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Quantifying the impact of human mobility on malaria

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Abstract

Human movements contribute to the transmission of malaria on spatial scales that exceed the limits of mosquito dispersal. Identifying the sources and sinks of imported infections due to human travel and locating high-risk sites of parasite importation could greatly improve malaria control programs. Here we use spatially explicit mobile phone data and malaria prevalence information from Kenya to identify the dynamics of human carriers that drive parasite importation between regions. Our analysis identifies specific importation routes that contribute to malaria epidemiology on regional spatial scales.

Local “hotspots” of malaria prevalence, resulting from complex interactions between the malaria parasite *Plasmodium falciparum* and its human and mosquito hosts, provide specific targets for the strategic deployment of malaria interventions (1–4). Movements of infected humans can increase the dispersal of parasites beyond what would be possible for mosquitoes alone (5,6). National malaria control programs must account for this human travel-mediated spread of parasites because frequent introduction of imported parasites could undermine local control or elimination strategies (5, 7–9). Mapping the routes of parasite dispersal by human carriers will allow for additional targeted control by identifying both the regions where imported infections originate and where they may contribute significantly to transmission. International migrants can contribute to continental parasite dispersal across Africa, and census surveys have provided insights into these routes of

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The geographical spread of malaria parasites was analyzed by combining the daily movements of 15 million Kenyans with malaria prevalence estimates.

importation (6). The vast majority of travelers that will impact malaria parasite dispersal are those moving within a country between regions of variable malaria receptivity on a daily or weekly basis, however.

Here, we use mobile phone data to analyze the travel patterns of nearly 15 million individuals over the course of a year in Kenya, combining these data with a simple transmission model of malaria based on highly spatially resolved malaria infection prevalence data to map routes of parasite dispersal. Previous small-scale studies have used mobile phones to estimate importation rates of malaria parasites by residents of Zanzibar following journeys to mainland Tanzania, but these data lacked resolution on the infection risk at their journey destinations, as well as information about infected visitors to the island (8, 9). Here we identify networks of parasite movements within Kenya and pinpoint both "source" and "sink" regions.

We estimated the daily locations of 14,816,521 Kenyan mobile phone subscribers between June 2008 and June 2009, mapping every call or text made by each individual to one of 11,920 cell towers located within the boundaries of 692 settlements (Figures 1A and B) that were defined by satellite imagery as previously described (11–13 and see SI for methods). Each individual was assigned to a primary settlement where they spent the majority of their time over the course of the year, and the destination and duration of each journey made out of the primary settlement was calculated (Figure S1). We used a malaria prevalence map from 2009 (14) with a $1km^2$ resolution to assign each settlement a malaria endemicity class ranging from 1 (<0.1% prevalence of *Plasmodium falciparum* infection in 2–10 year olds, $PfPR_{2–10}$) to 7 (>=40% $PfPR_{2–10}$), and these estimates were used to infer i) a resident's probability of being infected and ii) the daily (nightly) probability that visitors to the settlement will become infected. Data on the seasonality of infection risk was not available, so these estimates likely represent an upper bound (see SI). Settlements were grouped into risk regions via a clustering algorithm to define geographically contiguous groups with the same malaria endemicity (Figure 1C, see SI).

The travel network (Figures 2A and S2A) is dominated by the Kenyan capital Nairobi, which forms a hub for human movements to and from all regions of the country. Although the highest volume of travel occurs between Nairobi and the central regions of the country, substantial movement also occurs between the central region and Lake Victoria (for values see Tables S1, S2).

There are two sources of importation of parasites. First, individuals visiting endemic areas may become infected during their stay, depending on the malaria endemicity of the destination, carrying parasites back to their primary settlement (see SI for methods). We term these individuals "returning residents" and they are equivalent to "passive acquirers" of infections (1). Parasite networks resulting from travel by returning residents are shown in Figure 2B (see Figure S2B and Tables S3, S4). Second, infected individuals can carry parasites with them when they visit other settlements, potentially contributing to onward infections if the destination is receptive to transmission (see SI for methods). Figure 2C illustrates the network of parasite movement by "visitors", and these individuals are equivalent to "active transmitters" in previous frameworks (1, Figure S2C and Tables S5, S6). For this analysis, we assume that receptivity to transmission is reflected by the prevalence of infection, although this simplification does not account for current control measures, which we discuss further below. The structures of these networks were remarkably stable over the course of the year (see Figures S3–S5), so although seasonal changes in transmission might cause our estimates of parasite movement to be generally high, the routes and relative volumes will remain unaffected.

Parasite movement networks represent only a subset of the human mobility network underlying them, due to the spatial heterogeneity in malaria risk across the country. The human travel network is denser than the parasite networks, as expected, with more edges and a higher mean degree per settlement, as well as greater connectivity (see Table S7). Returning residents contribute to some movements of parasites between regions within the Lake Victoria and coastal areas (Figure 2B), but Nairobi imports the largest fraction of infections in this way, with infected residents returning after journeys to the coast, Lake Victoria, and low endemicity regions in central Kenya. Visitors contribute to transmission anywhere that is receptive to transmission (see SI and Figure 2C), but may have less impact in the capital, for example, where vectors are scarce. Hence, the visitor network is dominated by importation around Lake Victoria and shows relatively low importation rates between the lake and the coast, the two main foci of transmission. Visitors carrying parasites within regions are therefore likely to be a much more important consideration for control programs than inter-regional visitors, suggesting that the Lake Victoria and coastal regions may be considered as weakly connected but relatively independent entities for the purposes of malaria elimination.

To examine directional and net movements of people and parasites between settlements, we analyzed asymmetries between “source” and “sink” settlements. Here, we rank each settlement based on their contribution as net emitters (sources) and net receivers (sinks) of people and parasites (human travel in Figure 3A, parasite movement in Figure 3B, see SI for Methods). The difference between each settlement’s source and sink rank distinguishes those that are primarily as sources of people or parasites versus those that are primarily sinks. Sources and sinks of human travel are almost entirely overlapping and reflect patterns of population density and regular travel. In contrast, the parasite routes show directional movement between source settlements in the Lake Victoria region and parasite sinks on the periphery of this focus of transmission and in the Nairobi area (see SI). The capital city and its surroundings are thus a major destination for both humans and parasites, but most of the parasite importation that can contribute to onward transmission occurs on the periphery of the highly endemic Lake Victoria region. Therefore, even though malaria prevalence is low in these regions, elimination efforts must encompass control of imported infections to be successful.

The high spatial resolution of our mobility data allowed us to pinpoint particular settlements that are expected to receive or transmit an unexpectedly high volume of parasites compared to surrounding regions. Figures 4A and 4B show the result of an analysis of outlying settlements identified by means of an anomaly detection algorithm (see SI for methods). Here, the size of the circle represents Rc; the basic reproductive number of the parasite under control (15). This measure provides insights into how important outliers are likely to be for transmission, since importation can only contribute to transmission if local conditions and vector populations allow it. Combining local estimates of importation with information about locally heterogeneous transmission, including vector behavior, ecology, and population distributions on a fine scale, will play an important role in future regional elimination efforts. Again, the settlements on the edge of Lake Victoria are major sources of parasites, and the neighboring settlements further inland are most vulnerable to importation. Returning residents played an important role in importing parasites to major parasite sinks, with residents from the top 10% of outlying settlements taking on average 29 trips during the year, compared to 20 trips by individuals from the remaining 90% of settlements (medians 10.4 versus 7.6, respectively, Mann Whitney U test, $p < 0.0001$). These sinks also received substantial numbers of visitors from higher malaria endemicity settlements (24% of visitors) compared to settlements that were not considered sinks (12% of visitors). In contrast, individuals from the top 10% of major parasite source settlements did not travel more frequently, but 62% of journeys made were to settlements with lower malaria

endemicity compared to 0.08% of journeys made from the remaining 90% of settlements ($p < 0.0001$) (Tables S8–S9).

In Nairobi, the density of cell towers enabled further localization of these estimates and a comparison with cross-sectional clinical surveys of malaria incidence carried out in 2010 (16). Frequent malaria epidemics occurred in the capital at the beginning of the 20th century, but declined significantly following substantial control efforts, rapid population growth and urbanization (16–19). The current potential for local transmission within the city is controversial, with studies showing substantial infection prevalence and ongoing treatment of presumed clinical cases despite the scarcity of suitable mosquito vectors (16–19). Figure 4C shows the ratio of monthly clinical cases to our predicted monthly imported cases from mobile phone data at the location of each hospital survey (see SI for methods, Table S10, Figure S6). Areas in the highly urbanized center of the city, where transmission is unlikely, show a very high ratio of estimated imported to clinical cases. In contrast, hospitals on the periphery of the city have a higher ratio of clinical cases to estimates from the mobile phone data. The patterns suggest some local transmission may be occurring in these residential and less developed areas. Although caution must be exercised in the interpretation of comparisons between clinical and mobile phone estimates, this approach provides a starting point for the identification of transmission foci in urban settings and the local implementation of surveillance programs.

There are limitations to this approach (10), since we can only measure mobility among phone owners in areas where there are cell towers (20, see SI for discussion), we cannot capture cross-border migration, and our importation calculations are constrained by the available, non-seasonal malaria prevalence estimates. Nevertheless, we believe this analysis has made it possible to assess the degree of connectivity among different regions of Kenya – the resulting estimates can be used to cost regional elimination strategies, identify “source” regions where reducing transmission would provide benefit to surrounding areas, evaluate patterns of importation and endemicity in low intensity areas such as Nairobi, and pinpoint likely importation hotspots. On an extremely local scale, driven primarily by vector biology and habitat and local variability in household structures etc., hotspots of transmission that occur can be targeted by indoor residual spraying, vector habitat removal, insecticides, drug administration and bed net use. Control program activities targeting the large volumes of human traffic between regions that we have identified here will be completely different to those that concentrate on local transmission hotspots, focusing on communicating risks to travelers to alter their behaviors, restricting travel patterns, and/or conducting routine surveillance in high-risk areas.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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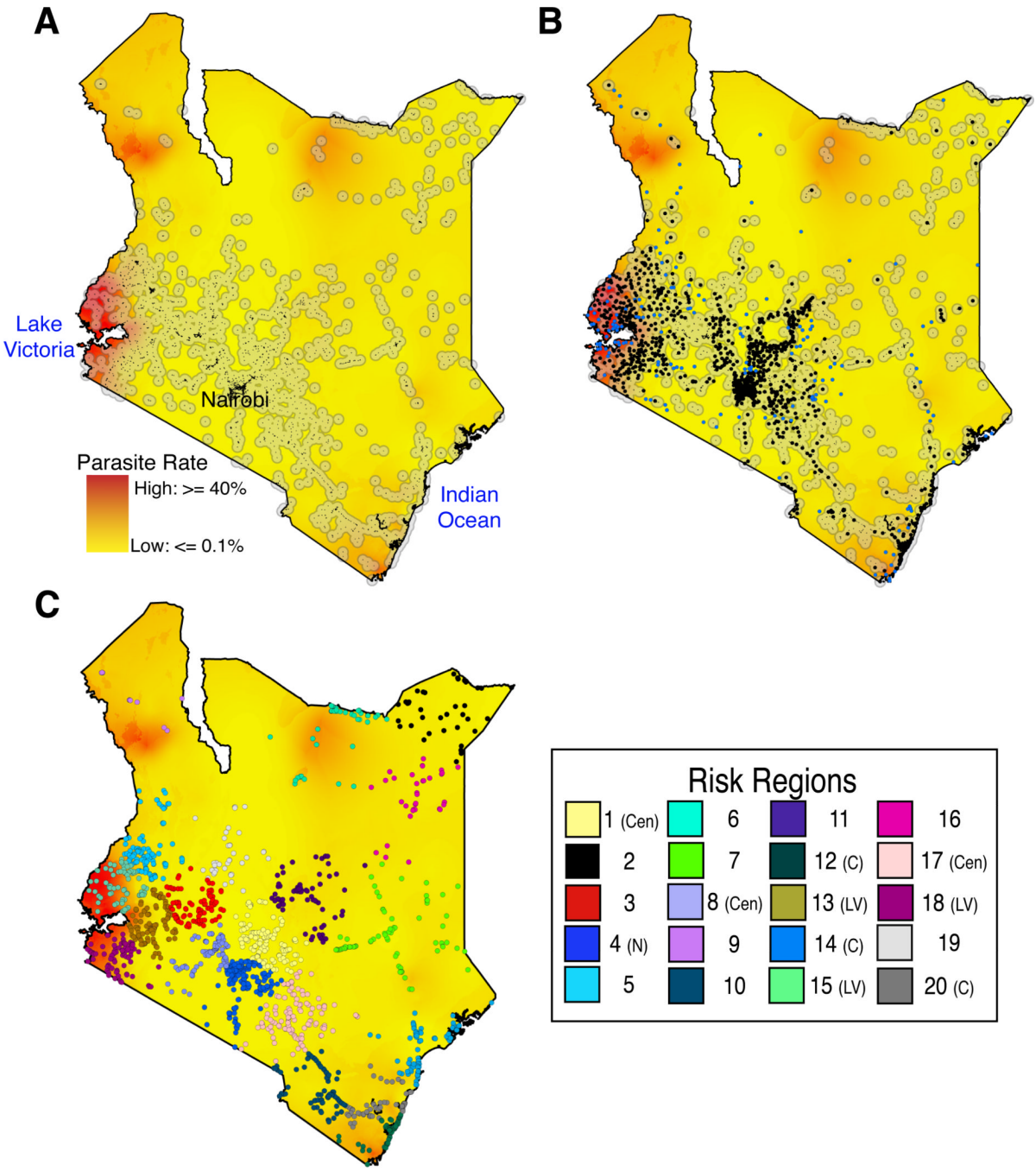

Figure 1. The distribution of settlements, cell towers, and malaria risk in Kenya

A) Malaria prevalence in Kenya in 2009 (from $PfPR_{2-10}$<0.1% in yellow to $PfPR_{2-10}$>40% in red) and the locations of settlements used in the analysis (settlement centers are shown in black, and mapped with a 10km extent around the perimeter of the settlement in grey). **B)** Mobile phone towers (black or blue dots) are overlaid over the extended settlement boundaries. Towers that fall within a settlement are shown in black and those excluded from the analysis are shown in blue. **C)** Regions used for visual mapping of transmission routes. Each settlement was allocated to one of twenty regions by a clustering algorithm (see Methods in the SI) based on homogenous malaria risk and geography, as shown. Regions

near Lake Victoria (LV), in Nairobi (Nairobi), the central areas (Cen), and along the coast (C) are labeled accordingly.

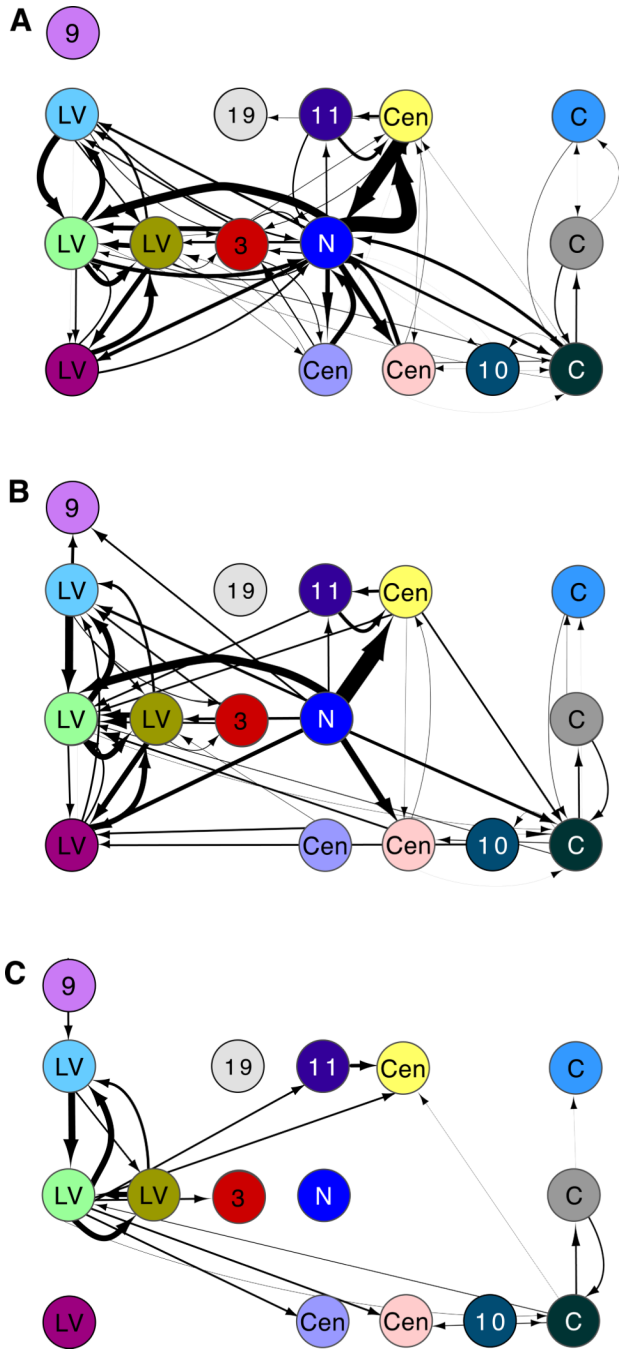

Figure 2. Travel networks of people and parasites between settlements and regions

A) Average monthly travel between regions (nodes), with edges weighted by volume of traffic. For clarity, the top 50% of routes are shown with arrows indicating the direction of movement (humans or parasites) from a primary settlement to a visited settlement. **B)** Average monthly parasite importation by returning residents, by region. **C)** Average monthly parasite importation by visitors, where importation is not considered if the destination has extremely low transmission (see SI). The labeling of nodes is as described in Figure 1. For each network, node layout is roughly based on geographic location.

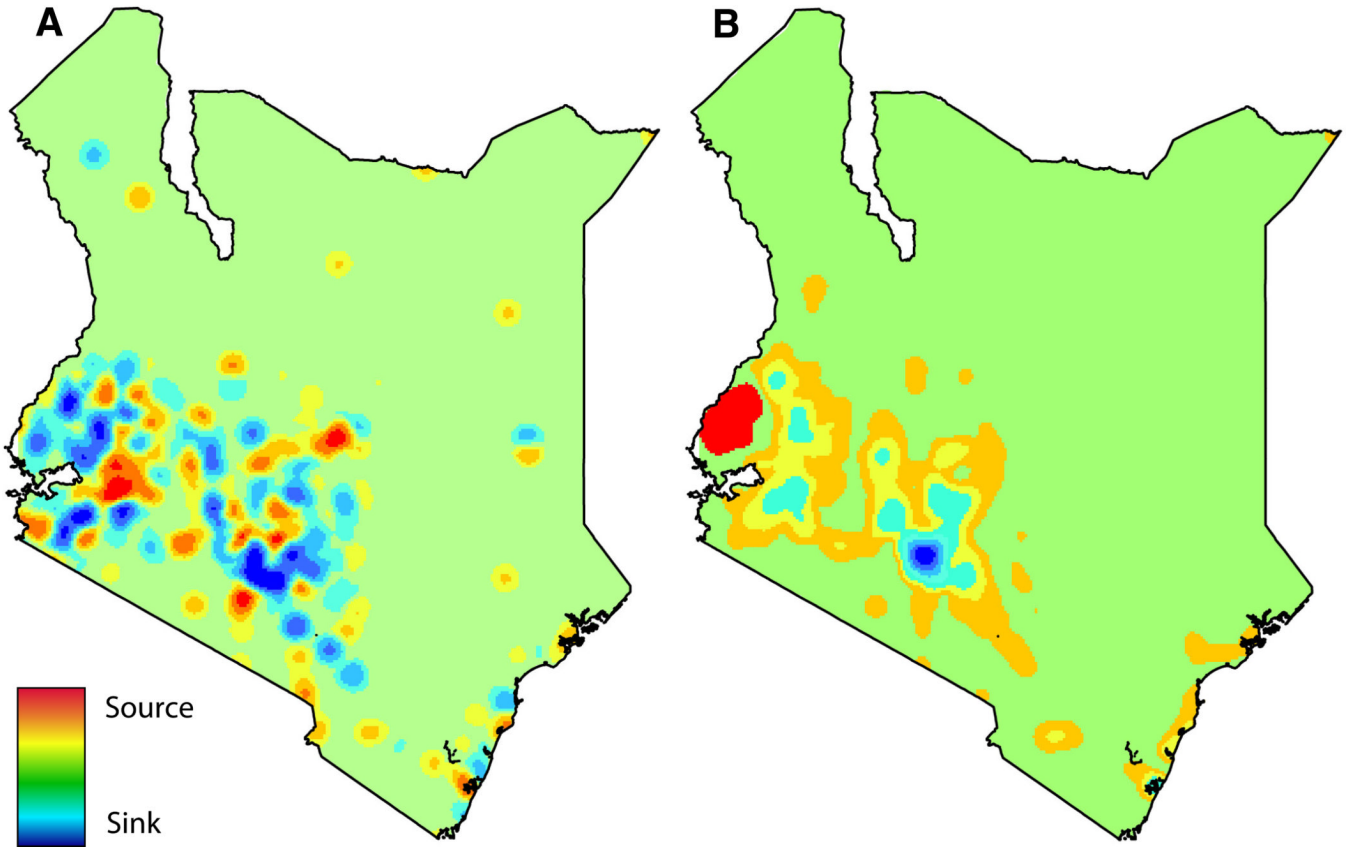

Figure 3. Sources and sinks of human and parasite dispersal

Kernel density maps showing ranked sources and sinks of human travel and total parasite movement in Kenya. A) Settlements were designated as primarily sources or sinks based on yearly estimates of human travel. The direction movement is shown highlighting principal sources (in red) versus principal sinks (in blue). B) The directional parasite movements, major parasite sources (in red) and sinks (in blue) are shown.

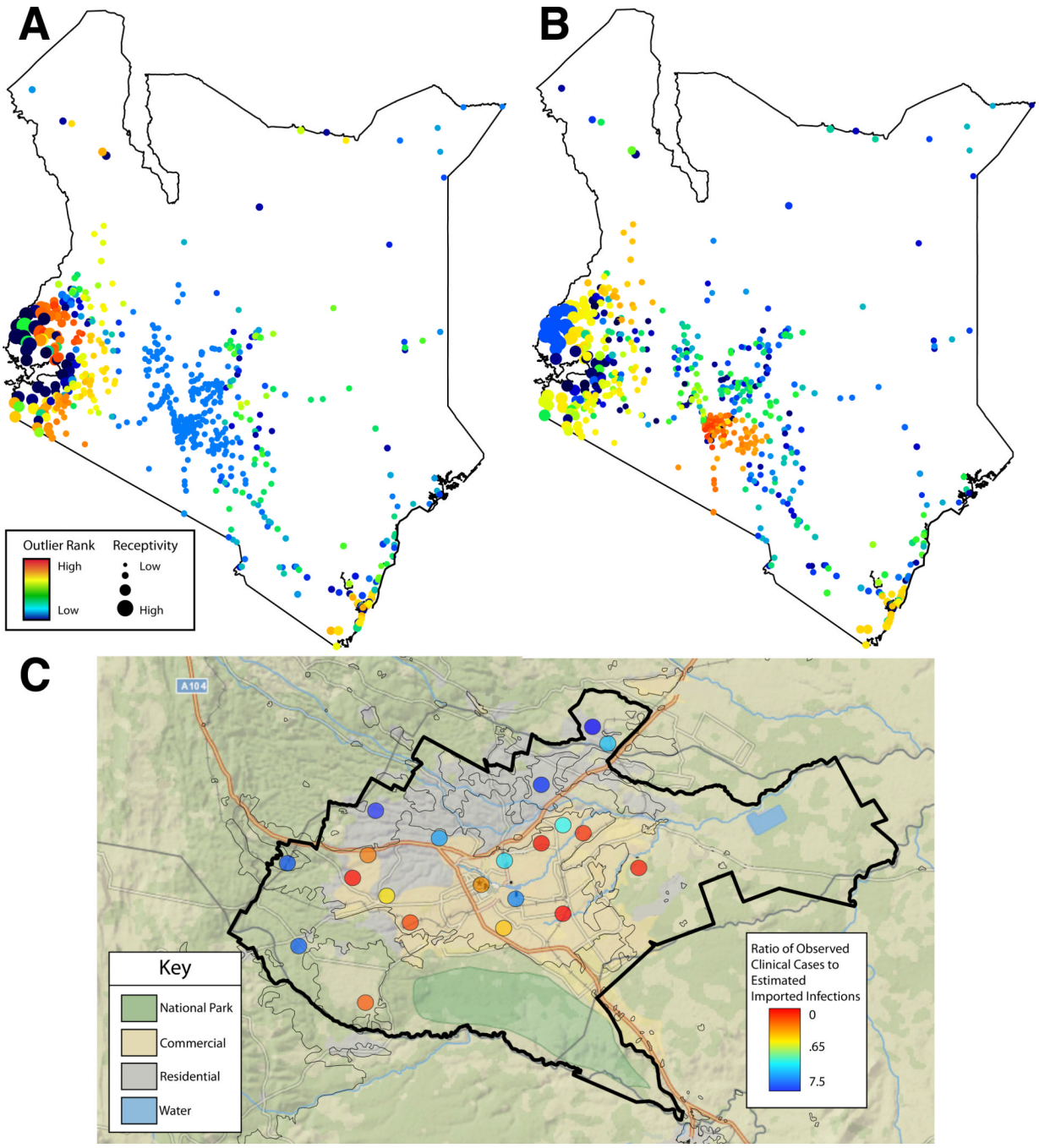

Figure 4. Local analysis of source/sink anomalies

A) Source outliers and B) sink outliers. Settlements are colored by their outlier rank (from low values in blue to high values in red) and sized according to $R_c$an indicator of receptivity (see Methods in SI). C) The localized importation into Nairobi compared to clinical cases. A topographic map of Nairobi was provided from National Geographic and ESRI highlighting the national park, commercial, and residential areas of the city.