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Assessing the Effect of Fever and Influenza like Illness on Human Movement in Iquitos Peru

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B.S., B.A., Arizona State University, 2014

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An abstract of

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of
Master of Public Health
Epidemiology

2016

Abstract

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By Zachary Heth

Background: Influenza like illness is a common global disease which causes broad public health problems. It is however poorly understood in ambulatory and non-healthcare seeking populations. Movement within urban centers is also poorly understood when looking at resource poor areas, the effect of influenza like illness and fever on movement is of particular interest in understanding the spread of infections.

Objective: The purpose and aim of this study is to examine the relationship between circulatory movement in a developing urban area and what effect having a fever and experiencing an ILI may have on said movement. This study also aimed to look at the application of iButtons as a means of tracking peripheral skin temperature over time.

Methods: Participants were enrolled based on the presence of fever. Once enrolled they were followed for seven days during which time they were interviewed daily about symptoms. Participants were also given GPS and iButton data loggers to record movement and peripheral skin temperature.

Results: ANOVA testing in which random effects and mixed effects were taken account of showed no significant difference between those experiencing fever and those not experiencing fever when it came to any of the three distance measures distance (maximum distance F=0.59 p-value=0.4453, average distance F=0.82 p-value=0.3683, total number of GPS points greater than 10m from home F=1.03 p-value=0.3142). When compared to tympanic measures for participants iButton measures were found to have no statistically significant association even with random and mixed effects modeling (p-value = 0.0922).

Discussion: Though there was found to be no significant relationship between all people and who either were or were not febrile and movement, there was significance among individuals based on if they had a fever. It was also of note that many of the assumptions about non-healthcare seeking and ambulatory care populations made in more developed areas were found to be true in Iquitos, Peru. The reasons behind both the significant difference and the contradiction of assumptions are not yet fully understood as the data set was limited both by missing data and a small sample size.

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Acknowledgements

I would like to thank the amazing friends I have made here at Rollins without whom I would have been unable to spend so many night in the GCR basement. I would also like to thank my friends and family for their support throughout my entire academic life.

I would also like to thank my advisor, Gonzalo Vazquez-Prokopec, who has helped me learn so much about what it is I want to do in public health and helped me to grow as a researcher. A special thanks should also be given to those at UC Davis and the researchers at NAMRU-6 who collected this data. Last, but not least, I would like to thank the participants of this study.

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Introduction

The way in which humans move throughout urban areas is important for a variety of reasons, it informs and shapes transportation and communication networks, informs urban development, and aids in both the spread and prevention of infection (1-9). Broadly speaking there are two main types of human movement that are of interest when discussing the spread of infection. The first, is migratory movements, which are large scale movements occurring between continents, countries, and regions it is migratory movement which can lead to pandemics and the global spread of infection as well as the introduction or reintroduction of a disease into an area (8). The second type of movement is circulatory which, is movement at a smaller scale, this may include movement between rural and urban areas, intra urban movement, or neighborhood movement (8). Circulatory movement is important for the spread of disease locally in cities and urban areas it is important in the spread of vector borne and contact associated diseases throughout a city and leads to introduction of disease into different neighborhoods (8). Movement though, is not the sole reason infections spread, as many diseases require direct human to human contact, or for humans to be in close proximity to one another. Movement is a behavior associated with contact patterns, which play a central role in the spread of infection as an infected host interacts with non-infected individuals (10). Since most populations do not have high amounts of random contact mixing, it is these networks of contact that too play an important role in the spread of infection (10).

Most studies have focused on human movement in developed cities, and have found that people have days which are dominated by a lack of variability in movement (11-14). However a study done in Iquitos, Peru showed that people in resource poor urban areas do not necessarily follow this idea of routine movement; instead, for several potential reasons such as loosely structured economies and unstructured daily routines, movement is more variable and less dominated by a work-home routine than in highly developed urban centers (2). This random movement may actually contribute more to the spread of vector borne diseases and influenza like illnesses (among others) in resource poor urban areas, and as resource poor urban areas make up the majority of the world's urbanization it is of increasing importance to understand what causes the movement and contact patterns of people living in such environments and what factors may affect circulatory travel (2, 15, 16).

Influenza like illness (ILI) is of keen interest in Iquitos, Peru because ILI is a global public health problem and though influenza and ILI are understood well in more temperate areas where there is a distinct seasonality, transmission in the tropics and the effects of ILI in the tropics is poorly understood (17). Very few studies have looked at the effects of ILI on hospitalized or ambulatory populations, and even fewer have looked at the characterization of ILI in populations that sought no medical attention (18-22). Most of these studies have also focused predominantly on costs associated with ambulatory care in highly developed non-tropical areas. The epidemiology of ILI in Iquitos shows that ILIs are endemic year round with different influenza types showing seasonality and there is an incident rate of 46.7 per 1000 person years once adjusted for age (17). In the region of Latin America and the Caribbean, year round influenza is a problem, and one study found that the region has an annual rate of 36,080 influenza like illnesses per 100,000 person years (20). The same study found that significant factors for contracting

ILI included being under the age of 5 years old and living in crowded homes (defined as having 2+ people per room) (17).

Ambulatory care for ILI is of increasing importance and interest. This interest is in part due to the fact that surveillance for ILI in ambulatory care settings has a tendency to misdiagnose and thus underrepresent ILI, because syndromic surveillance which is commonly used is fast but has a positive predictive rate of only 60-80% (23, 24). Having a correct diagnosis of ambulatory cases of ILI is particularly important because those who may be asymptomatic or have mild symptoms can still shed virus, misdiagnosis of ILI may also lead to patients being prescribed antibiotics which commonly occurs (25-27). In addition, the effect of ambulatory fever and the effects of influenza like illness over time of illness have not been well studied in resource poor urban areas. This is in part due to the fact that most methods of taking temperature are at least slightly invasive or time consuming. New technology though may be promising in recording temperature 24 hours a day with minimal invasiveness, the iButton is a temperature data logger ("iButton DS1922L", Maxim CA) which has been used in limited health related studies (28-38). Generally these studies have been small with the number of participants ranging from seven to 70 (34, 35). These iButton studies have also predominantly focused on foot or wrist temperatures and have primarily been done in highly controlled research settings (31-33, 36, 37). Though iButtons have been shown to be comparable to wired skin temperature units, and have been reported as having high accuracy (31, 32, 34-36). Most studies have only looked at limited time windows in controlled environments ranging from 40 minutes to three days, many sleep studies have used iButtons for single nights (31-37). The potential for iButtons to serve as long term temperature measuring devices is something of great interest, and can fill a needed knowledge gap when it comes to looking at ambulatory fever. This is so, because iButtons have been shown to provide reliable measures of peripheral skin temperatures, a proxy for core body temperature. Being able to record temperature along with semi structured interviews, and GPS units will increase our ability to look at the effect fever has on ambulatory care and non-healthcare seeking populations movement through urban areas.

The purpose and aim of this study is to examine the relationship between circulatory movement in a developing urban area and what effect having a fever and experiencing an ILI may have on said movement. This study also aimed to look at the application of iButtons as a means of tracking peripheral skin temperature over time.

Methods

Study Area

The study area is the city of Iquitos, Peru (73.2ºW, 3.7 ºS, 120m above sea level), located in the north-eastern Department of Loreto; Iquitos is an isolated city bordered by three rivers and the Amazon Rainforest making it only accessible via plane or boat (1, 2, 39). Iquitos has a high population density with roughly 400,000 inhabitants living in a roughly 30 sq. Km urban area (2, 38). Economic activity in Iquitos is dominated by lumber, oil, fishing, agriculture, tourism, and small commercial enterprises with a considerable amount of economic activity done informally with roughly 33.4% of the economically active population either unemployed or engaged in informal economic activity(1, 2, 39). With limited personal automobiles and public transportation most intra-urban travel in Iquitos is done through personal motorcycles, motorized rickshaws, or limited bus lines running throughout the city (2, 39). Being a tropical environment Iquitos experiences an average daily temperature of 25.8ºC (22.0-32.2ºC) with limited temperature changes throughout the year; and the average rainfall in Iquitos is 3.6m occurring throughout the year (17). Influenza like illness is reported in Iquitos throughout the year with lows typically occurring from August to January and peaking from March to May (17). Iquitos has been the site of long term projects focused on health and vector borne disease involving the University of California at Davis, the U.S. Naval Medical Research Unit 6-Iquitos Group, and Emory University for over 15 years (39).

Study Design

Participants were recruited through active febrile surveillance studies currently happening Iquitos (process depicted in **Figure 1**). To be recruited participants had to have a fever of 38 ºC or higher, once identified as febrile and consent was obtained iButtons and GPS were used for seven days to track temperature and location, respectively. During the tracking period participants were visited daily to be interviewed about symptoms and use of antipyretics. Participants tympanic temperature was taken twice daily in each ear (using Braun Thermoscan Ear Thermometer with ExacTemp Technology, IRT450USSM). GPS data loggers were replaced every three days. Case definitions for influenza like illness (ILI) were based on European Centre for Disease Prevention and Control recommended surveillance standards (40). Upon completion of the one week period a retrospective survey was given to characterize movement of participants.

Instruments

Three distinct instruments were used to obtain information: 1. GPS data loggers (“i-gotU GT120”, Mobile Action Technology Inc.), 2. Semi-Structured Interviews (SSIs), and 3. Skin temperature data loggers (“iButton DS1922L”, Maxim CA).

The GPS data loggers were used to continuously track the movements of participants for a seven day period. The accuracy of these units is 4.4m for point data and 10.3m for line data, the acceptability of using these GPS data loggers and their effectiveness in deployment have been described in previous studies (1, 41). Reasoning for choosing these GPS units has been reported in previous studies, but includes: 1. data storage capacity, 2. spatial accuracy, 3. durability and water proofing, 4. light weight, 5. wide acceptability of carrying mechanism, 6. low maintenance on part of study participants, 7. low cost, and 8. security (38). GPS units were programmed at a 2 min collection frequency and ran for 24 hours. Participants were provided with a charger for the GPS units so they could charge them before use.

Different SSIs were conducted throughout the study period using tablets and mobile data collection platforms ODK and Commcare HQ (Dimagi, inc.). When participants were enrolled they completed a registration and socio-demographic survey to provide different indicators of socioeconomic status. A daily survey was conducted to provide information on symptoms and severity of those symptoms. At the end of the period a retrospective survey was done to provide information on where participants had visited and for how long they visited various locations throughout the study area. The design and development for this SSI has been described previously (38).

iButton data loggers were affixed via hypoallergenic tape (Tegaderm) to record axillary temperature of participants. This placement was decided on following a pilot study and focus group to determine acceptability and use of iButtons among residents of Iquitos. iButtons have been used in several studies previously and found to accurately record peripheral skin temperatures (28-31, 38). These temperature loggers where chosen because 1. They were highly acceptable to the population of Iquitos, 2. They had the desirable range of 15-46ºC, 3. They have been found to have high accuracy, 4. They are non-invasive, light weight, and waterproof, 5. They have password protection, and 6. They have high memory capacity (28-31). iButtons were programed to record axillary skin temperature every 2 minutes continuously for the study period.

Study Analysis

Variables under selection included indicators of SES, severity of symptoms (reported intensity and calculated average intensity for each symptom by day), type of symptoms (dichotomous yes, no variable), and use of antipyretics (dichotomous yes, no variable). Analysis of the SSIs was done in SAS version 9.4 to determine which variables held a significant effect on movement.

To determine variable significance Pearson's chi-squared was used when comparing frequencies that were not time dependent or involved multiple observations for single individuals. Fischer's exact test, was used for ANOVA testing where mixed and random effects were taken into account, as well as for model building for general linear mixed models. Student's T-test, was used to compare means that were not time dependent or involved multiple observations for single individuals. General linear modeling taking into account mixed effects and random effects was used in bivariate analysis and model building. For all tests, a p-value < 0.05 is considered statistically significant. Modeling of the data was done through the use of mixed effects and random effects modeling to allow for the multiple days of observation and measurement each participant has. Collinearity was assessed for and determined by using a Condition Index value > 30 and a Variance Inflation Factor > 0.5, testing for the best fitting model was attempted though backwards elimination, but proved impossible due to overparameterization so forward building methods were used (42).

All GIS related work was conducted in ArcGIS 10.3 (ESRI, Redlands, CA). Use of ArcGIS involved the reading and cleaning of GPS data collected from the GPS Data

Loggers, and mapping of the data collected (data management has been described elsewhere) (2). All data is projected in WGS 1984 UTM Zone 18S. Distance from home was calculated three ways as, 1. Total number of GPS points greater than 10m from home 2. Average distance traveled per day and 3. Maximum distance traveled per day. Statistical analyses were done in SAS 9.4 using Students T-Tests and ANOVA with mixed effects to determine differences in distance traveled between those who were and were not febrile as well as to assess differences in distance traveled for individuals during the study time period.

Ethical Approvals

The study was approved by the IRB of Naval Medical Research Unit No. 6 who did the data collection and with whom Emory has a common IRB agreement. Human subject's approval was granted for this project on the 3rd of March 2015.

Results

Table one shows the demographic breakdown for the Semi-Structured Interviews and population of interest in Iquitos. The majority of participants were Female (67.86%) and there was a median age of 31 (IQR=34). Though there were relatively low levels of unemployed participants (3.70%) and of participants engaged in agriculture (7.41%), most participants were either students (37.04%) or Housewives (37.04%). The initial appearance of health for participants as determined by a medical professional was recorded prior to the start of the study and generally, 92.86%, of participants appeared to be of average health. All participants were found to have average or better hydration and only two participants were determined to have lower than average nutrition. Other general health factors considered included perceived stress which showed 21.74% of participants said they had stress. Most participants had either no preconditions upon enrolling (53.57%) or one precondition (32.14%).

Medicine use during the study period changed over time as fewer people reported using either paracetamol or another drug for illness (day one, 80% used paracetamol by day four less than half did as seen in **Table 2**). The maximum number of doses of paracetamol reduced over time as well from a max of six doses on day one to a low of only one dose on day four. Overall 95% of the study population reported a positive effect from paracetamol (**Table 2)**. **Table 3** shows the frequency of reported symptoms over the enrollment period of participants, later surveys have a loss to follow up and frequencies become a reflection of shrinking n values. The mean intensity of symptoms (defined as the average of reported symptom intensity per day across participants) tends to decrease over time (**Figure 2**). The largest drop in symptom intensity comes from malaise which began with a self-reported average intensity of greater than 5 on day one and dropped to one by day six. Malaise along with abdominal pain lasted longest among participants, shortest lasting symptoms included photophobia and chest pain each only occurring one day during the study period. The symptoms affecting most participants at some point in the study included fever, chills, weakness, anorexia, headache, retro orbital pain, body pain, and muscle pain as seen in the first column of **Table 3** where reported frequencies were over 50%. As seen in **Table 4** the frequency of participants who sought medical attention was very low (17.86%) despite 39.39% saying their illness caused a major change in activity and 46.43% claiming a minor change in activity. **Table 4** also shows that for most people symptoms were not constant throughout the day they were experienced.

When looking at what if any differences exist between those who sought medical attention for their symptoms (ambulatory care) and those who did not (non-healthcare seeking) it was found that there were no significant differences. There was no significant difference in the mean number of symptoms reported (defined as the mean number of symptoms from the maximum reported symptoms for each unique ID) (p-val=0.5597), nor was there any significant difference in the duration of symptoms between groups (reported in days) (fever p-value= 0.5597, chills p-value=0.4828, fatigue p-value=0.5763, headache p-value=0.3237, retro orbital p-value=0.8801) (median number of days duration for symptoms is displayed in **Table 5**). Along these lines no significant difference was found when looking at activity level (p-value=0.6067), intensity of symptoms (p-value=0.0723), or paracetamol use (p-value=0.2113) between those who reported seeking medical care for symptoms and those who did not.

Overall, the average core body temperature changed significantly throughout the period of enrollment for participants, this was determined by using an ANOVA accounting for both mixed and random effects (F-value = 23.17, p-value <0.0001). Further ANOVA testing with Tukey adjustment (and accounting for mixed and random effects) revealed a significant difference lay between the first two days and the rest of the time in enrollment as core body temperature decreased from day zero (first day of enrollment) to day three where it remained statistically insignificant relative to the other days as seen in **Figure 3.** The average of daily temperature within days and overall was found to be normal through looking at plots of the jackknife residuals as suggested in the literature for assessing normality in mixed and random effects models (43). This pattern is also true no matter when temperature was assessed as no significant difference existed between morning and afternoon temperature readings as seen in **Figure 4** (p-value = 0.3481). When looking specifically at only fever over time (**Figure 5**), the mean temperature of fever lowers over time (F=3.53 p-value =0.0017). Further ANOVA testing with Tukey adjustment (and accounting for mixed and random effects) revealed that the only significant difference in variance between days was between the first day and the rest of the days during enrollment, as with temperature as a whole the fever data also was shown to be normal when plotting jackknife residuals.

Analysis of the iButton data collected involved simple and generalized linear mixed model regressions with tympanic temperature as the gold standard, taking into account mixed effects and potential random effects. Higher order modeling (p-value = 0.0922) produced a better result than simple linear regression (p-value = 0.4932) however, both were similarly insignificant. Both models measured the average core temperature against the iButton temperature, the higher order model controlled for the random effect associated with the multiple measures for participants. The change in iButton temperature over time can be seen in **Figure 6** and is consistently lower than that of the tympanic temperature.

Using the acquired GPS data, it was shown that no significant difference exists between those who were febrile and those who were not when it comes to distance in any of the three measured ways, ANOVAs were run with mixed and random effects taken into consideration and looking at plots of residuals for normality, log transformations were used for all three measures of distance (maximum distance F=0.59 p-value=0.4453, average distance F=0.82 p-value=0.3683, time spent away from home F=1.03 p-value=0.3142). **Figure 7** depicts the spatial layout of participants by fever. Looking at differences within individuals and not as a group revealed seven individuals who did have significant differences in the average distance traveled between when they were febrile and when they were not febrile all p-values for the paired t-test were below 0.05 and considered significant t-test results and p-values for tests are located in **Table 6**.

Full modeling of the data was limited to 11 unique participants. Bivariate analysis between the outcome of distance (defined as average distance per day) and the various symptoms and semi-structured interview data showed 14 significant or borderline significant variables (**Table 7)**. Assessing for collinearity reduced this number to 10 variables of interest: fever, average intensity of symptoms, fever intensity, weakness intensity, abdominal pain intensity, paracetamol doses, cough, diarrhea, bad taste, and abdominal pain. Modeling through the backwards elimination method resulted in overparameterization of the model and modeling required a forward addition strategy be used instead. Taking mixed and random effects into account the best model created included the beta coefficients fever, average intensity of symptoms, fever intensity, and paracetamol doses (**Table 8)**. However none of the beta coefficients were found to be significant.

Discussion

Influenza and influenza like illnesses (ILI) have the proven capacity to spread around the world and cause global pandemics (44). Annually they affect millions of people and cause a large cost not only in money for treatment but time lost from work, as well as increasing morbidity (18-20, 22, 45). However, even with their global importance influenza and ILI are not well studied in ambulatory and non-healthcare seeking populations (18). This study is the first to look specifically at how fever associated with ILI and potential influenza affects the movement of individuals in a resource poor urban environment, it is also one of the first to look at the behaviors and characteristics of non-healthcare seeking and ambulatory care patients in the Amazon basin.

Medicine use in the study was shown to reduce over time as symptoms decreased in both number and severity. The medicine of interest was paracetamol also known as acetaminophen or APAP, a common fever and pain reliever. At the beginning of the study 80% of participants reported using APAP, this dropped to below 50% by day four as participants began reporting feeling better. Other drugs taken during the study period may have come from either co-infections or pre-existing conditions, most medication associated with preconditions came from reported asthma or hypertension. Of those who did take APAP 95% reported it relieving either some or all symptoms that they were experiencing. Despite more than 30% of the participants having one or more preconditions overall stress was low (21.74%) and the general health, nutrition, and hydration of the population were either average or higher.

As ILI still does not have a true definition and definitions vary across studies, ILI was defined here as a fever of greater than 37.2°C and one symptom from the following two groups, group one: fever, chills, body aches, muscle pain, headaches, fatigue and group 2: sore throat, cough, runny or stuffy nose. These criteria were based on the case definition form the European Centre for Disease Prevention (40). Overall 25 symptoms were reported as occurring, the most frequent in occurrence during the study period were fever, chills, weakness, anorexia, headache, retro orbital pain, body pain, bone pain, and muscle pain. Those lasting five or more days were anorexia, abdominal pain, malaise, cough, and sputum. All symptoms show a steady decline in intensity and occurrence as time passed, this should be expected as people heal and become better.

A few studies have looked at the cost and severity of ILI in those who go to hospital and those who use ambulatory care, and at least one study has compared ambulatory care and non-healthcare seeking populations (18). These studies have generally found that those who seek care have 1. More reported symptoms 2. Longer duration of symptoms 3. Used more medication, and more often 4. Reported frequent interruption of activities as opposed to those who did not seek care (18). These were not the results found in the population in our study; very few participants reported seeking medical care for their symptoms (17.86%). When comparing the participants who sought medical attention to those who did not there was no significant difference in the mean number of total symptoms reported (P-value= 0.5597). The duration of symptoms were also not significantly different when looking at the two comparison groups, fever, chills, fatigue, headache, and retro orbital pain all had non-significant reported duration (p-values= 0.5328, 0.4828, 0.5763, 0.3237, and 0.8801 respectively). For the two comparison groups medication use (APAP) did not significantly differ either (p-value=0.2113). The intensity of pain was thought to be a driving force for seeking medical care, however in the population studied even though those who sought medical care had a higher mean in average pain from symptoms their mean score was not statistically significant form those who did not seek care (p-value=0.0723). It also happened that a disruption of normal activity levels was also not statistically associated with seeking medical care (p-value=0.6067) this occurred despite 39.39% of participants claiming a major change in activity and 46.43% stating a minor effect in activity change. All previous studies looking at these differences between healthcare seeking and non-healthcare seeking populations took place in developed European cities, these differences may be due to the fact that the study area is a resource poor urban area with a less structured economy and fewer healthcare facilities (2). These differences may be very important in understanding why and how disease spreads in developing urban areas.

Looking specifically at fever and core body temperature (CBT) it was seen that there was a significant difference in CBT during the study period (p-value=<.0001), this is a reflection of the fact that at enrollment participants were febrile and after two days of observation, the majority of participants became non-febrile and average CBT dropped into a healthy range. In terms of fever specifically this also changed as it should, it became lower over time with a significant change after the first day (p-value=0.0017). There was not found to be any significant difference in fever or temperature recordings depending on the time of day, allowing for reliable measurements regardless of time. Comparison of the iButton to the tympanic temperature showed that iButtons differed significantly from tympanic temperatures, as they were uniformly lower than tympanic temperature and underperformed in recording fever accurately. When compared in both linear and mixed effects and random effects modeling they were still not a good match with tympanic, though the higher order modeling did produce a smaller p-value, it was still not significant. The reason for the poor performance may be due to any number of reasons including interference from sweat, ambient temperature, or other unknown causes. It may be the case that including other beta coefficients could improve the outcome and create a model which better represents CBT.

Distance in this study was measured in three different ways to test if one would be a better representation of movement than the others. Of the three methods one was a simple count of GPS points more than 10m away from the participants' home, 10m was chosen as a buffer because that is the error in the GPS units. This measurement simply represents the total amount of time spent away from home. The second measure of distance was average distance traveled, this is simply the mean of all distances associated with points more than 10m from home. The third measure of distance was maximum distance traveled, this is the absolute maximum distance a person traveled in a day. When looked at in comparing those with fever to those without fever none of the three yielded statistically significant results with maximum distance performing the worst (F=0. 59 p-value=0.4453). Subsequent bivariate analysis between symptoms and other factors was done with both of the other measurements and compared both globally among all participants and locally comparing movement for individual participants. Based on the results of these, average distance was seen as the overall better measure of distance as it found better relationships with variables of interest. When looking specifically at differences among individuals seven participants of 53 were found to have statistically significant differences in the amount they traveled based solely on whether or not they had a fever.

Full modeling of the data was restricted only to those who could contribute symptom, GPS, and temperature data, this resulted in a very small number of participants (n=11). After conducting bivariate analysis and testing for collinearity it was clear that several variables did have significant relationships with average distance traveled. However, modeling proved to be difficult as adding too many of these variables led quickly to over parameterization. When limited numbers of coefficients were used in model building and did run, no significant coefficients were found. This study has served as a foray into the variables which may be of interest in developing models later from which to predict the amount of movement expected based on medicine use, symptoms, and other factors.

Strengths and Weaknesses

The strengths of this study lie in the foundation that it was built on, and the history of similar pilot studies in the area (1, 2, 39). The population of Iquitos is very enthusiastic about participation and was a true source of strength for the study. In addition the repeated surveys and daily measures of tympanic temperature also help to reinforce the robustness and accuracy of the data.

The weaknesses of the study include not only a small sample size, but data which is sometimes intermittent and present for some days but missing on others due to either human error or rollover occurring in devices. The small size of the study also means all conclusions should be considered in the context of a small study and that the results may not be as robust as a larger study. The intermittent data also leaves the study unable to draw conclusions about why individuals may have differences in movement as opposed to looking at movement in the overall population. The overperameterization which occurred also means that interaction assessment was not done as interaction terms increased parameterization.

Public Health Implications and Future Directions

The public health implications for this study are predominantly concerned with understanding how it is that ILIs spread throughout resource poor urban environments. With a better understanding of how movement and fever interact it will be possible to produce better models for the spread of disease and address specific needs in resource poor urban areas as they are the dominant areas of urbanization globally (15). Such understanding will also allow public health officials to produce better syndromic surveillance, improve, develop, and refine interventions to prevent the spread of ILIs, and improve the prediction of how ILIs will move through an environment. Future directions for this research revolve around bringing in more data and varied data to see what other variables may be important as well as to build more robust models. Use of iButton in the future is also of interest, though it did not perform well, it may be possible to adjust for limitations in the temperature loggers.

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Tables

Table 1. Demographic Breakdown of Participants with Influenza like Illness in Iquitos, Peru

Variable Name	n	Frequency (%)	Median [Q1, Q3]
Sex (Female)	28	67.86	
Age	28		31 [10, 44]
Primary Occupation	27		
Agriculture		7.41	
Driver		3.70	
Housewife		37.04	
Student		37.04	
Vendor		3.70	
Unskilled Labor		3.70	
Unemployed		3.70	
Other		3.70	
Appearance	28		
General			
Good		7.14	
Average		92.86	
Hydration			
Good		10.71	
Average		89.29	
Nutrition			
Good		14.29	
Average		78.57	
Bad		7.14	
Preconditions*	28		
Three Preconditions		3.57	
Two Preconditions		10.71	
One Preconditions		32.14	
Zero Preconditions		53.57	
Experiencing Stress(Yes)	23	21.74	

*These are the total number or pre-existing medical conditions reported by participants at the time of enrollment.

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Table 1 is a breakdown of the demographic information we have for the study participants.

Table 2. Medicine Use among Participants with Influenza like Illness in Iquitos, Peru

Variable Name	*n*	Frequency (%)
Paracetamol Help (yes)	20	95
Medicine Type		
Day 1	25	80
Paracetamol		20
Other		
Day 2	19	
Paracetamol		73.68
Other		26.32
Day 3	7	
Paracetamol		57.14
Other		42.86
Day 4	3	
Paracetamol		33.33
Other		66.67
Day 5	1	
Paracetamol		0
Other		100
Day 6	1	
Paracetamol		0
Other		100
Doses of Paracetamol		
Day 0	20	
1		40
2		45
3		5
4		5
6		5
Day 1	16	
1		43.75
2		50
4		6.25
Day 2	5	
1		40
2		60
Day 3	1	
1		100

Table 2 looks at the reported frequency of medicines and doses of paracetamol over time. The n drops rapidly over time.

Table 3. Symptom Presence among Participants with Influenza like Illness in Iquitos, Peru

Variable												
Day	1		2		3		4		5		6	
	n	Frequency (%)	n	Frequency (%)	n	Frequency (%)	n	Frequency (%)	n	Frequency (%)	n	Frequency (%)
Fever	28	96.43	23	47.83	10	40						
Chills	28	89. 29	23	47.83	10	30						
Weakness	28	89.29	23	82.61	10	50	3	33.33				
Anorexia	28	82.14	23	73.91	10	40	5	40	3	33.33		
Headache	28	89.29	23	78.26	10	50	4	50				
Retro orbital	28	89.29	23	21.74	10	30	4	25				
Body Pain	28	75	23	56.52	9	4.44	5	40				
Bone Pain	28	57.14	22	31.82	9	33.33	5	40				
Joint Pain	28	50	23	43.48	9	33.33	5	40				
Muscle Pain	28	78.57	22	45.45	9	55.56	5	60				
Abdominal Pain	28	32.14	21	14.29	8	12.5	5	40	3	33.33	1	100
Nausea	28	42.86	20	5	8	12.5						
Vomiting	28	25	21	4.76	8	12.5						
Diarrhea	28	25	21	9.52	8	12.5						
Congestion	27	29.63	19	15.79								
Sore Throat	27	29.63	19	31.58								
Cough	27	37.04	19	26.32	9	22.22	5	20	3	66.66		
Erysipelas	27	11.11	19	15.79								
Bad Taste	27	33.33	19	21.05	9	11.11	5	20				
Chest Pain	27	11.11										
Sputum	27	18.52	19	21.05	9	22.22	5	20	3	66.66		
Photophobia	27	3.7										
Faint	27	22.22	19	26.32	9	33.33	5	20				
Itch	26	3.85	19	5.26								

Table 3 depicts the frequency symptoms were reported over time by those who were surveyed.

Table 4. Symptom Frequency and Duration among Participants with Influenza like Illness in Iquitos, Peru

Variable	*n*	*Frequency (%)*
Medication Use	28	96.43
Seek Medical Attention	28	17.86
Change in Activity	28	
Major Effect		39.29
Minor Effect		46.43
No Effect		14.29
Frequency of Symptoms		
Malaise	27	
Constant		40.74
Come and Go		59.26
Fever/Chills	27	
Constant		25.93
Come and Go		74.07
Headache	25	
Constant		28
Come and Go		72
Musculoskeletal Pain	23	
Constant		28
Come and Go		72
Abdominal Pain	9	
Constant		9
Come and Go		8

Table 4 displays medical attention seeking behavior and the frequency with which participants experiences various symptoms, as either constant of as coming and going.

Table 5. Symptom Duration among Participants with Influenza like Illness in Iquitos, Peru

Variable	*n*	*Median [Q1, Q3]*
Symptom Duration (days)		
Malaise	26	2 [1, 3]
Fever	26	2 [1, 3]
Chills	24	2 [1, 3]
Fatigue	24	2 [1, 3]
Headache	23	2 [1, 3]
Retroorbital	11	2 [1, 3]
Body Pain	18	1 [1, 2]
Bone Pain	13	1 [1, 2]
Joint Pain	13	1 [0, 2]
Muscle Pain	19	1 [1, 2]
Abdominal Pain	9	2 [1, 2]
Nausea	10	2 [1, 2]
Vomit	7	2 [2, 2]
Diarrhea	6	2 [1, 2]

Table 5 shows the duration for which participants were experiencing symptoms most had a median of 2 days.

Table 6. Significance Test from Comparison between Febrile and Non-Febrile Movements within Individual Participants

Participant	*T-test*	*p-value*
1	-3.32	0.0293
2	-17.11	0.0372
3	-3.04	0.0289
4	18.45	0.0345
5	-207.97	0.0031
6	-7.42	0.0177
7	-758.48	<.0001

Table 6 displays the t-test and p-values for the seven participants who were found to have a significant difference with their own travel based on fever alone. The table shows the relative scale of significance.

Table 7. Bivariate Analysis between Log Average Distance and Variables of interest

Variable	*p-value*	*R-Sq.*
Abdominal Pain	0.0099	0.2071
Fever	0.0923	0.0707
Bad Taste	0.0305	0.1525
Diarrhea	0.062	0.0978
Cough	0.0387	0.1369
Malaise Intensity	0.0463	0.57
Fever Intensity	0.0098	0.795511
Chills Intensity	0.0995	0.194851
Weakness Intensity	0.0301	0.562732
Retroorbital Intensity	<.0001	0.998095
Body Pain Intensity	0.038	0.68
Joint Pain Intensity	0.0162	0.946
Frequency of Paracetamol	0.0929	0.428888
Job	0.0782	0.295621

Table 7 is the results of the bivariate analysis done to test for significant relationships btween Average distance and the variables of interest, these are only those found to be significant or borderline significant.

Table 8. Model Coefficients and Measures for Best Fitting Model

	Variable	*F-Value*	*P-Value*
Beta 1	Fever	6.31	0.2411
Beta 2	Average Intensity	1.27	0.4620
Beta 3	Frequency of Paracetamol	0.00	0.9719
Beta 4	Fever Intensity	3.18	0.3255

Table 8 shows the results of the best model that was created form the limited data using a general linear mixed model. It was not overparameterized, but it also did not generate any significant coefficients in the model.

Figures

Figure 1. Depiction of Enrollment and Study Design Process

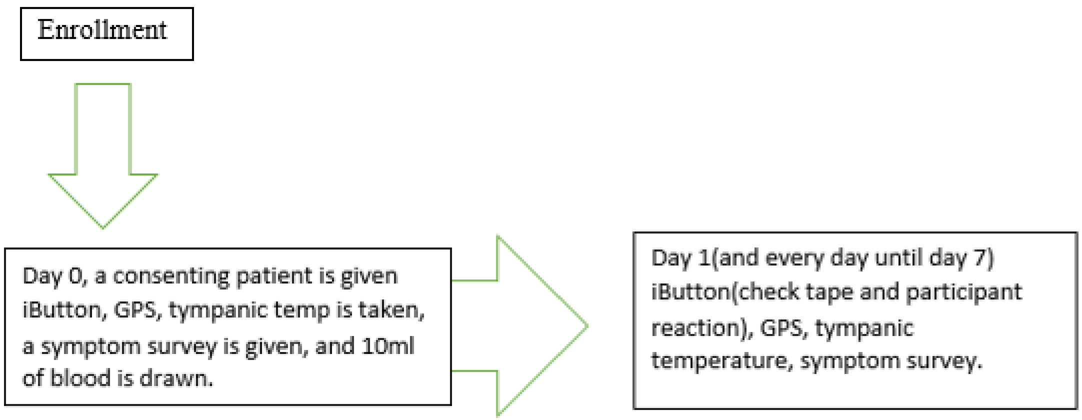
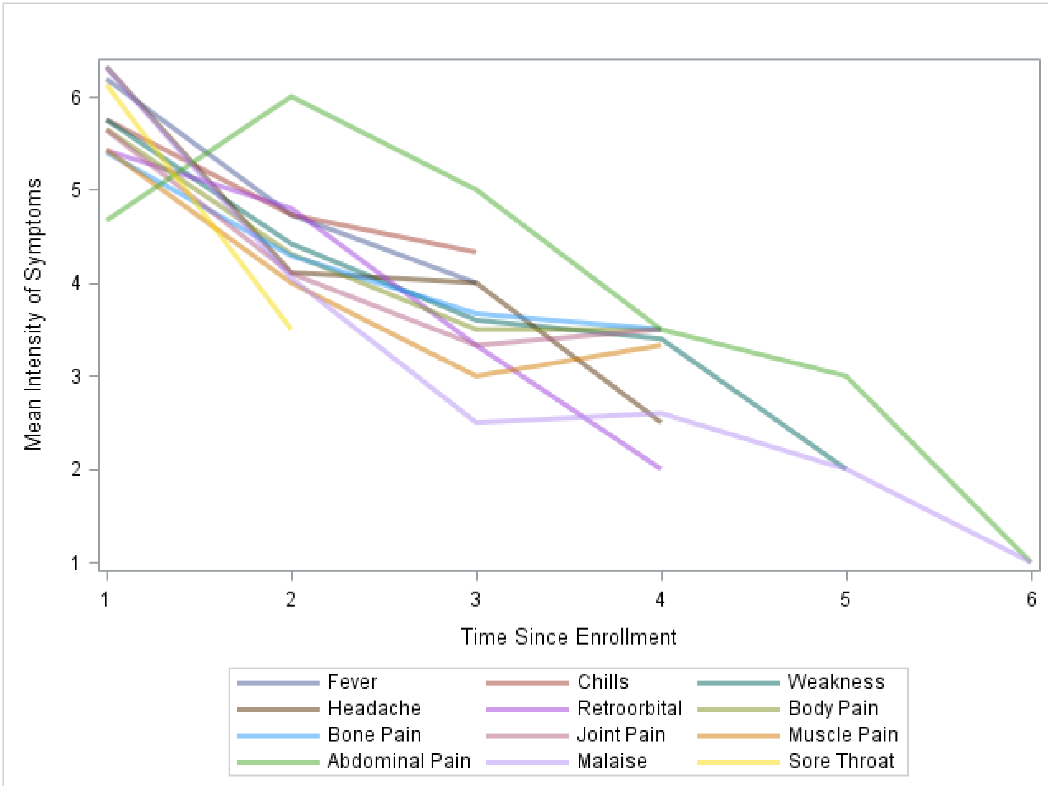
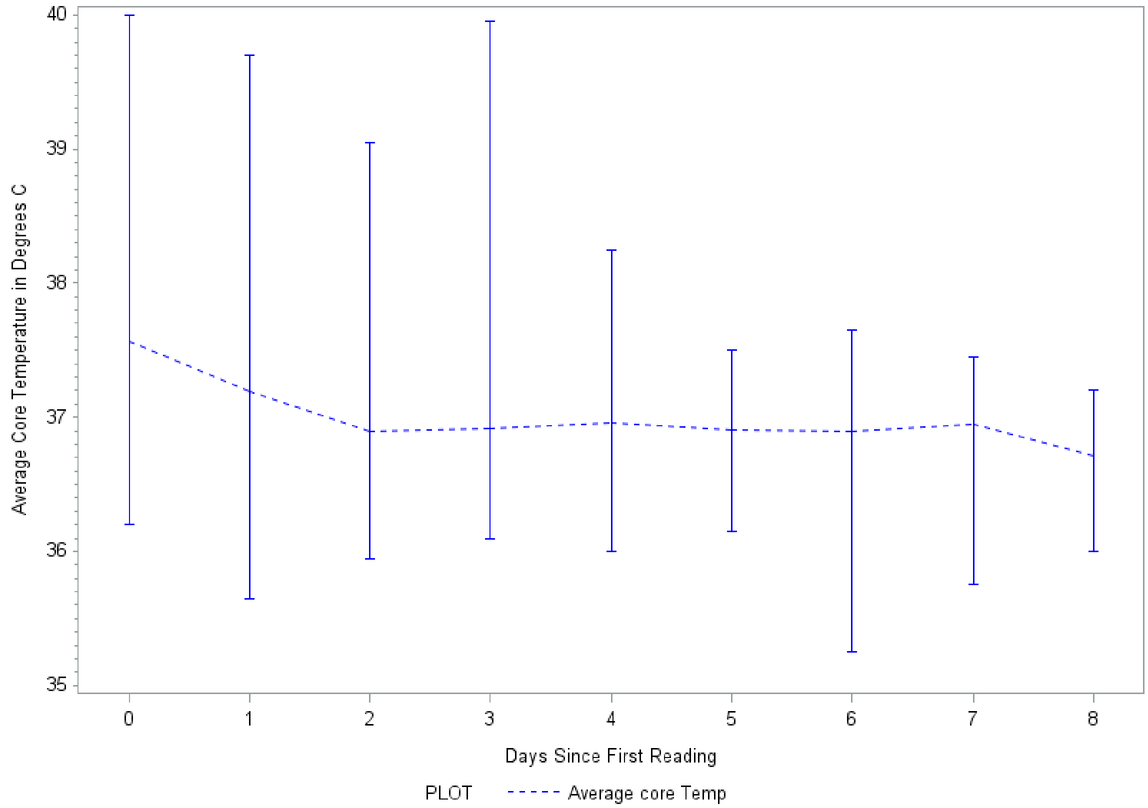


Figure 2. Average Intensity of Symptoms over the Study Period by Day



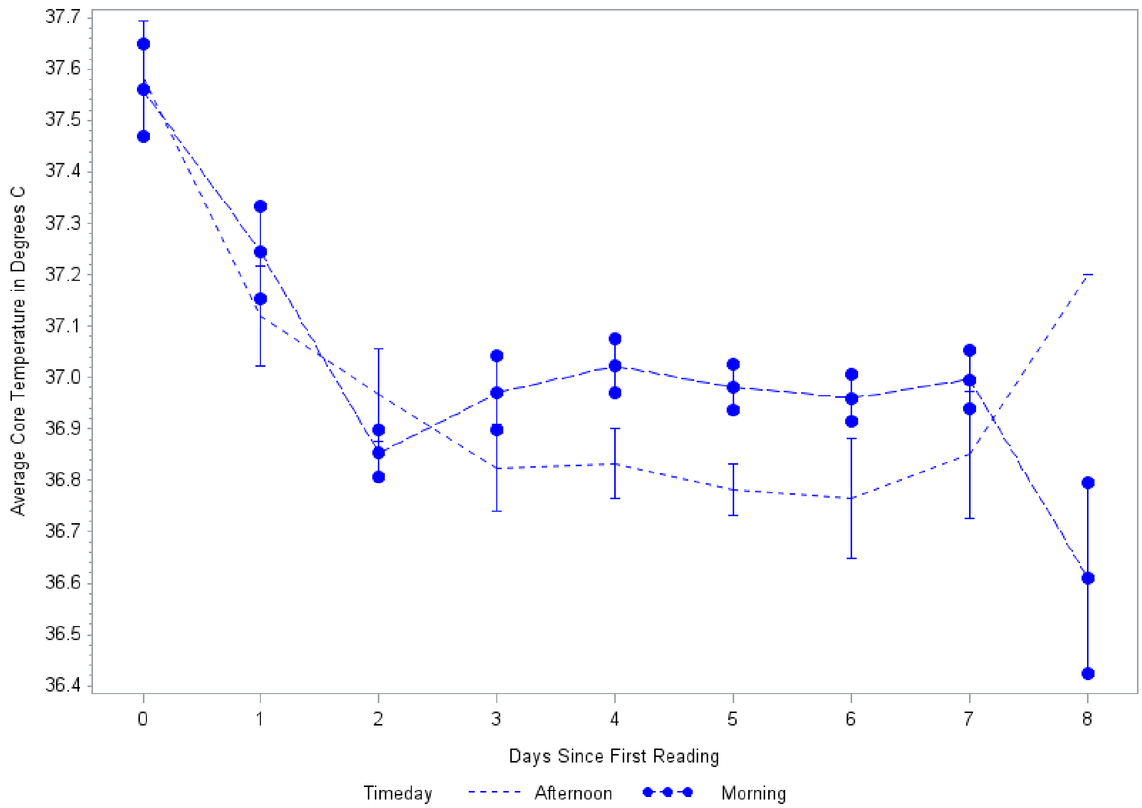
The average reported intensity for each symptom is reported by day. Average intensity was calculated by adding all reported intensities on the reported day and dividing by the total number of participants experiencing the symptom. The maximum reportable intensity is 10 and the minimum reportable intensity is 0.

Figure 3. Average Core Body Temperature (°C) Measured over Time of Enrollment



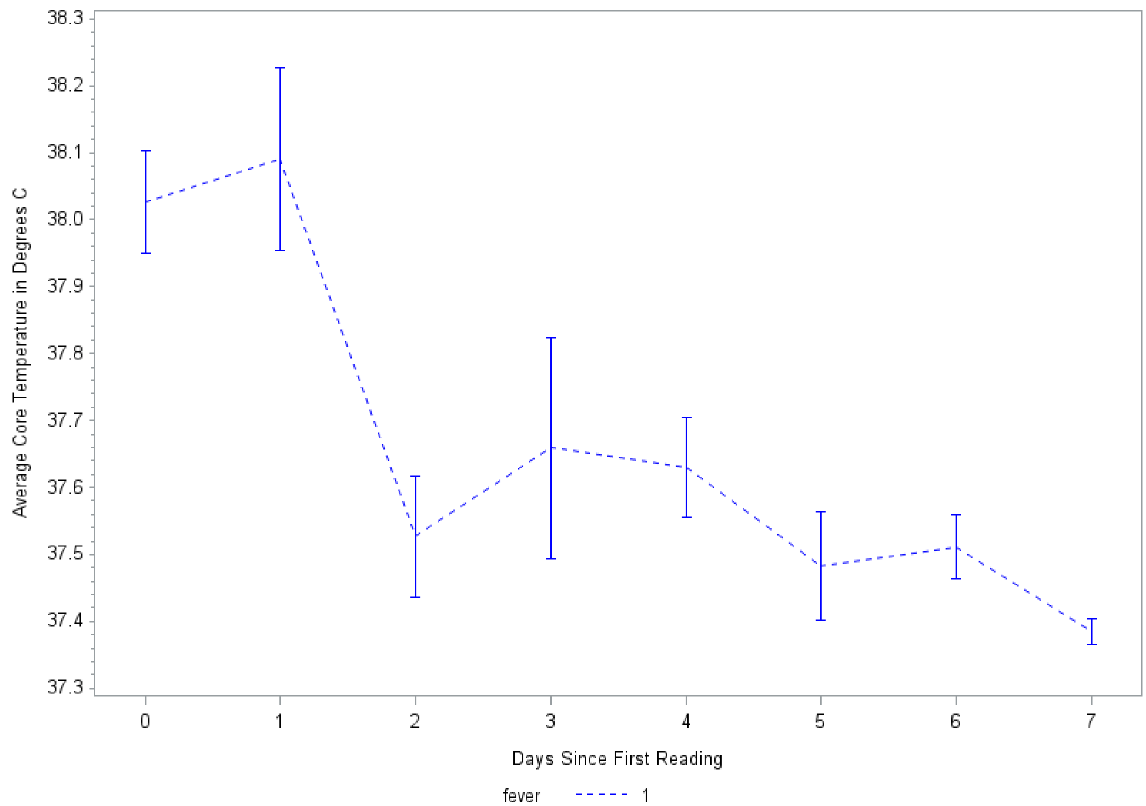
Each point represents the mean temperature for the given day for all temperatures taken that day, regardless of time. Points are encompassed by standard error bars for the day.

Figure 4. Average Core Body Temperature taken over Time during Mornings and Afternoons



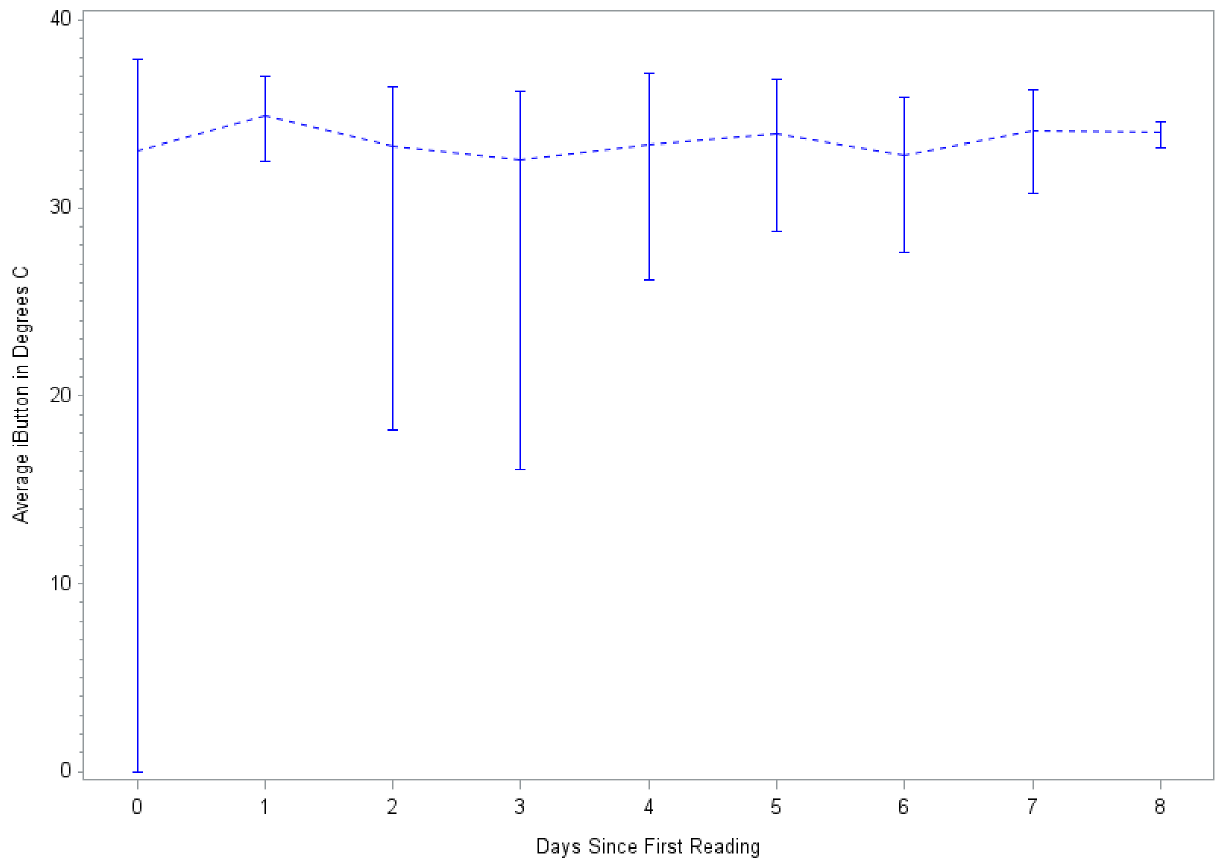
Each point represents the mean temperature for the given day for all temperatures taken that day during the specified period of time (morning or afternoon). Points are encompassed by standard error bars for the day and time.

Figure 5. Average Fever Temperature Taken over Time of Enrollment



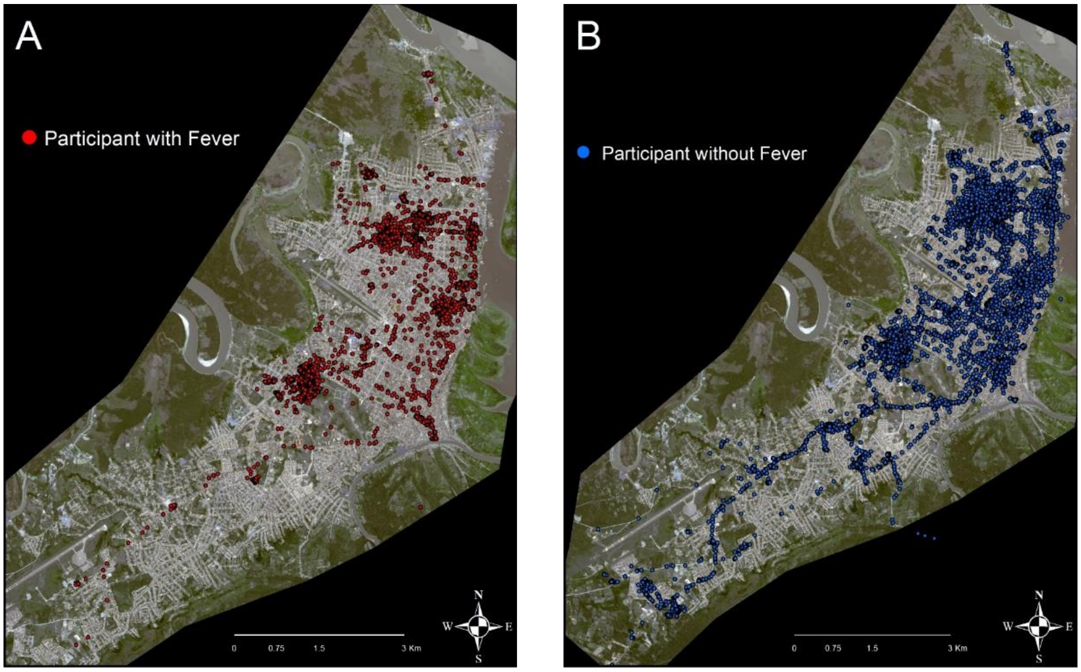
Each point represents the mean temperature for the given day for all temperatures >37.2°C taken that day, regardless of time. Points are encompassed by standard error bars for the day.

Figure 6. Average iButton Temperature Taken over Time of Enrollment



Each point represents the mean iButton temperature for the given day for all iButton temperatures taken that day, regardless of time. Points are encompassed by standard error bars for the day.

Figure 7. Maps Depicting the Distribution of Participant Travel for Febrile and Non-Febrile Participants



Map A shows the movement patterns and spatiality of those participants who were diagnosed with fever (>37.2°C). Map B shows the movement patterns and spatiality of those participants who were not diagnosed with fever.