Nutrition and Preventing Tuberculosis and TB deaths: The **RATIONS** (**R**educing **A**ctivation of **T**uberculosis by **I**mprovement **O**f **N**utritional **S**tatus) Trial

"*Good ideas are not necessarily new ideas but old ideas resurrected at the proper time*"- Charles Handy *in* The Hungry Spirit.

Collaborating Institutions

ICMR-NIRT, Chennai

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The OUTCOME

UpToDate® Jharkhand McGill University

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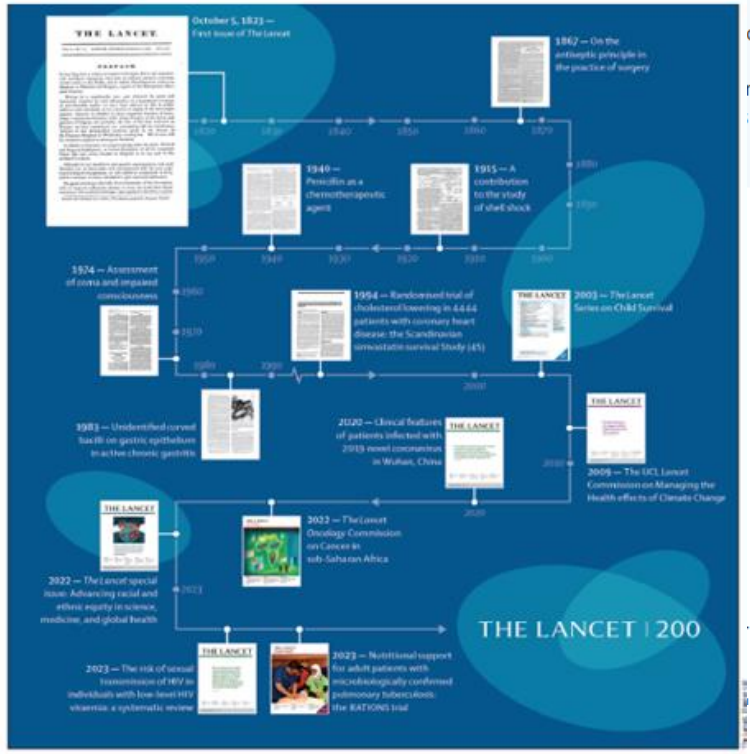
Prevention of tuberculosis: BCG immunization and nutritional supplementation

Topic Graphics (2)



opics are updated as new evidence becomes available and our peer review process is complete.

rature review current through: **Nov 2024.**
topic last updated: **Sep 28, 2023.**

'B)

upplementation for prevention of TB are discussed below.

Food: the tuberculosis vaccine we already have

CrossMark

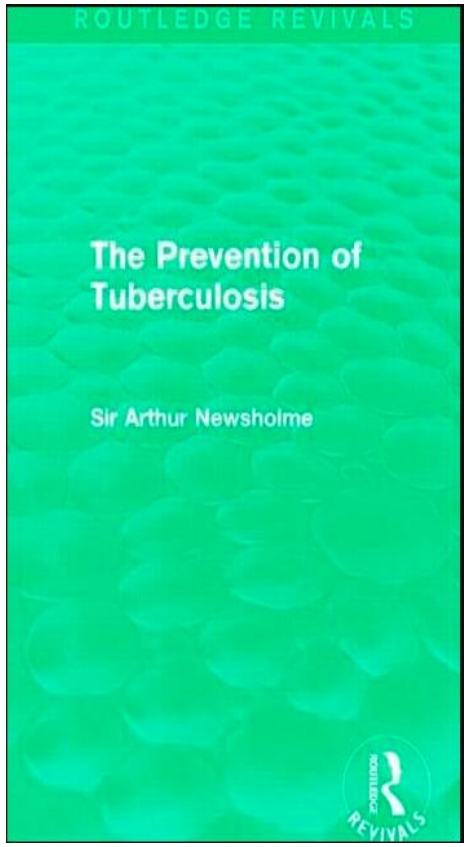
Sinha P, Mehta S. Food: the tuberculosis vaccine we already have. Lancet. 2023;402(10402):588-90.

The RATIONALE

1. Nutrition is central to survival, health, and protection from disease.
2. A well-functioning Immune system confers 90% lifetime protection against TB.
3. The presence of active TB indicates some impairment of immunity
4. Undernutrition followed by HIV is the most common cause of immunodeficiency globally- Nutritionally acquired immune deficiency(**N-AIDS)**
5. This trial addressed **N-AIDS** in a rural population with high levels of TB and undernutrition.

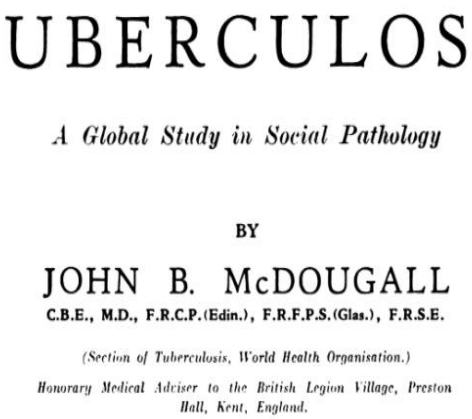
Beisel WR. The Journal of Nutrition. 1996;126(10 Suppl):2611S-5S1. Bhargava A. BMJ [Internet]. 2016; 355. http://www.bmj.com/content/bmj/355/bmj.i5407.full.pdf.

1908



"No system of measures for controlling tuberculosis can be considered final, which omits to do what is practicable for preventing malnutrition"-Sir Arthur Newsholme

1949


TUBERCULOSIS

A Global Study in Social Pathology

BY

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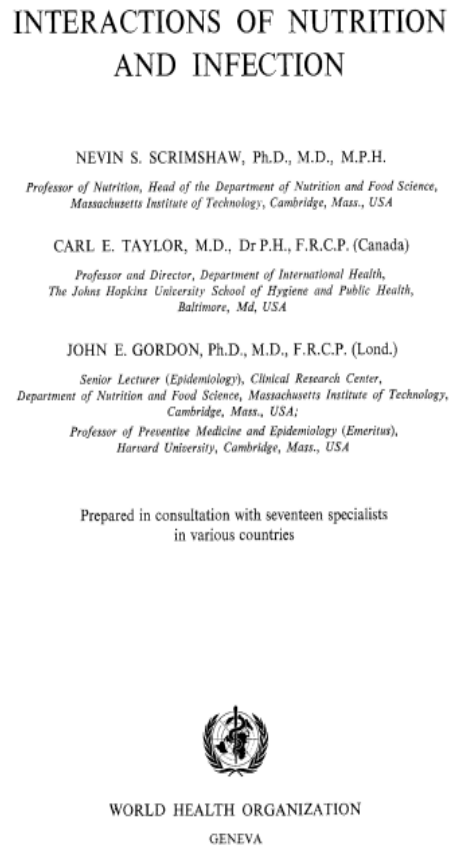
"The nutrition of the individual, using the term in its widest sense, is in the author's opinion, the most vital factor in the prevention in tuberculous disease"-

1935

A principal determinant of mortality in tuberculosis is nutrition- Major Greenwood in Epidemic and Crowd Diseases

1968


INTERACTIONS OF NUTRITION AND INFECTION

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Prepared in consultation with seventeen specialists in various countries

WORLD HEALTH ORGANIZATION

GENEVA

TB affects nutrition. Malnutrition risk factor for TB

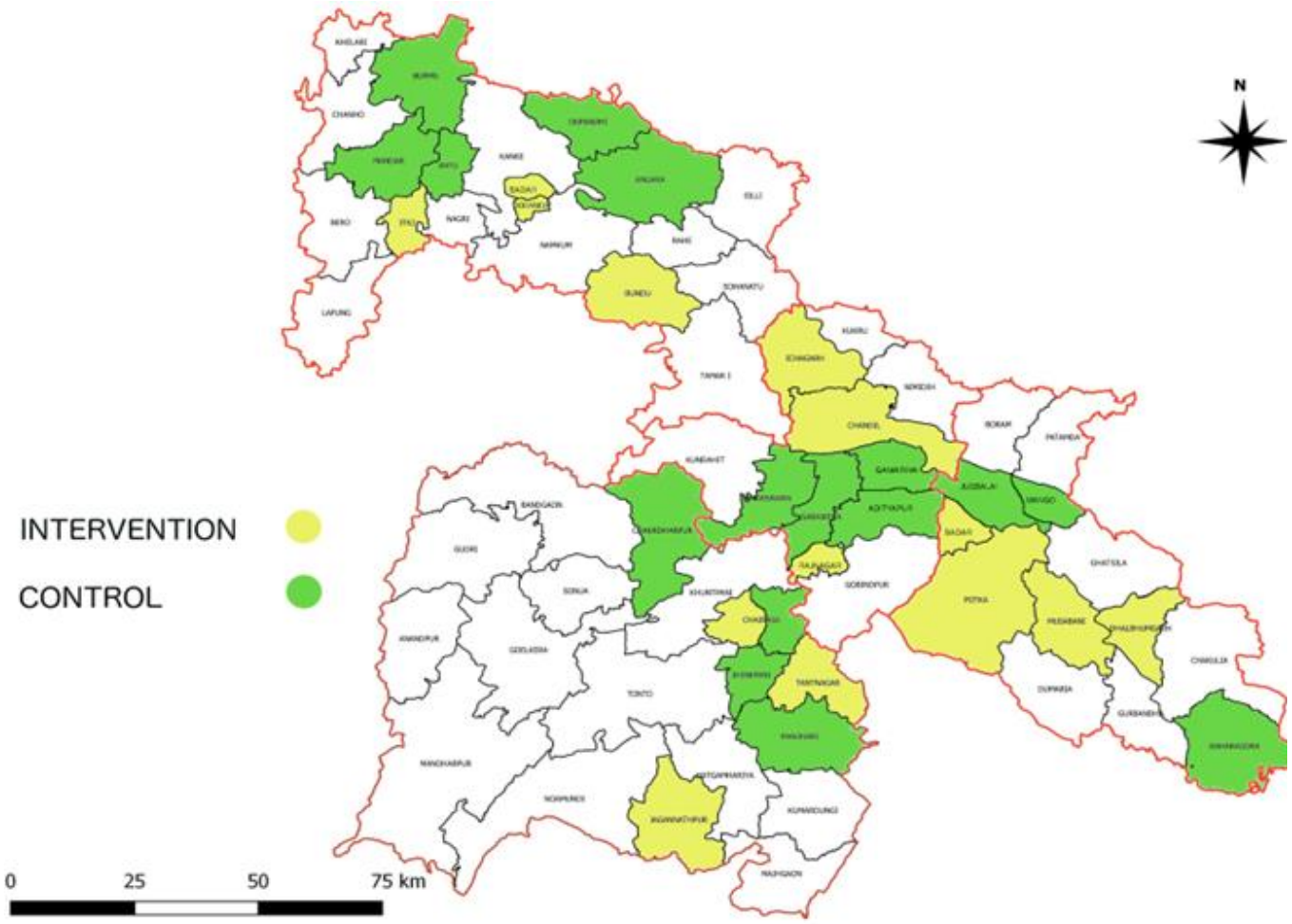
A natural experiment of the impact of nutrition on TB: From 1945

	TB incidence
Britishers: usual prison diet+ 1000 calorie+ 30 g proteins/day	6 /500 (1.2%)
Russians: Usual prison diet	300/2000 (15%)

	French (1,200)	Russian (1,200–1,000)	British (250)
1943, July–Dec.	0	6	0
1944, Jan.–June	1	14	0
,, July–Dec.	1	31	0
1945, Jan.–April (3 months) ..	4	11	0

Leyton GB. Effects of Slow starvation. The Lancet. 1946;248(6412):73-9.
Cochrane AL. Tuberculosis among prisoners of war in Germany. British Medical Journal 1945:656-8.

Trial setting: Jharkhand (The land of trees)



Trial Area

- 4 districts: Ranchi, Seraikela Kharsawan, East Singhbhum, West Singhbhum
- 28 TB units
- 2100 Km^2

Trial Timeline

Start date of trial: 14th May 2019
Start of Enrolment : 16th Aug 2019
Trial duration: 3 years
End date: 13th August 2022

Study population

RATIONS TRIAL and its populations

10345 Household contacts followed for 2 years

2800 Patients (1400 in each arm) with infective PTB

Control group: 4724 household contacts were on usual diet

Intervention group: **5621** contacts received food baskets + multivitamins for 6 months

Objectives

Primary Objective

- Difference in incident cases in Household Contacts in both arms in 24 months of follow-up

Secondary Objectives

- TB mortality
- Weight change, BMI, functional status
- Loss to follow-up
- Severe adverse effects to TB drugs

Study Intervention: a million kg study

Study arms	Intervention
Intervention arm	• **Patient**: 5 Kg Rice + 3 Kg Pulses + 1.5 Kg milk powder + 500 ml Oil + **multivitamins** per capita per month (1200 Kcal + 52 gm protein per day) • **Family**: 5 Kg Rice +1.5 Kg pulses+ **Multivitamins** per capita per month (750 Kcal + 23 g proteins per day)
Control arm	• **Patient:** 5 Kg Rice + 3 Kg Pulses + 1.5 Kg milk powder+ 500 ml Oil + multivitamins • **Family:** Nutritional assessment + dietary advice

Cost of basket per patient per month: Rs. 1100 /USD 15.6 (2019 prices) Cost per adult contact: Rs. 325 /USD 4.6 per month

Glimpses from the field

Baseline characteristics of contacts

- People who had access to PDS: **85%**
- Tobacco consumption: **9%**
- Alcohol consumption: **14%**
- Presence of BCG Scar: **70%**
- Tuberculosis preventive treatment*: **16%**

Children <5 years: 11%
Children 6-17 years: 30%

Adults: 59%

Prevalence of Undernutrition across age groups

	Control	Intervention
Adults	**35%**	**39%**
Children	**47%**	**49%**
Adolescents	**21%**	**27%**

Outcomes in contacts of the RATIONS trial

PRIMARYOUTCOME

Incident TB in contacts:

96/5602(2.6%) vs. 22/4712(1.7%):

Incident TB rates in contacts:

1270 /10^5p-y vs. **780** / 10^5p-y

Adjusted Incidence rate ratio (all forms of TB): **0.61**

(**39% reduction in incidence rate**)

Adjusted Incidence rate ratio (Lung TB): 0.52

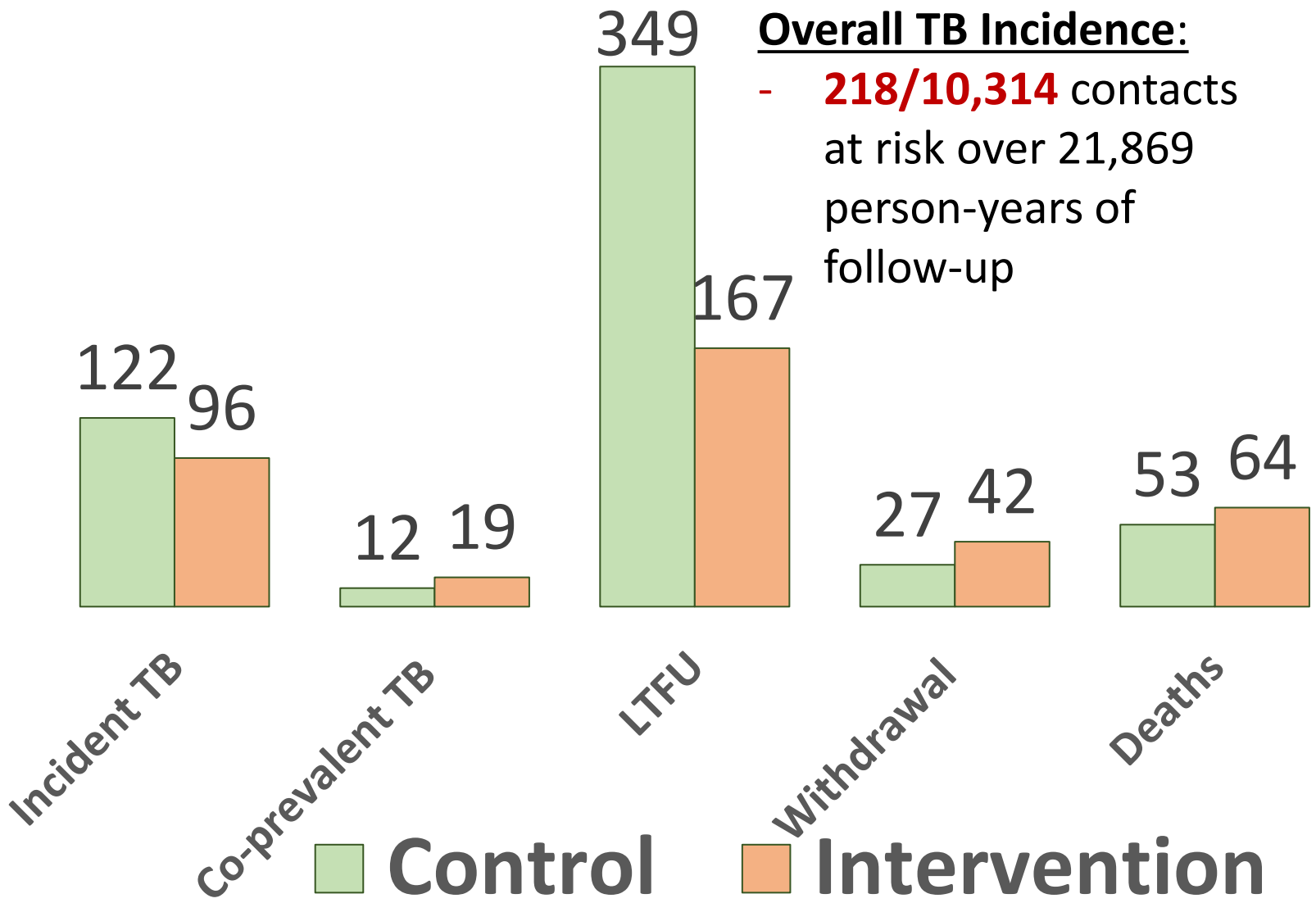
(48% reduction in incidence rate)

Adjusted HR(all forms): 0.59

Adjusted HR (Lung TB): 0.51

Overall TB Incidence:

- **218/10,314** contacts at risk over 21,869 person-years of follow-up



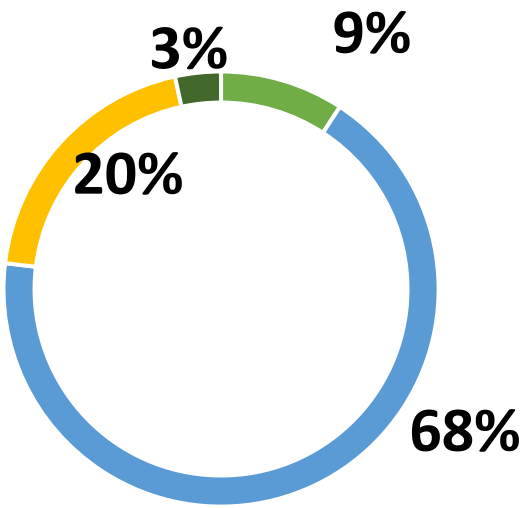
Key baseline characteristics and outcomes in patients

Underweight (BMI<18.5 kg/m^2): **82%**

- Severely underweight (BMI<16 kg/m^2)**: 48.6%**
- Extremely severely underweight (BMI<14 kg/m^2)**: 17%**

70.7%

29.3%



The severely ill patients with TB:

- Hypotension **– 10.4%**
- Hypoxia: **9%**
- Anemia : **88%**
- Severe anemia: **7.5%**

Performance status at b**aseline**
Able to do normal work: **3%**
Limited activity or bed bound: **12 %**

Outcomes:

Treatment success: 94%

Loss to follow up : 1%

Treatment failure: 0.2%

Deaths: 3.9%

Return to normal work : 75%

Undernutrition as a serious comorbidity in patients with TB:globally

- **Systematic review of Prevalence of Undernutrition (Low BMI) in pulmonary TB: 48%**
- The prevalence of mild, moderate, and severe malnutrition was 21.4%, 14.0%, and 29.4%.
- **Systematic review of prevalence of anemia in patients with TB : 61.5%**
- Prevalence of mild, moderate and severe anemia was 35.7%, 31.2%, and 11.6%.
- **Undernutrition is the *single most prevalent , easily identifiable and treatable comorbidity* increasing TB mortality**

(Li A etal. Front Med (Lausanne). 2023;10:1173619. . Barzegari S, etal Indian J Tuberc. 2019;66(2):299-307)

TB Deaths and their predictors

- **Most deaths in first 2 mos. Median Time to death was 46 (18,96)**
- Most deaths occurred at home (77%)

- **3 major predictors of death:**
- 5% decrease in Incidence of death per kg increase in weight: 23% decline with 5 kg.
- 3 fold higher risk with diabetes.
- 5 fold higher risk with bed –ridden or limited mobility patients

Adequate weight gain ↓ deaths. Lack of weight gain ↑ deaths

- **5%** weight gain in first two months reduced the hazard (instantaneous risk) of death by **60% [aHR = 0.39, 95% CI 0.18-0.86]**
- Even females: 18.8 kg and 8.6 kg/m^2 Males: 24.2 kg and 10.7 kg/m^2 survived
- In cohorts without nutritional support, 60% had static or decreasing BMIs in 2 months *(Sinha P etal. CID. 2022)* and this was associated with 5 fold risk of death

Key learning from RATIONS trial for **TB Prevention: A B F** as a vaccine

Nutritional supplementation is a potential public health intervention for TB prevention in communities with a burden of TB and undernutrition

- Nutritional supplementation reduced the incidence of TB by nearly 40-50%.
- NNS in contacts to prevent 1 case of TB over 2 years: **111 (30 households)**
- **No. of TB cases prevented per 1000 contacts supplemented vs. treated with TPT: 9 cases vs. 11 cases.**
- Nutritional supplementation can complement other strategies for TB prevention
- Efficacy of protection: ~ to recently developed vaccine (M72/AS01$_E$)- 49.7%
- Oral, Polyvalent, safe in children and pregnant women, promotes growth and development.
- Ryckman T, Weiser J, Gombe M etal . The Lancet Global Health. 2023;11(8):e1205-e16.

Effect of nutritional care on other infectious morbidity; Daily supplementary feeding vs. daily medical care.

TABLE 3

Illness of children aged 0–58 mo in two Guatemalan highland Indian villages, one with daily supplementary feeding and one with daily medical care[1]

	Santa Maria Cauqué Medical treatment village		Santa Cruz Balanya Supplementary feeding village	
Year	No. children	Illnesses per child	No. children	Illnesses per child
1960	189	3.4/y	118	1.3
1961	207	4.7	139	1.3
1962	212	5.9	151	1.4
1963	211	4.7	146	2.6
1960–1964	205 average	18.7 in 4 y	138 average	6.6 in 4 y

[1] Source: Scrimshaw and Guzman 1995 (12).

Scrimshaw NS. Historical concepts of interactions, synergism and antagonism between nutrition and infection. J Nutr. 2003;133(1):316s-21s.

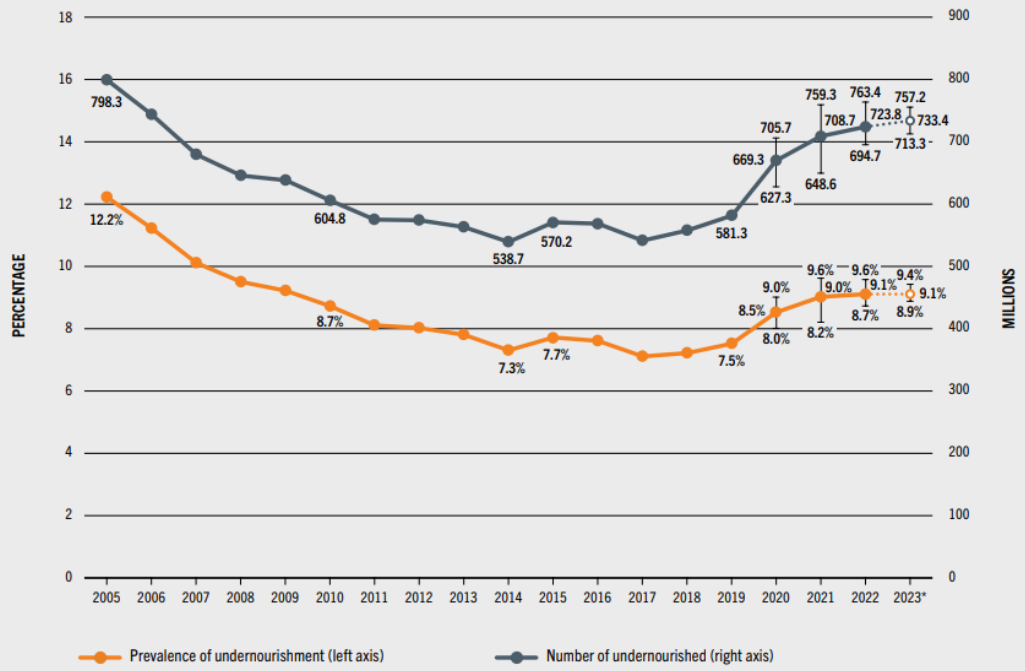
Poverty, extremely severe undernutrition and recovery with person-centred care in RATIONS




Nutritional Support: Essential Not Optional Component Of Person-centered Care

Nutrition: The challenges:Global hunger has risen and is persistent
The opportunities: Nutrition is a super-investment

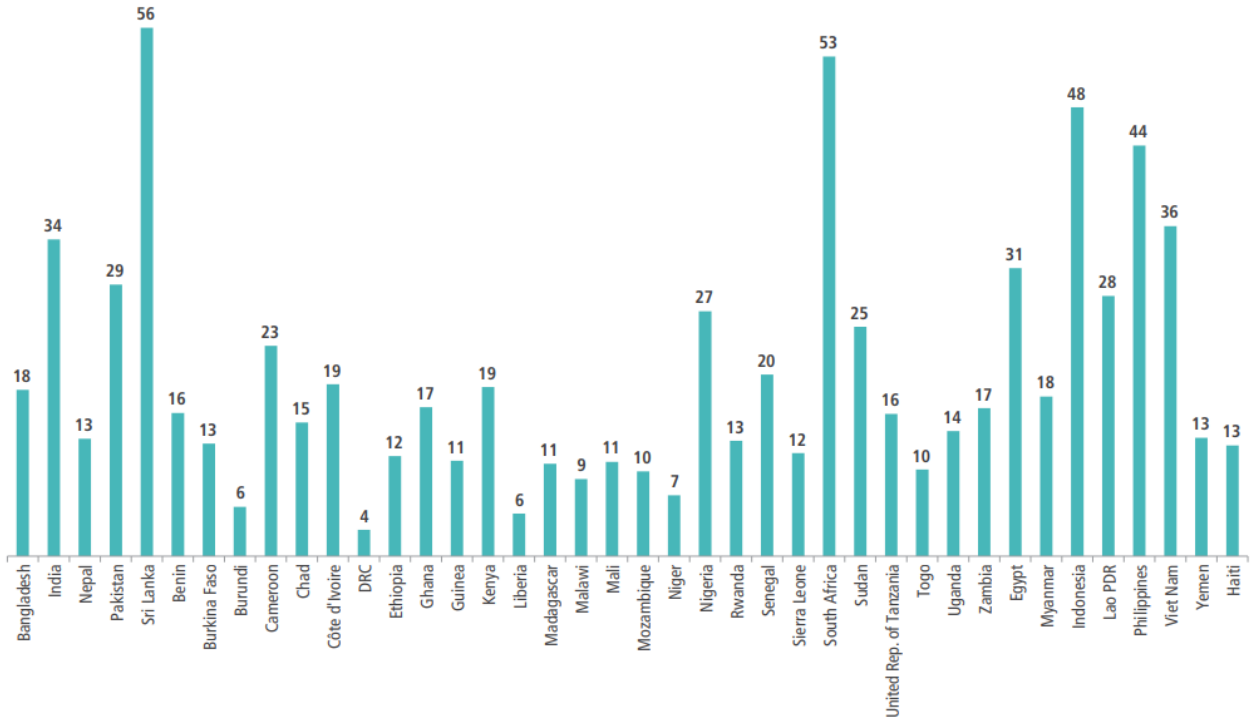
FIGURE 1 GLOBAL HUNGER ROSE SHARPLY FROM 2019 TO 2021 AND PERSISTED AT THE SAME LEVEL TO 2023



NOTES: Bars show lower and upper bounds of the estimated range. * Projections based on nowcasts for 2023 are illustrated by dotted lines.
SOURCE: FAO. 2024. *FAOSTAT: Suite of Food Security Indicators*. [Accessed on 24 July 2024]. https://www.fao.org/faostat/en/#data/FS.
Licence: CC-BY-4.0.

The State of Food Security and Nutrition in the World 2024

FIGURE 2.1 BENEFIT-COST RATIOS OF SCALING UP NUTRITION-SPECIFIC INTERVENTIONS FOR STUNTING REDUCTION IN SELECTED COUNTRIES



Source: Hoddinott et al. (2013), and additional country estimates made by the authors based on the methodology in Hoddinott et al. (2013).
Note: The benefit-cost ratios are for scaling up the nutrition-specific interventions described in Bhutta et al. (2013a).

Global Nutrition Report 2014

Dr. Martin Luther King in his Nobel Prize acceptance speech(1964)

"I have the audacity to believe that people everywhere can

have three meals a day for their bodies,

education, and culture for their minds and

dignity, equality and freedom for their spirits."