Helminth Influences in Leprosy: Indicators, Treatment, Reactions and Clinical Outcomes

LRI Project 703.15.41

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LEPROSY RESEARCH INITIATIVE

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Soil-Transmitted Helminths (STH)

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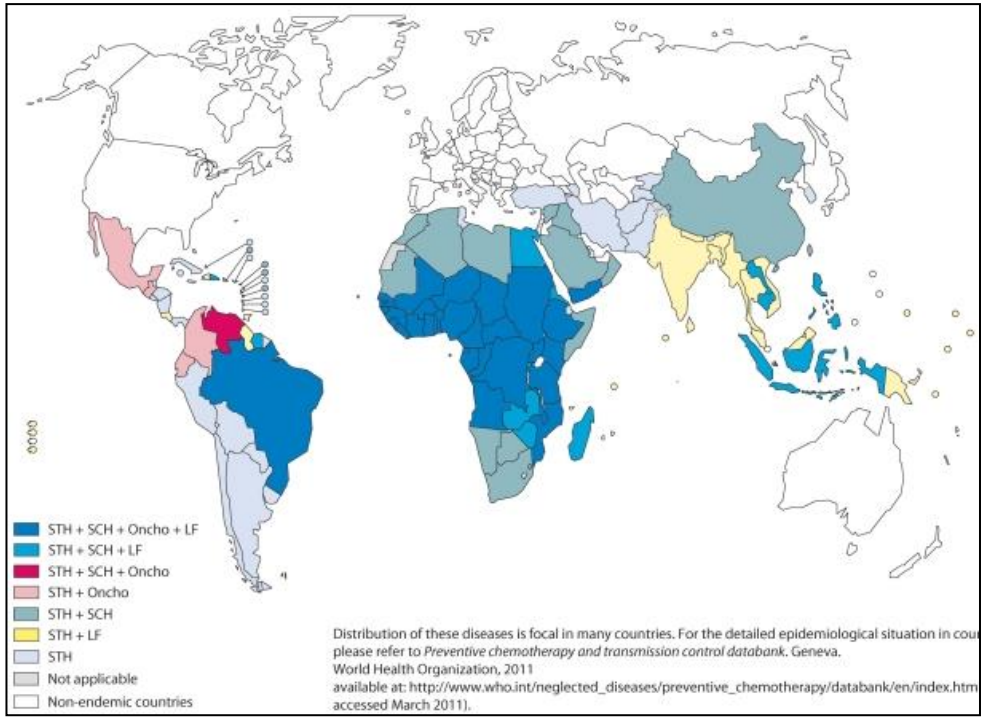
- NTD: 2 billion infected worldwide
- 5 main species seen in humans:
  - Roundworm (*Ascaris lumbricoides*)
  - Whipworm (*Trichuris trichiura*)
  - Hookworm (*Necator americanus, Ancyclostoma duodenale*)
  - Threadworm (*Strongyloides stercoralis*)
- Other helminth NTDs (associated with water):
  - Onchocerciasis – >99% in 31 African countries
  - Schistosomiasis – 90% in Africa



Endemic Population Control

Periodic Deworming + Health Education + Improved Sanitation

- Periodic Deworming → Mass Drug Administration (MDA)
- Health Education → WASH
- Improved Sanitation → (Extreme) Poverty, Crowding, Housing, And National Infrastructure

More than 94% of annual new leprosy cases are from areas co-endemic for soil-transmitted helminths (STH).

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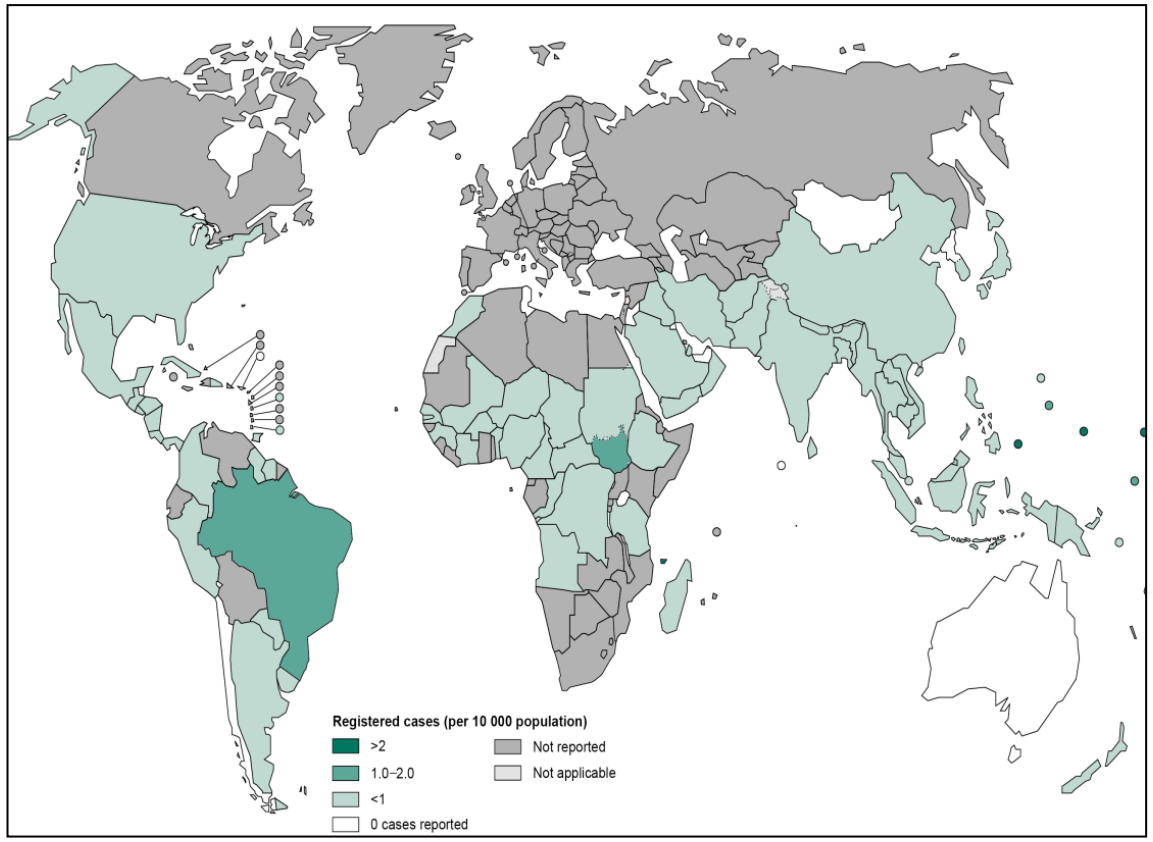
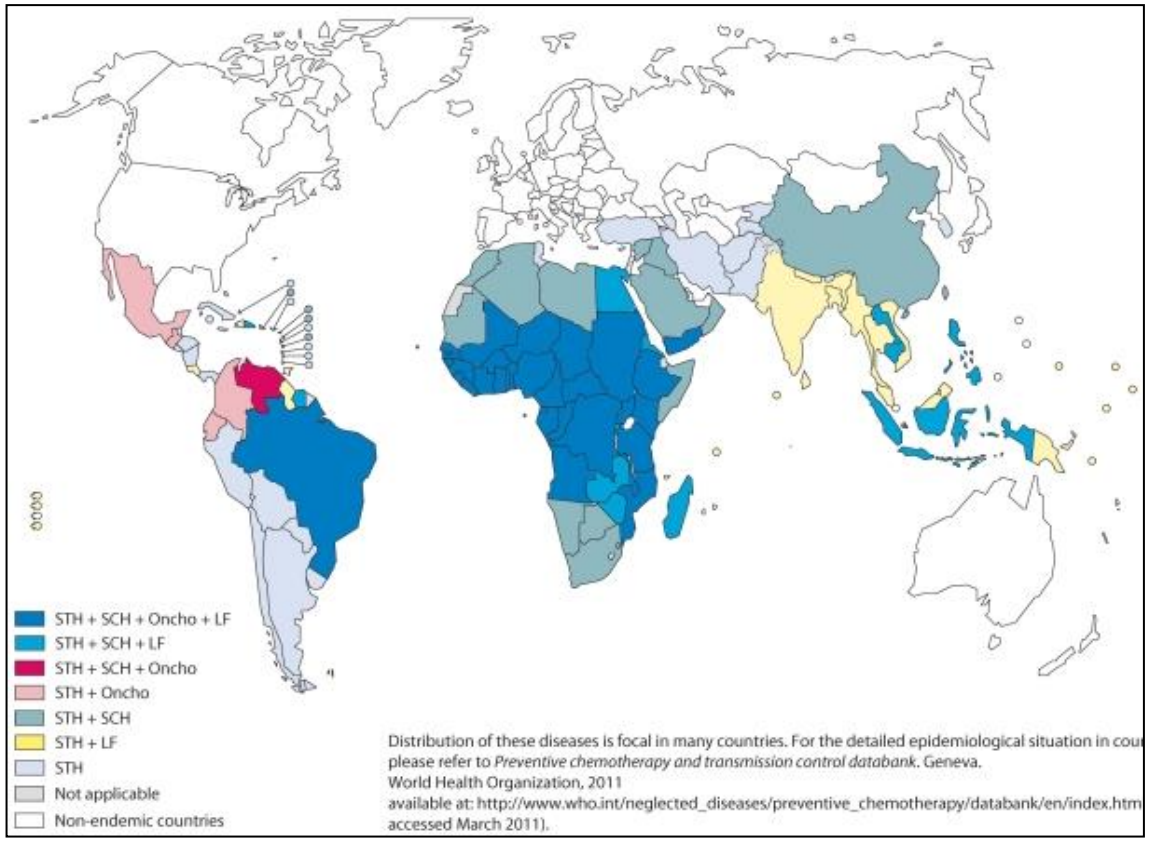
Global Distribution of Leprosy



Global Distribution of Helminths



Helminths and Leprosy: Co-endemic Populations

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Chronic helminth infection can supress cellular immunity and create systemic bias towards an antibody response

Retrospective or Observational Cohorts

M.leprae evidence can persist for years

Helminths: DNA can be cleared within a week after deworming

Repopulating T cell responses can vary from months to years (burden, disease, species, multiplicity, duration)

Reduces ability to kill or limit *M.leprae* growth

MB, BL/LL leprosy

Deworming?

Destabilize Co-infection? Immune Shift or Reconstitution?

Leprosy Reactions

Helminth Influences in Leprosy: Indicators, Treatment, Reactions and Clinical Outcomes

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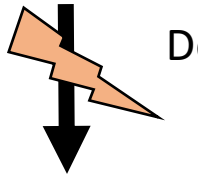
Prospective, longitudinal cohort study

Baseline Cohort

1. *New Leprosy without Reaction*
2. *New Reaction*
3. *New Leprosy Household Contacts*



Deworming (6 monthly)
WASH training

Follow-up Quarterly for up to 2 years

Sampling for Analysis

Clinical Exam → leprosy indicators and outcomes

Stool sample → microscopy, qPCR → Nepal's STH (all 5 species)

Blood → immune response to *M. leprae*

Questionnaire → socio-economic context, sanitation access
WASH → Habits, implementation and sustainability

Very well defined → Tremendous amount of data and analysis

1st National Mass Drug Administration Campaign in Nepal began in 2003

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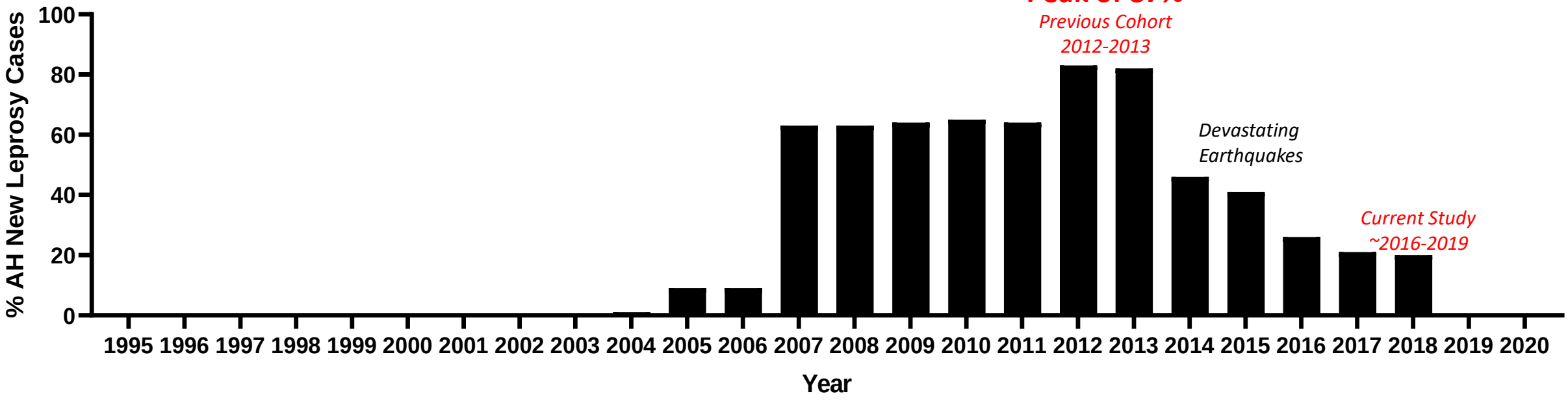
Mass Drug Administration (MDA)

Albendazole: 4-5 year annual campaigns step-wise across districts

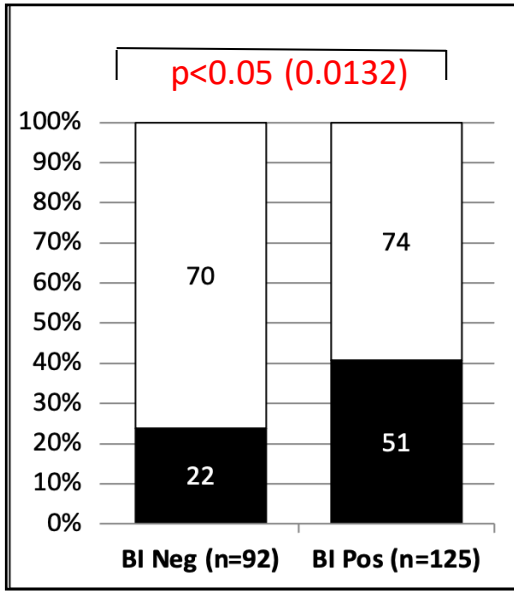
Percentage of TLM Nepal's New Leprosy Cases reporting from MDA-active Districts



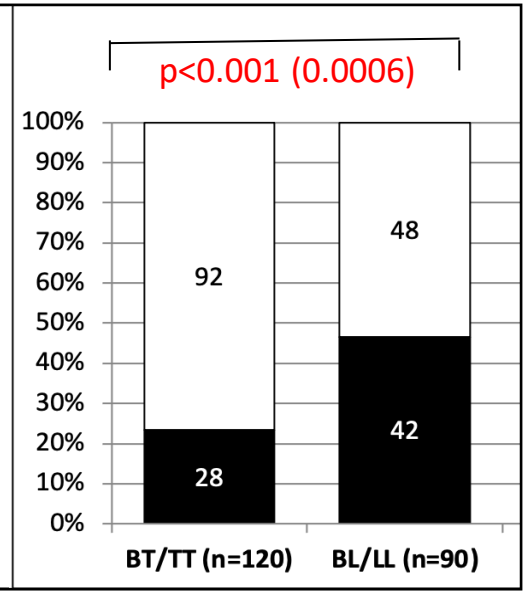
New Leprosy and Helminth Co-infection at Baseline

Helminth Co-infection Analysis	Association
BI	STH+ ~ BI+ **(p < 0.05)**
Across BI counts (0-6+)	STH+ linear trend **(p < 0.0013)**
TT/BT or BL/LL	STH+ ~ BL/LL **(P < 0.001)**
Across Ridley-Jopling Classifications	STH+ linear trend **(p < 0.0001)**
Leprosy Reactions	-

BI vs STH infection



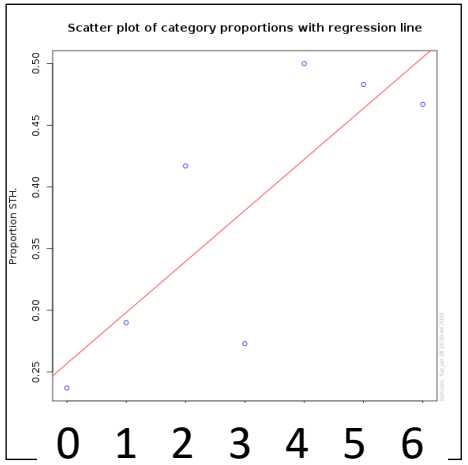
RJ vs STH infection



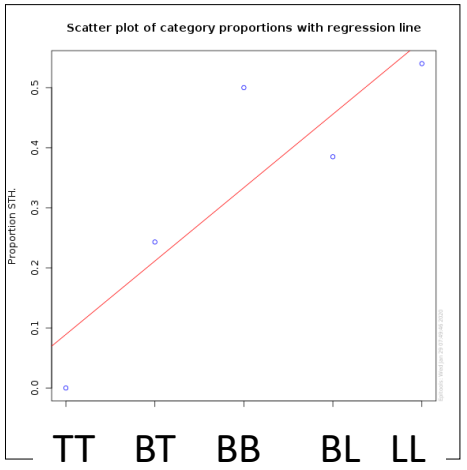
STH co-infection is significantly associated with leprosy indicators

Directly relate to host immune response and duration of disease

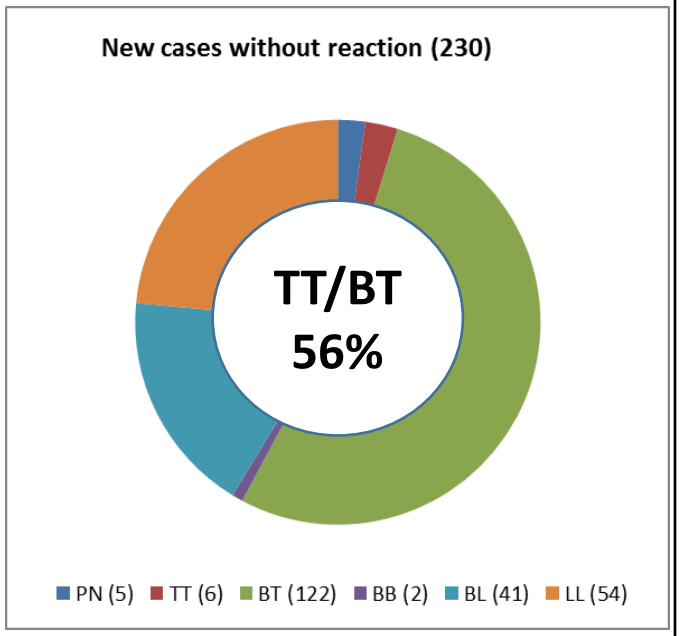
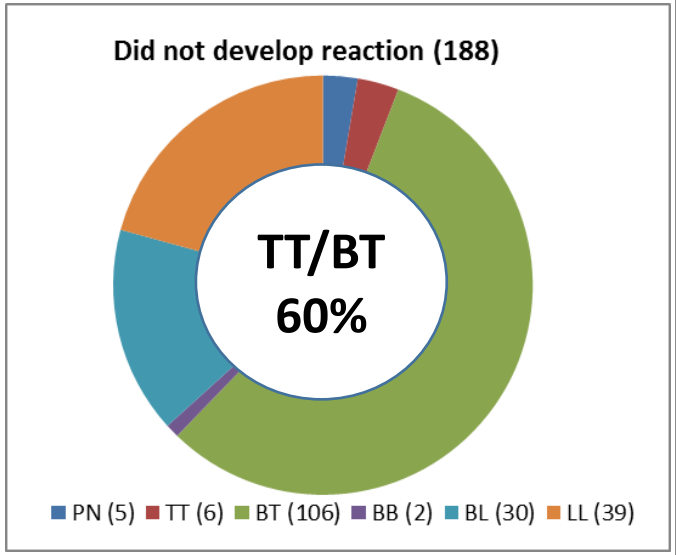
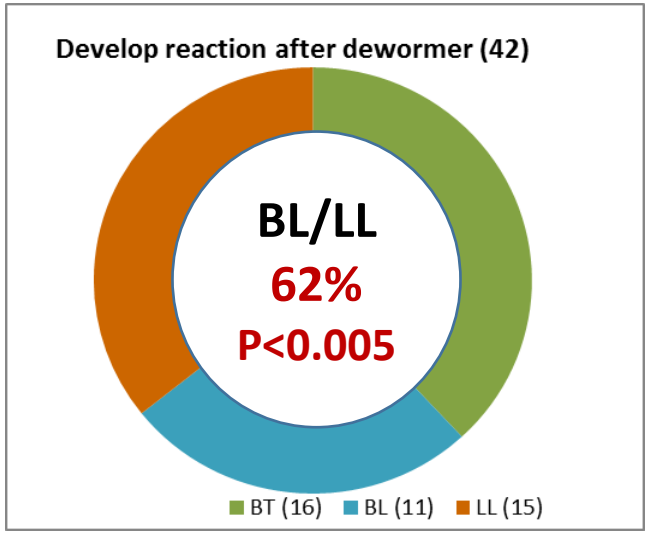
BI Score



Ridley-Jopling Classification



New Cases that Developed Reaction after Deworming: How were they different?

Indicator	230 New leprosy without reaction	188 never developed reaction	42 developed reaction
BI	58% BI+ Average BI 2.77	51% BI+ Average BI 1.7	83% BI+ Average BI 3.1 **(p < 0.0001)**
Ridley-Jopling			

STH association with leprosy reaction at baseline?

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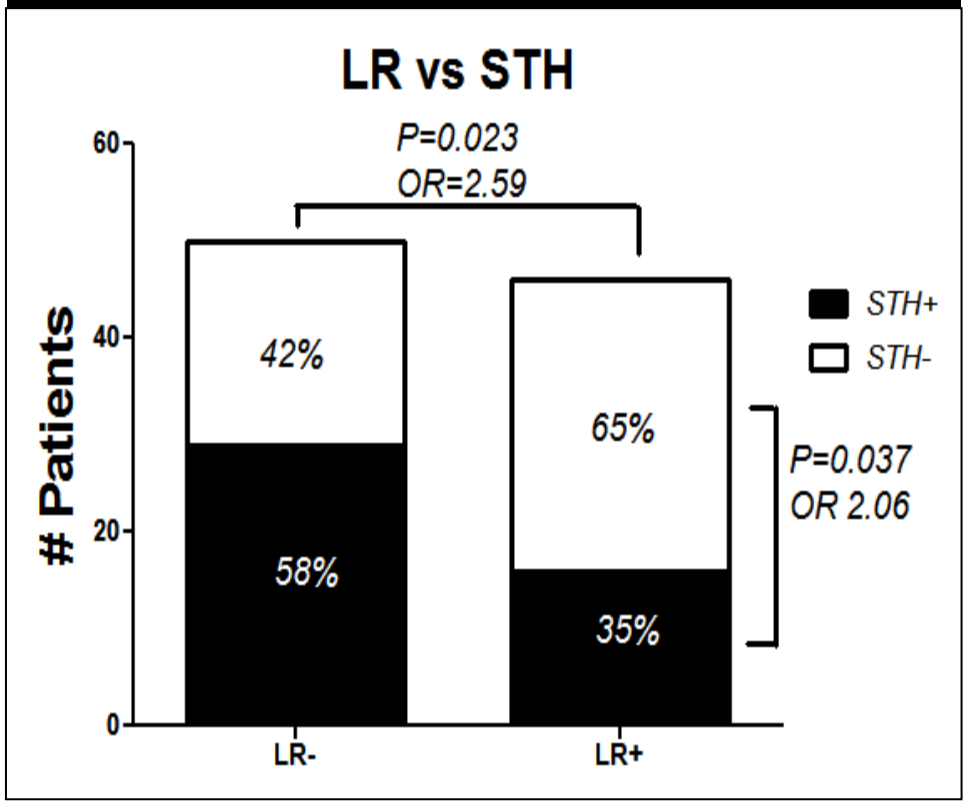
Peak MDA 87%

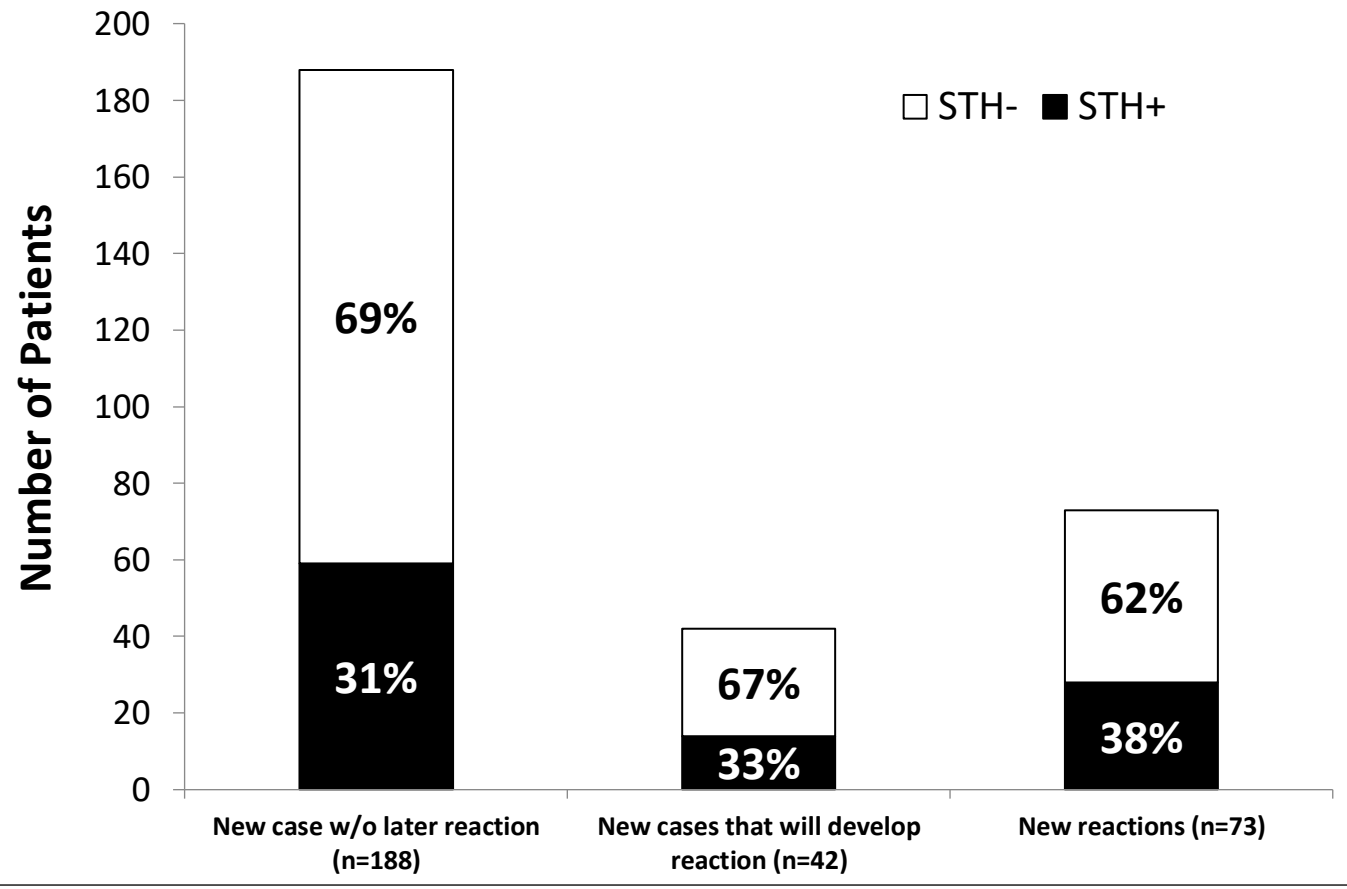
Significant Inverse Relationship

2012-2013 Cohort

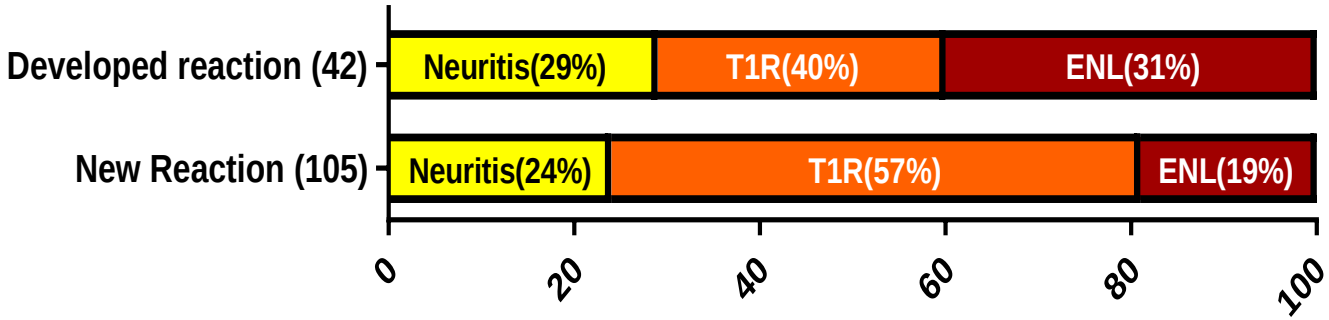


Post-MDA 80%

2016-2019 Cohort



Was Leprosy Reaction Presentation Different when New Cases were dewormed at MDT start?



Duration to Reaction Development

Group (220)	Neuritis (11)	Type 1 Reaction (18)	ENL (13)
New Leprosy + MDT + Dewormer	82% ≤ 6 months	71% ≤ 6 months	69% ≥ 6 months

*Follow-Up data still pending

M.leprae & Helminth Co-infection Summary

Co-endemic population

Soil-Transmitted Helminths

Significantly Associated

Disease Duration

BI

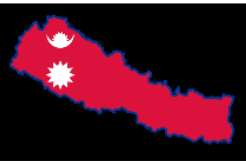
Ridley-Jopling

Long-term immunological response to *M.leprae*

Significantly Associated

Leprosy Clinical Outcomes:
Reactions, Neuropathy → Disability Development

Study Relevance and Pending Work



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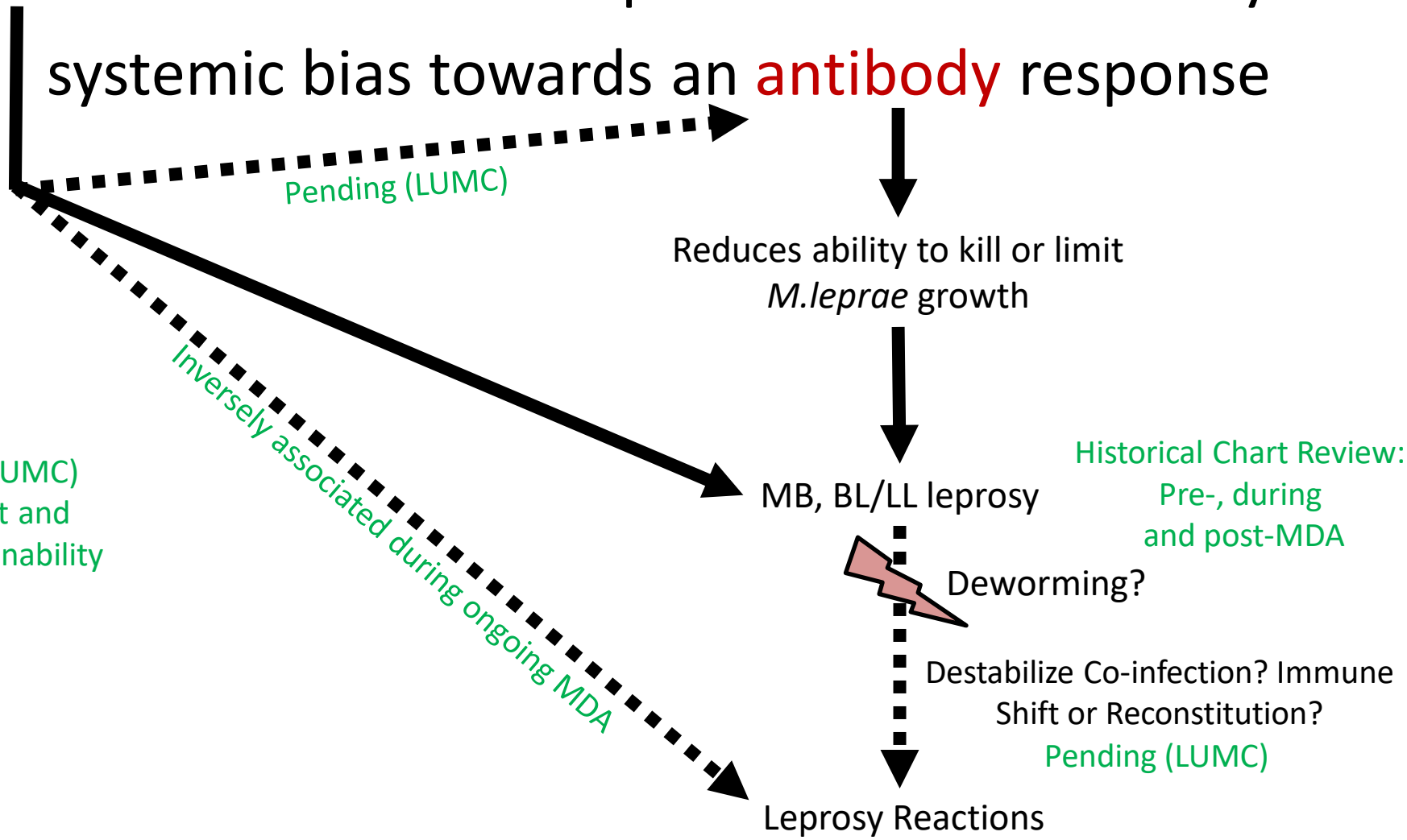
Chronic helminth infection can supress cellular immunity and create systemic bias towards an antibody response



- Final follow-up via call or patient visit
- Finish Follow-Up Stool qPCR
- Subset: Immune Analysis (Diagnostics, LUMC)
- Correlation with socio-economic context and WASH → habits, implementation, sustainability

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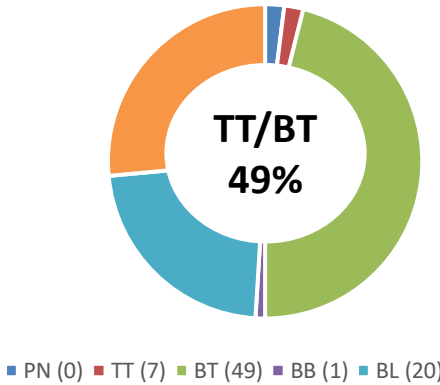
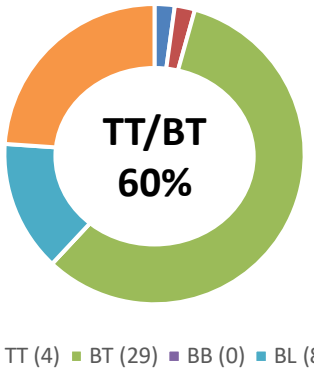
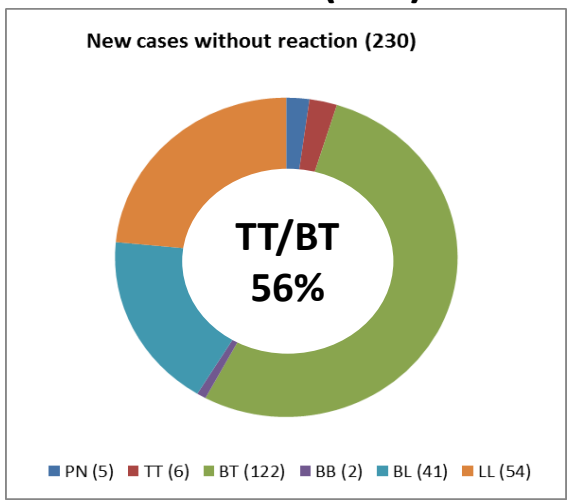
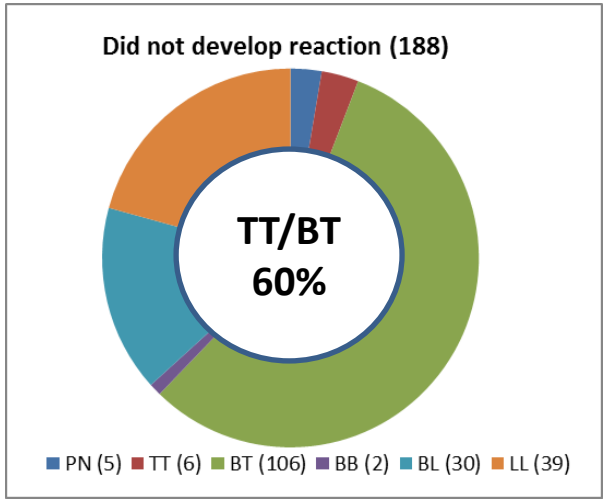
Peak MDA vs Post-MDA: Are Indicators and Reaction Patterns Different?

MDA Status	New without Reaction	New Case + Dewormer: No Reaction Development	Reaction
87% Peak MDA (2012-2013)	**40% BI+ (60)** 		**52% BI+ (94)** 
80% Post-MDA (2016-2019)	**58% BI+ (230)** 	**51% BI+ (188)** 	83% BI+ (Avg BI 3.1) **(p < 0.0001)**