

Providing Contraceptive Service in HIV Prevention Trials

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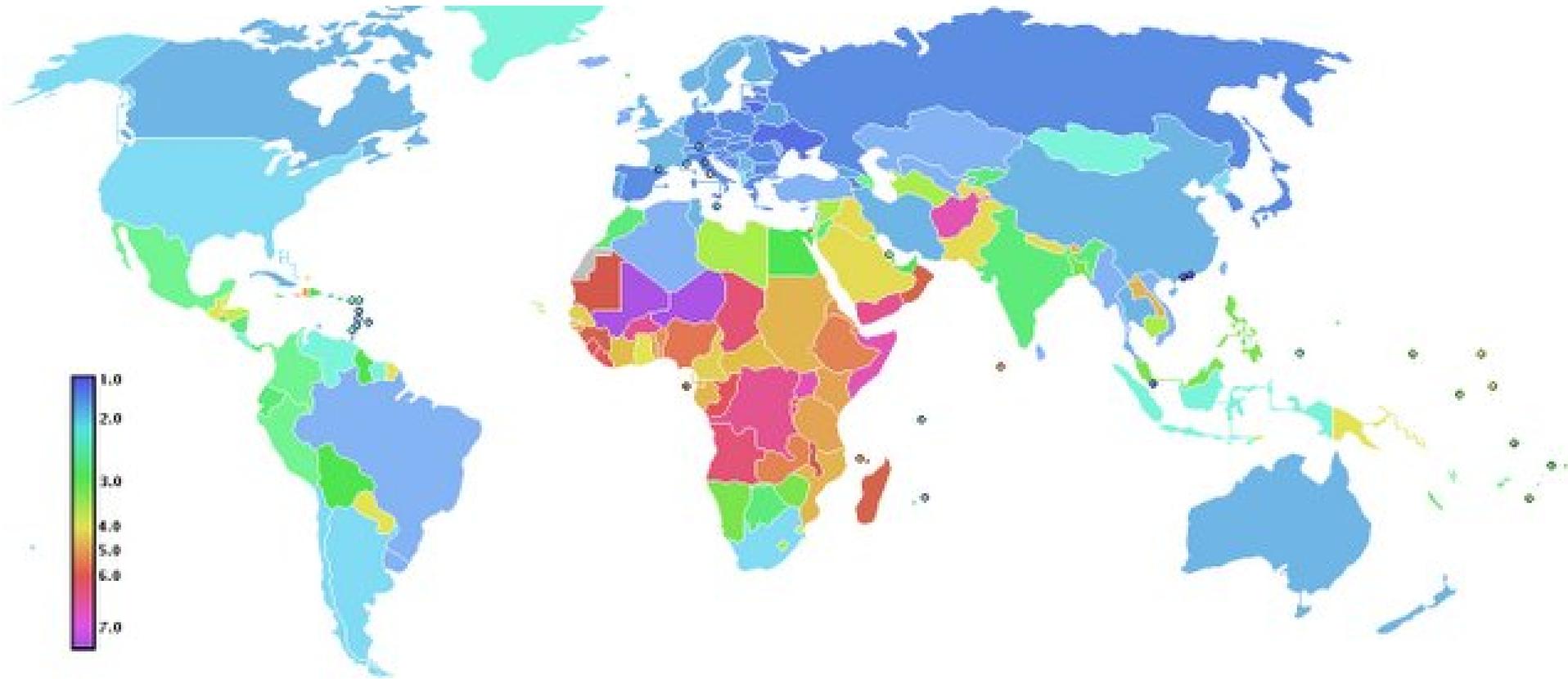
Outline

- Importance in the context of clinical trials
- Share experience of two HIV prevention trials
- Predictors of Pregnancy in these cohorts
- Strategies suggested to reduce pregnancy incidence

Introduction

- Relevance of Prevention Research in our setting
 - Sub-Saharan Africa
 - Vulnerability of women
- Protocols of biomedical interventions
 - Oral antiretroviral PrEP and topical vaginal microbicides
 - Women of reproductive age : fertility desires
- Counseling and provision of contraception on-site
- Safety and efficacy of new interventions
- Impact of pregnancies on statistical power of trials

Total Fertility Rate



Total Number of children a woman would have at the end of her reproductive period given age specific fertility rates

Objectives

Effect of contraception provision on pregnancy rates in :

- HPTN 039

- Pregnancy, Contraception, and HIV Acquisition in HPTN 039: Relevance for HIV Prevention Trials (JAIDS)

Analyses to :

- characterize the prevalence and predictors of pregnancy,
- evaluate the effect of contraceptive use on pregnancy and HIV risk
- assess the association between pregnancy and incident HIV infection



Acquisition in HPTN 039: Relevance for HIV Prevention Trials (JAIDS)

Analyses to :
• characterize the prevalence and predictors of pregnancy, evaluate the effect of contraceptive use on pregnancy and HIV risk

• assess the association between pregnancy and incident HIV infection

- MDP 301

- Secondary data analysis of MDP 301 clinical trial data

- Incident cases of HIV infection from October 2005 to September 2009
- To describe the relationship between pregnancy and incident HIV infection



Incident cases of HIV infection from October 2005 to September 2009

To describe the relationship between pregnancy and incident HIV infection

HPTN 039

Methods

- Enrolment : 1358 HIV negative, HSV-2 seropositive women from SA, Zambia, and Zimbabwe
- 18 month follow-up (Oct 03 to Nov 07)
- Consent included counselling to avoid pregnancy
- Pregnant women were excluded from enrollment
- Urine pregnancy testing
- Study drug was withheld in pregnancy during follow-up
- Resumption of study drug after a pregnancy was completed
- Status of infants born

Table 1: Pregnancy Incidence and Outcomes

| | South Africa | | Zambia | | Zimbabwe | | Total | |
|--|--------------|------------|--------|------------|----------|------------|-------|------------|
| | N | % | N | % | N | % | N | % |
| Total number of pregnancies | 47 | 100 | 139 | 100 | 42 | 100 | 228 | 100 |
| Number of women with 1 pregnancy | 37 | | 118 | | 40 | | 195 | |
| Number of women with >1 pregnancy | 5 | | 9 | | 1 | | 15 | |
| Time from enrollment to first pregnancy in months, median (IQR) | 7.0 | (3.7/12.1) | 7.8 | (5.0/12.8) | 8.9 | (4.9/13.8) | 7.9 | (4.9/12.8) |
| Pregnancy incidence throughout follow-up (per 100 woman-years) | 9.9 | | 18.3 | | 8.4 | | 13.2 | |
| Pregnancy outcome | | | | | | | | |
| Full term live birth | 15 | 31.9 | 67 | 48.2 | 27 | 64.3 | 109 | 47.8 |
| Premature live birth | - | - | 2 | 1.4 | 1 | 2.4 | 3 | 1.3 |
| Foetal death/still birth | 1 | 2.1 | 2 | 1.4 | 1 | 2.4 | 4 | 1.8 |
| Miscarriage | 15 | 31.9 | 42 | 30.2 | 12 | 28.6 | 69 | 30.3 |
| Ectopic pregnancy | 2 | 4.3 | - | - | - | - | 2 | 0.9 |
| Elective termination | 14 | 29.8 | 2 | 1.4 | - | - | 16 | 7.0 |
| Missing | - | - | 24 | 17.3 | 1 | 2.4 | 25 | 11.0 |

Enhanced FP services at sites : 15.9 to 12.8 per 100 wys (p=0.23)

SA Site: 14.9 to 9.6 per 100 wys

Zambia : 21.1 to 17.8 per 100wys

Zimbabwe: 6.7 to 8.6 per 100 wys

Table 2. Risk Fa

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"But I take the pill everytime I become pregnant, and it doesn't help."

| |
|--|
| |
| |
| Age |
| <21 |
| 21-24 |
| 25-29 |
| 30-34 |
| ≥35 |
| Contraceptive |
| None |
| Oral |
| Injectable |
| IUD/other |
| Condom |
| Menopause |
| Missing |
| Unprotected vaginal sex at last 3 months |
| 0 |
| 1-12 |
| 12-36 |
| >36 |

| | |
|-----|---------|
| ate | |
| I | p-value |
| | Ref |
|) | 0.23 |
|) | 0.02 |
|) | 0.02 |
|) | <0.0001 |
| | Ref |
|) | <0.0001 |
|) | <0.0001 |
|) | 0.03 |
|) | 0.09 |
|) | 0.97 |
|) | <0.0001 |
| | |
|) | <0.0001 |
|) | <0.0001 |
|) | 0.001 |

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MDP 301

Methods

- Enrolment : 2508 HIV seronegative women from Soweto and Orange Farm (26.7% of trial cohort)
- 12 month follow-up (Oct 05 to Sept 09)
- Consent included counselling to avoid pregnancy
- Pregnant women were excluded from enrollment

- Quick Vue Urine rapid test on-site
- Confirmation by serum β HCG

- Study drug was withheld in pregnancy during follow-up
- Resumption of study drug after a pregnancy was completed
- Status of infants born

Figure 1 : Reported Contraception use at Enrolment and Wk 52 visit

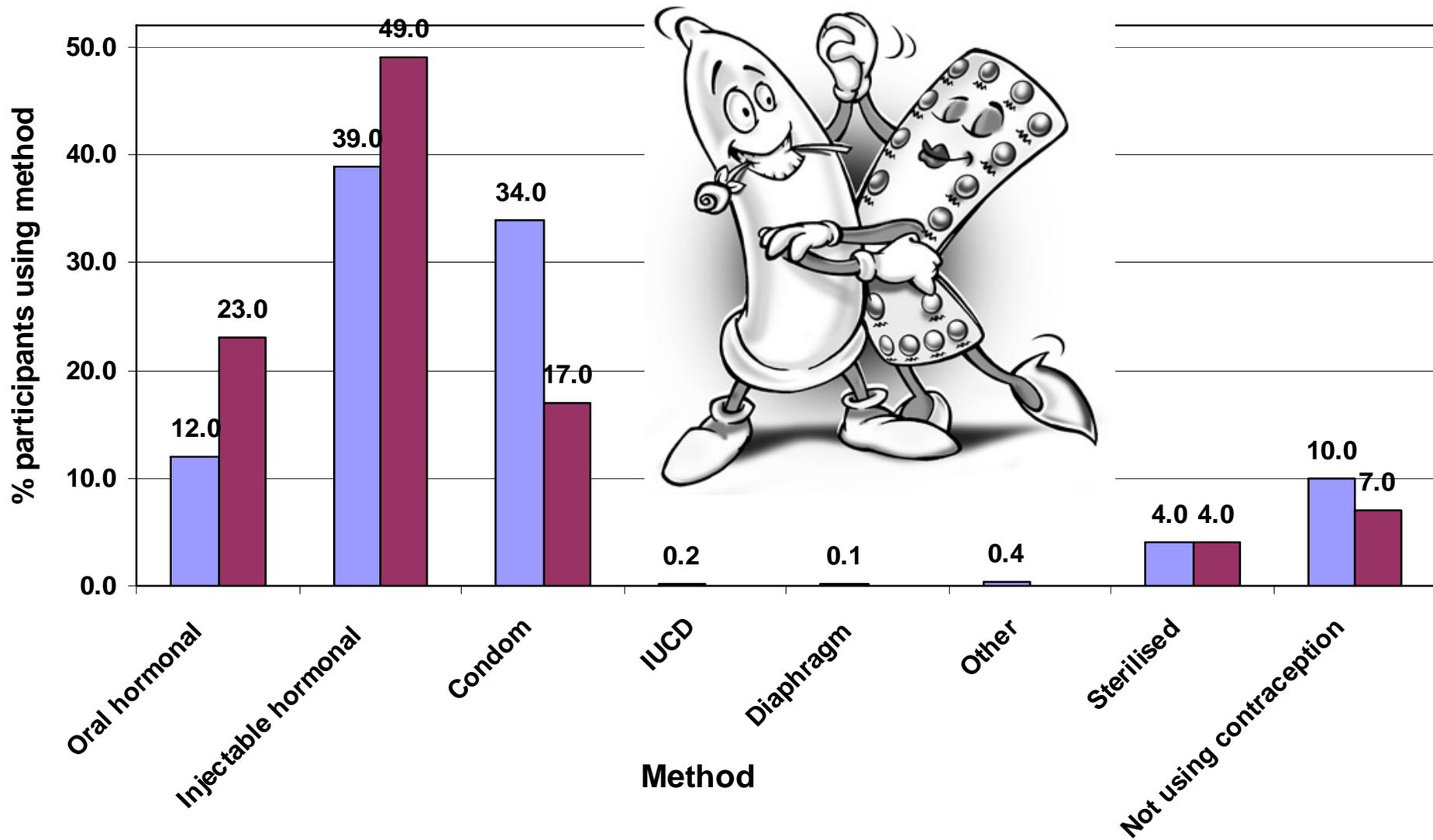


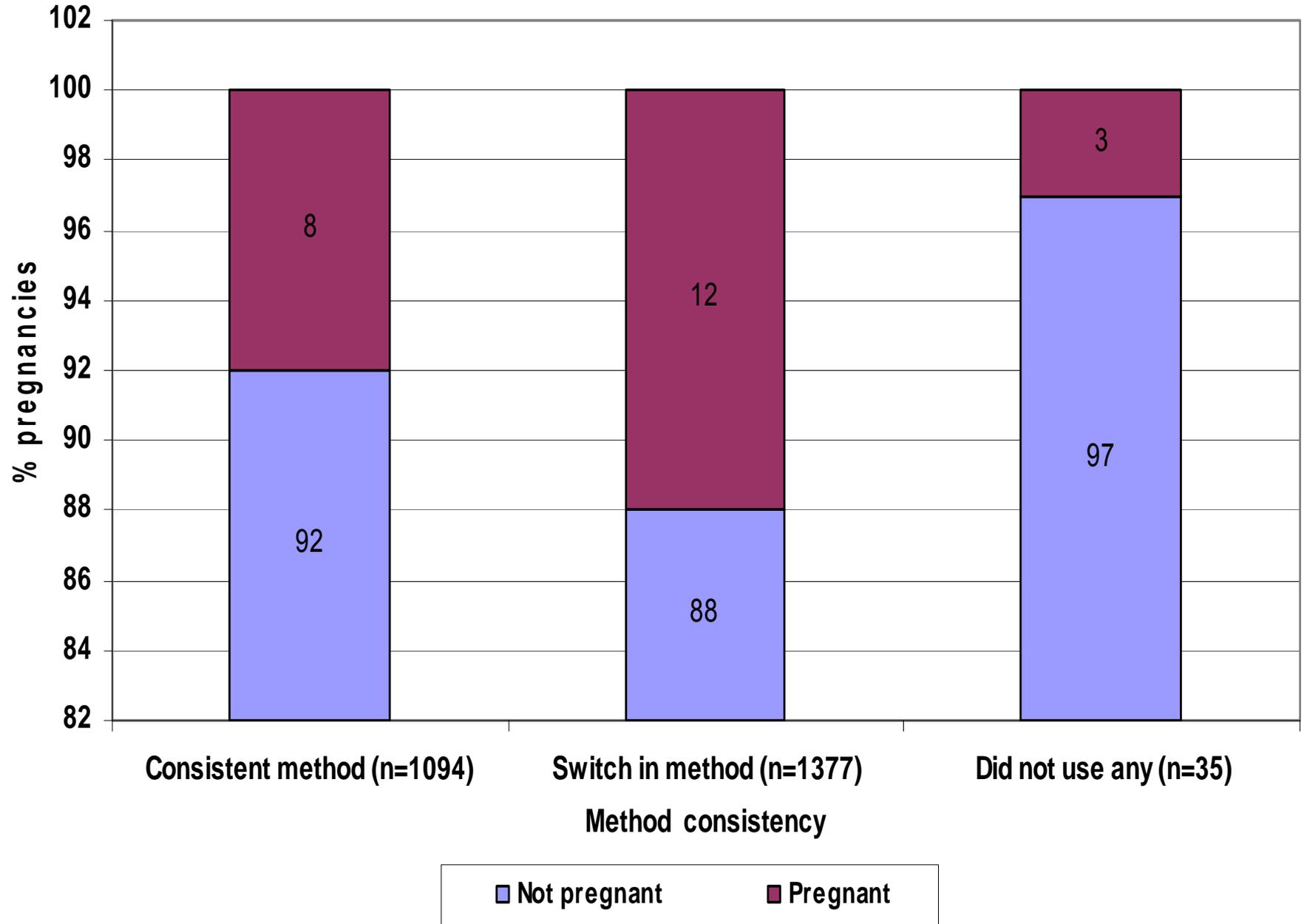
Table 3: Risk Factors for Pregnancy in MDP 301, Jhb Sites

Total : n=246

Pregnancy incidence: 10.7 per 100 woman-years (95% CI 9.4 – 12.1)

| | Univariate | | | Multivariate | | |
|------------------------|------------------------|---|-------|----------------------|---|-------|
| | HR | 95% CI | p | HR | 95% CI | p |
| Age | | | | | | |
| 18-24 | Ref | | | Ref | Ref | |
| 25-34 | 0.85 | 0.65 - 1.12 | 0.272 | 0.9 | 0.69 - 1.12 | 0.349 |
| ≥35 | 0.35 | 0.22 - 0.56 | 0.000 | 0.44 | 0.27- 0.71 | 0.001 |
| Education Level | | | | | | |
| None | Ref | | | | | |
| Primary | 5.01 x 10 ⁷ | | | 6.37x10 ⁷ | | |
| Secondary | 1,94x10 ⁸ | 7.20x10 ⁷ - 5.21x10 ⁸ | 0.000 | 1.28x10 ⁸ | 5.57x10 ⁷ - 4.24x10 ⁸ | 0.000 |
| Tertiary | 1.38x10 ⁸ | 4.4x10 ⁷ - 4.36x10 ⁸ | 0.000 | 8.74x10 ⁷ | 3.12x10 ⁷ - 3.25x10 ⁸ | 0.000 |
| Method | | | | | | |
| Switching method | Ref | | | | | |
| Consistent | 0.70 | 0.54-0.92 | 0.010 | 0.78 | 0.59-1.01 | 0.061 |

Figure 2: Pregnancies by consistency of contraceptive method used



Percentage of pregnancies by month of follow up

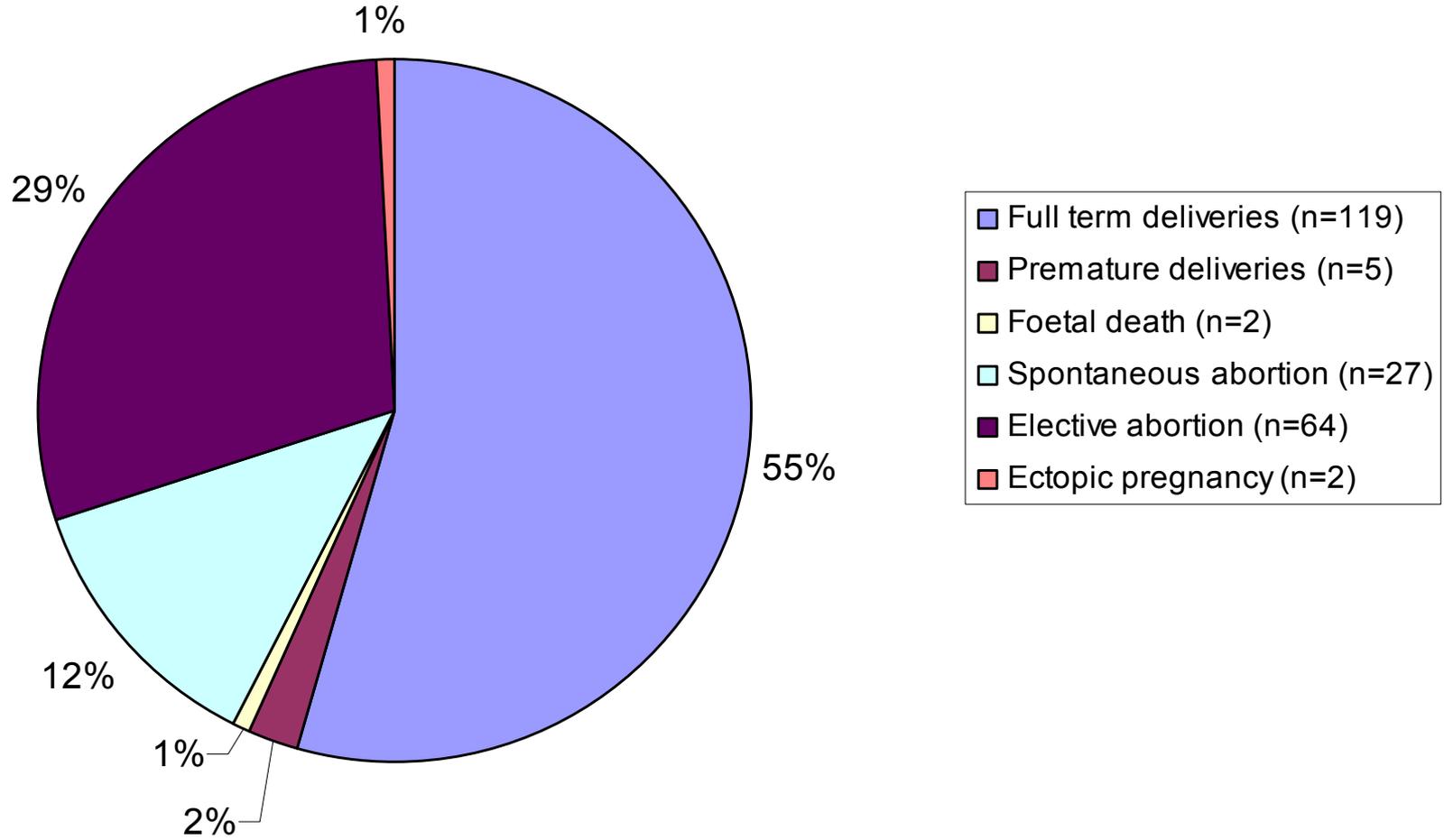
| | n | % |
|------------------|-----------|-----------|
| Month 3 | 78 | 32 |
| Month 6 | 73 | 30 |
| Month 9 | 43 | 18 |
| 1 year | 48 | 20 |
| 1 year 1m | 2 | 1 |

Percentage of pregnancies by year of trial

| | n | % |
|---------------|------------|-----------|
| Year1* | 48 | 20 |
| Year2 | 72 | 29 |
| Year3 | 102 | 41 |
| Year4 | 24 | 10 |

*year 1 was from 10/10/2005 to 09/10/2006, similarly for years 2 to 4

Figure 3 : Pregnancy outcomes





"Fortunately, we caught the problem before it grew too big!"

Strategies

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"THEY STOP HER GOING ON
ABOUT US STARTING A FAMILY!"

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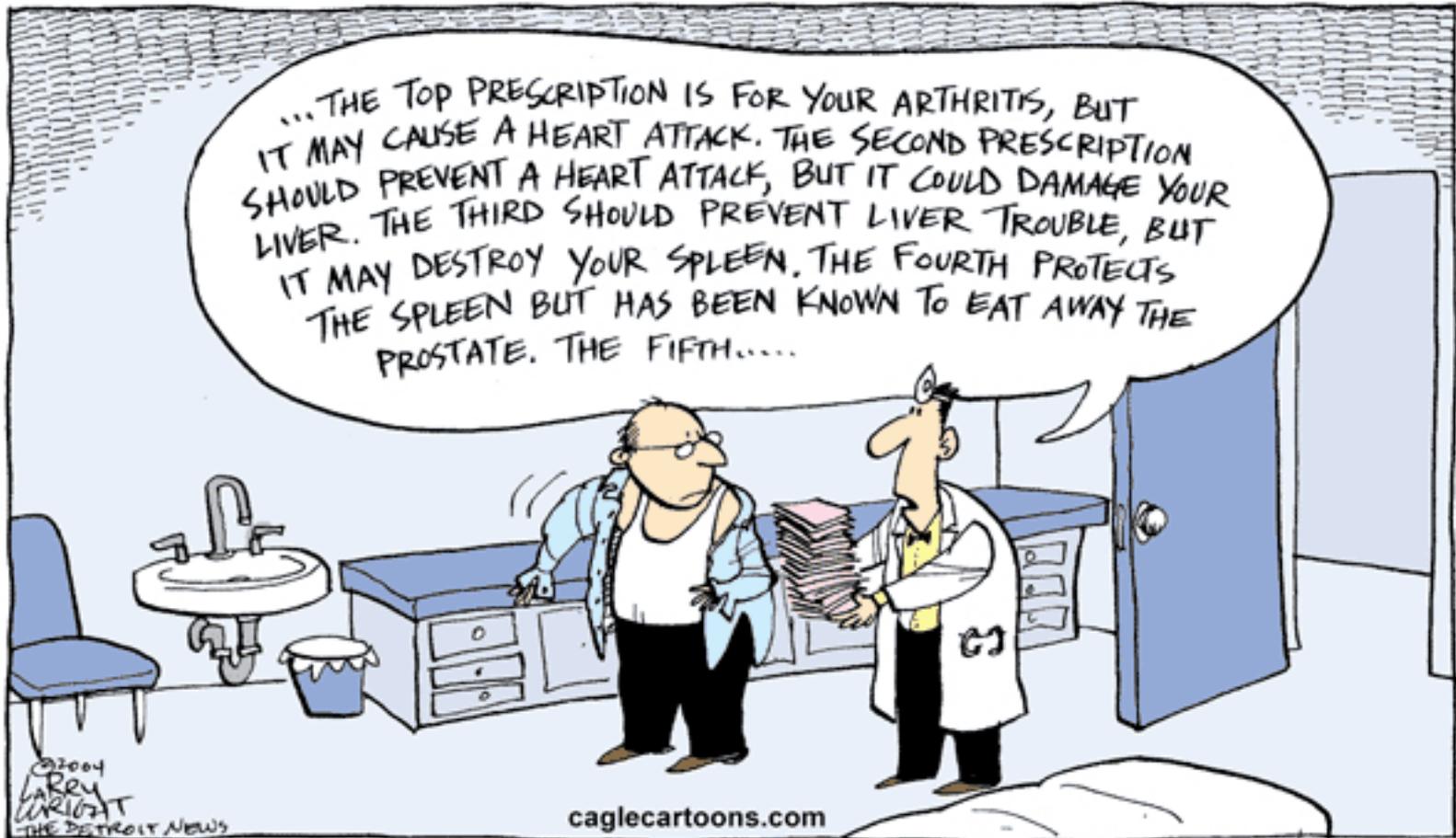


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"You look like a strong man —
could you get the lid off this
container of birth control pills?"

Male involvement

Strategies



More options with less side effects

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