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Title:

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Date:

2022-05-01

Citation:

Muhi, S., Ko, D. K., McGuinness, S. L., Biggs, B. A., Mahanty, S. & Delany, C. (2022). Mixed-method analysis of screening for *Strongyloides stercoralis* prior to immunosuppression: a problem of limited bandwidth?. *Internal Medicine Journal*, 52 (5), pp.790-799. <https://doi.org/10.1111/imj.14991>.

Persistent Link:

<https://hdl.handle.net/11343/248451>



A mixed-method analysis of screening for *Strongyloides stercoralis* prior to immunosuppression: A problem of limited bandwidth?

Journal:	<i>Internal Medicine Journal</i>
Manuscript ID	IMJ-0483-2020.R1
Manuscript Type:	Original Article
Date Submitted by the Author:	12-Jul-2020
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Keywords:	Strongyloides stercoralis, Immunocompromise, screening, preventative health
Abstract:	<p>Background Guidelines recommend screening for strongyloidiasis prior to immunosuppression in those at epidemiological risk, as hyperinfection following immunosuppression is often fatal. The uptake of this recommendation is unknown, and we aimed to explore this in our setting.</p> <p>Aims 1. Determine the proportion of adult patients at epidemiological risk for strongyloidiasis who were screened prior to immunosuppression at the Royal Melbourne Hospital, 2. Explore the factors that influenced clinicians' decision to screen for strongyloidiasis prior to immunosuppression.</p> <p>Methods This study used a mixed-methods approach. First, a 12-month (1 January 2018 to 1 January 2019) retrospective observational study was used to quantify the proportion of those at epidemiological risk who were screened prior to immunosuppression, while also identifying variables that were positively or negatively associated with screening. Second, clinicians from relevant specialties were recruited for focus group sessions to explore factors that influenced their decision to screen according to an interpretivist framework.</p>

	<p>Results 230 newly immunosuppressed patients at epidemiological risk of strongyloidiasis were identified, of whom 87 (37.8%) were screened prior to immunosuppression. In multivariate analysis, older patients, outpatients and people from non-English speaking backgrounds were significantly less likely to be screened. In focus groups, a number of barriers and enablers to screening were identified. Notably, clinicians reported that a major barrier was the cognitive load required to clinically reason about this uncommon disease, in addition to other priorities.</p> <p>Conclusion We identified many missed opportunities to screen patients at risk of hyperinfection, particularly those most vulnerable. To improve screening, this study</p>

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12 July 2020

A mixed-method analysis of screening for *Strongyloides stercoralis* prior to immunosuppression: A problem of limited bandwidth?

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No conflicts of interest to declare.

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Abstract

Key words: *Strongyloides stercoralis*, screening, preventative health, immunocompromised.

Background

Guidelines recommend screening for strongyloidiasis prior to immunosuppression in those at epidemiological risk, as hyperinfection following immunosuppression is often fatal. The uptake of this recommendation is unknown, and we aimed to explore this in our setting.

Aims

1. Determine the proportion of adult patients at epidemiological risk for strongyloidiasis who were screened prior to immunosuppression at the Royal Melbourne Hospital,
2. Explore the factors that influenced clinicians' decision to screen for strongyloidiasis prior to immunosuppression.

Methods

This study used a mixed-methods approach. First, a 12-month (1 January 2018 to 1 January 2019) retrospective observational study was used to quantify the proportion of those at epidemiological risk who were screened prior to immunosuppression, while also identifying variables that were positively or negatively associated with screening. Second, clinicians from relevant specialties were recruited for focus group sessions to explore factors that influenced their decision to screen according to an interpretivist framework.

Results

230 newly immunosuppressed patients at epidemiological risk of strongyloidiasis were identified, of whom 87 (37.8%) were screened prior to immunosuppression. In multivariate analysis, older patients, outpatients and people from non-English speaking backgrounds were significantly less likely to be screened. In focus groups, a number of barriers and enablers to screening were identified. Notably, clinicians reported that a major barrier was the cognitive load required to clinically reason about this uncommon disease, in addition to other priorities.

Conclusion

We identified many missed opportunities to screen patients at risk of hyperinfection, particularly those most vulnerable. To improve screening, this study highlights the importance of reducing cognitive load by using decision-support tools, which may facilitate screening in vulnerable patients and in time-constrained settings.

Introduction

Strongyloides stercoralis is a soil-transmitted parasitic nematode endemic to many tropical and subtropical regions, including northern Australia.^{1,2} Despite affecting between 30 – 100 million people worldwide, strongyloidiasis is considered a neglected tropical disease.³ Due to the parasite's unique auto-infective capability, strongyloidiasis has been reported up to 75 years following exposure.⁴ It is often asymptomatic, with no significant consequences in the majority of otherwise healthy people.⁵ However, when exposed to immunosuppression, *S. stercoralis* can multiply at an accelerated rate, with large numbers of parasites entering the auto-infective cycle (“hyperinfection syndrome”) or disseminating to other organs.⁶ Hyperinfection has a mortality rate approaching 80%,⁷ with death occurring due to sepsis and multiorgan failure.⁸

A number of immunosuppressive therapies have been associated with hyperinfection. High-dose corticosteroids have a particularly strong and specific association,⁹ especially in the setting of solid organ transplantation.¹⁰ However, the absolute risk of hyperinfection remains unknown. Hyperinfection is a largely preventable condition. Australian¹¹ and international¹² guidelines recommend screening prior to immunosuppression for patients at epidemiological risk, which includes those who have lived or travelled to an endemic area. Serology is readily available, with high sensitivity (~90%) and specificity (~98%); however, false negatives may occur in the immunosuppressed, highlighting the importance of screening before immunosuppression.¹³ In those diagnosed with strongyloidiasis, hyperinfection can be prevented by treating with ivermectin prior to commencement of immunosuppression.

In temperate Australia, strongyloidiasis is predominantly seen in migrants from endemic areas.¹⁴ Previous serosurveys of Melbourne migrants have noted seroprevalences of 11% in East African and 42% in Cambodian migrants.¹⁴ A 1998-2005 case series from a Melbourne Hospital¹⁶ reported 33 cases of strongyloidiasis; this included six cases of hyperinfection, all of which occurred in immigrants, with the majority due to commencement of immunosuppressive therapy without prior screening. Notably, diagnosis was delayed in immigrants (11.5 months) compared to travellers (4.0 months).¹⁶ The authors concluded that a screening policy would have prevented hyperinfection in the majority of immigrants in their series. Based on this limited literature, screening for *Strongyloides* prior to immunosuppression is hypothesised to be under-performed in non-endemic Australian settings.

Objectives

1. To determine the proportion of adult patients at epidemiological risk of strongyloidiasis that were screened prior to immunosuppression over a 12-month period at the Royal Melbourne Hospital (RMH),
2. To explore the factors that influenced clinicians' decision to screen for strongyloidiasis prior to immunosuppression.

Methods

1. Methods: Quantitative study (retrospective observational study)

Inclusion criteria

All adult patients (≥ 18 years of age) prescribed immunosuppressive therapy at RMH between 1 January 2018 and 1 January 2019 and at epidemiological risk for strongyloidiasis were eligible for inclusion. Patients with multiple episodes of immunosuppression were included at the first episode only.

Immunosuppressive therapy was defined as one or more of:

- Prednisolone ≥ 20 mg per day for ≥ 14 days (or equivalent) and/or
- Anti-rejection therapy in solid organ or haematopoietic transplant recipients and/or
- Cytotoxic drugs (e.g. cyclophosphamide, myeloablative chemotherapy) and/or
- Biological therapies (tumour necrosis factor (TNF) inhibitors and anti-CD20 agents)

Epidemiological risk for strongyloidiasis was defined according to previous guidelines,^{11,12} and included migrants and expatriates from endemic areas and Aboriginal and Torres Strait Islanders (ATSI). Patients were defined as "screened" if *S. stercoralis* serology was performed in the 12 months prior to, or within two weeks after commencement of immunosuppression.

Data collection

Immunosuppressive therapy prescriptions were captured using hospital pharmacy dispensing records, and medical records of all patients meeting inclusion criteria were manually reviewed (medical records at our institution are paper-based but scanned for electronic review). Demographic variables (age, sex, country of birth, travel or living in endemic area, non-English

speaking background [NESB], ATSI status) and clinical variables (number of comorbidities, including malignancy, autoimmune disease, neurological, pulmonary, hepatic, renal, cardiac or cardiovascular disease; presence of eosinophilia at the time of immunosuppression, hepatitis B serology, QuantiFERON-TB) were collected for all patients meeting inclusion criteria. Data was collated in a Microsoft Excel spreadsheet. Serological results of *S. stercoralis* IgG enzyme immunoassay from 1 January 2017 were obtained from the Victorian Infectious Diseases Reference Laboratory (VIDRL), currently the only pathology provider performing *S. stercoralis* serology in Victoria. Patients for whom data were insufficient to determine epidemiological risk were excluded. Proxy variables for epidemiological risk were used if required, including primary language spoken at home and use of an interpreter.

Data analysis

Statistical comparison between groups (patients screened and patients not screened) were performed using univariate and multivariate logistic regression analysis. Categorical variables were reported as frequency and percentage, continuous variables as mean and range. Results were considered to be statistically significant if $p < 0.05$. Data were analysed using the IBM SPSS statistical software package (SPSS Inc., Chicago, IL, USA).

2. Methods: Qualitative study (focus group interviews)

Theoretical framework

To answer the second objective, a qualitative interpretivist approach was used to look for the meaning and motivation behind people's actions by seeking their thoughts, ideas and values.¹⁷ Interpretivist methodologies enable exploration of people's behaviour, including their interpretation of the context and environment in which they work. This paradigm was used to obtain a more complete picture of the clinical reasoning and decision making related to *Strongyloides* screening.

Sample

Clinicians from specialties identified in the quantitative study as prescribing immunosuppressive therapies (Fig. 1) were invited for focus group discussions to examine attitudes towards screening for *Strongyloides*. Clinicians at all levels of training were included. In accordance with previous guidelines,¹⁸ this study aimed to conduct a minimum of 4-5 focus

groups, each with approximately 10 participants, in order to reach saturation (i.e. identify common and recurring themes across the data).

A total of six focus groups including Residents (Res), Registrars (Reg) and Consultants (Con) (n = 54) were conducted from August to October 2019. Participating specialities were responsible for the management of approximately 80% of the patients from the quantitative study and included (number of participants in brackets):

- Nephrology (10)
- Rheumatology (10)
- Haematology / BMT (9)
- Infectious Diseases (7)
- Dermatology (8)
- General Medicine (10)

Recruitment strategy

Speciality units were invited to participate in a voice-recorded focus group session (45 minutes) followed by a brief 15-minute educational presentation on strongyloidiasis. Information about focus groups was provided in a Participant Information and Consent Form, distributed via email and provided in hard copy to participants before the focus group. Consent forms were collected at the end of the session and filed securely. Representation across training levels was pre-arranged, in order to thoroughly explore factors influencing screening behaviours.

Data collection

Drawing from the available literature, a discussion guide (Appendix 1) was developed to stimulate discussion and to probe participants' perspectives about *Strongyloides* screening.¹⁸ Focus groups occurred in locations selected by the coordinating participants. These were recorded with participants' consent using a digital microphone and securely stored for transcription and analysis. During focus group discussions, closed-ended questions were used to clarify areas of agreement or disagreement, in order to elucidate whether the moderator had appropriately captured the group's perspectives, and ensure no misinterpretation occurred.

Data analysis

Focus group audio recordings were transcribed verbatim. Transcribed data were coded and analysed manually using an inductive coding methodology.¹⁹ First, each section of text was summarised according to key discussion points and scrutinised for recurring patterns, which were colour-coded. These emerging patterns of information and ideas were then analytically

coded and categorised into two overarching themes, labelled as “enablers” and “barriers” to screening. A barrier was defined as a process or situation which might impede screening for *Strongyloides* in accordance with current guidelines, whereas an enabler was a process or condition which might facilitate screening. Double coding was performed by a co-researcher, with a subsequent comparison of identified themes to ensure consistency in coding and theme development. Illustrative and representative participant quotes were selected to support results and are presented with additional text for attribution.

Ethics

Ethics and Governance was approved by the Melbourne Health Human Research and Ethics Committee (MH HREC 2019.102).

Results: Retrospective observational study

Between 1 January 2018 to 1 January 2019, the search strategy identified 1,908 patients who received an immunosuppressive agent, of which 230 met inclusion criteria (Table 1). No patients were excluded due to inadequate epidemiological information. File review identified that 82 out of 230 patients (35.7%) were screened in the 12 months prior to, or within two weeks after commencing immunosuppression. Review of VIDRL data identified an additional five patients who were screened at external sites, increasing the number screened to 87 out of 230 (37.8%), of whom two were positive (2.3%). An additional 12 patients were identified who had serology more than two weeks following commencement of immunosuppression. Of these, three were seropositive, increasing seroprevalence to 5.1%. Screening rate by speciality unit ranged from 5% to 73%.

The mean age of patients was 54.9 years. The majority were male (57.0%), inpatients (89.6%), and 89 patients (38.7%) had at least five medical comorbidities. 80 patients (34.8%) were from NESB and were mostly migrants, predominantly from Asia (52.6%). Only two patients identified as being of ATSI origin. Nephrology, haematology and bone marrow transplant (BMT) were the predominant specialty units responsible for the care of these patients (Fig. 1). The principal immunosuppressive therapy was corticosteroids (68.7%); those receiving steroids included 48 renal transplant recipients (20.9%).

In multivariate analysis (Table 2), patients of older age were significantly less likely to be screened for *Strongyloides*. There was no association between screening and patients with ≥ 5 comorbidities. Patients categorised as NESB were over 2.5 times less likely to be screened. In multivariate analysis, those born in Africa were over five times more likely to be screened for *Strongyloides* than those born in Asia. Inpatients were over 20 times more likely to be screened than outpatients. Those with eosinophilia were also more likely to be screened, although this did not reach statistical significance. Patients who were screened for tuberculosis and/or hepatitis B were over seven times more likely to be screened for *Strongyloides*.

Results: Thematic analysis

Five enablers and five barriers to screening were identified. Barriers were often linked to a related enabler, employed by the clinician in order to address the barrier (Fig. 2).

Cognitive overload is a barrier to screening, addressed by policies, systems and tools

An overarching barrier that emerged was the phenomenon of *cognitive overload*. Clinicians reported that it was cognitively taxing to consider screening for strongyloidiasis in addition to their many other clinical priorities. “We can’t know everything, we all go to conferences, and all of these things contribute to what’s vying for your attention” [FG1, Con]. This phenomenon was often described using computer analogies: “I only have enough bandwidth to handle a few things, so *Strongyloides* probably dropped off” [FG3, Con]. A relationship with rarity emerged: “In any rare condition, we learn it, we forget it, we learn it again and forget it. It’s a cycle of stuff going in and out of the hard drive” [FG1, Con]. To overcome this, clinicians described processes designed to automate screening. Tools were also developed (Fig. 3). Nurse practitioners were reportedly crucial: “We use a checklist and it’s rare for a patient to start on a biologic without [them] checking” [FG2, Reg].

Perceived rarity of infection is a barrier, overcome by experience to cases encountered

“We have decades worth of data of these patients being treated with steroids, and we haven’t come across any problems yet” [FG1, Con]. Clinicians asked: “We screen them but we haven’t really found any yet. I wonder if we should be screening them at all?” [FG5, Con]. Clinicians described the impact of experience: “I had a case. The patient had disseminated *Strongyloides*

and a rash, and died of septic shock, so, I screen for it” [FG6, Con]. “I’ve never actually seen a case, so it’s way down on the list for things I’m screening for” [FG3, Con].

Unclear cost-effectiveness is a barrier to screening

Participants raised concerns that protocolised screening would result in unnecessary costs: *“Who’s going to wear the cost of the test, and what are the consequences?” [FG2, Con]. This was most relevant in the context of rarity: “I’ve been prescribing immunosuppression for 15 years. Nor have I seen a patient with it, and if I turn around and start screening everybody, I’m not necessarily certain about the cost effectiveness” [FG1, Con].*

Cognitive links to other infections with risk of reactivation (“chunking”) enables screening

Overcoming cognitive load through “chunking”, or cognitively linking *Strongyloides* with other infections that reactivate during immunosuppression was an enabler to screening: *“I think with the TB experience, we just kind of put it into that framework” [FG2, Reg]. One physician described their paradigm: “I also look for two other infections in someone I’m going to immunosuppress, hepatitis B and tuberculosis, as other illnesses that can potentially reactivate with steroids, my cluster of three” [FG6, Con].*

Collaboration and sharing of information are an enabler to screening

Collaborating with perceived experts, particularly ID physicians, was an enabler to screening: *“We may rely on the Infectious Diseases doctors to tell us where we’re deficient, I suspect” [FG3, Con]. An ID clinician illustrated how their input was connected to reducing the cognitive load: “My job on those rounds, if there’s someone from an endemic country, is to make sure someone’s thinking about it” [FG4, Reg].*

Knowledge gaps and lack of guideline awareness barriers

Awareness of *Strongyloides* was demonstrated across all groups. Although the FG2 unit had developed a protocol to screen patients prior to biological therapy, data from the retrospective study demonstrated that they were only screening one-third of patients, highlighting a knowledge gap: *“We often don’t think about screening before steroids” [FG2, Con]. Another barrier was in guideline relevance: “We would go to the [Australian] therapeutic guidelines if the screening came back positive. I wouldn’t use it for my screening guideline” [FG5, Reg].*

Time constraints are a barrier to screening, especially in the outpatient setting

Time constraints were a clear barrier, particularly in the outpatient setting: “*When we only have 10 or 20 minutes with a patient anyway, this poses a serious barrier*” [FG2, Reg]. This barrier was also linked to cognitive load: “*If it’s busy, you might forget to screen for Strongyloides, because it’s lower down on the list of things to screen*” [FG1, Reg].

No patient-specific factors are recognised as barriers

Patient demographic factors were further explored. All focus group participants believed they would screen people regardless of age: “*With things like TB, you consider more so in an older age group. The latency is relevant*” [FG3, Con]. The influence of language was also probed, and in conflict with the findings of the retrospective study, participants reported “*we probably have a bias to screen for more unusual infections*” [FG3, Reg].

Discussion

Strongyloidiasis truly is a neglected tropical disease, exemplified by the low rate (37.8%) of screening for strongyloidiasis prior to immunosuppression in those at greatest epidemiological risk. Use of a mixed-methods approach to data analysis (through triangulation of quantitative and qualitative data), provided insights into why screening was underperformed. Although clinicians understood the latency of infection, and self-reported that age would not be a barrier, older age was significantly associated with reduced screening. This may reflect an unconscious bias towards screening those who have more recently arrived from an endemic area, consistent with the findings of Einsiedel and Spelman.¹⁶

Awareness of strongyloidiasis was insufficient to support screening. Clinicians reported that other elements of care took priority, and cognitive overload was an overarching barrier to screening. Many of the barriers and enablers identified were linked to this concept. Cognitive load theory (CLT), well established in the health education literature,²⁰ posits that the human cognitive system has a limited working memory.^{21,22} Furthermore, working memory is fragile, and distractions easily result in forgetting.²³ CLT proposes that expertise develops as learners organise and combine simple ideas into more complex ones.²¹ By bringing elements together, information *chunking* frees up working memory capacity for other activities.²¹

To overcome barriers, clinicians had independently developed tools to enable screening. Participants often described infections with a risk of reactivation within the same cognitive framework (i.e. *chunking*). Quantitative data corroborated this by demonstrating that patients were over seven times more likely to be screened for *Strongyloides* if they were screened in a panel with tuberculosis and/or hepatitis B. This implies that methods that limit cognitive load and enhance automation and chunking will tip the balance back in the favour of screening (Fig. 2). Clinicians reported the introduction of an electronic medical record (EMR) would create the possibility of using electronic “smart-sets” as decision-support tools, although they could paradoxically increase cognitive load if too many ‘pop-ups’ were encountered (this may be interpreted as extraneous cognitive load or ‘white noise’). However, previous hospital systems with EMRs have shown that, in general, EMRs reduce cognitive load.²³ Therefore, if feasible, electronic tools may re-introduce *Strongyloides* into the working memory of busy clinicians.

A number of clinicians were concerned that indiscriminate use of automated tools may lead to over-screening. Cost-effectiveness is therefore a concern that must be addressed. As of October 2019, the cost of *Strongyloides* serology is AUD\$13. Current estimates report that 24 hours in an Australian ICU will cost AUD\$4,500.²⁴ If all 230 patients included in this study had received screening, at \$13 per test, this would have cost approximately AUD\$3,000. By comparison, the cost of a renal transplant is approximately \$81,000 in the first year, alone.²⁵ Unfortunately, the absolute risk of reactivation is unknown, so it remains difficult to predict which patients warrant targeted chemoprophylaxis. Expecting clinicians to perform a detailed epidemiological risk assessment may actually *increase* intrinsic load by augmenting the task complexity. Although universal screening may be attractive, it will also result in increased serological false-positivity, due to the reduced pre-test probability of infection and known cross-reactivity with other nematodes. This may lead to unnecessary medical intervention and unacceptable cost, as described by clinicians. It is ultimately at the clinician’s discretion to decide whether targeted screening is cost-effective, but cost-effectiveness is a difficult argument to maintain in light of these comparatively low costs and the otherwise preventable nature of hyperinfection.

Over one-third of patients were from NESB, and they were over 2.5 times *less* likely to be screened compared to those whose primary language was English. Analysis of clinicians’ attitudes could not explain this counter-intuitive finding. Previous research acknowledges the importance of communication in the provision of quality healthcare, reporting that language barriers have deleterious effects on patient outcomes.²⁶ Patients who face language barriers are

less likely than others to access preventative medicine²⁷ and less likely to receive the same standard of care, with significant ethnic disparities.²⁸ It is hypothesised that language barriers may have contributed to the many factors which increase extraneous cognitive load (e.g. need for interpreter). Given that clinicians did not recognise language as a barrier, the impact of this cognitive load is clearly much greater in reality than appreciated, in addition to the complexities of managing immunocompromised patients.

Consistent with previous reports,¹⁵ clinicians in at least one unit were not aware that screening should be performed prior to high dose, prolonged courses of corticosteroids, and clinicians in multiple units were unaware of guidelines recommending screening in their patients. Clinicians reported seeking guidance to better understand their screening obligations. By sharing this responsibility, the burden of cognitive load may be distributed with other colleagues involved in their patient's care, allowing them to focus on more pressing issues in their own field of expertise. Future research aims to assess the uptake of automated screening interventions with serial evaluation of screening rate.

Limitations

Seroprevalence was lower than anticipated. Although universal screening for strongyloidiasis is not required for immigration, patients may have been previously treated in accordance with national guidelines.²⁹ A characteristic of *Strongyloides* serology is that it is expected to serorevert 6 to 12 months after treatment.³⁰ Some patients included in the study may have received low-level immunosuppression prior to inclusion, reducing the reliability of serology. Although no cases of hyperinfection were documented, clinicians in the Northern Territory (an endemic setting) note that overwhelming sepsis in the absence of a microbiological diagnosis is relatively common in the immunocompromised.³¹ Selection bias in the favour of inpatients was likely, as outpatients commenced on immunosuppression may have filled scripts in community pharmacies. The focus group participants confirmed that many outpatients were prescribed biological therapy on a private script. Finally, incorrectly recorded epidemiological risk may have resulted in under-ascertainment.

A limitation of the qualitative study is that the scope is limited to doctors who practice within a well-resourced hospital, limiting generalisability. Although participants were encouraged to express alternate viewpoints through probing questions, there is potential for focus groups to generate confirmation bias and 'socially desirable' replies. In order to enhance generalisability,

focus groups were conducted with clinicians from different levels of training. Junior doctors may not have been willing to fully express their opinions in the presence of their consultants, out of fear that they may be perceived as lacking knowledge, leading to conformity bias.³²

Strengths

Although biological therapies were difficult to capture, the vast majority of patients included in this study were receiving corticosteroids, which are thought to be the most significant immunosuppressive agent attributed to latent *Strongyloides* reactivation. A strength of the qualitative study was that the target level of participant recruitment was achieved, facilitating identification of barriers and enablers to screening. The mixed-method design of this study allowed a deeper exploration of clinicians' screening behaviour and explained some important themes identified in the focus groups (e.g. rarity) while also revealing unexpected barriers that would not have otherwise been described in the focus groups alone.

Conclusion

This study highlights the continuing neglect of this uncommon but potentially deadly parasite. Even in this well-resourced, non-endemic setting, vulnerable patients remain at greatest risk. Policies and automated interventions must be implemented with expert input, in order to reduce cognitive pressures and enable “chunking” of information. These will be most useful in time-constrained settings such as the outpatient clinic, while facilitating screening in the elderly and patients from non-English speaking backgrounds.

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Tables and Figures

Table 1: Descriptive statistics of patients included in retrospective analysis

Characteristic (n = 230)	Number (%)
Screened (at time of immunosuppression)	87 (37.8)
Sex (male)	131 (57.0)
Non-English speaking background	80 (34.8)
<u>Continent of birth</u>	
Asia	121 (52.6)
S, E. Europe	67 (29.1)
Oceania	17 (7.4)
Africa	16 (7.0)
S. America	9 (3.9)
Aboriginal and Torres Strait Islander	2 (0.9)
Peripheral eosinophilia	13 (5.7)
Inpatients	206 (89.6)
Patients with ≥ 5 comorbidities	89 (38.7)
<u>Immunosuppression</u>	
Corticosteroids	158 (68.7)
Prednisolone	83 (36.1)
Dexamethasone	27 (11.7)
Renal transplant	48 (20.9)
Cytotoxic chemotherapy	25 (10.9)
Bone marrow transplant	18 (7.8)
Anti-CD20 agent	19 (8.3)
TNF inhibitor	3 (1.3)
Other	7 (3.0)
Positive serology (at time of immunosuppression)	2 / 87 (2.3)
Positive serology (including all patients tested)	5 / 99 (5.1)

Table 2: Factors associated with screening in univariate and multivariate analyses.

Characteristic	Screened (n=87) (%)	Not screened (n=143) (%)	Univariate			Multivariate		
			OR	95% CI	p	OR	95% CI	p
Age ≤ 55 (n=103)	50 (57.5)	53 (37.1)	2.30	1.33 - 3.95	< 0.01	2.51	1.33 - 3.95	0.02
Sex (male) (n=131)	53 (60.9)	78 (54.5)	1.30	0.76 - 2.23	0.34	1.08	0.76 - 2.23	0.83
NESB (n=80)	19 (21.8)	61 (42.7)	0.34	0.21 - 0.69	< 0.01	0.39	0.21 - 0.69	0.01
ATSI origin (n=2)	1 (1.2)	1 (0.7)	1.65	0.10 - 26.74	0.72	1.65	0.10 - 26.74	0.39
Inpatient (n=206)	86 (98.9)	120 (83.9)	16.48	2.18 - 124.4	< 0.01	21.72	2.54 - 185.8	< 0.01
≥ 5 comorbidities (n=89)	34 (39.1)	55 (38.5)	1.03	0.59 - 1.77	0.93	1.20	0.59 - 1.77	0.62
Coinfection test (n=176)	82 (94.3)	94 (65.7)	8.55	3.25 - 22.50	< 0.01	7.32	3.25 - 22.50	< 0.01
Eosinophilia (n=13)	7 (8.1)	6 (4.2)	2.00	0.65 - 6.15	0.23	1.37	0.65 - 6.15	0.67
<i>Continent of birth:</i>								
Asia (n=121)	46 (52.9)	75 (52.4)	1.07	0.62 - 1.82	0.82	<i>Reference</i>		
Oceania (n=17)	9 (10.3)	8 (5.6)	1.71	0.62 - 4.73	0.30	2.20	0.58 - 8.43	0.25
Africa (n=16)	13 (14.9)	3 (2.1)	8.31	2.29 - 30.10	< 0.01	5.14	1.21 - 21.80	0.03
S, E Europe (n=67)	16 (18.4)	51 (35.7)	0.41	0.21 - 0.77	< 0.01	0.85	0.35 - 2.08	0.72
S. America (n=9)	3 (3.4)	6 (4.2)	0.82	0.20 - 3.35	0.78	0.46	0.10 - 2.14	0.32

Abbrev: OR, odds ratio; CI, confidence interval; NESB, non-English speaking background; ATSI, Aboriginal and Torres Strait Islander. Coinfection tests included hepatitis B (serology) and/or tuberculosis (QuantIFERON-TB Gold).

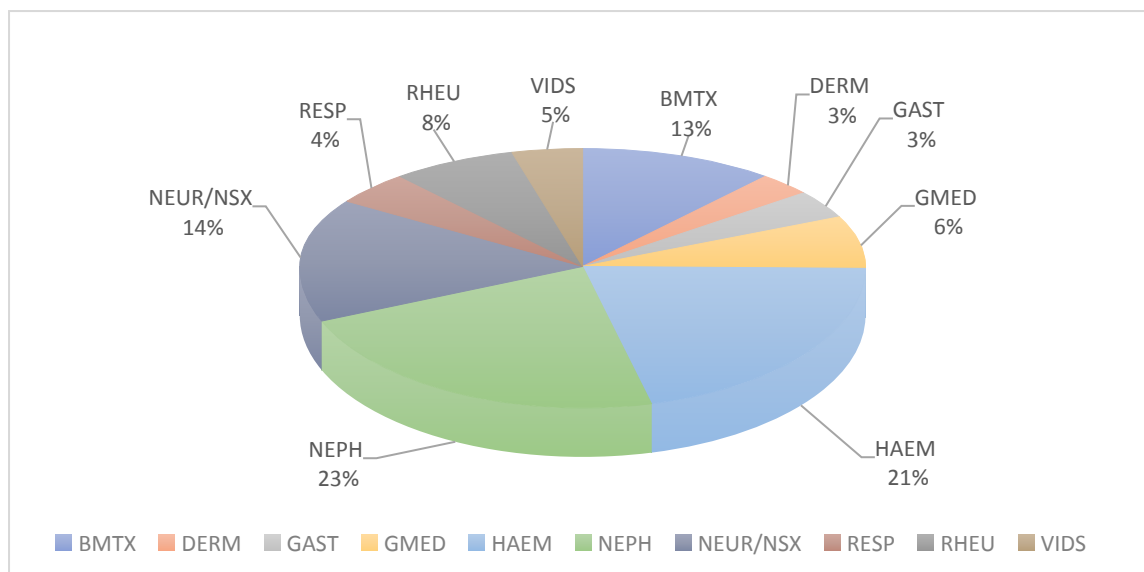


Figure 1: Full list of specialties invited to participate and proportion of patients included in the retrospective study by specialty unit.

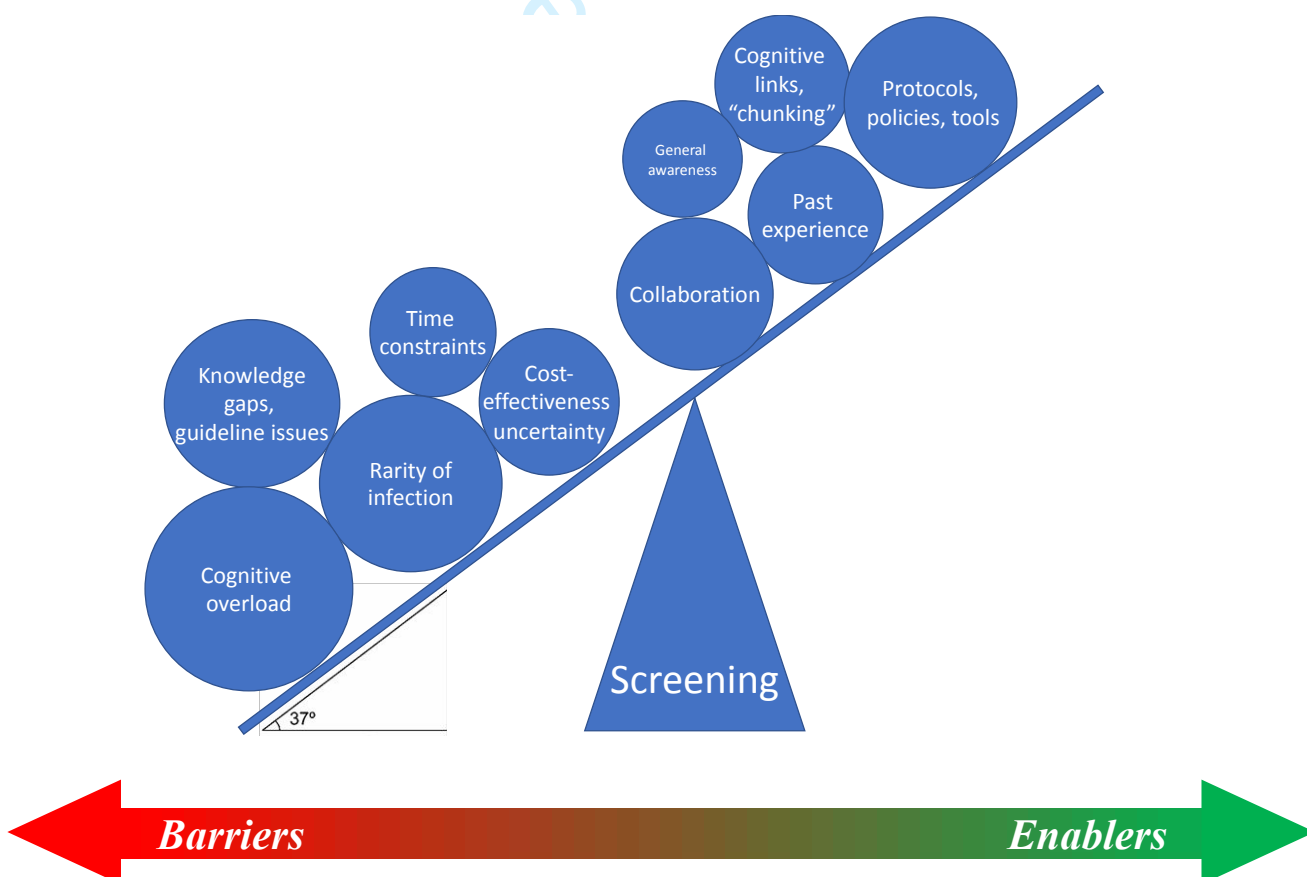


Figure 2: Summary of thematic analysis findings. Graphical representation of the barriers and enablers to screening, where relative sizes are estimated from thematic analysis. 37° angle represents screening rate.

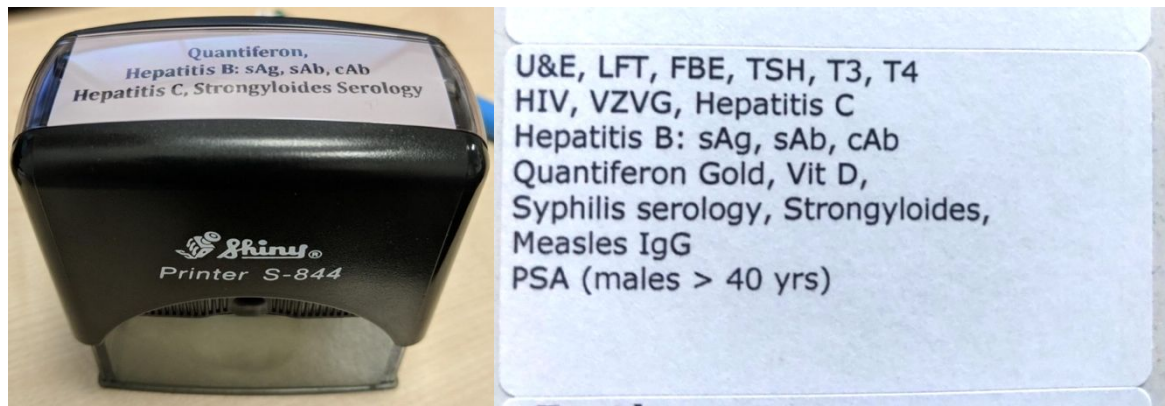


Figure 3: Screening stamp and pathology sticker developed by clinicians to streamline screening.

APPENDIX 1: Focus Group Discussion Guide

Opening question

“I am interested in gaining insight into your understanding about strongyloidiasis and especially about screening for it in patients who are immunocompromised. I want to emphasise the exploratory nature of this session...”

Who, in this room, prescribes immunosuppressive treatment? Describe your role in this process.

General knowledge and experience of strongyloidiasis

Tell me, in general terms, what you know about *Strongyloides*?

Can you describe any cases, stories or clinical experiences?

How have these experiences (or lack of experiences) influenced the way you approach screening for strongyloidiasis?

Perceived relevance of strongyloidiasis in particular clinical area

Is knowledge of this parasite important to you and your patients?

In comparison to your day-to-day patient care, how do you rate its importance in your specialty?

How does it compare to other infections that you may screen for?

General experience of screening for infections in immunocompromised

What is your unit’s approach to screening for infections in immunocompromised patients?

Is this left up to the individual doctor or is there a system or policy / guideline in place?

Frequency of screening and perceived barriers and enablers to screening

Do you have a view about the frequency of screening for *Strongyloides*—do you think is done often enough in your area at the moment?

What would trigger you to screen for *Strongyloides* prior to immunosuppression?

What do you believe are the barriers to screening prior to immunosuppression in your area of practice? [Specific barriers then discussed]:

- a. Lack of awareness?
- b. Not relevant to your specialty?
- c. Rare occurrence?
- d. Lack of education? (Are knowledge or educational gaps a barrier?)
- e. Patient-specific factors (i.e. explanatory analysis), e.g. non-English speaking background, older age.
- f. Clinical setting: Inpatients vs outpatients?

Educational factors: Further exploration

How do you acquire knowledge or seek information in regards to preventing infection in immunocompromised patients? [More closed-ended questions to follow-up:]

What format is this education and who is responsible for facilitating it?

Are you predominantly self-directed in your own education?

What resources do you use to guide your practice?

What guidelines (if any) do you use to inform your decision-making around screening?

Do you find these resources to be credible and relevant to your practice?

Do you find guidelines to be accessible? E.g. cumbersome, expensive, restrictive to individual decision-making?

Future direction

How can we improve screening for strongyloidiasis in our patients before immunosuppression? What needs to be done?

Do you believe your unit would like to be involved in future educational activities or the development of tools to guide or educate clinicians?

Thank you for your time today. Is there anything that we haven't covered, or should have talked about but didn't?

Non-verbal cues:

Non-verbal: communication (including body language) and overall level of engagement:

For Peer Review