

***The Preterm Prevention Project:  
Development of an Evidence-Based  
Intervention***

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# Reference

**Recruitment and retention of women in a large randomized control trial to reduce preterm birth: The Philadelphia Collaborative Preterm Prevention Project. *BMC Medical Research Methodology* 2010 10.88.**

# Background Research

- ◆ Risk factors tend to co-occur.
- ◆ Many risk factors for PTB are associated with inflammation.
- ◆ Risk of PTB is retained across pregnancies.
- ◆ Normal shift towards Th2-type cytokines across gestation.
- ◆ When the shift to Th2-type immunity is incomplete may result in PTB.

# Background Research

- ◆ Normal term labor may be initiated as a result of a reversal from the Th2 to the Th1 type cytokine profile.
- ◆ Women entering pregnancy with an enhanced inflammatory state may fail to achieve the Th2 dominance or reach a Th1 threshold early.
- ◆ Almost every intervention conducted to reduce PTB, including those targeted at infection have been conducted during pregnancy.

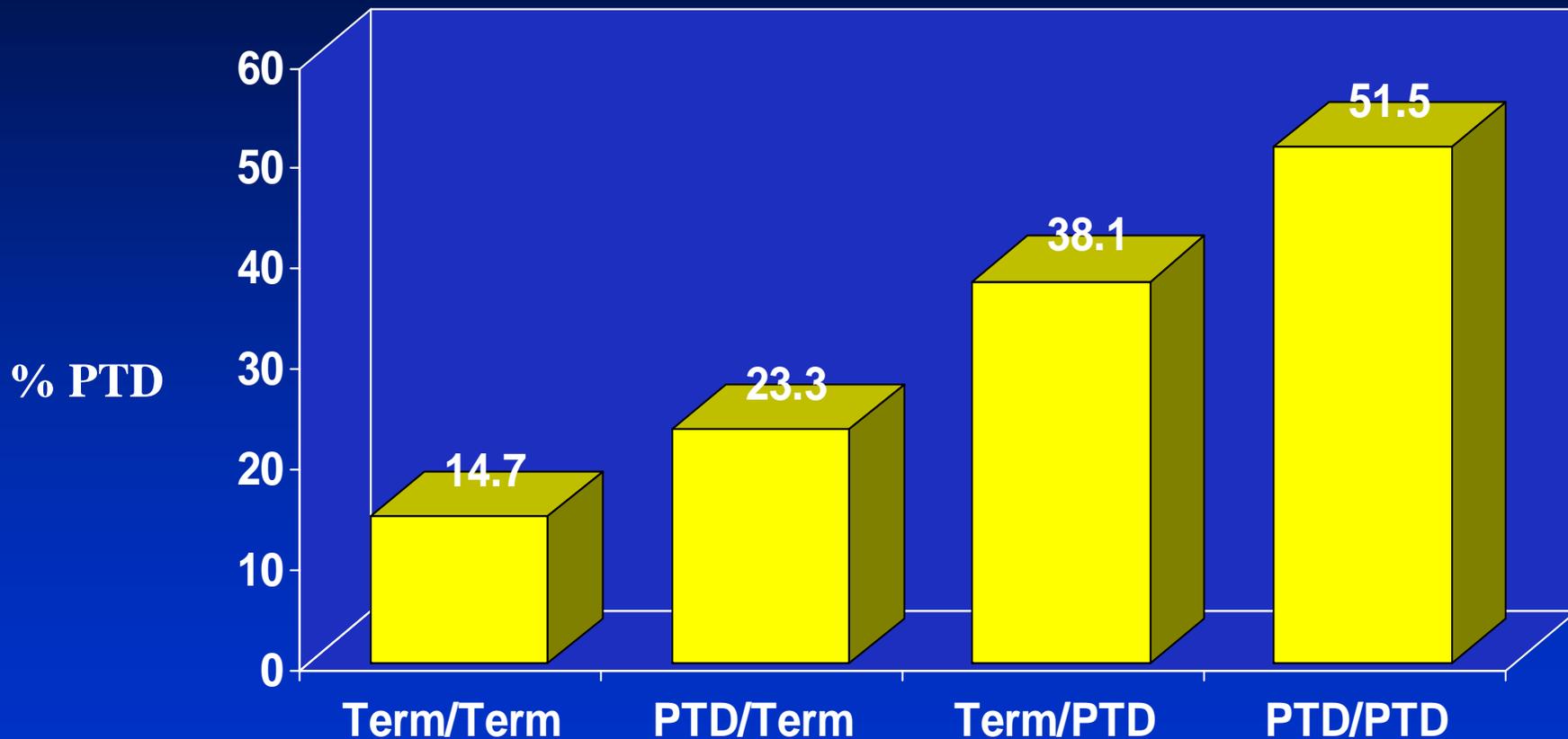
# **Aim**

- **Reduce smoking, depression, infection, stress and achieving an appropriate BMI in the interconception period among women experiencing a previous PTB, to reduce markers of systemic inflammation and the rate of repeat PTB.**

# **Study Development : Why the Interconception Period**

- ◆ **Interventions during pregnancy to reduce PTB have little efficacy - timing?**
- ◆ **Best predictor of preterm delivery is a previous preterm delivery- risk retained?**

# Prematurity Risk Based on Prior Pregnancy Outcome



Salama et al, 1994

# Prematurity Rates Based Upon Previous Pregnancy Outcomes

- ◆ Results from the MFMU progesterone trial
- ◆ 50% of women in the usual care group with a history of a prior PTB at <32 weeks had a repeat preterm birth

# **Selected Interventions: Evidence of Association with Inflammation and PTB**

- **Maternal Stress (housing/health literacy)**
- **Periodontal disease- moderate to severe**
- **Urogenital Tract Infections**
- **Depression**
- **Nutritional counseling - emphasis on pre pregnancy BMI's <19**
- **Smoking cessation**

# **Maternal Stress: Association with PTB and Inflammation**

- **Women experiencing psychosocial stress in pregnancy are between 1.5 -2.0 times as likely to have a PTB even after adjustment for biomedical and behavioral attributes.**
- **Stress influences the immune system in very complex ways and may have opposite effects systemically and locally.**

# **Maternal Stress: Association with PTB and Inflammation**

- ◆ Evidence suggests that glucocorticoids and catecholamines may systemically shift the Th1/Th2 balance towards Th2.
- ◆ Evidence also suggests that both also up regulate production of pro-inflammatory cytokines locally.

# **Infection: Association with PTB and Inflammation**

- **Urogenital tract infections confer 1.5 – 4.0 times the risk of PTB.**
- **Infection can activate the decidua and fetal membranes to produce TNF- $\alpha$ , IL-1 $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, G-CSF, proteases and prostiglandins**

# **Smoking: Association with PTB and Inflammation**

- **Smoking confers 1.2 – 2.0 times the risk of PTB after adjustment for other risk factors.**
- **IL-6 and CRP levels are significantly elevated in smokers as compared to non-smokers.**

# **BMI: Association with PTB and Inflammation**

- **Adipose tissue makes IL-6 driving up the production of CRP in the liver.**
- **There is a linear association between BMI and CRP.**
- **BUT.....**

# BMI

- **Thin women have substantially more preterm and growth restricted infants than average sized women**

# **Depression: Association with PTB & Inflammation**

- Association with PTB inconsistent with some data showing women with depressed mood 2-3 times as likely to experience a PTB
- Reduced NK cell activity
  - Improves with remission of depression
- Cytokines levels correlated with depressive symptoms (IL-1  $\beta$ , TNF  $\alpha$ ).
- Treatment with immune activators (interferon) associated with depression.
  - Treatment with antidepressants (SSRIs) counteract this adverse effect.

# The Study

- **Enrolled before discharge**
  - **Consent**
  - **Medical chart**
  - **Survey**
  - **Randomization**
  - **Smoking Intervention begins**
  - **Schedule 1<sup>st</sup> postpartum visit (1 month)**

# Postpartum Study Visits

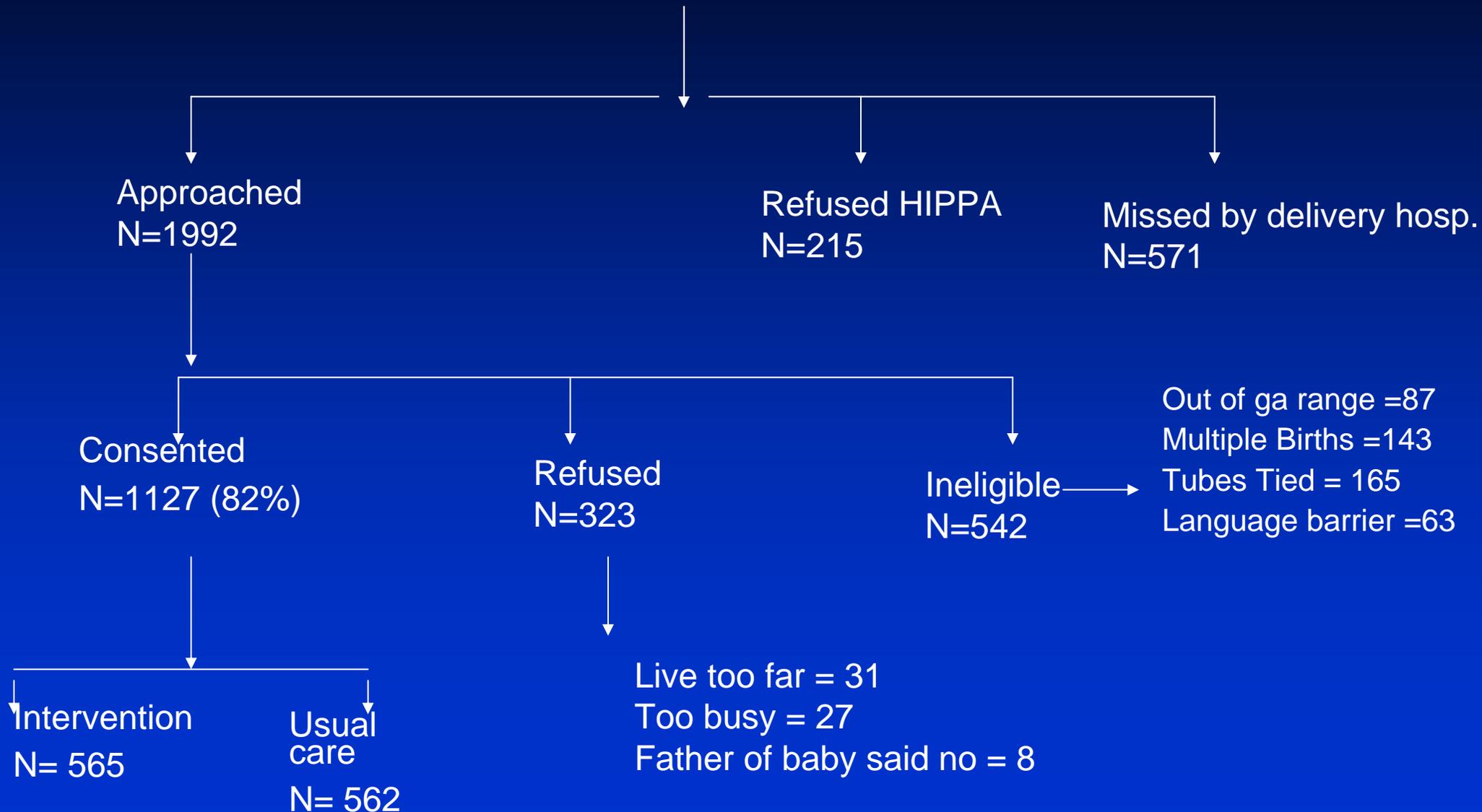
- When: 1, 6, 12, 18, and 24 months postpartum
- Or, at 20 weeks gestation of the subsequent pregnancy (n=200)

# Postpartum Study Visits

- Survey
- Periodontal exam (1, 12 and 24 months only)
- Vaginal fluid (self collection)
- Blood
- Urine
- Anthropometric measurements
- Blood pressure
- Transportation, flexible hours, childcare, barriers eliminated

# Recruitment

2778 Women Identified



# Sample Characteristics

<b>Black Race/ethnicity</b>	<b>71.5%</b>
<b>Mean Maternal Age</b>	<b>25 +/- 6</b>
<b>Single</b>	<b>80%</b>
<b>&lt; HS Ed</b>	<b>32%</b>
<b>Medicaid</b>	<b>68%</b>
<b>Income &lt;\$10,000/yr</b>	<b>18.5%</b>

# **Summary: Prevalence of risk factors**

**n = 562**

<b>Housing Inadequacies</b>	<b>75%</b>
<b>Periodontal Disease</b>	<b>55%</b>
<b>Depression Symptoms</b>	<b>45%</b>
<b>Smoking</b>	<b>38%</b>
<b>Urogenital Tract Infections</b>	<b>35%</b>
<b>Clinical Depression</b>	<b>31%</b>
<b>Low Literacy</b>	<b>23%</b>
<b>Low BMI</b>	<b>19%</b>

# Multiple Risk Factors

Number of Risk Factors	Percent
0	23.1
1	15.9
2	19.2
3	20.9
4+	20.5

# Summary of Participation Rates

Intervention	Accepting	Participating
Infections	100%	89%
Housing	92%	83%
Periodontal	89%	52%
Literacy	68%	48%
Nutrition	63%	44%
Depression	71%	40%
Smoking	52%	29%

\* The percent of women completing treatment is significantly less than those participating

# **Selected Findings**

- ◆ **Exposures associated with adverse outcomes are moderately prevalent and co-occur.**
- ◆ **There is a wide range of participation across interventions- even with every traditional barrier to care addressed.**
- ◆ **Volunteering for treatment is MUCH different than random assignment to treatment- people who really need the intervention may not seek care**

# **Important Research Questions**

- ◆ **Why don't some women avail themselves of care?**
  - **Not just traditional barriers to care**
  - **Complex decision making that may seem irrational to providers but may make perfect sense in certain contexts- what are those contexts?**

# Important Research Questions

RHIME factors (Racism, Housing challenges, Insufficient resources, Multiple burdens and Emergencies) play a role in women's everyday lives and influence care participation

We need to become aware of, document and *address* the ways various institutional structures, rules and ways of doing business create additional burdens for already stressed women

# Summary

**Targeting a single risk factors may not be sufficient – common mechanism**

**Timing of intervention is critical- PNC too late**

**Truly ‘at risk’ women may not participate**

**Even if an intervention “works” it may not be successfully implemented- what do we mean by works?**

**More research needed to understand complex barriers to participation**