SITA

11° CONGRESSO NAZIONALE

FIRENZE | 3 dicembre 2021

Malattie Tropicali Neglette e problematiche relative al trattamento

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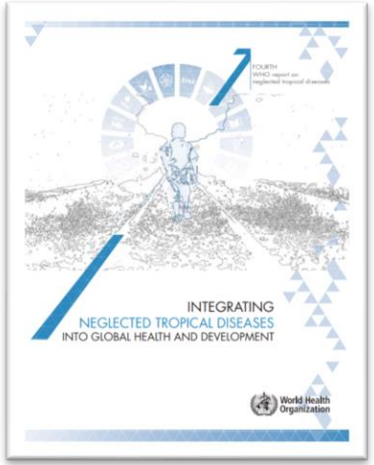
Firenze

Neglected Tropical Diseases (NTDs)



Bacterial

Buruli ulcer

Leprosy

Trachoma

Endemic treponematosis

Viral

Dengue & Chikungunya

Rabies

Protozoan

Chagas disease

Sleeping sickness

Leishmaniasis

Helminthic

Dracunculiasis

Cystic echinococcosis

Foodborne trematodiasis

Lymphatic filariasis

Onchocerciasis

Schistosomiasis

Soil transmitted helminthiases

Taeniasis/cysticercosis

Ectoparasites

Scabies

Fungal

Mycetoma, chromoblastomycosis, and other deep mycoses

Snake bite envenoming

WHO http://www.who.int/neglected_diseases/diseases/en/ accessed 03/10/2019

Neglected tropical diseases (NTDs) are ancient diseases of poverty that impose a devastating human, social and economic burden on more than 1 billion people worldwide, predominantly in tropical and subtropical areas among the most vulnerable, marginalized populations.

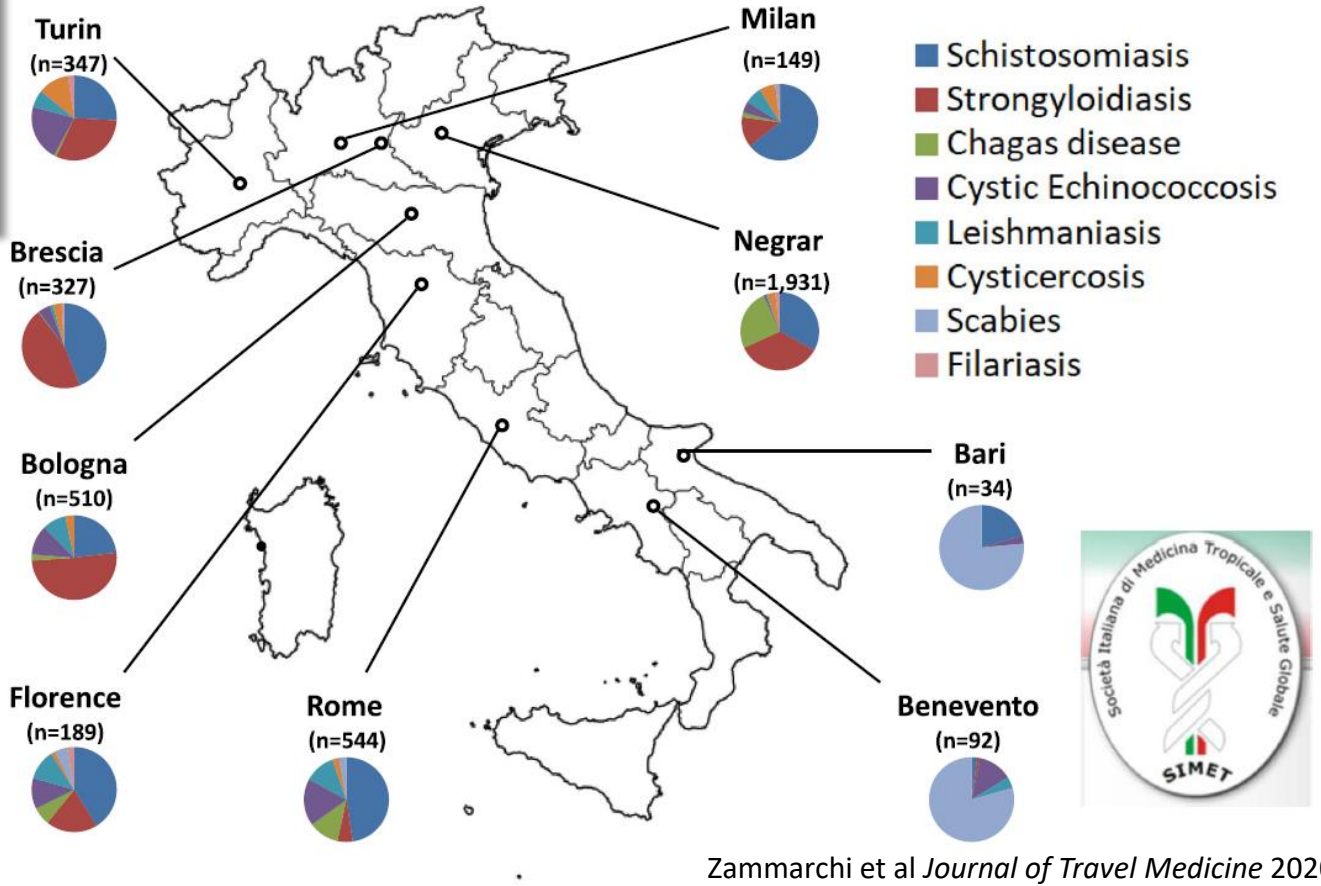
NTDs in Italy –SIMET survey

Journal of Travel Medicine, 2019, 1–9
doi: 10.1093/jtm/taz100
Original Article

Original Article

Schistosomiasis, strongyloidiasis and Chagas disease: the leading imported neglected tropical diseases in Italy

Lorenzo Zammarchi MD[1,*], Federico Gobbi PhD[2], Andrea Angheben MD[2], Michele Spinicci MD[1], Dora Buonfrate MD[2], Guido Calleri MD[3], Mirella De Paola MD[3], Nazario Bevilacqua MD[4], Stefania Carrara MD[4], Luciano Attard MD[5], Elisa Vanino MD[5], Maurizio Gulletta MD[6], Elena Festa MD[6], Tiziana Iacovazzi MD[7], Anna Grimaldi MD[8], Alessio Sepe MD[9], Angelo Salomone Megna MD[10], Giovanni Gaiera MD[11], Antonella Castagna PhD[11], Patrizia Parodi MD[12], Marco Albonico PhD[2,13], Zeno Bisoffi PhD[2,14], Francesco Castelli MD[6], Piero Olliaro PhD[15] and Alessandro Bartoloni MD[1]

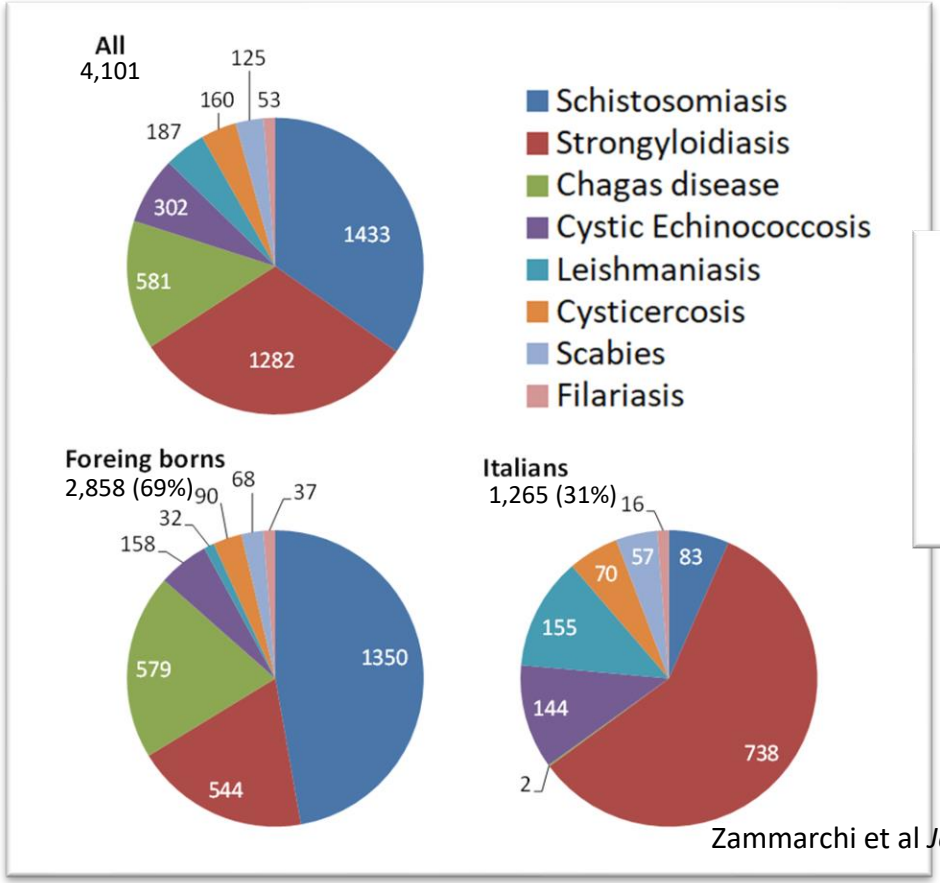


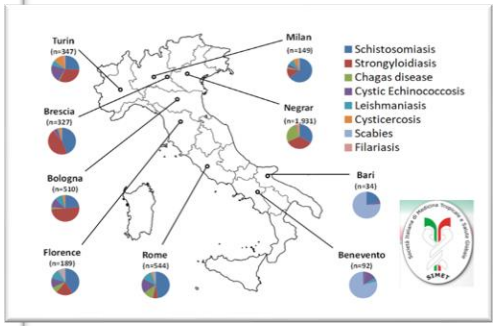
- Period 2011-2017
- 9 SIMET centres

Zammarchi et al *Journal of Travel Medicine* 2020

NTDs in Italy –SIMET survey

- Period 2011-2017
- 9 SIMET centres
- 4,101 NTD cases
  - 35% schistosomiais
  - 31% strongyloidiasis
  - 14% Chagas diseases
  - 7% echinococcosis
  - 5% leishmaniasis
  - 4% cysticercosis
  - 3% scabies
  - 1% filariasis

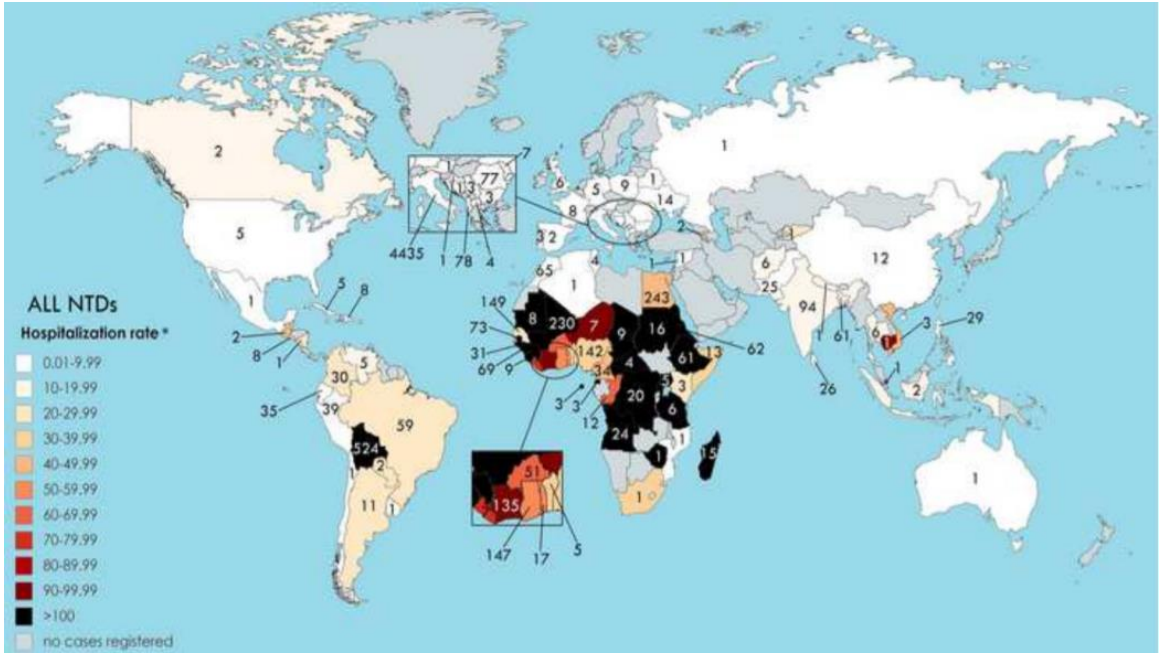




Zammarchi et al *Journal of Travel Medicine* 2020

Hospitalizations for NTDs in Italy (2011-2016)

- 7,195 hospitalizations
- 60% Italians
- 40% in foreigners
- leishmaniasis (34%)
- schistosomiasis (29%)
- strongyloidiasis (12%)
- Chagas disease (8%)
- dengue (8%)



Tilli M et al *Infection 2020*

Chikungunya: From Indian Ocean to Romagna

Estimated **254 locally acquired infections in 2007 (1 death)**

Courtesy Dr Rezza

Chikungunya in Italia per la 2° volta

Ministero della Salute

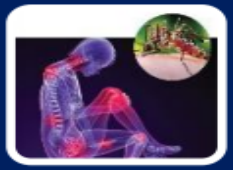
Istituto Superiore di Sanità

Primo caso esordito 26/06/17

Primo caso diagnosticato 15/09/17

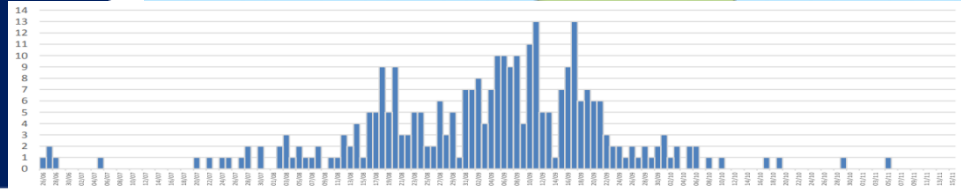
Ultimo caso esordito 05/11/17

ECSA strain ; Non ha mutazione E1-A226V
100% homology with two strains from Pakistan and India from 2016



489 Total notified cases:
384 Lazio Region
97 Calabria Region
5 Emilia-Romagna Region
1 Marche Region
2 European Countries (France/Germany)

1 death



http://www.salute.gov.it/portale/temi/documenti/chikungunya/bollettino_chikungunya_ULTIMO.pdf

RAPID COMMUNICATION

First autochthonous dengue outbreak in Italy, August 2020

Luca Lazzarini[1], Luisa Barzon[2,3,4], Felice Foglia[5], Vinicio Manfrin[1], Monia Pacenti[4], Giacomina Pavan[6], Mario Rassu[6], Gioia Capelli[2,7], Fabrizio Montarsi[2,7], Simone Martini[2,8], Francesca Zanella[2,9], Maria Teresa Padovan[5], Francesca Russo[2,9], Federico Gobbi[2,10]

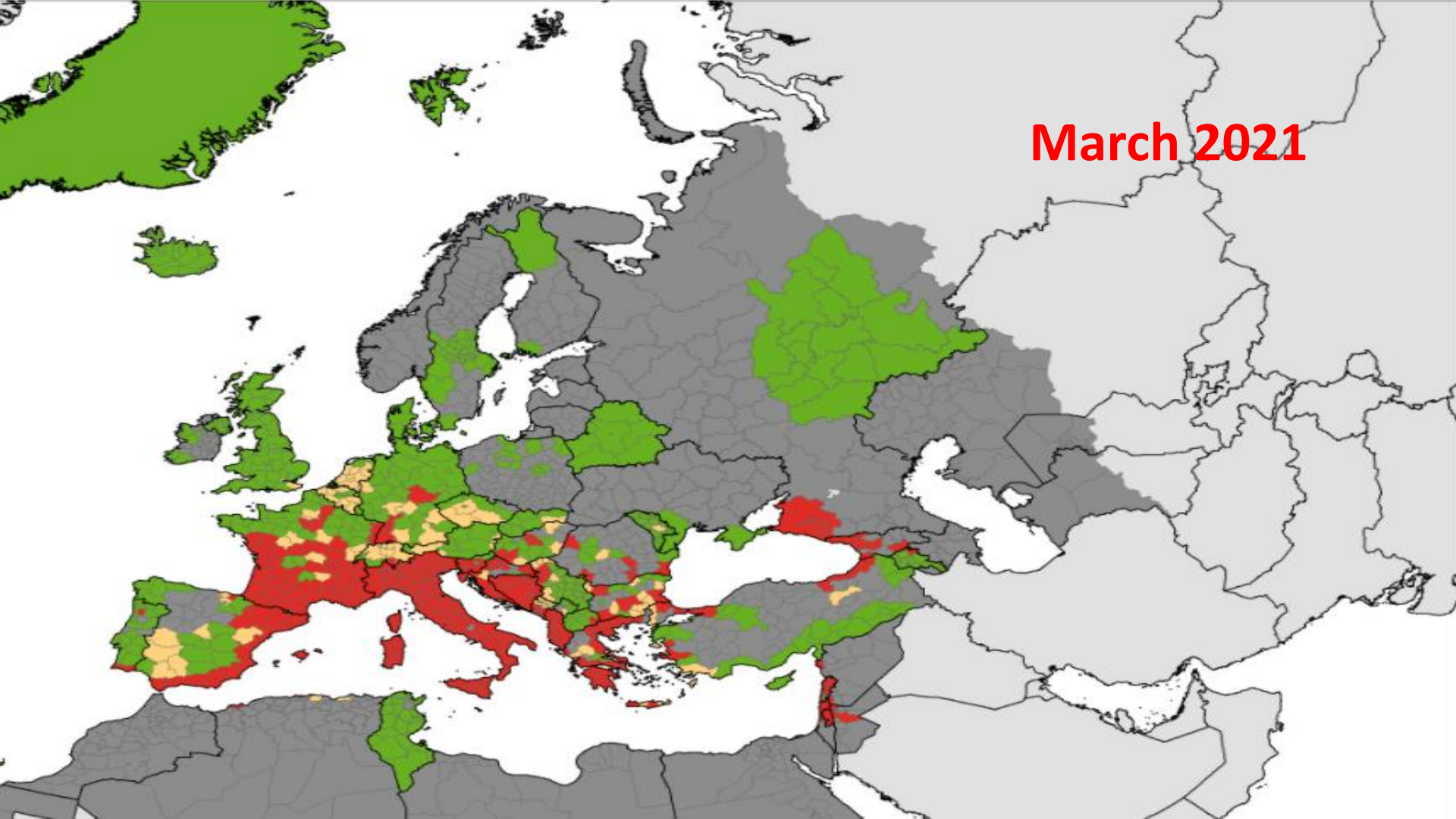
In August 2020, during the coronavirus disease (COVID-19) pandemic, five locally acquired cases of dengue virus type 1 were detected in a family cluster in Vicenza Province, North-East Italy where Aedes albopictus mosquitoes are endemic. The primary case was an importation from West Sumatra, Indonesia. This is the first outbreak of autochthonous dengue reported in Italy. During the COVID-19 pandemic, screening of febrile travelers from endemic countries is crucial in areas where competent vectors are present.

TABLE

Clinical and laboratory findings in outbreak (family cluster) of autochthonous dengue, Vicenza Province, Italy, July to August 2020 (n=6)

Clinical, epidemiological and laboratory parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Date of symptom onset	30 Jul	16 Aug	16 Aug	16 Aug	18 Aug	18 Aug
Delay between sample collection and onset of symptoms (days)	27	10	6	10	8	8
Symptoms	Fever (38° C), arthralgia, myalgia, headache	Fever (39° C), arthralgia, myalgia, headache	Fever (38° C), arthralgia, upper limb itching	Fever (38° C)	Fever (38.5° C)	Fever (39° C)
Epidemiological link	Source case	Household contact of Case 1	Index case and household contact of Case 1	Household contact of Case 1	Household contact of Case 1	Household contact of Case 1
DENV RNA in blood[a]	Negative	DENV-1	DENV-1	Negative	DENV-1	DENV-1
DENV RNA in urine[a]	Negative	DENV-1	DENV-1	DENV-1	DENV-1	DENV-1
DENV RNA in saliva[a]	Negative	Negative	DENV-1	Negative	DENV-1	DENV-1
DENV NS1 antigen[b]	Negative	Positive	Positive	Negative	Positive	Positive
DENV IgM[c]	Positive	Positive	Negative	Positive	Positive	Positive
DENV IgG[c]	Positive	Negative	Negative	Negative	Negative	Negative

Montecchio Maggiore (Vicenza, Agosto 2020): 6 casi (uno importato e 5 autoctoni)


March 2021

Chagas disease

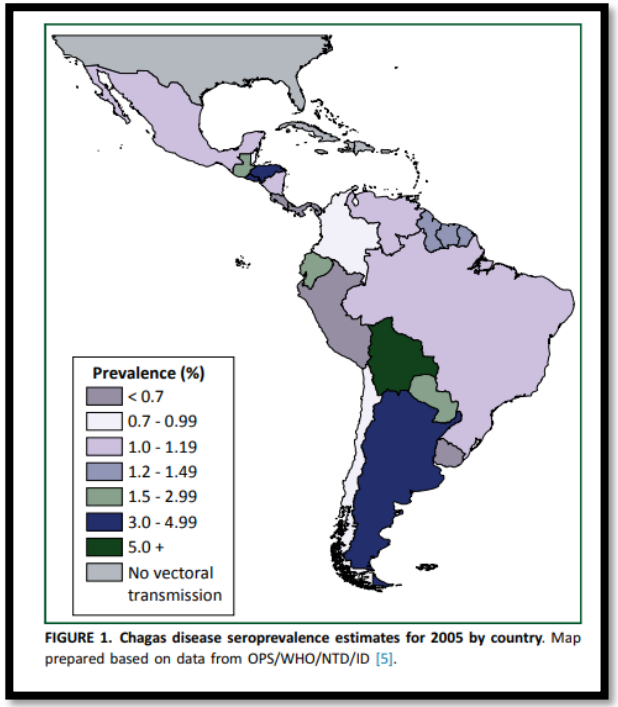
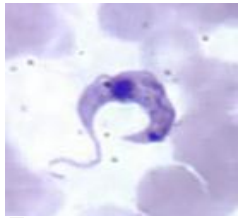


FIGURE 1. Chagas disease seroprevalence estimates for 2005 by country. Map prepared based on data from OPS/WHO/NTD/ID [5].

Carlos Chagas 1879-1934



Trypanosoma cruzi

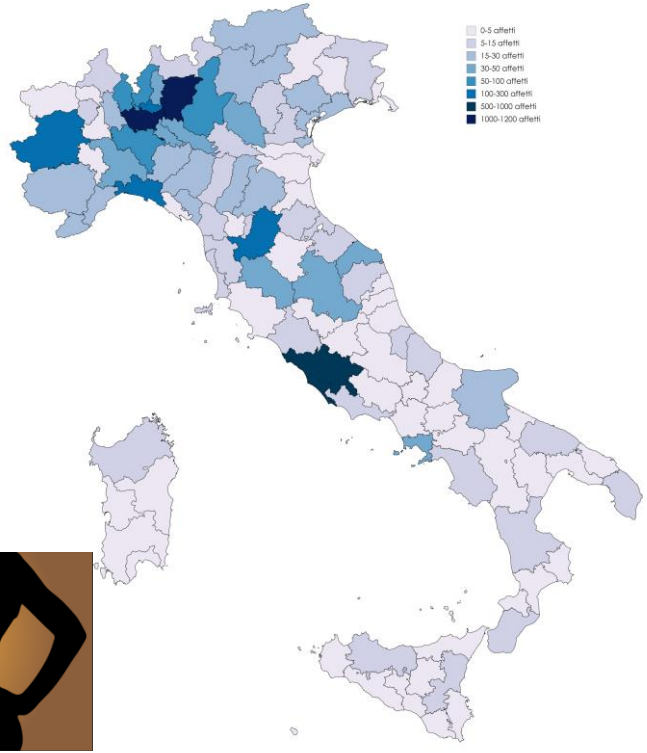
Tratomine

- ~8 milion subjects infected
- 10,000 deaths per year

Stanaway JD Glob Heart 2015

Estimated number of affected migrants:

3,268 - **5,015** [Campolmi I et al *Intern Emerg Med* 2020]



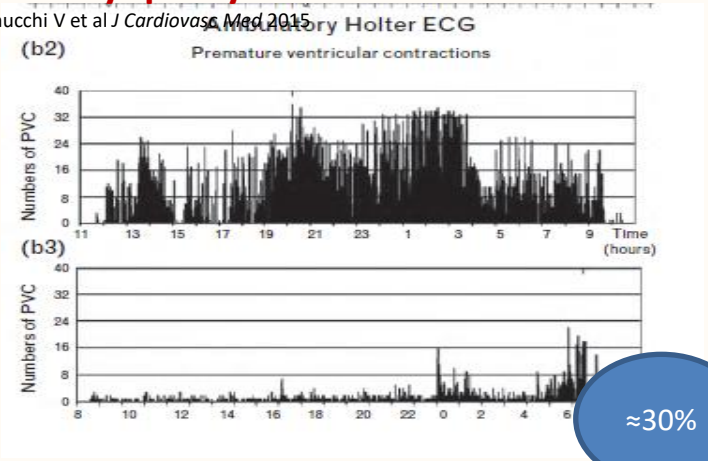
Estimated number of congenital CD cases acquired in Italy (2014-2018):

16 (95% CI 12-21) [Zammarchi et al *J Trav Med* 2021]

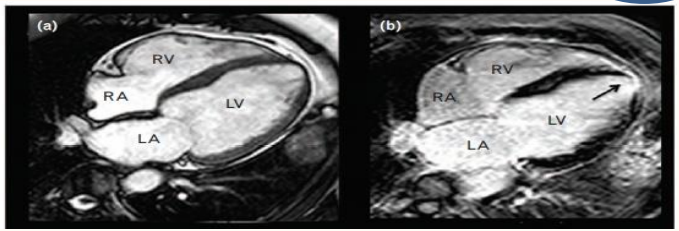
Chagas disease

Arrhythmogenic and structural cardiomyopathy

Vannucchi V et al *J Cardiovasc Med* 2015



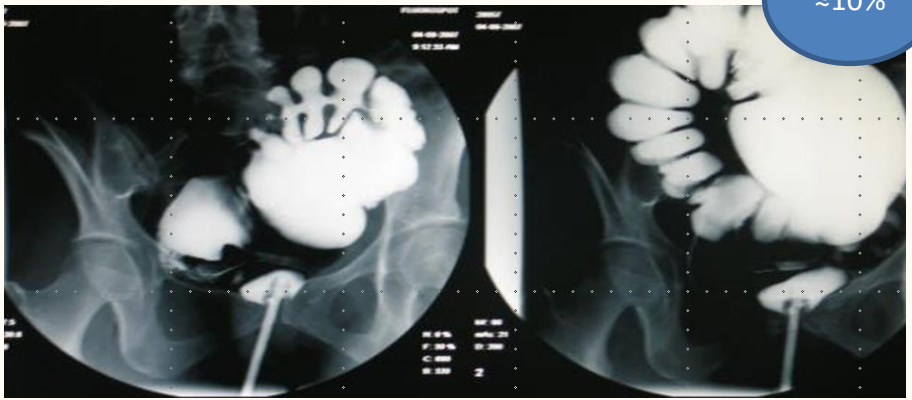
≈30%



Intestinal megasyndrome

Di Martino C et al *Surg Infect* 2014

≈10%



Reactivations in immunocompromised

Angheben A et al *Blood Transfus* 2012

CASE REPORT

Reactivation of Chagas disease after a bone marrow transplant in Italy: first case report

Andrea Angheben[1], Elena Giaconi[2], Mariacristina Menconi[2], Gabriella Casazza[2], Mohammad Najajreh[2], Mariella Anselmi[4], Federico Gobbi[1], Zeno Bisoffi[1], Carlo Tascini[3], Claudio Favre[2]

Congenital Infection

Bargiggia G et al *Infez Med* 2018

Le Infezioni in Medicina, n. 1, 93-96, 2018

CASE REPORT

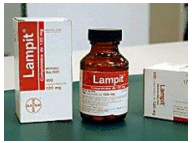
Congenital Chagas disease in a Bolivian newborn in Bergamo (Italy)

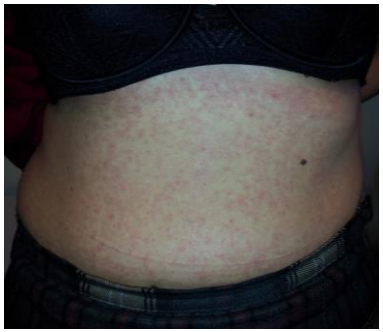
Graziano Bargiggia[1], Maurizio Ruggeri[2], Gaia Ortalli[1], Simona Gabrielli[3], Paola Rodari[4], Lorenzo D'Antiga[2], Claudio Farina[1]

Chagas disease: diagnosis and treatment

Diagnosis:

- **Serology (*T. cruzi* IgG)**: test of choice for chronic infections (symptomatic or asymptomatic)
- **Parasitological methods** (thin and thick blood slide, microhematoctit): congenital infection, reactivation, acute infection





Treatment:

- **Benznidazole (or Nifurtimox) for 60 days (oral)**
- ≈100% effective in acute and **congenital** infections
- **≈60% effective in recent chronic infections (children)**
- ≈20% in long lasting chronic infections (adults)
- Treatment before pregnancy **prevent vertical transmission**
- **Side effects are common (rash …)**

Effetto del trattamento prima della gravidanza

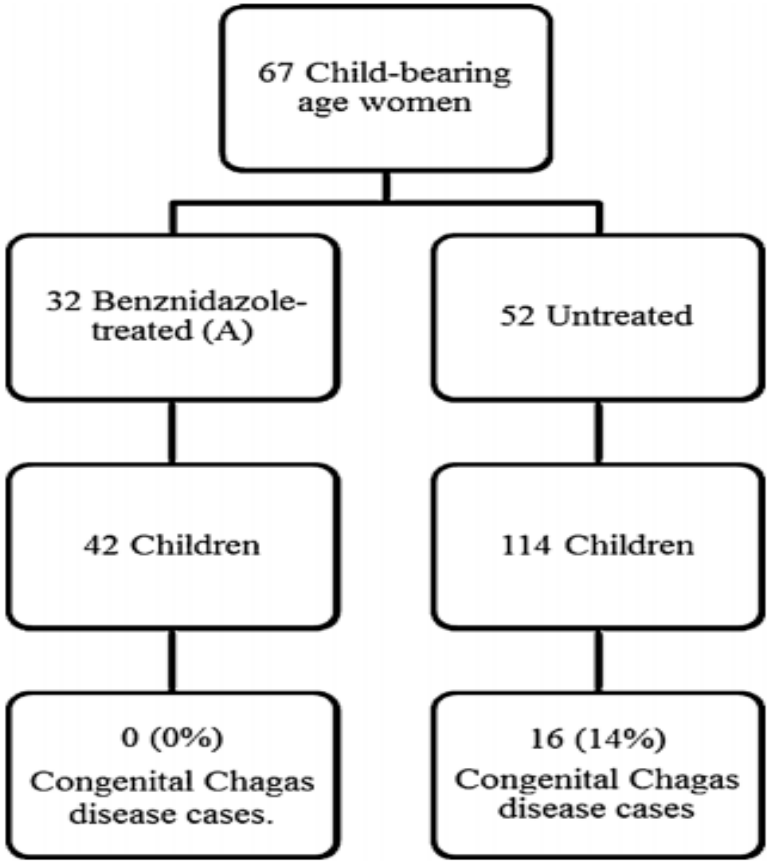


Fig. 1. Flow diagram of congenital Chagas disease in a cohort study comparing women of reproductive age with and without benznidazle treatment prior to pregnancy.
[A]Seventeen women also gave birth in the untreated status of the disease.

Alvarez MG Acta Tropica 2017

Risultati analoghi in:
Murcia L Clin Infect Dis 2013
Fabbro DL PLoS Negl Trop Dis 2014

Cost-effectiveness of Chagas disease screening in Latin American migrants at primary health-care centres in Europe: a Markov model analysis

Ana Requena-Méndez, Sheila Bussion, Edelweiss Aldasoro, Yves Jackson, Andrea Angheben, David Moore, Maria-Jesús Pinazo, Joaquim Gascón, Jose Muñoz, Elisa Sicuri

Summary

Background Chagas disease is currently prevalent in European countries hosting large communities from Latin America. Whether asymptomatic individuals at risk of Chagas disease living in Europe should be screened and treated accordingly is unclear. We performed an economic evaluation of systematic Chagas disease screening of the Latin American population attending primary care centres in Europe.

Methods We constructed a decision tree model that compared the test option (screening of asymptomatic individuals, treatment, and follow-up of positive cases) with the no-test option (screening, treating, and follow-up of symptomatic individuals). The decision tree included a Markov model with five states, related to the chronic stage of the disease: indeterminate, cardiomyopathy, gastrointestinal, response to treatment, and death. The model started with a target population of 100 000 individuals, of which 4·2% (95% CI 2·2–6·8) were estimated to be infected by *Trypanosoma cruzi*. The primary outcome was the incremental cost-effectiveness ratio (ICER) between test and no-test options. Deterministic and probabilistic analyses (Monte Carlo simulations) were performed.

Findings In the deterministic analysis, total costs referred to 100 000 individuals in the test and no-test option were €30 903 406 and €6 597 403 respectively, with a difference of €24 306 003. The respective number of quality-adjusted life-years (QALYs) gained in the test and no-test option were 61 820·82 and 57 354·42. The ICER was €5442. In the probabilistic analysis, total costs for the test and no-test option were €32 163 649 (95% CI 31 263 705–33 063 593) and €6 904 764 (6 703 258–7 106 270), respectively. The respective number of QALYs gained was 64 634·35 (95% CI 62 809·6–66 459·1) and 59 875·73 (58 191·18–61 560·28). The difference in QALYs gained between the test and no test options was 4758·62 (95% CI 4618·42–4898·82). The incremental cost-effectiveness ratio (ICER) was €6840·75 (95% CI 2545–2759) per QALY gained for a treatment efficacy of 20% and €4243 per QALY gained for treatment efficacy of 50%. Even with a reduction in Chagas disease prevalence to 0·05% and with large variations in all the parameters, the test option would still be more cost-effective than the no-test option (less than €30000 per QALY).

Interpretation Screening for Chagas disease in asymptomatic Latin American adults living in Europe is a cost-effective strategy. Findings of our model provide an important element to support the implementation of *T cruzi* screening programmes at primary health centres in European countries hosting Latin American migrants.

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Economic evaluation of Chagas disease screening of pregnant Latin American women and of their infants in a non endemic area

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ABSTRACT

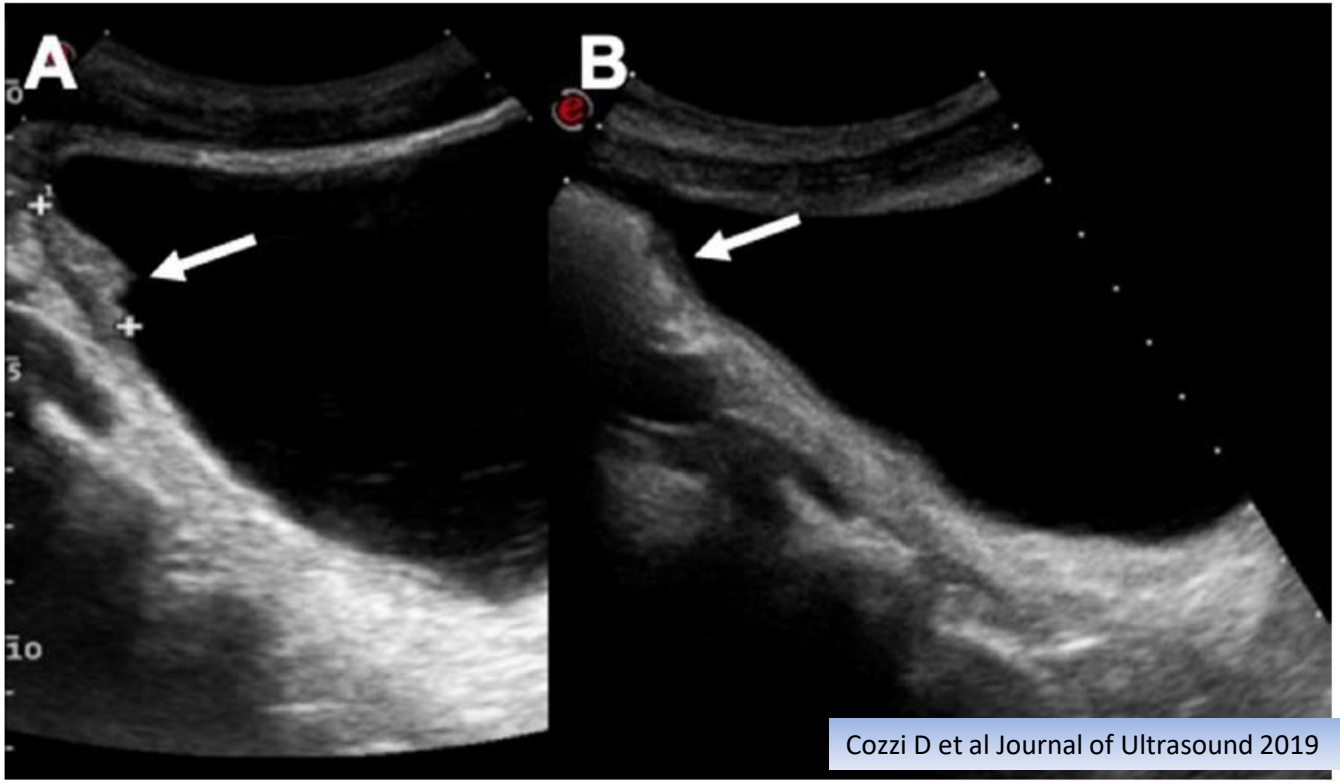
Migration is a channel through which Chagas disease is imported, and vertical transmission is a channel through which the disease is spread in non-endemic countries. This study presents the economic evaluation of Chagas disease screening in pregnant women from Latin America and in their newborns in a non endemic area such as Spain. The economic impact of Chagas disease screening is tested through two decision models, one for the newborn and one for the mother, against the alternative hypothesis of no screening for either the newborn or the mother. Results show that the option "no test" is dominated by the option "test". The cost effectiveness ratio in the "newborn model" was 22 €/QALYs gained in the case of screening and 125 €/QALYs gained in the case of no screening. The cost effectiveness ratio in the "mother model" was 96 €/QALYs gained in the case of screening and 1675 €/QALYs gained in the case of no screening. Probabilistic sensitivity analysis highlighted the reduction of uncertainty in the screening option. Threshold analysis assessed that even with a drop in Chagas prevalence from 3.4% to 0.9%, a drop in the probability of vertical transmission from 7.3% to 2.24% and with an increase of screening costs up to €37.5, "test" option would still be preferred to "no test". The current study proved Chagas screening of all Latin American women giving birth in Spain and of their infants to be the best strategy compared to the non-screening option and provides useful information for health policy makers in their decision making process.

Schistosomiasis

Treatment: praziquantel 40mg/kg per *os* per 1-3 giorni

Fig. 5 Vesical parietal thickening (arrow—**a**) and follow-up US control after 4 months of therapy (**b**)

Not registered in Italy



Cozzi D et al Journal of Ultrasound 2019

Journal of Travel Medicine
International Society of Travel Medicine
Promoting healthy travel worldwide
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Original Article

Original Article

Prospective cohort study using ultrasonography of Schistosoma haematobium–infected migrants

Francesca Tamarozzi, PhD[1,*], Tamara Ursini, MD[1], Niccolò Ronzoni, MD[1], Geraldo Badona Monteiro, MD[1], Federico G Gobbi, PhD[1], Andrea Angheben, MD[1], Joachim Richter, MD[2], Dora Buonfrate, MD[1] and Zeno Bisoffi, MD[1,3]

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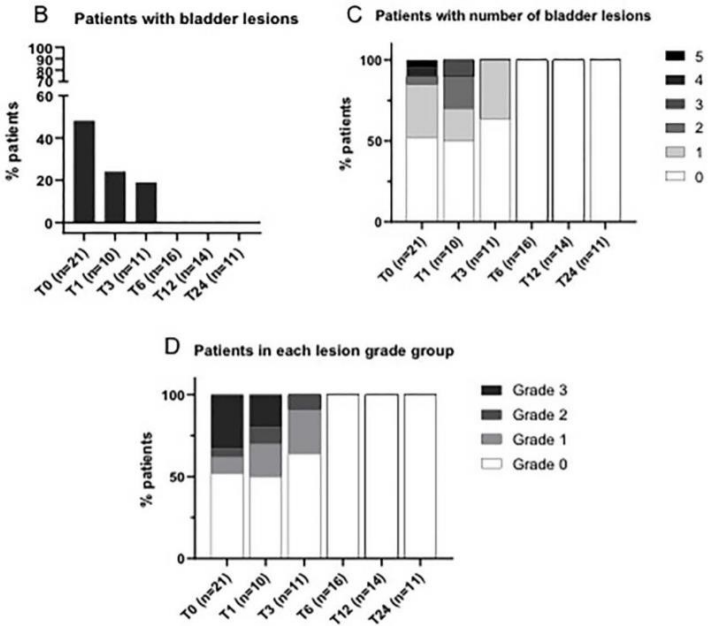
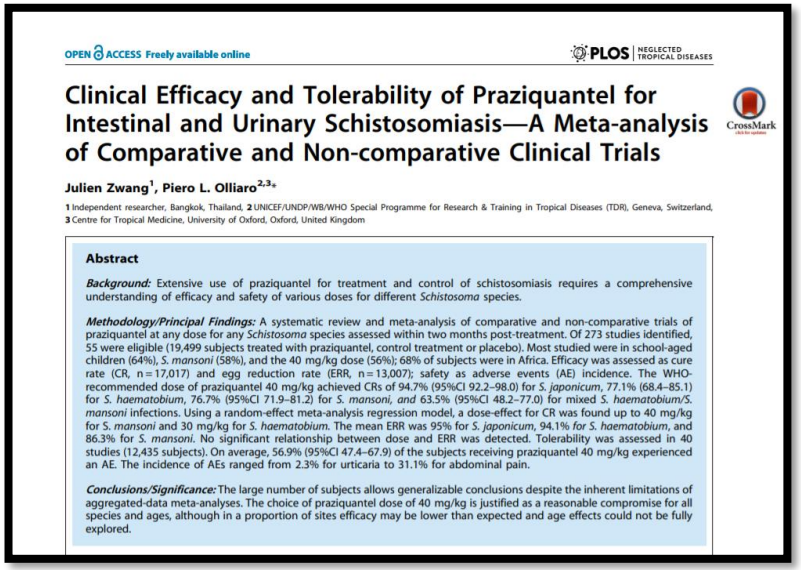


- Twenty-one patients, aged 18–29 years
- Ultrasound at 0, 1, 3, 6, 12, 24 months after PZQ
- Follow-up ≥6 months was completed by 16 (76.2%) patients; ≥12 months by 14 (66.7%) and 24 months by 11 (52.4%)
- All patients with bladder lesions on enrolment completed a follow-up of ≥6 months
- Lesions resolved completely by 6 months in all cases and no new development/re-appearance was observed

Praziquantel, how many doses?



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PLOS | NEGLECTED TROPICAL DISEASES

Clinical Efficacy and Tolerability of Praziquantel for Intestinal and Urinary Schistosomiasis—A Meta-analysis of Comparative and Non-comparative Clinical Trials

Julien Zwang[1], Piero L. Olliaro[2,3]*

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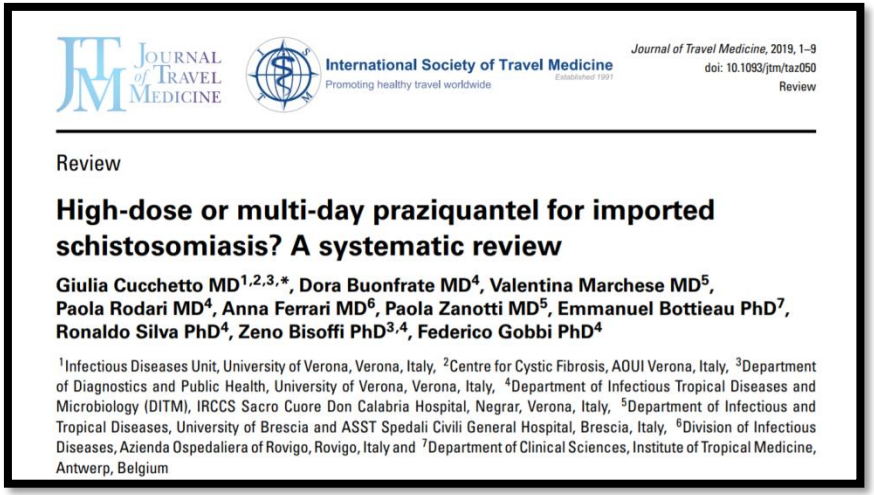
Abstract

Background: Extensive use of praziquantel for treatment and control of schistosomiasis requires a comprehensive understanding of efficacy and safety of various doses for different *Schistosoma* species.

Methodology/Principal Findings: A systematic review and meta-analysis of comparative and non-comparative trials of praziquantel at any dose for any *Schistosoma* species assessed within two months post-treatment. Of 273 studies identified, 55 were eligible (19,499 subjects treated with praziquantel, control treatment or placebo). Most studied were in school-aged children (64%), *S. mansoni* (58%), and the 40 mg/kg dose (56%); 68% of subjects were in Africa. Efficacy was assessed as cure rate (CR, n = 17,017) and egg reduction rate (ERR, n = 13,007); safety as adverse events (AE) incidence. The WHO-recommended dose of praziquantel 40 mg/kg achieved CRs of 94.7% (95%CI 92.2–98.0) for *S. japonicum*, 77.1% (68.4–85.1) for *S. haematobium*, 76.7% (95%CI 71.9–81.2) for *S. mansoni, and* 63.5% (95%CI 48.2–77.0) for mixed *S. haematobium/S. mansoni* infections. Using a random-effect meta-analysis regression model, a dose-effect for CR was found up to 40 mg/kg for S. *mansoni* and 30 mg/kg for *S. haematobium*. The mean ERR was 95% for *S. japonicum*, 94.1% *for S. haematobium*, and 86.3% for *S. mansoni*. No significant relationship between dose and ERR was detected. Tolerability was assessed in 40 studies (12,435 subjects). On average, 56.9% (95%CI 47.4–67.9) of the subjects receiving praziquantel 40 mg/kg experienced an AE. The incidence of AEs ranged from 2.3% for urticaria to 31.1% for abdominal pain.

Conclusions/Significance: The large number of subjects allows generalizable conclusions despite the inherent limitations of aggregated-data meta-analyses. The choice of praziquantel dose of 40 mg/kg is justified as a reasonable compromise for all species and ages, although in a proportion of sites efficacy may be lower than expected and age effects could not be fully explored.



JTM Journal of Travel Medicine

International Society of Travel Medicine
Promoting healthy travel worldwide
Established 1991

Journal of Travel Medicine, 2019, 1–9
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Review

Review

High-dose or multi-day praziquantel for imported schistosomiasis? A systematic review

Giulia Cucchetto MD[1,2,3,*], Dora Buonfrate MD[4], Valentina Marchese MD[5], Paola Rodari MD[4], Anna Ferrari MD[6], Paola Zanotti MD[5], Emmanuel Bottieau PhD[7], Ronaldo Silva PhD[4], Zeno Bisoffi PhD[3,4], Federico Gobbi PhD[4]

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Praziquantel 40 mg/kg cure rate:
94.7% (95%CI 92.2–98.0) for *S. japonicum*
77.1% (68.4–85.1) for *S. haematobium*
76.7% (95%CI 71.9–81.2) for *S. mansoni*

Praziquantel	
Medical Contraindications	*Other Contraindications*
• Known cysticercosis or neurocysticercosis* • Seizures or neurologic disorders of unknown etiology (suggestive of possible neurocysticercosis)	• Children <4 years old • Known hypersensitivity or allergy

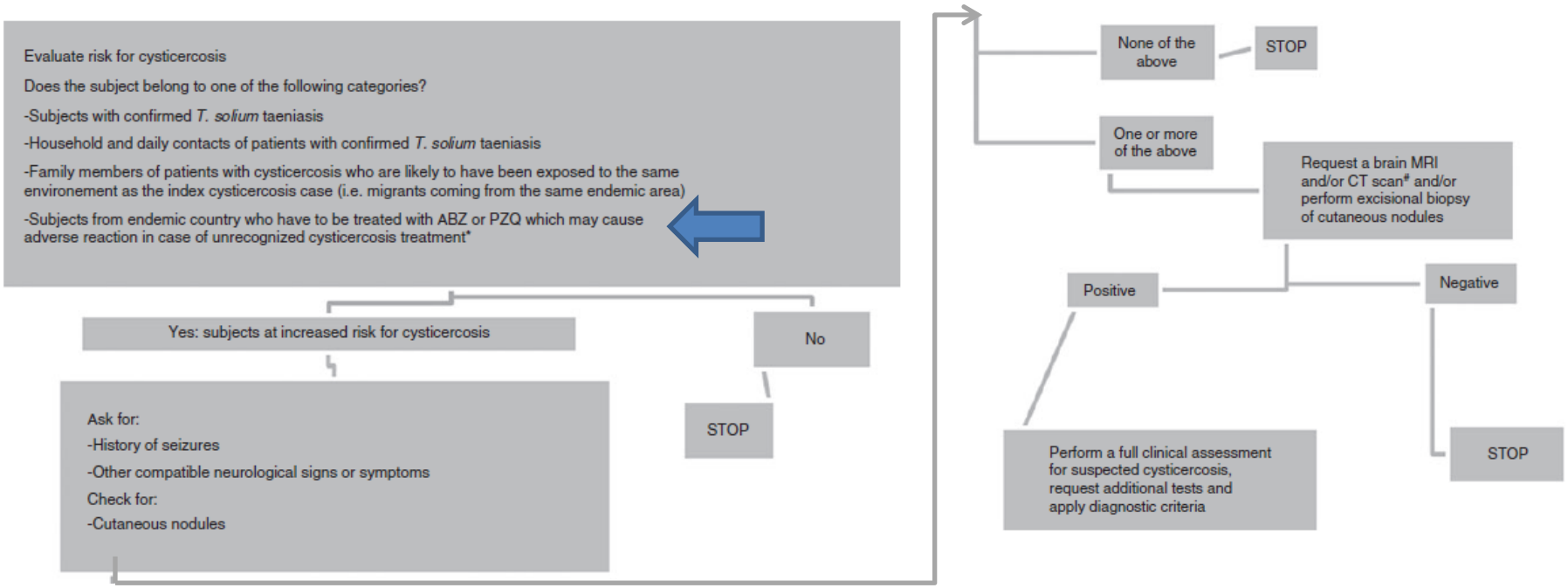
*Cysticercosis (e.g., subcutaneous nodules) is a parasitic tissue infection caused by Taenia solium. Taenia brain cysts (neurocysticercosis) may cause seizures or other neurologic disorders. Presumptive treatment with albendazole and/or praziquantel is contraindicated in these cases, and expert consultation is strongly recommended.

5.2 Central Nervous System (CNS) Effects

Biltricide can exacerbate central nervous system pathology due to schistosomiasis, paragonimiasis, or *Taenia solium* cysticercosis. As a general rule, consider whether to administer Biltricide to individuals reporting a history of epilepsy and/or other signs of potential central nervous systems involvement such as subcutaneous nodules suggestive of cysticercosis unless the potential benefit justifies the potential risk. Hospitalize the patient for duration of treatment when schistosomiasis or fluke infection is found to be associated with cerebral cysticercosis.

https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/intestinal-parasites-domestic.html

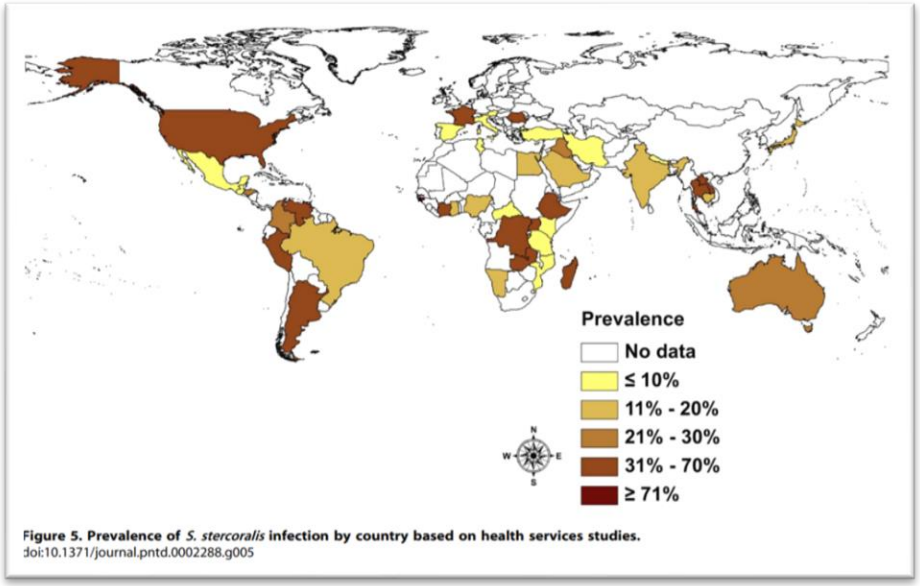
Appendix I
Algorithm: Screening for unrecognised symptomatic cysticercosis



Zammarchi L et al TMIH 2016

Strongyloides stercoralis infection (strongyloidiasis)

30–100 million people estimated to be infected worldwide



Schar F et al Plos NTD 2013

Prevalence:
8% in Italians aged >60 with eosinophilia
17% in migrants aged >18 with eosinophilia

Buonfrate D et al Euro Surveill 2016

Strongyloidiasis: clinical aspects

Uncomplicated

Table 3
Clinical characteristics of cases of strongyloidiasis (total and by group)

	Total (n = 178) (100%), n (%)
Symptomatic, n (%)	85 (47.8)
Gastrointestinal symptoms, n (%)	54 (30.3)
Nausea	4 (2.2)
Vomiting	4 (2.2)
Reflux	6 (3.4)
Dyspepsia	13 (7.3)
Abdominal pain	20 (11.2)
Constipation	8 (4.5)
Diarrhea	22 (12.4)
Pulmonary symptoms, n (%)	6 (3.4)
Cough	4 (2.2)
Sputum	0 (0)
Wheezing	1 (0.6)
Cutaneous symptoms, n (%)	38 (21.3)
Urticaria	32 (18)
Larva currens	5 (2.8)
Purpura	2 (1.1)
Comorbidity, n (%)	72 (40.4)

Ramirez-Olivencia et al IJID 2014

Eosinophilia
≈60-70%

Disseminated / Hyperinfection

Convegno Scientifico di Parassitologia e Medicina Tropicale
a tema libero

Firenze, 12 dicembre 2008

Strongiloidiasi disseminata in paziente con linfoma a cellule T indifferenziato: presentazione di un caso

Letizia Attala

A Cavallo, M Bonizzoli, F Bartalesi, M Strohmeyer, A Bartoloni

SOD Malattie Infettive e Tropicali - AOU Careggi

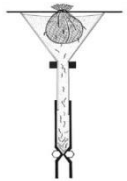
Anestesia e Rianimazione DAI 9 - AOU Careggi

Letality 50-60%

Risk factors:

- Corticosteroids
- HTLV-1 infection
- Transplant
- Chemotherapy
- Malnutrition
- Alcoholism
- (HIV)

Strongyloidiasis: diagnosis



Low sensitivity

- Standard parasitological examination of stool (very low)
- **Agar-plate stool colture (45%)**
- **PCR on stool (57%)**
- **Serology (89-95%)**

Higher sensitivity

Strongyloidiasis: treatment

IVERMECTIN

- Uncomplicated cases and immunocompetent: Ivermectin 200 mcg/kg po single dose
- Hyperinfection / dissemination OR immunosuppressed: ivermectin po multiple dose +/- albendazole po. Possible use of subcutaneous ivermectin (veterinary preparation)

Buonfrate D et al Lancet Infect Dis 2019

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

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

Summary

Background *Strongyloides stercoralis* infection is a neglected condition that places people who are immunocompromised at risk of hyperinfection and death. Ivermectin is the drug of choice for the treatment of *S stercoralis* infection, but there is no definitive evidence on the optimal dose. This trial aimed to assess whether multiple doses of ivermectin were superior to a single dose for the treatment of non-disseminated strongyloidiasis.

Methods Our study was designed as a multicentre, open-label, phase 3, randomised controlled superiority trial. Participants were enrolled in four centres in Italy, three in Spain, and two in the UK, and recruiting sites were predominantly hospitals. Eligible patients were older than 5 years, weighed more than 15 kg, were residents in an area not endemic for *S stercoralis*, and either were positive for *S stercoralis* in faecal tests and on serology (any titre) or had a positive serological test with high titres, irrespective of the result of faecal tests. Patients were randomly assigned (1:1) using a computer-generated, blinded allocation sequence (with randomly mixed block sizes of six, eight, and ten participants) to receive either one dose of ivermectin 200 µg/kg or four doses of ivermectin 200 µg/kg (given on days 1, 2, 15, and 16). The primary endpoint was the proportion of participants with clearance of *S stercoralis* infection at 12 months, which was assessed in all randomly assigned participants who were not lost to follow-up (modified full-analysis set) and in participants in the modified full-analysis set who did not deviate from the assigned treatment regimen (per-protocol set). All participants were included in the safety analysis. The trial was registered with ClinicalTrials.gov, NCT01570504, and is now closed for recruitment.

Findings Of the 351 patients assessed for eligibility, 309 recruited between March 26, 2013, and May 3, 2017, were randomly assigned to one dose (n=155) or four doses (n=154) of ivermectin. At 12 months in the modified full-analysis set, 86% (95% CI 79 to 91; 102 of 118 participants) had responded to treatment in the single-dose group compared with 85% (77 to 90; 96 of 113 participants) in the four-dose group (risk difference 1·48%, 95% CI −7·55 to 10·52; p=0·75); similar results were observed in the per-protocol set. Adverse events were generally of mild intensity and more frequent in the multiple-dose than in the single-dose group. The trial was terminated early due to futility.

Interpretation Multiple doses of ivermectin did not show higher efficacy and was tolerated less than a single dose. A single dose should therefore be preferred for the treatment of non-disseminated strongyloidiasis.

Lancet Infect Dis 2019

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See Online/Comment
https://doi.org/10.1016/S1473-3099(19)30519-5

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Am. J. Trop. Med. Hyg., 92(6), 2015, pp. 1257–1260
doi:10.4269/ajtmh.14-0716

Evitare albendazolo (minore efficacia)

Case Report: Persistent Strongyloidiasis Complicated by Recurrent Meningitis in an HTLV Seropositive Peruvian Migrant Resettled in Italy

Lorenzo Zammarchi,† Francesca Montagnani,† Giacinta Tordini, Eduardo Gotuzzo, Zeno Bisoffi, Alessandro Bartoloni,* and Andrea De Luca

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Abstract. We describe a case of persistent strongyloidiasis complicated by recurrent meningitis, in a human T cell lymphotropic virus type 1 (HTLV-1) seropositive Peruvian migrant adult resettled in Italy. He was admitted with signs and symptoms of acute bacterial meningitis, reporting four other meningitis episodes in the past 6 years, with an etiological diagnosis of *Escherichia coli* and *Enterococcus faecium* in two cases. He had been previously treated with several antihelmintic regimens not including ivermectin, without eradication of strongyloidiasis, and he had never been tested for HTLV before. During the described episode, the patient was treated for meningitis with broad-spectrum antibiotic therapy and 200 μg/kg/dose oral ivermectin once daily on day 1, 2, 15 and 16 with full recovery and no further episodes of meningitis. The presented case underlines several critical points concerning the management of poorly known neglected diseases such as strongyloidiasis and HTLV infection in low-endemic areas. Despite several admissions for meningitis and strongyloidiasis, the parasitic infection was not adequately treated and the patient was not previously tested for HTLV. The supply of ivermectin and the choice of treatment scheme was challenging since ivermectin is not approved in Italy and there are no standardized guidelines for the treatment of severe strongyloidiasis in HTLV seropositive subjects.

Ivermectin	
Medical Contraindications	*Other Contraindications*
• Presence of *Loa loa* microfilaremia**	• Children weighing <15 kg • Pregnancy or breastfeeding an infant <1 week old • Known hypersensitivity or allergy

**Treatment of identified strongyloidiasis is contraindicated in patients with high-burden Loa loa parasitemia (see Loa loa endemic country list, above). In these cases, ivermectin may precipitate encephalopathy.

https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/intestinal-parasites-domestic.html

Loa loa & ivermectin

Am. J. Trop. Med. Hyg., 97(6), 2017, pp. 1833–1835
doi:10.4269/ajtmh.17-0337

Absence of *Loa loa* Microfilaremia among Newly Arrived Congolese Refugees in Texas

Jessica Montour,[1] Deborah Lee,[2*] Cathy Snider,[1] Emily S. Jentes,[2] and William Stauffer[2,3]
[1]Texas Department of State Health Services, Austin, Texas; [2]Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, Atlanta, Georgia; [3]University of Minnesota, Departments of Medicine and Pediatrics, Infectious Diseases and International Medicine, Minneapolis, Minnesota

PanAfrican Medical Journal

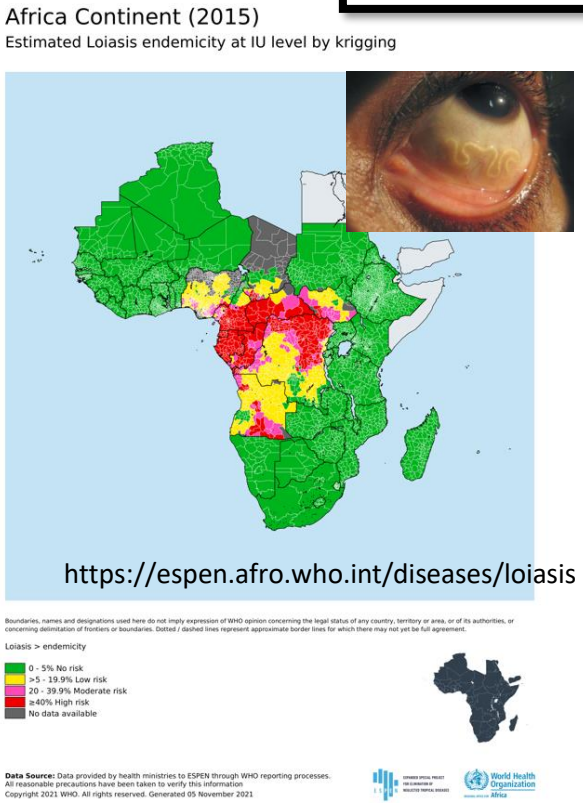
Open Access

Case report

Post-ivermectin encephalopathy in Senegal: a case report

Daniel Gams Massi [1,&], Mohamed Lelouma Mansare[1], Mariétou Traoré[1], Moustapha Ndiaye[1], Amadou Gallo Diop[1], Mouhamadou Mansour Ndiaye[1]

Presumptive or targeted treatment with ivermectin for strongyloidiasis is contraindicated in patients with high-burden *Loa loa* parasitemia. In these cases, ivermectin may precipitate encephalopathy. A **thin and thick blood smear between 10 a.m. and 2 p.m.** for *Loa loa* microfilaria should be performed before treatment with ivermectin **in patients coming for a *Loa loa* endemic country**



Loa loa endemic countries

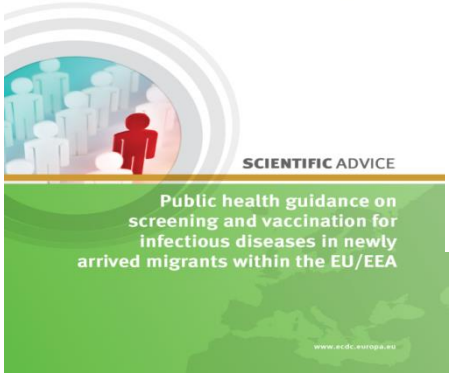
1. Angola
2. Cameroon
3. Central African Republic
4. Chad
5. Congo
6. Ethiopia
7. Equatorial Guinea
8. Gabon
9. Nigeria
10. South Sudan
11. Democratic Republic of Congo

https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/intestinal-parasites-domestic.html

Screening sierologico è raccomandato nei migranti provenienti da paesi endemici

R9.4 – Nei migranti, anche asintomatici, che hanno vissuto o viaggiato in aree endemiche per strongiloidosi* e schistosomiasi (si veda allegato 6), è raccomandato l'esame sierologico, nell'ambito della presa in carico sanitaria. Il riscontro di sierologia positiva per *Strongyloides stercoralis* e *Schistosoma spp*, in soggetti non trattati di recente, deve essere considerato come infezione in atto e come tale meritevole di trattamento.
(ASID, RHeaNA 2016; NCEZID/CDC 2013; CCIRH 2011) **Grado A**

June 2017



Evidence-based statement (schistosomiasis)

Offer serological screening and treatment (for those found to be positive) to all migrants from countries of high endemicity in sub-Saharan Africa and focal areas of transmission in Asia, South America, and North Africa (see Figure 14).

(Certainty of evidence: low)

December 2018

Travel Medicine and Infectious Disease xxx (xxxx) xxxx

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Strategies for management of strongyloidiasis in migrants from Sub-Saharan Africa recently arrived in Italy: A cost-effectiveness analysis

Lorenzo Zammarchi[a,b,*], Marta Tilli[a], Annarita Botta[a], Dora Buonfrate[c], Alessandro Bartoloni[a,b], Sara Boccalini[d]

MILANO 28 NOVEMBRE - 01 DICEMBRE 2021

XX Congresso Nazionale SIMIT

Valutazione economica di differenti strategie per la gestione della schistosomiasi in migranti provenienti dall'Africa Sub-Sahariana arrivati in Italia.

Dr.ssa Annarita Botta

Scuola di Specializzazione in Malattie Infettive e Tropicali

Università degli Studi di Firenze

Infection (2019) 47:3–5
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EDITORIAL

Neglected tropical diseases in Europe: rare diseases and orphan drugs?

Guido Calleri[1] · Andrea Angheben[2] · Marco Albonico[2,3]

Table 1 Orphan drug licensing in Italy, Spain and Germany

Drug	Main target conditions	License AIFA Italy	License AEMPS Spain	License BfArM Germany
Benznidazole	Chagas disease	No	No	No
Diethylcarbamazine	Lymphatic filariasis	No	No	No
Eflornithine i.v.	African trypanosomiasis	Withdrawn	No	No
Ivermectin tabs	Strongyloidiasis, onchocerciasis	No	No	Yes (for scabies only)
Meglumine antimoniate	Leishmaniasis	Withdrawn	Yes	No
Melarsoprol	African trypanosomiasis	No	No	No
Miltefosine	Leishmaniasis	No	No	Yes
Nitazoxanide	Giardiasis amoebiasis, cryptosporidiosis	No	No	No
Praziquantel	Schistosomiasis, cestodes, trematodes	No	No	Yes
Primaquine	P. vivax/P. ovale malaria	Withdrawn	No	No
Quinacrine*	Refractory giardiasis	No	No	No
Suramin	African trypanosomiasis	No	No	Yes
Thiabendazole	Strongyloidiasis, ancylostomiasis	Withdrawn	Withdrawn	No
Triclabendazole	Fascioliasis	No	No	No

*Not in the WHO essential medicines list

Possibili soluzioni? Legge 648/96?

Azienda Ospedaliero Universitaria Careggi

MODULO IMPORTAZIONE FARMACI

Richiesta di importazione di medicinali
ai sensi del D.M. 11/02/1997

M/ 521/13/18
Ed. 2
Rev. 0
Del 04/10/2017

AL MINISTERO DELLA SALUTE
USMAF-SASN……
UNITA' TERRITORIALE……

Il sottoscritto Dr. ……
Residente in…… via ……tel……
iscritto nell'Albo dell'Ordine dei Medici-Chirurghi di ……
al n…… cod. regionale ……
Reparto/ Struttura di appartenenza……Cdc……
Chiede di importare il medicinale (contenente il seguente/i principio/i attivo/i)……
……
nome commerciale: ……
forma farmaceutica……
nella quantità di numero …… confezioni contenenti …… di farmaco cadauna.
prodotto dalla ditta: …… (specificare il nome dell'azienda)
Precisa che tale medicinale è regolarmente registrato nel Paese di provenienza: ……
per il trattamento di ……

- Tale medicinale è indispensabile per la cura del Sig. (iniziali o codice) ……

affetto da: ……

- Tale medicinale è indispensabile per scorta di reparto.

Motivo per cui viene richiesta la scorta di reparto****……
Dichiara altresì che il farmaco:

- non ha valida alternativa terapeutica con altri medicinali registrati in Italia;
- non contiene sostanze stupefacenti o psicotrope;
- non è un emoderivato;
- verrà impiegato sotto la propria diretta responsabilità, dopo aver ottenuto il consenso informato scritto del paziente;
- che le generalità del paziente ed i documenti relativi al consenso informato sono custoditi presso il medico curante per la durata prevista dalla normativa vigente.

Particolari condizioni di conservazione del medicinale:
Temperatura (es. -20°C, da 2 a 8°C, < 25°, <30°, nessuna indicazione): ……
Altro: ……

Luogo e data _____

_____ _____

Timbro e firma leggibile del Farmacista Timbro e firma leggibile del Medico

****Da compilare solo in caso di scorta reparto

Dichiara che
a) Tale medicinale è indispensabile per la cura del Sig. (iniziali o codice)
oppure
b) Tale medicinale è indispensabile per scorta reparto
Motivo per cui viene richiesta scorta reparto

- Verrà impiegato sotto la propria responsabilità dopo aver ottenuto il consenso informato scritto del paziente

Legge 648/1996

La Legge 648/1996 consente di erogare un farmaco a carico del Servizio Sanitario Nazionale (SSN), previo parere della Commissione Tecnico-Scientifica (CTS) di AIFA:

Quando non esiste un'alternativa terapeutica valida:

- per medicinali innovativi autorizzati in altri Stati, ma non in Italia
- per medicinali non ancora autorizzati, ma in corso di sperimentazione clinica
- per medicinali da impiegare per una indicazione terapeutica diversa da quella autorizzata

In tutti questi casi è necessaria l'esistenza di studi conclusi, almeno di fase II, che dimostrino un'efficacia adeguata con un profilo di rischio accettabile a supporto dell'indicazione richiesta.

In presenza di una alternativa terapeutica valida (Art. 3 Legge 79/2014):

- per medicinali da impiegare per una indicazione terapeutica diversa da quella autorizzata, purché tale indicazione sia nota e conforme a ricerche condotte nell'ambito della comunità medico-scientifica nazionale e internazionale, secondo parametri di economicità e appropriatezza.

ITALIAN NETWORK
on Neglected Tropical Diseases

IN-NTD

We support the Sustainable Development Goals

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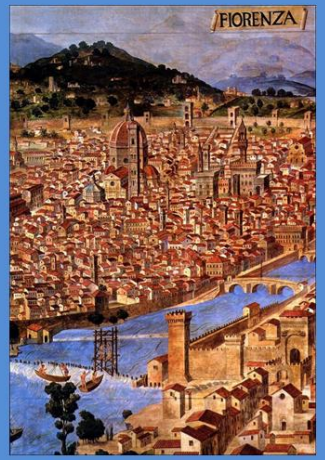

Argomenti principali

- COVID-19 e Salute Globale
- Malattie Tropicali Neglette
- One Health
- Vaccini e Salute Globale
- Cooperazione Internazionale
- Medicina delle migrazioni e dei viaggi

PRESIDENTE
Prof. Alessandro Bartoloni
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