

## Supplementary material

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**Supplementary Table S1. Microscopy counts of cercariae in rinse water after exposure.**

		<b>Reinfection group (n=12), median (range)</b>	<b>Infection control group (n=12) , median (range)</b>
<b>Exposure 1 Week 0</b>	Heads Tails Whole cercariae	0.5 (0-1) 8.5 (2-15) 0 (0-2)	0 (0-0)* 0 (0-0)* 0 (0-0)*
<b>Exposure 2 Week 9</b>	Heads Tails Whole cercariae	0 (0-2) 5 (1-8) 0.5 (0-1)	0 (0-0)* 0 (0-0)* 0 (0-0)*
<b>Exposure 3 Week 18</b>	Heads Tails Whole cercariae	0 (0-3) 7 (5-14) 0 (0-2)	0 (0-2) 4 (1-8) 0.5 (0-2)

\* Mock exposures with water.

**Supplementary Table S2. Risk of PZQ-related symptoms after treatment.**

	Reinfection (n=12)			Infection control (n=12)		
	Treatment 1	Treatment 2	Treatment 3	Treatment 1*	Treatment 2*	Treatment 3
Any PZQ symptom#						
Mild	2 (17%)	2 (17%)	3 (25%)	1 (8%)	0	3 (25%)
Moderate	2 (17%)	4 (33%)	2 (17%)	0	0	1 (8%)
Severe	4 (33%)	0	1 (8%)	0	0	1 (8%)
Abdominal Pain						
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	1 (8%)
Severe	0	0	0	0	0	0
Nausea						
Mild	2 (17%)	1 (8%)	2 (17%)	1(8%)	0	3 (25%)
Moderate	1 (8%)	2 (17%)	0	0	0	0
Severe	2 (17%)	0	0	0	0	1(8%)
Heartburn						
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	1(8%)
Dizziness						
Mild	2	2 (17%)	3 (25%)	0	0	1(8%)
Moderate	1(8%)	2 (17%)	2 (17%)	0	0	1(8%)
Severe	4	0	0	0	0	0
Disturbance of smell or taste						
Mild	0	0	1(8%)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
Fever						
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	1(8%)	0	0	0
Headache						
Mild	0	0	1(8%)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
Malaise/fatigue						
Mild	0	0	0	0	0	0
Moderate	0	4 (33%)	0	0	0	0
Severe	3 (25%)	0	1(8%)	0	0	1(8%)
Loss of appetite						
Mild	0	0	0	0	0	0
Moderate	0	1(8%)	0	0	0	0
Severe	1(8%)	0	0	0	0	0

\* Treatment with placebo

# Only maximum severity counted

PZQ: praziquantel

**Supplementary Table S3. Number of related AEs reported after each PZQ treatment.**

	<b>Reinfection group, n (%)</b>	<b>Infection control group, n (%)</b>
<b>Treatment 1, week 8</b>	17 (42%)	3 (18%)*
<b>Treatment 2, week 17</b>	13 (31%)	0*
<b>Treatment 3, week 30</b>	14 (27%)	14 (82%)
<b>Total</b>	41 (100%)	17 (100%)

\* treatment with placebo

PZQ = praziquantel

**Supplementary Table S4. Risk of *Schistosoma*-related symptoms after (re)infection.**

	Reinfection (n=12)			Infection control (n=12)		
	Exposure 1	Exposure 2	Exposure 3	Exposure 1*	Exposure 2*	Exposure 3
Any local symptom#						
Mild	10 (83%)	11 (92%)	8 (67%)	0	4 (33%)	7 (58%)
Moderate	0	0	0	0	1 (8%)	0
Severe	0	0	1 (8%)	0	0	0
Rash						
Mild	9 (75%)	11 (92%)	8 (67%)	0	3 (25%)	7 (58%)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
Itch						
Mild	9 (75%)	2 (17%)	7 (58%)	0	3 (25%)	5 (42%)
Moderate	0	0	0	0	1 (8%)	0
Severe	0	0	1 (8%)	0	0	0
Any systemic symptom#						
Mild	3 (25%)	2 (17%)	1 (8%)	0	1 (8%)	2 (17%)
Moderate	2 (17%)	3 (25%)	1 (8%)	1 (8%)	2 (17%)	2 (17%)
Severe	2 (17%)	1 (8%)	2 (17%)	1 (8%)	1 (8%)	2 (17%)
Acute schistosomiasis						
Mild	0	0	0	0	0	1 (8%)
Moderate	1 (8%)	2 (17%)	1 (8%)	0	0	1 (8%)
Severe	2 (17%)	0	0	0	0	2 (17%)
Fever						
Mild	0	0	0	0	1 (8%)	1 (8%)
Moderate	0	0	0	0	1 (8%)	0
Severe	1 (8%)	0	0	0	0	2 (17%)
Chills						
Mild	0	0	0	0	0	1 (8%)
Moderate	0	0	0	0	0	0
Severe	0	0	1 (8%)	0	0	0
Night sweats						
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	1 (8%)	0	0	0	0	0
Headache						
Mild	0	0	0	0	0	1 (8%)
Moderate	0	0	1 (8%)	1 (8%)	0	1 (8%)
Severe	1 (8%)	1 (8%)	0	0	0	2 (17%)
Malaise/fatigue						
Mild	2 (17%)	3 (25%)	0	1 (8%)	0	1 (8%)
Moderate	2 (17%)	1 (8%)	2 (17%)	0	1 (8%)	2 (17%)
Severe	1 (8%)	1 (8%)	0	0	0	1 (8%)
Myalgia						
Mild	0	0	0	0	0	1 (8%)
Moderate	2 (17%)	1 (8%)	0	0	0	0
Severe	1 (8%)	0	0	0	0	1 (8%)
Urticaria						
Mild	0	0	1 (8%)	0	0	1 (8%)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
Facial oedema						
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	1 (8%)
Severe	0	0	0	0	0	0
Lymphadenitis						
Mild	0	0	0	0	0	1 (8%)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
Cough						
Mild	0	0	1 (8%)	0	1 (8%)	1 (8%)
Moderate	0	0	0	0	1 (8%)	0
Severe	0	0	0	0	0	0
Sore throat						
Mild	0	0	0	0	2 (17%)	1 (8%)
Moderate	1 (8%)	1 (8%)	1 (8%)	0	0	0
Severe	0	0	0	0	0	0

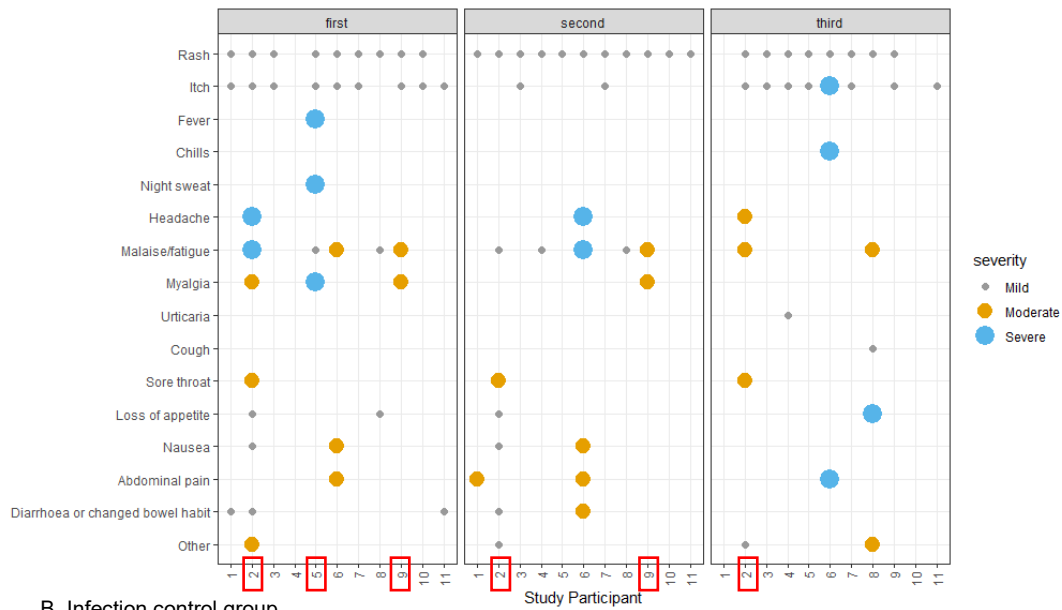
	Reinfection (n=12)			Infection control (n=12)		
	Exposure 1	Exposure 2	Exposure 3	Exposure 1*	Exposure 2*	Exposure 3
Loss of appetite						
Mild	2 (17%)	1 (8%)	0	0	0	0
Moderate	0	0	0	0	0	1 (8%)
Severe	0	0	1 (8%)	0	0	0
Nausea						
Mild	1 (8%)	1 (8%)	0	0	0	0
Moderate	1 (8%)	1 (8%)	0	0	0	0
Severe	0	0	0	1 (8%)	0	0
Abdominal pain						
Mild	0	0	0	0	0	0
Moderate	1 (8%)	2 (17%)	0	1 (8%)	0	1 (8%)
Severe	0	0	1 (8%)	0	1 (8%)	0
Diarrhoea or changed bowel habit						
Mild	3 (25%)	1 (8%)	0	1 (8%)	0	1 (8%)
Moderate	0	1 (8%)	0	0	1 (8%)	0
Severe	0	0	0	1 (8%)	1 (8%)	0
Other						
Mild	0	1 (8%)	1 (8%)	0	0	1 (8%)
Moderate	1 (8%)	0	1 (8%)	0	0	0
Severe	0	0	0	0	0	0

\* Mock exposure with water

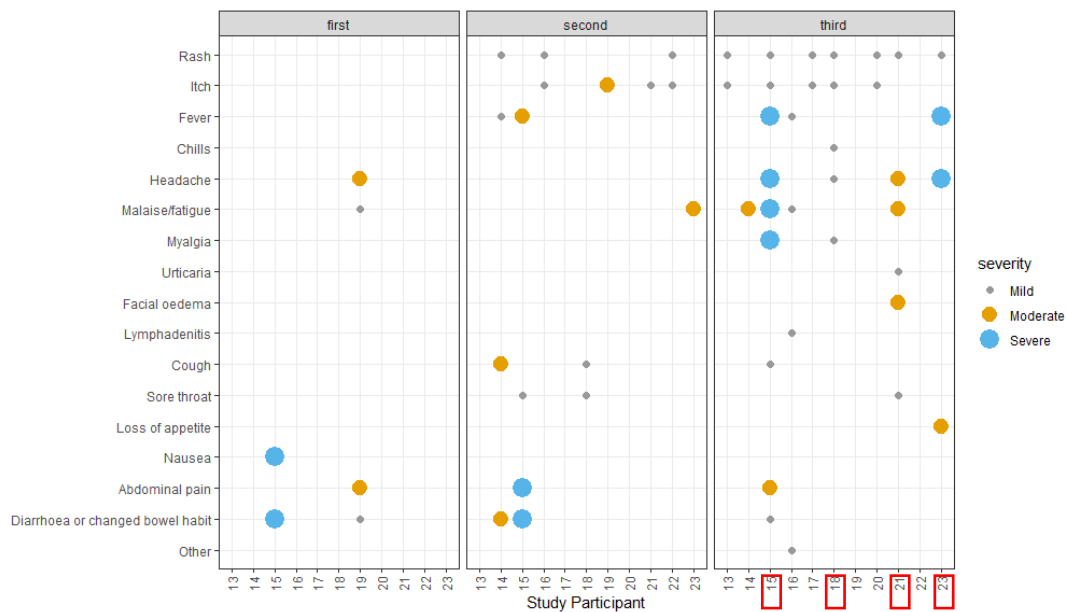
# Only maximum severity counted

**Supplementary Fig. S1. Severity and type of adverse events after Schistosoma (re)exposure stratified by group and exposure.**

**A. Reinfection group**

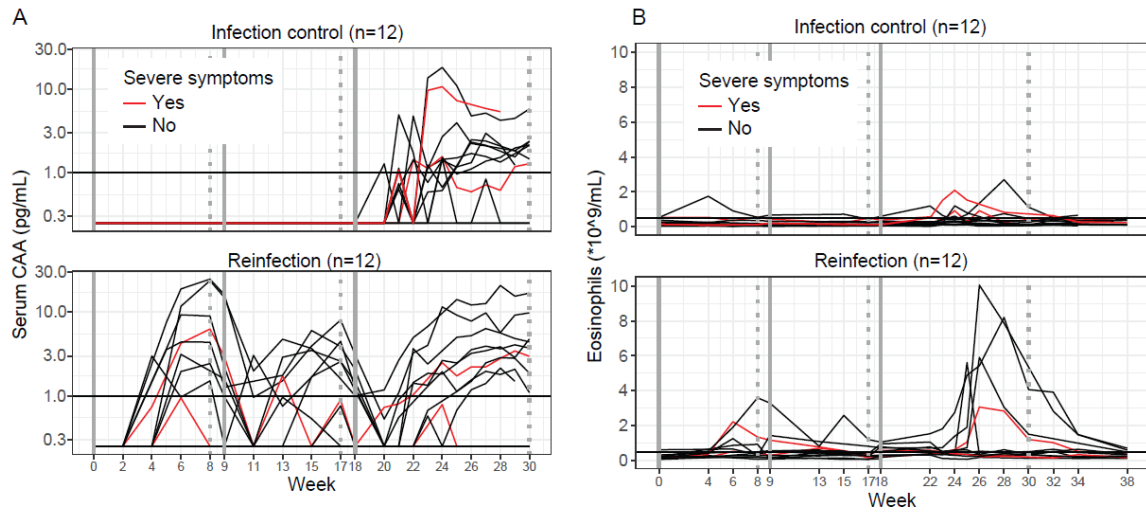


**B. Infection control group**



Graphs show the incidence of local and systemic Schistosoma-related adverse events. It shows clustering of symptoms in particular participants, suggestive of acute schistosomiasis (in red boxed). Only the maximum severity for each adverse event after each exposure is plotted. Note that participants 12 and 24 did not report related adverse events and are therefore not shown in the graph.

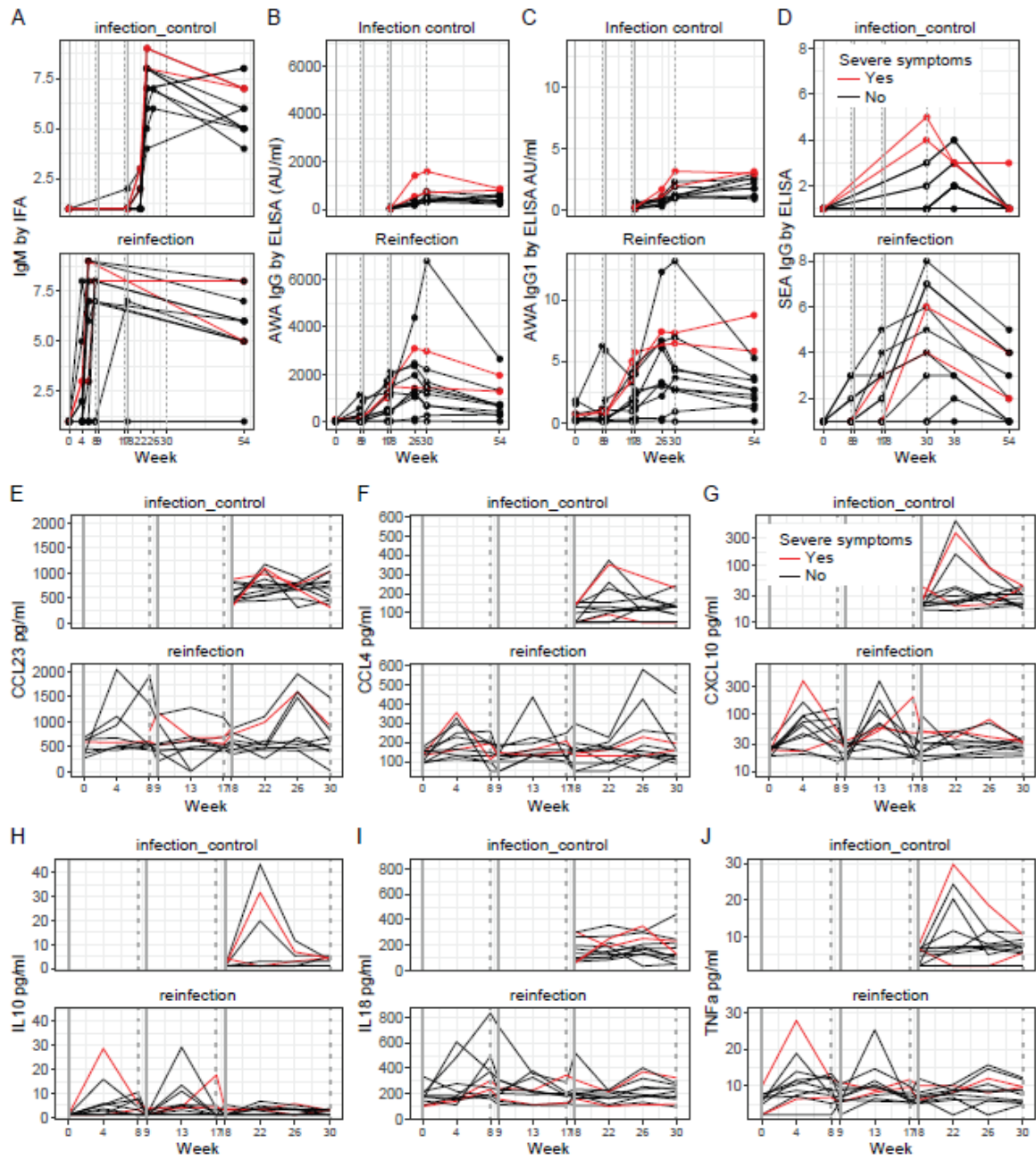
## Supplementary Fig. S2 CAA levels and eosinophil counts after (re)exposure to *Sm* cercariae, stratified by severe acute schistosomiasis symptoms



Plots show the changes over time in CAA (A) and eosinophils (B) in infection control (n=12) and reinfection (n=12) participants stratified by severe acute schistosomiasis symptoms (yes, n=4). Individual participant data is plotted. The horizontal black line shows the cut-off for abnormal counts ( $\geq 0.5 \times 10^9/\text{mL}$  for eosinophils;  $\geq 1.0$  pg/mL for CAA). The solid, grey vertical line shows *Sm* exposure weeks, while the grey, black vertical line shows when PZQ treatment was given.



**Supplemental Fig. S3: Antibody, chemokine, and cytokine responses after (re)exposure to *Sm* cercariae, stratified by severe acute schistosomiasis symptoms**



Plots show the individual changes in antibody levels in worm-specific IgM (A), AWA-specific IgG (B), AWA-specific IgG1 (C), and SEA IgG (D). For CCL23 (E), CCL4 (F), CXCL10 (G), IL-10 (H), IL-18 (I), and TNF (J) individual participant data are plotted. Data is stratified for severe acute schistosomiasis symptoms (red, yes, n=4). The solid, grey vertical line shows *Sm* exposure weeks (0,9,18), while the dotted, grey vertical line shows when PZQ treatment was given (8,17,30). AWA = adult worm antigen; SEA = soluble egg antigen