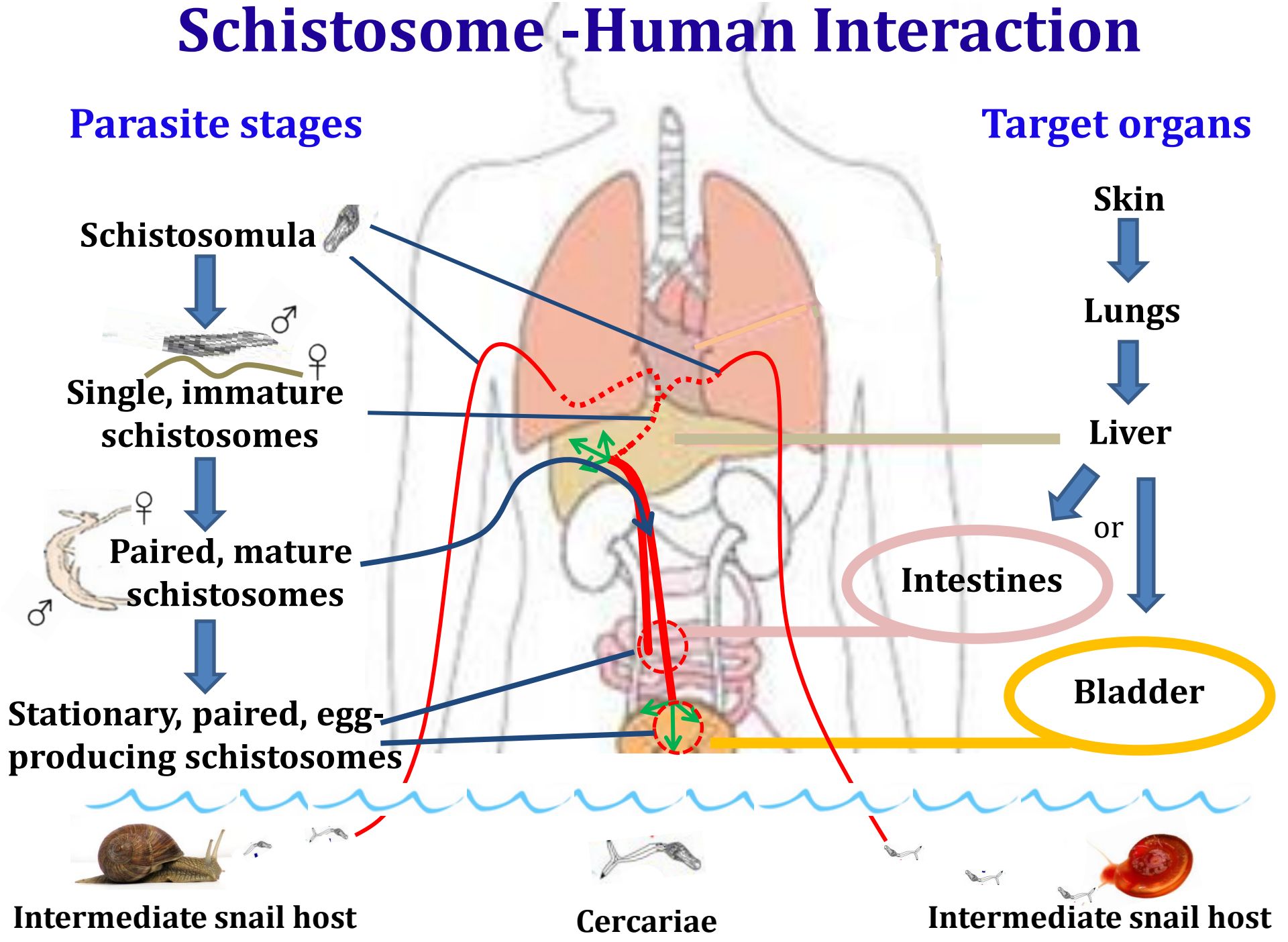
”Building on a decade of progress with WASH to control, eliminate and eradicate the NTDs”

Paper published in January 2021 by Boisson et al. in the Trans Roy Soc Trop Med Hyg in support of WHO’s new

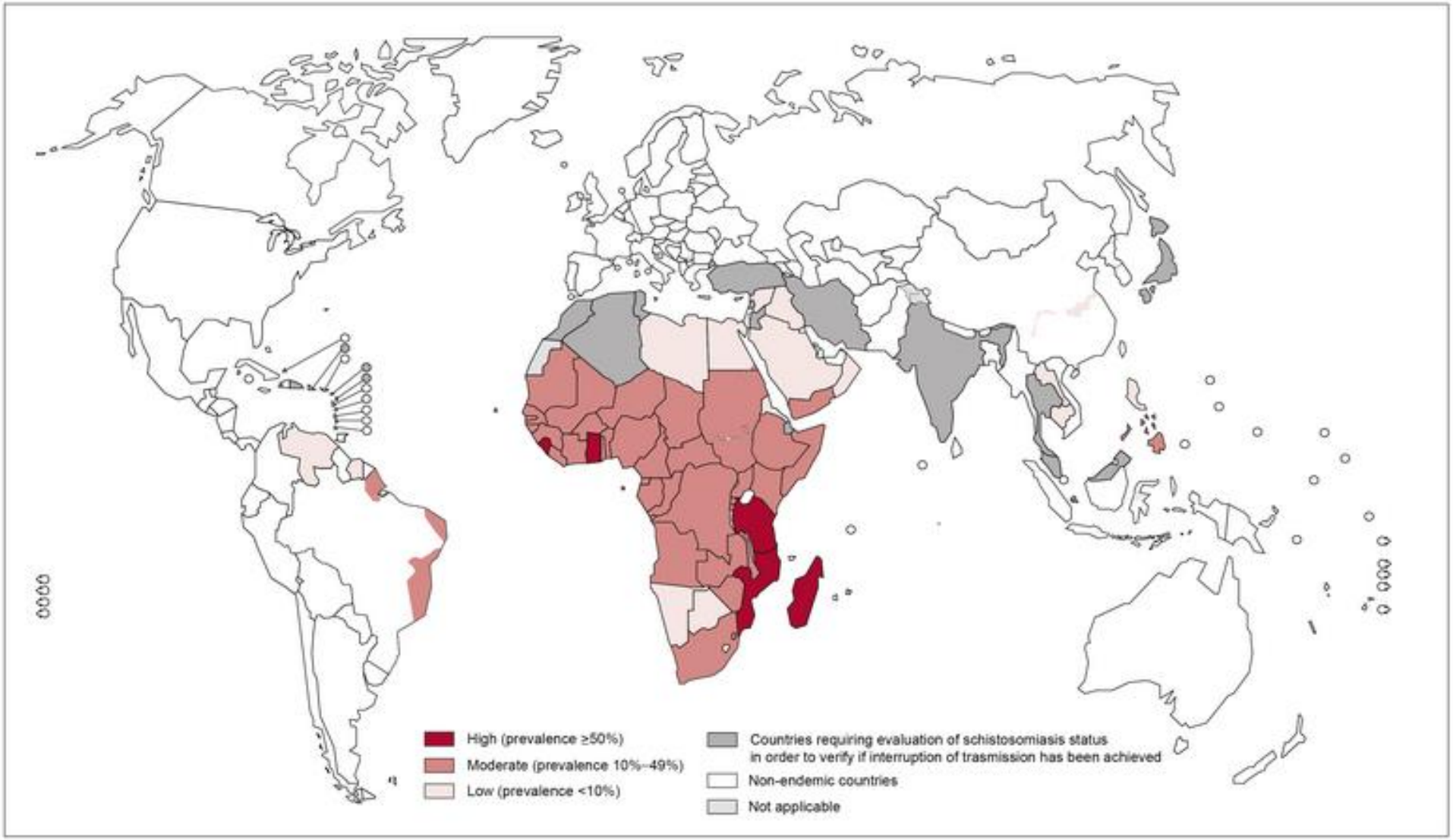
Road Map for the NTDs 2021-2030

…but where are the vaccines?

Schistosome -Human Interaction



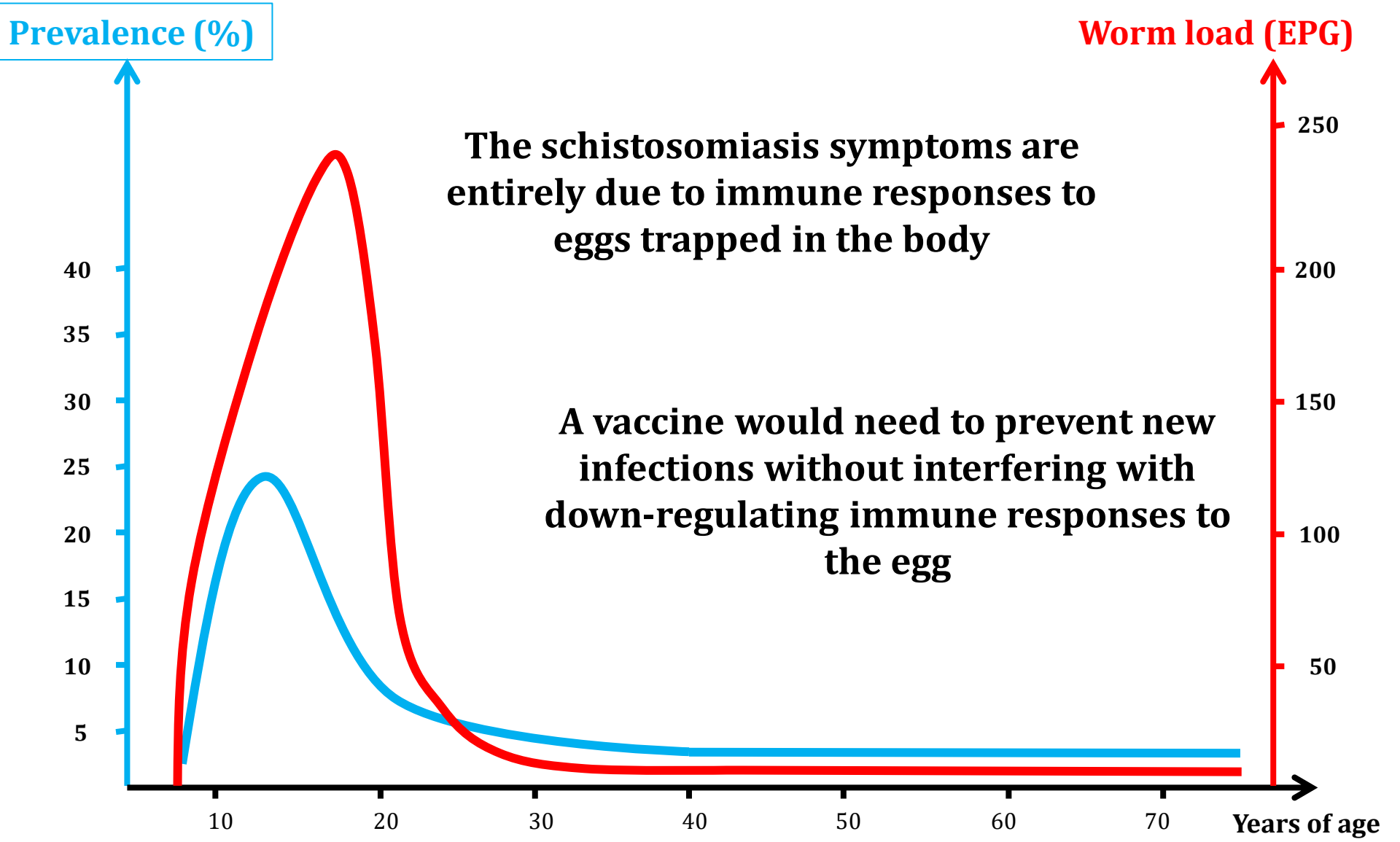
The endemic areas – situation 2013



Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

World Health Organization

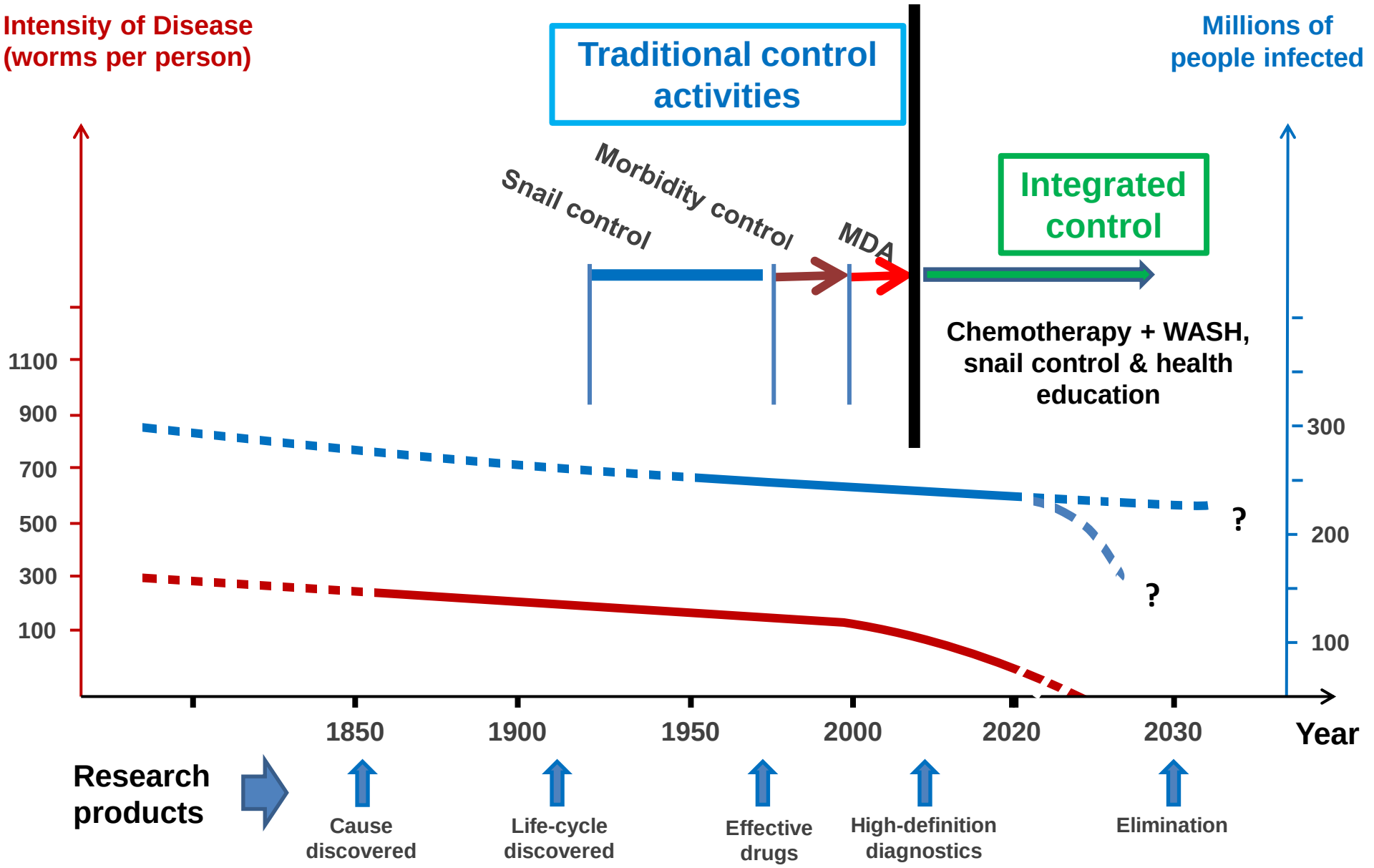
Age is a Predominant Correlate of Disease Intensity in the Endemic Areas



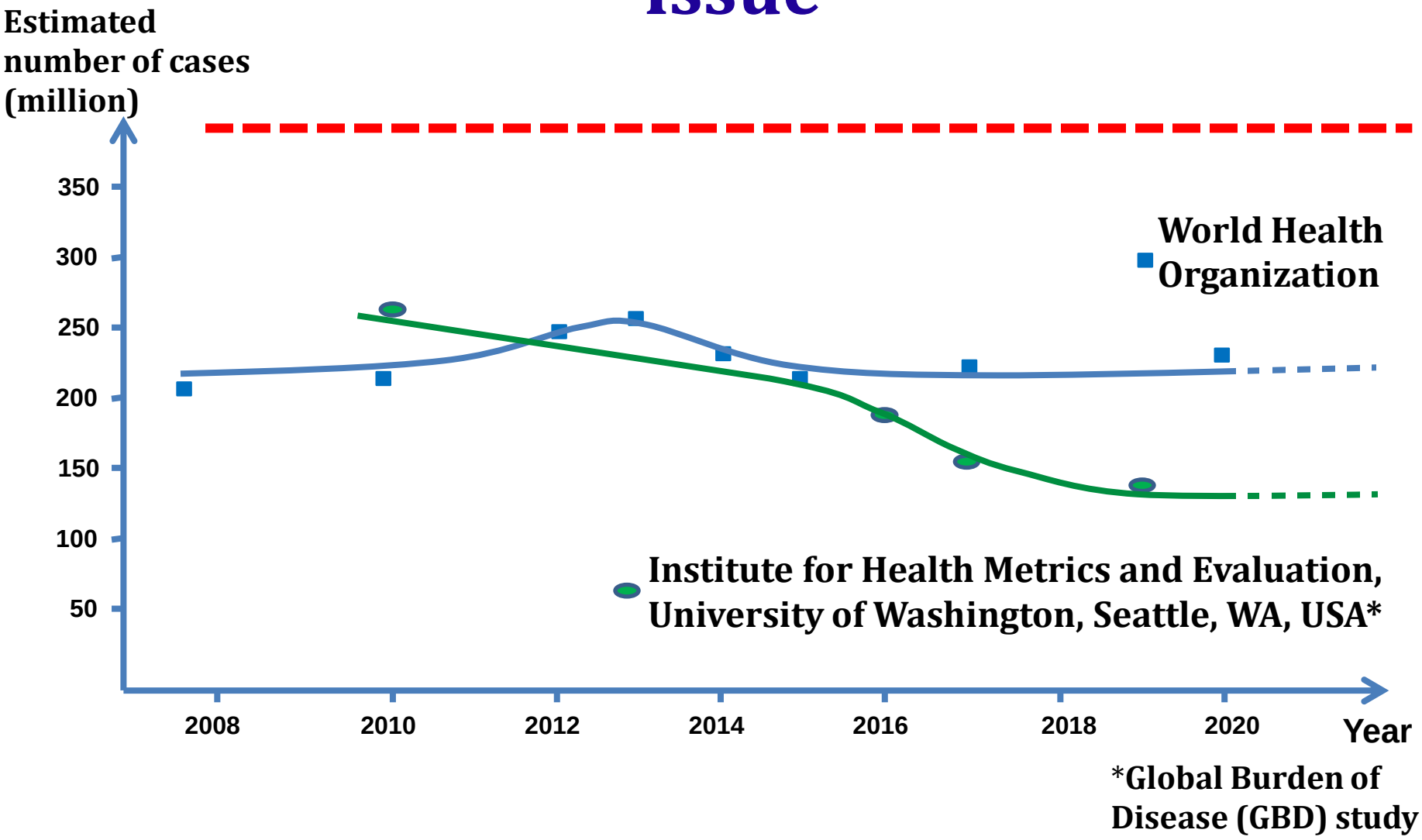
Chemotherapy with Praziquantel Remains the Cornerstone for Schistosomiasis Control

- **Chemotherapy kills adult worms (>80% effect) but immature schistosomes are unaffected and reinfection restores the previous level of worm burden within weeks**
- **Risk for development of drug resistance**
- **Only marginal effect against transmission**

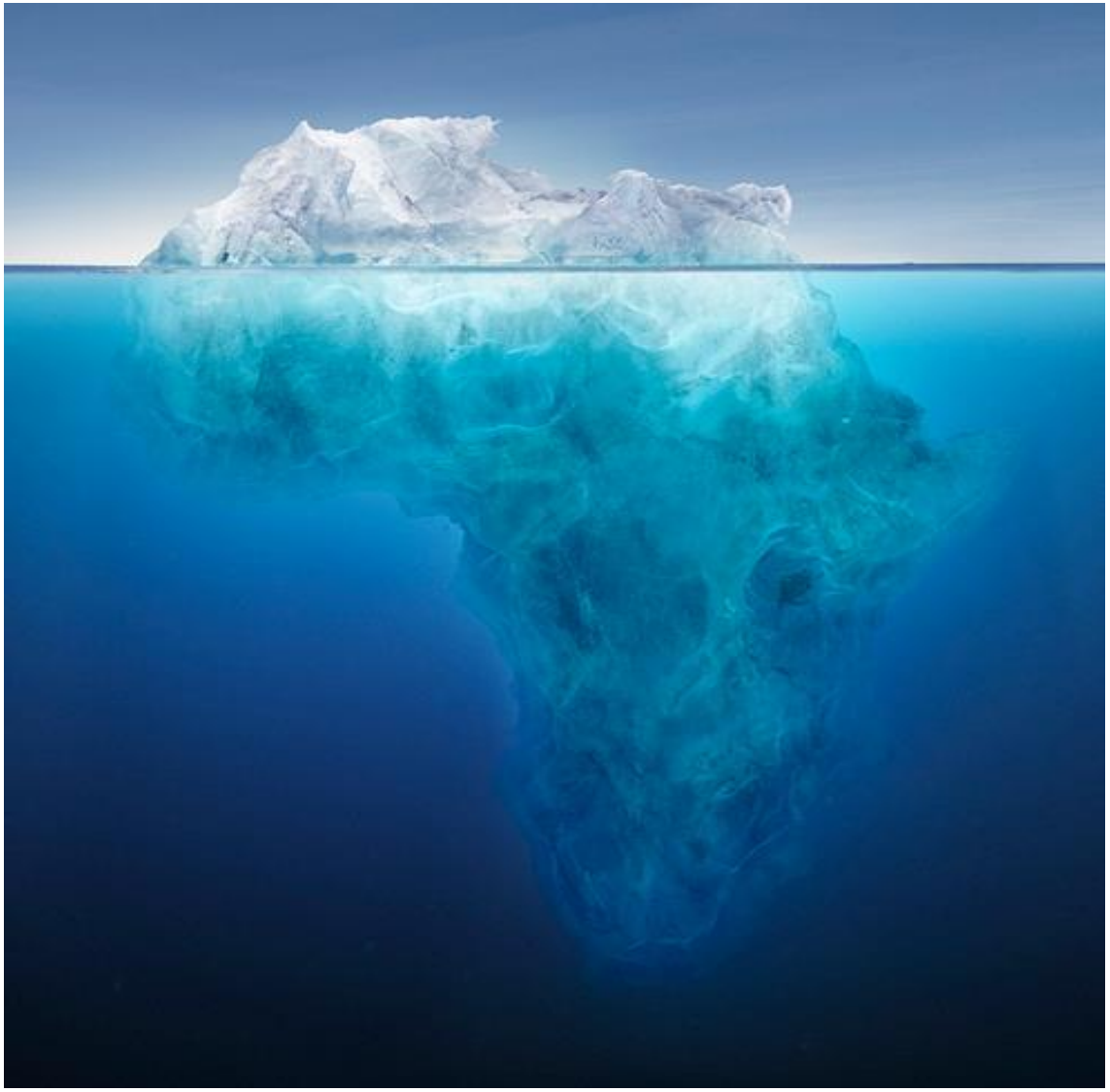
Schistosoma: quo vadis?



About 800 million People are at Risk but the Number of Infected is a Contended Issue



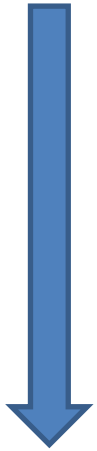
Low-level Infections Not Yet Fully Recognized



Potential for vaccination against Schistosomiasis: Supporting Evidence

- Strong immunity (around 80% protection) in mice after vaccination with attenuated cercariae
- Good protection from veterinary helminth vaccines
- Field investigations in humans show lower levels of infection in older people
- Laboratory and field studies demonstrate the presence of human protective immune responses in endemic areas

General



Specific

Key Arguments for Schistosomiasis Vaccine Development

Chemotherapy		Supporting evidence	Vaccination	
POSITIVE	NEGATIVE		POSITIVE	NEGATIVE
Praziquantel safe and effective	Short-term effect	Vaccines repeatedly proven cost-effective for control of infectious diseases	Long-term effect	Cold-chain delivery
Current control successful	Risk of reduced compliance	High-level protection consistently achieved with irradiated cercariae	Lower delivery cost over time	Relocation of people affects follow-up boosting
	Risk for drug resistance	Partial immunity acquired naturally in endemic areas	Partial effect acceptable - absence of replication in the host	

Would a Combination of Two Intervention Approaches be Useful?

Chemotherpy

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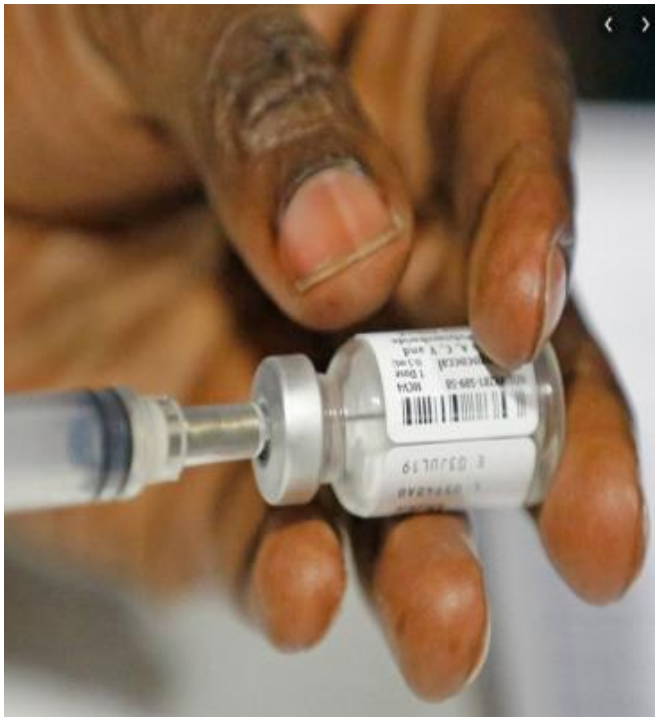
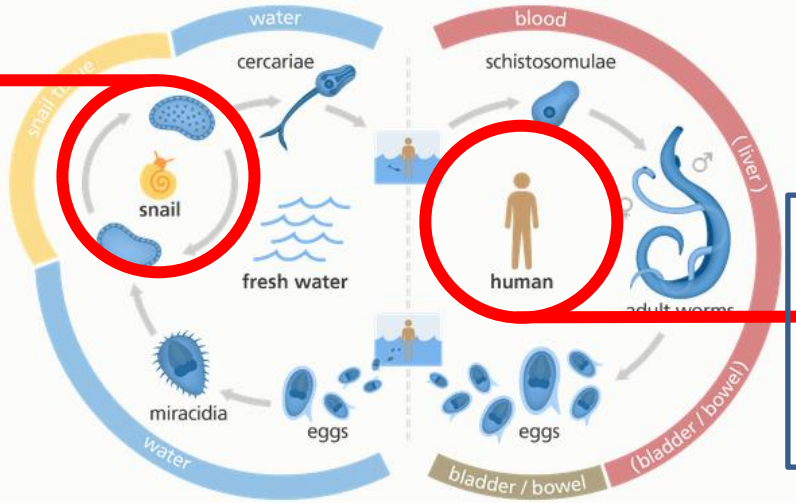


Vacination

This appproach would potentially achieve both killing of the adult worms and prevention of reinfection

Important Vaccine Trial Prerequisites

Level of snail infections = risk



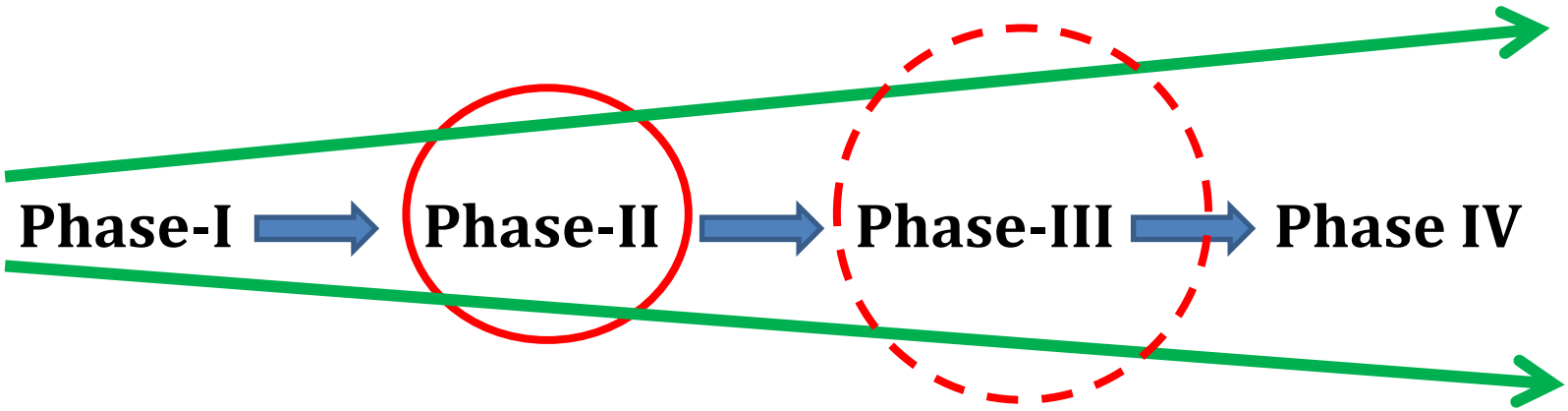
Worm burdens in humans = disease & risk

1. **Trial areas need to be surveyed and graded with respect to endemicity, as reflected by the rate of infection in the snail populations in the study area**

2. **Measurements of the intensity of infection in the definitive host most be 100% reliable**

Vaccine candidate	Phase I	Phase II	Phase III
Smp-80 (a 78 kDa subunit of calpain, a calcium-dependent cysteine protease)	Acceptable safety and immunogenicity results shown	Multi-factorial activity will require multiple endpoints	
Sh28-GST (a 28 kDa glutathione S-transferase)	Acceptable safety and immunogenicity results shown	Acceptable safety and immunogenicity results shown in the field	Delay of reinfection measured over a 3-year period
Sm14-FABP (a 28 kDa fatty acid-binding protein)	Acceptable safety and immunogenicity results shown	Acceptable safety and immunogenicity results shown in the field	
SmTSP-2 (a 9 kDa extracellular tetraspanin subunit domain)	Acceptable safety and immunogenicity results shown		
SjCTPI (a 28 kDa triose phosphatase isomerase)* *veterinary vaccine	Acceptable safety and immunogenicity results shown	Reduced bovine egg excretion shown in an endemic area	Reduced transmission of naturally acquired schistosomiasis

Endpoints for Clinical Vaccine Trials



- **Should these endpoints be the same as for chemotherapy?**
- **Should we aim for discontinued egg excretion from the host?**
- **Is reduced intensity of infection sufficient or do we need to aim for sterile immunity?**

The younger the age at vaccination, the less the risk of anti-egg responses