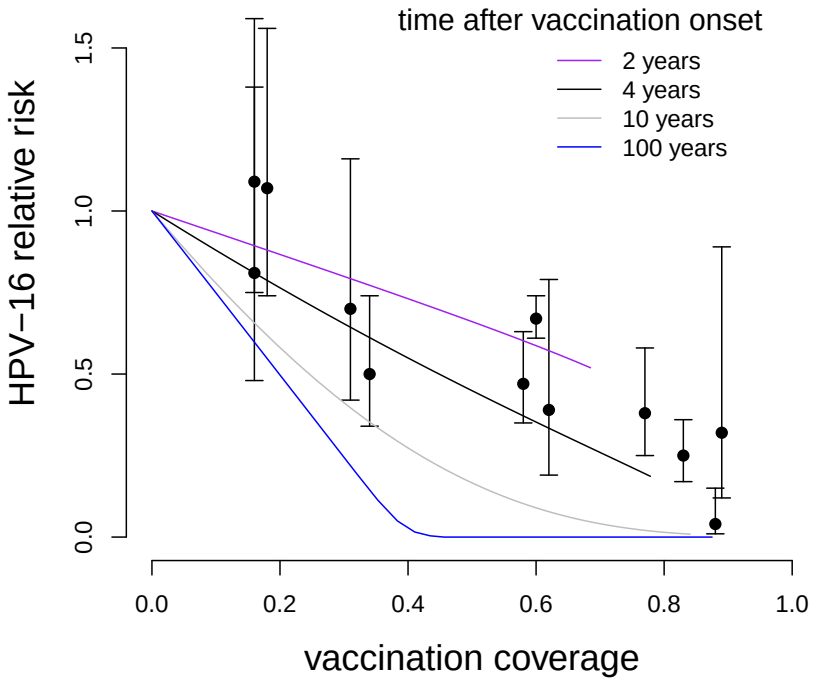

Figure S2. Reduction in HPV-16 prevalence as a function of vaccination coverage. The solid lines represent the modeled HPV-16 prevalence, normalized and expressed as a relative risk (RR), after 2, 4, 10 and 100 years of vaccination. The data represent the change in HPV-16/18 prevalence between the pre- and post-vaccination periods from several countries as reported in the systematic review by Drolet et al. [6]. Individual points represent data with different vaccination coverage from either 13–19 or 20–24 year old girls in the US, United Kingdom or Australia. The difference between the pre-vaccination and post-vaccination periods ranged between 1–4 years.

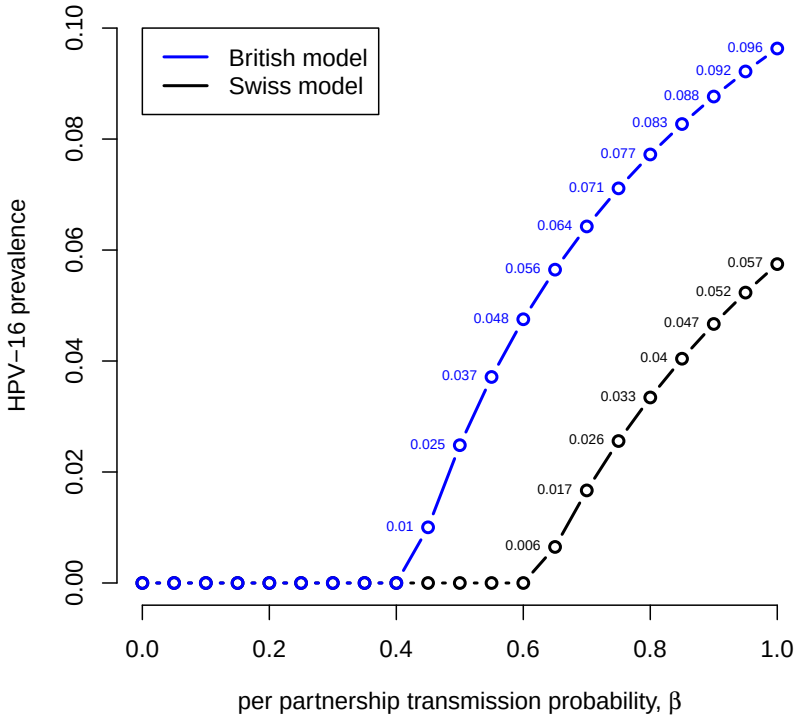

Figure S3. Prevalence of HPV-16 as a function of the per partnership transmission probability. The modeled pre-vaccination prevalences are based on Swiss (black) and British (blue) data (SIR and Natsal-3 survey, respectively).

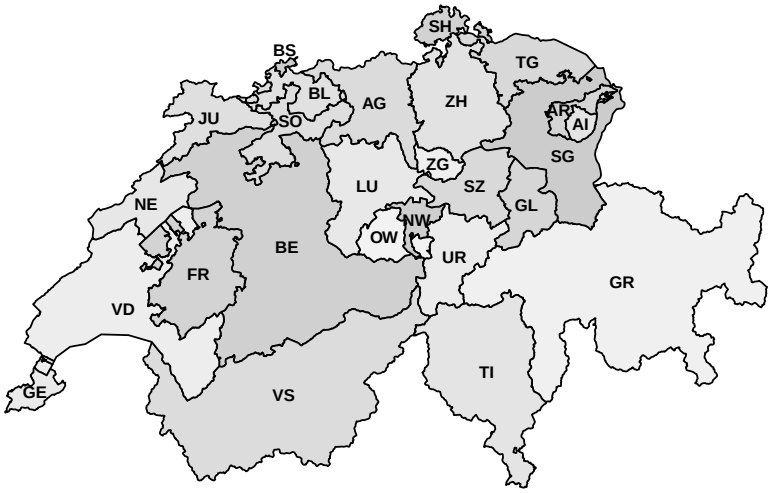

Figure S4. Swiss map with the cantonal boundaries. The acronyms of the cantons are explained in Table S1.

5 Additional tables

Table S1. HPV vaccination uptake in 16 year old girls in Switzerland. Data represent the last completed survey period (2011–2013) of the Swiss National Vaccination Coverage Survey (SNVCS). Data for Geneva and Appenzell Innerrhoden are from 2010 and 2014, respectively.

Canton	Acronym	% three dose	% two dose	% one dose
Zürich	ZH	44	3	2
Bern	BE	37	5	2
Luzern	LU	50	4	2
Uri	UR	40	5	1
Schwyz	SZ	27	3	1
Obwalden	OW	31	2	1
Nidwalden	NW	61	0	0
Glarus	GL	47	7	2
Zug	ZG	17	3	4
Fribourg	FR	71	1	1
Solothurn	SO	53	3	2
Basel-Stadt	BS	52	4	0
Basel-Landschaft	BL	64	1	1
Schaffhouse	SH	40	4	3
Appenzell Ausserrhoden	AR	24	3	2
Appenzell Innerrhoden	AI	34	3	3
St.Gallen	SG	59	5	0
Graubünden	GR	44	6	2
Aargau	AG	59	3	0
Thurgau	TG	35	6	2
Ticino	TI	38	7	0
Vaud	VD	66	1	2
Valais	VS	75	3	1
Neuchâtel	NE	59	3	3
Genève	GE	62	5	0
Jura	JU	63	0	1

Table S2. Cantonal population sizes of 18–24 year old women and men in Switzerland. For the transmission model, we assumed a 1:1 sex ratio. Data are from the Swiss Federal Statistical Office (FSO).

Canton	Acronym	Population size
Zürich	ZH	105,586
Bern	BE	80,549
Luzern	LU	35,656
Uri	UR	3269
Schwyz	SZ	12,641
Obwalden	OW	3269
Nidwalden	NW	3513
Glarus	GL	3477
Zug	ZG	8838
Fribourg	FR	27,666
Solothurn	SO	22,161
Basel-Stadt	BS	13,441
Basel-Landschaft	BL	21,313
Schaffhausen	SH	6587
Appenzell Ausserrhoden	AR	4847
Appenzell Innerrhoden	AI	1595
St.Gallen	SG	46,129
Graubünden	GR	16,474
Aargau	AG	52,832
Thurgau	TG	23,722
Ticino	TI	25,780
Vaud	VD	69,060
Valais	VS	29,800
Neuchâtel	NE	15,849
Genève	GE	40,033
Jura	JU	6418

Table S3. Comparison of model parameters and outputs between Switzerland (SIR survey) and Britain (Natsal-3). The model outputs are based on a per partnership transmission probability of 80% [5].

Parameter/Output	SIR	Natsal-3
Partner change rate low activity (y^{-1})	0.17	0.37
Partner change rate high activity (y^{-1})	2.41	3.60
Pre-vaccination prevalence of HPV-16	3.34%	7.72%
Basic reproduction number, R_0	1.29	1.90
Vaccination threshold for one sex	39.6%	72.3%

Table S4. National HPV-16 prevalence after 15 years of heterogeneous and homogeneous vaccination uptake for different assumptions about sexual activity, cantonal population sizes and overall vaccination uptake. The first three scenarios are those from the main text.

Sexual activity	Cantonal population sizes	Inter-cantonal sexual mixing	Overall vacc. uptake	HPV-16 prev. (heterogeneous)	HPV-16 prev. (homogeneous)
SIR survey	Swiss FSO	Assortative	52%	0.58%	0.49%
SIR survey	Swiss FSO	Proportional	52%	0.54%	0.49%
SIR survey	Swiss FSO	Mobility-inf.	52%	0.55%	0.49%
SIR survey	All same size	Assortative	52%	0.63%	0.49%
SIR survey	Swiss FSO	Assortative	26%	1.58%	1.55%
Natsal-3	Swiss FSO	Assortative	52%	2.49%	2.39%
Natsal-3	All same size	Assortative	52%	2.53%	2.39%
Natsal-3	Swiss FSO	Assortative	26%	4.98%	4.98%

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