



Transmission Reduction and Prevention with HPV Vaccination

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Couple-based studies

- ▶ HPV transmission investigated in longitudinal couple-based studies
- ▶ Recently formed relationships: optimal for examining transmission dynamics
- ▶ HITCH: only HPV couple-based transmission study to target recently formed couples
 - ▶ Vaccination → transmission reduction (*Wissing, Cancer Epidemiol Biomarkers Prev, 2019*)
- ▶ No RCTs on the reduction of HPV transmission in couple-based studies

TRAP-HPV

- ▶ **Objective:** To determine the efficacy of an HPV vaccine in reducing transmission of genital and oral HPV infection to sexually active heterosexual partners of HPV vaccinated individuals.

The screenshot shows the ClinicalTrials.gov website interface. At the top left is the NIH logo and the text "U.S. National Library of Medicine". To the right are two menu items: "Find Studies" and "About Studies", both with downward-pointing triangles. Below this is the "ClinicalTrials.gov" logo in a blue, italicized serif font. A breadcrumb trail below the logo reads "Home > Search Results > Study Record Detail". The main content area displays "Trial record 1 of 1 for: NCT01824537." followed by navigation links: "Previous Study | Return to List | Next Study". At the bottom, the study title is shown in bold black text: "Transmission Reduction and Prevention With HPV Vaccination (TRAP-HPV) Study (TRAP-HPV)".

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Trial record **1 of 1** for: NCT01824537.

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Transmission Reduction and Prevention With HPV Vaccination (TRAP-HPV) Study (TRAP-HPV)

2x2 Factorial Design

	Male (M) vaccination	
Female (F) vaccination	HPV (Gardasil 9: T)	Placebo (Hepatitis A: P)
HPV (Gardasil 9: T)	M^{TF^T}	M^{PF^T}
Placebo (Hepatitis A: P)	M^{TF^P}	M^{PF^P}

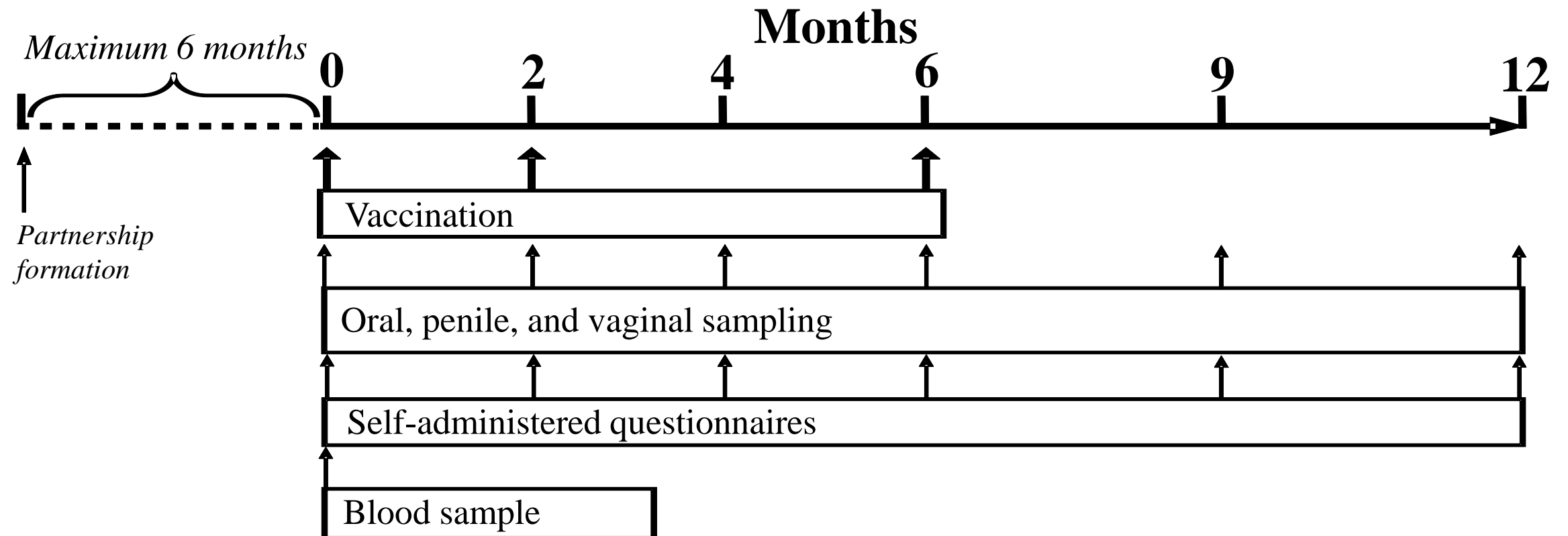
Sample size

- ▶ **500 couples needed**
- ▶ Based on Bernstein and Lagakos approach (*Bernstein, J Clin Microbiol, 2006*)
 - ▶ 90% power
 - ▶ type one error: 0.05
 - ▶ one-sided hypothesis for reductions: 40% rate of transmission
 - ▶ assuming cumulative 16% loss to follow-up at month 12
 - ▶ attrition rate: 2.7% per-visit

Eligibility criteria

- ▶ Volunteer couples must:
 - (1) not have been vaccinated with the intervention vaccine.
 - (2) plan on remaining in Montreal for at least 1 year.
 - (3) be in a new relationship that started no more than six months prior to study entry.
 - (4) plan on having continued sexual contact with partner.
 - (5) be between 18-45 years old.
 - (6) have no history of cervical, penile, oral or anal cancers.
 - (7) be willing to comply with study procedures.

Time points



HPV Testing

- ▶ Master Pure extraction kit (Epicenter, Madison, Wisconsin) (*Habis, Cancer Epidemiol Biomarkers Prev, 2004*)
- ▶ Linear Array HPV Genotyping Test (Roche Molecular Systems, Indianapolis, Indiana) (*Coutlée, J Clin Microbiol, 2006*)
 - ▶ Detects 36 HPV types
 - ▶ 6, 11, 16, 18, 26, 31, 33-35, 39, 40, 42, 44, 45, 51-54, 56, 58, 59, 61, 62, 66-73, 81-84, and 89
 - ▶ PGMY09/11 consensus primer system targets L1 gene

Outcomes

- ▶ Reduction of HPV infections with target HPV vaccine types in multiple anatomic sites in Avaxim-administered sexual partners of HPV vaccinated individuals
- ▶ Reduction in HPV type concordance, evaluable as per these group contrasts

	Male (M) vaccination	
	HPV (Gardasil 9: T)	Placebo (Avaxim: P)
Female (F) vaccination		
HPV (Gardasil 9: T)	M^{TF^T}	M^{PF^T}
Placebo (Avaxim: P)	M^{TF^P}	M^{PF^P}

Statistical analysis

- ▶ Advanced regression methods
- ▶ Kaplan-Meier: plot the cumulative probability of HPV infection in sexual partners of vaccinated versus unvaccinated individuals against follow-up time
- ▶ Log-rank test: comparisons in HPV transmission between vaccine & control groups
- ▶ Additional cumulative risk models fitted with type-specific transmission as an outcome

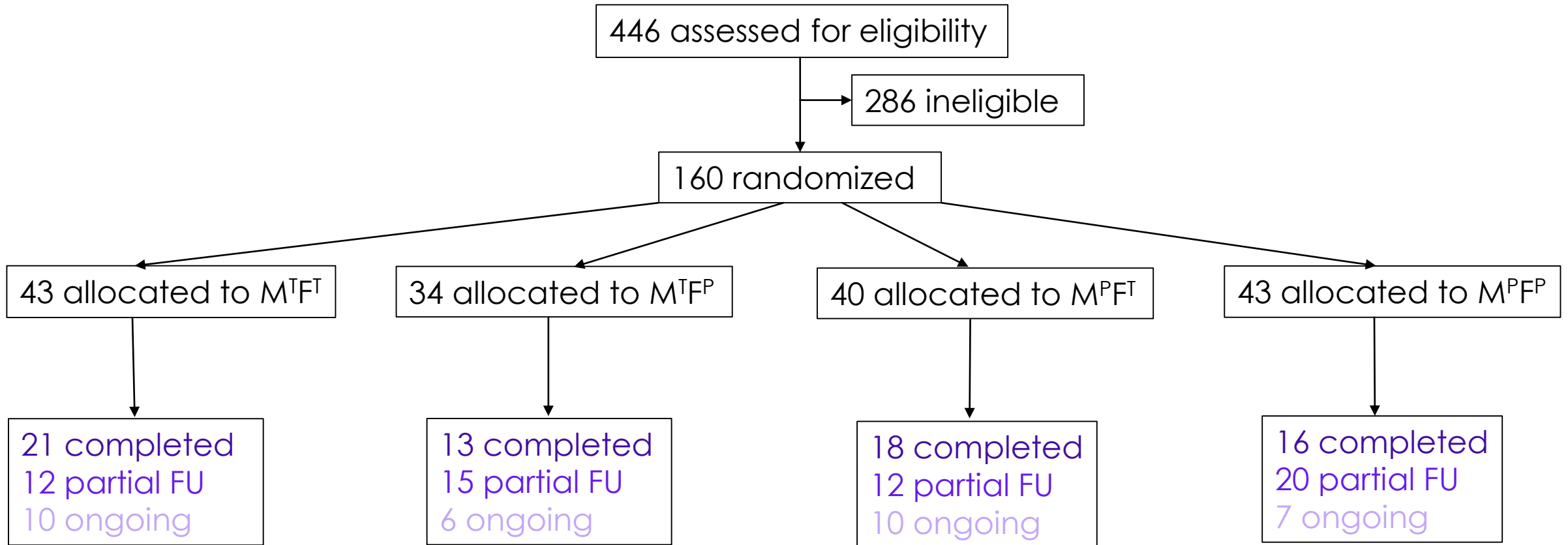
Strengths

- ▶ First RCT to investigate HPV transmission reduction via vaccination within couples
- ▶ Few couple-based studies have recruited a target sample size ≥ 500 couples
 - ▶ 502 (*El-Zein, JMIR Res Protoc, 2019*)
 - ▶ 874 (*Liu, Sci Rep, 2015*)
- ▶ TRAP-HPV could provide empirically-derived estimates for health economic models and mathematical models predicting herd immunity

Challenges & 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
- ▶ Collection of anal samples discontinued
- ▶ Gardasil replaced with Gardasil 9 as intervention vaccine
- ▶ Havrix (GlaxoSmithKline) replaced with Avaxim (Sanofi Pasteur) as placebo vaccine

Consort Diagram



Acknowledgements

▶ TRAP-HPV study group

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