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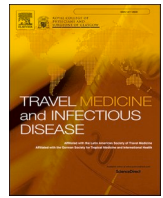
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Infections with long latency in international refugees, immigrants, and migrants seen at GeoSentinel sites, 2016–2018

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ABSTRACT

Background: The continued increase in global migration compels clinicians to be aware of specific health problems faced by refugees, immigrants, and migrants (RIM). This analysis aimed to characterize RIM evaluated at GeoSentinel sites, their migration history, and infectious diseases detected through screening and diagnostic workups.

Methods: A case report form was used to collect data on demographics, migration route, infectious diseases screened, test results, and primary infectious disease diagnosis for RIM patients seen at GeoSentinel sites. Descriptive statistics were performed.

Results: Between October 2016 and November 2018, 5,319 RIM patients were evaluated at GeoSentinel sites in 19 countries. Africa was the region of birth for 2,436 patients (46 %), followed by the Americas (1,644, 31 %), and Asia (1,098, 21 %). Tuberculosis (TB) was the most common infection screened and reported as positive (853/2,273, 38 % positive by any method). TB, strongyloidiasis, and hepatitis B surface antigen positivity were observed across all migration administrative categories and regions of birth. Chagas disease was reported only among RIM patients from the Americas (393/394, 100 %) and schistosomiasis predominantly in those from

Abbreviations: (RIM), refugees, immigrants, and migrants; (TB), tuberculosis; (TBI), tuberculosis infection; (PBHA), protocol-based health assessment; (IGRA), interferon gamma release assay; (TST), tuberculin skin test.

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Africa (480/510, 94 %). TB infection (694/5,319, 13 %) and Chagas disease (524/5,319, 10 %) were the leading primary infectious disease diagnoses.

Conclusions: Several infections of long latency (e.g. TB, hepatitis B, and strongyloidiasis) with potential for long-term sequelae were seen among RIM patients across all migration administrative categories and regions of origin. Obtaining detailed epidemiologic information from RIM patients is critical to optimize detection of diseases of individual and public health importance, particularly those with long latency periods.

1. Introduction

The number of international refugees, immigrants, and migrants (RIM) worldwide tripled from 1970 to 2020, reaching an estimated 281 million. RIM now comprise 3.5 % of the global population, with just over half having migrated outside of their original global region [1,2]. Common health issues affecting RIM include infectious diseases and chronic non-infectious diseases (particularly in older individuals), psychological conditions, and psychiatric diseases, with multiple diagnoses being common [3]. These health issues are compounded by healthcare-related challenges, including fragmentation of care and lack of access to services provided to country nationals [4].

Infectious diseases encountered in RIM reflect the country in which they were born, social determinants of health, and geographic exposures (e.g. countries traversed during the migratory journey) [5–7]. Many infectious diseases encountered by RIM have long latency periods and long-term sequelae. Unrecognized asymptomatic infection, diagnostic delays, and underdiagnosis of chronic infections in the host country may lead to preventable morbidity and mortality (such as hepatocellular carcinoma due to chronic hepatitis B, heart failure due to Chagas disease, schistosomiasis leading to bladder cancer or portal hypertension, or *Strongyloides* hyperinfection or dissemination leading to death). Although immediate focus on communicable diseases of public health concern in acutely displaced populations is paramount (e.g. active tuberculosis disease, measles, cholera), chronic infections that have fewer public health implications but are associated with high disease burden and mortality warrant systematic screening and treatment [5].

GeoSentinel is a global surveillance network consisting of specialized sites established to detect emerging infections and track trends in travel-associated infections [8,9]. The GeoSentinel Network last examined data from RIM populations served across its sites from 1997 to 2009. In one analysis of protocol-based health assessments (PBHA) at two US-based GeoSentinel sites serving predominantly refugees, 43 % of those screened had latent or asymptomatic tuberculosis infection (TBI), 15 % eosinophilia, and 6 % hepatitis B infection [10]. Active tuberculosis (TB) disease, soil-transmitted helminths, malaria, and systemic febrile illnesses were rare (though refugees in this analysis would have received pre-departure screening and presumptive treatment for malaria and other parasitic diseases through the U.S. Refugee Resettlement Program) [11]. Another GeoSentinel analysis addressed diseases in predominantly non-refugee migrants resettled in 19 countries on 5 continents and evaluated for specific infectious diseases of concern [12]. The most frequent diagnoses were TBI (22 % of all diagnoses), viral hepatitis (17 %), and active tuberculosis (10 %). A limitation of both studies was the lack of certain key data points pertaining to RIM health, such as route of migration, which were not available due to data collection at the time. As displaced populations vary over time, both studies may lack generalizability to infectious disease risks faced by contemporary RIM populations.

In 2016, a panel of experts in migration health within the GeoSentinel Network convened to standardize the data collected for RIM, allowing more detailed insights into the dynamics of infectious diseases in RIM within GeoSentinel. In this analysis, we provide updated and more detailed data about infectious diseases affecting RIM globally, and describe the complexity of migration route and other factors such as migration administrative categories.

2. Methods and materials

We performed a cross-sectional analysis of RIM patients seen within the GeoSentinel Network from October 2016 to November 2018 using data collected via a GeoSentinel case report form for RIM patients who crossed at least one international border and had possible travel-related illness (es) (Figure A.1, Case Report Form). All GeoSentinel sites were included. Some of these sites function as referral centers for specific diseases whereas others focus on protocol-based screening [9].

2.1. Definitions and site protocols

Sites chose a migration administrative category based on international definitions and how administrative classes were determined in their countries (Table A1) [13]. We analyzed those designated as refugees, asylum seekers, asylees, and refugee/asylum seeker/asylees together as one category, given the overlap in definitions used in different countries [14]. We use the term “documented” for patients who do not fall into any other category and have legal permission to stay in the country of the GeoSentinel site, and “undocumented” for those not in any other category who do not have legal permission to stay.

Sites could choose among nine reasons for the visit to the GeoSentinel site, ranging from PBHA for newly arrived RIM patients to specialty care visit for a problem unrelated to screening (Figure A1). A standardized screening protocol was not provided to sites. Screening protocols were defined as a combination of tests applied universally to specific populations of RIM, generally assumed to be used to identify clinically important infections in asymptomatic patients. Some site protocols were driven by national guidelines such as those available in the United States, Canada, Australia, and some European countries, while others were addressed to identify specific infectious diseases such as Chagas disease screening programs in Spain [15–18]. Sites were asked to indicate the patient had a primary care provider/medical home if he or she could identify a name or practice when asked “who is your doctor?”

Information about screening for eleven common infectious diseases or conditions associated with migration (tuberculosis, hepatitis B and C, HIV, Chagas disease, strongyloidiasis, schistosomiasis, syphilis, intestinal parasitosis identified by stool examination, malaria, and filarial diseases) was collected via multiple choice selection on the case report form. This section included whether screening was done, what test was used, and the results of the testing (Figure A1). For TB screening, the case report form included both screening for TB disease via chest X-ray as well as screening for TBI via interferon gamma release assay (IGRA) or tuberculin skin testing (TST).

Sites recorded information about diagnoses identified during the patient encounter and documented a single primary diagnosis. A primary diagnosis could also reflect a syndrome if no confirmed diagnosis was arrived upon at the time of completion of the case report form. Diagnoses could be those identified clinically, from screening, from referral from an outside clinic, or by diagnostic tests not included in the screening protocols. The primary diagnoses were reviewed by one clinician (EB) and assigned to one of sixteen categories for most common primary infectious diseases or ‘other’ (Table A2).

2.2. Statistical analysis

The descriptive analyses performed summarized continuous variables with means and standard deviations (SD) and categorical variables with frequency proportions and frequency counts. Hypothesis testing was not included in the study design. Analysis was performed using SAS version 9.4 (SAS Institute Inc, Cary, NC, USA). Sample size calculation was not performed as the analysis included all RIM patients seen within the GeoSentinel Network from October 2016 to November 2018.

The GeoSentinel data collection protocol has been reviewed by a human subject's advisor at the Centers for Disease Control and Prevention's National Center for Emerging and Zoonotic Infectious Diseases

and has been classified as public health surveillance and not human subject research. Individual sites obtained Investigational Review Board clearance as required by local regulations.

3. Results

3.1. Demographics

Data were collected on 5,319 RIM patients in 19 countries. Demographic data, GeoSentinel site information, and reason for site visit are presented in Table 1. Women comprised 43 % of the cohort and the overall mean age was 30.7 years (standard deviation 16.2). Refugees/

Table 1

Characteristics of refugee, immigrant, and migrant patients and GeoSentinel sites across all migration administrative categories, October 2016–November 2018.

	All RIM ^a patients (N = 5319) – no. (%)	Refugees/Asylees/asylum seekers ^b (N = 1978) – no. (%)	Documented migrant (N = 1840) – no. (%)	Undocumented migrant (N = 659) – no. (%)	Unknown/other (N = 842) – no. (%)
Sex – N with data	5309	1977	1837	658	837
Female	2269 (43)	707 (36)	1015 (55)	196 (30)	351 (42)
Age – N with data	5305	1972	1836	659	838
0–4 years	199 (4)	104 (5)	28 (2)	1 (0)	66 (8)
5–17 years	1008 (19)	615 (31)	121 (7)	79 (12)	193 (23)
18–64 years	3909 (74)	1233 (63)	1587 (86)	554 (84)	535 (64)
>65 years	189 (4)	20 (1)	100 (5)	25 (4)	44 (5)
Unaccompanied minor – N with data	4317	1711	1583	509	514
Yes	305 (7)	146 (9)	19 (1)	52 (10)	88 (17)
Region of birth – N with data	5319	1978	1840	659	842
Africa	2436 (46)	1269 (64)	439 (24)	364 (55)	364 (43)
Americas	1644 (31)	120 (6)	1037 (56)	242 (37)	245 (29)
Asia	1098 (21)	546 (28)	313 (17)	43 (7)	196 (23)
Other	141 (3)	43 (2)	51 (3)	10 (2)	37 (4)
Time lived in country of birth – N with data	5301	1968	1837	657	839
0–<5 years	2039 (39)	882 (45)	508 (28)	254 (39)	395 (47)
5–<10 years	418 (8)	206 (11)	159 (9)	5 (1)	48 (6)
10–<15 years	389 (7)	168 (9)	168 (9)	19 (3)	34 (4)
15–<20 years	601 (11)	270 (14)	156 (9)	97 (15)	78 (9)
>20 years	1854 (35)	442 (23)	846 (46)	282 (43)	284 (34)
GeoSentinel site region – N with data	5319	1978	1840	659	842
Europe	3246 (61)	813 (41)	1358 (74)	426 (65)	649 (77)
North America	1857 (35)	1040 (53)	407 (22)	224 (34)	186 (22)
Other	216 (4)	125 (6)	75 (4)	9 (1)	7 (1)
Time elapsed since arrival to GeoSentinel site country – N with data	5008	1837	1771	608	792
0–<1 years	2878 (58)	1590 (87)	445 (25)	425 (70)	418 (53)
1–<2 years	364 (7)	140 (8)	113 (6)	59 (10)	52 (7)
2–<3 years	180 (4)	45 (2)	73 (4)	31 (5)	31 (4)
3+ years	1586 (32)	62 (3)	1140 (64)	93 (15)	291 (37)
Reason for visit – N with data	5319	1978	1840	659	842
Protocol-based health assessment	2727 (51)	1484 (75)	545 (30)	270 (41)	428 (51)
Primary care	304 (6)	82 (4)	55 (3)	125 (19)	42 (5)
Post-travel illness	147 (3)	50 (3)	66 (4)	16 (2)	15 (2)
Pre-travel visit	13 (0)	7 (0)	5 (0)	0 (0)	1 (0)
Inpatient consult	152 (3)	26 (1)	60 (3)	46 (7)	20 (2)
Management of TB/TBf ^c	384 (7)	65 (3)	257 (14)	39 (6)	23 (3)
Specialty referral arising from screening	859 (16)	155 (8)	506 (28)	74 (11)	124 (15)
Specialty referral not related to screening	602 (11)	106 (5)	303 (17)	66 (10)	127 (15)
Other	131 (3)	3 (0)	43 (2)	23 (4)	62 (7)
Language different from clinic site country – N with data	5319	1978	1840	659	842
Yes	2980 (56)	1606 (81)	525 (29)	502 (76)	347 (41)
Has primary care medical home – N with data	5319	1978	1840	659	842
Yes	2055 (39)	305 (15)	1222 (66)	161 (24)	367 (44)

^a RIM = refugee, immigrant, migrant.

^b Includes migrant status categories refugees, asylum seekers, and asylees, as well as those categorized as refugee/asylum seeker/asylee (no difference in GeoSentinel site country). Refugee status was reported for 782 (15 %), asylum seeker for 204 (4 %), asylee for 100 (2 %), and not otherwise specified (i.e. at GeoSentinel sites with no differentiation between these categories) for 892 (17 %).

^c Tuberculosis/Tuberculosis infection.

Table 2

Proportion of positive tests for screening of eleven targeted infectious diseases, stratified by complexity of migration route^a in GeoSentinel, October 2016–November 2018.

	All RIM patients (N = 5319) – no. (%)	Migration route from country of birth to receiving country – no. (%)		
		Direct (N = 4368)	One intermediary country (N = 620)	Two or more intermediary countries (N = 331)
Tuberculosis (any test) ^b	853/2273 (38)	591/1617 (37)	151/479 (32)	111/177 (63)
Stool ova and parasite ^c	540/2106 (26)	471/1736 (27)	25/148 (17)	44/222 (20)
Schistosomiasis ^d	510/1495 (34)	396/1199 (33)	43/116 (37)	71/180 (39)
Strongyloidiasis ^e	429/2240 (19)	361/1945 (19)	27/137 (20)	41/158 (26)
Chagas disease ^f	393/850 (46)	391/831 (47)	0/9 (0)	2/10 (20)
Hepatitis B (surface antigen positive)	219/3382 (7)	162/2623 (6)	27/509 (5)	30/250 (12)
Malaria ^g	90/585 (15)	75/474 (16)	7/36 (19)	8/75 (11)
Syphilis ^h	78/2463 (3)	63/1937 (3)	11/360 (3)	4/166 (2)
HIV ⁱ	67/3178 (2)	62/2497 (3)	3/489 (1)	2/192 (1)
Hepatitis C	52/2627 (2)	45/2060 (2)	6/408 (2)	1/159 (1)
Filaria ⁱ	48/483 (10)	43/412 (10)	0/19 (0)	5/52 (10)

^a These results should not be interpreted as prevalence data, as the denominator does not reflect a standardized population that was screened. All percentages in this table reflect number reported positive divided by number screened (%).

^b Testing methods listed on data collection form included interferon-gamma release assay, tuberculin skin testing, and chest X-ray.

^c Stool ova and parasites testing methods listed were antigen, microscopy, and PCR. There was no further specification of the organisms tested for by antigen and PCR.

^d Testing methods included *Schistosoma* spp. serology and microscopy.

^e Testing methods included serology and microscopy.

^f Testing by *Trypanosoma cruzi* serology.

^g Testing by microscopy.

^h Testing methods listed included rapid plasma reagin (RPR)/venereal disease research laboratory test (VDRL) for non-treponemal testing or *Treponema pallidum* particle agglutination test (TP/PA)/fluorescent treponemal antibody absorption test (FTA-ABS) listed as treponemal testing options.

ⁱ Testing methods included serology or antibody/antigen.

asylees/asylum seekers accounted for 1,978 (37 %) patients included in this analysis, followed by documented migrants (1,840, 35 %), undocumented migrants (659, 12 %), and migrants of unknown (718, 14 %) and other status (124, 2 %). Within the refugee/asylee/asylum seeker group, refugee status was reported for 782 (15 %), asylum seeker for 204 (4 %), asylee for 100 (2 %), and not otherwise specified (i.e. at GeoSentinel sites with no differentiation between these categories) for 892 (17 %).

Africa was the region of birth for 2,436 RIM patients (46 %), followed by the Americas for 1,644 (31 %), and Asia for 1,098 (21 %). Most RIM patients (4,368/5,319, 82 %) arrived directly from their country of birth while 620/5,319 (12 %) traveled to one other country between country of birth and country of GeoSentinel site, and 331/5,319 (6 %) had a complex migration route consisting of two or more countries from country of birth to country of GeoSentinel site. Data were recorded from GeoSentinel sites in 19 countries, of which 10 were in Europe, three were in Asia, three in North America, and one each in sub-Saharan Africa, South America, and Australia. More than 85 % of RIM patients were

seen at GeoSentinel sites in four countries: Spain for 2,171 (41 %), the United States for 1,498 (28 %), Italy for 501 (9 %), and Canada for 358 (7 %).

3.2. Migration administrative category

Demographic and migration route characteristics differed by migration administrative category. Undocumented migrants were predominantly male (462/658, 70 %); most documented migrants were female (1,015/1,840, 55 %). Refugees/asylees/asylum seekers, in particular, were young (mean age 24.2 years, SD 13.7 years), frequently spoke a language different from that of the GeoSentinel site country (1,606/1,978 or 81 %), and rarely identified a primary care site or medical home at the time of the GeoSentinel site visit (305/1,978 or 15 %). Most RIM who were refugees/asylees/asylum seekers were from countries in Africa (1,269/1,978, 64 %), whereas most documented migrants were from countries in the Americas (1,037/1,840, 56 %). Almost all documented migrants (1,772/1,840, 96 %) arrived in the GeoSentinel site country directly from their country of birth; undocumented migrants had the highest proportion of migration routes traversing two or more countries outside the country of birth (101/659, 15 %). GeoSentinel sites in the United States saw the highest proportion of refugees/asylees/asylum seekers (907/1,978, 46 %). The highest proportions of documented (1,214/1,840, 66 %), undocumented (361/659, 54 %), and unknown/other (452/842, 53 %) migrants were seen at sites in Spain.

The subset of RIM patients seen for the purpose of PBHA included 2,727 patients, of whom most were seen at GeoSentinel sites in Spain (1,157, 42 %), the United States (969, 36 %), and Italy (327, 12 %). Asylees/asylum seekers/refugees were the group seen most often for PBHA (1,484/1,978, 75 %); documented migrants were seen in similar proportions for PBHA (545/1,840, 30 %) and specialty referral arising from screening (506/1,840, 28 %).

3.3. Screening test results

Sites reported screening for at least one of 11 common pre-selected infections for 4,165 (78 %) RIM patients (Table 2). Screening tests for Hepatitis B and HIV were reported most frequently (3,382 and 3,178 patients, respectively). There was some variability in test methods across sites (e.g. TST, IGRA, or chest X-ray for TB; treponemal or non-treponemal test for syphilis). Of the tests performed and reported, there was a high proportion of positive tests for several of the conditions listed, notably TB (314/663 [47 %] by TST, 552/1,634 [34 %] by IGRA, and 109/616 [18 %] by chest X-ray), strongyloidiasis (418/2,002, 21 % by serology), Chagas disease (393/850, 46 % by serology), and schistosomiasis (474/1,356, 35 % by serology). Compared to the frequency proportions among patients who arrived directly from their country of birth, the proportion of TB and hepatitis B surface antigen positivity was nearly double among those whose migration routes involved two or more countries: positive screening tests for TB were seen in 111/177 (63 %) of those with complex migration routes vs. 591/1,617 (37 %) of those who traveled directly from their country of birth to the GeoSentinel site country, and positive hepatitis B screening in 30/250 (12 %) and 162/2,623 (6 %) respectively. There also were higher proportions of positive tests for strongyloidiasis (41/158, 26 %) and schistosomiasis (71/180, 39 %) among the group with a complex migration route (Table 2).

3.4. Key infections identified on screening

Characteristics of RIM patients who screened positive for TB, schistosomiasis, strongyloidiasis, Chagas disease, and hepatitis B are listed in Table 3. RIM patients from all continents were tested for TB and strongyloidiasis with these infections identified in varying proportions from every region. The largest proportion of positive tests for hepatitis B

Table 3

Characteristics of individuals with positive screening tests for tuberculosis, Chagas disease, schistosomiasis, strongyloidiasis, and hepatitis B, GeoSentinel, October 2016–November 2018.

Characteristic	Infection n with characteristic/N total individuals who tested positive for infection (%)				
	Positive TB screening (N = 853)	Schistosomiasis ^a (N = 510)	Strongyloidiasis ^a (N = 429)	Chagas disease (N = 393)	Hepatitis B (surface antigen positive) (N = 219)
Sex – N with data	851	509	429	392	218
Female	283 (33)	105 (21)	172 (40)	282 (72)	44 (20)
Age – N with data	849	508	428	392	217
<5 years	19 (2)	2 (0)	2 (0)	1 (0)	2 (1)
5- <18 years	110 (13)	89 (18)	24 (6)	2 (1)	30 (14)
18- < 65 years	697 (82)	405 (80)	374 (88)	374 (95)	181 (83)
>65 years	23 (3)	12 (2)	28 (7)	15 (4)	4 (2)
Region of birth – N with data	853	510	429	393	219
Africa	558 (65)	480 (94)	191 (45)	0 (0)	174 (80)
Americas	137 (16)	10 (2)	201 (47)	393 (100)	7 (3)
Asia	139 (16)	20 (4)	33 (8)	0 (0)	35 (16)
Other	19 (2)	0 (0)	4 (1)	0 (0)	3 (1)
Time lived in country of birth – N with data	852	508	428	391	219
0-<5 years	380 (45)	292 (56)	114 (27)	3 (1)	109 (50)
5-<10 years	43 (5)	28 (6)	20 (5)	13 (3)	8 (4)
10-<15 years	58 (7)	26 (5)	20 (5)	10 (3)	15 (7)
15-<20 years	103 (12)	74 (15)	48 (11)	25 (6)	24 (11)
>20 years	268 (32)	88 (17)	226 (53)	340 (87)	63 (29)
Time elapsed since arrival to GS site country – N with data	814	483	422	388	204
0-<1 years	595 (73)	353 (73)	172 (41)	26 (7)	148 (73)
1-<2 years	51 (6)	40 (8)	27 (6)	7 (2)	18 (9)
2-<3 years	19 (2)	15 (3)	13 (3)	4 (1)	9 (4)
3+ years	149 (18)	75 (16)	210 (50)	351 (90)	29 (14)
Migration administrative category – N with data	853	510	429	393	219
Asylee/refugee/asylum seeker ^b	362 (42)	222 (42)	99 (23)	0 (0)	105 (48)
Documented migrant	200 (23)	113 (22)	211 (49)	374 (95)	43 (20)
Undocumented migrant	198 (23)	123 (24)	79 (18)	6 (2)	50 (23)
Unknown/other	93 (11)	52 (10)	40 (9)	13 (3)	21 (10)

‡Positive screening for TB by any method, including interferon-gamma release assay, tuberculin skin testing, and chest X-ray.

^a Positive by any screening method (serology or microscopy).

^b Includes Migrant Status categories refugees, asylum seekers, and asylees, as well as those categorized as Refugee/Asylum Seeker/Asylee (no difference in GeoSentinel site country).

surface antigen was found among patients from Africa (174/219, 79.5 %), though all regions contributed cases except Oceania (none were tested). Schistosomiasis was detected almost exclusively in those from Africa (480/510, 94 %) with smaller proportions from the Americas and Asia. Chagas disease was found only in RIM patients whose country of birth was in the Americas. Most (340/391, 87 %) patients diagnosed with Chagas disease had lived in their country of birth more than 20 years, whereas most with positive *Schistosoma* serology (292/508, 58 %) and hepatitis B surface antigen (109/219, 50 %) had lived in their country of birth for ≤5 years. Most patients with Chagas disease had lived in the GeoSentinel country for over three years and nearly all (390/394, 99 %) were seen at sites in Spain.

3.5. Primary infectious disease diagnoses

A primary infectious disease diagnosis was designated by the treating clinician for 3,877 (73 %) RIM patients (Table 4). TBI was the most frequent primary infectious disease diagnosis (694, 13 %), followed by Chagas disease (524, 10 %), schistosomiasis (440, 8 %), and strongyloidiasis (373, 7 %). Though not a specific disease or infection, eosinophilia was listed as a primary diagnosis in 208/5,319 (4 %) of RIM patients. When stratified by migration administrative category, TBI (312/1,978, 16 %) and schistosomiasis (217/1,978, 11 %) as primary diagnoses were more frequent among the refugee/asylum seekers/asylees group, whereas Chagas disease was more frequent among documented migrants (412/1,840, 22 %). With the exception of Chagas disease, all of the most frequent primary diagnoses were found in every

migration administrative group. Outside of the 16 most frequent diagnoses that were coded, other primary diagnoses that were infectious disease-related varied widely (Table A3). Frequently reported non-infectious etiologies included vitamin D deficiency, anemia, and abnormal urinalysis; 542 (10 %) RIM patients had a primary diagnosis of “healthy” (i.e., no abnormal laboratory tests or clinical findings).

4. Discussion

Infections with long-latency and long-term health consequences such as TBI, hepatitis B, strongyloidiasis, schistosomiasis, and Chagas disease were reported frequently in this analysis of global RIM patients seen at diverse sites in 19 countries across the GeoSentinel surveillance Network. Most infections occurred in RIM groups across all geographic regions and migration administrative categories.

This analysis highlights the diversity of RIM patients seen at GeoSentinel sites and the nature of healthcare provided across the GeoSentinel Network. A wide range in screening practices were observed and no disease was screened for universally, including TB and HIV. This is also reflected in the wide spectrum of various primary diagnoses documented by GeoSentinel sites. Most of the infections identified would not have been diagnosed by current domestic health screening guidance used for the general population of these resettlement countries [19].

Despite the diversity of patients, sites, and clinical practices, certain unifying themes emerged across RIM groups. TBI was the most frequently reported primary diagnosis and TBI, hepatitis B, and

Table 4
Most common primary infectious diseases visit diagnoses, GeoSentinel, October 2016–November 2018^a.

Diagnosis	All Migrants N = 5319 – no. (%)	Migration administrative category – no. (%)			
		Refugees/Asylees/Asylum seekers ^b N = 1978	Documented N = 1840	Undocumented N = 659	Unknown/Other N = 842
TBI ^c	694 (13)	312 (16)	202 (11)	100 (15)	80 (10)
Chagas disease	524 (10)	0 (0)	412 (22)	12 (2)	100 (12)
Schistosomiasis ^d	440 (8)	217 (11)	93 (5)	72 (11)	58 (7)
Strongyloidiasis ^d	373 (7)	67 (3)	172 (9)	74 (11)	60 (7)
Active TB disease	314 (6)	59 (3)	168 (9)	51 (8)	36 (4)
Hepatitis B (surface antigen positive)	218 (4)	80 (4)	59 (3)	38 (6)	41 (5)
Eosinophilia ^e	208 (4)	57 (3)	64 (4)	29 (4)	58 (7)
Malaria	159 (3)	42 (2)	54 (3)	38 (6)	25 (3)
<i>Giardia</i>	82 (2)	30 (2)	23 (1)	7 (1)	22 (3)
HIV	75 (1)	25 (1)	25 (1)	14 (2)	11 (1)
Soil-transmitted helminths	53 (1)	14 (1)	12 (1)	12 (2)	15 (2)
Tapeworm ^f	45 (1)	13 (1)	19 (1)	1 (0)	12 (1)
Filarial disease ^g	34 (1)	12 (1)	08 (0)	3 (1)	11 (1)
Hepatitis C	34 (1)	8 (0)	15 (1)	1 (0)	10 (1)
<i>Helicobacter pylori</i> ^h	30 (1)	11 (1)	10 (1)	6 (1)	3 (0)
Sexually transmitted infection	25 (1)	5 (0)	10 (1)	2 (0)	8 (1)
Other infectious diseases	569 (11)	152 (8)	170 (9)	87 (13)	160 (19)
Other non-infectious diseases ⁱ	846 (16)	589 (30)	132 (7)	59 (9)	66 (8)
Other unspecified	21 (0)	11 (1)	04 (0)	3 (1)	3 (0)
Healthy	542 (10)	265 (13)	174 (10)	47 (7)	56 (7)
No primary diagnosis reported	33 (1)	9 (0)	14 (1)	3 (0)	7 (1)

^a “Primary diagnosis” for visit was derived from an open text field completed by the clinician on the GeoSentinel form and was coded by EB into the 16 most common diagnoses, followed by “other”.

^b Includes migration administrative categories Refugee/Asylum Seeker/Asylee (no difference in GeoSentinel site country), refugee, asylum seeker, and asylee.

^c Tuberculosis infection (i.e. latent or asymptomatic tuberculosis infection).

^d Includes primary diagnosis by any method (e.g. serology and microscopy).

^e While not a specific diagnosis, “eosinophilia” was listed as the primary visit diagnosis on the case report form in these cases.

^f Species of causative pathogen not further specified.

^g Includes primary diagnosis by any method (e.g. serology, microscopy, biopsy, etc.).

^h Includes primary diagnosis by any method (e.g. antigen testing, urea breath test, serology and others).

ⁱ For full list of primary diagnoses, including those listed as “Other,” see Supplementary Appendix.

strongyloides were identified in RIM patients from all global regions and administrative migration categories. In contrast, Chagas disease was seen only in those originally from the Americas (*Trypanosoma cruzi*, the causative parasite is only endemic in Latin America), and schistosomiasis predominantly in RIM from Africa. Despite the high proportions of TBI and hepatitis B among primary diagnoses, these diagnoses comprised an even greater proportion of GeoSentinel diagnoses in earlier analyses [12]. Both our analysis and the earlier analyses were done before the COVID-19 pandemic disrupted global TB programs. Our analysis highlights the importance of screening for TB in virtually all global RIM patients.

Certain findings in our analysis merit further study. First, the group of patients whose migration route included two or more countries in addition to their country of birth had disproportionately high proportions of positive TB screening, hepatitis B, and strongyloidiasis among those tested. A number of factors might account for this finding: exposures during a protracted migration, heightened social vulnerability of this group, more directed referrals as opposed to asymptomatic screening as few refugees fell into this category, exposure to larger numbers of people, or higher baseline prevalence in the country of birth. Future studies may focus on better characterizing the epidemiology of patients with complex migration routes, with a focus on factors that may increase disease acquisition or transmission. Second, undocumented migrants most frequently had a complex migration journey. GeoSentinel is well-positioned to provide information about the infectious disease burden faced by undocumented migrants, because information about this group may not be captured by other surveillance systems, such as refugee resettlement programs. For clinicians, these data underscore the importance of obtaining a detailed migration history beyond soliciting only the patient’s country of birth. Future studies should inform the development of evidence-based guidelines and, ideally, provision of

services at multiple points along the migration path, including for undocumented migrants. Third, among patients diagnosed with hepatitis B and schistosomiasis, a substantial proportion (50 % and 58 %, respectively) had lived in their country of birth for less than five years. These populations may have had a higher baseline prevalence of these diseases in the country of birth at the time they departed (i.e., 5 years or less was ample time for exposure), moved from a lower endemic setting (birth country) to a higher one (non-birth country), or encountered an outbreak or exposures in a specific setting en route to the GeoSentinel site country. In the case of hepatitis B, it is unclear how many cases in our analysis were acquired via perinatal transmission, which more commonly results in chronic hepatitis B than transmission in adulthood. [20] Coverage with the birth dose of hepatitis B vaccine varies greatly by region, from 17 % in the WHO African Region to 78 % in the WHO Western Pacific Region and has increased over time but not simultaneously throughout the world [21]. Although RIM patients from Africa comprised 46 % of the cohort, they accounted for 80 % of the hepatitis B diagnoses, which may reflect later initiation, or less coverage, of vaccine programs. The reason for the high proportion of schistosomiasis cases in patients who had spent less than 5 years in their country of birth is unclear. Again, most (94 %) of these diagnoses were among patients from Africa, and we do not have sufficient information to know if these were infections acquired at young age or later during the migration journey. Schistosomiasis tends to be more focal, with high prevalence in defined geographic areas, and more detailed information about migration route will be needed to know if migrants may be more likely to encounter these high prevalence areas during their migration [11]. Future studies focusing on hepatitis B and schistosomiasis acquisition are warranted and should focus on differentiation of childhood vs adult acquisition; knowing the risk of acquiring these diseases before migration vs during migration would be helpful for prevention efforts.

Chagas disease tests were reported positive in exceptionally high proportions, almost exclusively from sites in Spain. These proportions should not be interpreted as generalizable data for all Latin American groups for two reasons. First, Spanish sites see many patients from higher prevalence countries (e.g. predominantly Bolivian communities) and second, because some of these sites serve as referral centers for Chagas disease and are located in areas of Spain with active Chagas disease screening programs. Since Chagas disease has not been part of traditional RIM screening programs, this analysis raises the possibility of underdiagnosis or under-reporting of Chagas disease at other sites in the GeoSentinel Network who see RIM patients from Latin America. The demonstrated value of the Chagas disease screening programs created in Spain have informed development of similar programs for Central and South American migrants to North America and other countries in Europe where Chagas disease is underrecognized [22–25].

4.1. Limitations

As with all GeoSentinel analyses, this analysis cannot be used to determine disease prevalence or calculate risk for specific diseases within populations as it lacks adequate denominator data and representative sampling. The high proportions of positive tests for certain infections by no means represent true rates of disease, but more likely reflect that astute clinicians at GeoSentinel sites are aware of the possibility of these infections in their patients, or are sites that participate in health assessment programs for RIM, and use a standardized protocol. Data were collected from a range of encounter types, including a substantial portion of specialty referrals for specific diagnoses. Refugees/asylum seekers/asylees were seen more frequently for PBHA whereas specialty referrals (possibly for a specific diagnosis) were higher for documented migrants, introducing bias in comparisons between administrative categories. Data for this analysis were collected primarily from sites in Spain, the United States, Italy, and Canada, and therefore may not be generalizable to other countries, even those with participating GeoSentinel sites. For example, certain refugees arriving to the United States and Canada complete pre-travel assessments, and prior to arrival to the United States, may receive presumptive treatment for schistosomiasis, strongyloidiasis, malaria, and soil-transmitted helminthiasis, which are expected to affect data on diagnostic yield within this group [15,16]. Information on pre-departure screening and presumptive treatment was not available systematically so could not be accounted for in this assessment. Although sites were encouraged to use standardized migration administrative categories, patients do not always fall into a specific group and terminology is historically used differently in different places, which may have created conflicting classification between GeoSentinel sites (Table A1).

5. Conclusion

Infections of long latency with long-term health implications are common among RIM patients from around the world. A summary of major take-aways for clinicians and public health practitioners is available in Box 1. These data stress the importance of taking a detailed migration and travel history, and of tailoring screening protocols to exposures that could have occurred along the migration route, in order to optimize detection of diseases of individual and public health importance, particularly those with long latency periods. Clinicians should be aware of the ubiquity of TB and hepatitis B and the endemicity of Chagas disease (Latin America) and schistosomiasis (Africa) when evaluating RIM patients in their practice. Prompt screening and diagnosis is the first step in providing appropriate treatment and management. Further research studies with representative sampling should investigate the full cascade of care for these infections of importance.

CRedit authorship contribution statement

Elizabeth D. Barnett: Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Alyse B. Wheelock:** Investigation, Supervision, Writing – review & editing. **William B. MacLeod:** Data curation, Formal analysis, Methodology. **Anne E. McCarthy:** Conceptualization, Investigation, Writing – original draft, Writing – review & editing. **Patricia F. Walker:** Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Christina M. Coyle:** Conceptualization, Investigation, Writing – review & editing. **Christina A. Greenaway:** Investigation, Methodology, Writing – review & editing. **Francesco Castelli:** Investigation, Writing – review & editing. **Rogelio López-Vélez:** Investigation, Writing – review & editing. **Federico G. Gobbi:** Investigation, Writing – review & editing. **Elena Trigo:** Investigation, Writing – review & editing. **Martin P. Grobusch:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Philippe Gautret:** Investigation, Writing – review & editing. **Davidson H. Hamer:** Formal analysis, Investigation, Methodology, Writing – review & editing, Funding acquisition. **Susan Kuhn:** Conceptualization, Methodology, Supervision, Writing – original draft, Writing – review & editing. **William M. Stauffer:** Conceptualization, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

Dr. Barnett receives royalties from UpToDate for her contribution to Evaluation of Newly Arrived Adult Immigrants. Dr. Greenaway

Box 1

Major take-aways and notable findings for refugees, immigrants, and migrants in the GeoSentinel Network

Major take-aways for clinicians and public health practitioners	Notable findings
Obtain a detailed migration history and use available resources to help guide screening recommendations* Though many infections of long latency pose long-term consequences and merit screening, some are excluded from screening guidelines that inform current practice	Over 15 % of migrants had traversed at least one additional country before arriving at the GeoSentinel site country The top three most common primary visit diagnoses listed by clinicians (latent tuberculosis infection, strongyloidiasis, and Chagas disease) are all infections with potential late-onset complications which may occur years to decades after migration
Be aware of the ubiquity of tuberculosis and hepatitis B infection	Tuberculosis infection and hepatitis B were seen in migrants across all regions of origin
Be aware of Chagas disease in migrants from continental Latin America and schistosomiasis in migrants from Africa	Almost all migrants diagnosed with Chagas disease originated from the Americas and most migrants diagnosed with schistosomiasis originated from Africa

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Appendix A. Supplementary data

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