

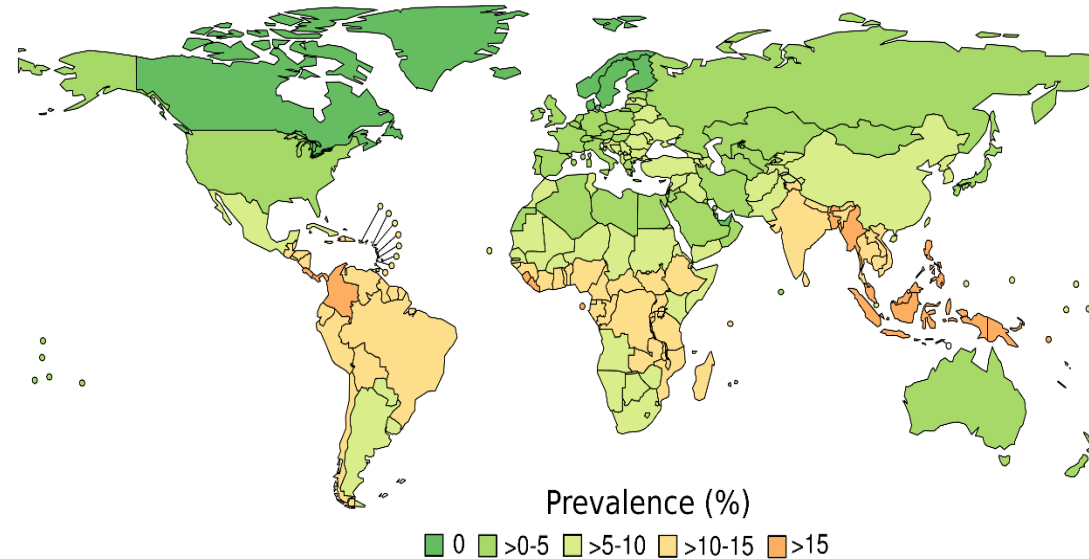
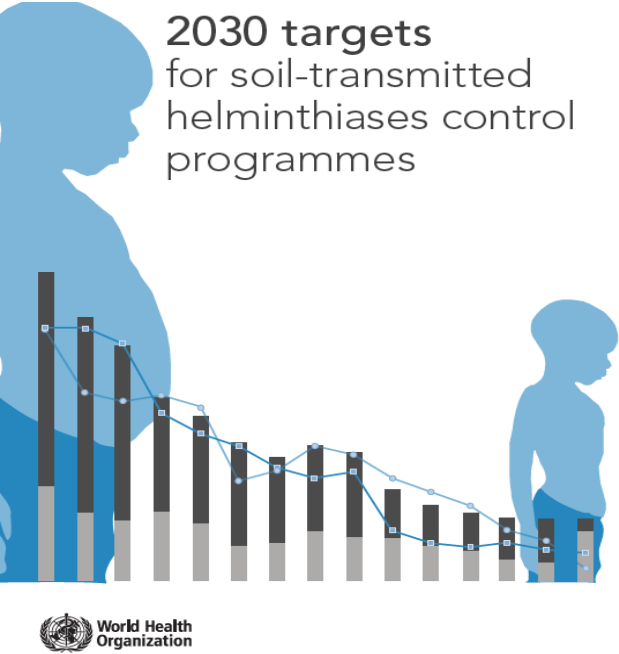
Strongiloidosi



Dora Buonfrate



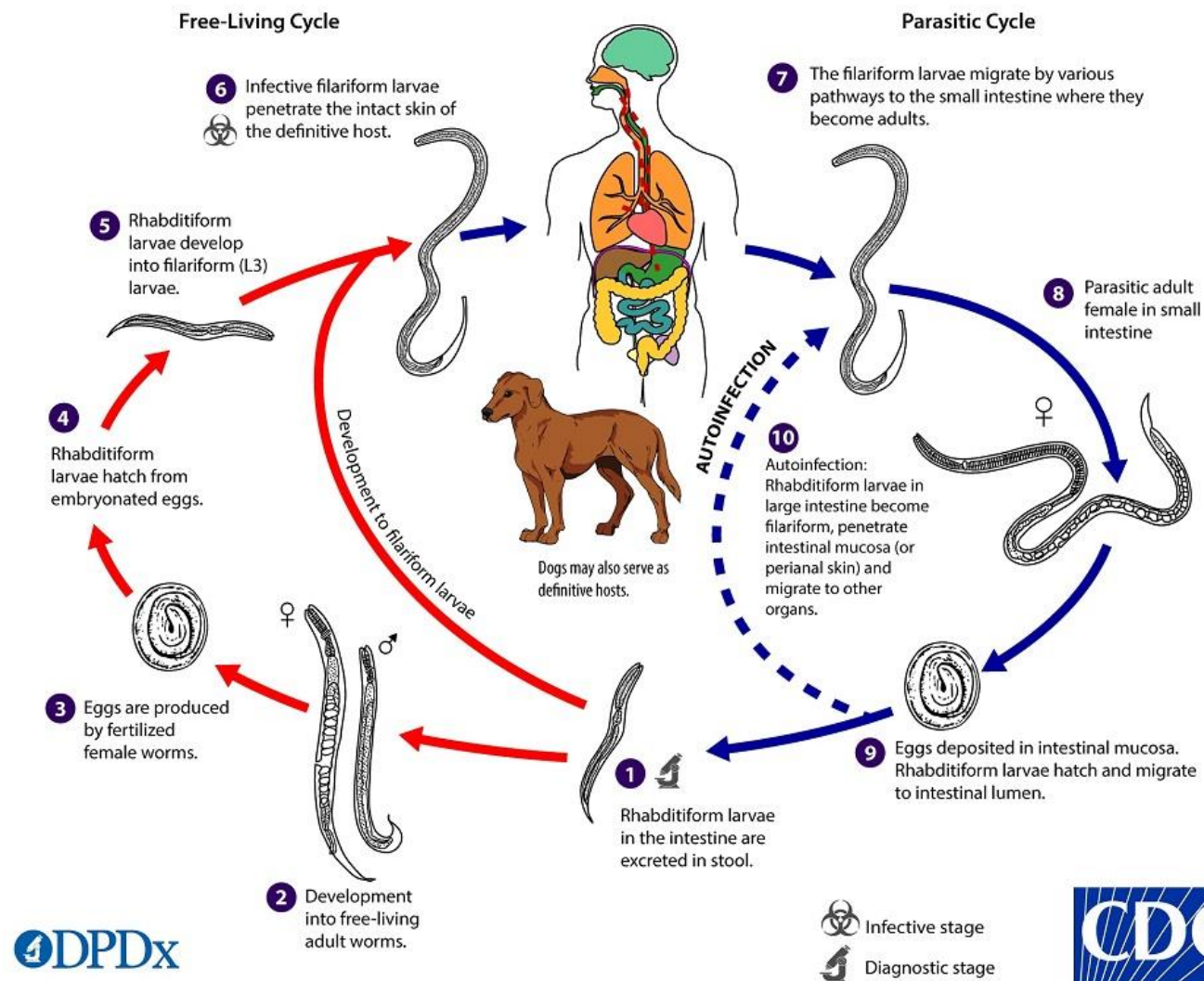
WHO Collaborating Center on
strongyloidiasis and other
Neglected Tropical Diseases



613.9 million infected individuals (95% CI: 313.1–910.1 million)



Strongyloides stercoralis



Prevalenza in Italia: memoria del passato...



Silvana Mangano in “Riso amaro” (1949)

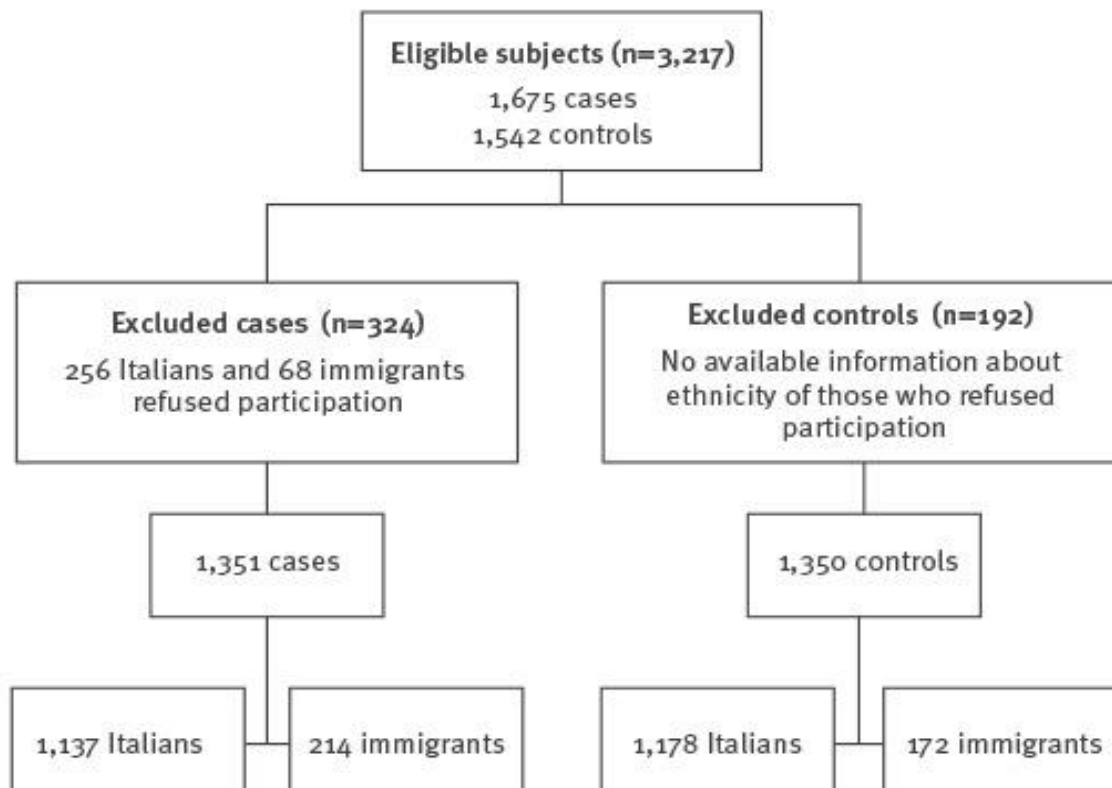
Epidemiology of *Strongyloides stercoralis* in northern Italy: results of a multicentre case–control study, February 2013 to July 2014

D Buonfrate ¹, M Baldissera ², F Abrescia ³, M Bassetti ⁴, G Caramaschi ⁵, M Giobbia ⁶, M Mascarello ⁷, P Rodari ⁸, N Scattolo ⁹, G Napoletano ², Z Bisoffi ¹, on behalf of the CCM *Strongyloides* Study Group ¹⁰



INCLUSION CRITERIA

- Patients presenting to one of the participating sites' lab for **FBC**
- Individuals born in Italy before 1951, without significant history of travel abroad («Italians»)
- Individuals born and having lived for at least 2 years outside EU («Immigrants») ≥ 18 years



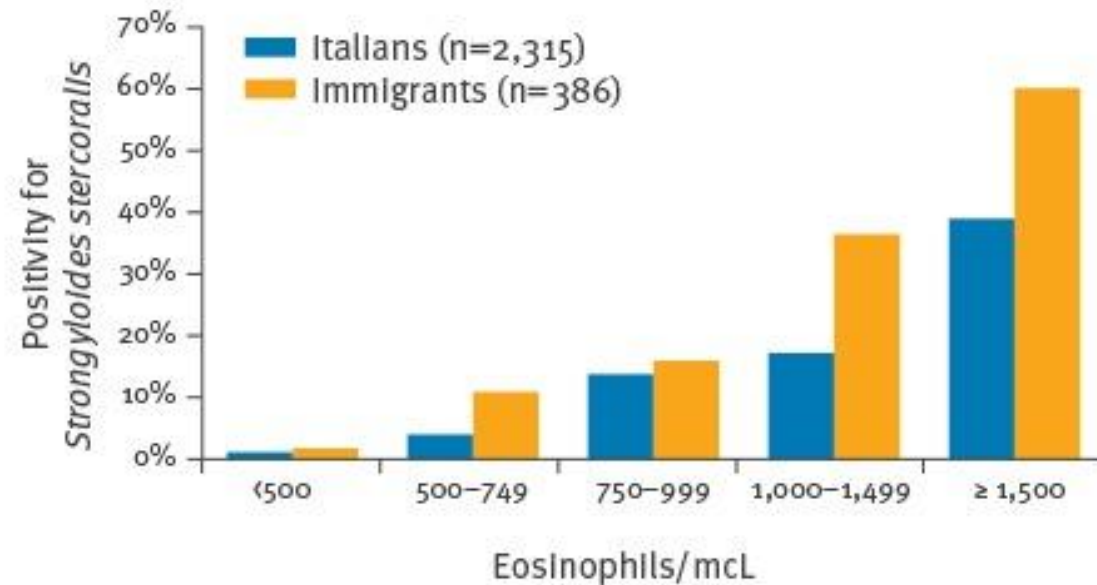
8.5%

16.8%

1.1%

1.7%

Ss positive



Multivariate analysis - **Italians**

Factors	OR	95% CI	P value
Eosinophil count $\geq 500/\text{mCL}$	8.18	4.53–14.76	< 0.001
Sex (male vs female)	0.93	0.63–1.39	0.730
Year of birth			
1947–1951	1.00	Reference	NA.
1937–1946	2.56	1.24–5.28	0.011
1936 or before	3.95	1.90–8.20	< 0.001
Recruitment site			
Trieste	1.00	Reference	NA
Udine	1.34	0.54–3.32	0.52
Negrar	1.67	0.69–4.00	0.25
Mantova	2.33	1.00–5.41	0.050
Brescia	2.47	1.07–5.70	0.033
Treviso	2.97	1.33–6.64	0.008
San Bonifacio	3.43	1.54–7.68	0.003

Multivariate analysis - migrants

Factors	OR	95% CI	P value
Eosinophil count $\geq$ 500/mcL	9.62	2.85–32.41	< 0.001
Sex (male vs female)	1.70	0.82–3.54	0.16
Age (+ 1 year)	1.00	0.97–1.03	0.83
Geographical area of origin			
Europe	1.00	Reference	NA
North Africa/Middle East	1.77	0.28–11.27	0.55
Asia	5.01	1.02–24.59	0.047
Latin America	6.33	1.20–33.40	0.030
Sub-Saharan Africa	9.54	2.01–45.19	0.004

SCIENTIFIC ADVICE

**Public health guidance on
screening and vaccination for
infectious diseases in newly
arrived migrants within the EU/EEA**

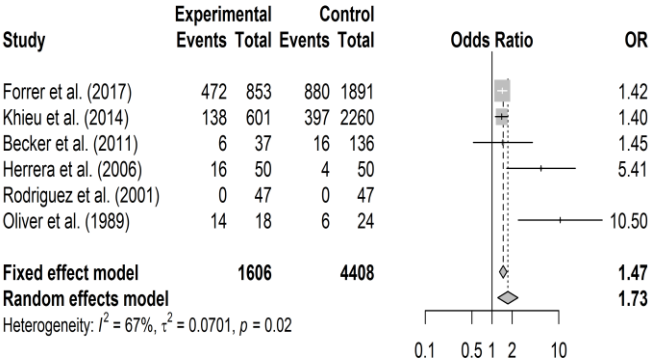
Evidence-based statement (strongyloidiasis)

Offer serological screening and treatment (for those found to be positive) for strongyloidiasis to all migrants from countries of high endemicity in Asia, Africa, the Middle East, Oceania and Latin America (see Figure 15).

(Certainty of evidence: low)

Aspetti clinici

URTICARIA

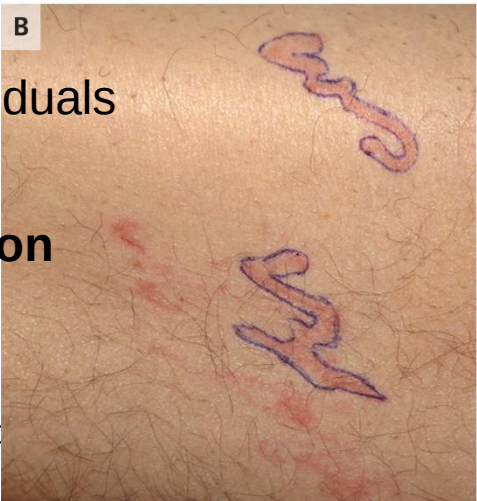


Abdominal pain: reported by **61.86%** individuals

Diarrhea by **50.54%** individuals

Urticaria/rash by **33.35%** individuals

40-50% asymptomatic infection



currents

Tamarozzi F et al. Morbidity associated with *Strongyloides hyperinfection syndrome*. *Am J Trop Med & Hyg* 2019 Apr 8. doi: 10.4269/ajtmh.18-0895.

Pichard DC, et al. Rapid development of migratory, linear, and serpiginous lesions in association with immunosuppression. *J Am Acad Dermatol*. 2014 Jun;70(6):1130-4. doi: 10.1016/j.jaad.2013.11.036. PMID: 24831316; PMCID: PMC4024165.

Puerta-Peña M, Calleja Algarra A. Larva Currens in *Strongyloides* Hyperinfection Syndrome. *N Engl J Med*. 2022 Apr 21;386(16):1559. doi: 10.1056/NEJMmicr2115708. PMID: 35443110.

La forma grave – iperiinfestazione/disseminazione

CASE REPORT

Late post-kidney transplant *Strongyloides* hyperinfection syndrome

Transpl Infect Dis. 2018;20:e12975.
<https://doi.org/10.1111/tid.12975>

Case of *Strongyloides* hyperinfection syndrome

To cite: Kuriakose K, Carpenter K, Wanjalla C, et al. *BMJ Case Rep*
Published online: [please include Day Month Year]
doi:10.1136/bcr-2016-210000

MOF Sepsi da batteri intestinali Meningiti da batteri intestinali

Fatal Multiorgan Failure Syndrome in Coinfected Patient, after Treatment with

Case Reports in Critical Care
Volume 2021, Article ID 5554810, 5 pages
<https://doi.org/10.1155/2021/5554810>

Am. J. Trop. Med. Hyg., 101(2), 2019, pp. 418–421
doi:10.4269/atmh.19-0347
Copyright © 2019 by The American Society of Tropical Medicine and Hygiene

Case Report: Two Cases of Strongyloidiasis Presenting with Thrombotic Events

Mara Waters,^{1*} Sigmund Krajden,^{2,3} Christie Kim,² Reem Elsobky,² Bohdan Lychacz,² Matthew Cheung,^{1,4} Mark Crowther,⁵ and Jay Keystone^{1,6}

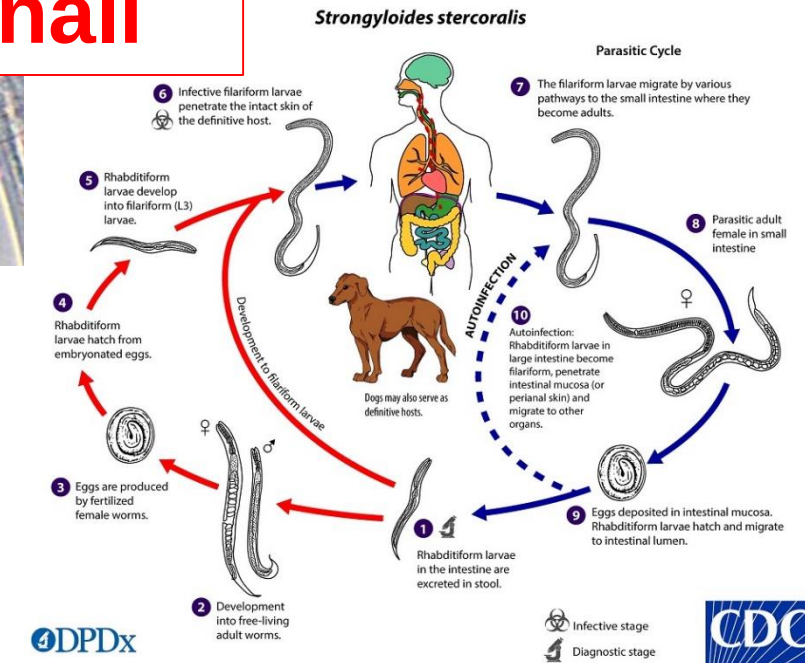
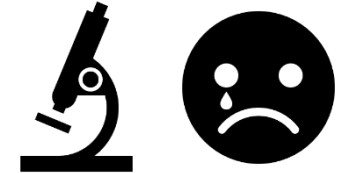


Table 1. Conditions associated with hyperinfection syndrome

Drugs/biologics
Immunosuppressives
Corticosteroids
Azathioprine
Cyclophosphamide
Methotrexate
Anti-neoplastic agents
6-mercaptopurine
Adriamycin
Bleomycin
Carmustine
Chlorambucil
Doxorubicin
Daunorubicin
Ifosfamide
Melphalan
Mitoxantrone
VP16
Vinca alkaloids
Biologics
Etanercept
Inflixumab
Rituximab
Antithymocyte globulin
Anti-CD3 (OKT3)
Mycophenolate mofetil
Total body irradiation
Diseases/syndromes
HTLV-1
Hypogammaglobulinaemia (nephrotic syndrome and multiple myeloma)
Haematologic malignancies and myelodysplastic syndromes
Solid Organ Transplantation
HSCT
HIV/IRIS
Malnutrition

Nutman TB. Human infection with *Strongyloides stercoralis* and other related *Strongyloides* species. *Parasitology*. 2017 Mar;144(3):263-273. doi: 10.1017/S0031182016000834.

Il problema della diagnostica



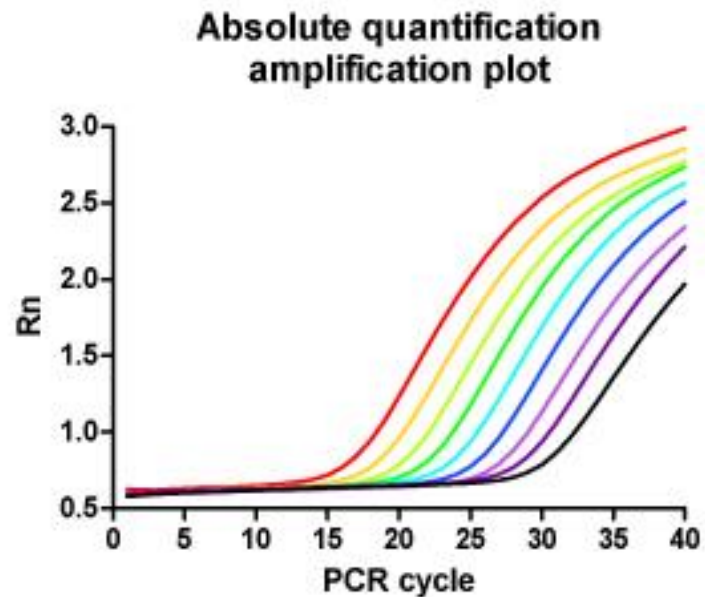
- Metodi diretti (riscontro di larve o di DNA):
 - Esame microscopico diretto delle feci - sensibilità intorno al 20%

- Coltura in agar
- Baermann
- PCR



- Metodi indiretti:
Ricerca anticorpale (sierologia)

PCR



Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Ahmad 2013	3	0	14	37	0.18 [0.04, 0.43]	1.00 [0.91, 1.00]		
Amor 2016	22	31	29	314	0.43 [0.29, 0.58]	0.91 [0.87, 0.94]		
Becker 2015_a	14	20	14	208	0.50 [0.31, 0.69]	0.91 [0.87, 0.95]		
Becker 2015_b	14	17	14	211	0.50 [0.31, 0.69]	0.93 [0.88, 0.96]		
Buonfrate 2017_a	18	7	2	196	0.90 [0.68, 0.99]	0.97 [0.93, 0.99]		
Buonfrate 2017_b	23	2	117	81	0.16 [0.11, 0.24]	0.98 [0.92, 1.00]		
de Paula 2015_a	23	11	7	99	0.77 [0.58, 0.90]	0.90 [0.83, 0.95]		
de Paula 2015_b	27	10	3	60	0.90 [0.73, 0.98]	0.86 [0.75, 0.93]		
Knopp 2014	8	9	38	138	0.17 [0.08, 0.31]	0.94 [0.89, 0.97]		
Lohd 2016	27	29	8	61	0.77 [0.60, 0.90]	0.68 [0.57, 0.77]		
Meurs 2017	88	46	12	157	0.88 [0.80, 0.94]	0.77 [0.71, 0.83]		
Shar 2013	25	13	16	164	0.61 [0.45, 0.76]	0.93 [0.88, 0.96]		
Sharifdini 2015_a	85	32	0	349	1.00 [0.96, 1.00]	0.92 [0.88, 0.94]		
Sharifdini 2015_b	72	16	13	365	0.85 [0.75, 0.92]	0.96 [0.93, 0.98]		
Sultana 2013	14	1	27	118	0.34 [0.20, 0.51]	0.99 [0.95, 1.00]		
Ten Hove 2009	1	0	0	120	1.00 [0.03, 1.00]	1.00 [0.97, 1.00]		
Verweij 2009	33	12	21	146	0.61 [0.47, 0.74]	0.92 [0.87, 0.96]		
Zueter 2014	3	0	6	184	0.33 [0.07, 0.70]	1.00 [0.98, 1.00]		

Sensibilità 56-64%

Buonfrate D, et al. Accuracy of molecular biology techniques for the diagnosis of Strongyloides stercoralis infection-A systematic review and meta-analysis. PLoS Negl Trop Dis. 2018 Feb 9;12(2):e0006229. doi: 10.1371/journal.pntd.0006229

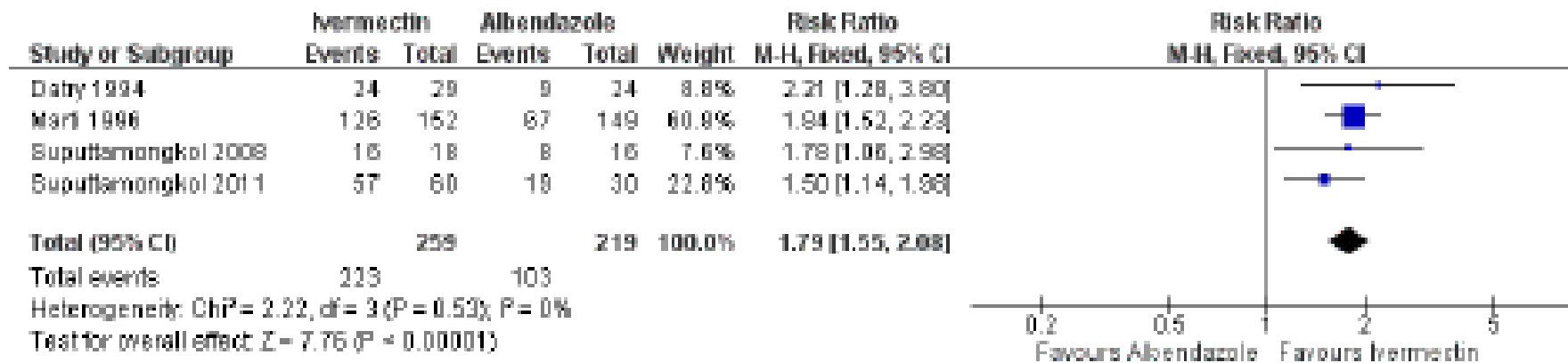
SEROLOGY – PROS and CONS

PROS	CONS
Best sensitivity*	Lower specificity *
Useful for screening	Can be negative in immunosuppressed individuals
Can be used for post-treatment monitoring	Needs several months for seroconversion/decrease in titre after treatment

*Though widely differ between diverse assays

Terapia

Figure 4. Forest plot of comparison: I Ivermectin versus albendazole, outcome: I.I Parasitological cure.



Multiple-dose versus single-dose ivermectin for *Strongyloides stercoralis* infection (Strong Treat 1 to 4): a multicentre, open-label, phase 3, randomised controlled superiority trial

Lancet Infect Dis 2019
Published Online
September 23, 2019
[https://doi.org/10.1016/S1473-3099\(19\)30289-0](https://doi.org/10.1016/S1473-3099(19)30289-0)

Dora Buonfrate, Joaquin Salas-Coronas, José Muñoz, Begoña Trevino Maruri, Paola Rodari, Francesco Castelli, Lorenzo Zammarchi, Leila Bianchi, Federico Gobbi, Teresa Cabezas-Fernández, Ana Requena-Mendez, Gauri Godbole, Ronaldo Silva, Marilena Romero, Peter L Chiodini, Zeno Bisoffi

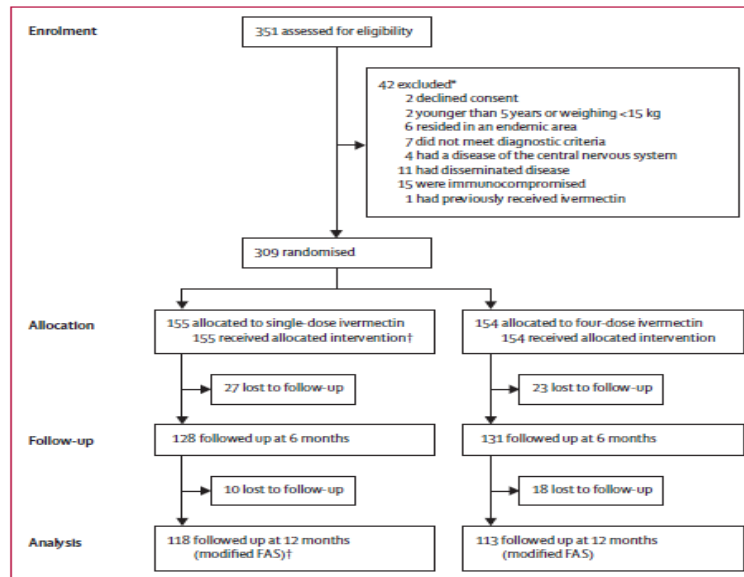


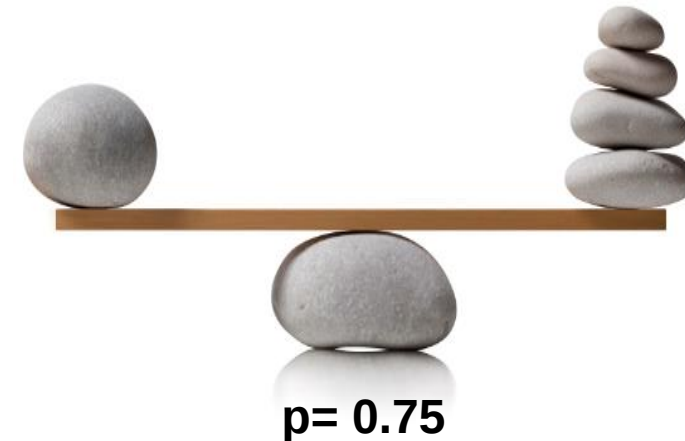
Figure 1: Trial profile
FAS=full analysis set. *Some participants had more than one reason for exclusion. †One patient took a further four doses before the 6-month follow-up visit and was excluded from the per-protocol analysis.

**Dose singola
(200 mcg/kg)
di ivermectina**

86% (95%CI 79-91)

**Dosi multiple
(200 mcg/kg x 4)
di ivermectina**

85% (95%CI 77-90)



➡ **BASTA UNA DOSE**



U.S. CENTERS FOR DISEASE
CONTROL AND PREVENTION

Trattamento delle forme disseminate

If possible, immunosuppressive therapy should be stopped or reduced, and:

Ivermectin 200 µg/kg per day orally, until stool and/or sputum exams are negative for 2 weeks

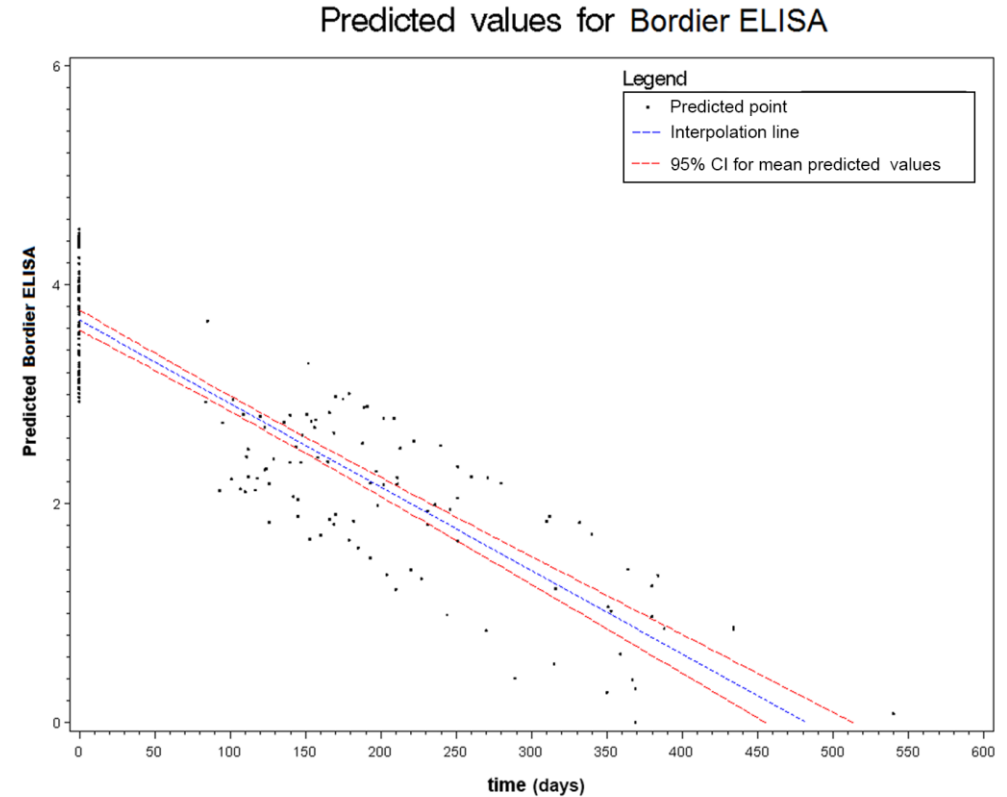
Evidence in support of these recommendations..?

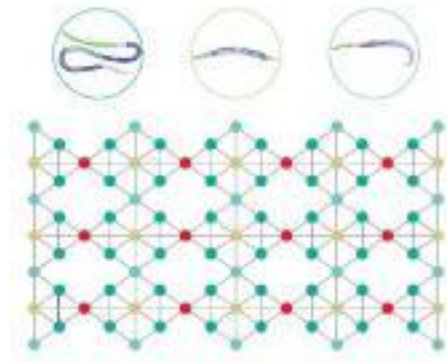
Monitoraggio del trattamento

- Se al baseline ho test fecali positivi, vanno ripetuti a breve distanza dal trattamento (anche 1 settimana dopo)



- La sierologia va ripetuta, a distanza però di almeno 3-4 mesi





Review of the WHO guideline on preventive chemotherapy for public health control of strongyloidiasis



Nathan C Lo, David G Addiss*, Dora Buonfrate*, Arancha Amor, Melaku A negagrie, Zeno Bisoffi, Richard S Bradbury, Jennifer Keiser, Stella Kepha, Virak Khieu, Alejandro Krolewiecki, Jean B Mbonigaba, Jose Muñoz, Francisca Mutapi, Valdemiro Novela, Susana Vaz Nery, Luc E Coffeng, Sake J de Vlas, Jessica Bartoszko, Lorenzo Moja, Denise Mupfasoni, Antonio Montresor

Strongyloidiasis is a soil-transmitted helminthiasis that is estimated to affect 300–600 million people across Asia, Africa, South and central America, and the Pacific. This neglected parasitic disease is most known for its ability to persist as a lifelong infection due to autoinfection and its risk of hyperinfection and disseminated disease during immunosuppression, which has a more than 60% case fatality. Despite the large global burden of strongyloidiasis, there have been no large-scale public health programmes or WHO guidelines directed towards its control and elimination. However, over the past decade, key scientific and policy changes along with requests from endemic countries have led to WHO incorporating strongyloidiasis into its 2021–30 roadmap and public health targets for control and elimination of neglected tropical diseases. In 2024, WHO published its first guideline on public health control of strongyloidiasis with a single recommendation: in endemic settings with a *Strongyloides stercoralis* infection prevalence of 5% or higher (measured either with Baermann or agar plate culture from stool specimens), WHO conditionally recommends mass drug administration with single-dose ivermectin (200 µg/kg; oral therapy) in all age groups from 5 years and older to reduce strongyloidiasis. This Review, written by the 2023–24 strongyloidiasis guidelines development group along with WHO colleagues and international experts, presents a summary of the recently published WHO guideline recommendation for strongyloidiasis, and the supporting evidence, considerations for public health implementation, and future research needs.

Lancet Infect Dis 2024

Published Online
October 28, 2024
[https://doi.org/10.1016/S1473-3099\(24\)00595-4](https://doi.org/10.1016/S1473-3099(24)00595-4)

*Contributed equally

Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University, Stanford, CA, USA (N C Lo MD); The Task Force for Global Health, Decatur, GA, USA (D G Addiss MD); IRCCS Sacro Cuore don Calabria Hospital, Negrar, Verona, Italy (D Buonfrate MD, Z Bisoffi PhD); Fundación Mundo Sano, Bahir

Grazie per l'attenzione!

dora.buonfrate@sacrocuore.it

