



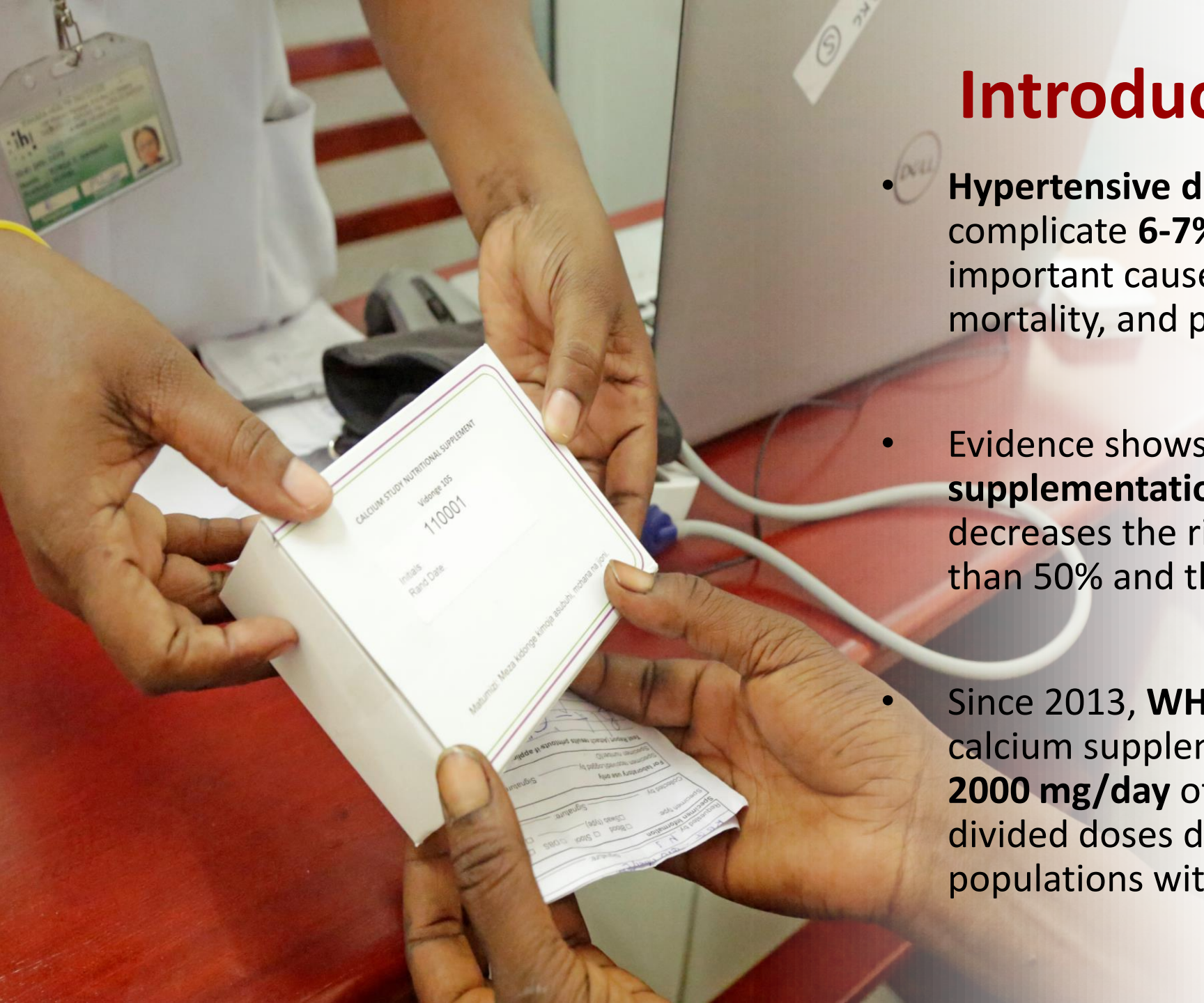
Low-Dose Calcium Supplementation for Prevention of Preeclampsia and Preterm Births

ARISE ANNUAL SCIENTIFIC SYMPOSIUM

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Introduction

- **Hypertensive disorders** of pregnancy complicate **6-7%** of pregnancies and are important causes of maternal morbidity, mortality, and preterm birth.
- Evidence shows that **calcium supplementation** during pregnancy decreases the risk of pre-eclampsia by more than 50% and that of preterm birth by 25%.
- Since 2013, **WHO recommends** high-dose calcium supplementation (**1500–2000 mg/day** of elemental calcium) in three divided doses during pregnancy in populations with low dietary calcium intake.



Suggested scheme for calcium supplementation in pregnant women

Dosage	1.5–2.0 g elemental calcium/day ^a
Frequency	Daily, with the total daily dosage divided into three doses (preferably taken at mealtimes)
Duration	From 20 weeks' gestation until the end of pregnancy
Target group	All pregnant women, particularly those at higher risk of gestational hypertension ^b
Settings	Areas with low calcium intake

^a 1 g of elemental calcium equals 2.5 g of calcium carbonate or 4 g of calcium citrate.

^b Women are regarded as being at high risk of developing gestational hypertension and pre-eclampsia if they have one or more of the following risk factors: obesity, previous pre-eclampsia, diabetes, chronic hypertension, renal disease, autoimmune disease, nulliparity, advanced maternal age, adolescent pregnancy and conditions leading to hyperplacentation and large placentas (e.g. twin pregnancy). This is not an exhaustive list, but can be adapted/complemented based on the local epidemiology of pre-eclampsia.



**World Health
Organization**

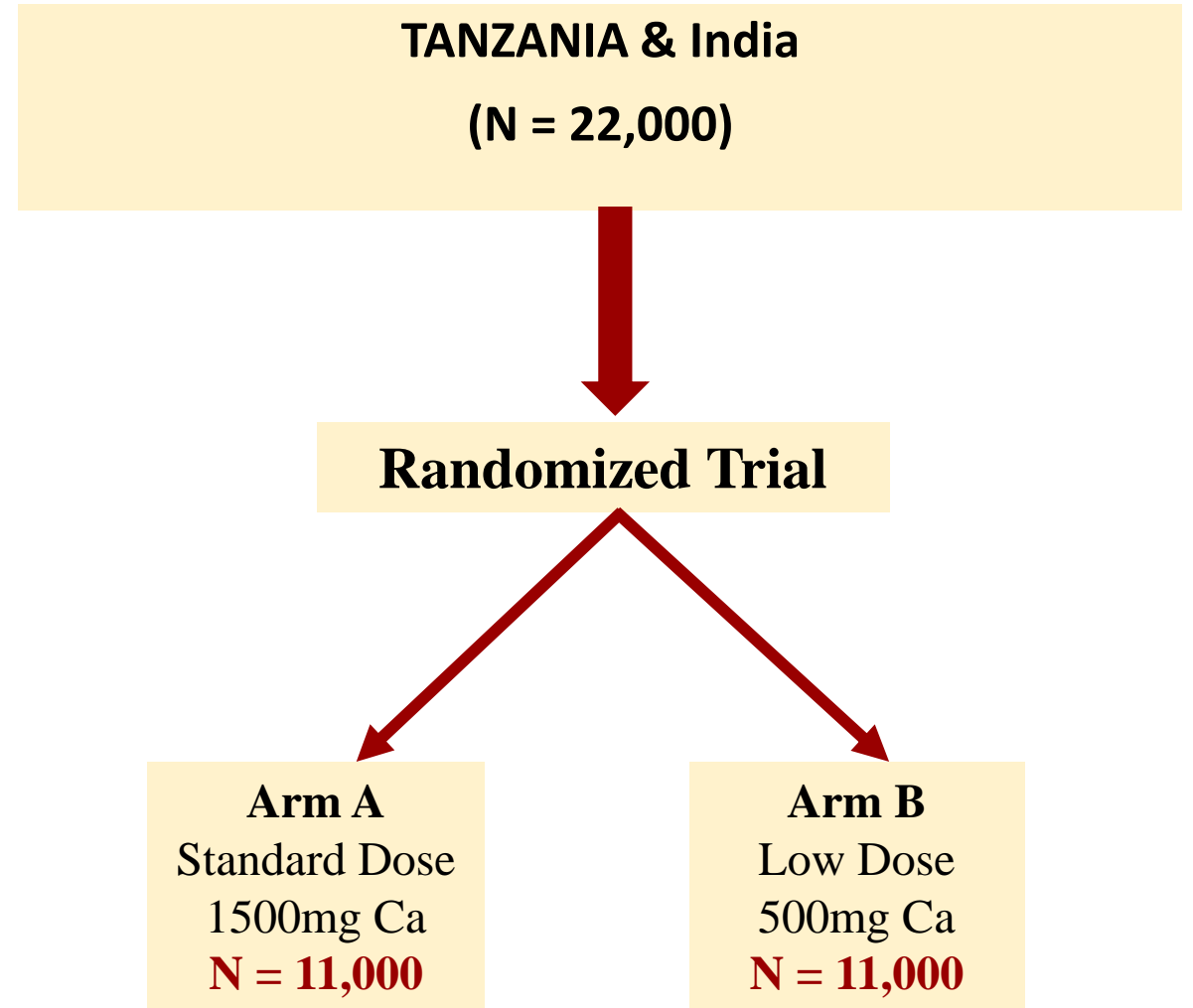
Study Rationale

- Despite its proven efficacy, and being recommended by WHO, calcium supplementation is not yet standard of care in most LMICs due;
 - High cost of calcium supplements
 - Complexity of the suggested dosing schedule
 - Logistical challenges related to transportation and storage
- An equally effective **lower dose of calcium** (500 mg) administered as a single dose, may help overcome these barriers and increase individual and health system adoption of this effective intervention.

Low dose?

What Did We Do?

- 2 independently powered randomized clinical trials in Tanzania and India (N=22,000).
- Trial aimed at assessing effects of low-dose calcium supplementation (500mg/day) compared to high-dose (1500mg/day) in reducing preeclampsia and preterm births.



Randomized Trial Regimen

Arm A Standard WHO Dose (1500 mg/day)

Morning Tablet 1 → 500mg

Afternoon Tablet 2 → 500mg

Evening Tablet 3 → 500mg

Arm B Low Dose (500 mg/day)

Morning Tablet 1 → 500mg

Afternoon Tablet 2 → Placebo

Evening Tablet 3 → Placebo

RESULTS

WHAT ARE THE FINDINGS?

The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Two Randomized Trials of Low-Dose Calcium Supplementation in Pregnancy

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Primary Outcomes

TANZANIA



	Low Dose	High-Dose	RR (95% CI)	P-value
Preeclampsia	3.0% 165/5,503	2.7% 150/5,497	1.10 (0.88 – 1.36)	<0.001
Preterm	10.4% 531/5,109	9.7% 493/5,081	1.07 (0.95 – 1.21)	0.10

INDIA



	Low Dose	High-Dose	RR (95% CI)	P-value
Preeclampsia	3.0% 164/5,497	3.6% 196/5,503	0.84 (0.68 – 1.03)	<0.001
Preterm	11.4% 593/5,195	12.8% 665/5,193	0.89 (0.80 – 0.98)	<0.001

Secondary and Safety Outcomes - TANZANIA

Outcome	Low Dose	High-Dose	RR (95% CI)
Gestational Hypertension	4.1	4.0	1.02 (0.85-1.22)
Severe PE	1.8	1.7	1.06 (0.80-1.40)
Maternal deaths	0.1	0.1	1.33 (0.30-5.95)
Fetal deaths	6.6	7.2	0.93 (0.81-1.07)
Stillbirths	3.1	3.0	1.05 (0.85-1.35)
Low birth weight	8.8	8.7	1.03 (0.90-1.18)
Infant deaths	1.6	1.8	0.90 (0.67-1.22)
Small for Gestational Age Births	22.2	22.0	1.02 (0.94-1.09)
Maternal hospitalization	40/38,164	25/38,702	1.6 (0.97-2.63)
Severe anemia (3 rd Trimester)	0/4229	0/4215	-

Secondary and Safety Outcomes - INDIA

Outcome	Low Dose	High-Dose	RR (95% CI)
Gestational Hypertension	3.2	3.8	0.85 (0.70-1.03)
Severe PE	1.1	1.8	0.63 (0.46-0.87)
Maternal deaths	0.04	0.04	1.00 (0.14-7.10)
Fetal deaths	5.2	5.1	1.03 (0.87-1.20)
Stillbirths	2.1	2.3	0.92 (0.71-1.18)
Low birth weight	17.3	17.5	0.98 (0.90-1.06)
Infant deaths	0.5	0.3	1.60 (0.84-3.06)
Small for Gestational Age Births	32.8	34.2	0.96 (0.90-1.01)
Maternal hospitalization	11/43,223	24/43,332	0.46 (0.22-0.94)
Severe anemia (3 rd Trimester)	1/4475	2/4478	0.50 (0.05-5.52)

CONCLUSION AND RECOMMENDATIONS

Conclusions

- In Tanzania and India, **low-dose calcium supplementation was noninferior** to high-dose calcium supplementation with respect to the **risk of preeclampsia**.
- **Low-dose calcium supplementation was noninferior** to high dose calcium supplementation with respect to the **risk of preterm live birth in the India** but not in the Tanzania.
- Meta-analysis of pooled data from both trials, **low-dose** supplementation appeared to be **as effective as high-dose** calcium supplementation in reducing the risk of both preeclampsia and preterm birth

Recommendations

- Findings of the two trials show that providing **a single calcium pill to pregnant women is as effective as providing three pills**:
 - There is a **need to revisit the recommendation** of high-dose calcium supplementation to enable Tanzania and other LMICs to afford and implement this important intervention.
 - **Reducing the number calcium pills** will also **improve uptake and adherence** by pregnant women given that they also have to take iron folic acid supplements.

Acknowledgements

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GATES *foundation*



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Medical Officers In
Charges

Staff at the Study



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RCH Clinics

Study Nurse

Participants



Tanzania Medicines & Medical Devices authority

