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Gaps in Surveillance: Referral of Acutely Ill Returned Travelers in the Emory Healthcare System for Specialty Care and Entry into an International Surveillance Network

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By

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Abstract

Gaps in Surveillance: Referral of Acutely Ill Returned Travelers in the Emory Healthcare System for Specialty Care and Entry into an International Surveillance Network

By Phuong-Vi Nguyen

Background: The monitoring and treatment of travel-related illnesses is a critical aspect of public health, especially in major travel hubs like Atlanta. This thesis explores the epidemiological patterns and healthcare utilization among returning travelers with acute illnesses within the Emory Healthcare Network and the Emory TravelWell Center, part of the GeoSentinel Surveillance Network.

Objective: To analyze the demographic and clinical characteristics of travelers seen at Emory Healthcare and Emory TravelWell Center, determine the overlap in patient populations, and identify significant factors associated with malaria diagnosis.

Methods: A primary data analysis was conducted using datasets from Emory Healthcare and the GeoSentinel Surveillance Network, encompassing 2870 patients seen between March 2, 2009 and December 31, 2022. The study employed a retrospective observational design, aligning patients by visit date, age, and gender. Statistical analyses included the Kruskal-Wallis test for age comparison and chi-square tests for categorical variables such as gender distribution and malaria positivity rates.

Results: There were a total of 1,412 patients seen only at an Emory Healthcare site, 794 patients seen only at the TravelWell Center, and 332 patients seen in both systems. The analysis revealed significant differences in the mean ages of patients across the three groups (Emory, TravelWell, and both), with p-values less than 0.0001. Gender distribution also varied significantly, with a higher proportion of females in the TravelWell group. Malaria positivity rates were markedly different across Emory (7.1%) and TravelWell (1.6%), with the highest prevalence observed in patients seen at both Emory and TravelWell (14.5%). The chi-square test confirmed the statistical significance of these differences ($p < 0.0001$).

Conclusions: The findings highlight distinct demographic and clinical profiles among returning travelers with acute illnesses, emphasizing the need for integrated surveillance and standardized data collection protocols across healthcare networks. The study underscores the importance of continued collaboration between Emory Healthcare and the GeoSentinel Surveillance Network to enhance the identification and management of travel-related diseases.

Implications: This research contributes to the understanding of travel-related illness patterns and the effectiveness of surveillance systems. Recommendations include the standardization of data collection, improved real-time communication between networks and within the healthcare systems, and the expansion of prospective studies to further explore and mitigate travel-related health risks.

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Chapter I: Introduction

The rapid increase in international travel has facilitated the global spread of infectious diseases, posing significant public health challenges. This dynamic movement of human pathogens from areas of endemicity to new locations has the potential to ignite large outbreaks among naïve populations. Returned travelers who develop acute illnesses are thus a critical population for public health surveillance to help prevent transmission in local populations and mitigate potential outbreaks before they escalate. In addition, domestic providers are often unfamiliar with diseases that may manifest among returned travelers, making their appropriate referral important for medical care as well.

GeoSentinel, the Global Surveillance Network of the International Society of Travel Medicine, has played a pivotal role in enhancing public health surveillance of diseases among returning travelers in the United States[15] and abroad. Funded by the Centers for Disease Control and Prevention (CDC), this network collects data on post-travel illnesses across 71 specialized travel and tropical medicine sites on six continents[13], including the "ATL" site at the Emory TravelWell Center in midtown Atlanta. Despite the comprehensive nature of this network, it faces inherent limitations common to large, diffuse, passive surveillance systems. Specifically, it relies on the timely referral of individuals to designated sites for data capture and entry by specific providers, leading to significant gaps in tracking and accurately characterizing patients with post-travel illnesses.

A crucial aspect of this research is to assess how many patients within the Emory Healthcare system present with symptoms possibly related to acute illness acquired during travel, and where these presentations occur. Currently, there is a gap in understanding at Emory regarding the number and location of patients seeking care for travel-related illnesses, which

hinders accurate diagnosis and their potential inclusion in the GeoSentinel network. Additionally, it is essential to determine if patients seen at the Emory TravelWell Center differ in significantly from the broader Emory Healthcare population, as this could potentially skew the data used for analysis in GeoSentinel. Understanding whether these patients exclusively seek care at the travel clinic or if they also visit other healthcare facilities, such as emergency rooms, without being captured by the surveillance network, is critical. This knowledge gap underscores the importance of accurately tracking and managing diseases associated with travel, compelling us to investigate these questions to address the existing challenges effectively.

Problem Statement

Despite the efforts of the GeoSentinel network and Emory TravelWell Center, there are significant limitations in identifying and tracking returned travelers with acute illnesses in the United States. This issue arises from the reliance on timely referrals and data entry by specific providers, leading to gaps in information and the potential underreporting of cases. Consequently, the accurate characterization and surveillance of post-travel illnesses remain challenging, compromising public health responses and disease containment efforts.

Theoretical Framework

The theoretical framework for this study is grounded in the principles of epidemiological surveillance and public health informatics. The surveillance system's effectiveness is evaluated through its capacity to accurately capture and track disease occurrences among returned travelers. This study employs a retrospective observational design to compare the data captured by the Emory TravelWell Center and the broader Emory Healthcare network. By analyzing discrepancies in data capture and patient characteristics, the research aims to enhance the

understanding of surveillance system efficacy and inform improvements in public health monitoring and response strategies.

Purpose Statement

The purpose of this study is to estimate the magnitude of the discrepancy between cases of acute illness post-travel data captured at the Emory TravelWell Center and entered into the GeoSentinel surveillance network versus those seen within the broader Emory Healthcare network. The study aims to characterize the two patient populations and identify high-yield sites for improved capture of case patients, thereby enhancing the study of post-travel illnesses in the greater Atlanta area and increasing data entry into the GeoSentinel Network.

Research Question

The primary research question driving this study is: What proportion of individuals who undergo malaria testing, indicative of international travel and acute illness, are captured in the GeoSentinel surveillance network within the Emory Healthcare system compared to those seen at the Emory TravelWell Center? Additional inquiries include examining differences in patient populations between the TravelWell Center and other Emory Healthcare facilities and identifying key challenges in effectively tracking and integrating data on travel-related acute illnesses into surveillance systems like GeoSentinel.

Significance

The significance of this research extends beyond Emory and Atlanta to a broader context with implications for major metropolitan areas and busy international airports. By identifying gaps in case capture and data entry, the study aims to enhance local and national surveillance systems for travel-related illnesses. Improvements in surveillance can lead to earlier detection

and containment of disease outbreaks, thereby reducing morbidity and mortality associated with these illnesses. Furthermore, this research aligns with CDC objectives in public health surveillance, providing valuable insights that can inform policymaking, public health practice, and future research efforts both locally and potentially setting a precedent for enhanced detection capabilities at other sites globally.

Definition of Terms

- *GeoSentinel Surveillance Network*: A global surveillance network that collects data on post-travel illnesses across specialized travel and tropical medicine sites.
- *Emory TravelWell Center*: A clinic within the Emory Healthcare system that provides pre-travel counseling and manages post-travel illnesses, contributing data to the GeoSentinel network.
- *Acute Illness*: A condition characterized by a sudden onset and typically short duration, which in this context is associated with recent travel.
- *Surveillance System*: A systematic collection, analysis, and interpretation of health data essential for planning, implementation, and evaluation of public health practice.
- *Retrospective Observational Design*: A study design where researchers look back in time to examine exposures and outcomes that have already occurred.
- *Data Capture*: The process of collecting and recording data relevant to patient health and disease surveillance.

By addressing these elements, this study seeks to provide a comprehensive analysis of the current limitations in travel-related illness surveillance and propose methods for improving data accuracy and public health outcomes.

Chapter II: Review of Literature

Understanding the prevalence and implications of malaria among international travelers is critical for developing effective prevention and treatment strategies. Previous research has highlighted the patterns of travel-related malaria, yet gaps remain in our knowledge regarding specific risk factors, diagnostic challenges, and optimal intervention strategies. This review synthesizes existing literature to provide a comprehensive background for the current study, focusing on the incidence of malaria post-travel, diagnostic approaches, and the role of travel history in predicting malaria outcomes[1,3,20].

Current State of Knowledge

Malaria-related

Travel-related malaria is a significant concern, with numerous studies documenting its incidence and characteristics among international travelers[1,3]. A GeoSentinel analysis covering 2003 to 2016 revealed a substantial number of malaria cases among travelers, emphasizing the need for continuous monitoring and intervention[9,13]. Another study from the GeoSentinel Network underscored the importance of differential diagnosis for travelers returning from malaria-endemic regions, particularly from West Africa[2,6]. The variation in malaria incidence among different regions also suggests the need for region-specific preventive measures and diagnostic protocols[10,15].

Research has shown that travelers visiting friends and relatives (VFR) are at a higher risk of contracting malaria compared to other traveler groups[18,20]. This elevated risk is attributed to longer stays, less stringent use of prophylaxis, and exposure to higher transmission areas[8,19]. The CanTravNet surveillance data further supports these findings, indicating a significant burden of

travel-acquired infections and illnesses among Canadian travelers[22]. Moreover, VFR travelers often perceive themselves to be at lower risk, which leads to lower compliance with preventive measures[18].

Studies also highlight the role of socioeconomic and demographic factors in influencing malaria risk among travelers[21]. Young adults and male travelers are more frequently affected, possibly due to greater exposure to outdoor activities and less adherence to protective measures. Additionally, the emergence of drug-resistant malaria strains poses a significant challenge, necessitating ongoing research and updates to treatment protocols[12,17].

Other Post-Travel Illnesses

In addition to malaria, travelers often contract other acute febrile illnesses. Research indicates that dengue, chikungunya, Zika virus, and COVID-19 are significant causes of fever in returning travelers[4]. For instance, a study published in the New England Journal of Medicine highlighted the prevalence of various febrile illnesses among travelers, emphasizing the need for comprehensive diagnostic evaluations beyond malaria[4]. Surveillance networks such as GeoSentinel have documented cases of these emerging viruses among international travelers, indicating the broad spectrum of travel-related illnesses[15].

The challenge of differentiating between malaria and other febrile illnesses is compounded by overlapping clinical presentations and the variable availability and performance of diagnostic tests. For example, dengue and chikungunya can present with symptoms similar to malaria, such as fever, headache, and myalgia, making clinical differentiation challenging[5]. This underscores the importance of using a combination of diagnostic tests and clinical history to accurately diagnose the cause of fever in returning travelers[15].

Gaps in Knowledge

Despite extensive research, several gaps remain in understanding travel-related malaria. One major gap is the variability in diagnostic practices and the resulting impact on malaria detection rates[10,13]. For instance, studies have shown inconsistent use of rapid diagnostic tests (RDTs) and microscopy, leading to potential underdiagnosis or misdiagnosis of malaria cases[14]. Additionally, there is a need for more detailed data on the specific travel behaviors and protective measures of travelers who contract malaria[21]. The effectiveness of pre-travel health advice and interventions remains under-researched, especially in diverse traveler populations.

Furthermore, while the overall incidence of malaria among travelers is well-documented, less is known about the long-term outcomes and complications associated with travel-acquired malaria. Research has primarily focused on acute presentations, with limited data on the chronic impacts of malaria on travelers. Understanding these long-term effects is crucial for developing comprehensive care strategies for affected individuals. Moreover, the psychological and economic burden of travel-related malaria on individuals and healthcare systems is an area that warrants further exploration[15].

The effectiveness of different preventive measures, such as insecticide-treated nets (ITNs) and chemoprophylaxis, in various settings is another area that needs more attention[23]. Current guidelines may not be uniformly applicable across different regions and traveler demographics, leading to varying degrees of protection. Research on personalized preventive strategies based on individual risk profiles could enhance the efficacy of these interventions[7,18].

Addressing the Gaps: The Current Study

The present study aims to address these gaps by leveraging the wealth of knowledge about malaria as a surrogate marker and using it as a control where we know with relative certainty the actual diagnosis. This approach will help us understand where these cases go and how many get followed up at TravelWell. Specifically, we will analyze data from multiple surveillance networks, including GeoSentinel and CanTravNet, to identify specific travel-related factors that increase the risk of malaria and to evaluate the effectiveness of current diagnostic practices[23].

Additionally, this study will explore the follow-up of malaria-negative cases, including those with co-infections with arboviruses like dengue, chikungunya, and Zika. Previous studies have noted the detection of these arboviruses in individuals with and without parasitemia, although this is not a key focus of the current study. Our goal is to provide insights into the long-term health outcomes of travelers diagnosed with malaria and other febrile illnesses, thereby contributing to a more comprehensive understanding of the disease's impact[5].

Synthesizing Previous Research

Travel-Related Malaria

A synthesis of previous research reveals that travel-related malaria is influenced by a variety of factors, including destination, duration of travel, and adherence to prophylactic measures[2,9,20]. Studies have consistently shown that sub-Saharan Africa is the most common region of exposure for travelers diagnosed with malaria[1,3,6]. Furthermore, research highlights the critical role of pre-travel health advice and interventions in mitigating the risk of malaria[10,15,18]. Effective pre-travel consultations should include tailored advice based on the traveler’s itinerary, health status, and risk factors[5,13].

The literature also emphasizes the importance of timely and accurate diagnosis in managing travel-related malaria[22]. Delayed diagnosis can lead to severe complications and increased morbidity, underscoring the need for improved diagnostic tools and protocols in both travel and clinical settings[21]. Recent advancements in molecular diagnostics, such as polymerase chain reaction (PCR) assays, have shown promise in enhancing the detection of malaria parasites, particularly in low-density infections[7,18]. Combining traditional diagnostic methods with new technologies could improve accuracy and speed in malaria detection[23].

Studies have also explored the role of travel clinics and their impact on reducing malaria incidence among travelers[6,8,18]. Clinics that provide comprehensive travel health services, including vaccination, prophylaxis, and education, have been shown to significantly reduce the risk of malaria and other travel-related illnesses[14,19,20]. Enhancing the accessibility and reach of these clinics, particularly in remote and underserved areas, is crucial for broadening the impact of preventive measures[7,17].

Research on travel-related malaria also underscores the significance of international collaboration and information sharing[3,9]. Multinational studies and data pooling from different countries enable a more comprehensive understanding of malaria patterns and trends among travelers[2,15]. Collaborative efforts between countries can lead to the development of standardized guidelines and policies, ensuring consistency in prevention and treatment practices[13,18]. Additionally, partnerships between public health organizations, academic institutions, and the travel industry can enhance the dissemination of information and resources to travelers[19,23].

Non-Malaria Acute Travel-Related Illness

In addition to malaria, travelers are at risk for a wide range of non-malarial acute illnesses. These include gastrointestinal diseases, respiratory infections, and sexually transmitted infections, which can be influenced by travel destination, duration, and pre-travel health practices[12,16,21]. Effective management of these illnesses involves a combination of pre-travel advice, timely diagnosis, and appropriate treatment strategies[11,20,22].

Pre-travel consultations should provide comprehensive advice on food and water safety, personal hygiene, and vaccination[4,11,14]. For instance, gastrointestinal diseases are commonly reported among travelers, often due to contaminated food or water[8,14]. Vaccinations and preventive measures against diseases such as hepatitis A, typhoid fever, and traveler's diarrhea are essential components of pre-travel health advice[9,14,17].

Respiratory infections, including influenza and COVID-19, are also significant concerns for travelers[7,10,13]. Preventive measures such as vaccinations, wearing masks, and maintaining social distancing in crowded places can reduce the risk of respiratory infections during travel[6,10,13].

Sexually transmitted infections (STIs) represent another critical aspect of non-malarial travel-related illnesses. Travelers engaging in high-risk sexual behaviors are at increased risk for STIs, and pre-travel consultations should emphasize safe sex practices and provide access to prophylactic measures, such as condoms[12,19,20].

Overall, research highlights the importance of travel clinics in providing comprehensive health services that address both malarial and non-malarial travel-related illnesses[5,15,23]. These clinics play a crucial role in educating travelers, administering vaccinations, and offering prophylaxis, thereby reducing the incidence of travel-related illnesses[3,13,21]. Enhancing the reach

and accessibility of these clinics, particularly in remote areas, is essential for improving travel health outcomes on a global scale[6,9,22].

The Importance of Surveillance Networks

Surveillance networks like GeoSentinel, CanTravNet, and EuroTravNet play a crucial role in monitoring travel-related infections and providing valuable data for public health interventions[11,13,18]. These networks facilitate the collection and analysis of data on travel-associated illnesses, enabling the identification of emerging trends and high-risk groups[2,12,22]. TravelWell, by participating in GeoSentinel, which is the largest international network, ensures that travelers are seen by providers who interact with these groups and stay updated with the latest information and guidelines. Studies utilizing GeoSentinel data have contributed significantly to our understanding of travel-related malaria, highlighting the need for continued surveillance and research collaboration[8,23].

The data from these networks have been instrumental in identifying patterns of malaria transmission and informing policy changes[15,18]. For instance, surveillance data have led to updates in travel health guidelines, emphasizing the importance of tailored advice and interventions based on the latest epidemiological trends[1,6,17]. The integration of artificial intelligence (AI) and machine learning algorithms in surveillance systems could further enhance their predictive capabilities and improve response times during outbreaks.

Surveillance networks also play a pivotal role in tracking the spread of drug-resistant malaria strains[9,19]. Data from these networks have helped identify regions with high prevalence of drug resistance, informing treatment protocols and public health responses[2,4,23]. By

maintaining robust surveillance systems, public health authorities can promptly detect and respond to changes in malaria epidemiology, mitigating the risk of widespread outbreaks[13,18].

Relevance to Target Population

The relevance of travel-related malaria to the target population is evident in the significant health burden it imposes on international travelers. The findings from surveillance data indicate that travelers returning from malaria-endemic regions are at a high risk of contracting the disease, necessitating targeted prevention and intervention strategies[13,14,22]. This population includes not only tourists and business travelers but also expatriates, VFR travelers, and humanitarian aid workers[2,9,19].

Understanding the unique risk profiles and behaviors of these traveler groups is crucial for designing effective health interventions[7,8,21]. For example, VFR travelers often face challenges in accessing and adhering to preventive measures due to cultural beliefs, financial constraints, and perceived risk[12,18,20]. Tailoring interventions to address these specific barriers can significantly enhance their effectiveness and reduce the incidence of travel-related malaria[17].

The role of pre-travel health services is particularly relevant in this context[13,18]. Comprehensive pre-travel consultations that include risk assessment, vaccination, prophylaxis, and education are essential for mitigating the risk of malaria among travelers[10,15]. Enhancing the accessibility and quality of these services, especially in regions with high outbound travel rates, can have a substantial impact on reducing the burden of travel-related malaria[3,4,6].

Societal Impact

The societal impact of travel-related malaria extends beyond individual health outcomes, affecting public health systems and economies[18,22]. While travel-related malaria is a significant

concern, malaria-negative cases (or those co-infected with other pathogens) are arguably more important overall. These cases include infections with arboviruses such as chikungunya, Zika, and dengue, which have significant public health implications, particularly in regions like Florida where these diseases are emerging[4]. Additionally, the impact of COVID-19 on travel and subsequent health outcomes cannot be ignored. The costs associated with diagnosing, treating, and managing these cases among travelers can be substantial, placing a strain on healthcare resources[13].

Public health initiatives aimed at preventing travel-related malaria can yield significant societal benefits[13]. By reducing the incidence of malaria among travelers, these initiatives can lower healthcare costs, enhance workforce productivity, and promote safer travel practices[2,18]. Moreover, effective prevention strategies can contribute to broader public health goals, such as controlling malaria transmission in endemic regions and preventing the spread of drug-resistant strains[7,15,23].

International collaboration and policy development are crucial for addressing the societal impact of travel-related malaria[3,6,19]. Harmonizing travel health guidelines, sharing surveillance data, and fostering partnerships between public health authorities and the travel industry can enhance the effectiveness of prevention and response efforts[8,14,20]. These collaborative efforts can also facilitate the development of innovative solutions, such as digital health tools and community-based interventions, to improve malaria prevention and management among travelers[1].

Public Health Initiatives and Future Directions

Public health initiatives aimed at preventing travel-related malaria have focused on enhancing surveillance, improving diagnostic practices, and promoting adherence to preventive measures[15,18,19]. Programs that provide education and resources to travelers, such as pre-travel consultations and online health information, play a vital role in mitigating malaria risk[2,6,22]. Additionally, initiatives that integrate modern technologies, such as mHealth applications, can improve the accessibility and effectiveness of travel health services[13,21].

Future research should continue to explore the long-term health outcomes of travel-acquired malaria, including the potential for chronic complications and the effectiveness of different treatment regimens[18]. Studies should also examine the impact of emerging diagnostic technologies and personalized preventive strategies on malaria incidence among travelers[2,10,12]. By addressing these research gaps, we can develop more targeted and effective interventions to protect travelers from malaria[1].

The integration of digital health tools into travel health practices holds promise for enhancing malaria prevention and management[17,23]. Mobile applications that provide real-time health advice, track adherence to prophylaxis, and facilitate timely diagnosis and treatment can empower travelers to take proactive steps in protecting their health[9,14]. Additionally, leveraging big data and AI to analyze travel patterns and predict malaria risk can inform public health strategies and optimize resource allocation[7,8,20].

International collaboration remains a cornerstone of effective malaria prevention and control efforts[6,22]. By sharing data, harmonizing guidelines, and fostering partnerships, countries can collectively address the challenges posed by travel-related malaria[2,10,18]. These collaborative efforts can also support capacity building in malaria-endemic regions, enhancing local surveillance and response capabilities[15,18].

Research should continue to focus on understanding the unique risk factors and behaviors of different traveler groups, such as VFR travelers, to design tailored interventions[13,23]. By addressing the specific needs and challenges of these groups, we can enhance the effectiveness of malaria prevention strategies and reduce the overall burden of travel-related malaria[2,9].

The development and dissemination of comprehensive pre-travel health services are crucial for protecting travelers from malaria[1]. These services should include risk assessment, vaccination, prophylaxis, and education, tailored to the individual traveler's itinerary and health status[8,10,14]. Ensuring the accessibility and quality of pre-travel consultations, particularly in regions with high outbound travel rates, can have a substantial impact on reducing malaria incidence among travelers[17,21].

Public health initiatives should also focus on the broader societal benefits of malaria prevention[3,6,22]. By reducing the incidence of malaria among travelers, we can lower healthcare costs, enhance workforce productivity, and promote safer travel practices[13,18,19]. Effective prevention strategies can contribute to controlling malaria transmission in endemic regions and preventing the spread of drug-resistant strains[2,7,18].

International collaboration and policy development are essential for addressing the societal impact of travel-related malaria[12,15,20]. Harmonizing travel health guidelines, sharing surveillance data, and fostering partnerships between public health authorities and the travel industry can enhance the effectiveness of prevention and response efforts[1,9]. These collaborative efforts can also facilitate the development of innovative solutions, such as digital health tools and community-based interventions, to improve malaria prevention and management among travelers[9,23].

Conclusion

In conclusion, travel-related malaria and other travel-related illnesses remain a significant public health concern, with ongoing challenges in prevention, diagnosis, and management[1,6,23]. This review has highlighted the complexity of malaria transmission dynamics among international travelers and the critical role of surveillance networks in monitoring and responding to travel-related infections[3,18]. Future research should focus on addressing the identified gaps in knowledge, including the long-term health impacts of travel-acquired malaria and the effectiveness of new diagnostic and preventive strategies[13].

By advancing our understanding of travel-related infections and implementing targeted interventions, we can mitigate the burden of preventable diseases and ensure the health and safety of global travelers[9,21]. Enhancing the accessibility and effectiveness of travel health services, leveraging emerging technologies, and fostering international collaboration are key to achieving these goals[15,18,19]. The continued integration of surveillance data into public health practice will be vital in adapting to the evolving landscape of travel-related malaria[2,17].

Chapter III: Methodology

The purpose of this thesis is to analyze travel-related infections among returning travelers to the Atlanta area who present with acute illnesses. By utilizing datasets from the Emory Healthcare Network and the Emory TravelWell Center, part of the GeoSentinel Surveillance Network, this study aims to identify patterns and risk factors associated with these infections. This study has a narrower focus on understanding how representative the TravelWell (TW) population is compared to Emory as a whole, based on numbers, demographic variables, and the makeup of malaria/non-malaria infections. This will help target interventions and studies to better understand, prevent, and treat travel-related infections.

Population and Sample

Population Description

The population involved in this study consists of all returning travelers who presented with acute illnesses and had malaria testing performed at an Emory Healthcare site, as well as those seen at the Emory TravelWell Center. The participants were patients seen within the Emory Healthcare Network, which included 1,744 patients, and at the Emory TravelWell Center in midtown Atlanta, which accounted for 1,126 patients. The data covered the period from March 2, 2009, to December 31, 2022. The timeframe was selected based on the availability of malaria testing data from Emory's data warehouse, ensuring a consistent period for analysis across both systems.

Study Setting

The study was conducted in Atlanta, a major hub for domestic and international travel, making it a strategic location for analyzing travel-related infections. Emory Healthcare, a

comprehensive academic health system, serves as a major healthcare provider in the region. The Emory TravelWell Center, located at the Emory Midtown campus, specializes in travel medicine and participates in the GeoSentinel Surveillance Network as the Atlanta site. This integration allows for the collection of extensive data on travel-related illnesses, providing a robust foundation for this study.

Rationale for Population Selection

The choice of using malaria testing as a key identifier for inclusion in this study stems from its prevalence as a default diagnostic test for sick returning travelers. Malaria testing is readily accessible and commonly ordered by providers caring for sick returned travelers. Testing can be ordered without approval from infectious diseases specialists, and the order is available in the hospital ordering system, which eliminates the need to navigate specialized send-out/reference ordering systems. Moreover, malaria is predominantly travel-related, with very few domestic cases in the United States, making it a relevant and specific marker for assessing travel-related health risks.

Atlanta's status as a travel hub, coupled with the availability of detailed healthcare data from Emory's institutions, provides a unique opportunity to study travel-related infections. Malaria was chosen as the screening test because it is a common and serious travel-related infection with well-documented diagnostic procedures. This selection provides a reasonable way to search the Emory database due to the availability and specificity of malaria testing data. The dates were limited to ensure the availability of consistent and comparable data from both Emory Healthcare and GeoSentinel. GeoSentinel data was pulled based on patient visits and diagnostic records within the specified timeframe. As a tertiary care medical center and referral center, Emory attracts more complicated or unusual cases, making it an ideal setting for this study. The

selected population offers a diverse sample of travelers, facilitating a comprehensive analysis of various infections encountered by returning travelers. The inclusion criteria encompassed all patients with a recorded visit date between March 2, 2009, and the end of 2022. Exclusion criteria included patients who did not fall within this specified timeframe.

Research Design

The study design is a primary data analysis of a retrospective observational study. This design was chosen to leverage existing datasets from Emory Healthcare and GeoSentinel, facilitating a thorough examination of travel-related infections among the target population. The analysis involved aligning patients by date of visit to either healthcare setting, and then by age and gender when available.

Creation of Dataset Sets

Prior to matching, the data were compiled and separated into three distinct sets: Emory Healthcare, GeoSentinel, and both. This categorization allowed for a detailed analysis of each subset, providing insights into the patterns and prevalence of travel-related infections across different healthcare settings.

Matching Criteria

Patients were matched based on their date of visit to either healthcare setting, with matches expanded to within ±14 days of the visit dates. Further alignment was conducted based on age, gender, and ethnicity, allowing for matches with a ±1 year range for age if exact visit dates did not coincide and the patient's birthday fell between the visit dates. Malaria testing information was utilized to confirm matches, ensuring the accuracy and reliability of the dataset.

Procedures

Data Cleaning

To ensure consistency and accuracy, the GeoSentinel data for the TravelWell Center underwent thorough data cleaning to remove patients not within the same timeframe as provided in the Emory Healthcare data. This step was necessary due to the more limited timeframe availability of the Emory data. The Emory data also underwent additional cleaning to reclassify malaria test result information. This process involved isolating rapid antigen results, smear results, determining whether results indicated malaria positivity, and identifying the type of malaria if positive and known. Additionally, those with birthdates of 1/1/1955, 1/1/1975, or listed at age 0 in the Emory dataset were removed due to being quality control (QC) specimens (approximately 42 data points).

Coordination and Data Collection

As this was a new study, initial steps included coordinating meetings with the appropriate contacts from each surveillance system to pull all deidentified data before applying inclusion and exclusion criteria. This coordination ensured access to the necessary data for analysis. Subsequent data cleaning isolated workable datasets, preparing them for detailed analysis.

Data Collection Instruments

Given the nature of this study, no pre-existing datasets were available in a readily usable format. Data collection instruments included:

1. Surveillance Systems: The primary sources of data were the Emory Healthcare Clinical Data Warehouse and the GeoSentinel Surveillance Network. These systems provided data on travel-related illnesses.
2. Deidentified Data: Both data sources utilized deidentified patient information, ensuring compliance with privacy regulations and facilitating secure data analysis. It is important to note that the Emory data was not deidentified by the institution but rather by the researchers for this study. There were no codes linking GeoSentinel entries to individual participants or personal health information (PHI).
3. Data Cleaning Protocols: Detailed protocols were established for data cleaning and reclassification, particularly focusing on malaria test results and TW diagnostic codes to ensure accurate categorization.

Data Collection Process

The data collection process involved several key steps:

1. Initial Data Pull: Data were pulled from the Emory Healthcare Network and GeoSentinel Surveillance Network, focusing on the specified inclusion timeframe.
2. Data Cleaning: The initial datasets underwent extensive cleaning to remove irrelevant data and reclassify critical information, such as malaria test results. Malaria screens and smears were entered as separate results, requiring line-by-line cleaning. Reporting was not fully standardized, with free text boxes used, and individuals often underwent multiple tests per clinical episode.
3. Data Matching: Patients were matched based on visit dates, age, gender, and ethnicity, with specific criteria for confirming matches.

4. Dataset Separation: The cleaned and matched data were separated into three distinct sets (Emory Healthcare, GeoSentinel, and both) for detailed analysis.

Data Sources

Emory Healthcare Network

The Emory Healthcare Data Warehouse provided data exclusively accessible within Emory. This system logs patient visits, diagnoses, and test results, offering a rich dataset for analyzing travel-related infections.

Emory TravelWell Center and GeoSentinel Network

The Emory TravelWell Center, while part of the Emory Healthcare Network, contributes deidentified data to the GeoSentinel Surveillance Network as the "ATL" site. All data entered into GeoSentinel from Emory is coded as ATL followed by a 4-digit numeric code. GeoSentinel is a global network that collects data on travel-related illnesses from various sites worldwide. Using the ATL code, the network provided comprehensive data on patients seen at the TravelWell Center, enhancing the study's robustness.

Timeframe Adjustment

Due to the more limited timeframe of data available in the Emory Healthcare Data Warehouse, the GeoSentinel data had to be adjusted to include only patients from the same timeframe. The early timepoint (March 2, 2009) was selected as the earliest timepoint for available data, and the later timepoint (December 31, 2022) marked the end of the Cerner electronic medical record system at Emory and a changeover to a new system. This adjustment ensured standardization across datasets, facilitating accurate comparisons and analyses.

Relevant Variables

The analysis focused on several key variables:

- Visit Date: The date of each patient's visit to either healthcare setting.
- Gender: Included when available for demographic analysis.
- Ethnicity: Included when available to assess potential demographic patterns.
- Age: Used for matching and demographic analysis.
- Malaria Testing Information: Included rapid antigen results, thick and thin smear results, malaria diagnosis (defined as rapid antigen and/or thick and thin smear positive), and species of plasmodium parasite, if known.
- All Testing/Diagnoses: Specific to TravelWell data, encompassing diagnostic information available.

Data Analysis Methodology

Statistical Analysis

The data analysis involved several statistical techniques to identify patterns and associations in travel-related infections:

1. Descriptive Statistics: Initial analysis included descriptive statistics to summarize the demographic characteristics of the study population (see appendix Table 1).
2. Matching Analysis: Matching criteria were analyzed to ensure accuracy and reliability, focusing on the alignment of visit dates, age, gender, and ethnicity.
3. Comparative Analysis: Comparative analyses were conducted across the three dataset sets (Emory Healthcare, GeoSentinel, and both) to compare rates of malaria diagnosis and identify differences and similarities in infection patterns.

4. Multivariable Analysis: Multivariable regression models were employed to identify predictors associated with a positive malaria diagnosis, adjusting for potential confounders such as age, gender, ethnicity, and presence of repeat visits.

Data analysis was conducted using Microsoft Excel and SAS 9.4. These tools facilitated complex analyses and the visualization of results, ensuring accurate and interpretable findings.

Ethical Considerations

The study adhered to ethical standards, with all data deidentified to protect patient privacy. The study protocol was reviewed and approved by the Emory University Institutional Review Board (IRB), ensuring compliance with ethical guidelines for research involving human subjects.

Conclusion

This chapter outlined the methodology employed in this study, detailing the population and sample, research design, procedures, instruments, and data analysis methodology. By following these detailed steps, similarly trained scientists or public health practitioners can replicate this study, contributing to the broader understanding of travel-related infections. The comprehensive approach ensures the reliability and validity of the findings, supporting the development of effective public health strategies to mitigate the impact of travel-related infections.

Chapter IV: Results

This chapter presents the major findings of the study derived from the data summarized in Tables 1, 2, and A1. The data includes demographic variables and the malaria/non-malaria makeup of patients seen at Emory Healthcare and the Emory TravelWell Center. This detailed dataset provides a foundation to explore the patterns and risk factors associated with travel-related infections among returning travelers to the Atlanta area.

In total, there were 1,744 patients tested for malaria at an Emory Healthcare site, of which 332 (19.0%) were also seen at the TravelWell Center and entered into the GeoSentinel database. Additionally, 794 patients were seen at the TravelWell Center without having malaria testing recorded in the Emory system.

Age Distribution Among Groups

The age distribution among patients seen at Emory Healthcare, the TravelWell Center, and those with visits logged in both systems was examined. The Kruskal-Wallis test was conducted due to the violation of ANOVA assumptions and yielded a p-value of <0.0001, indicating a statistically significant difference in the mean ages among the three groups. This result suggests that the ages of patients seen at Emory Healthcare, TravelWell Center, and those who had overlapping visits differ significantly (Table 2).

Demographic Characteristics

Significant differences in demographic and clinical characteristics were explored, notably the distribution of age, gender, and ethnicity across the groups. A critical finding was the very low representation of the Hispanic population—specifically, no Hispanic women were captured

in the dataset. This highlights a significant gap, potentially pointing to an underrepresentation in the healthcare system's data capture mechanisms or accessibility (Table 1).

Table 1. Categorical characteristics of patients seen March 2, 2009 - December 31, 2022 at an Emory Healthcare site in comparison to patients who were seen at both an Emory campus and TravelWell Center using data pulled from the Emory Healthcare Data Warehouse.

	Emory Healthcare (n = 1412)		Both (n = 332)		p-value
Variable	**Frequency**	**Percent**	**Frequency**	**Percent**	
Female	637	45.11	183	55.12	0.0010
Ethnicity					0.0108
African American or Black	491	34.80	85	25.60	
American Indian or Alaskan Native	9	0.64	1	0.30	
Asian	108	7.65	16	4.82	
Caucasian or White	549	38.91	151	45.48	
Hispanic	2	0.14			
Native Hawaiian or Other Pacific Islander	3	0.21			
Multiple	10	0.71	3	0.90	
Patient Declines	4	0.28			
Unknown/Unreported	236	16.71	76	22.89	
Malaria					<0.0001
No	1312	92.92	284	85.54	
Yes	100	7.08	48	14.46	
Episodes					0.4296
A	1360	96.32	324	97.59	
B	49	3.47	7	2.11	
C	3	0.21	1	0.30	
Campus					
Emory Crawford Long Hospital	195	20.83	30	11.86	
Emory Johns Creek Hospital	117	12.50	10	3.95	
Emory University Hospital	324	34.62	38	15.02	
The Emory Clinic	169	18.06	98	38.74	
Emory Occupational Injury	3	0.320			
Unknown/Unreported	604	42.78	156	46.99	
Antigen Results					<0.0001
Neg	1249	88.46	286	86.14	
Pos	89	6.30	42	12.65	
	74	5.24	4	1.20	
Smear Results					<0.0001
Neg	1088	77.05	269	81.02	
Pos					
facliparum	63	4.46	30	9.04	
malariae	1	0.07	1	0.30	
ovale	2	0.14	4	1.20	
spp	1	0.07			
vivax	14	0.99	5	1.51	
mixed (falciparum & ovale)	1	0.07			
Gametocytes only			1	0.30	
Other					
Babesia	1	0.07			
No Borrelia	1	0.07			
No Morulae	1	0.07			
No spirochetes	2	0.14			
Unknown/Unreported	237	16.78	22	6.63	

Table 2. Demographic and Malaria Positive Cases Among Patients Seen at Emory Healthcare, Emory TravelWell Center, and Both Locations.

	Emory	TravelWell	Both	Intergroup *p-value*
***n* (% female)**	1412 (45.1)	794 (58.1)	332 (55.1)	< 0.0001
age, mean (SD)	43 (16.3)	40 (14.4)	39 (12.4)	< 0.0001
malaria pos, *n* (%)	100[1] (7.1)	12[2] (1.6)	48[3] (14.5)	< 0.0001

Note: [1]missing for 4 patients, [2]missing for 32 patients, [3]missing for 1 patient.

The p-values for each within-group comparison are as follows:
% Female: Emory: 0.0002, TravelWell: <0.0001, Both: 0.0620
Age: Emory: <0.0001, TravelWell: <0.0001, Both: <0.0001
Malaria pos: Emory: <0.0001, TravelWell: <0.0001, Both: <0.0001

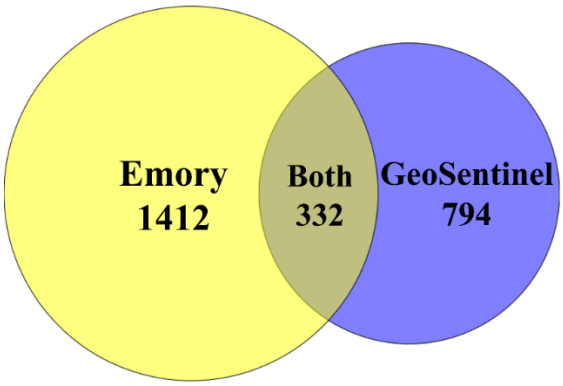

Figure 1. Proportional Venn diagram illustrating the sample sizes of patients seen within the Emory Healthcare Network (n=1412), Emory TravelWell Center (n=794), and both (n=333). The diagram highlights the overlap and unique contributions of each dataset to the study population.

Malaria-Positive Cases Among Groups

The primary hypothesis posited that the Emory TravelWell Center sees a minority of cases of acute illness in returned travelers compared to the entire Emory Healthcare system. This hypothesis is supported by the observation that, although more malaria cases are diagnosed in number within the broader Emory Healthcare network, malaria is over-represented in the "Both" category when considering proportions. Specifically, while 19% of the total malaria cases tested at Emory were also seen at TravelWell, the proportion of malaria diagnoses is notably higher in

the "Both" category compared to the total cases seen only within Emory Healthcare. This indicates a significant concentration of malaria-positive cases among patients who utilize both the Emory and TravelWell facilities.

A chi-square test for independence was conducted to investigate whether there was a significant difference in the number of malaria-positive cases among the three groups. The test resulted in a p-value of <0.0001, indicating that the differences in positive malaria tests among the three groups are statistically significant (Table 2, Figure 2). Additionally, while the choice of malaria testing as a focus for our study might seem pertinent due to its routine use as a default diagnostic test for sick returning travelers, which any provider can order without infectious diseases specialist approval, we must acknowledge a limitation in our data. Ideally, to fully justify malaria testing as a key investigative tool, we would need comprehensive data on the total number of acute febrile illness cases following international travel that underwent malaria smear testing. This data is challenging to collect comprehensively, which influenced our decision to focus on malaria as a proxy for assessing the burden of travel-related diseases.

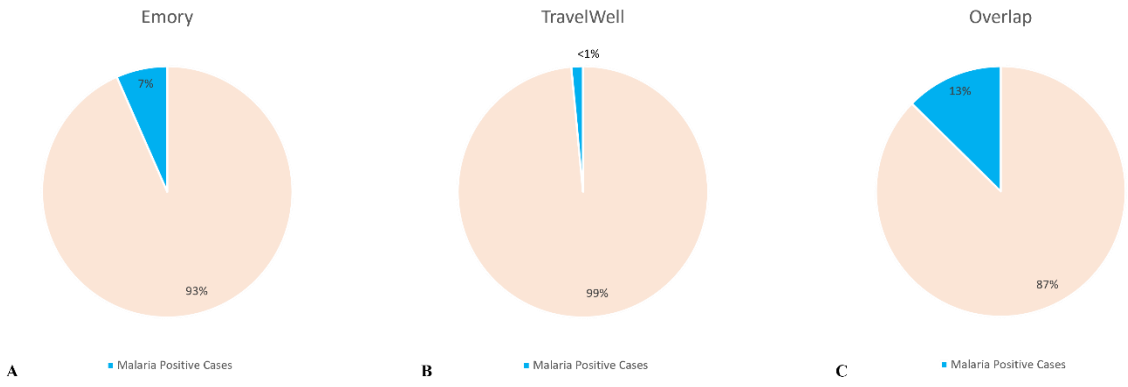

Figure 2. Proportion of malaria cases in A) all Emory-only cases, B) all TravelWell-only cases, and C) all cases of patients seen at Both Emory and TravelWell.

Discrepancies Between the "Both" Category and the Rest of the GeoSentinel Group

Our analysis aims to understand how the "Both" category (patients seen at both Emory Healthcare and the TravelWell Center) differs from the broader GeoSentinel group. The hypothesis posits that the TravelWell Center services are sought by a different patient population than those seen at Emory Healthcare as a whole.

The existence of the TravelWell Center and its affiliations with organizations like the CDC and Delta Airlines does not necessarily influence the cases recorded in GeoSentinel. Instead, limiting data capture to specialized referral clinics may skew what is entered into GeoSentinel compared to the entire returned traveler population. Knowledge about the TravelWell Center's services likely directs a specific subset of returning travelers to the facility, impacting the data captured and emphasizing the need for broader awareness and understanding of the center’s role in travel health. Consequently, this may result in a distinct demographic and clinical profile of patients within the GeoSentinel database, particularly in the "Both" category, as compared to the overall patient population at Emory Healthcare.

These observations underscore the need to consider the differences in patient populations when interpreting data from specialized travel health clinics versus general healthcare settings. Understanding these differences is crucial for accurately assessing travel-related health risks and developing targeted public health interventions.

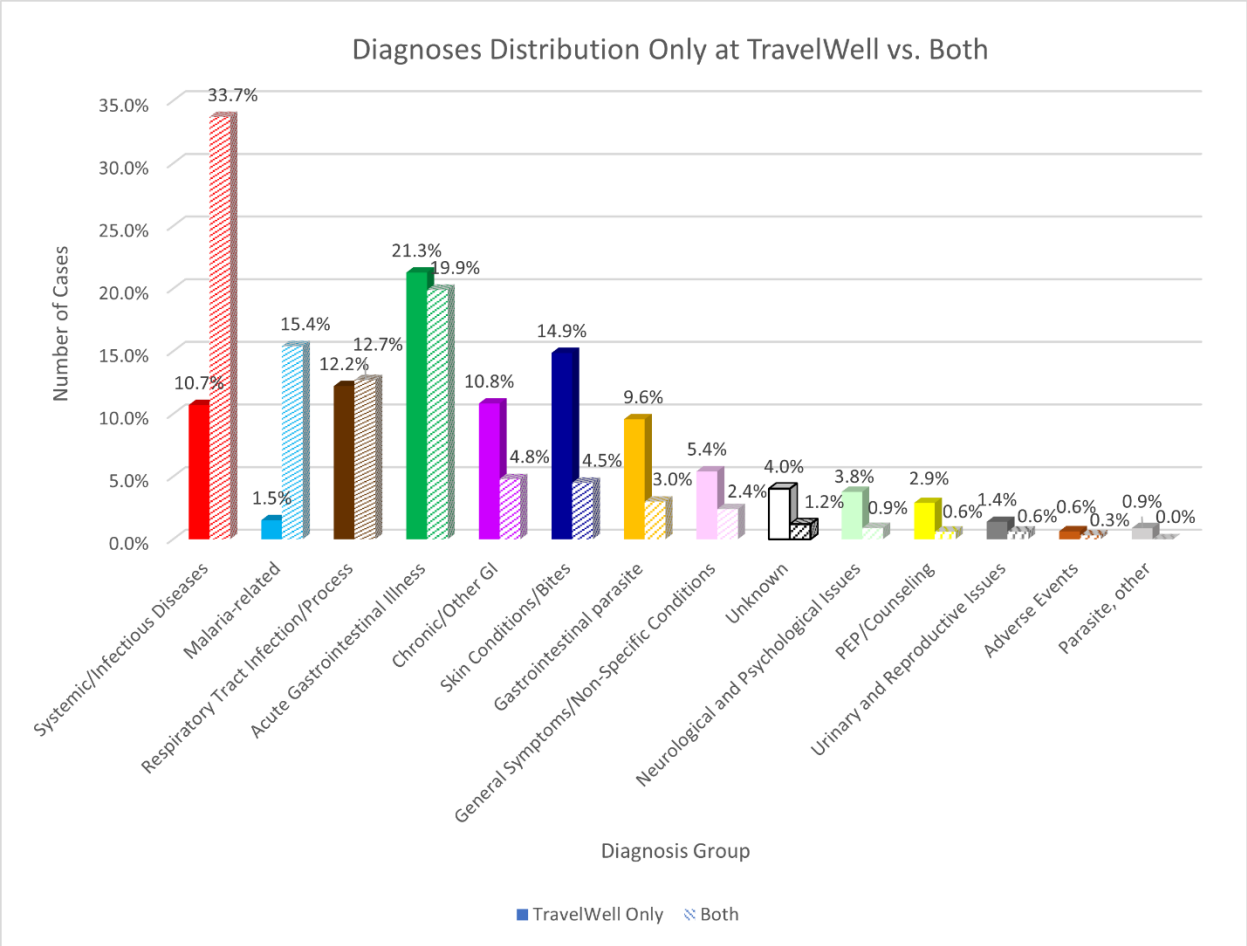

Figure 3. Comparison of the categorical diagnoses distribution between patients documented in GeoSentinel data with and without malaria testing: those seen exclusively at the TravelWell Center versus those seen at both Emory Healthcare and TravelWell. For detailed breakdowns of diagnoses within each category, refer to Tables A2 and A3.

Figure 3 illustrates significant differences in the distribution of diagnostic categories between patients seen at the Emory TravelWell Center and entered in the GeoSentinel database that had malaria testing (i.e. the “both” category) and those who did not have malaria testing performed. Further expansion of specific diagnoses within each category is detailed in Tables A2 and A3. To clarify the composition of the "both" category, of the total number entered, 58% (192 patients) were seen only at TravelWell, while 42% (140 patients) represent follow-up or subsequent visits within the Emory system or at TravelWell following an initial visit elsewhere. This categorization does not necessarily suggest more complex or severe cases among

overlapping patients. Instead, the prevalence of systemic and infectious diseases among these overlapping patients (33.7%) compared to TravelWell-only patients (10.7%) reflects the nature of conditions managed at these sites, not a higher complexity of cases. Malaria-related diagnoses are notably more common in the 'Both' category (15.4%) compared to TravelWell-only patients (1.5%), which aligns with our focus on malaria testing in the Emory search criteria. Additionally, conditions like chronic or other gastrointestinal illness and skin conditions/bites are more prevalent in TravelWell-only patients, at 10.8% and 14.9% respectively, compared to 4.8% and 4.5% among overlapping patients. The observations hint that the 'Both' category might approximate the Emory-only group in terms of case mix, an assumption based on comparative data analysis. However, this assumption remains conservative, and actual disparities could potentially be more pronounced, though current data limitations prevent further speculation. Despite these possible similarities, significant differences in specific health conditions between groups are evident, underscoring the need for targeted healthcare strategies tailored to the primary reasons for patient visits. These findings reveal distinct patterns in healthcare utilization and diagnostic outcomes, influenced by the type of healthcare facility accessed by returning travelers.

Other Findings

Both Emory/TravelWell Cases Analysis

In addition to the primary findings, the study provided detailed insights into the cases overlapping between Emory Healthcare and the TravelWell Center. It's crucial to clarify how these overlapping cases are defined for the purpose of this analysis. Specifically, if the GeoSentinel entry date matched the malaria test date, the visit was classified as an acute TravelWell visit. Out of the 332 cases categorized as 'Both,' analysis revealed that 140 cases

(42%) had visits that occurred 1-14 days apart, indicating follow-up or coordinated care between the two facilities. Conversely, the majority, representing 58% of the 'Both' group, involved patients who were seen or tested on the same day at both TravelWell and Emory Healthcare. Further breaking down the 140 cases with staggered visits, 74.3% were seen initially at an Emory facility and followed up at TravelWell, while the remaining 25.7% had their initial visit at TravelWell and subsequent follow-up at an Emory facility. This distribution highlights the dynamic interaction between the two healthcare settings in managing patient care, particularly for those requiring specialized follow-up related to travel-associated health issues. This observation indicates that initial evaluations or treatments at Emory Healthcare often led to subsequent follow-up or specialized consultations at the TravelWell Center, particularly when travel-related health concerns were identified (Figure 4).

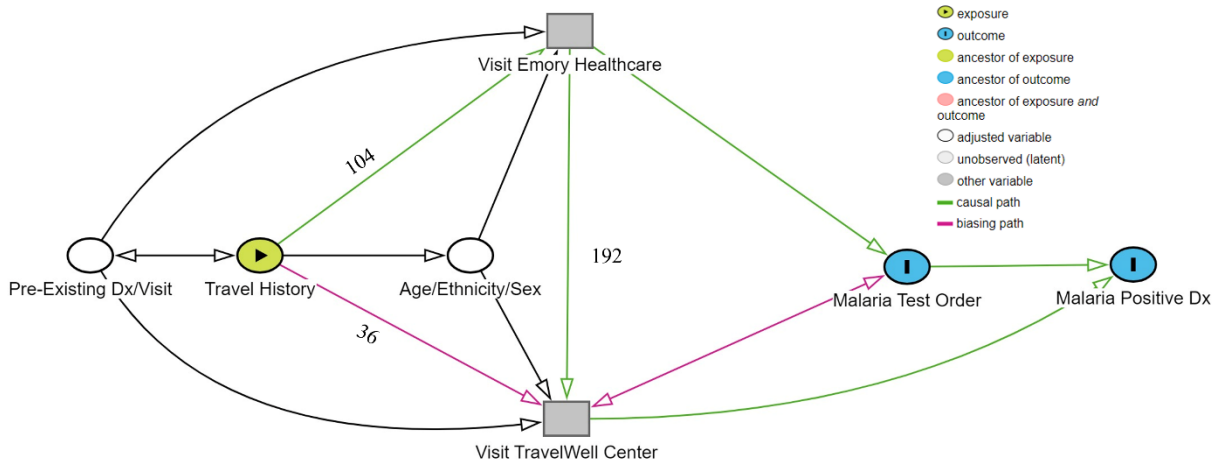

Figure 4. Directed Acyclic Graph (DAG) depicting the relationship pathway between exposure (travel history), malaria testing, and subsequent positive malaria diagnosis among returning travelers in the study population.

Multivariable Analysis of Malaria Diagnosis Predictors

A comprehensive multivariable analysis was conducted to identify the predictors most influential in determining the outcome of a positive malaria diagnosis among patients seen at

Emory Healthcare and those with encounters at both Emory and the TravelWell Center. This analysis utilized logistic regression to evaluate the effects of age, sex, ethnicity, and number of episodes on the likelihood of a malaria diagnosis.

Key Findings (Table 3):

- Age: In the Emory Healthcare group, each additional year of age slightly decreased the likelihood of a positive malaria diagnosis (Odds Ratio [OR]: 0.985, $p = 0.0352$), suggesting that younger individuals are at a higher risk. Conversely, age did not significantly affect malaria diagnosis likelihood in the Both group (OR: 1.019, $p = 0.1713$).
- Gender: Males were significantly more likely to be diagnosed with malaria compared to females in both groups, with males at Emory Healthcare over twice as likely (OR: 2.043, $p = 0.0018$) and in the Both group, more than three times as likely (OR: 3.29, $p = 0.0009$) to have a positive diagnosis.
- Ethnicity: African American or Black patients had significantly higher odds of receiving a malaria diagnosis in both settings, with odds ratios indicating over four times the likelihood compared to Caucasian or White patients, who served as the reference category. This finding was consistent across both groups, emphasizing a stark disparity in malaria incidence among ethnicities.
- Number of Episodes: The number of visits or episodes did not significantly impact the likelihood of a malaria diagnosis in either group, indicating that repeated healthcare encounters were not associated with an increased diagnosis rate of malaria.

The results emphasize the complex interplay of demographic factors in the epidemiology of malaria among returned travelers. The analysis reveals that younger males and African American or Black individuals have a higher incidence of malaria. This increased incidence is likely associated with inadequate healthcare prevention activities rather than inherent genetic or sex-hormone-based susceptibility. Identifying this demographic is crucial for focusing targeted interventions and preventive measures to reduce malaria cases effectively.

Interestingly, the analysis found no significant impact from the number of healthcare episodes on the likelihood of a positive malaria diagnosis. This suggests that malaria is often identified early in the healthcare process, supporting the efficacy of initial screening practices. However, it also raises a concern about the "learning" effect. Ideally, individuals who had a malaria scare during their initial (A) visit should exhibit far fewer malaria cases in subsequent (B/C) visits. The lack of a decrease in malaria cases in follow-up visits might indicate that patients are not sufficiently adopting preventive behaviors after their initial diagnosis. This highlights the need for improved educational efforts and follow-up practices to ensure that patients understand and implement effective malaria prevention strategies after their initial encounter with the healthcare system.

Implications of Multivariable Analysis Findings

The findings from the multivariable analysis provide critical insights into the factors that contribute to malaria diagnoses in a travel medicine setting. Understanding these factors can help refine diagnostic protocols and tailor educational and preventive strategies to address the needs of the most affected demographics. Moreover, the distinct patterns observed between single-location and overlapping healthcare visits may influence how healthcare providers approach the

evaluation and treatment of returned travelers, especially in settings like the TravelWell Center that specialize in travel medicine.

$$y = \propto + \beta_1(age) + \beta_2(sex) + \beta_3(ethnicity) + \beta_4(singlevisit)$$

Table 3. Multivariable analysis identifying predictors most important to the outcome (positive malaria diagnosis) for patients using information from the Emory Healthcare Data Warehouse and the GeoSentinel Surveillance Network.

		Emory Healthcare		Both	
Variable	**Level**	**Odds Ratio (95% CI)**	***p-value***	**Odds Ratio (95% CI)**	***p-value***
Age		0.985 (0.972, 0.999)	0.0352	1.019 (0.992, 1.047)	0.1713
Sex	1 = Male	2.043 (1.304, 3.202)	0.0018	3.29 (1.633, 6.627)	0.0009
	0 = Female	ref		ref	
Ethnicity	1 = African American or Black	4.381 (2.584, 7.428)	<.0001	4.574 (2.129, 9.828)	<.0001
	2 = American Indian or Alaskan Native	<0.001 (<0.001, >999.999)	0.9881	<0.001 (<0.001, >999.999)	0.9943
	3 = Asian	1.292 (0.47, 3.552)	0.6198	2.949 (0.703, 12.365)	0.1392
	4 = Hispanic	<0.001 (<0.001, >999.999)	0.9943		
	5 = Native Hawaiian or Other Pacific Islander	<0.001 (<0.001, >999.999)	0.9929		
	6 = Multiple	2.901 (0.345, 24.384)	0.3268	<0.001 (<0.001, >999.999)	0.9912
	7 = Patient Declines/Unknown/Unreported	0.86 (0.368, 2.009)	0.7271	1.342 (0.492, 3.66)	0.565
	0 = Caucasian or White				
Episodes	1 = multiple visits	1.517 (0.608, 3.788)	0.3719	1.419 (0.157, 12.791)	0.7552
	0 = single visit	ref		ref	
		# of obs in dataset = 1412 # of obs used = 1409		# of obs in dataset = 332 # of obs used = 331	

Summary

The results of this study provide significant insights into the age distribution, malaria-positive cases, other demographic differences, and expansion on the breakdown of other common diagnoses seen among returning travelers seen at Emory Healthcare, the TravelWell Center, and those with overlapping visits. The key findings are summarized as follows:

1. Age Distribution: There is a statistically significant difference in the mean ages among the three groups, with the TravelWell Center having the youngest mean age and Emory Healthcare the oldest.
2. Demographic Differences: The ability to capture some ethnicities versus others was highlighted, indicating which populations are not being adequately represented. Notably, very few Hispanic individuals were captured in the study data, with no Hispanic women recorded at all.
3. Malaria-Positive Cases: The rates of malaria-positive cases vary significantly across the groups, with the TravelWell Center having the highest percentage of positive cases.
4. Non-Malaria Diagnoses: Analysis of diagnostic outcomes for patients seen exclusively at the TravelWell Center compared to those seen at both TravelWell and other Emory Healthcare sites reveals distinct patterns in disease prevalence. Patients with overlapping healthcare visits exhibited higher rates of systemic and infectious diseases (33.7%) compared to those seen only at TravelWell (10.7%). Similarly, malaria-related diagnoses were significantly more common in the overlapping group (15.4%) compared to the TravelWell-only group (1.5%). While respiratory conditions were similarly prevalent across groups, acute gastrointestinal illnesses were slightly less common among overlapping cases. Conversely, chronic gastrointestinal conditions, skin conditions, bites,

and gastrointestinal parasites were predominantly diagnosed in TravelWell-only patients, indicating that these conditions are frequently managed within the specialized travel medicine setting.

5. Multivariable Analysis Findings: The multivariable analysis identified key predictors for malaria diagnosis, with younger age and male gender associated with increased likelihood of a positive malaria diagnosis. Ethnicity also played a significant role, with African American or Black patients more likely to receive a malaria diagnosis. These factors highlight critical areas for targeted interventions and preventive measures within travel medicine.
6. Integrated Healthcare Response: The analysis of overlapping cases revealed that a significant number of patients visited an Emory Healthcare site shortly before their visit to the TravelWell Center. This suggests a coordinated healthcare response to travel-related illnesses and underscores the importance of integrated surveillance and healthcare systems in managing and mitigating travel-related health risks.

Additionally, the analysis of overlapping cases revealed that a significant number of patients visited an Emory Healthcare site shortly before their visit to the TravelWell Center, suggesting a coordinated healthcare response to travel-related illnesses. These findings underscore the complex interplay of demographic factors, disease prevalence, and healthcare utilization among travelers. They highlight the need for continued surveillance, targeted public health interventions, and enhanced integration of healthcare services to improve health outcomes for international travelers.

Chapter V: Conclusions, Implications, and Recommendations

This study aimed to analyze and compare the demographics and health outcomes of returning travelers to the Atlanta area who were seen at Emory Healthcare facilities and the Emory TravelWell Center, which is part of the GeoSentinel Surveillance Network. The primary focus was to identify significant differences in age distribution and malaria-positive cases among these groups. The study employed a secondary data analysis of a retrospective dataset, utilizing data from Emory Healthcare and GeoSentinel. Major findings indicated statistically significant differences in the age distribution and the number of malaria-positive cases, emphasizing the importance of integrated surveillance and healthcare systems in managing travel-related health risks.

Age Distribution

The analysis revealed that the TravelWell Center tended to serve a younger demographic compared to Emory Healthcare. This could be attributed to the differing nature of services provided at each facility. Emory Healthcare data does not include the pediatric population because patients under the age of 18 are often seen at the Children's Hospital of Atlanta instead. As such, any analyses with Emory patients are limited with age range, unlike the GeoSentinel Network.

Other studies in travel medicine support these findings, indicating that travel clinics tend to serve younger populations due to the nature of travel-related health issues, which often affect younger, more mobile individuals.[11] The context of our findings aligns with these observations, suggesting that the age distribution differences are reflective of the specialized roles of these healthcare settings.

Malaria-Positive Cases

The analysis of malaria-positive cases showed significant differences among the three groups, with the TravelWell Center having the highest percentage of positive cases. This finding is consistent with the TravelWell Center's focus on diagnosing and treating travel-related illnesses, including malaria. The higher rate of malaria-positive cases at the TravelWell Center underscores the importance of specialized travel medicine services in managing diseases endemic to travel destinations.

Influence of TravelWell Center's Existence

The presence of the TravelWell Center within the GeoSentinel database significantly impacts the types and volumes of cases reported. Its contracts with major entities like the CDC and Delta mean that travelers returning with illnesses are more likely to be referred there, potentially skewing data towards certain demographics and conditions. This selective referral could create an education gap, where not all potential patients are aware of the Center's resources or choose to utilize its services.

Limitations

Despite the robust methodology, several limitations could affect the findings. First, each surveillance system has different methods and requirements for electronic health records (EHR). Emory's system can review identified records, while GeoSentinel stores deidentified data, creating potential challenges in accurately matching patient records across systems. Additionally, missing values and incomplete entries, especially in the GeoSentinel system, may have impacted the data quality. Incomplete entries could be aborted and later added as separate unique records, complicating data analysis.

These limitations may have introduced biases or inaccuracies in the findings. For example, the inability to perfectly match patients between systems could have led to overestimations or underestimations of certain health outcomes.

Strengths

The study also has several methodological strengths. The use of large original datasets allowed for a comprehensive analysis of a diverse population with varied travel histories. The inclusion of many variables enabled a detailed examination of demographic and health outcomes, providing a robust dataset for analysis. Furthermore, the study's focus on returning travelers in a major travel hub like Atlanta enhances the generalizability of the findings to other urban centers with high travel volumes.

Public Health Implications

The findings have significant implications for public health practice, particularly in the management of travel-related health risks. The observed differences in age distribution and malaria-positive cases highlight the need for targeted health interventions tailored to the demographics of travelers. The results underscore the importance of integrated surveillance systems that can seamlessly share information across different healthcare settings.

For public health theory, the study reinforces the necessity of specialized travel medicine services and the role they play in early diagnosis and treatment of travel-related illnesses. It also highlights the importance of continuous surveillance to monitor and respond to emerging health threats among travelers.

Future Recommendations

1. Harmonized Data Collection: Standardize data collection practices across both Emory Healthcare and the GeoSentinel network to improve data quality and comparability.
2. Capture Underrepresented Populations: Develop strategies to better capture data on populations currently underrepresented in the dataset, such as the Hispanic population, to ensure all traveler demographics are monitored.
3. Efficient Case Capture: Explore mechanisms to capture cases either while travelers are still abroad or immediately upon their return, rather than waiting for patients to present at healthcare facilities.
4. Education and Awareness: Increase awareness about the TravelWell Center's services among the general public and within corporate entities that frequently send employees abroad, to ensure all travelers know where to seek care.

Conclusion

The study successfully identified significant differences in age distribution and malaria-positive cases among returning travelers seen at Emory Healthcare, the TravelWell Center, and those with overlapping visits. These findings highlight the importance of specialized travel medicine services and integrated surveillance systems in managing travel-related health risks. While there are limitations, the methodological strengths and implications for public health practice underscore the value of this research. Continued surveillance, standardized data collection, and prospective studies are recommended to further enhance the management of travel-related health issues and improve public health outcomes.

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Appendix

Table A1. Categorical characteristics of patients seen March 2, 2009 - December 31, 2022 at the Emory TraveWell Center in comparison to patients who were seen at both an Emory campus and TravelWell using data pulled from GeoSentinel.

	TravelWell Center (n = 794)			Both (n = 332)		
Variable	**Frequency**	**Percent**	**Missing**	**Frequency**	**Percent**	**Missing**
Female	461	58.06		183	55.12	
Immigrant Status						
No	694	87.41		282	84.94	
Yes	100	12.59		50	15.06	
Expatriate Status						
No	776	97.73		326	98.19	
Yes	18	2.27		6	1.81	
Travel Reason			20			1
Education/Student	32	4.13		7	2.11	
Medical	4	0.52		1	0.30	
Migration	27	3.49		4	1.21	
Military	2	0.26		1	0.30	
Missionary/Humanitarian	158	20.41		73	22.05	
Occupational/Professional	218	28.17		94	28.40	
Other	7	0.90		5	1.51	
Research	11	1.42		8	2.42	
Retirement	1	0.13				
Tourism (Vacation)	263	33.98		89	26.89	
VFR (non-traditional)	7	0.90		2	0.60	
VFR (traditional)	44	5.68		47	14.20	
Clinical Visit			21			1
Migration Travel Only	18	2.33		4	1.21	
Seen After Travel	738	95.47		322	97.28	
Seen During Travel	17	2.2		5	1.51	
PreTravel Encounter			216			68
No	213	27.99		107	33.02	
Yes	365	47.96		157	48.46	

Table A2. Complete diagnoses collected from GeoSentinel for patients seen only at the TravelWell Center between March 2, 2009 and December 31, 2022.

Group	Diagnoses	Count
Malaria-Related	MALARIA, P. FALCIPARUM	5
	MALARIA, P. OVALE	1
	MALARIA, P. VIVAX	3
	MALARIA, SEVERE AND COMPLICATED	1
	MALARIA, SPECIES UNKNOWN	2
Acute Gastrointestinal Illness	ACUTE GASTROENTERITIS < 12 HOURS (FOOD POISONING)	1
	ACUTE GASTROENTERITIS > 12 HOURS	11
	C. DIFFICILE ASSOCIATED DISEASE	6
	CAMPYLOBACTER	3
	COLITIS	1
	DIARRHEA, ACUTE UNSPECIFIED	139
	DIARRHEA, ACUTE, OTHER SPECIFIED ORGANISM	1
	DYSENTERY, ACUTE UNSPECIFIED	2
	SALMONELLA PARATYPHI	1
	SALMONELLA SPECIES	1
	SALMONELLA TYPHI	1
	TYPHOID FEVER (ENTERIC FEVER), UNSPECIFIED	2
Gastrointestinal parasite	ASCARIS, INTESTINAL	4
	BLASTOCYSTIS Sp.	7
	CRYPTOSPORIDIUM	1
	DIENTAMOEBIASIS (D. FRAGILIS)	2
	ENTAMOEBA HISTOLYTICA, AMEBOMA	2
	ENTAMOEBA HISTOLYTICA, DIARRHEA/DYSENTERY	5
	ENTAMOEBA HISTOLYTICA, EXTRAINTESTINAL (e.g. liver abscess)	1
	ENTEROBIASIS (PINWORM)	2
	GIARDIA	29
	HOOKWORM (A. DUODENALE, N. AMERICANA)	2
	INTESTINAL PARASITE, UNSPECIFIED (PROTOZOA OR HELMINTH)	2
	PATHOGENIC INTESTINAL PARASITE, OTHER SPECIFIED (PROTOZOA OR HELMINTH)	1
	SCHISTOSOMIASIS, HUMAN SPECIES UNKNOWN	2
	SCHISTOSOMIASIS, S. HEMATOBIUM	2
	SCHISTOSOMIASIS, S. MANSONI	9
	STRONGYLOIDES, SIMPLE INTESTINAL	4
	TAPEWORM, D. LATUM	1
Chronic/Other GI	ABDOMINAL PAIN, UNSPECIFIED ETIOLOGY	5
	CIGUATERA INTOXICATION	1
	DIARRHEA, CHRONIC UNSPECIFIED	22
	FAILURE TO THRIVE (ALL AGES)	3
	GASTROINTESTINAL SYMPTOMS, OTHER	3
	GERD/NON-INFECTIOUS ESOPHAGITIS/NON-SPECIFIC GASTRITIS, PEPTIC ULCER DISEASE (H. PYLORI NEGATIVE)	1
	H.PYLORI	2
	INFLAMMATORY BOWEL DISEASE (CROHN'S OR ULCERATIVE COLITIS), PRE-EXISTING	1
	INFLAMMATORY BOWEL DISEASE, NEW ONSET OR EXACERBATION POST-TRAVEL (CROHN'S or ULCERATIVE COLITIS)	1
	IRRITABLE BOWEL SYNDROME NEW ONSET, POST-INFECTIOUS OR EXACERBATION	44
	IRRITABLE BOWEL SYNDROME, CHRONIC	2
	SPRUE, TROPICAL	1
Respiratory Tract Infection/Process	ADENOVIRUS 4/41	1
	BRONCHITIS, ACUTE	9
	CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)/CHRONIC BRONCHITIS	1
	COVID-19 (SARS-CoV-2)	1
	INFLUENZA - LIKE ILLNESS	14
	INFLUENZA A	2
	INFLUENZA B	3
	LATENT TUBERCULOSIS, POSITIVE IFN-RELEASE ASSAY (e.g. Quantiferon or T-SPOT) (NOT ACTIVE DISEASE)	8
	MYCOBACTERIUM TUBERCULOSIS, EXTRAPULMONARY, OTHER	3
	OTITIS EXTERNA	1
	OTITIS MEDIA, ACUTE	3
	PHARYNGITIS, OTHER OR UNSPECIFIED	3
	PHARYNGITIS, STREPTOCOCCAL	1
	PNEUMONIA, ATYPICAL/NON-LOBAR, UNSPECIFIED	2
	PNEUMONIA, LOBAR, UNSPECIFIED	3
	RESPIRATORY TRACT INFECTION (UPPER) (no known etiology)	38
	SINUSITIS, ACUTE	2
	TONSILLITIS	2
Systemic/Infectious Diseases	CHIKUNGUNYA VIRUS INFECTION	3
	CYTOMEGALOVIRUS	2
	DENGUE, UNCOMPLICATED	11
	ENDOCARDITIS	1
	EPSTEIN-BARR VIRUS	2
	FEBRILE ILLNESS, UNSPECIFIED (< 3 WEEKS)	4
	HEPATITIS A, ACUTE	1
	HEPATITIS, ACUTE UNSPECIFIED (<3 MONTHS)	2
	LYME DISEASE - ACUTE OR EARLY DISEASE (INCLUDING ERYTHEMA CHRONICUM MIGRANS AND OTHER MANIFESTATIONS)	1
	MONONUCLEOSIS, UNSPECIFIED	2
	MUMPS	1
	VIRAL SYNDROME (WITH/WITHOUT RASH)	48
	ZIKA VIRUS, VECTOR-ACQUIRED	7

Parasite, other	CHAGAS DISEASE, CHRONIC	1
	FILARIA, LOA LOA	3
	FILARIA, SPECIES UNKNOWN	2
	LEISHMANIA, VISCERAL	1
Skin Conditions/Bites	BITE, ANIMAL OTHER	1
	BITE, DOG	3
	BITE, MONKEY	3
	BITE, SPIDER	1
	BITE, TICK	3
	CERCARIAL DERMATITIS (SWIMMER`S ITCH)	1
	CUTANEOUS LARVA MIGRANS, HOOKWORM-RELATED	2
	ERYTHEMA MULTIFORME	1
	FUNGAL INFECTION (SUPERFICIAL/SUBCUTANEOUS/CUTANEOUS MYCOSIS)	3
	HERPES ZOSTER, SHINGLES	4
	INSECT OR OTHER ARTHROPOD BITE/STING (WITH OR WITHOUT SUPRAINFECTION)	19
	LEISHMANIA, CUTANEOUS	9
	LEPROSY	17
	MPOX (formerly MONKEYPOX)	5
	MYCETOMA/MADURA FOOT	1
	MYIASIS	3
	RASH, ATOPIC DERMATITIS, ECZEMA	5
	RASH, DERMATITIS (incl contact dermatitis)	11
	RASH, UNKNOWN ETIOLOGY (NON-FEBRILE)	11
	RASH, URTICARIA, OR ANGIOEDEMA	4
	SKIN AND SOFT TISSUE INFECTION (SKIN ABSCESS or SECONDARY BACTERIAL INFECTION OF EXISTING LESION)	4
	SKIN AND SOFT TISSUE INFECTION, SUPERFICIAL: IMPETIGO, FOLLICULITIS, FURUNCLE, CARBUNCLE, PARONYCHIA, ECTHYMA	2
	SKIN AND SOFT TISSUE INFECTION: ERYSIPELAS, CELLULITIS, GANGRENE	4
	WARTS, NON-GENITAL	1
Neurological and Psychological Issues	ANXIETY DISORDER/PANIC ATTACKS	1
	DELUSIONAL PARASITOSIS	6
	ENCEPHALOPATHY, UNSPECIFIED	1
	FATIGUE < 1 MONTH (NOT FEBRILE)	2
	FATIGUE >=1 MONTH (NOT FEBRILE)	3
	GUILLAIN BARRE SYNDROME	1
	HEADACHE	3
	NEUROCYSTICERCOSIS	4
	PSYCHOSIS	1
	STRESS - POST TRAUMATIC STRESS DISORDER (PTSD)	1
	STRESS: MARITAL, WORK-RELATED, OR OTHER	3
	SYNCOPE	2
	VERTIGO	2
General Symptoms/Non-Specific Conditions	ANEMIA	3
	ARTHRALGIA/BONE PAIN	2
	ARTHRITIS, NONSEPTIC	1
	DEHYDRATION	1
	EOSINOPHILIA	4
	EXPOSURE, DOG, NON-BITE	5
	EXPOSURE, MONKEY, NON-BITE	4
	HEALTHY	6
	JET LAG	1
	LYMPHADENITIS, LYMPHADENOPATHY	1
	NAUSEA, VOMITING, UNSPECIFIED ETIOLOGY	1
	Other	11
	WEIGHT LOSS	3
PEP/ Counseling	HIV PEP (post exposure prophylaxis)	1
	PPD or IFN-RELEASE ASSAY CONVERSION	1
	RABIES PEP (post exposure prophylaxis)	14
	ZIKA SCREENING	7
Urinary and Reproductive Issues	ABNORMAL URINALYSIS (HEMATURIA, PROTEINURIA)	1
	CYST	1
	PREGNANCY	1
	PROSTATITIS (ACUTE OR CHRONIC)	1
	PYELONEPHRITIS	1
	URINARY TRACT INFECTION (UTI), ACUTE	5
	VAGINITIS	1
Adverse Events	ADVERSE EVENT, DRUG-RELATED [NOT SERIOUS]	4
	SERIOUS ADVERSE EVENT (SAE), VACCINE-RELATED (INCLUDING YF)	1
Unknown	(blank)	32
	Total	794

Table A3. Complete diagnoses collected from GeoSentinel for patients seen at both an Emory Healthcare site and the TravelWell Center between March 2, 2009 and December 31, 2022.

Group	Row Labels	Count
Malaria-related	MALARIA, P. FALCIPARUM	36
	MALARIA, P. MALARIAE	1
	MALARIA, P. OVALE	5
	MALARIA, P. VIVAX	5
	MALARIA, SPECIES UNKNOWN	4
Acute Gastrointestinal Illness	ACUTE GASTROENTERITIS > 12 HOURS	7
	C. DIFFICILE ASSOCIATED DISEASE	3
	CAMPYLOBACTER	7
	DIARRHEA, ACUTE UNSPECIFIED	46
	DYSENTERY, ACUTE UNSPECIFIED	1
	SALMONELLA SPECIES	1
	SALMONELLA TYPHI	1
Gastrointestinal parasite	ASCARIS, INTESTINAL	1
	GIARDIA	6
	PATHOGENIC INTESTINAL PARASITE, OTHER SPECIFIED (PROTOZOA OR HELMINTH)	1
	STRONGYLOIDES, SIMPLE INTESTINAL	2
Chronic/Other GI	ABDOMINAL PAIN, UNSPECIFIED ETIOLOGY	1
	CHOLECYSTITIS, CHOLANGITIS, OTHER BILIARY DISEASE OR PANCREATITIS	2
	DIARRHEA, CHRONIC UNSPECIFIED	7
	DIARRHEA, CHRONIC, OTHER SPECIFIED ORGANISM	1
	IRRITABLE BOWEL SYNDROME NEW ONSET, POST-INFECTIOUS OR EXACERBATION	5
Respiratory Tract Infection/Process	BRONCHITIS, ACUTE	1
	INFLUENZA - LIKE ILLNESS	10
	INFLUENZA A	5
	INFLUENZA B	2
	OTITIS MEDIA, ACUTE	1
	PHARYNGITIS, OTHER OR UNSPECIFIED	1
	PHARYNGITIS, STREPTOCOCCAL	2
	PNEUMONIA, ATYPICAL/NON-LOBAR, UNSPECIFIED	2
	PNEUMONIA, LOBAR, UNSPECIFIED	3
	RESPIRATORY TRACT INFECTION (UPPER) (no known etiology)	13
	SINUSITIS, ACUTE	2
Systemic/Infectious Diseases	BACTEREMIA	2
	CHIKUNGUNYA VIRUS INFECTION	1
	CYTOMEGALOVIRUS	2
	DENGUE, COMPLICATED	1
	DENGUE, UNCOMPLICATED	7
	EPSTEIN-BARR VIRUS	1
	FEBRILE ILLNESS, UNSPECIFIED (< 3 WEEKS)	14
	FEBRILE ILLNESS, UNSPECIFIED (FEVER OF UNKNOWN ORIGIN) (>=3 WEEKS)	3
	HEPATITIS, ACUTE UNSPECIFIED (<3 MONTHS)	2
	LEPTOSPIROSIS	2
	MONONUCLEOSIS, UNSPECIFIED	2
	REACTIVE ARTHRITIS	2
	RICKETTSIA, TICK BORNE SPOTTED FEVER (R. AFRICAE, R. CONORII, R. RICKETTSII, AND OTH	5
	VIRAL SYNDROME (WITH/WITHOUT RASH)	66
	ZIKA VIRUS, VECTOR-ACQUIRED	2
Skin Conditions/Bites	HERPES SIMPLEX	1
	HERPES ZOSTER, SHINGLES	1
	INSECT OR OTHER ARTHROPOD BITE/STING (WITH OR WITHOUT SUPRAINFECTION)	3
	LEPROSY	1
	MYIASIS	3
	RASH, UNKNOWN ETIOLOGY (NON-FEBRILE)	2
	RASH, URTICARIA, OR ANGIOEDEMA	1
	SKIN AND SOFT TISSUE INFECTION, SUPERFICIAL: IMPETIGO, FOLLICULITIS, FURUNCLE, CA	2
	SKIN AND SOFT TISSUE INFECTION: ERYSIPELAS, CELLULITIS, GANGRENE	1
Neurological and Psychological Issues	FATIGUE < 1 MONTH (NOT FEBRILE)	1
	HEADACHE	1
	MENINGITIS, VIRAL/ASEPTIC, UNKNOWN ETIOLOGY	1
General Symptoms/Non-Specific Conditions	LYMPHEDEMA	1
	ARTHRALGIA/BONE PAIN	1
	EXPOSURE, MONKEY, NON-BITE	1
	HEALTHY	2
	LYMPHADENITIS, LYMPHADENOPATHY	1
	Other	2
PEP/ Counseling	PPD or IFN-RELEASE ASSAY CONVERSION	1
	ZIKA SCREENING	1
Urinary and Reproductive Issues	URINARY TRACT INFECTION (UTI), ACUTE	1
	VAGINITIS	1
Adverse Events	ADVERSE EVENT, DRUG-RELATED [NOT SERIOUS]	1
Unknown	(blank)	4
	Total	332