



PREVENTION RESEARCH SKILLS-BUILDING FOR US ACTIVISTS AND ADVOCATES

HIV Prevention Research Update from the  
2009 Conference on Retroviruses and Opportunistic Infections (CROI)

## Introduction: How to Read an Abstract and Understanding Research Language

Thursday, February 19, 2009  
2:00 – 3:15 PM EST

*Speakers:*

Richard Jefferys, Treatment Action Group  
Walt Senterfitt, CHAMP

1

## How To Read A Research Abstract

- Dictionary definition of abstract: *A statement summarizing the important points of a text.*
- There are no universal, exact rules about how abstracts should be formatted, they vary between publications and conferences.
- Different types of research can use slightly different formats (e.g. a social science survey vs .a trial of a drug treatment)
- Overall goal is to give a brief summary of the research (there are always word count limits!).

## How To Read A Research Abstract

- Often when searching for information in conference or scientific literature databases, the abstract is all that is available, so they can be thought of as a tool to help decide whether to get the full research paper or view a conference presentation
- Because abstracts are a summary, a lot of information is left out, so it's not a good idea to rely on an abstract as the sole source of information about a study

## How To Read A Research Abstract

- The overall purpose is to explain:
  - the background as to why a research project was undertaken
  - the methods that were used
  - the results that were obtained
  - the conclusions the researchers have drawn from those results

# How To Read A Research Abstract

- **48LBSafety and Effectiveness of Vaginal Microbicides BufferGel and 0.5% PRO 2000/5 Gel for the Prevention of HIV Infection in Women: Results of the HPTN 035 Trial**
- Salim Abdool Karim\*<sup>1</sup>, A Coletti<sup>2</sup>, B Richardson<sup>3</sup>, G Ramjee<sup>4</sup>, I Hoffman<sup>5</sup>, M Chirenje<sup>6</sup>, T Taha<sup>7</sup>, M Kapina<sup>8</sup>, L Maslankowski<sup>9</sup>, and L Soto-Torres<sup>10</sup> Ctr for the AIDS Prgm of Res in South Africa, Durban; <sup>2</sup>Family Hlth Intl, Medford, MA, US; <sup>3</sup>Univ of Washington, Seattle, US; <sup>4</sup>South African Med Res Council, Durban; <sup>5</sup>Univ of North Carolina at Chapel Hill, US; <sup>6</sup>Univ of Zimbabwe, Harare; <sup>7</sup>Johns Hopkins Univ Bloomberg Sch of Publ Hlth, Baltimore, MD, US; <sup>8</sup>Ctr for Infectious Disease in Zambia, Lusaka; <sup>9</sup>Univ of Pennsylvania, Philadelphia, US; and <sup>10</sup>NIAID, NIH, Bethesda, MD, US
- **Background:** The development of female initiated HIV prevention methods is a high priority. The purpose of this study was to assess the safety and effectiveness of 2 microbicides—BufferGel and 0.5% PRO 2000/5 gel—for the prevention of male to female HIV transmission.
- **Methods:** A phase 2/2B, four-arm, randomized, placebo-controlled trial was conducted in Malawi, South Africa, Zambia, Zimbabwe, and the US. The 3 study gel arms were double-blinded, while the no gel arm was open label. The study participants were followed monthly for pregnancy, safety assessments, and study product resupply; and quarterly to assess gel and condom use and HIV infection. Gel products were temporarily discontinued at the time of first positive pregnancy test. The primary analysis of HIV effectiveness is a comparison of HIV incidence, in each active gel arm compared to each control arm.
- **Results:** We randomized 3099 women and followed them for an average of 20.4 months with a retention rate of 93.6%. There were no statistically significant differences in adverse events. Adherence to gel use was 81% across gel arms. Condom use was 72% in gel arms and 81% in no gel arm ( $p < 0.05$ ). There were 610 pregnancies for a rate of 11.3 per 100 woman-years. In a per-protocol analysis excluding time off product (5.9% of total woman-years of those on gel), 0.5% PRO 2000/5 Gel was 36% protective against HIV compared to no gel ( $p = 0.04$ ). The 0.5% PRO 2000/5 Gel was most effective among women who reported low condom use and high gel adherence.
- **Conclusions:** Women in the 0.5% PRO 2000/5 Gel arm had a 30% lower rate of HIV acquisition compared to controls, although not statistically significant in the intent-to-treat analysis. BufferGel did not alter the risk of HIV infection. Both products were safe.

# How To Read A Research Abstract

- **Background:** The development of female initiated HIV prevention methods is a high priority. The purpose of this study was to assess the safety and effectiveness of 2 microbicides—BufferGel and 0.5% PRO 2000/5 gel—for the prevention of male to female HIV transmission.

# How To Read A Research Abstract

- **Methods:** A **phase 2/2B, four-arm, randomized, placebo-controlled** trial was conducted in Malawi, South Africa, Zambia, Zimbabwe, and the US. The 3 study gel arms were **double-blinded**, while the no gel arm was **open label**. The study participants were followed monthly for pregnancy, safety assessments, and study product resupply; and quarterly to assess gel and condom use and HIV infection. Gel products were temporarily discontinued at the time of first positive pregnancy test. The **primary analysis** of HIV effectiveness is a comparison of **HIV incidence**, in each **active gel arm** compared to each **control arm**.

# How To Read A Research Abstract

- **Phase 2/2B:** Clinical trials are divided into different phases. Phase I is typically the first time something has been tried in people, so these trials are very small and look intensely at safety (and generally not efficacy). Phase 2 trials are larger and may take a first look for signs of efficacy. Phase 2B trials look at efficacy but may not be large enough to prove efficacy for certain. Phase III trials are much larger and aim to definitively show whether an intervention works or not. A large phase III trial of PRO2000 is ongoing, with results expected at the end of this year.
- **Four-arm:** An arm is the name given to different groups in a trial – different arms receive different interventions.
- **Randomized:** As participants are enrolled, they are randomly assigned to one of the different arms. The goal is to ensure the make-up of different arms is comparable (e.g. in terms of age, demographics, etc.). If one arm ends up with more young people, for example, it could influence the outcome because it might turn out that young people responded better to the intervention. This is called **bias** and randomization lessens the possibility of this happening.

# How To Read A Research Abstract

- **Placebo-controlled:** One or more arms of the study receives an inactive substance called a placebo. Placebo microbicides are not as easy to make as you might think!
- **Double-blinded:** Neither the person in the trial nor the people running the trial know which arm a participant has been assigned to.
- **Open label:** Everyone knows what they are getting. The PRO2000 trial is unusual because three arms were double-blinded, whereas one arm involved not receiving any gel at all so this arm was “open label.”
- **Primary analysis:** The main outcome measure that the researchers wanted to look at. This is specified clearly in advance in the trial protocol.
- **HIV incidence:** The rate of HIV infection. This is usually expressed as a rate per 100 “person-years” which we’ll come back to.
- **Active gel arm:** Arms of the trial receiving a microbicide gel that might have activity against HIV.
- **Control arm:** The arms of the trial receiving either a placebo gel or no gel at all.

# How To Read A Research Abstract

- Results: We randomized 3099 women and followed them for an average of 20.4 months with a **retention rate** of 93.6%. There were no **statistically significant** differences in adverse events. **Adherence** to gel use was 81% across gel arms. Condom use was 72% in gel arms and 81% in no gel arm ( $p < 0.05$ ). There were 610 pregnancies for a rate of **11.3 per 100 woman-years**. In a **per-protocol analysis** excluding time off product (5.9% of total woman-years of those on gel), 0.5% PRO 2000/5 Gel was 36% protective against HIV compared to no gel ( $p = 0.04$ ). The 0.5% PRO 2000/5 Gel was most effective among women who reported low condom use and high gel adherence.

Intention-to-treat analysis	HIV Events [woman-years]	Incidence per 100 woman-years	Hazards Ratio vs Placebo	Hazards Ratio vs No Gel
0.5% PRO 2000/5 Gel	36 [1332]	2.70	0.7 (0.5 to 1.1), $p = 0.10$	0.7 (0.4 to 1.0), $p = 0.06$
BufferGel	54 [1304]	4.14	1.1 (0.8 to 1.6), $p = 0.63$	1.1 (0.7 to 1.6), $p = 0.78$
Placebo Gel	51 [1305]	3.91		
No Gel	53 [1318]	4.02		
Overall	194 [5258]	3.69		

# How To Read A Research Abstract

- **Retention rate:** Proportion of people who remained in the trial. Participants are free to leave a trial at any time, for any reason.
- **Statistically significant:** A calculation of whether any differences between arms represent real differences or could have occurred by chance. In this case, no arm experienced more adverse events than any other. Walt Senterfitt will explain this in more detail.
- **Adherence:** The extent to which participants used the gels as the protocol instructed.
- **11.3 per 100 woman-years:** “Person years” is a way of describing the duration for which people were observed and the rate at which events occurred during that period of observation. 100 woman-years could be 100 women observed for a year, or 50 women observed for two years. In this case the 610 pregnancies that occurred in the total trial population of 3099 is being expressed as a rate: for every 100 women observed for a year, 11.3 pregnancies occurred.
- **Incidence per 100 woman-years:** The same approach as above, but used to calculate the rare at which women in each arm acquired HIV infection.

# How To Read A Research Abstract

- **Per-protocol analysis:** Per-protocol analysis is in contrast to the “Intention to treat analysis.” It is a strategy of analysis in which only patients who complete the entire clinical trial or other procedure are analyzed, not like the Intention to treat analysis which also includes the patients who dropped out. It is also sometimes called the “on treatment analysis.” In this particular case, they analyzed only the time women were using the microbicide gel, and excluded time when they weren’t (due to pregnancy, for example).
- **Hazard ratio:** This is a statistical method for measuring the difference in risk of events (in this case, acquisition of HIV infection) between arms. The researchers are measuring the difference in the rate of HIV infection among women that used PRO2000 or BufferGel compared to women that used a placebo gel or no gel at all. The first step is to calculate the rate of HIV infection per 100 person years, e.g. the rate was 2.7 for women in the PRO2000 arm vs. 3.91 for women in the placebo gel arm. This reduction in the rate of HIV infection is then expressed as a hazard ratio of 0.70, which means that there women who received PRO2000 had 30% less chance of acquiring HIV infection. But the statistics also show that this result is not quite significant and so might have occurred by chance.

# How To Read A Research Abstract

- **Conclusions:** Women in the 0.5% PRO 2000/5 Gel arm had a 30% lower rate of HIV acquisition compared to controls, although not statistically significant in the **intent-to-treat analysis**. BufferGel did not alter the risk of HIV infection. Both products were safe.

# How To Read A Research Abstract

- **Intent-to-treat analysis:** An analysis that includes information from everyone that enrolled into each arm of the trial, regardless of whether they stopped using the intervention or left the trial. The goal is to eliminate the possibility of misleading results being obtained. For example, if people who respond poorly to an intervention drop out of the trial, then an analysis of efficacy restricted to those that stayed may make it look like the intervention worked. For the purposes of ITT analysis, everyone who begins the treatment is considered to be part of the trial, whether they finish it or not. This explanation came from an excellent Wikipedia entry: [http://en.wikipedia.org/wiki/Intention\\_to\\_treat\\_analysis](http://en.wikipedia.org/wiki/Intention_to_treat_analysis)

# How To Read A Research Abstract

- Online Resources:
  - How to Read a Scientific Paper *By Carlton Hogan*
    - Pt. 1 <http://www.gmhc.org/health/treatment/ti/ti1504.html#paper>
    - Pt. 2 <http://www.gmhc.org/health/treatment/ti/ti1505.html#paper>
    - Pt. 3 <http://www.gmhc.org/health/treatment/ti/ti1506.html#paper>
- Clinical Trials Glossary: <http://clinicaltrials.gov/ct2/info/glossary>