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MCHIP Maternal and Child Health Integrated Program

Maternal Anemia and Blood Loss at Childbirth and Postpartum in Zanzibar, Tanzania

MCHIP Nutrition Brown Bag

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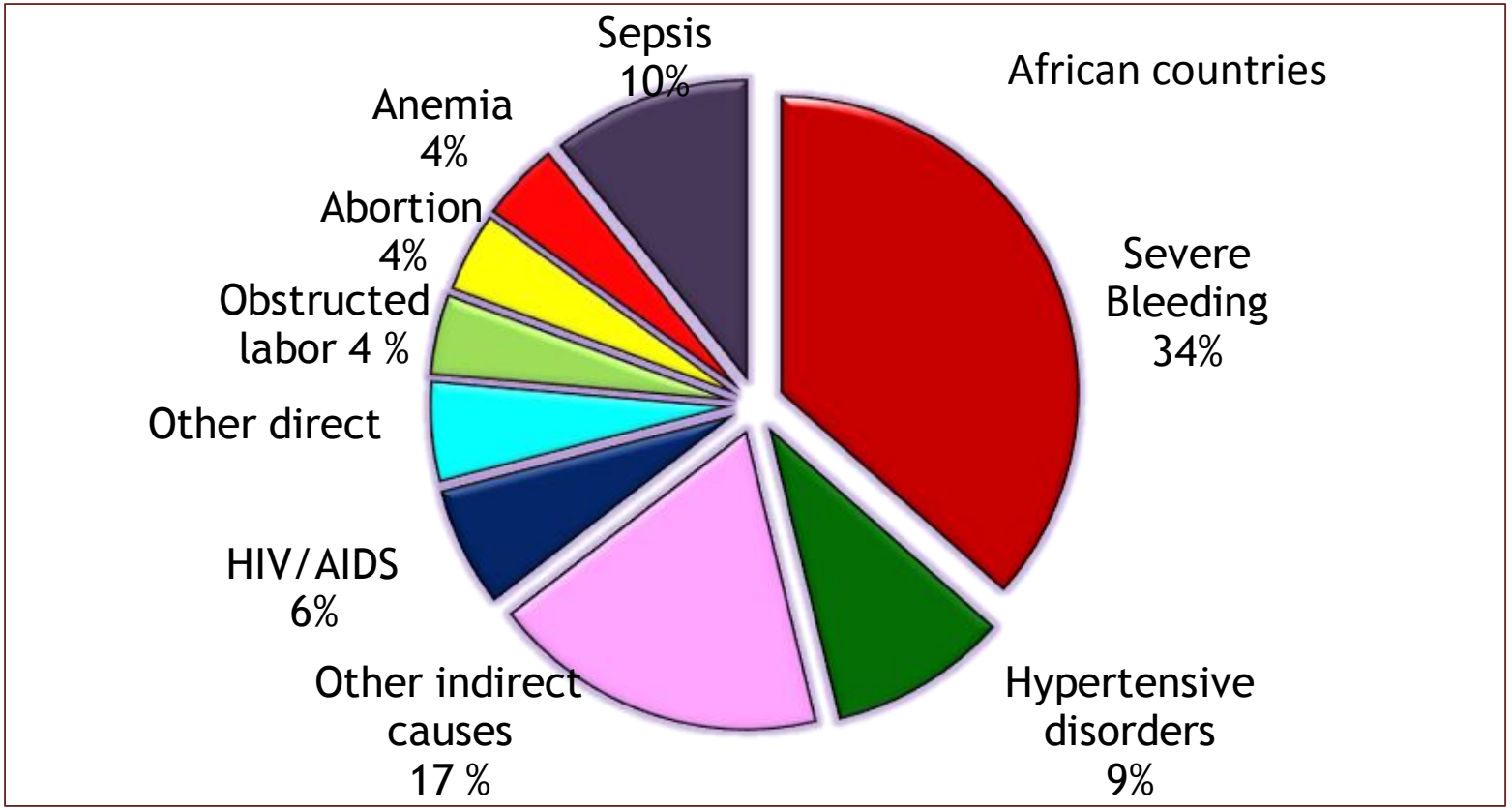
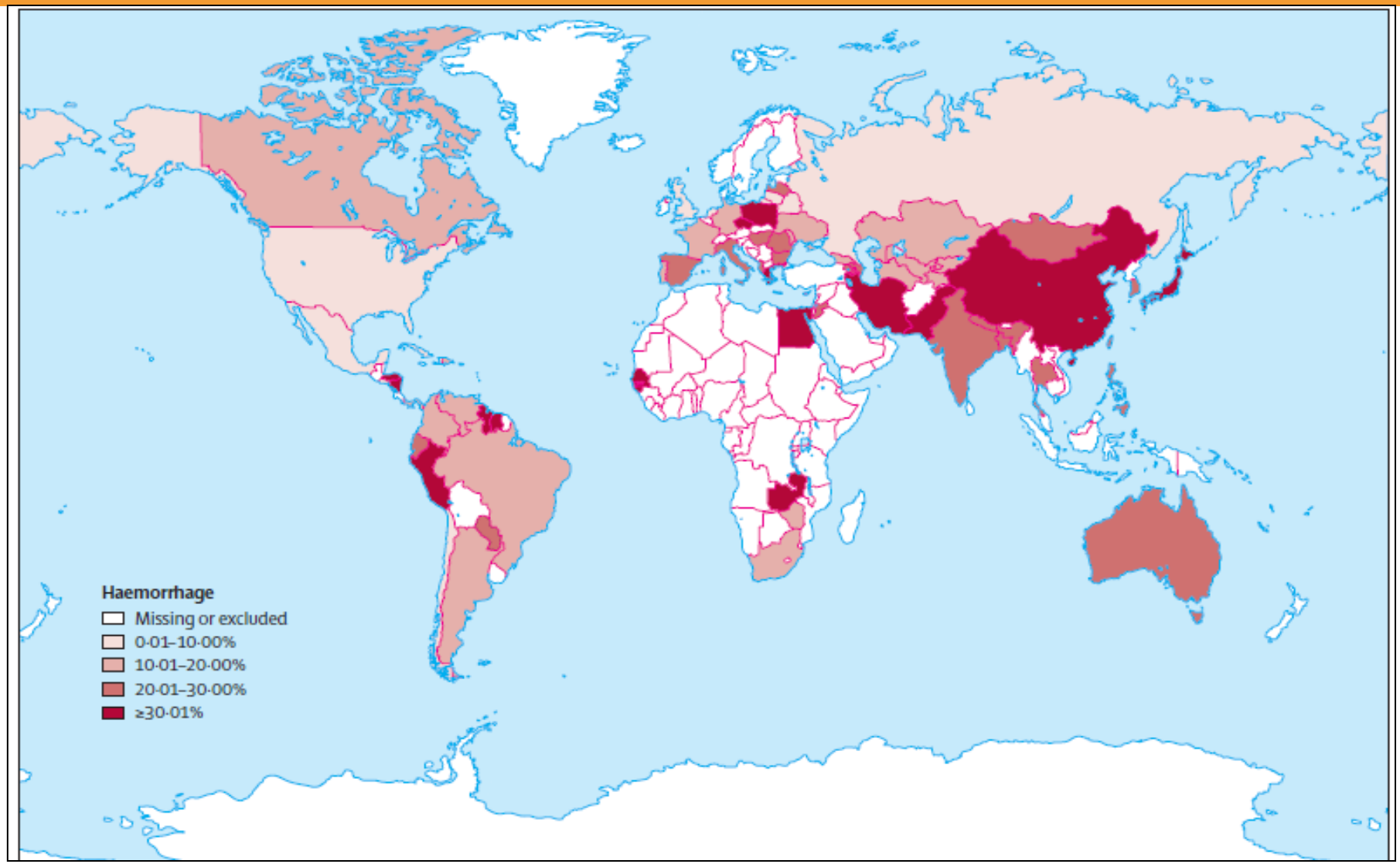
Hemorrhage (PPH) is the leading cause of maternal death
Anemia has been thought to underlie PPH



Khan et al, WHO systematic review 2006

Data is scant on maternal deaths due to PPH in Africa

(Khan, WHO systematic review, 2006)



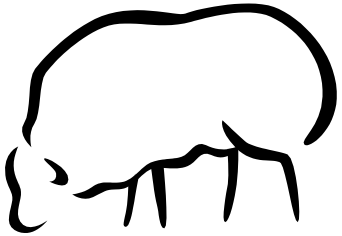
Maternal anemia is associated with poor birth outcomes, pregnancy complications and death

- Moderate to severe maternal anemia is associated with low birth weight and preterm deliveries

- Severe anemia is a cause of maternal mortality due to:
  - Heart failure
  - Excessive blood loss at delivery

Proposed biological mechanisms that play a role in PPH
Anemia is a plausible pathway

- Higher blood loss attributed to impaired uterine muscle strength for labor when prolonged
- Decreased resistance to infection, as infection may contribute to uterine dysfunction or inertia
- Decreased uterine blood flow or low uterine muscle strength may trigger inefficient uterine contractions, mediated by low body iron stores (serum ferritin) and iron deficiency anemia



Animal model, anecdotal evidence

What we know and don't know about anemia, PPH, and maternal mortality

- PPH is the leading cause of maternal death
- Yet, most women survive PPH and likely suffer morbidities affecting productivity and care practices, and they may become or remain anemic postpartum
- Lack of evidence in less developed countries, on the relationship between maternal anemia and blood lost at childbirth
- Need for such data in a setting where maternal mortality and severe anemia are prevalent

We addressed the following unanswered questions:

- What is the distribution of blood loss at childbirth and postpartum in less-developed countries where 99% of maternal deaths occur? How much do women actually lose?
- Can a reliable and valid measurement technique be utilized to measure blood loss at childbirth and postpartum in a less-developed country?
- Do women lose more blood at childbirth and postpartum in areas where maternal mortality and severe anemia are prevalent, as in east Africa?
- What are the risk factors or determinants for greater blood loss at childbirth and postpartum? Is anemia related?

Mothers and Health "Mama na Afya" community-based trial
Prevention and Treatment of Severe Anemia in Pregnancy

Study site: Northern Pemba Island, Zanzibar

Population: ~300,000, Muslim

Maternal mortality rate:449*

Staple foods: rice, cassava

P. falciparum malaria and soil-transmitted helminths endemic

* 2008 estimate, Hogan et al, 2010, Lancet

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Treatment groups: preventing and treating maternal anemia

Standard of Care

- Iron folic-acid (60 mg,400 ug), daily
- Anti-malarial: SP - 2 doses
- One dose deworming: 500 mg mebendazole

Enhanced Care

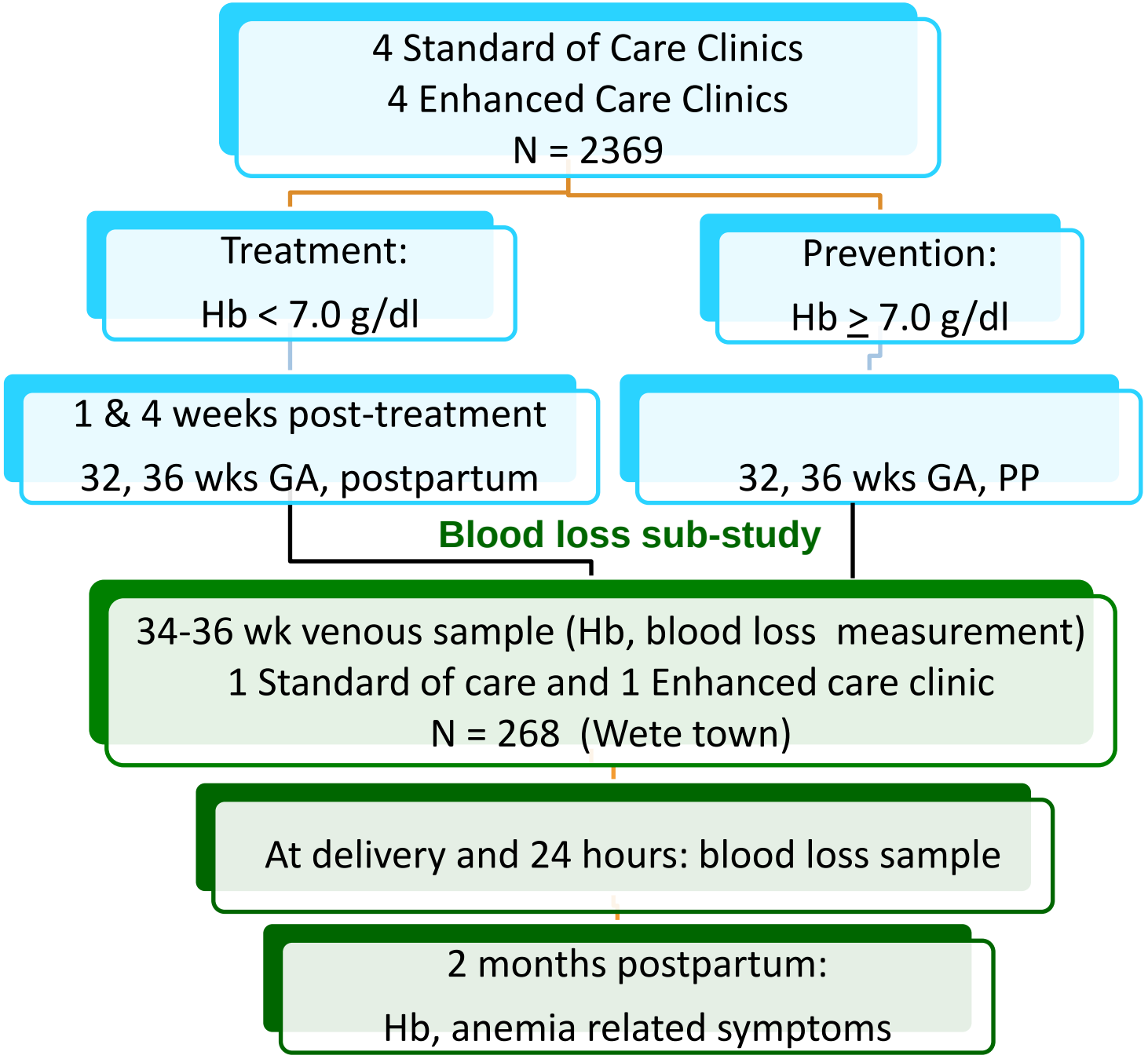
- Iron folic-acid, daily
- Antimalarial: SP – 2 doses
- Two dose deworming: 100 mg mebendazole, twice a day, 3 days
- Multivitamin (Vitamin A, C, E, B_1, B_2, B_3, B_5, B_6, B_{12}, folate)

Data collection was conducted in ANC clinics and through home visits

- Obstetric history
- Socioeconomic status
- Maternal morbidity
- Food Frequency
- Clinical Exam, treatments

- Pregnancy outcome
- Infant status
- Deliver treatments
- Compliance
- Birth weight

Mothers and Health study and Blood Loss Sub-study (2004-2005)



Research Aim 1

- To determine the distribution of blood loss at childbirth and 24-hours postpartum, utilizing the alkaline hematin technique

Diagnosing blood loss at childbirth is a challenge due to measurement

- Health workers rely on visual approximation for deciding if the amount of blood loss at childbirth is excessive
  - 30-50% under-estimation of blood loss
  - Can delay diagnosis, referral, and treatment
- Lack of consensus in research studies
  - No standard definition of excessive blood loss
  - Cutoff, duration and methods of measurement differ

(Brant 1967, Glover 2003)

Gold standard for measurement: alkaline hematin method

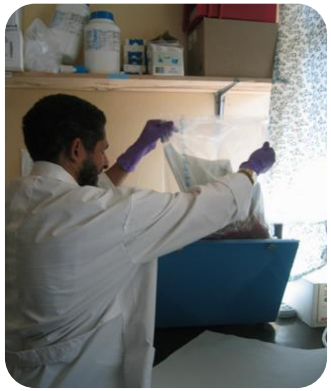
- Alkaline hematin method is the most widely used and most accurate method for objective quantification of blood loss in women
- Simple, reliable, practical
- A few early studies used alkaline hematin to quantify excessive menstrual bleeding and blood loss at childbirth and none in developing country settings

(Newton 1961, Hallberg, 1964, Chua 1998)

Using the gold standard – the alkaline hematin method to accurately quantify blood loss at childbirth and postpartum

At delivery and 24 hours postpartum in Wete Hospital:

Collect pads at childbirth and postpartum, dilute with NaOH solution



Denature hemoglobin in blood loss to alkaline hematin

Measure concentration of alkaline hematin

85% recovery rate

Compute blood loss at childbirth

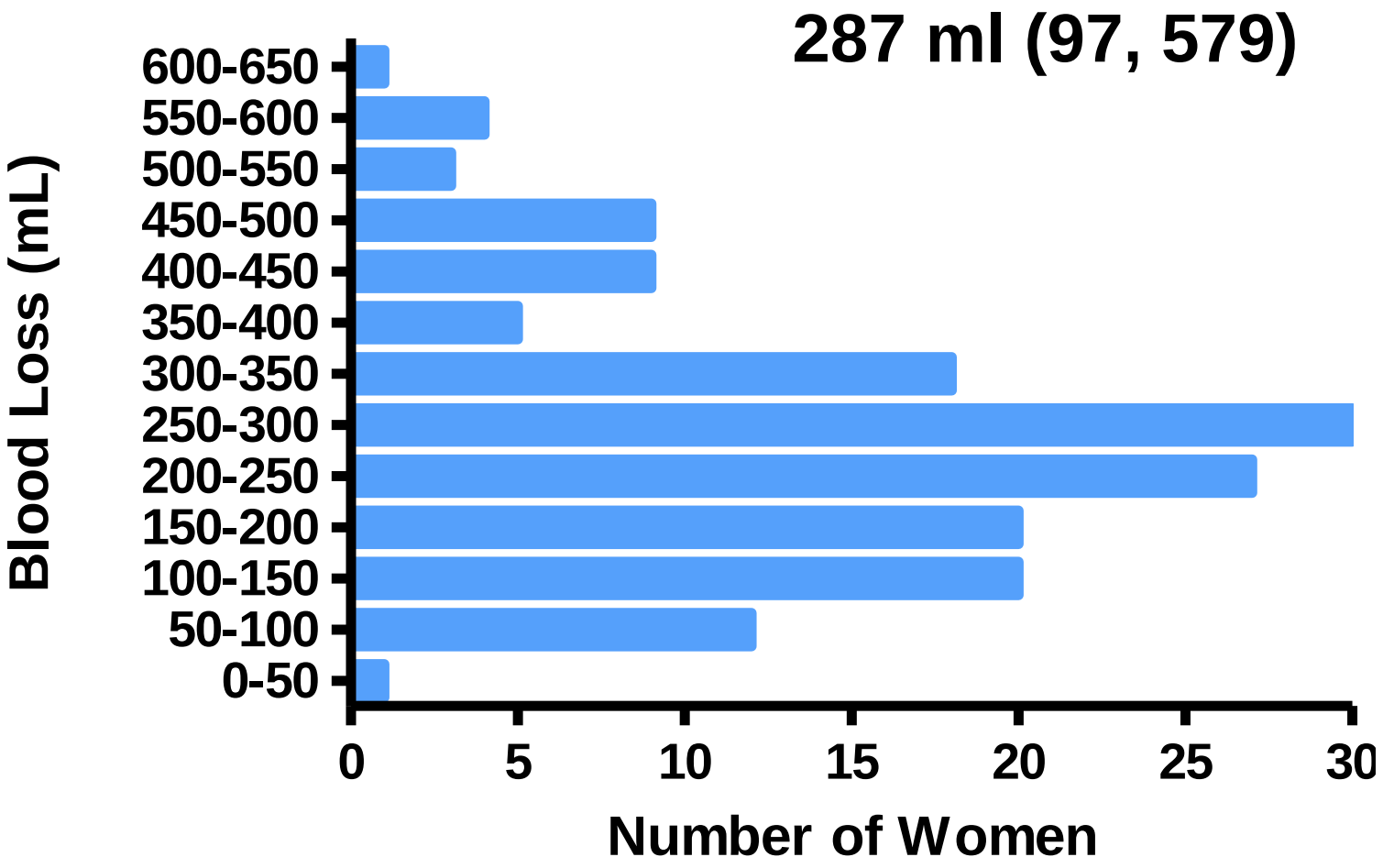
At ≥ 34 weeks gestational age:

Collect venous blood

Dilute with NaOH

Measure concentration of alkaline hematin

Distribution of blood loss was lower in hospital-based deliveries (N= 158)



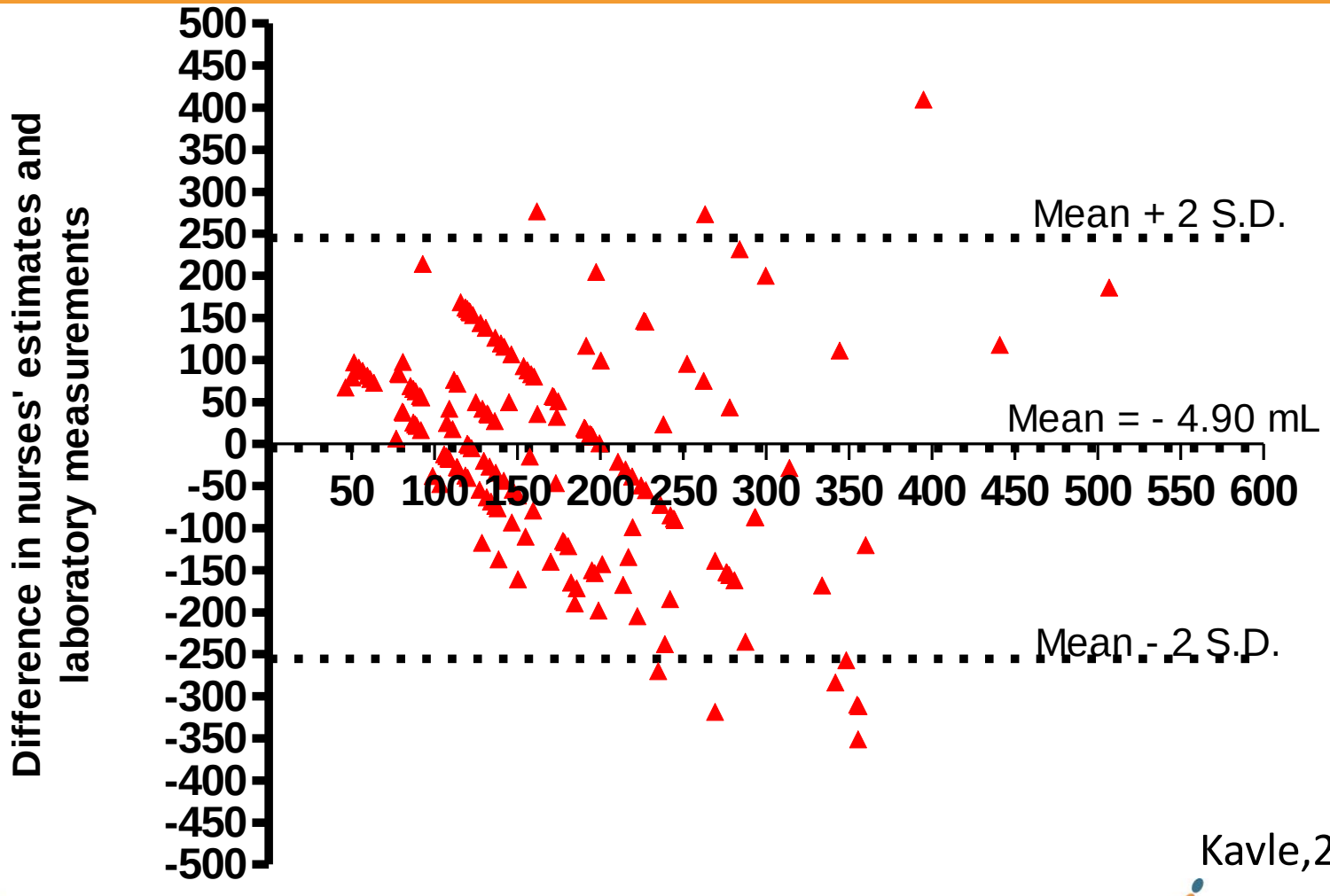
Kavle, 2006

Why was blood loss at childbirth and postpartum lower than expected?

- No complications of 3rd stage of labor
- Only two case of prolonged labor (3rd stage > 30 min.)
- Incidence of PPH low (5%)
- Breastfeeding following birth is universal
- Active management of third stage of labor (AMTSL) routinely practiced in hospital-based deliveries

Kavle, 2006

Nurse-midwives estimated blood loss accurately, when compared to laboratory measurements, yet had lower precision at higher losses



Kavle,2006

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Research Aim 2

- To evaluate the determinants of blood loss at childbirth, and 24- hours postpartum, specifically focusing upon the purported relationship between maternal anemia and blood loss at childbirth and postpartum

Little is known about factors which contribute to excessive blood loss at childbirth in less developed countries

- Nulliparity
- Grand multiparity
- Cervical trauma
- Maternal obesity
- Maternal anemia
- Instrumental delivery
- Induced labor
- Prolonged labor
- Third stage complications
- Pre- eclampsia
- Previous history of PPH
- Birth weight > 4000 grams

Geelhoed, 2006, Selo-Ojeme, 1997, Tsu, 1993

Statistical Methods

- Outcome: Total blood loss (mL) – childbirth and postpartum
- Bi-variate analyses
  - Nutritional factors
  - Socioeconomic factors
  - Obstetrical factors
- Multivariate regression analyses
  - Factors $p < 0.10$ in bi-variate analyses
  - Factors identified in previous literature
  - Universal confounders

Selected background characteristics
Zanzibari women, Wete town (N = 158)

Basic characteristics	**50th (5th, 95th) or %**
Age (years)	25.5 (18.0 - 38.0)
Gestational age (weeks)	29.0 (20.0 - 37.0)
Hemoglobin category	
No anemia (Hb >110 g/L)	38.6
Mild anemia (Hb 90-109 g/L)	45.6
Moderate to severe anemia (<90 g/L)	15.8
Parity	
0	21.5
1	15.2
2-5	37.3
≥5	25.9
Not employed	80%
Malarial infection; intestinal helminths	Low rate

Kavle, 2006

Selected labor and delivery characteristics, Zanzibari women, Wete town (N= 158)

Characteristics at childbirth	50th (5th, 95th) or %
Received oxytocin	44.9
Received ergometrine	95.6
Received oxytocin and ergometrine	40.5
Tear	7.6
Episiotomy	16.5
Gestational age (weeks)	39.1 (36.4 – 43.5)
Birthweight (grams)*	3,410 ± 434

* Mean ± SD, singleton births only

Kavle, 2006

Determinants for total blood loss: childbirth and 24-hrs postpartum

Independent variable	β estimate	SEM	p-value
Moderate - severe anemia vs. no anemia	90.63	28.38	0.002
Mild anemia vs no anemia	11.47	20.51	NS
First stage of labor (hr)	7.09	2.79	0.012
Placental weight (grams)	0.11	0.05	0.030
Oxytocin received	39.64	19.66	0.046
Pre-term birth < 37 weeks	-52.52	29.91	0.081

*NS = not significant p > 0.10

Kavle, 2008

Determinants for total blood loss: childbirth and 24-hrs postpartum

Independent variable	β estimate	SEM	p-value
Parity (0, Reference)			
1	34.19	34.18	NS
2 - 5	30.34	32.99	NS
≥ 5	59.61	35.17	0.09
Tear	25.01	37.61	NS
Episiotomy	18.77	34.00	NS
Standard of Care vs. Enhanced	1.90	19.32	NS

*NS = not significant p > 0.10

Kavle, 2008

Identified maternal anemia as determinant of blood loss, supports hypothesized relationship

Strong relationship between maternal anemia and blood loss

- Influence of maternal anemia on blood loss is more pervasive - affects a normal range of losses
- Relationships persisted following adjustment of confounding factors
- Internal validity due to rigorous prospective data collection of women during pregnancy delivery and postpartum
- Conducted in population where anemia and iron deficiency are prevalent

Study limitations

- Study sample restricted to semi-urban setting who were able to afford hospital delivery
- Access to health care may have contributed to lower blood loss
- Some loss to follow-up experienced
  - Delivered prior to obtaining venous sample
  - Delivered at home, could not get to hospital in time
  - Did not stay through 24 hours postpartum

Research and programmatic Implications

- Our findings likely underestimate the effect of anemia on blood loss in rural Africa, especially where anemia is untreated and in home births.
- Accurate measurement of blood loss can guide limits for “normal” blood loss and “excessive blood loss” which may vary by setting
- Consistency and accuracy of other measurement techniques vs. the gold standard needs further study
- Further exploration of the link between maternal anemia and postpartum hemorrhage
- Prevention of anemia is key


Thank you (Asante sana)!