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DEPARTMENT OF OB/GYN

PRENATAL CARE INTERVENTIONS AND CHILD HEALTH - PITFALLS AND OPPORTUNITIES

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PITFALLS

- I. INFLUENCE OF ‘STATUS’
- II. PERINATAL FUNNEL

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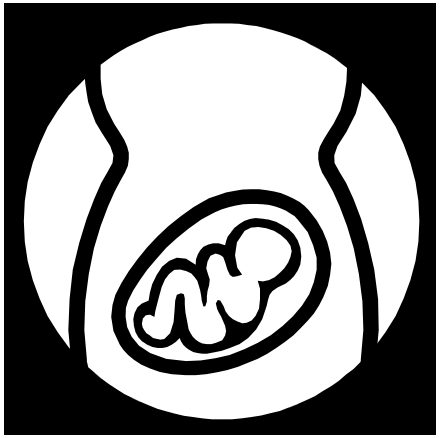

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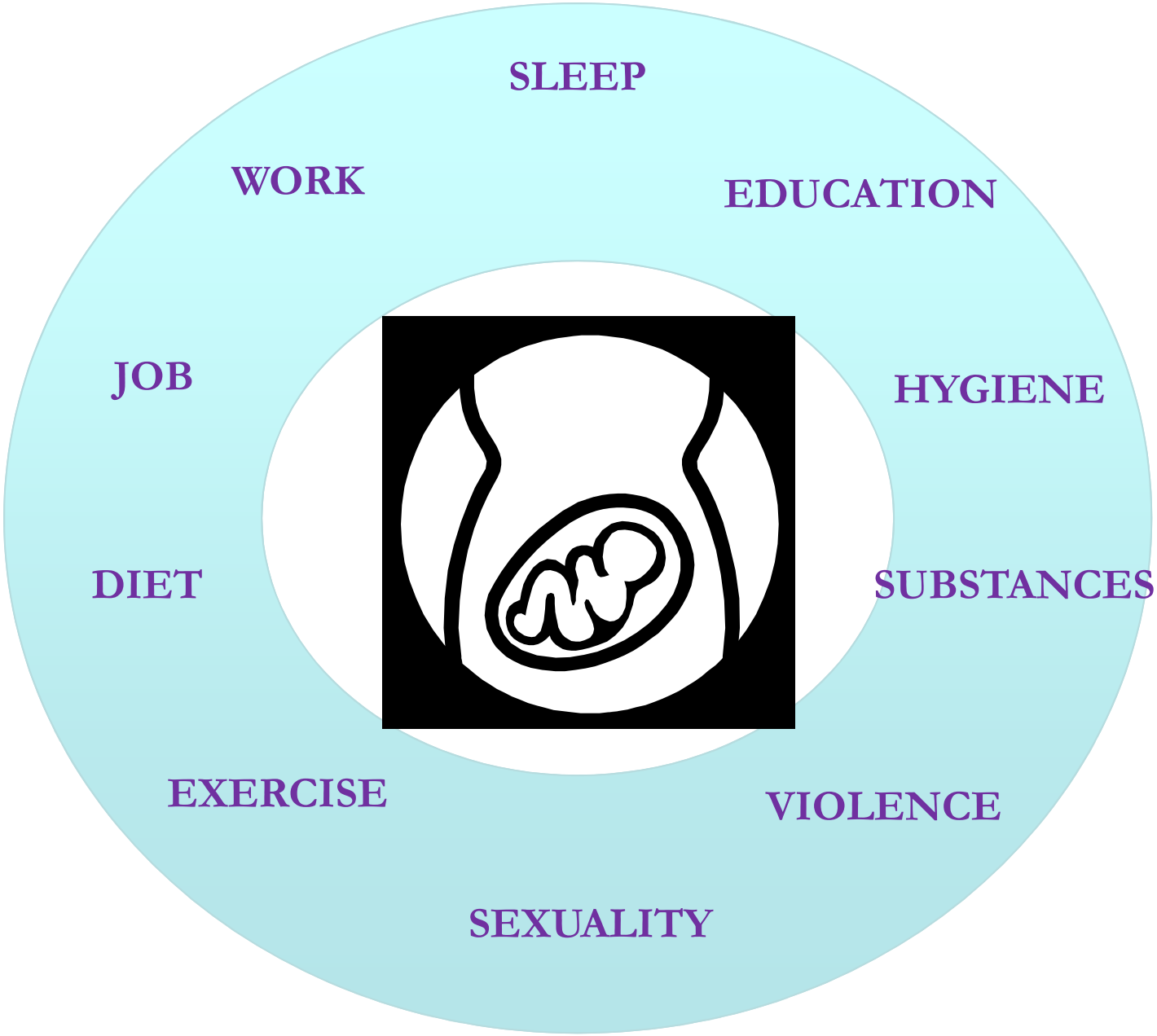

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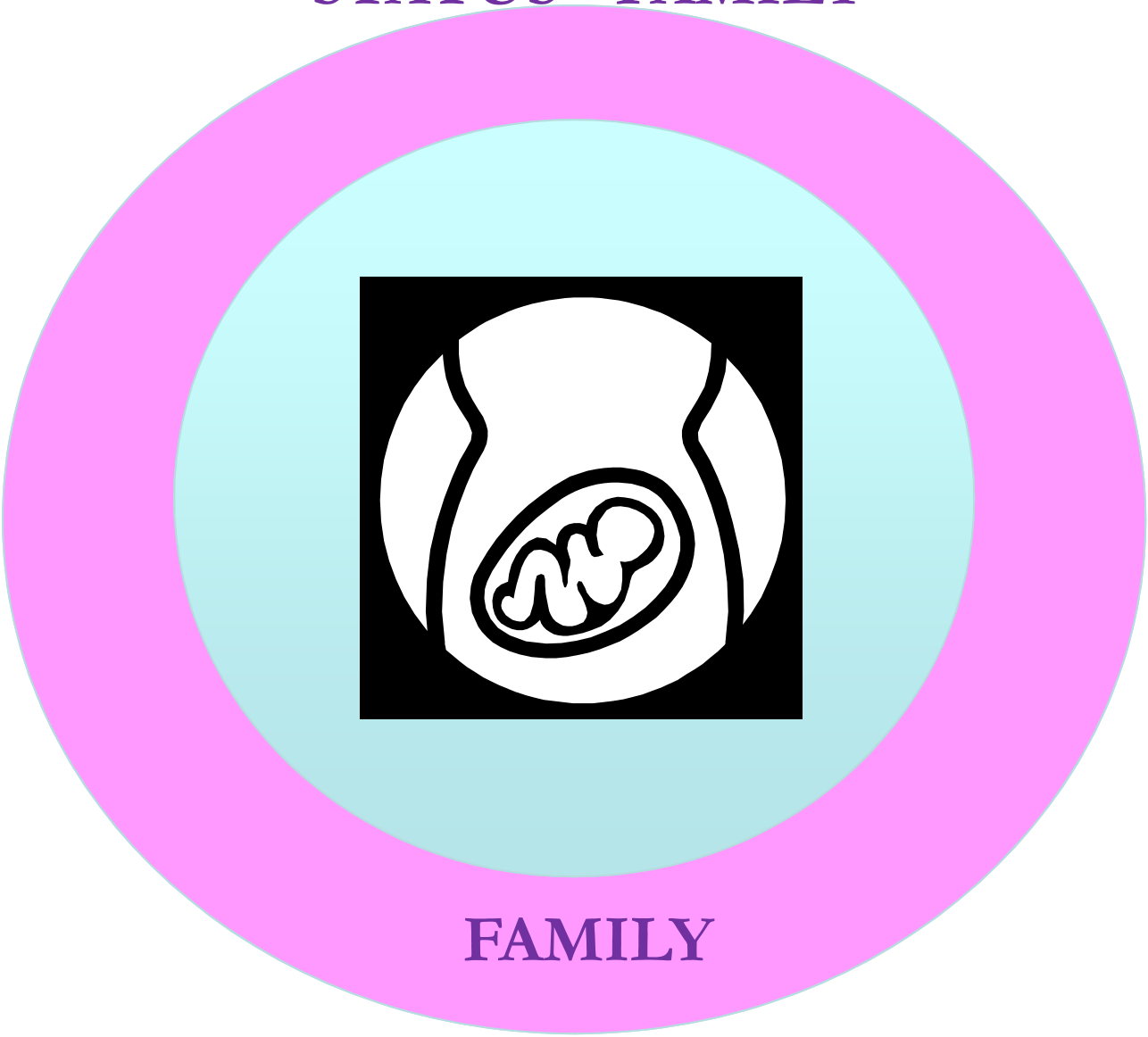
STATUS - FAMILY



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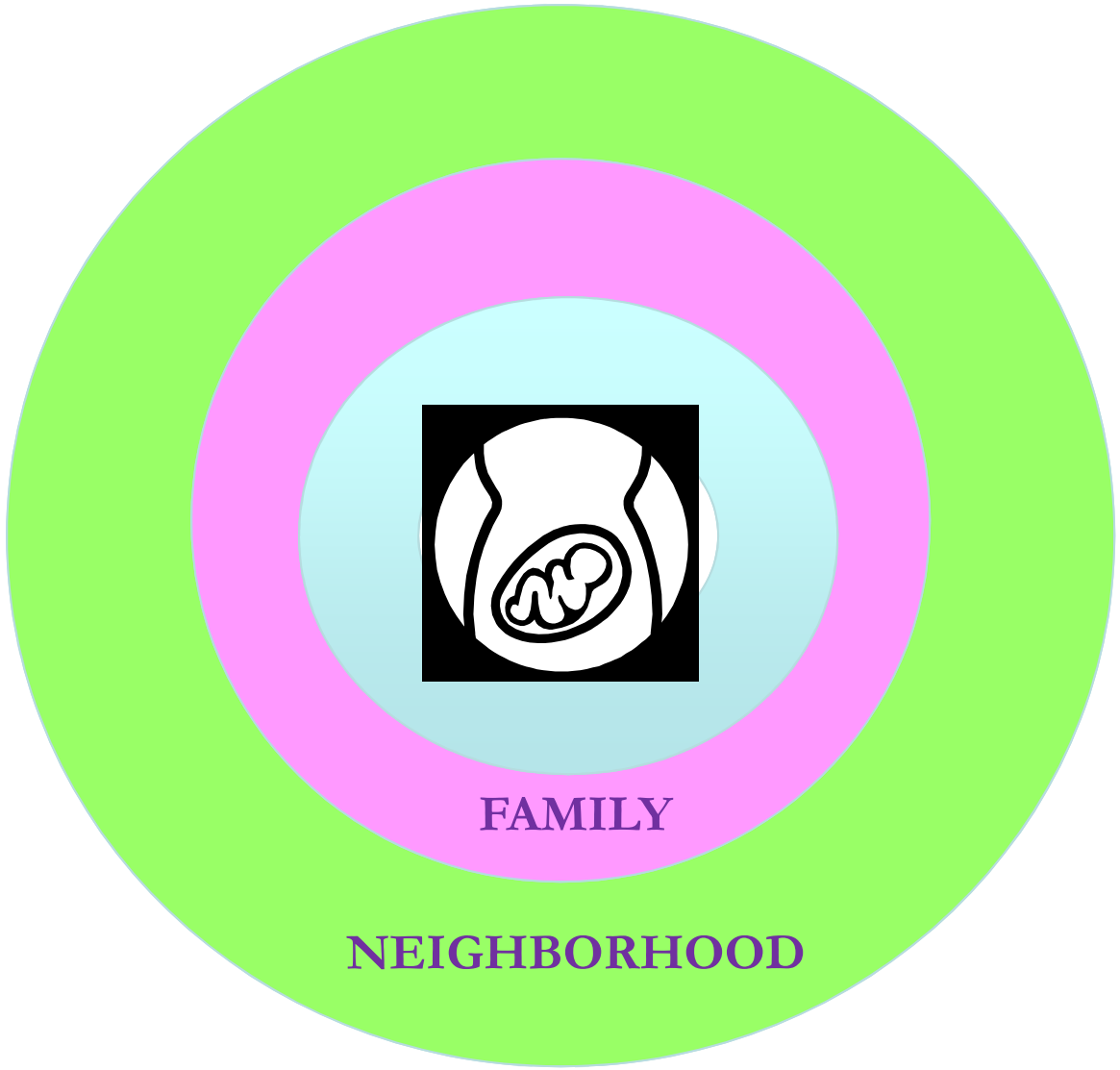
STATUS - NEIGHBORHOOD



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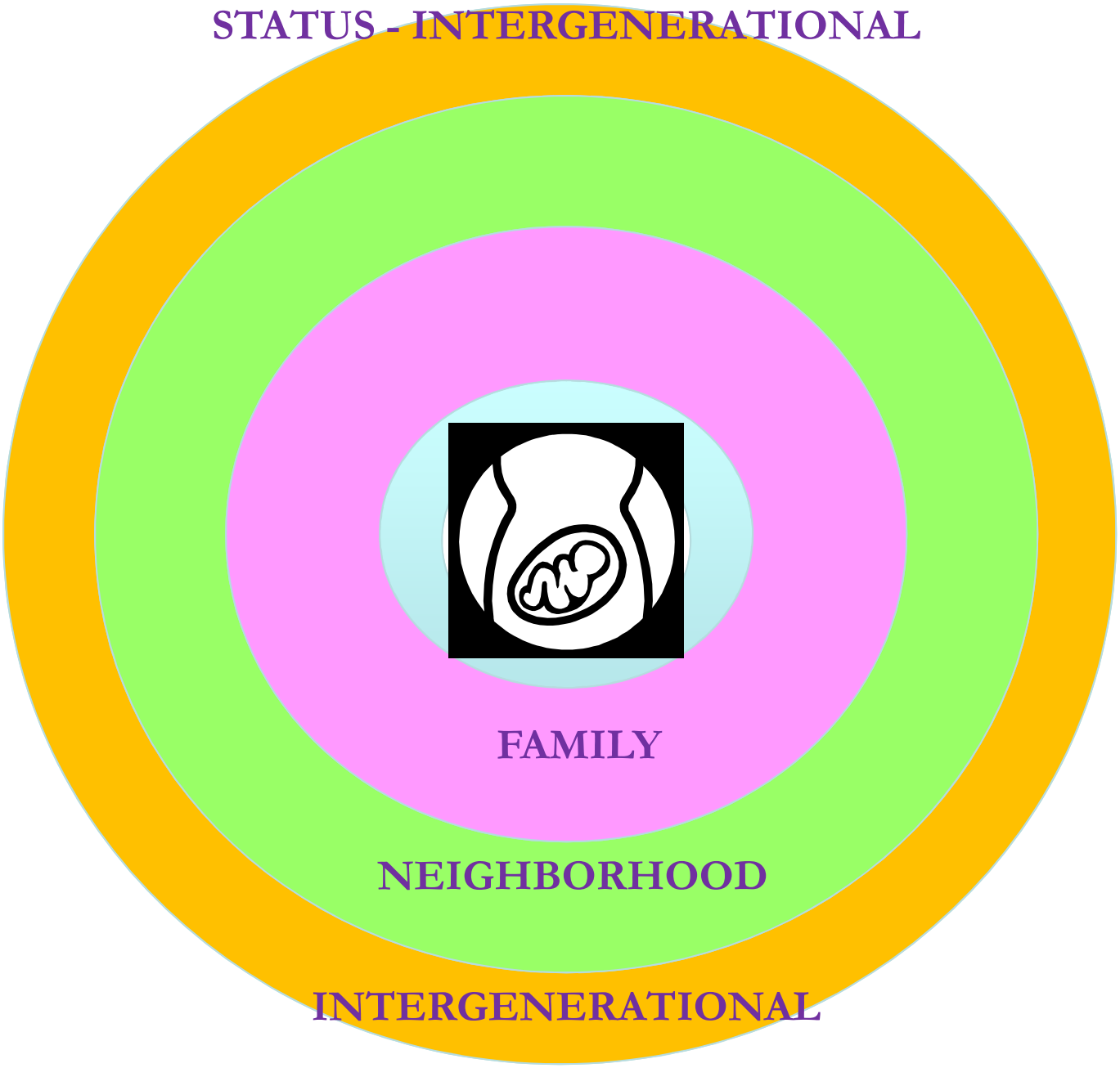

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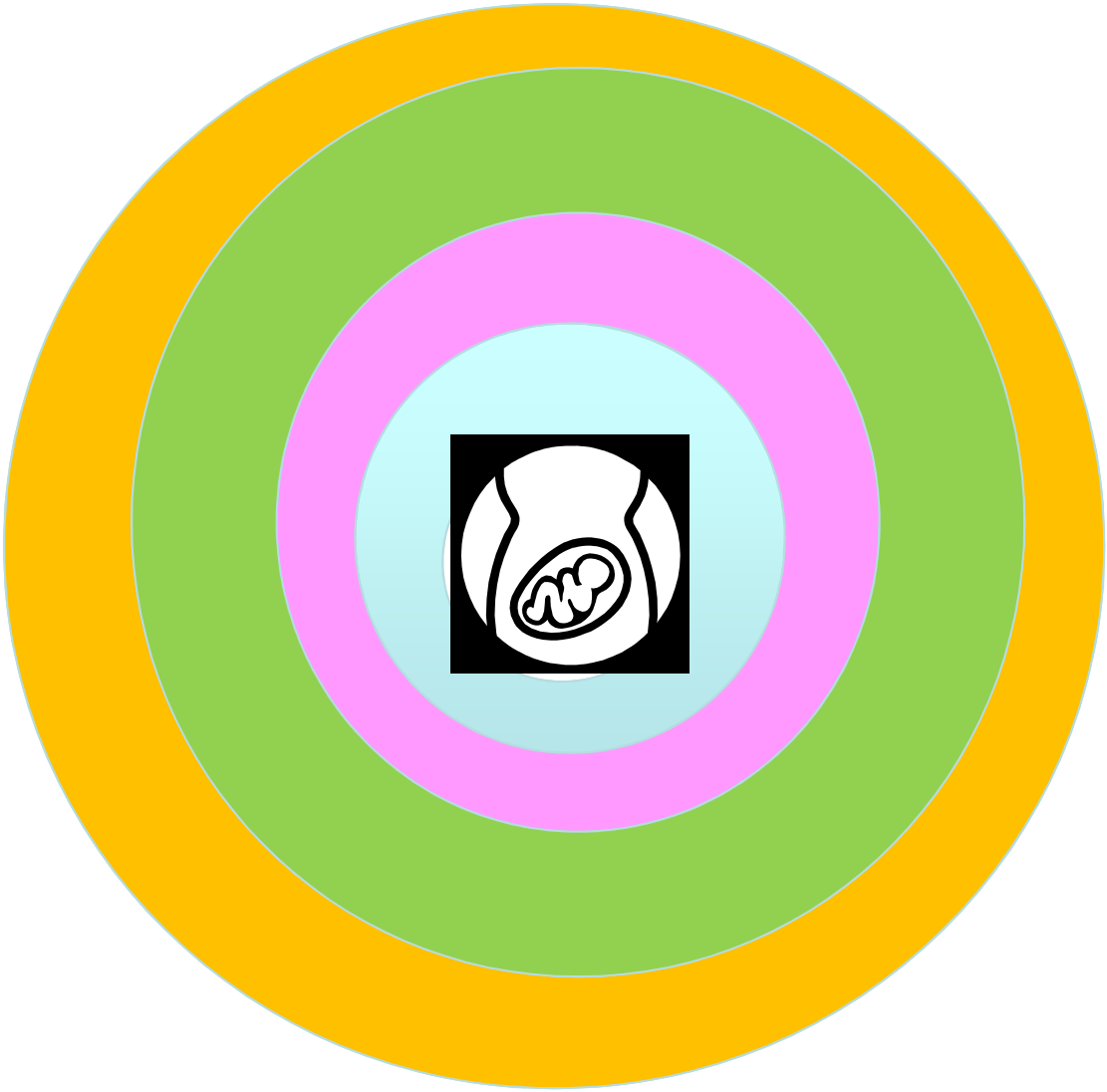
STATUS



TRADITION – "DEMOCRACY OF THE DEAD"

G.K.CHESTERTON

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STATUS – KEY POINTS

- 1. STATUS IS THE MOST POWERFUL PREDICTOR OF HEALTH OUTCOMES!
- 2. RISK FACTORS CLUMP TOGETHER IN INDIVIDUALS, FAMILIES, NEIGHBORHOODS, AND GENERATIONS OF LOW STATUS

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STATUS – CONFUSION SEQUENCE FOR PERINATAL EPIDEMIOLOGISTS AND CAREGIVERS

SELECT SINGLE RISK FACTOR

↓

MEASURE IT PRECISELY

↓

USE CRUDE PROXIES TO CONTROL FOR OTHER ASPECTS OF STATUS

↓

INFLATE MAGNITUDE OF RISK ESTIMATE

↓

ASSUME CAUSALITY

↓

IF "CAUSAL" - INTERVENE

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EXAMPLES

CONDITION	INITIAL ESTIMATE RISK PTB	WELL DONE RISK ESTIMATES	INTERVENTION RCTS
BACTERIAL VAGINOSIS	4-5	1.0-1.5	NEG
PERIODONTAL DISEASE	3-4	1.0-1.5	NEG
STRESS	2-3	1.0-1.5	-----
VITAMIN D DEFICIENCY	2-3	1.0-1.5	-----

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STATUS – END RESULTS

1. VERY FEW UNIVERSAL REMEDIES
   (? FOLIC ACID SUPPLEMENTATION)

2. LOTS OF FALSE STARTS

3. CLEAR NEED FOR EXCELLENCE IN EPIDEMIOLOGY

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PITFALL #2

- PERINATAL FUNNEL

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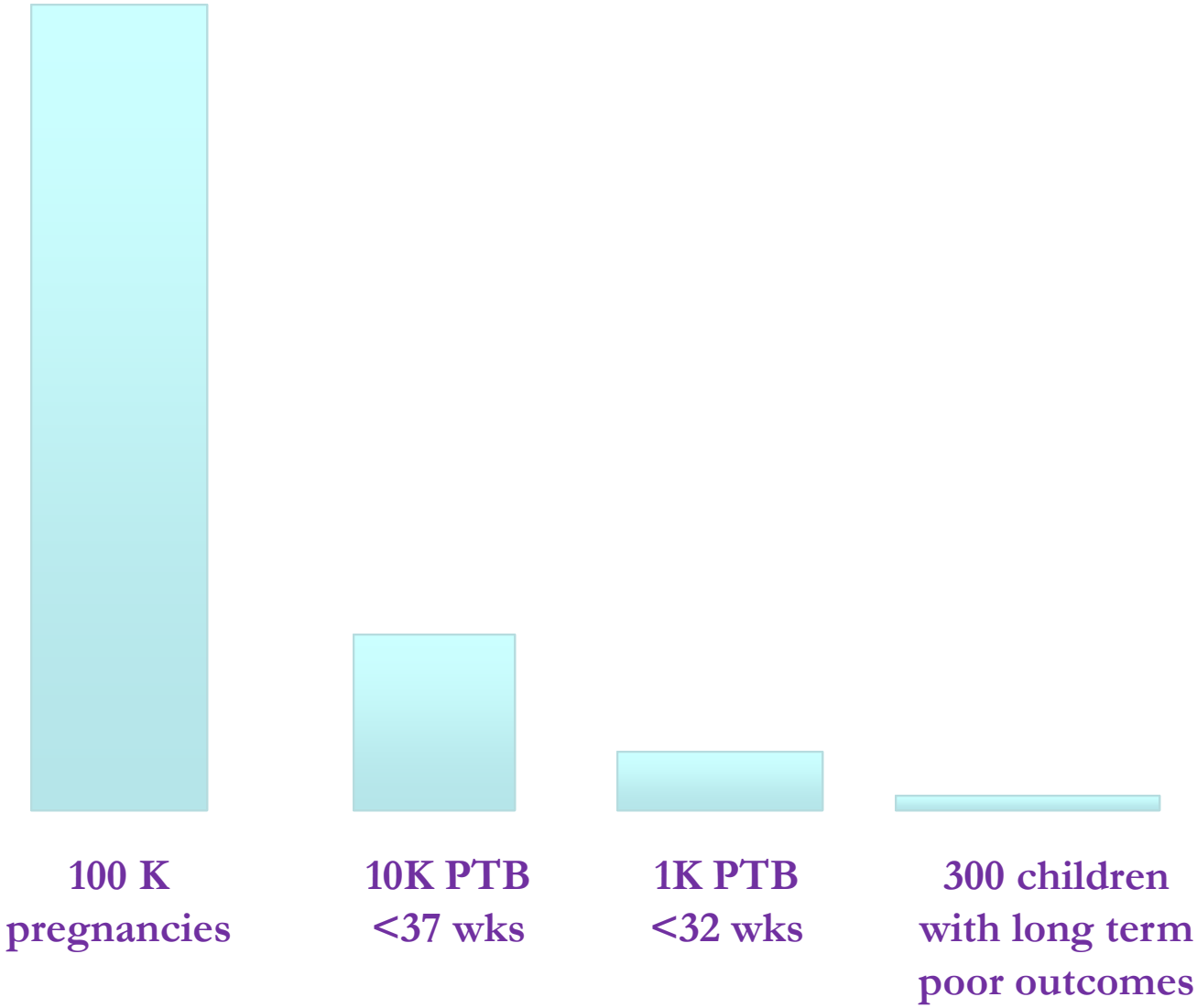
PERINATAL FUNNEL – PRETERM BIRTH



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PERINATAL FUNNEL – END RESULTS

- 1. UNIVERSALLY APPLIED INTERVENTIONS UNLESS QUITE CHEAP ARE VERY EXPENSIVE
- 2. EFFECTIVE TREATMENTS MAY HAVE THEIR EFFECTS DILUTED AND BECOME UNDETECTABLE WHEN APPLIED UNIVERSALLY
- 3. CLINICIANS AND PATIENTS PROPERLY SKEPTICAL ABOUT UNIVERSAL ADVIC E (BRIDGE ICES BEFORE ROAD)

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OVERCOMING THE PITFALLS – *TAILORED* INTERVENTIONS

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TAILORED INVERVENTIONS

OVERCOMING CLUMPING OF STATUS AND PERINATAL FUNNEL

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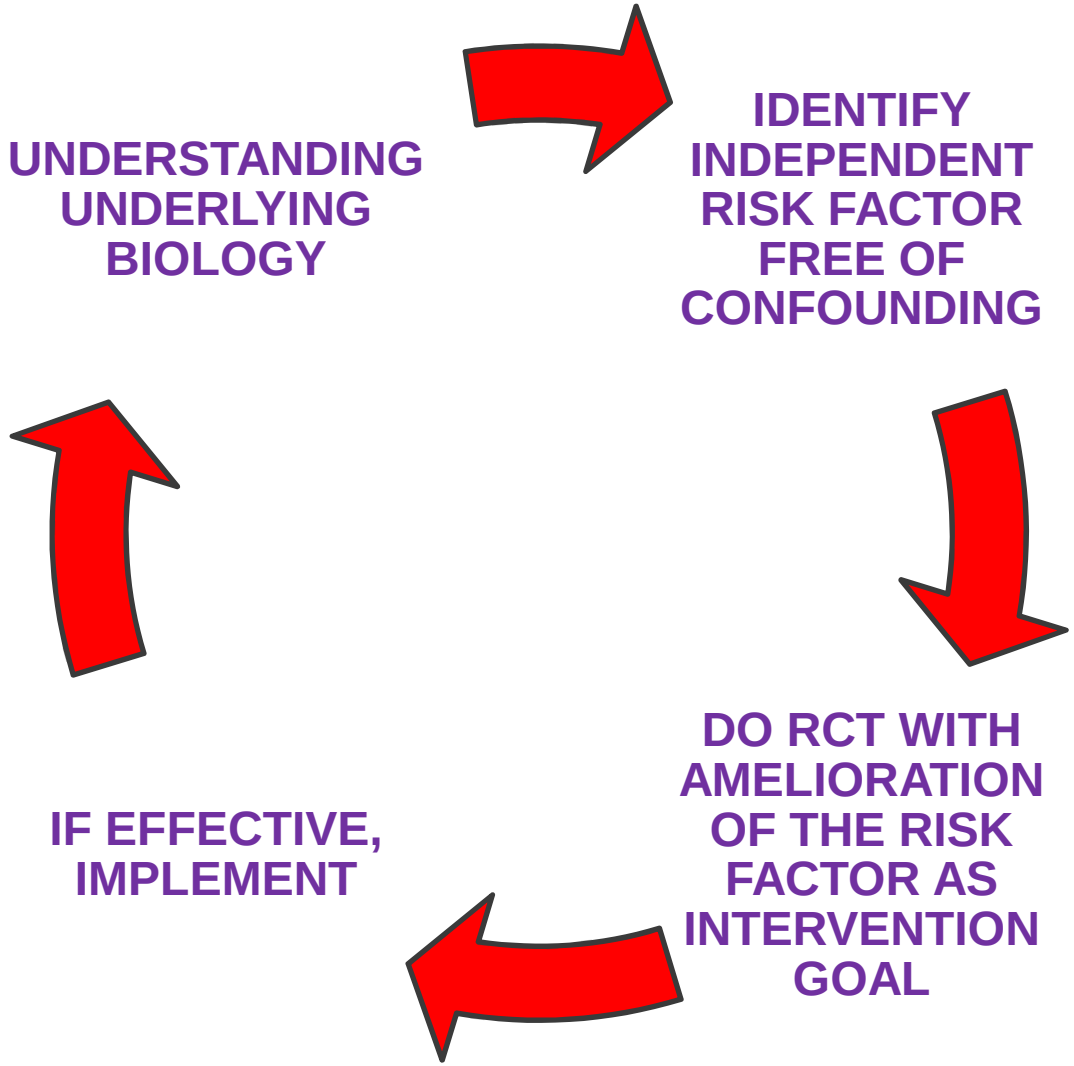
TAILORING



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A correction has been published »

Prevention of Recurrent Preterm Delivery by 17 Alpha-Hydroxyprogesterone Caproate

Paul J. Meis, M.D., Mark Klebanoff, M.D., Elizabeth Thom, Ph.D., Mitchell P. Dombrowski, M.D., Baha Sibai, M.D., Atef H. Moawad, M.D., Catherine Y. Spong, M.D., John C. Hauth, M.D., Menachem Miodovnik, M.D., Michael W. Varner, M.D., Kenneth J. Leveno, M.D., Steve N. Caritis, M.D., Jay D. Iams, M.D., Ronald J. Wapner, M.D., Deborah Conway, M.D., Mary J. O'Sullivan, M.D., Marshall Carpenter, M.D., Brian Mercer, M.D., Susan M. Ramin, M.D., John M. Thorp, M.D., and Alan M. Peaceman, M.D. for the National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network

N Engl J Med 2003; 348:2379-2385 | June 12, 2003

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TAILORING – MEISS ET AL.

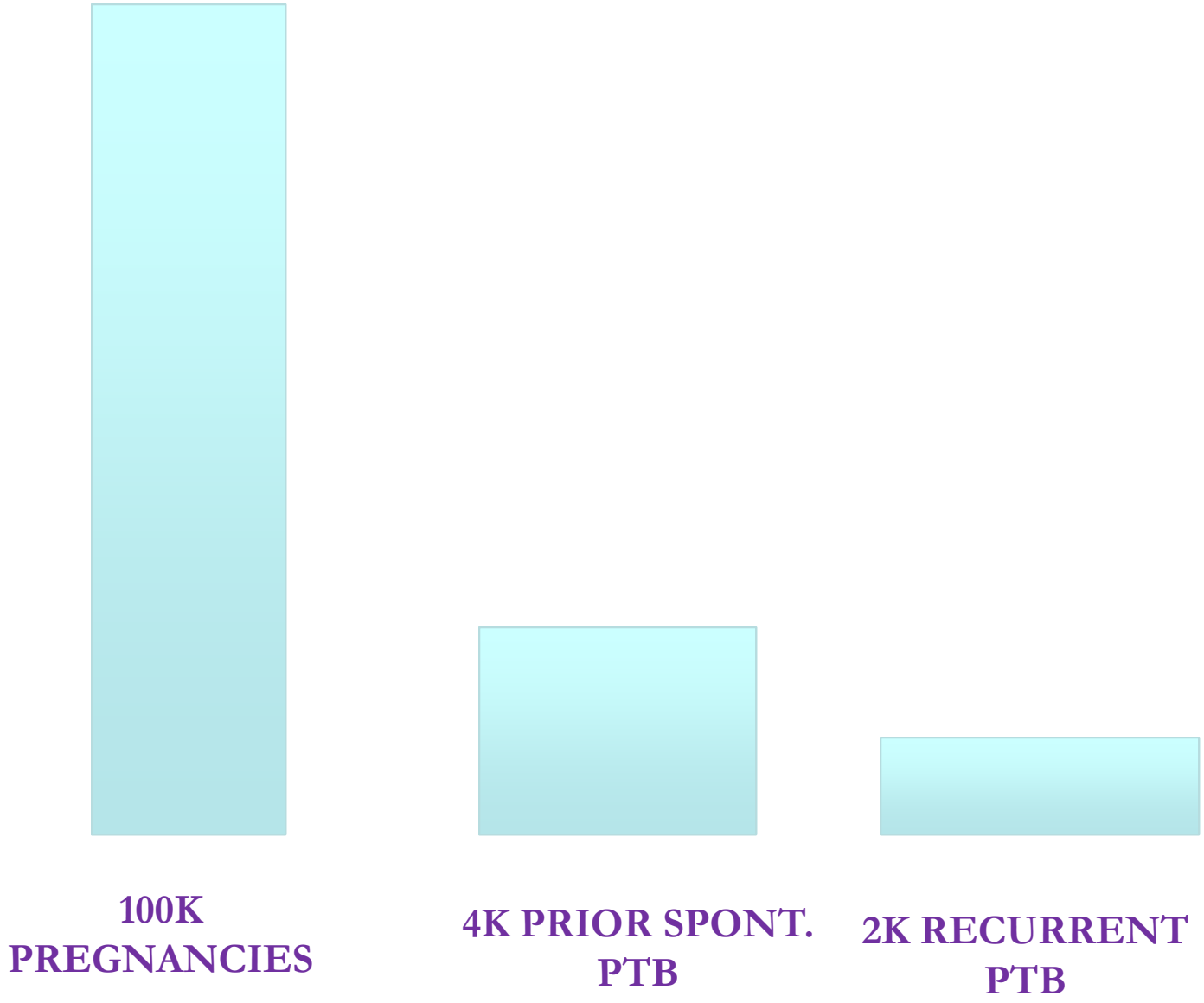

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Table 1. Characteristics of the 463 Women at Randomization.*

Characteristic	Progesterone Group (N=310)	Placebo Group (N=153)
Duration of gestation at the time of qualifying delivery — wk	30.6±4.6	31.3±4.2
No. of previous preterm deliveries	1.4±0.7	1.6±0.9†
>1 Previous preterm delivery — no. (%)	86 (27.7)	63 (41.2)
≥1 Previous term deliveries — no. (%)	153 (49.4)	71 (46.4)
Duration of gestation at randomization — wk	18.4±1.4	18.4±1.4
Age — yr	26.0±5.6	26.5±5.4
Race or ethnic group — no. (%)‡		
Non-Hispanic black	183 (59.0)	90 (58.8)
Non-Hispanic white	79 (25.5)	34 (22.2)
Hispanic	43 (13.9)	26 (17.0)
Asian	2 (0.6)	1 (0.7)
Other	3 (1.0)	2 (1.3)
Marital status — no. (%)		
Married or living with partner	159 (51.3)	71 (46.4)
Never married	119 (38.4)	64 (41.8)
Divorced, widowed, or separated	32 (10.3)	18 (11.8)
Body-mass index before pregnancy§	26.9±7.9	26.0±7.0
Yr of education	11.7±2.3	11.9±2.3
Smoking during pregnancy — no. (%)	70 (22.6)	30 (19.6)
Alcohol use during pregnancy — no. (%)	27 (8.7)	10 (6.5)
Substance use during pregnancy — no. (%)	11 (3.5)	4 (2.6)

* Plus–minus values are means ±SD.
† P=0.007.
‡ Race was self-assigned by the women.
§ The body-mass index is the weight in kilograms divided by the square of the height in meters.

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Table 2. Outcomes of Pregnancy According to Treatment Assignment.*

Outcome	Progesterone Group (N=306)	Placebo Group (N=153)	Relative Risk (95% CI)
	no. (%)		
Delivery before 37 wk of gestation	111 (36.3)	84 (54.9)	0.66 (0.54–0.81)
Spontaneous	90 (29.4)	69 (45.1)	0.65 (0.51–0.83)
Indicated because of complications	21 (6.9)	15 (9.8)	0.70 (0.37–1.32)
Black women	64 (35.4)	47 (52.2)	0.68 (0.51–0.90)
Nonblack women	47 (37.6)	37 (58.7)	0.64 (0.47–0.87)
Delivery before 35 wk of gestation	63 (20.6)	47 (30.7)	0.67 (0.48–0.93)
Delivery before 32 wk of gestation	35 (11.4)	30 (19.6)	0.58 (0.37–0.91)
Miscarriage at <20 wk of gestation	5 (1.6)	0	NA
Hospital visit for preterm labor	49 (16.0)	21 (13.8)	1.15 (0.72–1.86)
Tocolytic therapy	53 (17.3)	24 (15.9)	1.09 (0.70–1.69)
Corticosteroids for fetal lung maturity	52 (17.8)	30 (19.7)	0.91 (0.60–1.35)
Cesarean delivery	77 (25.2)	41 (26.8)	0.94 (0.68–1.30)
Chorioamnionitis	11 (3.6)	5 (3.3)	1.09 (0.39–3.09)

* Data on hospital visit for preterm labor were missing for 1 woman in the placebo group; data on tocolytic therapy were missing for 2 women in the placebo group; and data on corticosteroids for fetal lung maturity were missing for 14 women in the progesterone group and 1 woman in the placebo group. CI denotes confidence interval, and NA not applicable.

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Table 3. Fetal and Neonatal Outcomes According to Maternal Treatment Assignment.*

Outcome	Progesterone Group (N=306)	Placebo Group (N=153)	Relative Risk (95% CI)
	no./total no. with data (%)		
Fetal death, antepartum or intrapartum	6/306 (2.0)	2/153 (1.3)	1.50 (0.31–7.34)
Birth weight			
<2500 g	82/301 (27.2)	62/151 (41.1)	0.66 (0.51–0.87)
<1500 g	26/301 (8.6)	21/151 (13.9)	0.62 (0.36–1.07)
Neonatal death	8/306 (2.6)	9/153 (5.9)	0.44 (0.17–1.13)
Transient tachypnea	11/305 (3.6)	11/152 (7.2)	0.50 (0.22–1.12)
Respiratory distress syndrome	29/305 (9.5)	23/152 (15.1)	0.63 (0.38–1.05)
Bronchopulmonary dysplasia	4/305 (1.3)	5/152 (3.3)	0.40 (0.11–1.46)
Ventilatory support	26/303 (8.6)	22/151 (14.6)	0.59 (0.35–1.00)
Supplemental oxygen	45/303 (14.9)	36/151 (23.8)	0.62 (0.42–0.92)
Intraventricular hemorrhage			
Grade 3 or 4	2/305 (0.7)	0/153	NA
Any grade	4/305 (1.3)	8/153 (5.2)	0.25 (0.8–0.82)
Necrotizing enterocolitis	0/305	4/152 (2.6)	NA
Patent ductus arteriosus	7/305 (2.3)	8/151 (5.3)	0.43 (0.16–1.17)
Retinopathy	5/305 (1.6)	5/152 (3.3)	0.50 (0.15–1.70)
Proven sepsis	9/305 (3.0)	4/152 (2.6)	1.12 (0.35–3.58)

* Transient tachypnea was defined by a birth weight of less than 1000 g and a requirement for oxygen therapy, mechanical ventilation, or both during the first 24 hours of life in an infant in whom there was no evidence of other causes of respiratory distress. Respiratory distress syndrome was defined by a clinical diagnosis of type I respiratory distress syndrome and a requirement for oxygen therapy for at least 24 hours or by death before 24 hours in an infant who had received such a diagnosis and such therapy. Bronchopulmonary dysplasia was defined by a requirement for oxygen therapy (fraction of inspired oxygen, >0.21) for the first 28 days of life. Intraventricular hemorrhage was graded according to the most severe radiologic finding before hospital discharge. Necrotizing enterocolitis was defined by the unequivocal presence of intramural air on abdominal radiography, perforation seen on radiography, or stricture formation after an episode of suspected necrotizing enterocolitis. Infants were recorded as having patent ductus arteriosus if treatment for patent ductus arteriosus was documented in the medical records. Retinopathy was diagnosed by ophthalmologic examination. Proven sepsis was defined by positive cultures of blood, cerebrospinal fluid, or urine on admission to the nursery or (in the absence of positive cultures) clinical evidence of cardiovascular collapse or an unequivocal radiograph confirming the presence of infection in an infant with a clinical diagnosis of sepsis. CI denotes confidence interval, and NA not applicable.

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KEY POINT

TAILORING OVERCOMES PITFALLS!

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TAILORING – ANOTHER EXAMPLE

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Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Maternal-Fetal Medicine Units Network

Home	Research Projects	Publications	Presentations

Current Studies

TSH Trial	A Randomized Trial of Thyroxine Therapy for Subclinical Hypothyroidism or Hypothyroxinemia Diagnosed During Pregnancy

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A Randomized Trial of Thyroxine Therapy for Subclinical Hypothyroidism
or Hypothyroxinemia Diagnosed During Pregnancy

Objective: To determine whether thyroxine treatment of women with subclinical hypothyroidism or hypothyroxinemia diagnosed during the first half of pregnancy is associated with an intellectual improvement in their offspring at age 5 years using the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III)

Design Type: Double masked randomized clinical trial with 2 strata:

- 1) subclinical hypothyroid patients and
- 2) hypothyroxinemia patients

Outcome Measures:

Primary:

- IQ score (WPPSI-III) at age 5

Secondary:

- Composite neonatal outcome; neonatal TSH
- Bayley III at 12 and 24 months
- DAS II at age 3 and two subtests at age 4
- Connors' Rating Scales(S)-Revised at age 4
- Maternal thyroid status at 1 and 5 years postpartum

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TAILORING – SUBCLINICAL HYPOTHYROIDISM TRIAL

100K PREGNANT WOMEN

1K SUBCLINICAL HYPOTHYROIDISM

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REQUISITES FOR TAILORING

- 1. UNDERSTAND BIOLOGY;
- 2. OBSERVATIONAL DATA TO IDENTIFY AND VALIDATE RISK ASSESSMENT;
- 3. DESIGN INTERVENTIONS BASED ON #1 AND #2;
- 4. TEST EFFECTIVENESS OF INTERVENTION IN CLINICAL TRIALS;
- 5. IF EFFECTIVE, IMPLEMENT

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