Preventing Pregnancy in an HIV Prevention Trial: Lessons Learned from the VOICE Study

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Overview

- Introduction
- Strategies to prevent pregnancy in VOICE
- Baseline pregnancy related factors and contraceptive use
- Predictors of pregnancy
- Lessons learnt

Introduction

- Preventing pregnancy in HIV prevention trials is vital:
  - Safety of study product on pregnancy not established
  - To avoid the impact that time of study product will have on the power to detect an effective intervention
- Reported incidence ranges from 64/100 to 4/100 person years (P/Y)

Introduction

- SSA – an important region for HIV prevention trials due to increased incidence amongst young women
- High fertility rates secondary to:
  - Cultural norms and expectations
  - Gender dynamics
- Women not empowered to make decisions regarding reproductive health

VOICE (MTN 003)

- A randomized, double-blinded, placebo-controlled trial of daily oral tenofovir, oral tenofovir-emtricitabine, and 1% vaginal tenofovir gel for HIV-1 prevention.
- 360 women, between the ages of 18-45 were enrolled at CAPRISA eThekwini CRS
- Average period of follow up: 13 months (range 0-22 months)
- Women who agreed to use an effective method of contraception and had no pregnancy intention at enrolment were eligible

Contraceptive Services

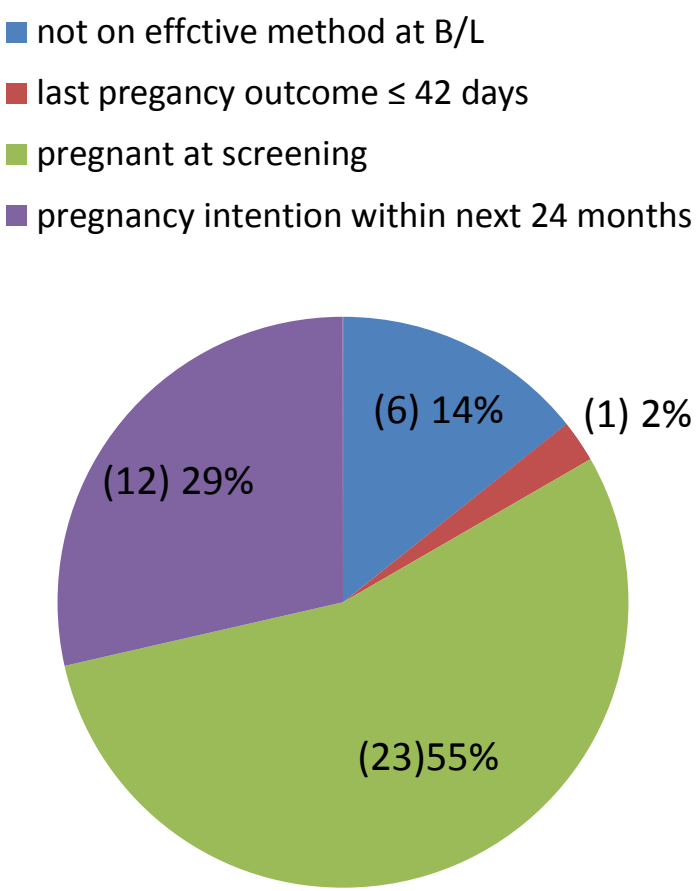
- Baseline and monthly contraceptive counselling: to assess contraceptive needs/pregnancy intention
- Pregnancy testing conducted at screening, enrolment and at monthly follow up visits
- Accessibility: Hormonal contraception (injectable –DMPA/NET-EN and combined oral contraceptives –COCs) provided on site
- Referrals facilitated for IUCD insertion and tubal ligation to public sector facilities

Monitoring of Contraceptive Use

- Contraceptive log and “Follow up Family Planning” CRF used to track contraceptive use
- Documentation of DOH accessed services- signed FP card
- Urine pregnancy testing conducted at every monthly follow up visit

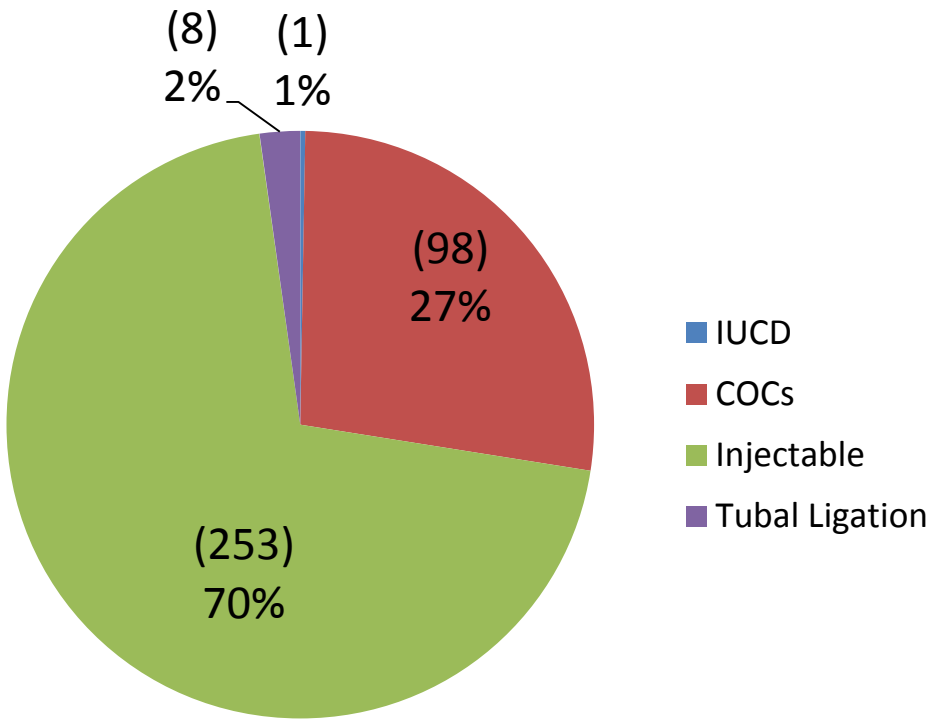
Pregnancy Screening Failures

- 772 screened/ 412 screening failures
- 42 (5,5%) of 772 women were ineligible due to pregnancy related factors



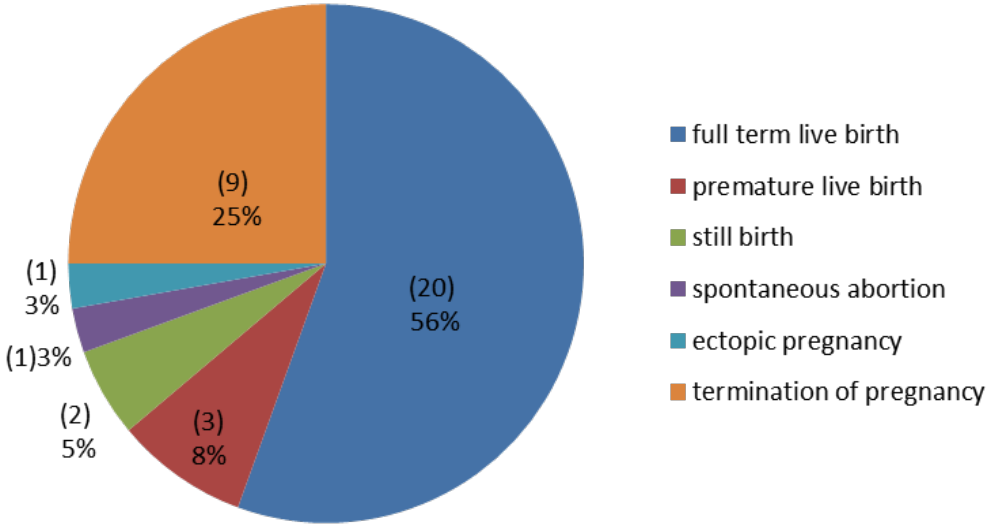
Baseline Contraceptive Use

- More than two thirds of women opted for injectable contraceptives
- 277 (77%) reported condom use at the time of enrolment



Pregnancy Incidence & Outcomes

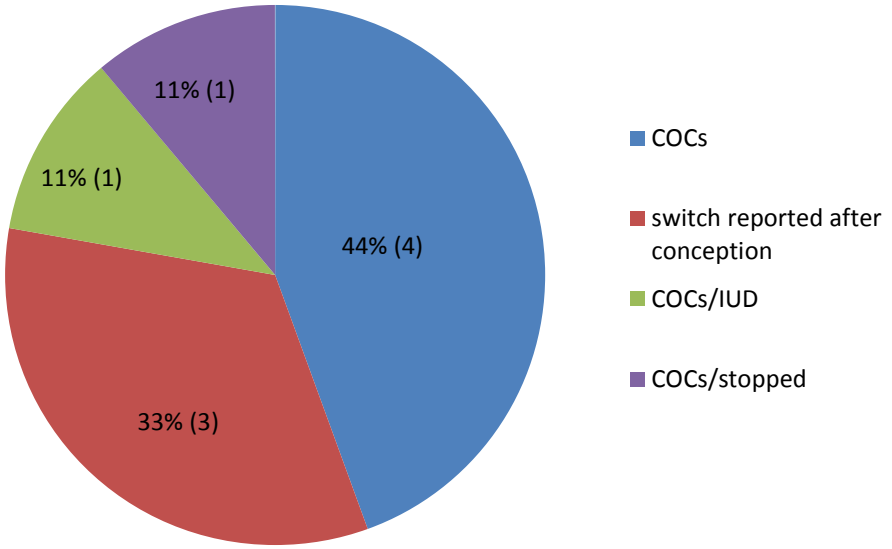
- 358 women followed up/ 35pregnancies/ 36 outcomes
- Pregnancy incidence 9.7/100 PY (95% CI: 6.7,13.5)
- 25% opted for termination of pregnancy



Contraception and Pregnancy

- COCs:
  - Baseline: 74% (26/35)
  - At conception: 83% (29/35)
- Injectable:
  - Baseline:26% (9/35)
  - At conception: 8,5% (3/35)

switch from injectable contraception



Pregnancy Incidence

	All arms	TDF	FTC/ TDF	Oral placebo	Tenofovir 1% gel	Gel placebo
Incidence rate (100 PY)	9.7	5.4	11.7	4.5	17.2	10.3
95% CI	[6.7,13.5]	[1.1,15.8]	[1.2,11.6]	[1.2,11.6]	[8.6,30.8]	[4.1,21.2]

P value testing comparison between the Tenofovir and gel placebo arms = 0.31

Time to Pregnancy

- 46% of pregnancies occurred during the first 6 months. 37% of total pregnancies occurred within first 3 months
- Pregnancy incidence increased slightly at month 24 because of pregnancies reported at study end visit

Table: Pregnancy Incidence Rates at 6 month intervals

Follow up time in months	6 months	12 months	18 months	24 months
Cumulative pregnancies	16	27	33	35
Incidence rate (per 100 PY)	9.3	8.8	9.2	9.7

Summary

The following were not conclusive risk factors for pregnancy in this data set:

- Randomization arm
- Younger age
- level of education
- Income source
- Marital status, having/living with primary partner

Summary

Risk factors for pregnancy:

- Not having living children at baseline (p 0.049)
- COCs as a method of contraception (p<0.001)

Limitations of this analysis:

- No accurate measure of contraceptive use at study end: missing data for contraceptive use within 3 months of study exit

Lessons Learnt

- Counselling around reasons for ineligibility must be discrete
- Active promotion of IUCD as a contraceptive method/on site provision of IUCD insertion
- In depth discussion around pregnancy intention taking into account social and cultural factors
- Addressing contraceptive related adverse events
- Addressing timing of contraceptive switching
- Importance of study in HIV prevention field and the effect of pregnancy/time of study product

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