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

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ABSTRACT

Background: The Italian and the European Centre for Disease Control and Prevention guidelines both recommend a systematic serological screening for strongyloidiasis in sub-Saharan migrants (SSA), however, studies on clinical and economic impact of this strategy in the Italian and European settings are lacking.
Methods: A population of 100,000 migrants from SSA to Italy was considered and a Markov decision tree model was developed to assess the clinical and economic impact of two interventions for strongyloidiasis compared with the current practice (passive diagnosis of symptomatic cases): a) universal serological screening and treatment with ivermectin in case of positive test b) universal presumptive treatment with ivermectin. One and 10-year time horizon in the health-care perspective were considered.
Results: In the one and 10-year time horizon respectively the costs for passive diagnosis was €1,164,169 and €9,735,908, those for screening option was € 2,856,011 and € 4,959,638 and those for presumptive treatment was €3,538,474 and € 4,883,272. Considering the cost per cured subject in the one-year time horizon, screening appears more favorable (€209.53), than the other two options (€232.55 per presumptive treatment and €10,197.29 per current strategy). Incremental cost-effectiveness ratio (ICERs) of screening strategy and presumptive treatment were respectively 265.27 and 333.19. The sensitivity analysis identified strongyloidiasis' prevalence as the main driver of ICER.
Conclusions: Compared to the current practice (passive diagnosis) both screening and presumptive treatment strategies are more favorable from a cost-effectiveness point of view, with a slight advantage of the screening strategy in a one-year time horizon.

1. Introduction

Strongyloidiasis is a helminthiasis endemic in rural areas of tropical and subtropical regions occurring sporadically in temperate areas, including some European regions [1]. Over 350 million people are estimated to be infected by this nematode worldwide [2]. The infection begins when human skin contacts filariform larvae (the infective larval stage) of *Strongyloides stercoralis*, which are found in soil or other materials contaminated with human feces. The infection has some important characteristics from the clinical and public health point of view. Firstly, only about half of infected subjects present symptoms (mainly uticaria, abdominal pain) [3,4], while most infected subjects do not experience any prominent symptoms, and peripheral eosinophilia may be the only clue. Hence, they often remain unaware that they harbor the infection. Secondly, *S. stercoralis* can cause a lifelong infection in the human host if left untreated due to the ability of the parasite to replicate indefinitely (auto-infective cycle) [2]. Thirdly, immunosuppressed patients can develop hyperinfection syndrome or dissemination, two potentially fatal complications with a fatality rate of 60–70% [2]. Unrecognized strongyloidiasis may lead to costly and inappropriate diagnostic tests due to unexplained itching, abdominal pain, including gastric pain [5] or eosinophilia and, in case of immunosuppression, even to hospital admissions and deaths [2]. Concerning the diagnosis, serology shows a much higher sensitivity (90–95% depending on the method [6] compared to fecal-based techniques [7] including Koga agar plate culture, and molecular methods

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(such as Polymerase Chain Reaction) which have a sensitivity of about 45 and 57% respectively [8]. Ivermectin is the treatment of choice of strongyloidiasis [9]. Recently an increased migration flow from Sub-Saharan Africa (SSA) to Europe has been recorded, with ~650,000 people (most of them from SSA) disembarked in Italy in the period 2014–2019 [10,11]. A high prevalence of strongyloidiasis is reported in SSA [1] and a recent systematic review of literature has estimated a prevalence of 14.6% (7.1–24.2%) in migrants coming from this area [12], highlighting an urgent need for the Italian National Health Service (NHS) to address the problem of the correct management of this disease. Even thus Italian guidelines on migrant health published in 2017 propose a systematic serological screening test for all migrants exposed in endemic areas, these guidelines are still not applied and the current practice in Italy is the passive diagnosis of patients who have or develop symptoms. Availability of diagnostic tools for strongyloidiasis is not uniform in the national territory and no guidelines for the management of positive cases are available [13]. Moreover ivermectin is not registered in Italy and have to be imported from abroad [14]. Possible alternatives to passive diagnosis are a universal screening for the presence of infection based on a reliable diagnostic test with the treatment of patients which tested positive, or a presumptive universal treatment of all subjects without any previous test. Thus far, studies on the optimal approach are lacking, as clinical and economic impact of this disease in non-endemic high-income countries have been addressed only partially, and only in the US setting [15,16]. Therefore, the main analytic objective of our study was to compare the benefits and costs of these strategies for immigrants from SSA arriving in Italy, in order to provide evidence on which could best serve the purpose of saving lives at an acceptable cost for the NHS.

2. Material and methods

2.1. Study design: decision model and strategies

A Markov decision tree model was developed in Microsoft Excel® to assess the clinical and economic impacts of two possible interventions for strongyloidiasis in immigrant from SSA:

a) serological screening of all immigrants from SSA and treatment in case of positive test, b) presumptive treatment with ivermectin single dose, compared with the passive diagnosis of patients who have or develop symptoms (current practice in Italy).

The time horizon of analysis was 10 years. The study was conducted according to the perspective of the Italian NHS. The Italian State guarantees a universal health coverage (including primary care, specialist care and hospitalization) for each subject present in the country, according to article 32 of the Italian Constitution. Concerning undocumented migrants, urgent treatment but also essential and continuous treatment, both outpatient and inpatient is ensured in public and accredited facilities, with particular regard to prophylaxis, diagnosis and treatment of infectious diseases (Decreto Legislativo 286/98, art. 35, comma 3) [17].The decision model and health status (with related transition rates and visits, diagnostic tests and treatments) are shown in Fig. 1 and Tables 1 and 2.

The results are reported as number of cured cases, cases of persistent symptomatic infection, deaths, costs and Incremental Cost-Effectiveness Ratio (ICER). ICER is defined as the difference in costs between two strategies divided by the difference in their effects, with the smaller ICER indicating better cost-effectiveness of one strategy versus the other. Particularly, the benefits of analysed strategies are reported as Life-Years Gained (LYG).

2.2. Input data

We assumed a population of 100,000 immigrants. In the model, each subject is assigned to a state of being either infected with *S. stercoralis* or uninfected, with a prevalence of infection of 17.9% [18]. The first strategy consists of the passive diagnosis of subjects who have or develop symptoms (current practice in Italy and, therefore, our comparator scenario in the analysis). Each infected subject can be (or become) symptomatic or not. According to literature data the percentage of symptomatic infected subjects is supposed to be 53.3% [3]. Only 14.8% of them in 10 years will undergo a diagnostic test, while the remaining will remain undiagnosed due to failure of the health care provider to suspect the diagnosis or requesting the right investigations [19]. In case the patient with symptoms will not receive a diagnostic test (and related medical treatment), or in case he/she will result falsely negative at the diagnostic test, he/she will move into a persistent symptomatic status, with subsequent economic costs linked to inappropriate interventions during the 10 years of analysis (point ι in Table 2). Two percent of these patients (subjects with no diagnostic test or with false negative results at diagnostic tests) will be hospitalized [20,21] during 10 years (hospitalization rate of 0.2% per year) due to hyperinfection/disseminated syndrome, with a fatality rate of 64.25% [22]. The second strategy (screening programme) identifies the infected subject who will undergo to the treatment. The screening test IgG ELISA has sensitivity of 89.5% and specificity of 98.3% [6]. As a consequence, some infected subjects will have false negative test results and they will have the same course as unscreened and therefore untreated infected subjects. A smaller proportion of non infected patients will have false positive screening tests, and will be improperly treated with additional costs because of misdiagnosis.

In the third strategy (presumptive treatment), both the infected and the uninfected subjects will be treated, and the uninfected subject category will create only additional costs and no benefit.

In all the scenarios, each subject that should be treated with ivermectin, coming from countries where loiasis is endemic [11], will undergo a peripheral blood smear for *Loa loa* microfilariae before receiving the drug. According to available data, subjects from countries endemic for loiasis account for about 30% of all SSA arrived in Italy [11]. In these subjects the expected loiasis prevalence was considered to range between 0 and 1% [23]. Subjects with loiasis will undergo a treatment with albendazole (200 mg bid for 21 days) before receiving ivermectin.

We assumed that the cure rate of the treatment with ivermectin was 85% [24]. Therefore, the treatment will not result in parasitological cure for 15% of subjects. In the passive diagnosis strategy these patients will remain in a state of persistent symptomatic infection during the 10 years of analysis, with mild to moderate symptoms (if any), that will generate costs due to inappropriate management and may lead to hospitalization and death with a probability that is equivalent to that of the patient who did not receive any diagnostic test at all. In the screening and presumptive treatment strategies we assumed that, although all patients will remain infected lifelong, only 53.3% of patients [3] will be symptomatic, and will remain in the state of persistent symptomatic infection that may lead to hospitalization and additional costs linked to misdiagnosis. In all the scenarios we assumed that initially infected asymptomatic patients who will remain untreated will remain asymptomatic and unaware of their status without requiring medical attention or generating costs. In other words this model does not consider the possibility of asymptomatic patients to get hospitalized for the severe condition (hyperinfection, disseminated syndrome), given the difficulty of finding reliable data on this risk. Counting these patients would have led to a higher number of hospitalizations than the ones estimated by the model, with subsequently higher costs for the NHS.

2.3. Costs

Concerning the passive diagnosis strategy, we attributed the cost δ to symptomatic subjects (53.3%) receiving the right investigations (14.8%), specifically serological test for strongyloidiasis, full blood count and an infectious diseases specialist consultation. We attributed

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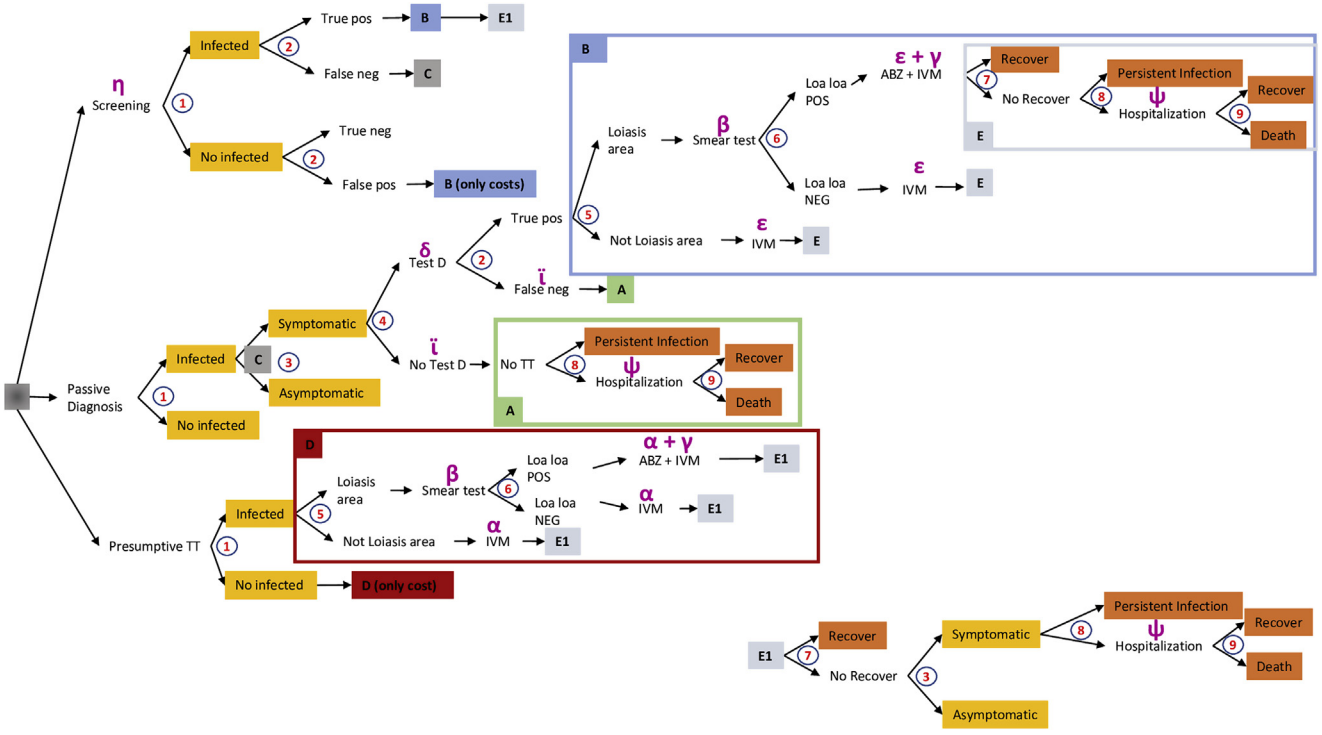

Fig. 1. The decision model and all health status and related treatments.
Text→*Screening*: screening strategy; *Passive diagnosis*: passive diagnosis strategy; *Presumptive TT*: presumptive treatment with ivermectin strategy; *True pos*: true positive; *False neg*: false negative; *True neg*: true negative ; *False pos*: false positive; *Test D*: diagnostic test performed; *No Test D*: diagnostic test not performed; *No TT*; treatment not given; *Smear test*: diurnal peripheral blood smear for *Loa loa* microfilariae; *Loiasis area*: subject coming from an area where loiasis is endemic; *Not Loiasis area*: subject coming from an area where loiasis is not endemic; *Loa Loa POS*: subject affected by loiasis; *Loa Loa NEG*: subject not affected by loiasis; *IVM*: treatment with ivermectin; *ABZ*: treatment with albendazole.
Latin letters→*A*: No treatment arm; *B*: positive diagnostic test arm, true positive; *B (only costs)*: positive diagnostic test arm, false negative. Only costs are applied to this arm; *C*: infected arm in passive diagnosis scenario; *D*: actions accomplished in presumptive treatment scenario in infected subjects; *D (only cost)*: actions accomplished in presumptive treatment scenario in not infected subjects. Only costs are applied to this arm; *E*: outcomes arm (in passive diagnosis scenario); *E1*: outcomes arm (in screening and presumptive treatment scenarios).
Numbers are referred to transition probabilities (see Table 1).
Greek letters are referred to costs (see Table 2).

the cost ι to symptomatic subjects receiving wrong investigations (85.2%). In details, we estimated the cost of misdiagnosis for infected symptomatic patients not receiving the right investigations, assuming that each patient will consult at least two specialists (for example a dermatologist and an allergologist or a gastroenterologist for unexplained itching and abdominal discomfort), and get routine blood check (blood count test, creatinine, ALT, γGT) and at least one abdominal ultrasound. In addition, the cost ι was be assigned to all subjects with persistent symptomatic infection each year during the overall 10-years period of analysis.

The cost of treatment for patients diagnosed with strongyloidiasis in the passive diagnosis strategy and in the screening strategy was those of ivermectin 3 mg five tablets once (corresponding approximately to the standard single dose of 200 μg/kg for subject with body weight 70 kg)

Table 1
Input data and rate of visits, diagnostic tests and treatments in the model.

	Parameter	Rate Base case	Minimum	Maximum	References
1	Strongyloidiasis prevalence	0.179	0.071	0.242	Buonfrate 2018 [18], Asundi 2019 [12]
2a	Sensitivity of IgG ELISA from Bordier (*Strongyloides ratti*; Bordier Affinity Products SA, Crissier, Switzerland)	0.895	0.838	0.951	Bisoffi 2014 [6]
2b	Specificity of IgG ELISA from Bordier (*Strongyloides ratti*; Bordier Affinity Products SA, Crissier, Switzerland)	0.983	0.959	1	Bisoffi 2014 [6]
3	Symptomatic patients	0.533	0.478	0.643	Ramirez-Olivencia 2014 [3]
4	Patients that will undergo a diagnostic test for strongyloidiasis	0.148	0.079	0.217	Boulware 2007 [19]
5	Subjects from *Loa loa* endemic countries[a]	0.300	0.16	0.36	Elaboration of UNHCR data [11]
6	*Loa loa* prevalence in Sub-Saharan immigrants	0.010[b]	0.00	0.020[b]	Montour 2007 [23]
7	Treatment cure rate	0.85	0.79	0.91	Buonfrate 2019 [24]
8	Hospitalization for strongyloidiasis hyperinfection/disseminated syndrome in 10 years	0.020	0.004	0.025	Milder 1981 [20], Salvador 2019 [21]
9	Lethality of strongyloidiasis hyperinfection/disseminated syndrome	0.6425	0.600	0.685	Buonfrate 2013 [22]

[a] Angola, Cameroon, Central African Republic, Chad, Republic of Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Nigeria, South Sudan.
[b] Assumption.

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Table 2
Cost of visits, diagnostic tests and treatments in the model (Euro).

Items	Costs (Euro)							
	α	B	Γ	Δ	ε	H	I	Ψ
5 tabs ivermectin (for 70 kg subject)	32.30	–	–	–	32.30	–	–	–
Diurnal peripheral blood smear for *Loa loa* microfilariae	–	4.00	–	–	–	–	–	–
Albendazole 1 tab/die x 3 week	–	–	47.25	–	–	–	–	–
Clinical visit with ID specialist	–	–	–	22.50	22.50	–	–	–
Serology test for *Strongyloides*	–	–	–	16.00	–	16.00	–	–
Blood count test	–	–	–	4.00	–	–	4.00	–
Clinical visit with two specialists	–	–	–	–	–	–	45.00	–
Creatinine	–	–	–	–	–	–	2.00	–
ALT	–	–	–	–	–	–	2.00	–
γGT	–	–	–	–	–	–	2.00	–
Abdominal Ultrasound	–	–	–	–	–	–	60.00	–
Estimated mean cost for a single hospitalization	–	–	–	–	–	–	–	3511.50[a]
TOTAL	32.30	4.00	47.25	42.50	54.80	16.00	115.00	3511.50

ID = Infectious Diseases.
[a] See Supplementary material.

plus those of an infectious diseases specialist consultation (cost ε). In the presumptive treatment strategy the only cost resulted from ivermectin 3 mg five tablets once since we suppose that the treatment could be delivered in the context of primary health care (Italian general practitioners are paid a quota per capita that is independent to the number of clinical interventions performed) without the referral to an infectious diseases specialist (cost α).

Regardless the strategy, subjects from *Loa loa* endemic countries that should receive ivermectin (both because diagnosed with strongyloidiasis or because of presumptive treatment) will have to undergo a diurnal peripheral blood smear for *Loa loa* microfilariae (cost β). Patients with a positive peripheral blood smear for *Loa loa* microfilariae will be treated with albendazole 200 mg (=½ tab) bid for 3 weeks (cost γ) before receiving ivermectin.

The costs of all visits, test, drugs and interventions were taken from the pricelist of Careggi University Hospital, Florence, Italy (Table 2). In order to approximately estimate hospitalization cost for strongyloidiasis (cost ψ), we selected from the Italian Pricelist for Hospital Care the codified "Reasons of hospitalization" that could possibly be associated to strongyloidiasis (Supplementary material).

We considered both admission in Intensive Care Units (ICU) and in ordinary hospitalization (surgery or medicine) units (Not-ICU) assuming that 10% of patients will be hospitalized in ICU and 90% in Not-ICU (Supplementary material).

All costs are in Euro and referred to 2018 pricelist. Discount rate of 3% was applied to all costs.

2.4. Sensitivity analysis

One-way deterministic sensitivity analysis was carried out in order to verify robustness of the base case and identify the main drivers of ICERs. This analysis was carried out by altering (according the above-described ranges in Table 1) single parameter inputs. In addition, ivermectin cost ranged from €5.73 to €8.17 [13]. Lastly, €8.50 was assumed in sensitive analysis as the cost of serological test, according to a possible special price of test in case of extensive use.

3. Results

Assuming a population of 17,900 infected people according to the prevalence rate, for passive diagnosis strategy (current practice), the model estimated 114 cured subjects, 9,414 persistent symptomatic infections and 12 deaths in the first year of analysis. The screening strategy leads to 13,630 cured subjects, 2,267 persistent symptomatic infections and 3 deaths. The presumptive treatment accounts for 15,216 recoveries, 1,428 persistent symptomatic infections and 2 deaths (Table 3). The persistent symptomatic infections value is the number of subjects with persistent symptomatic infection with annual inappropriate treatment year after year. The percentage of cured subjects increases from current strategy (0.6%) to screening (76.1%) and presumptive treatment strategies (85%). On the contrary, respectively 9,414, 2,267 and 1,428 subjects will have persistent symptomatic infection in passive diagnosis, screening and in presumptive treatment scenario (accounting for 52.6%, 12.7% and 8% of the whole infected population). Therefore, in the first year the passive diagnosis strategy has the lowest clinical impact, in term of number of cured cases and persistent symptomatic infected subjects. This calculation does not include the number of asymptomatic cases (8,359; 46.7% of infected subjects) not seen and not treated in the passive diagnosis scenario, contrarily to the other two strategies. The best strategy in terms of clinical outcomes (higher number of cured subjects and lower number of subjects with persistent symptomatic infection) is the presumptive treatment scenario. Table 3 also shows clinical outcomes in a 10-years time horizon: in the passive diagnosis scenario, the number of cured subjects increases greatly compared to the first year time horizon, while the number of subjects with persistent symptomatic infection leads to relevant economic losses due to inappropriate investigations in this time prospective. The best clinical impact of the presumptive treatment was confirmed also in this analysis.

From the economic point of view (Table 4), the passive diagnosis strategy is the least expensive, costing €1,164,169 per cohort of 100,000 migrants in the first year, as it is the least effective. The screening strategy (€2,856,011) is less expensive than presumptive treatment (€3,538,474). Considering the cost/recovery ratio it appears that screening is the least expensive option. However, in the 10-year time horizon the passive diagnosis strategy becomes the most expensive scenario (€9,735,908) from the NHS prospective, due to the inappropriate treatment of subjects with persistent symptomatic infection. The presumptive treatment is the least expensive strategy.

The distribution of costs in the 1-year and 10-year time horizons is reported in Table 5. The inappropriate costs (ι costs) for subjects with persistent symptomatic infection have a significant impact on the passive diagnosis scenario in the short (93.2% of expenses) and long term (93.1% of expenses). In 1-year time horizon the main costs are due to screening test (56% of expenses) and treatment (91.3% of expenses) in the specific strategies. In the long term, however, the ι cost becomes also relevant (Table 5).

In the time horizon of one year, ICER of both screening and presumptive treatment compared with the passive diagnosis strategy (no-screening and no-presumptive treatment) suggests that the screening strategy is more cost-effective than presumptive treatment (Table 6). In 10-years time horizon passive diagnosis strategies is dominated by the

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Table 3
Clinical outcomes estimated by the model.

Clinical outcomes					
Strategy	Number of cured subjects	Number of subjects with symptomatic persistent infection	Number of death	Percentage of recovery/ infected (%)	Percentage of persistent symptomatic infection/infected (%)
1-year time horizon					
Passive diagnosis	114	9414	12	0.6	52.6
Screening	13,630	2267	3	76.1	12.7
Presumptive treatment	15,216	1,428	2	85.0	8.0
10-years time horizon					
Passive diagnosis	1,138	89, 298	115	6.4	NA
Screening	13,746	22,044	29	76.8	NA
Presumptive treatment	15,225	14,154	18	85.1	NA

NA: Not applicable.

Table 4
Costs estimated by the model.

Costs (€)				
Strategy	1-year time horizon		10-years time horizon	
	Total costs	Cost/cured subject	Total costs	Cost/cured subject
Passive diagnosis	1,164,169	10,197.29	9,735,908	8,553.86
Screening	2,856,011	209.53	4,959,638	360.80
Presumptive treatment	3,538,474	232.55	4,883,272	320.74

Table 6
Costs estimated by the model.

Strategy	1-year time horizon			10-years time horizon	
	Δ Costs	Δ LYG	ICER	Δ Costs	Δ LYG
Screening vs Passive Diagnosis	1,691,842	6,378	265.27	−4,776,270	63,848
Presumptive TT vs Passive Diagnosis	2,374,305	7,126	333.19	−4,852,636	71,339

Legend→ *LYG*: Life Years Gained; *ICER*: Incremental Cost-Effectiveness Ratio.

others (more expensive with lower benefit).

The sensitivity analysis is reported in Table 7: the results of the base case are confirmed ranging the value of the data input. As expected, strongyloidiasis prevalence is the data with the major impact on ICER.

4. Discussion

The recent migratory flow from SSA to Italy poses major challenges to the Italian NHS with a possible risk of an overburden of public costs. It is believed that migrant-focused screening programs may be effective and cost-effective if they are highly targeted and well implemented. In line with that, various studies in EU countries have been conducted about the best cost-effective strategy to adopt regarding the management of diseases such as latent tuberculosis infection (LTBI), HIV and viral hepatitis which represent a global health problem [25–28].

In this context, this study aims to offer to healthcare policy-makers an evidence-based approach to the management of *S. stercoralis* infection in SSA immigrants arriving in Italy, which could both save lives and money for the NHS. We compared the benefits and costs of universal serological screening and universal presumptive treatment with ivermectin to the current passive diagnosis of symptomatic cases.

The results of the model suggest that both screening and presumptive treatment strategies, compared with the current strategy, are more favorable from a cost-effectiveness point of view, with a slight advantage of the screening strategy in a one-year time horizon.

Available guidelines in Europe recommend different strategies to manage strongyloidiasis in migrants. While Irish and UK guidelines suggest to offer screening only to migrants with symptoms/eosinophilia [29,30], Italian guidelines propose a systematic serological screening test for all migrants exposed in endemic areas, but are still not applied [31]. Availability of diagnostic tools for strongyloidiasis is not uniform in the national territory and no guidelines for the management of positive cases are available [13]. Moreover ivermectin is not registered in Italy and have to be imported from abroad [14].

Outside Europe, Australian and Canadian guidelines suggest

Table 5
Distribution of costs estimated by the model.

Costs (€) - 1-year time horizon								
	Screening	Diagnostic Test	Loa Loa Smear Test	Albendazole (γ)	Iota (ι)	Hospitalization	Ivermectin (α)	Total costs
Passive diagnosis		6,001	152	18	1,084,823	66,250	6,925	1,164,169
Screening	1,600,000	630	20,915	2,471	260,908	15,952	955,135	2,856,011
Presumptive TT			120,000	14,175	164,248	10,051	3,230,000	3,538,474
Distribution of costs (%) - 1-year time horizon								
Passive diagnosis	0.0	0.5	0.0	0.0	93.2	5.7	0.	100
Screening	56.0	0.0	0.7	0.1	9.1	0.6	33.4	100
Presumptive TT	0.0	0.0	3.4	0.4	4.6	0.3	91.3	100
Costs (€) - 10-years time horizon								
Passive diagnosis		52,726	1332	157	9,066,979	553,866	60,847	9,735,908
Screening	1,600,000	5,536	21,039	2485	2,232,590	137,190	960,797	4,959,638
Presumptive TT			120,000	14,175	1,430,790	88,306	3,230,000	4,883,272
Distribution of costs (%) - 10-years time horizon								
Passive diagnosis	0.0	0.5	0.0	0.0	93.1	5.7	0.6	100
Screening	32.3	0.1	0.4	0.1	45.0	2.8	19.4	100
Presumptive TT	0.0	0.0	2.5	0.3	29.3	1.8	66.1	100

Table 7
Sensitivity analysis.

	Screen vs No scren 1-year time horizon		Presum TT vs No screen 1-year time horizon	
	Minimum	Maximum	Minimum	Maximum
Base case	265.27		333.19	
Strongyloidiasis prevalence	669.64	196.07	1051.32	210.29
Sensitivity of IgG ELISA from Bordier (*Strongyloides ratti*; Bordier Affinity Products SA, Crissier, Switzerland)	283.12	249.83	333.14	333.24
Specificity of IgG ELISA from Bordier (*Strongyloides ratti*; Bordier Affinity Products SA, Crissier, Switzerland)	282.62	252.99	333.19	333.19
Symptomatic patients	250.29	308.99	311.09	397.69
Patients that will undergo a diagnostic test for strongyloidiasis	265.27	265.28	333.18	333.20
Subjects from *Loa loa* endemic countries*	263.57	266.00	324.41	336.95
Loa loa prevalence in Sub-Saharan immigrants	264.89	265.66	331.20	335.18
Treatment cure rate	295.81	238.76	368.88	302.20
Hospitalization for strongyloidiasis hyperinfection/disseminated syndrome in 10 years	272.25	263.10	340.32	330.97
Letality of strongyloidiasis hyperinfection/disseminated syndrome	265.32	265.22	333.25	333.13
Ivermectin cost	255.37	288.47	282.03	453.02
Cost of serological test	147.82		333.34	

universal serological screening too [32–34], while US guidelines suggest to perform routinely a pre-departure presumptive treatment, leaving both options of serological screening or presumptive treatment for subjects who did not received such a treatment in their countries of origin [35].

Recently the European Centre for Disease Prevention and Control (ECDC) released a guidance for screening and vaccination for infectious diseases in newly arrived migrants within the EU/EEA. The evidence-based statement on strongyloidiasis contained in the document suggests to offer serological screening and treatment (for those found to be positive) for strongyloidiasis to all migrants from countries of high endemicity with a “low certainty of evidence”. However, in the above document and also in a recently published systematic review funded by the ECDC the option of presumptive treatment for strongyloidiasis is also discussed and considered likely to be also cost-effective on the basis of economic modelling developed in non-European setting [36].

According to a study in the US setting, performed in 2004, potential cost savings of universal treatment with ivermectin were compared with no intervention (watchful waiting), universal treatment with albendazole and universal screening for eosinophilia (used as a proxy of *Strongyloides* infection) followed by treatment with ivermectin of subjects with eosinophilia [15]. In this analysis universal treatment with either ivermectin or albendazole appeared to be the most cost-effective option, while the screening option resulted to be the most expensive and less effective: this is probably linked to the low sensitivity (80%) and specificity (25%) of eosinophilia as a screening tool for strongyloidiasis, chosen by the authors since at the time methods with higher sensitivity and specificity were not available. It should be remembered that albendazole is clearly less effective than ivermectin and should not be considered any more an alternative treatment for strongyloidiasis [37].

Furthermore, an economic model with moderate quality evidence suggested that pre-departure presumptive treatment with single-dose ivermectin for all immigrants was cost-effective compared to five days’ post-departure treatment with albendazole and to serological screening in the US setting [16]. However, this study proposed a protocol that is not applicable to the Italian (and probably European) context, where no pre-departure control is possible due to the nature of the migratory flux of asylum seekers (people entering the country through dangerous sea-trip without preventively applying for visa).

In the Italian setting, a universal screening for strongyloidiasis in migrants from SSA could be applied if some criticalities were overcome. From a merely organizational point of view, the NHS has already in place tools that can be used to perform such a screening: each migrant, once relocated from first arrival ports, undergoes a visit to check obvious signs and symptoms of infectious diseases and to assess possible specific healthcare needs. The screening could be prescribed in this setting, or, alternatively, at the first visit to the general practitioner's cabinet. However, ivermectin is not registered in Italy and the administration of the drug imported from abroad is currently possible only in tertiary care centers, with subsequent increase of costs [14].

The main limitation of our study is that, as in all mathematical models, a number of assumptions were made, due to the lack of some specific data for the Italian setting. On the other hand, this is, at our knowledge, the first cost-effectiveness study in Europe that supports ECDC recommendations. Moreover we did not considered costs related to possible side effects related to ivermectin. However in a recent randomized controlled trial side effects related to ivermectin were mild and unlikely to determine additional cost for the NHS [24]. Finally possible additional benefits of the use of ivermectin in migrant populations such as the treatment of an highly prevalent disease such as scabies has not been taken in to account.

5. Conclusion

Recent ECDC guidelines suggest to offer universal serological screening of *S. stercoralis* infection to migrants from highly endemic countries, including Sub-Saharan Africa, pointing out that even if the level of evidence is low, potentially life-preserving benefits can arise from screening, linkage to care, and treatment [26]. The present analysis supports this conclusion in the Italian setting, and we hope this to be a useful decisional tool for policy-makers.

Ethic compliance

No approval from ethic committee was required since this study did not involved patients.

CRediT authorship contribution statement

Lorenzo Zammarchi: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **Marta Tilli:** Data curation, Investigation, Methodology, Validation, Writing - original draft, Writing - review & editing. **Annarita Botta:** Data curation, Investigation, Methodology, Validation, Writing - original draft, Writing - review & editing. **Dora Buonfrate:** Writing - review & editing. **Alessandro Bartoloni:** Writing - review & editing. **Sara Boccalini:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmaid.2020.101561.

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