

# The STEP Study

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## **Update on the Merck Ad5 Phase II Trial**

### **Merck V520 Protocol 023/HVTN 502**

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For the STEP Study Protocol Team

AIDS Vaccine 2007 Conference

Seattle, WA USA

August 22, 2007

# Topics to be discussed

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- Baseline characteristics of study participants
  - For more details, see Poster # P06-03
- Retention
- Safety data (blinded to treatment group)
  
- Not discussed
  - Risk behavior
    - See Poster # P06-07
  - Immunogenicity and efficacy: Data are still blinded
    - Final results available in late 2008/early 2009

# The STEP Study

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- Collaborative study between Merck, HIV Vaccine Trials Network (HVTN), and the Division of AIDS (DAIDS)/NIH
- aka, Merck Protocol V520-023 and/or HVTN 502
- Phase II Test-of-Concept study
  - Concept: Cell-mediated immune (CMI) responses elicited by the vaccine will
    - Prevent persistent HIV infection and/or
    - Control HIV viral replication if infection does occur
- [www.stepstudies.com](http://www.stepstudies.com)

# The STEP Study

## Study Population

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- ~3000 HIV-seronegative individuals in 2 cohorts:
  - ~1500 with low ( $\leq 200$ ) Ad5 titers
  - ~1500 with high ( $> 200$ ) Ad5 titers
- With sexual risk factors for acquiring HIV infection
  - Predominantly MSM and women with multiple sexual partners
  - Heterosexual men in the Caribbean
  - IDU are not excluded but must also have sexual risk factors
- In Clade B geographic regions
  - North America, Australia, South America, Caribbean
- Encourage enrollment of high risk women and diverse racial populations
- Stratified by gender, study site, baseline Ad5 titer

# STEP Study Sites



# STEP Study Sites



# STEP Study Sites

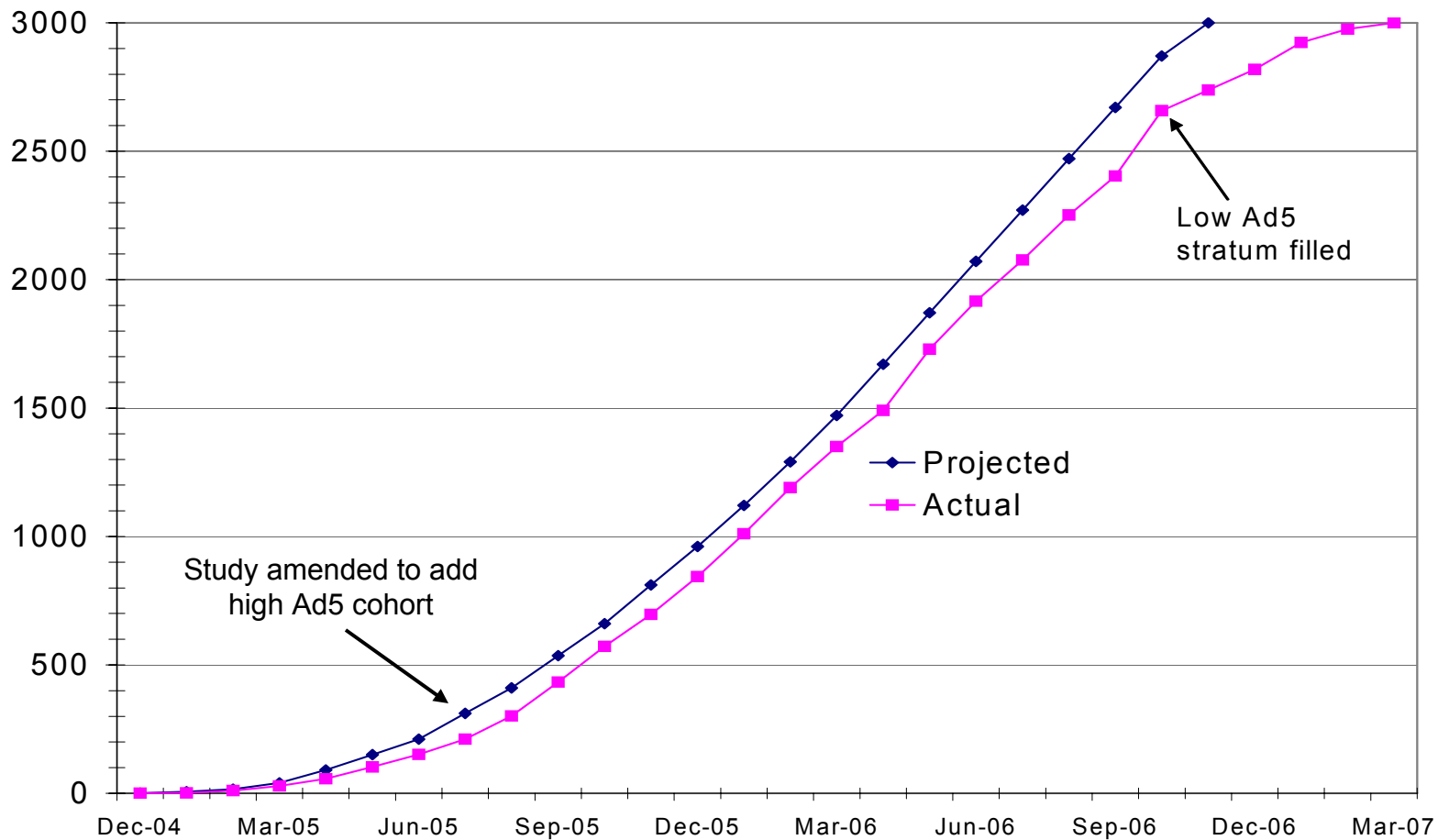


# STEP Study Sites



# The STEP Study

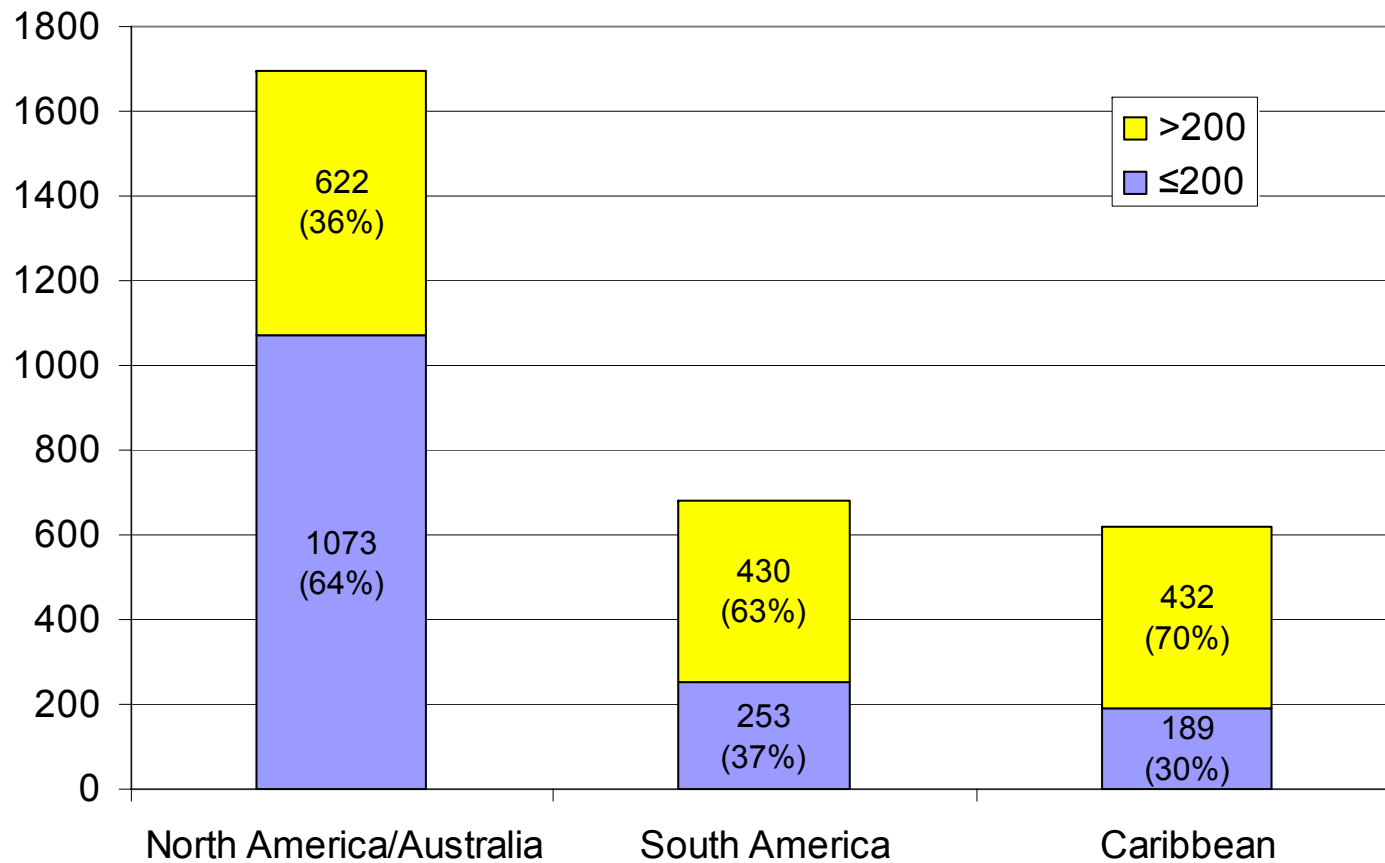
## Projected vs. Actual Enrollment



# The STEP Study

## Baseline Ad5 titer by region

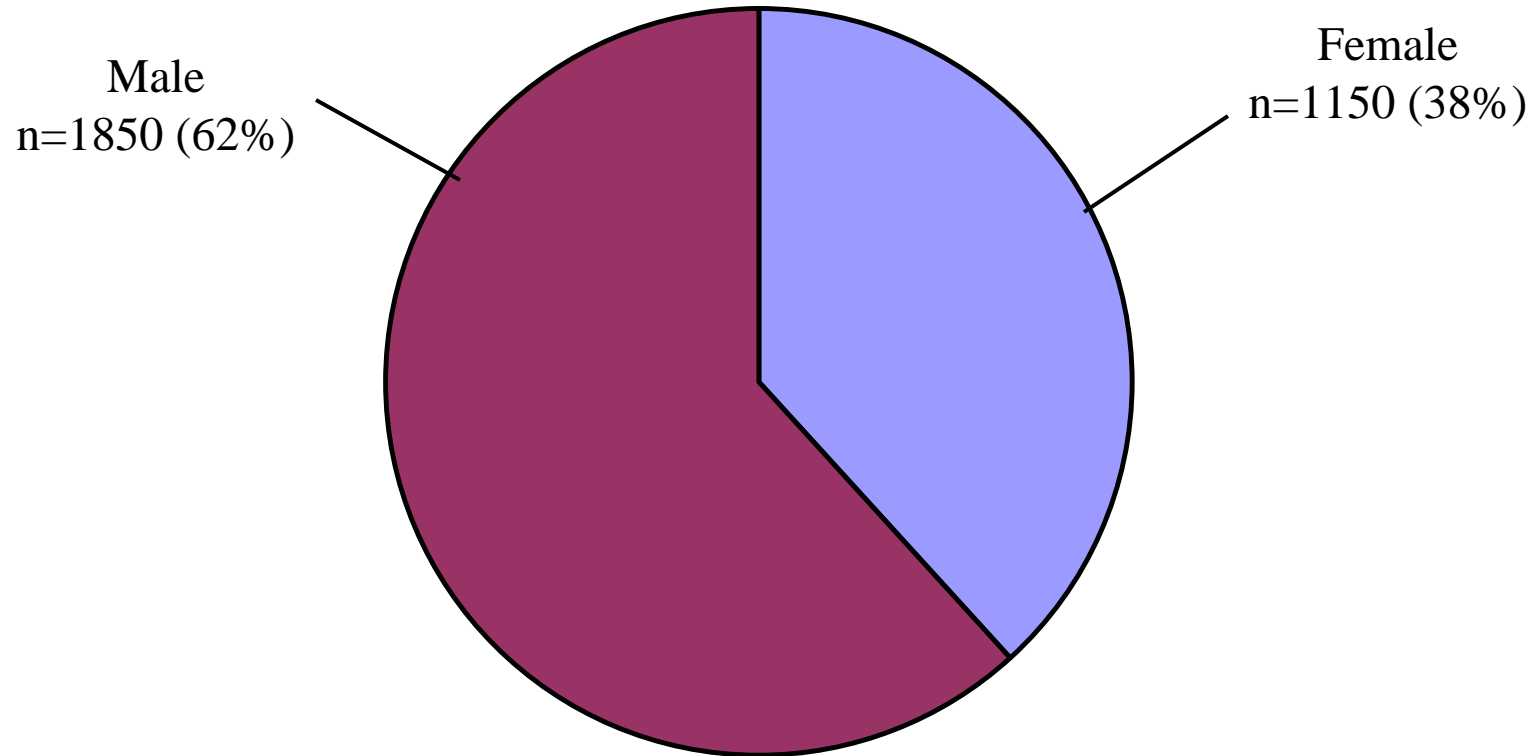
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# The STEP Study

## Enrollment by gender

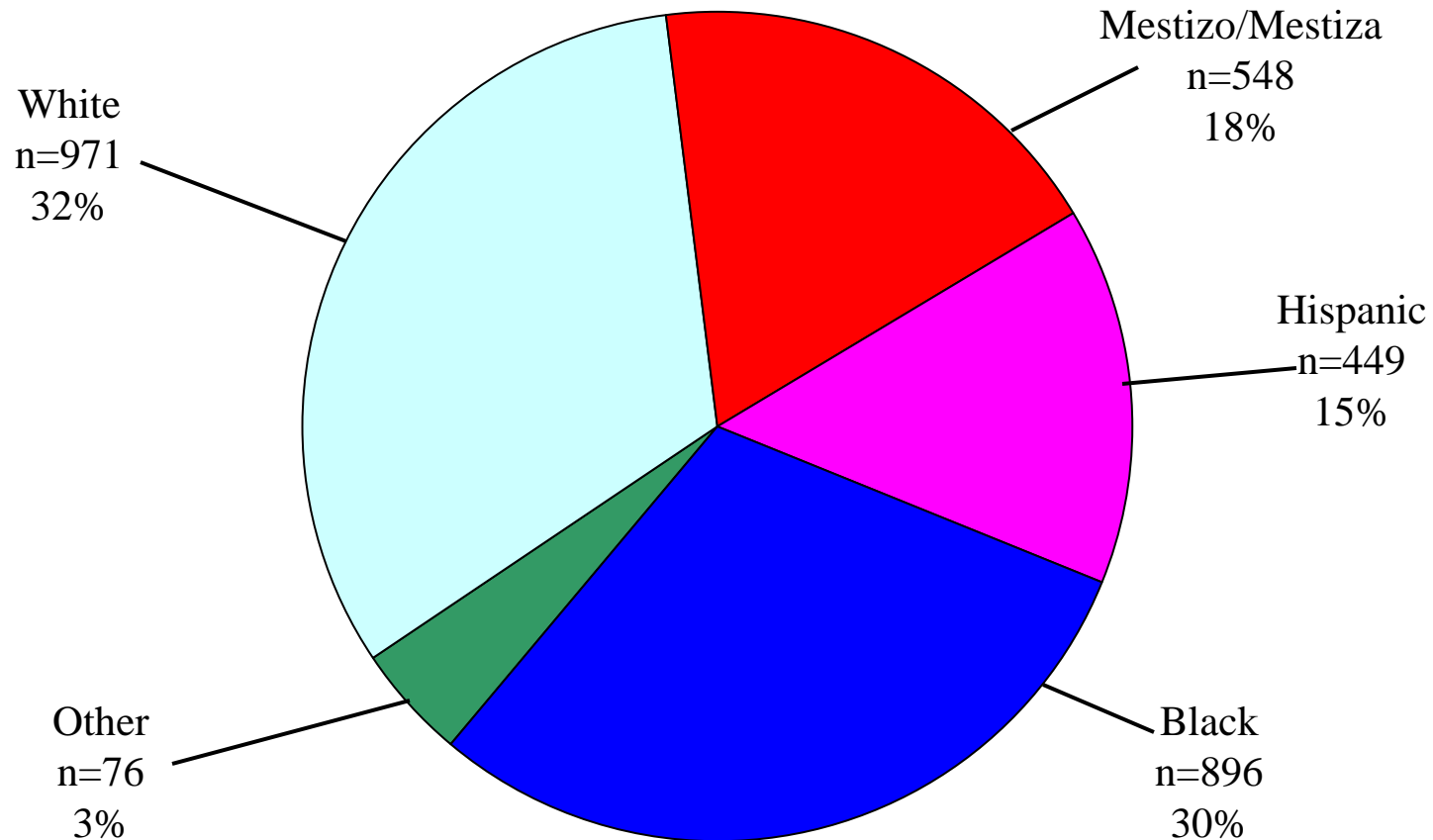
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# The STEP Study

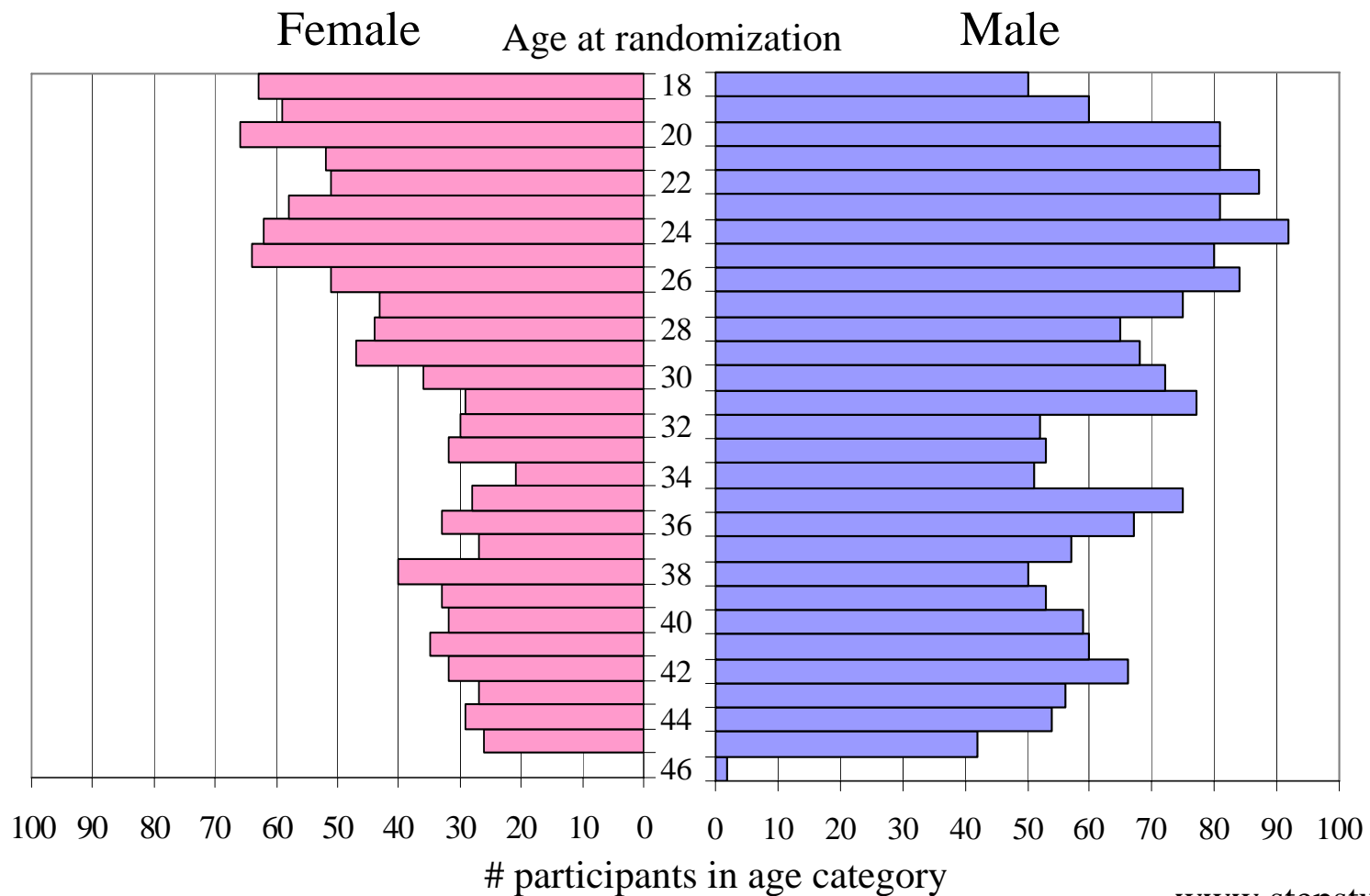
## Enrollment by ethnicity

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# The STEP Study

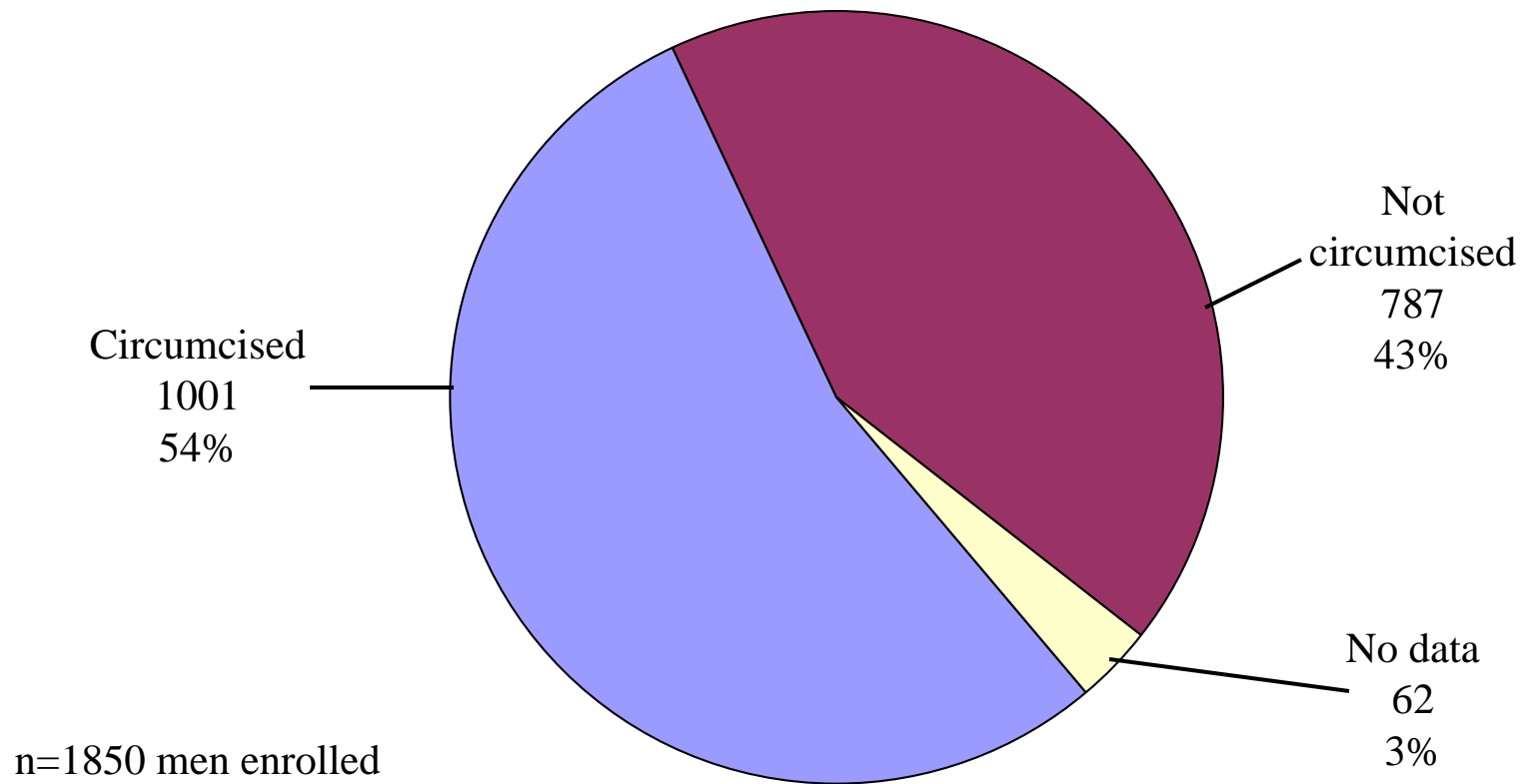
## Age distribution



# The STEP Study

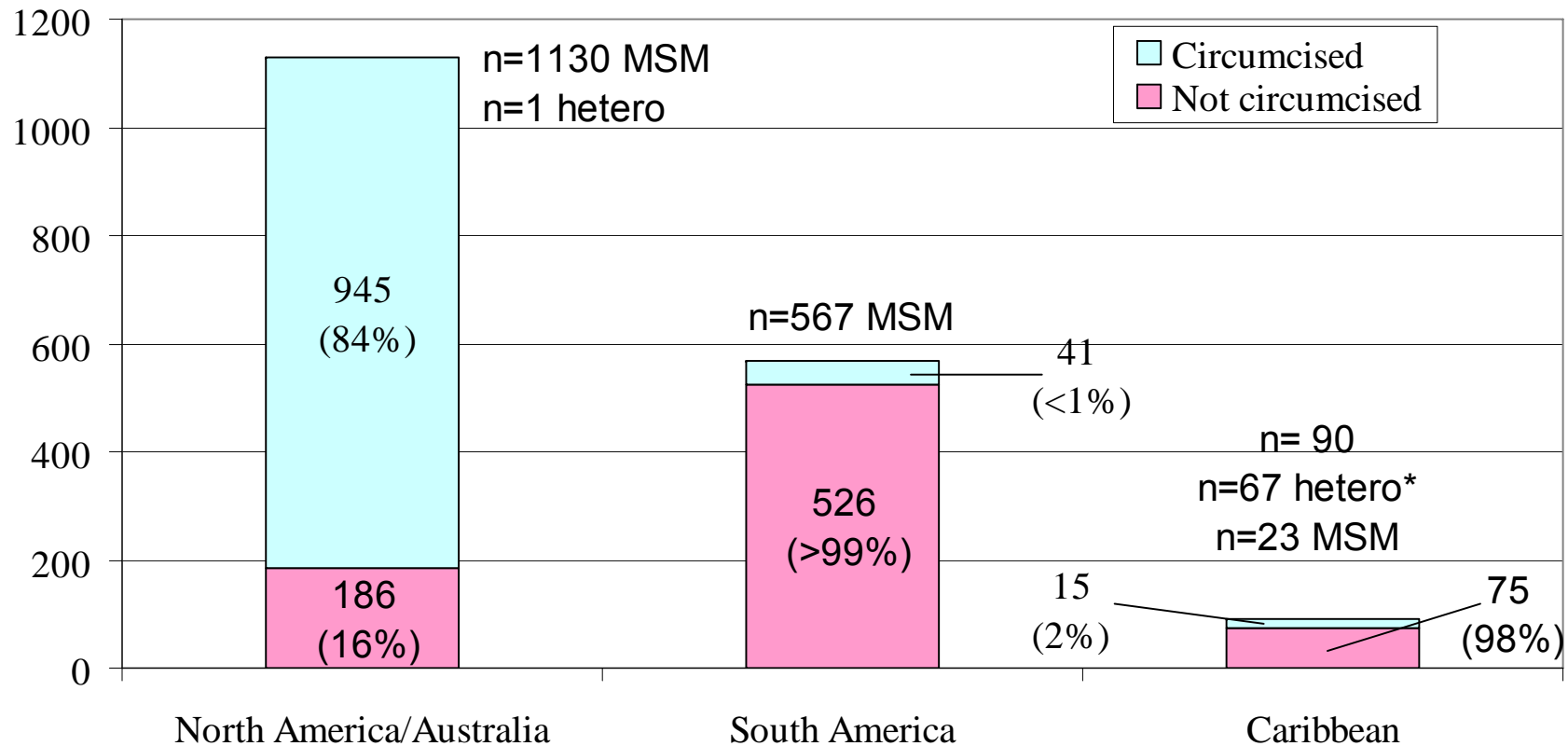
## Circumcision status

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# The STEP Study

## Circumcision status by region



\*Only 3/67 heterosexual men in the Caribbean are circumcised, compared to 12/23 MSM

# The STEP Study

## Retention

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Visit	Expected Visits*	Completed visits	
		n	%
Day 1	3000	3000	100%
Week 4	3000	2893	96%
Week 26	2860	2608	91%
Week 52	1969	1723	88%
Week 78	920	767	83%
Total	11749	10991	94%

\*Number of participants who have been in study long enough to reach each visit.  
Study injections are given at Day 1, Week 4, and Week 26.  
Data are preliminary.

# The STEP Study

## Blinded Safety

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- 79.2% (2358) of study participants reported one or more adverse experiences (AEs)
  - Majority of adverse experiences are of mild or moderate intensity
- 21 subjects reported SAEs
  - 18 subjects had SAEs that were not vaccine-related per the investigator
  - 3 subjects had SAEs that were at least possibly vaccine related per the investigator
    - Diarrhea
    - Hypertension, diarrhea, fever, and vomiting
    - Fever and chills

Based on available AE data as of 31-Jul-2007.

Percentages are calculated based on the number of patients with follow-up.

Data are blinded, so participants may have received vaccine or placebo.

Data are preliminary.

# The STEP Study

## Blinded Safety (cont.)

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- 5 Subjects discontinued from the study due to AEs
  - 4 study participants died from SAEs—none deemed to be vaccine related per the investigator
    - Drug overdose
    - Gastric cancer
    - Gunshot wound
    - Stab wound
  - 1 subject discontinued from the study due to multiple non-serious AEs
    - Dyskinesia, headache, eye pain, pruritis, paraesthesia, insomnia

Based on available AE data as of 31-Jul-2007.

Percentages are calculated based on the number of patients with follow-up.

Data are blinded, so participants may have received vaccine or placebo.

Data are preliminary.

# The STEP Study

## Most Commonly Reported AEs

N=2976 Study participants in analysis population: 2979	Mild		Moderate		Severe		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Injection Site Pain	969	(33.0)	171	(5.8)	14	(0.5)	1154	(39.3)
Headache	377	(12.8)	191	(6.5)	34	(1.2)	602	(20.5)
Fever	261	(8.9)	97	(3.3)	11	(0.4)	369	(12.6)
Injection Site Swelling	230	(7.8)	16	(0.5)	2	(0.1)	250	(8.5)
Injection Site Erythema	230	(7.8)	7	(0.2)	0	(0.0)	238	(8.1)
Fatigue	132	(4.5)	77	(2.6)	16	(0.5)	225	(7.7)
Diarrhea	122	(4.2)	59	(2.0)	9	(0.3)	190	(6.5)
Myalgia	72	(2.4)	44	(1.5)	8	(0.3)	124	(4.2)
Dizziness	69	(2.3)	27	(0.9)	3	(0.1)	99	(3.4)
Nausea	63	(2.1)	29	(1.0)	6	(0.2)	98	(3.3)
Sore throat	60	(2.0)	32	(1.1)	2	(0.1)	94	(3.2)

Data are preliminary.

Based on available AE data as of 31-July-2007.

AEs reported within 15 days of any study injection by  $\geq 3\%$  of study participants.

A given adverse experience assigned multiple intensity ratings is reported only once under the highest associated intensity rating.

Adverse experience terms are from MedDRA Version 10.0

Data are blinded, so participants may have received active vaccine or placebo.

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# The STEP Study

## Summary

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- High risk volunteers, including high risk women and diverse racial populations, were successfully enrolled
- Retention of high risk volunteers is challenging
- The study vaccine has been generally well tolerated
  - Study is still blinded
- Study is ongoing
  - Final results should be available by late 2008/early 2009

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# Acknowledgement

We acknowledge and thank the STEP Study participants and investigators for their dedication and commitment to this important trial

# The STEP Study Protocol Team

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- Sarah Alexander
- Susan Buchbinder
- Gail Broder
- Lisa Bull
- Ann Duerr
- Cheryl Ewing
- Dan Fitzgerald
- Paula Frew
- Lori Gabryelski
- Tirzah Griffin
- Soyon Im
- Dale Lawrence
- David Li
- Ellen MacLachlan
- Devan Mehrotra
- Robin Mogg
- Dewayne Mullis
- Gabriela O'Neill
- Mary Pleier
- Michael Robertson
- Steve Self
- Rosario Leon
- Amanda Vettori
- Steve Wakefield
- Amy Zhou

# US Sites

Investigator	Institution	City
Carlos Del Rio	Emory University	Atlanta
Paul Goepfert	University of Alabama at Birmingham	Birmingham
Ken Mayer	Fenway Community Health	Boston
Lindsey Baden	Brigham & Women's Hospital	Boston
Rick Novak	University of Illinois at Chicago	Chicago
Frank Judson	University of Colorado	Denver
Steve Tying	Center for Clinical Studies	Houston
Patricia Lee	Center for Clinical Studies	Houston
Steve Brown	AIDS Research Alliance	Los Angeles
Steve Santiago	Care Resource	Miami
Scott Hammer	Columbia University	New York City
Beryl Koblin	Project Achieve	New York City
Mike Marmor	New York University	New York City
Ronald Poblete	North Jersey Community Research Initiative	Newark
Ian Frank	University of Pennsylvania	Philadelphia
Mike Keefer	University of Rochester	Rochester
Susan Buchbinder	San Francisco Dept. of Public Health	San Francisco
Julie McElrath	University of Washington	Seattle
Sharon Frey	Saint Louis University	St Louis

# Sites outside US

Investigator	Institution	City
Martin Casapia	Asociacion Civil Selva Amazonica	Iquitos
Peter Figueroa	Ministry of Health	Kingston
Jorge Sanchez	Asociación Civil IMPACTA Salud y Educacion	Lima
Robinson Cabello	Asociación Vía Libre	Lima
Julie Bruneau	St-Luc Hospital	Montreal
Jean (Bill) Pape	Les Centres GHESKIO	Port-au-Prince
Mauro Schechter	Hospital Escola São Francisco de Assis	Rio de Janeiro
Carmen Zorilla	University of Puerto Rico	San Juan
Yeycy Donastorg	Unidad de Vacunas	Santo Domingo
Ellen Koenig	Zona Universitaria	Santo Domingo
Esper Kallas	Escola Paulista de Medicina	São Paulo
Artur Kalichman	Centro de Referência e Treinamento - DST/AIDS	São Paulo
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