HPV Prevention and Control Board

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Technical Meeting: Accelerating HPV-related Cancer Elimination
6-7 June 2024, Antwerp, Belgium

Session 3: Insights into HPV natural infection and transmission dynamics

Investigations to understand HPV transmission among heterosexual couples: TRAP-HPV trial & HITCH cohort study

Funding:
HITCH: CIHR, NIH, Merck
TRAP-HPV: CIHR, Merck

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Outline: Salient findings from HITCH and TRAP-HPV studies

- Anatomical routes in transmission: What have we learned?
- Viral load: Is transmission influenced by how productive an infection is?
- Is transmission mediated by HLA allele sharing between partners?
- Directionality of transmission between partners: Which is greater, M -> F or F -> M?
- Is a woman's new male partner likely to have the same HPV genotypes as those of her previous male partner?
- Can transmission be prevented by HPV vaccination?

HPV Infection and Transmission among Couples through Heterosexual Activity

Ann Burchell

HITCH COHORT STUDY

Eligibility screening

Inclusion criteria:
Females 18 – 24 years old, enrolled in post-secondary education in Montreal (intend to stay in Montreal for the following 2 years), sexually active with male partner initiated within the last 6 months, has intact uterus, no history of cervical lesions/cancer, not pregnant and not planning to be in following 2 years.
Males 18+ years old.

Month: 0 2 4 6 8 10 12 15 18 21 24

Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
502 F 548 M (502 M1, 42 M2, 4 M3)	454 F 422 M (387 M1, 31 M2, 4 M3)	415 F	377 F	332 F	276 F

Enrollment: May 2005 – January 2011

Last follow-up: January 2014

Web-based self-completed (Data collected: sociodemographic, smoking, reproductive history, lifetime sexual history, sexual activity, contraceptive history, medical history (including other STIs), knowledge of HPV, HPV vaccination)

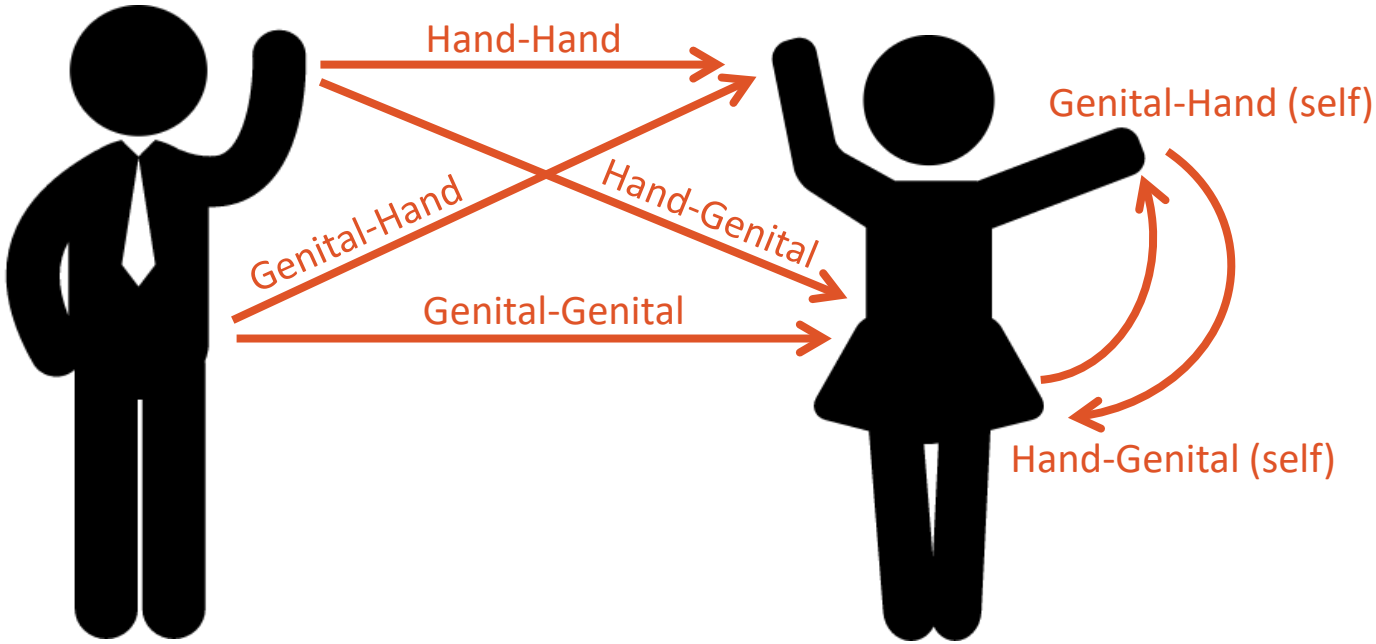
1. **Samples collected for HPV genotyping**: self-collected vaginal samples (females), nurse-collected penile and scrotal samples (males), [2008 onwards: oral rinses, swabs of index and middle fingers, and nails at visits for which both partners attended]
    - HPV DNA positivity: PCR of a 450 bp segment of HPV L1 capsid gene, Linear Array HPV genotyping assay (LA-HPV; Roche Molecular Systems)
        - Detectable genotypes: 6, 11, 16, 18, 26, 31, 33, 34, 35, 39, 40, 42, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84 and 89
    - Viral load: RT-qPCR for genotypes 16, 18, 31, 33, 45, 52
2. **Blood samples** collected for HPV antibody testing (L1, VLP-L1, E6)
    1. Antibody titers: bead-based multiplex serology assay
        1. Genotypes: 6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 58, 59, and 68

HPV sexual transmission modes

Talía Malagón

Karolina Louvanto

- Can Alpha HPV be transmitted through hand contact?
  - Multiple potential HPV sexual transmission modes
  - Direction of transmission between hands-genitals unclear



Malagón T, Louvanto K, Wissing M, Burchell AN, Tellier PP, El-Zein M, Coutlée F, Franco EL. Hand-to-genital and genital-to-genital transmission of human papillomaviruses between male and female sexual partners (HITCH): a prospective cohort study. Lancet Infect Dis. 2019 Mar;19(3):317-326.

Putative transmission routes for genital HPV DNA positivity

Talía Malagón

Karolina Louvanto

Hazard ratio of **genital** HPV type-specific positivity if other sites are positive vs. negative at previous visit

Exposure site	Univariate	
	Women	Men
	HR (95% CI)	HR (95% CI)
Hand (own)	9.8 (3.8-25.4)	10.5 (3.1-35.8)
Genital (partner)	19.2 (12.0-30.8)	43.3 (23.9-78.5)
Hand (partner)	5.0 (1.5-16.4)	20.3 (8.8-46.9)

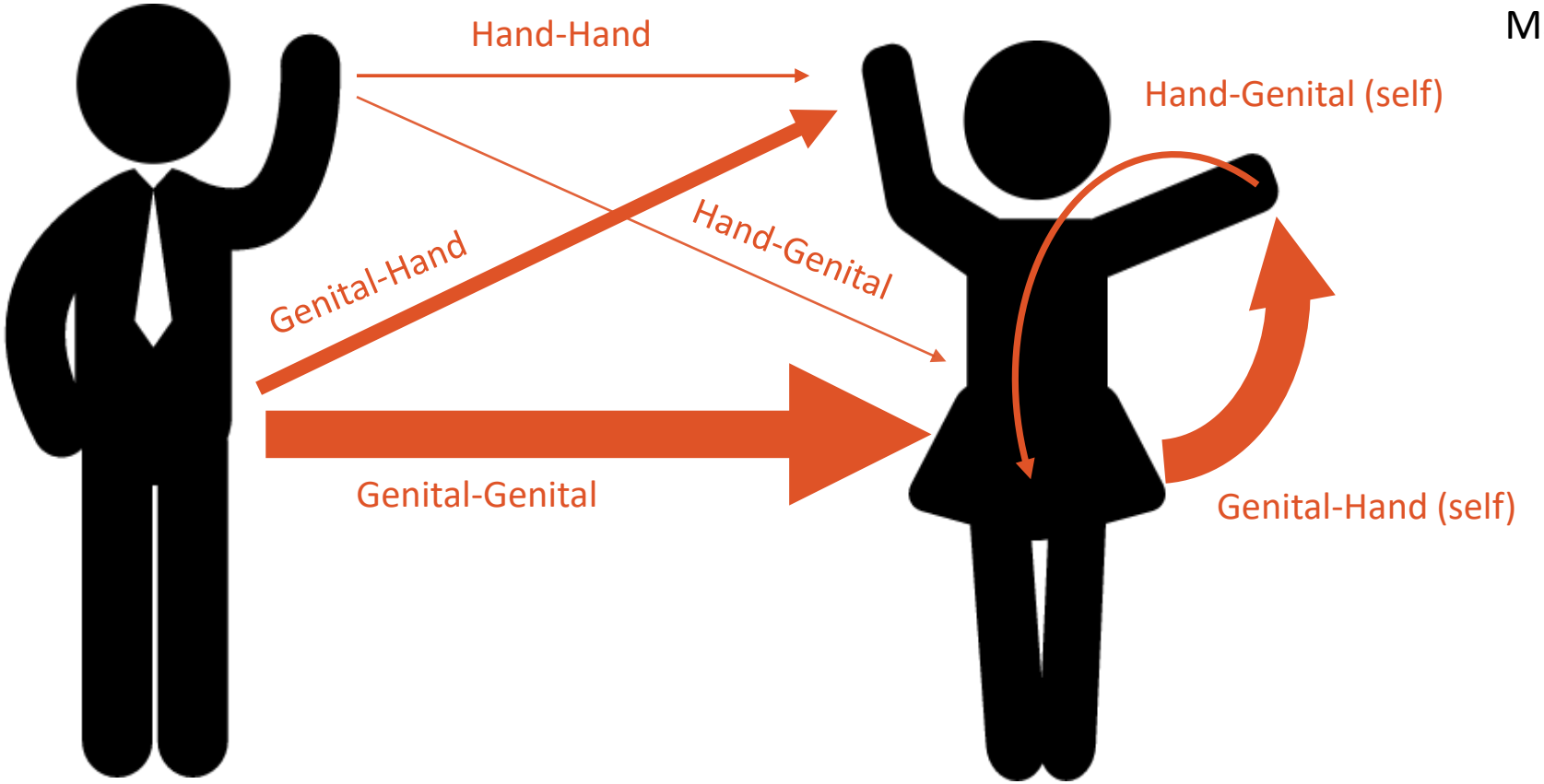
Malagón T, Louvanto K, Wissing M, Burchell AN, Tellier PP, El-Zein M, Coutlée F, Franco EL. Hand-to-genital and genital-to-genital transmission of human papillomaviruses between male and female sexual partners (HITCH): a prospective cohort study. Lancet Infect Dis. 2019 Mar;19(3):317-326.

What do we know? Direction of HPV transmission

Talía Malagón

Karolina Louvanto

Size of arrow corresponds to size of adjusted HR:

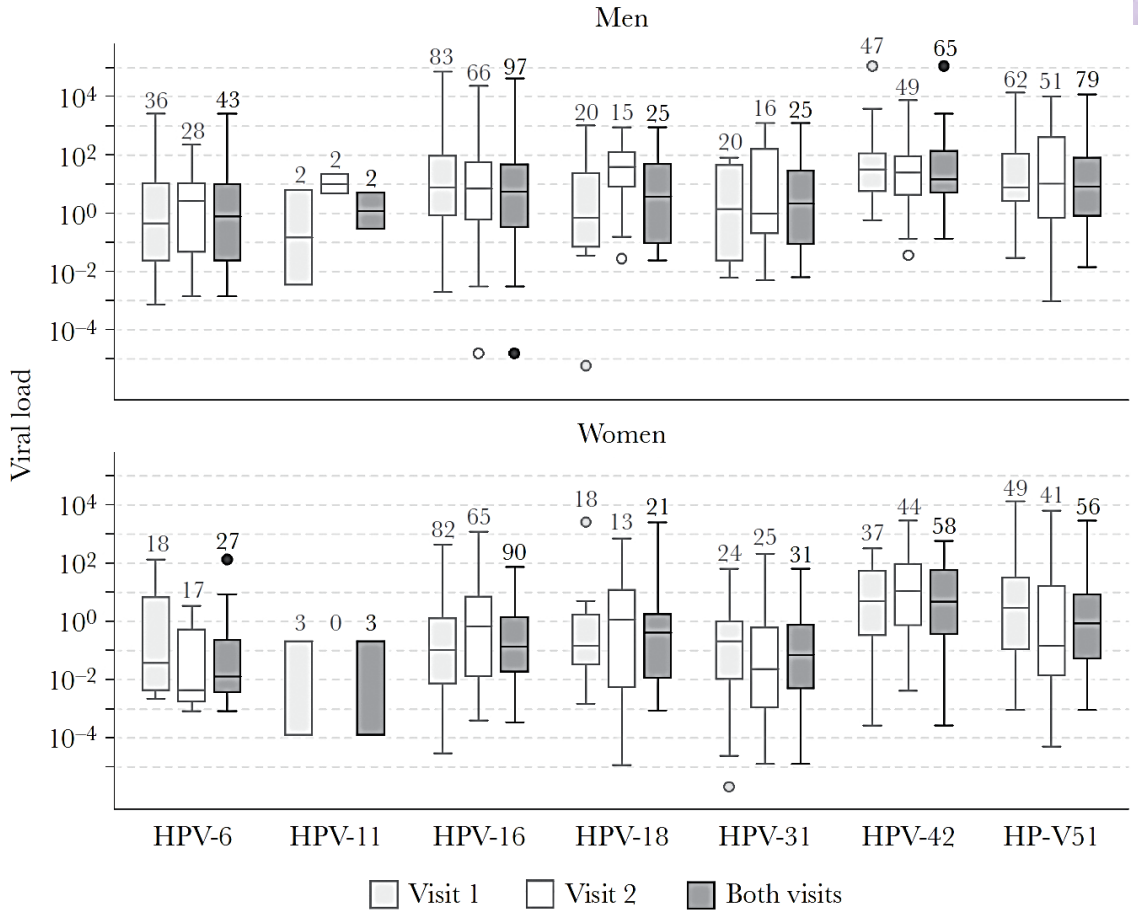


Malagón T, Louvanto K, Wissing M, Burchell AN, Tellier PP, El-Zein M, Coutlée F, Franco EL. Hand-to-genital and genital-to-genital transmission of human papillomaviruses between male and female sexual partners (HITCH): a prospective cohort study. Lancet Infect Dis. 2019 Mar;19(3):317-326.

HPV viral load by sex in HITCH

Michel Wissing

- Viral load was higher in penile than vaginal samples (p<0.001)
- Men with high viral load had more type-specific persistent HPV infections (OR=4.6, 95%CI: 2.0-10.5)
- High viral load in men was associated with prevalent (OR=5.3, 95%CI: 2.5-11.2) and incident (OR=6.7, 95%CI: 1.5-30.7) type-specific HPV infections in their female partner



Wissing MD, Louvanto K, Comète E, Burchell AN, El-Zein M, Rodrigues A, Tellier PP, Coutlée F, Franco EL. Human Papillomavirus Viral Load and Transmission in Young, Recently Formed Heterosexual Couples. *J Infect Dis.* 2019;220(7):1152-1161.

Does HLA mediate HPV transmission in heterosexual couples?

Karolina Louvanto

Rationale and Methods:

- Genes in the major histocompatibility complex mediate antigen presentation to the immune system
- Transmission of HPV infection involves exchanges of exfoliated epithelial cells during sex
- **Hypothesis:** HLA allele concordance would facilitate transmission of HPV infection by lowering the likelihood of HLA-mediated rapid clearing of exfoliated HPV-harboring cells exchanged during sex. Analogy to organ transplantation, i.e., mismatches would lead to faster destruction of partner's deposited cells
- **Approach:** We investigated whether the extent of HLA allele concordance between HITCH partners would influence HPV type concordance in members of the couple
- Direct DNA sequencing to type HLA-B07, -DRB1, -DQB1 and –G
- We identified a total of 106 different HLA alleles among 271 evaluable female and their 271 male partners

Louvanto K, Baral P, Burchell A, Ramanakumar A, El-Zein M, Tellier PP, Coutlée F, Roger M, Franco EL. Role of Human Leukocyte Antigen Allele Sharing in Human Papillomavirus Infection Transmission Among Heterosexual Couples: Findings From the HITCH Cohort Study. *J Infect Dis*. 2022;226(7):1175-1183.

Associations between the extent of HLA allele sharing and HPV concordance among heterosexual couples who were HPV positive

Inclusiveness of HLA Groupings Shared	Alleles Shared per Couple	Age-Adjusted OR (95% CI)[a]			
		All HPVs	Subgenus 1	Subgenus 2	Subgenus 3
HLA-B*07, -DRB1, and -DQB1	0	1.0	1.0	1.0	1.0
	1	1.1 (.8–1.7)	0.9 (.4–2.1)	1.3 (.8–2.2)	0.9 (.4–1.9)
	2–3	1.0 (.6–1.6)	0.8 (.3–2.2)	1.3 (.7–2.5)	0.6 (.2–1.5)
HLA-G	0	1.0	1.0	1.0	1.0
	1	1.1 (.7–1.6)	**0.4 (.2–.7)**	1.1 (.7–1.7)	**1.9 (1.0–3.5)**
	2	0.6 (.3–1.5)	0.6 (.1–2.7)	0.4 (.1–1.1)	3.0 (.5–16.7)
All HLAs	0	1.0	1.0	1.0	1.0
	1	1.6 (.7–1.9)	0.7 (.2–1.8)	1.1 (.6–2.0)	1.5 (.7–3.3)
	2	1.0 (.6–1.7)	0.8 (.3–2.4)	0.9 (.5–1.8)	1.2 (.5–2.9)
	3–5	1.1 (.5–2.1)	**0.2 (.0–1.0)**	1.6 (.7–3.7)	1.4 (.4–4.7)
HLA-G 3′UTR: 14 bp, +3142 C/G, +3187 G/A	0	1.0	1.0	1.0	1.0
	1	0.9 (.6–1.5)	1.4 (.6–3.5)	0.6 (.4–1.2)	**2.4 (1.0–5.7)**
	2	0.8 (.5–1.3)	0.9 (.3–2.5)	0.9 (.5–1.6)	0.8 (.4–1.9)
	3	0.7 (.4–1.2)	2.4 (.9–6.3)	0.6 (.3–1.1)	0.8 (.4–1.8)
HLA-G 3′UTR: 14 bp and all 8 different SNPs	0	1.0	1.0	1.0	1.0
	1	1.0 (.6–1.6)	1.5 (.6–3.7)	0.7 (.4–1.3)	**2.6 (1.0–6.3)**
	2	0.6 (.4–1.1)	0.8 (.3–2.5)	0.7 (.4–1.3)	0.7 (.3–1.7)
	3	0.7 (.3–1.2)	1.0 (.2–4.9)	0.6 (.3–1.2)	0.7 (.2–2.0)
	4	0.9 (.5–1.6)	2.4 (.8–7.3)	0.8 (.4–1.5)	0.8 (.3–1.9)
	5–6	0.9 (.3–2.5)	6.9 (.9–54.6)	0.4 (.1–1.4)	4.0 (.4–36.9)

Karolina Louvanto

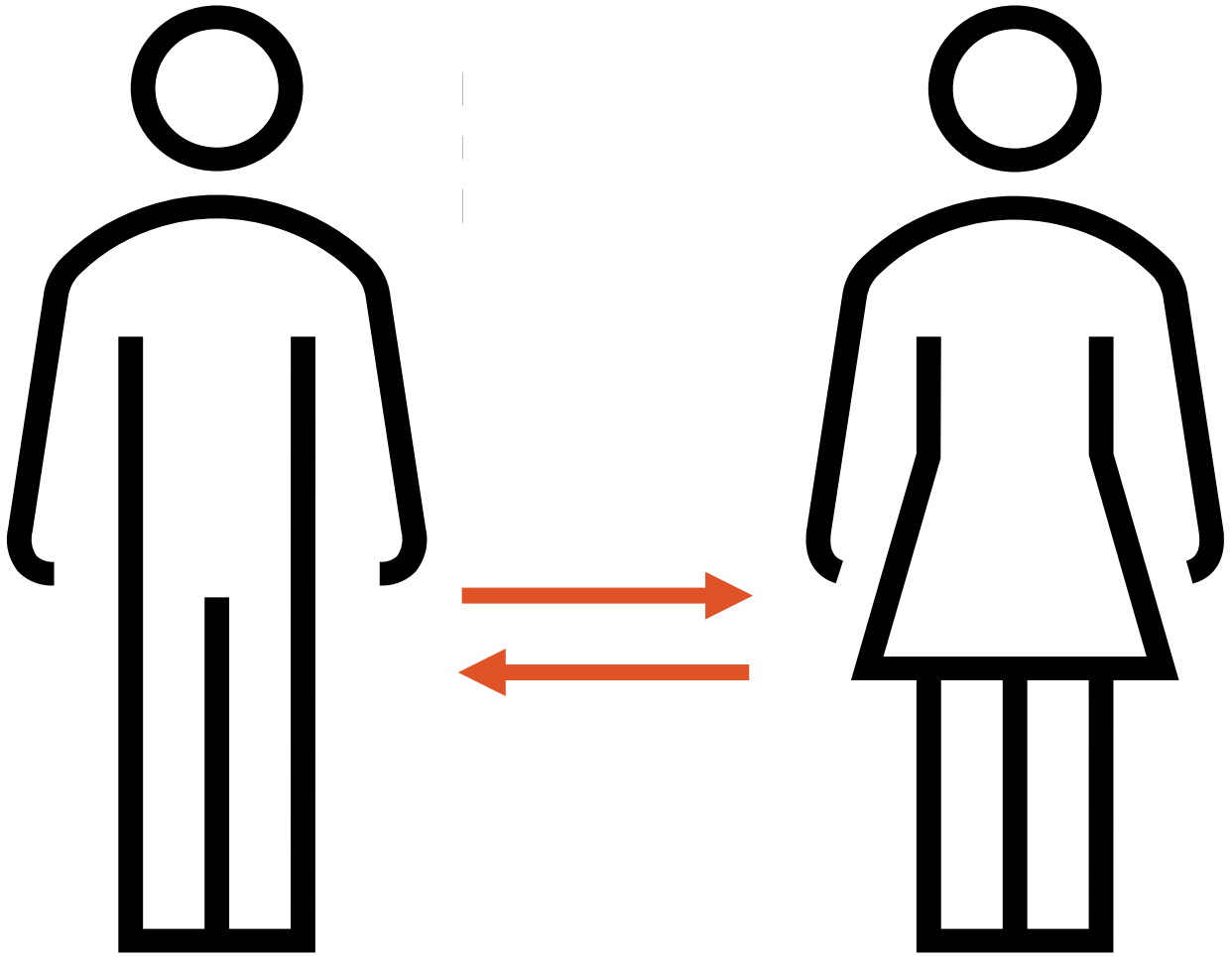
- Sixty comparisons, 5 significant associations, while one or two would be expected only by chance
- No consistent findings in terms of dose-response
- Conclusion: a role for HLA compatibility unlikely

Louvanto K, Baral P, Burchell A, Ramanakumar A, El-Zein M, Tellier PP, Coutlée F, Roger M, Franco EL. Role of Human Leukocyte Antigen Allele Sharing in Human Papillomavirus Infection Transmission Among Heterosexual Couples: Findings From the HITCH Cohort Study. *J Infect Dis*. 2022;226(7):1175-1183.

There seems to be a difference in propensity for the direction of genital HPV transmission

Rajshree Balaji

Aaron MacCosham



The propensity for transmission is greater from female to male than from male to female.

Balaji R, MacCosham A, Williams K, El-Zein M, Franco EL. Directionality of Genital Human Papillomavirus Infection Transmission Within Heterosexual Couples: A Systematic Review and Meta-analysis. J Infect Dis. 2020;222(11):1928-1937.

HPV transmission & clearance rates in HITCH

Talía Malagón

- Estimation of HPV incidence & clearance rates using a Bayesian model
- HPV type-specific transmission rates from women to men were 1.6 times higher than transmission rates from men to women

HPV type-specific transmission

	Events (n)	Rate (/100 person-months)	IRR	95% prediction interval
Transmission type-specific incidence				
Men to women	106	3.2	1.0	(ref)
Women to men	60	4.1	1.6	(1.0-2.5)

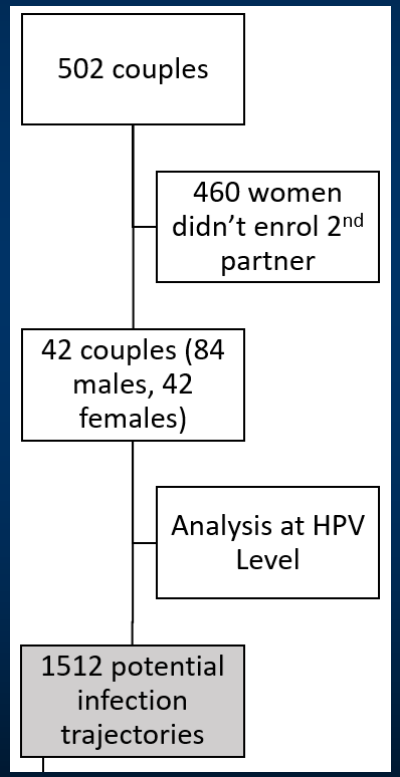
Malagón T, MacCosham A, Burchell AN, El-Zein M, Tellier PP, Coutlée F, Franco EL; HITCH Study Group. Sex- and Type-specific Genital Human Papillomavirus Transmission Rates Between Heterosexual Partners: A Bayesian Reanalysis of the HITCH Cohort. *Epidemiology*. 2021;32(3):368-377.

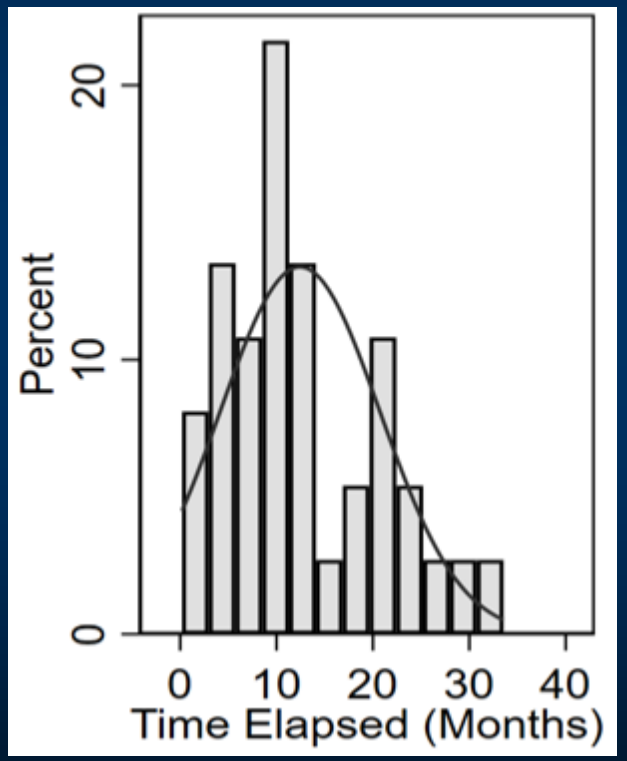
Sequential partner transmission of HPV infection:

Is there a tendency for the second male partner of a woman to have a comparable infection profile as the woman's previous male partner?

Andrew Arthur

Male 1 ⟷ Female ⟷ Male 2





Arthur AW, El-Zein M, Burchell AN, Tellier PP, Coutlée F, Franco EL. Epidemiology of genital human papillomavirus infections in sequential male sex partners of young females. Clin Microbiol Infect. 2024;30(2):247-253.

Sequential partner transmission of HPV infection:

Is there a tendency for the second male partner of a woman to have a comparable infection profile as the woman's previous male partner?

Andrew Arthur

Male 1 ⟷ Female ⟷ Male 2

Analysis	Odds Ratio (95%CI)
Crude	3.8 (2.4-5.8)
Adjusted for number of M1 and M2 testing opportunities	3.8 (2.4-6.0)
Restricted to dyads < 10.2 months* apart	4.6 (2.5-8.7)
Restricted to dyads >= 10.2 months apart	3.0 (1.5-5.9)
Restricted to M2 condom use 0-75% of the time	4.0 (2.2-7.2)
Restricted to M2 condom use 76-100% of the time	3.3 (1.6-7.1)
Adjusted for no. times female tested positive for M1's infection	1.3 (0.6-3.0)

Male 1	Male 2	
	HPV-	HPV+
HPV-	1283	109
HPV+	91	29
O/E ++	2.6 (1.9-3.4)	

* Median time between last HPV test for M1 and first one for M2

Arthur AW, El-Zein M, Burchell AN, Tellier PP, Coutlée F, Franco EL. Epidemiology of genital human papillomavirus infections in sequential male sex partners of young females. Clin Microbiol Infect. 2024;30(2):247-253.

Does HPV vaccination reduce infection transmission?

The role of reduced viral load

Michel Wissing

Table 5. Type-specific viral loads (copies/cell) in HPV-positive women, stratified by baseline vaccination status

	Unvaccinated women			Vaccinated women				
HPV type	***n***	**Median (IQR)**	**Geometric mean (95% CI)**	***n***	**Median (IQR)**	**Geometric mean (95% CI)**	***P* value[a]**	
HPV6	56	0.19 (0.007–4.13)	0.19 (0.07–0.51)	2	4.21 (0.0008–8.42)	0.08 (0.00–$3.4 \cdot 10^{24}$)	0.77	**0.001**
HPV11	7	0.02 (0.0002–0.22)	0.01 (0.0005–0.23)	0	—	—	—	
HPV16	106	3.09 (0.20–15.8)	1.44 (0.73–2.84)	8	0.006 (0.0004–0.43)	0.008 (0.0004–0.16)	**0.001**	
HPV18	29	1.21 (0.04–9.83)	0.60 (0.11–3.21)	1	0.36	0.36	0.86	
HPV31	46	0.47 (0.03–10.9)	0.34 (0.10–1.21)	3	0.13 (0.04–6.40)	0.32 (0.0004–238.5)	0.77	0.93
HPV42	74	26.3 (1.70–179.5)	12.9 (6.02–27.8)	14	24.8 (0.87–261.1)	18.0 (2.48–130.8)	0.86	
HPV51	73	7.36 (0.27–107.4)	3.81 (1.38–10.53)	12	4.77 (0.16–72.7)	3.87 (0.38–39.1)	0.81	

NOTE: Bold values indicate statistical significance ($P < 0.05$).

[a]*P* values for individual HPV types were calculated using Wilcoxon rank-sum tests. When HPV types were grouped based on whether the type is included in the quadrivalent vaccine, *P* values were calculated using the Friedman test, stratifying by HPV type.

- Lower viral loads for target types in vaccinated women.
- This could potentially translate into lower infectivity to partners.

Wissing MD, Burchell AN, El-Zein M, Tellier PP, Coutlée F, Franco EL. Vaccination of Young Women Decreases Human Papillomavirus Transmission in Heterosexual Couples: Findings from the HITCH Cohort Study. Cancer Epidemiol Biomarkers Prev. 2019 Nov;28(11):1825-1834.

HPV vaccination in reducing transmission to male partners

Michel Wissing

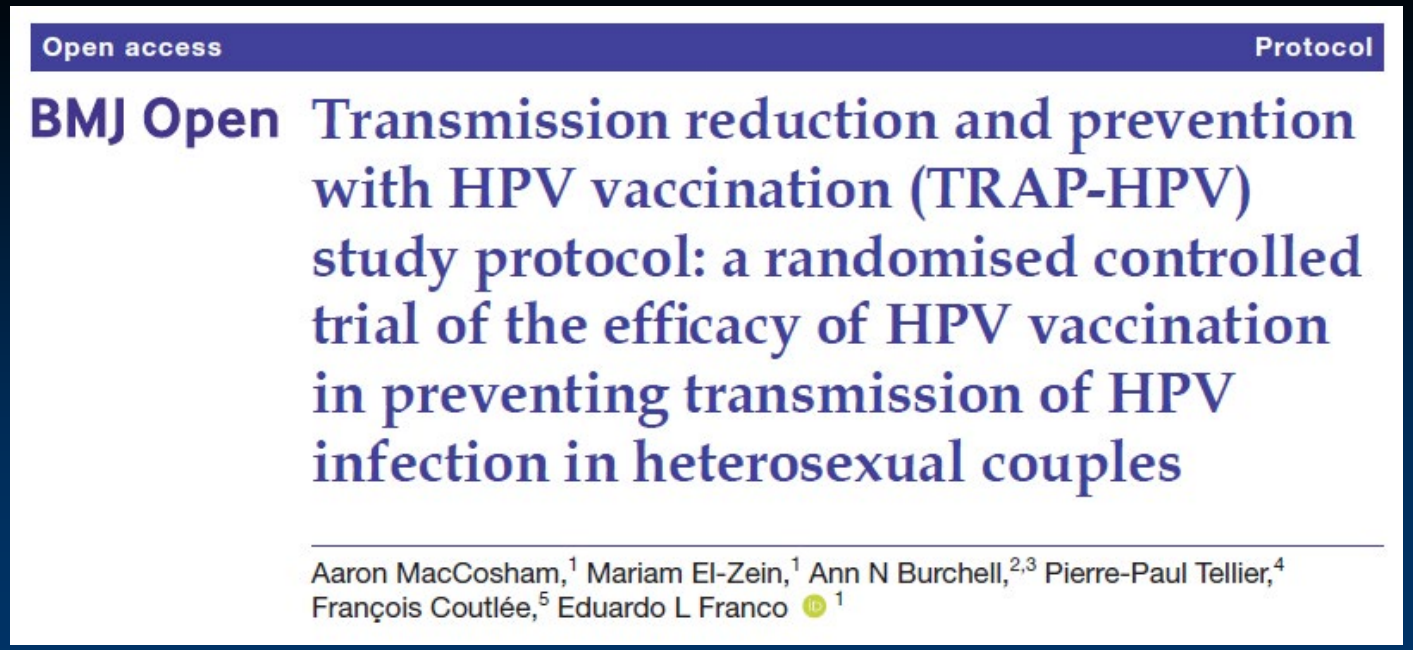
- Lower transmission rates of HPV from vaccinated women to their male partners
- 0% of the vaccinated women positive for HPV-6/11/16/18 transmitted these infections to their partners, whereas 33% of unvaccinated women positive for HPV-6/11/16/18 transmitted these infections to their partners.

HPV infection risk in male partners of vaccinated vs unvaccinated women

HPV TYPE	OR adjusted[a] (95% CI)
All (36 types)	0.80 (0.44-1.47)
Alpha 7, 9, 10 types	0.22 (0.05-0.95)
HPV-6/11/16/18	0.32 (0.04-2.53)

[a] adjusted for age, race, smoking status, age at first coitus, number of lifetime sex partners (coitus), whether the individual had same-sex partners and/or concurrent sex partners at the baseline visit, condom use, average frequency of coitus with HITCH partner per week, and duration of the sexual relationship.

Wissing MD, Burchell AN, El-Zein M, Tellier PP, Coutlée F, Franco EL. Vaccination of Young Women Decreases Human Papillomavirus Transmission in Heterosexual Couples: Findings from the HITCH Cohort Study. *Cancer Epidemiol Biomarkers Prev.* 2019 Nov;28(11):1825-1834.



Strengths and limitations:

- First RCT of the efficacy of vaccination to reduce HPV transmission.
- Couple members randomized independently to the treatment or placebo vaccine, allowing for comparison between 4 vaccination groups.
- Key logistical challenge in conducting a sexual transmission prevention study is the need for couples to have been recently formed.
- Anal sampling is a deterrent in participant recruitment.

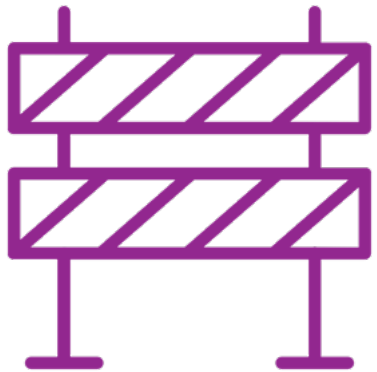
TR&P

2 x 2 Factorial Design

Female (F) vaccination	Male (M) vaccination	
	HPV (Gardasil 9: H)	Placebo (Hepatitis A: P)
HPV (Gardasil 9: H)	M^HF^H	M^PF^H
Placebo (Hepatitis A: P)	M^HF^P	M^PF^P

MacCosham A, El-Zein M, Burchell AN, Tellier PP, Coutlée F, Franco EL. Transmission reduction and prevention with HPV vaccination (TRAP-HPV) study protocol: a randomised controlled trial of the efficacy of HPV vaccination in preventing transmission of HPV infection in heterosexual couples. BMJ Open. 2020;10(8):e039383.

AMENDMENTS



Upper age limit: increased from 26 to 40 years old, and once more to 45 years old

Compensation: increased from $350 to $500 per couple and further to $1000

Discontinued collection of anal samples

Replaced Gardasil with Gardasil 9 as intervention vaccine

Replaced Havrix (GlaxoSmithKline) with Avaxim (Sanofi Pasteur) as placebo vaccine

Transmission Reduction And Prevention with HPV Vaccination (TRAP-HPV) study design and timeline

Eligibility screening

Inclusion/exclusion criteria - Participants were cisgender, heterosexual couples (aged 18 - 45) who had not received the intervention vaccine, had no anogenital cancer history, and had been together for 6 months or less, who were planning to stay in the Montreal area for at least a year, and to have ongoing sexual contact, and not planning to become pregnant in the next year.

Enrollment dates: March 26, 2014, to February 16, 2022.
Last follow-up visit: November 18, 2022.

Baseline: Visit 1 Randomization & informed consent	2 months : Visit 2	4 months: Visit 3	6 months: Visit 4	9 months: Visit 5	12 months: Visit 6
Total: 372 (Males: 186 / Females: 186) Males: 91 treatment, 95 control Females: 99 treatment, 87 control	**314** (M: 157 / F: 157) M: 76 treatment, 81 control F: 85 treatment, 72 control	**272** (M: 136 / F: 136) M: 67 treatment, 69 control F: 78 treatment, 58 control	**252** (M: 126 / F: 126) M: 63 treatment, 63 control F: 70 treatment, 56 control	**225** (M: 112 / F: 113) M: 57 treatment, 55 control F: 63 treatment, 50 control	**207** (M: 103 / F: 104) M: 52 treatment, 51 control F: 60 treatment, 44 control

Vaccination

Self-administered electronic questionnaires filled out.
Samples collected for HPV genotyping: oral (both partners), penile (males), and vaginal (females), anal (both partners, discontinued July 14, 2016) .

Blood sample

ORIGINAL STUDY

Protection to Self and to One's Sexual Partner After Human Papillomavirus Vaccination: Preliminary Analysis From the Transmission Reduction And Prevention with HPV Vaccination Study

Aaron MacCosham, MSc, Mariam El-Zein, PhD,* Ann N. Burchell, PhD,†‡ Pierre-Paul Tellier, MD,§ François Coutlée, MD,¶ and Eduardo L. Franco, DrPH,* for the TRAP-HPV study group*

Aaron MacCosham

Conclusions: Our study provides inconclusive evidence that individuals whose partner recently received an HPV vaccine are protected from vaccine-preventable types but demonstrates that vaccinated individuals are at a lower risk of incident infections.

MacCosham A, El-Zein M, Burchell AN, Tellier PP, Coutlée F, Franco EL; TRAP-HPV study group. Protection to Self and to One's Sexual Partner After Human Papillomavirus Vaccination: Preliminary Analysis From the Transmission Reduction And Prevention with HPV Vaccination Study. *Sex Transm Dis*. 2022 Jun 1;49(6):414-422.

Enrollment, randomization, and analytical sample in the TRAP-HPV study

Alissa Moore

788 inquiries received

→ 216 couples unreachable to assess eligibility

572 couples reachable and assessed for eligibility

→ 386 couples excluded pre-enrollment
- 213 ineligible
- 163 eligible but declined
- 8 eligible but did not respond
- 2 pending enrollment when study closed

186 couples enrolled (Mar. 2014- Feb. 2022)

→ 32 couples excluded from current analysis
- 29: only a baseline visit
- 3: invalid baseline genital sample, imputation based on subsequent samples not possible

154 couples at baseline, vaccine administered:
- **MuFu: male and female unvaccinated (40 couples)**
- **MvFu: male vaccinated, female unvaccinated (31 couples)**
- **MuFv: male unvaccinated, female vaccinated (39 couples)**
- **MvFv: male and female vaccinated (44 couples)**

N couples at follow-up visits:

Visit 2 - **month 2**: 154 couples, **vaccine administered** (**40 MuFu**, **31 MvFu**, **39MuFv**, **44 MvFv**)
Visit 3 - month 4: 133 couples (**31 MuFu**, **26 MvFu**, **36 MuFv**, **40 MvFv**)
Visit 4 - **month 6**: 125 couples, **vaccine administered** (**30 MuFu**, **26 MvFu**, **32 MuFv**, **37 MvFv**)
Visit 5 - month 9: 112 couples[a] (**26 MuFu**, **24 MvFu**, **28 MuFv**, **34[a] MvFv**)
Visit 6 - month 12: 103 couples[b] (**23[b] MuFu**, **21 MvFu**, **28 MuFv**, **31 MvFv**)

[a]112 females/111 males
[b]103 females/102 males

Moore et al. Manuscript in preparation

Results: HPV Incidence

Study arm	HPV	FEMALE			MALE		
		Events	Time[a]	Rate[b] (95% CI)	Events	Time[a]	Rate[b](95% CI)
MuFu n=40 couples	Vaccine-targeted	5	3560.54	1.40 (0.51, 5.34)	8	3311.79	2.42 (0.97, 7.63)
	Related	1	2713.97	0.37 (0.01, 2.05)[c]	3	2552.65	1.18 (0.21, 17.18)
	Unrelated	12	7153.20	1.68 (0.94, 3.29)	15	6784.93	2.21 (1.35, 3.88)
MvFu n=31 couples	Vaccine-targeted	5	3172.26	1.58 (0.55, 6.17)	3	3034.10	0.99 (0.17, 3.07)
	Related	5	2305.25	2.17 (0.94, 6.02)	5	2219.67	2.25 (1.00, 6.10)
	Unrelated	22	6081.94	3.62 (1.88, 7.80)	17	5887.70	2.89 (1.49, 6.24)
MuFv n=39 couples	Vaccine-targeted	4	3793.67	1.05 (0.42, 3.45)	12	3581.69	3.35 (1.95, 6.30)
	Related	3	2877.35	1.04 (0.34, 4.69)	6	2740.19	2.19 (1.05, 5.30)
	Unrelated	22	7499.06	2.93 (1.67, 5.59)	26	7286.07	3.57 (2.28, 5.93)
MvFv n=44 couples	Vaccine-targeted	7	4431.81	1.58 (0.71, 4.25)	7	4189.61	1.67 (0.75, 3.51)
	Related	9	3265.27	2.76 (1.43, 6.00)	10	3141.70	3.18 (1.58, 7.26)
	Unrelated	24	8712.42	2.75 (1.50, 5.63)	20	8307.32	2.41 (1.45, 4.26)

[a] Indicates infection-months at risk.
[b] Rates represent events /1000 infection-months at risk. Jackknife confidence intervals are reported wherever possible to account for intra-participant correlation.
[c] In instances where no events were observed, or there was an insufficient number of failures to calculate jackknife confidence intervals, exact Fisher's 95% confidence intervals were used.

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Results: HPV Transmission

Study arm	HPV	FEMALE			MALE		
		Events	Time[a]	Rate[b] (95% CI)	Events	Time[a]	Rate[b](95% CI)
MuFu n=40 couples	Vaccine-targeted	1	141.54	7.07 (0.18, 39.37)[c]	1	62.88	15.90 (0.40, 88.61)[c]
	Related	0	44.78	0 (0.00, 82.38)[c]	1	8.08	123.73 (3.09, 689.60)[c]
	Unrelated	4	172.82	23.15 (7.85, 76.83)	5	93.93	53.23 (28.79, 99.00)
MvFu n=31 couples	Vaccine-targeted	1	47.90	20.88 (0.52, 116.33)[c]	2	50.47	39.63 (4.79, 143.15)[c]
	Related	2	34.99	57.16 (11.98, 361.22)	2	38.11	52.48 (13.61, 271.55)
	Unrelated	9	147.78	60.90 (28.94, 141.46)	8	239.91	33.35 (14.26, 75.11)
MuFv n=39 couples	Vaccine-targeted	1	75.40	13.26 (0.33, 73.90)[c]	5	39.10	127.89 (41.84, 354.21)
	Related	1	62.49	16.00 (0.40, 89.17)[c]	2	65.25	30.65 (4.56, 245.92)
	Unrelated	2	131.78	15.18 (3.70, 108.35)	12	323.72	37.07 (20.92, 70.39)
MvFv n=44 couples	Vaccine-targeted	3	100.57	29.83 (7.26, 145.53)	0	81.58	0 (0.00, 45.22)[c]
	Related	2	77.50	25.80 (5.51, 199.62)	2	127.74	15.66 (3.65, 117.67)
	Unrelated	5	267.21	18.71 (7.33, 53.62)	7	333.80	20.97 (11.35, 40.69)

[a] Indicates infection-months at risk.
[b] Rates represent events /1000 infection-months at risk. Jackknife confidence intervals are reported wherever possible to account for intra-participant correlation.
[c] In instances where no events were observed, or there was an insufficient number of failures to calculate jackknife confidence intervals, exact Fisher's 95% confidence intervals were used.

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HITCH Study's Publications (as of May 2024)

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3. Burchell AN, Coutlée F, Tellier PP, Hanley J, Franco EL. Genital transmission of human papillomavirus in recently formed heterosexual couples. J Infect Dis. 2011;204(11):1723-9.
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12. Wissing MD, Burchell AN, El-Zein M, Tellier PP, Coutlée F, Franco EL. Vaccination of Young Women Decreases Human Papillomavirus Transmission in Heterosexual Couples: Findings from the HITCH Cohort Study. Cancer Epidemiol Biomarkers Prev. 2019;28(11):1825-1834.
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24. Arthur AW, El-Zein M, Burchell AN, Tellier PP, Coutlée F, Franco EL. Detection and Clearance of Type-Specific and Phylogenetically Related Genital Human Papillomavirus Infections in Young Women in New Heterosexual Relationships. J Infect Dis. 2024;229(3):691-706.
25. Ng K, Morais S, Wissing MD, Burchell AN, Tellier P-P, Coutlée F, Waterboer T, El-Zein M, Franco EL. Empirical sample-specific approaches to define HPV16 and HPV18 seropositivity in unvaccinated, young, sexually active women. Microbiol Spectr. 2024: e0022924.

TRAP-HPV Study’s Publications

1. MacCosham A, El-Zein M, Burchell AN, Tellier PP, Coutlée F, Franco EL. Transmission reduction and prevention with HPV vaccination (TRAP-HPV) study protocol: a randomised controlled trial of the efficacy of HPV vaccination in preventing transmission of HPV infection in heterosexual couples. BMJ Open. 2020;10(8):e039383.
2. MacCosham A, El-Zein M, Burchell AN, Tellier PP, Coutlée F, Franco EL; TRAP-HPV study group. Protection to Self and to One's Sexual Partner After Human Papillomavirus Vaccination: Preliminary Analysis From the Transmission Reduction And Prevention with HPV Vaccination Study. Sex Transm Dis. 2022;49(6):414-422.

Graduate Trainee Research – HITCH and TRAP-HPV Studies

MSc Students

Aaron MacCosham, 2018-21

Rajshree Balaji, 2019-20

Samantha Shapiro, 2019-21

Andrew Arthur, 2020-23

Alissa Moore, 2022-24

Kristy Ng, 2022-24

PhD Student

Ann Burchell, 2003-09

Postdoctoral Fellows

Karolina Louvanto, 2012-14, 2015

Kristina Dahlstrom, 2013-14

Talía Malagon, 2016-19

Michel Wissing, 2016-19

Samantha Morais, 2021-22