Assessing the role of geographical HIV hot-spots in the spread of the epidemic

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What is Health Geography?

- Health geography is the application of geographical perspectives and methods to the study of health, disease and health care

- Health geography uses the concepts and techniques of geography to investigate health-related issues

- Health geography, uses the tools and approaches of geography to tackle health-related questions focused on the importance of variations across space, with an emphasis on concepts such as location, direction, and place

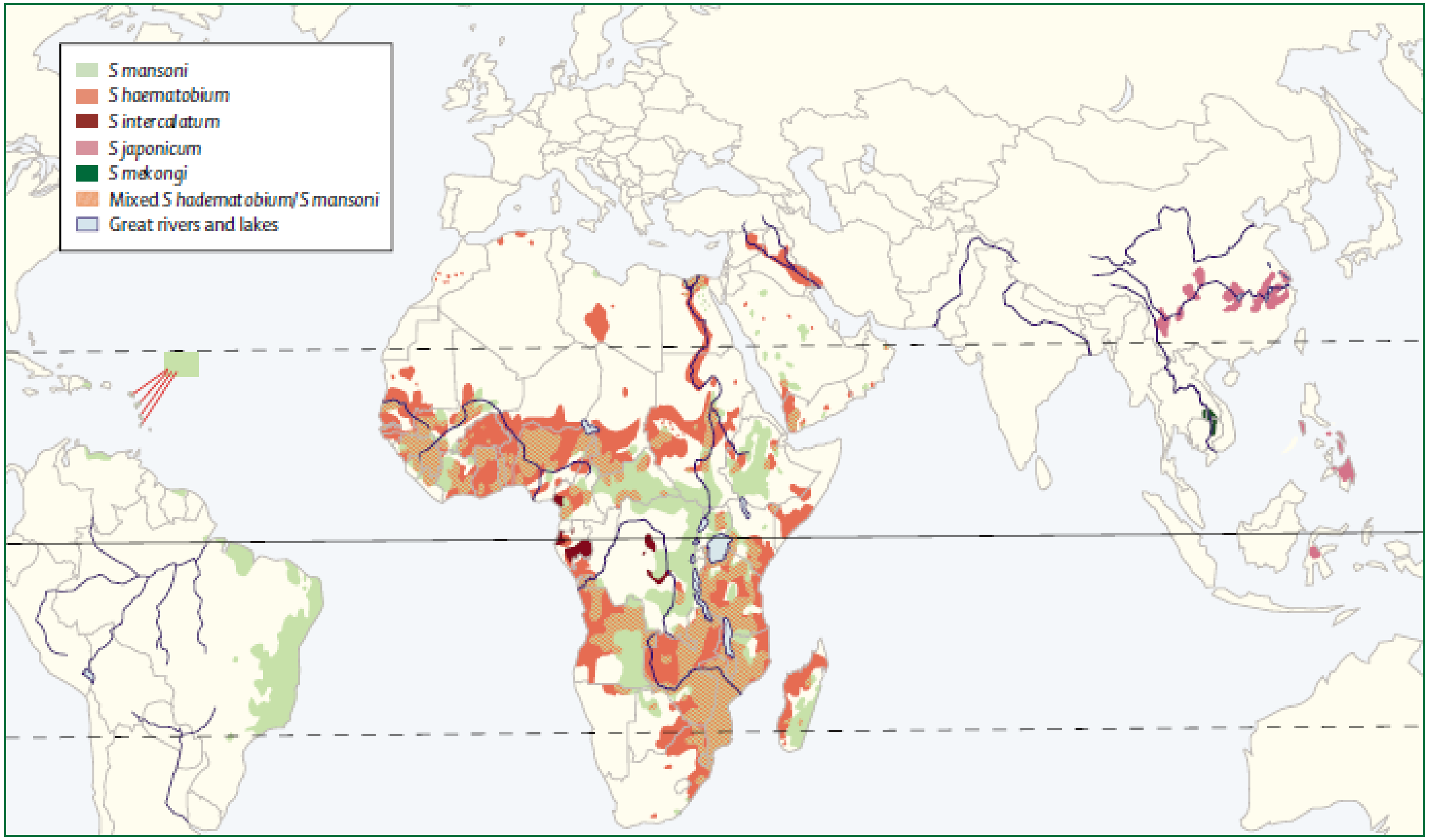
Maps: Great Communicators

- Graphic representations of data frequently more powerful than numeric or textual representations

- Maps seem authoritative to policy makers and stake holders

Disease mapping examples

Schistosomiasis



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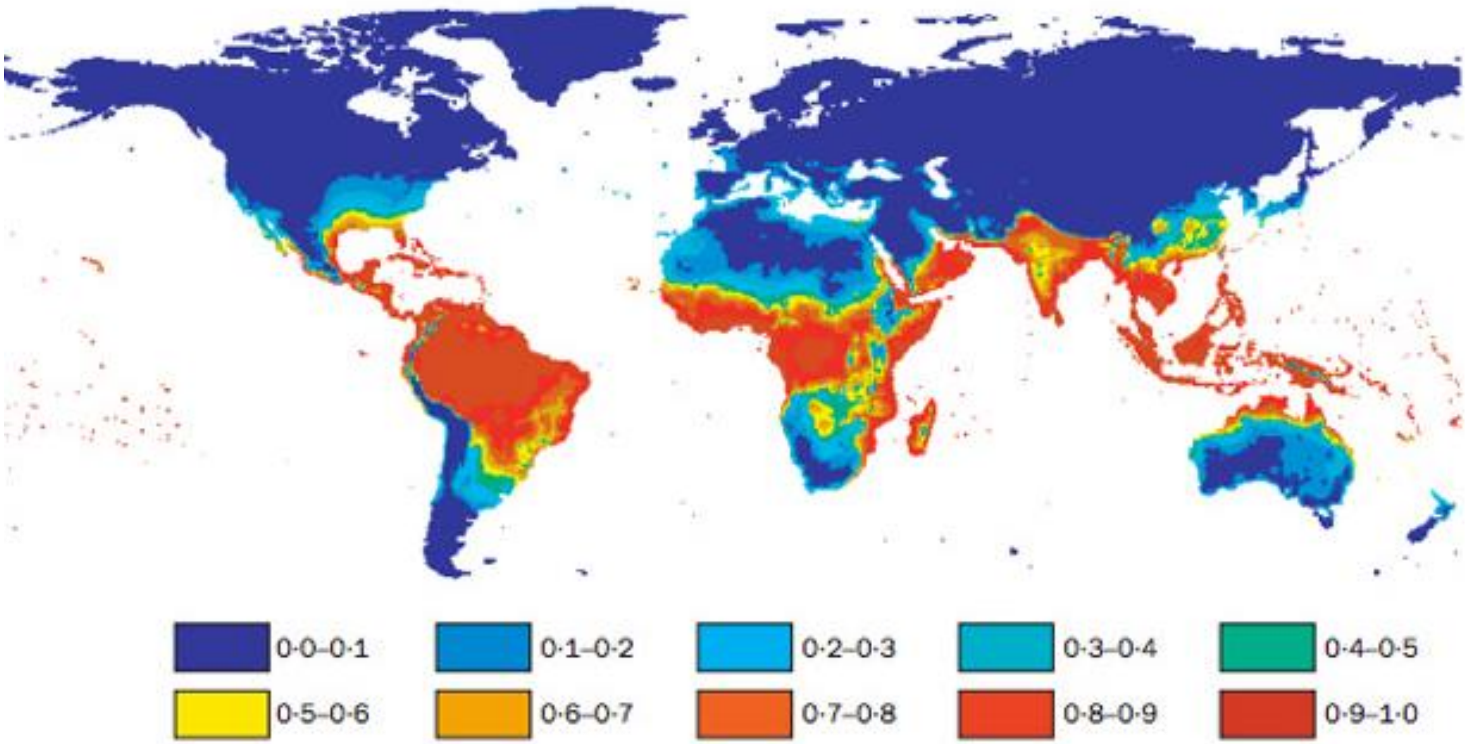
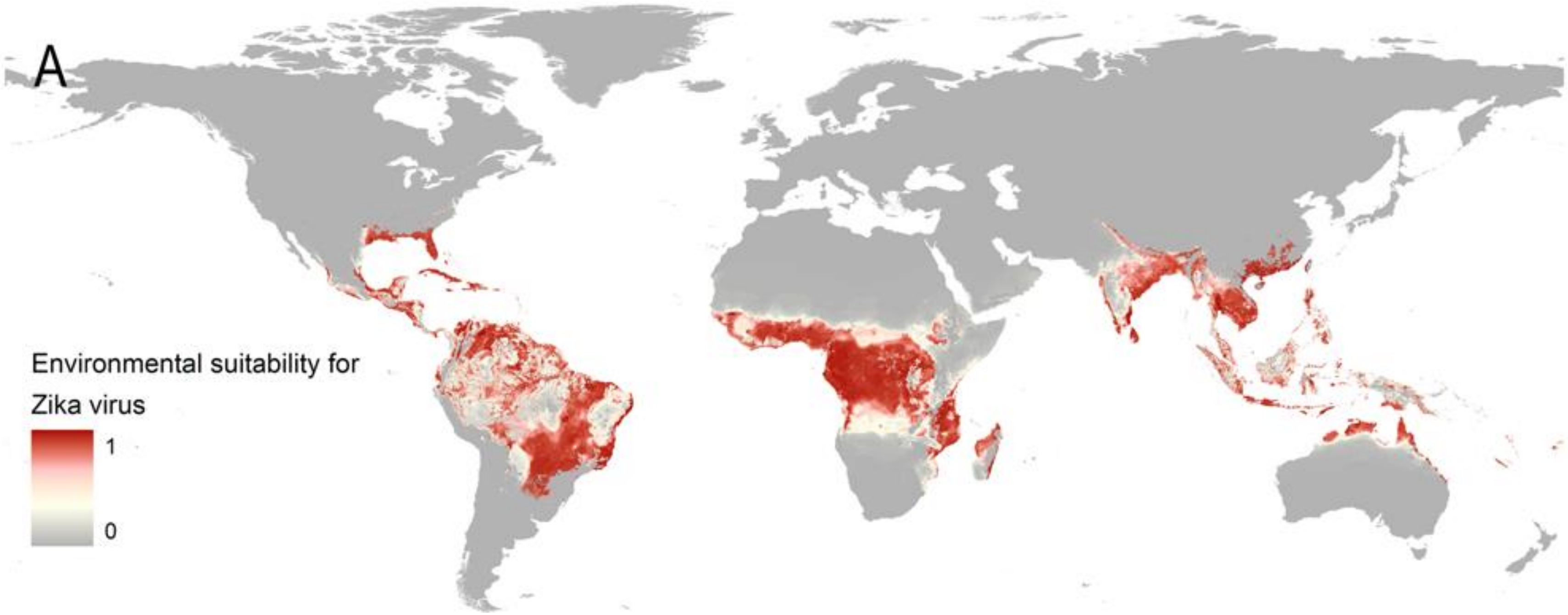
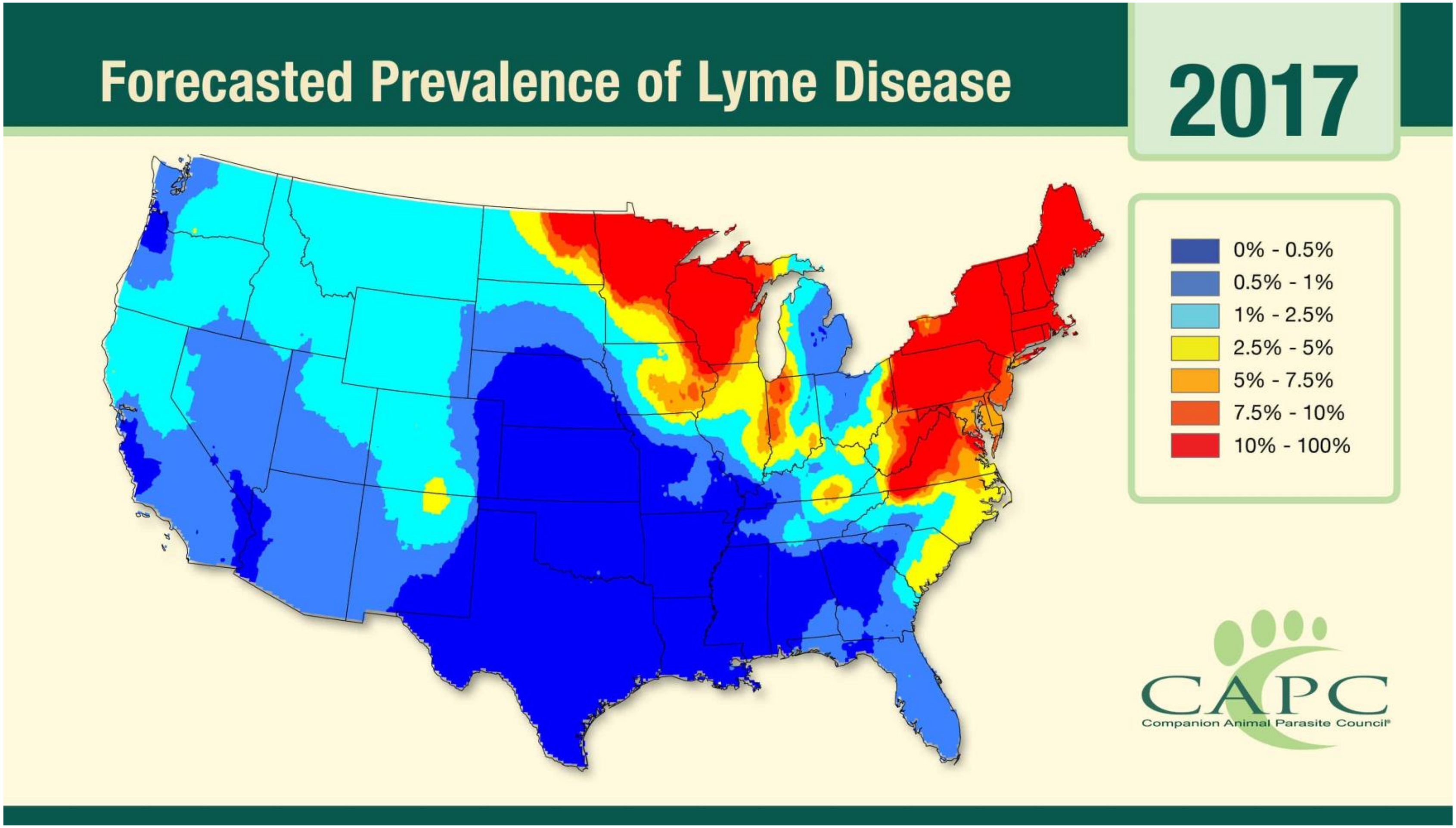
Dengue Fever

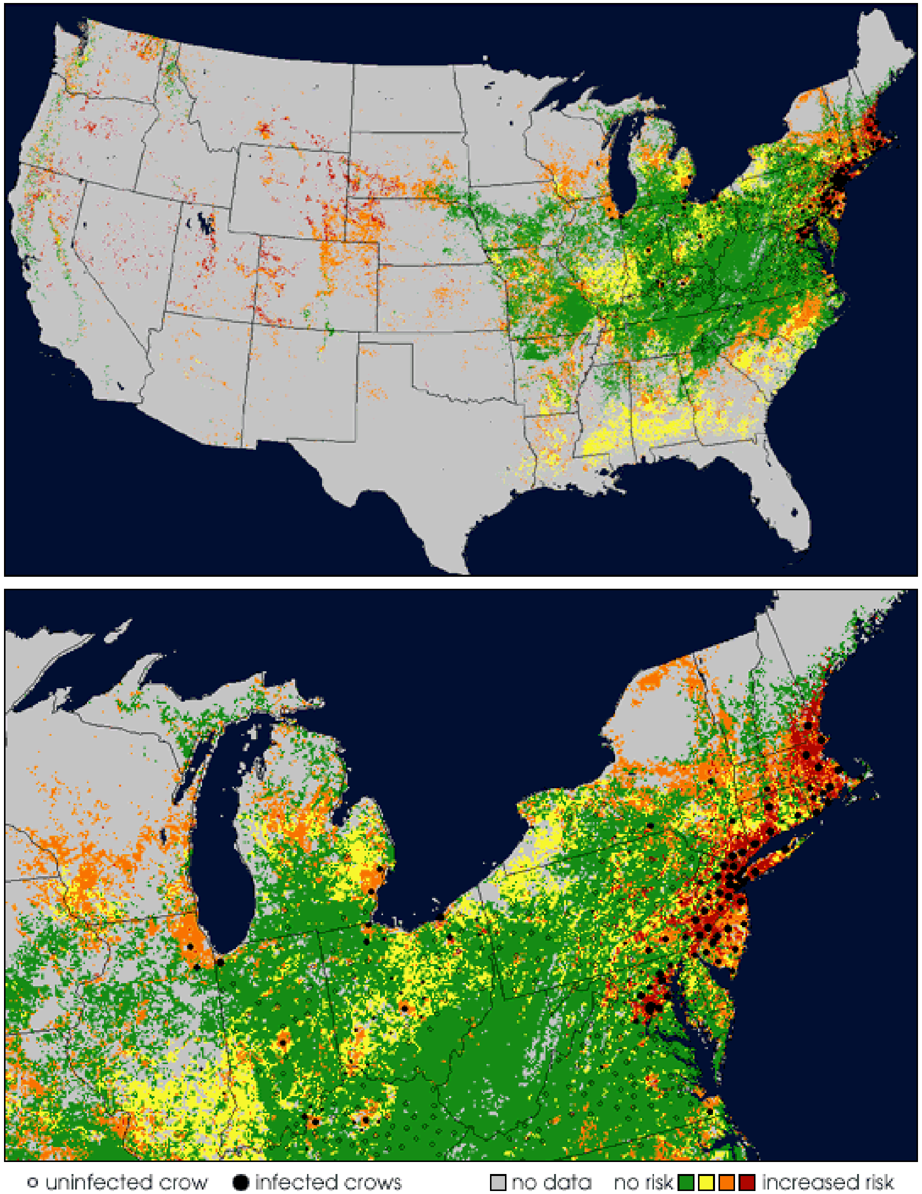


Zika virus

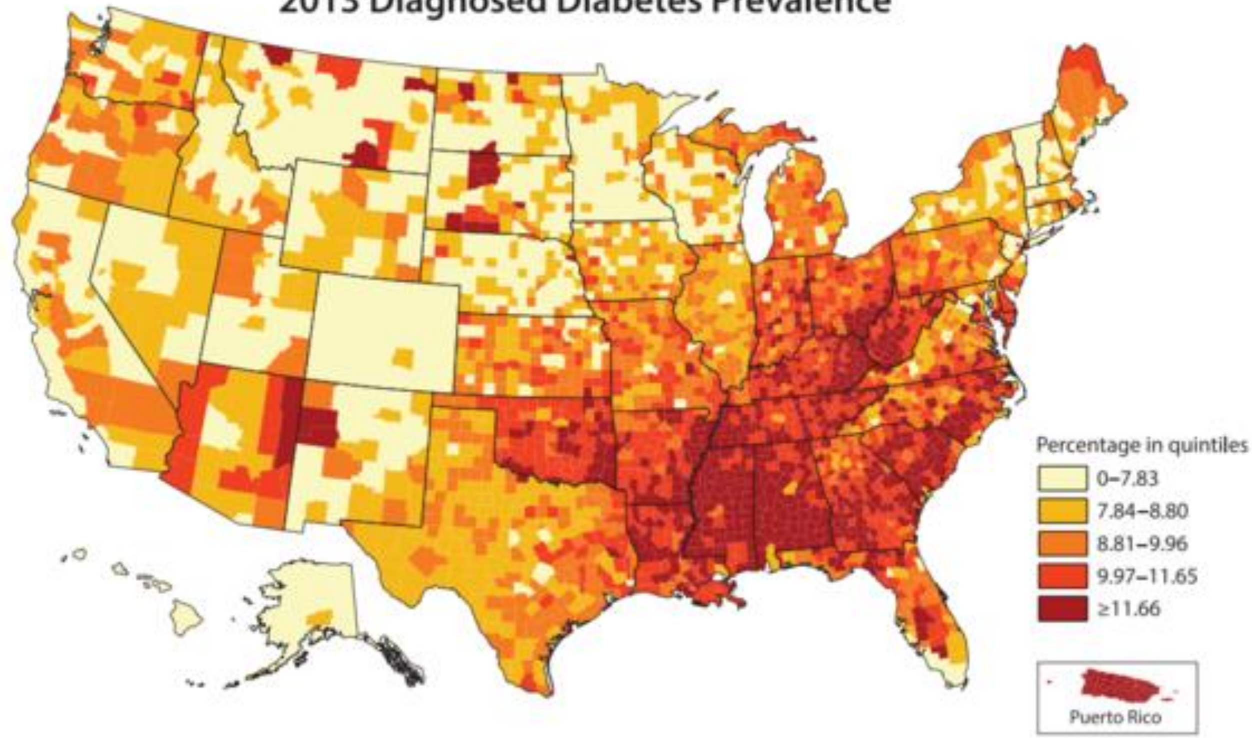



Forecasted Prevalence of Lyme Disease
2017
0% - 0.5%
0.5% - 1%
1% - 2.5%
2.5% - 5%
5% - 7.5%
7.5% - 10%
10% - 100%
CAPC
Companion Animal Parasite Council

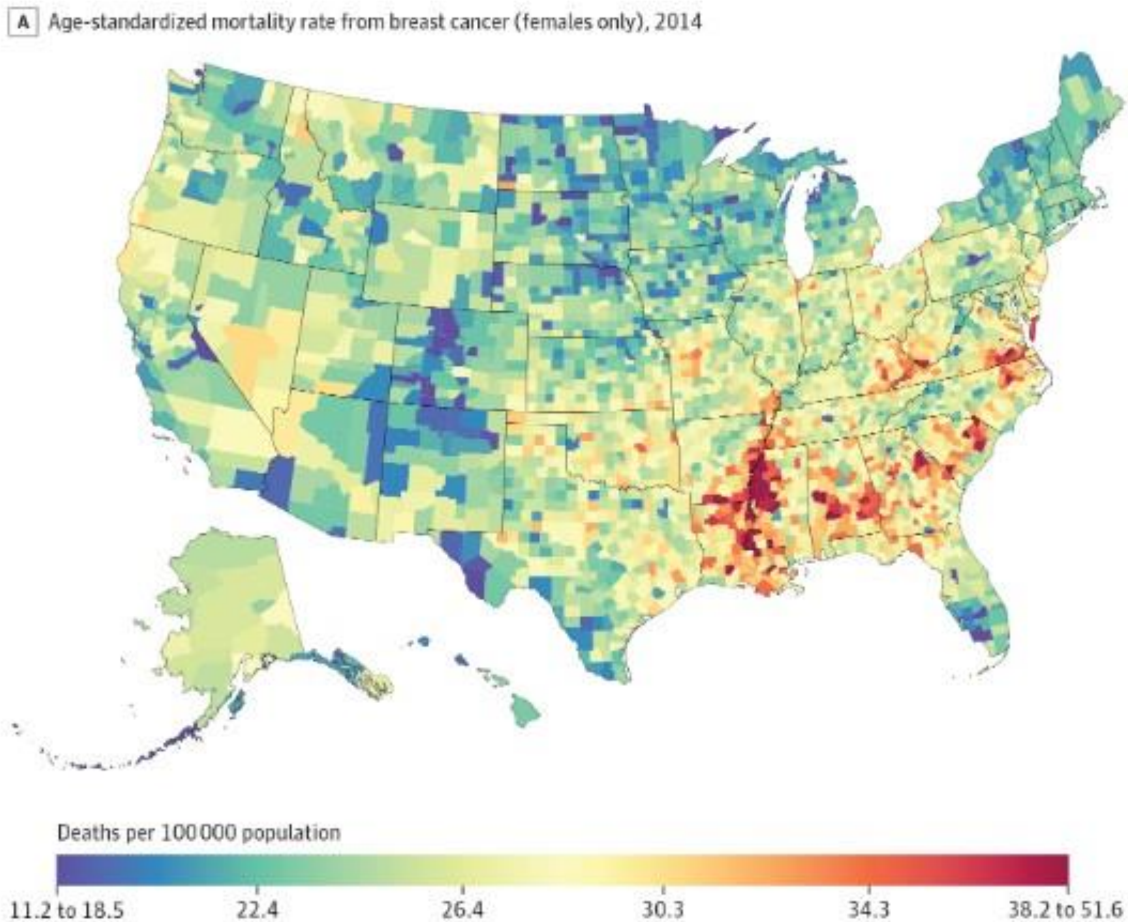
West Nile Virus



2013 Diagnosed Diabetes Prevalence



Data source: United States Diabetes Surveillance System.


A Age-standardized mortality rate from breast cancer (females only), 2014
Deaths per 100 000 population
11.2 to 18.5
22.4
26.4
30.3
34.3
38.2 to 51.6

Malaria Atlas Project

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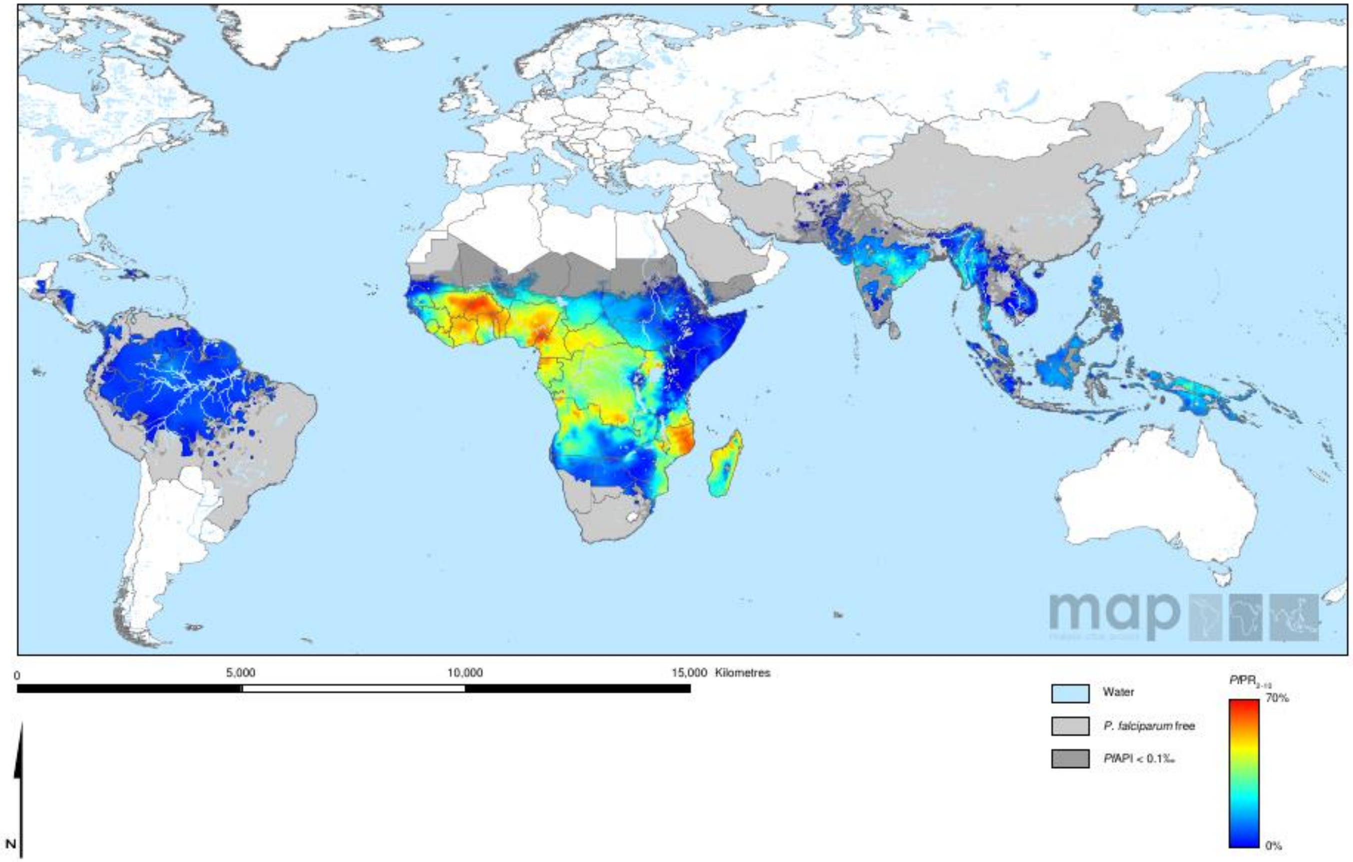
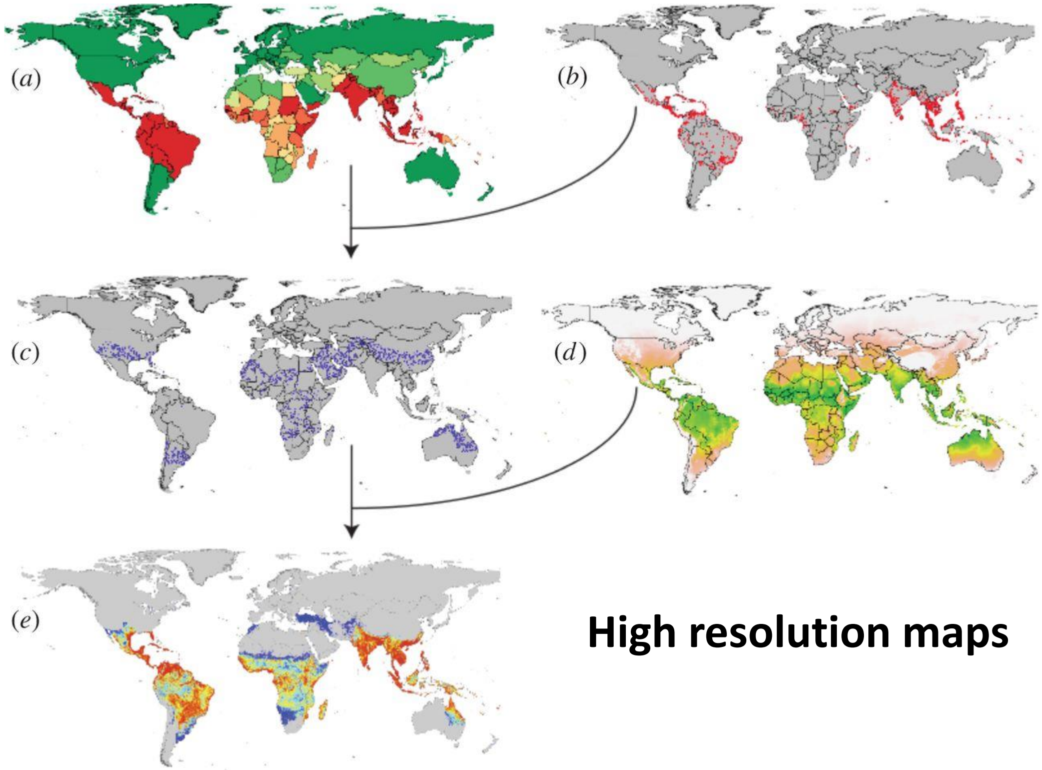
Malaria


map
0
5,000
10,000
15,000 Kilometres
N
Water
P. falciparum free
PfAPI < 0.1‰
70%
0%

Ecological Niche Modeling: Vector-borne diseases

Georeferenced data points

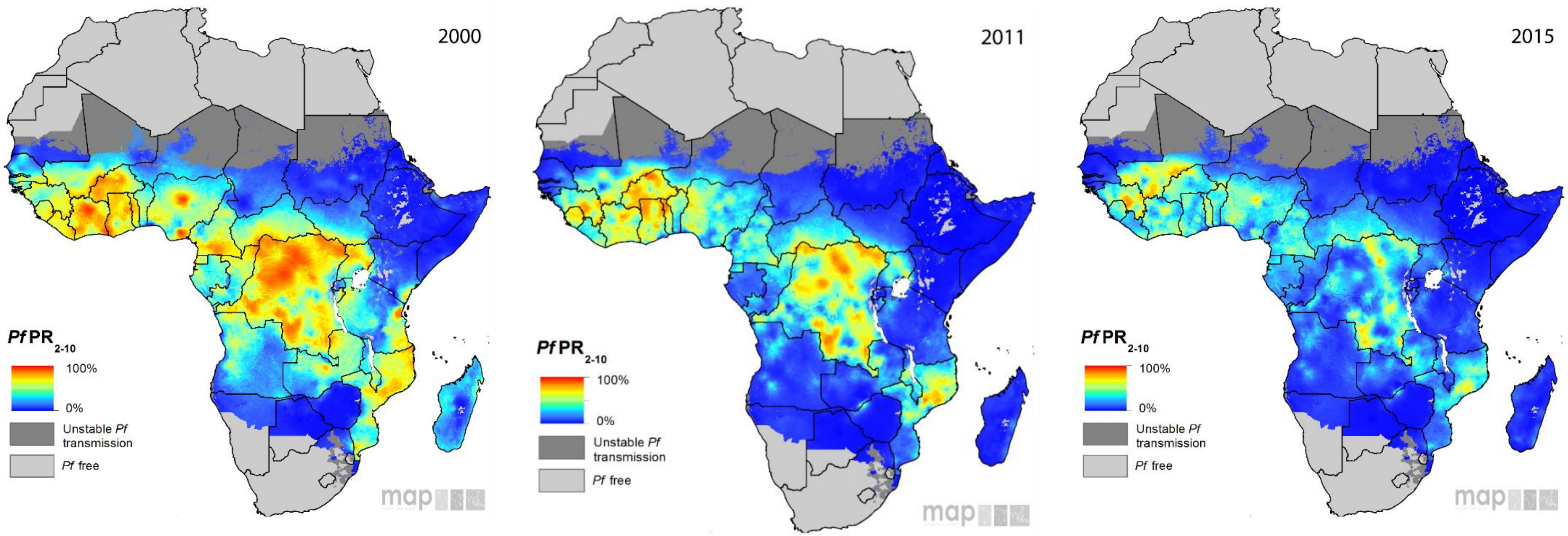


Environmental cofactors

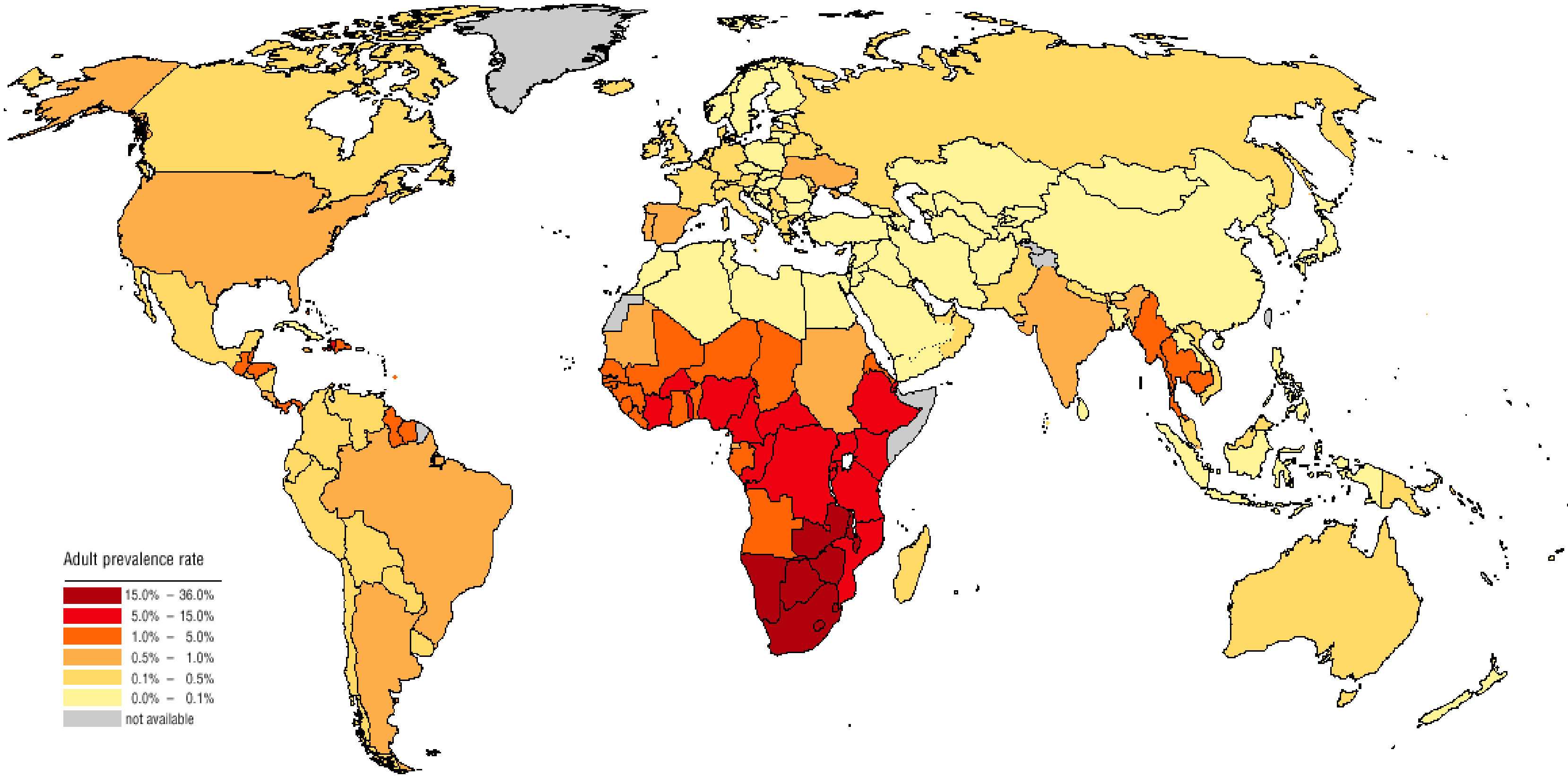
High resolution maps

High resolution maps of the **geographic distribution of a disease**. The use of the survey data from a **sample of locations** to predict continuous surfaces of risk, informed by **environmental and demographic covariates**

Spatio-temporal dynamics of malaria



HIV



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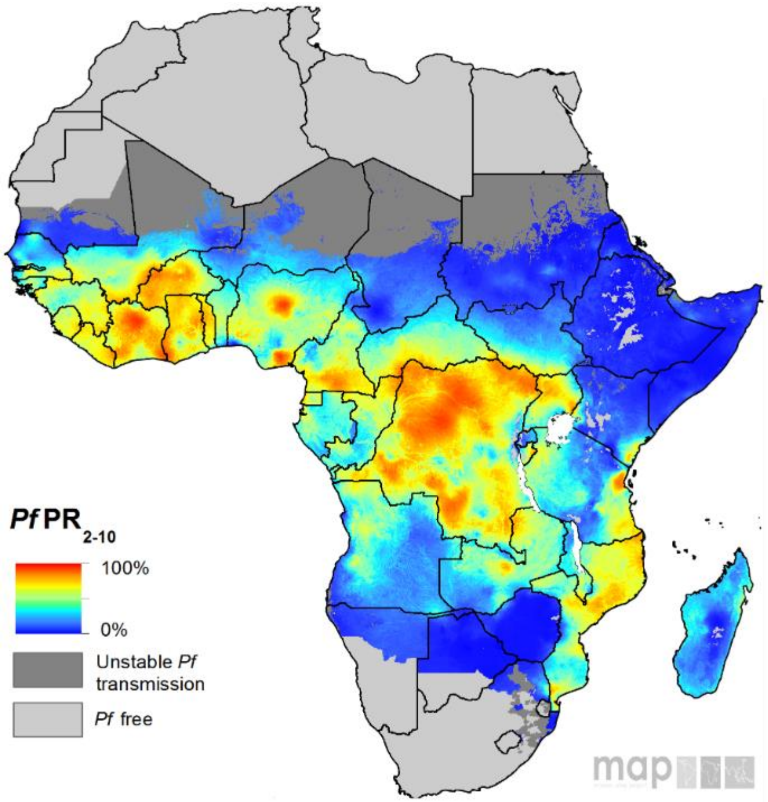

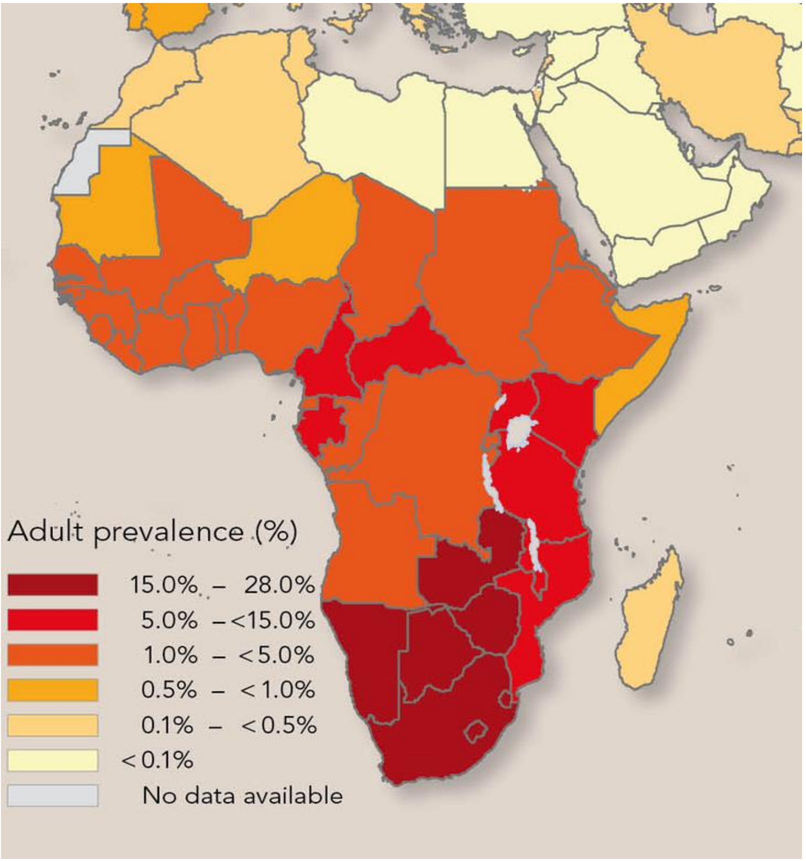

Malaria

HIV

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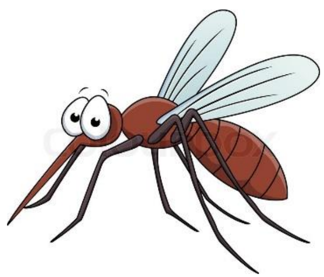
Introduction: HIV

- The human immunodeficiency virus (HIV) is retrovirus that causes HIV infection and over time acquired immunodeficiency syndrome (AIDS)
- AIDS is a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections to thrive
- Without treatment, average survival time after infection with HIV is estimated to be 9 to 11 years
- **Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, or breast milk**

Introduction: HIV

Vector-borne diseases

Pathogen | Vector | Host



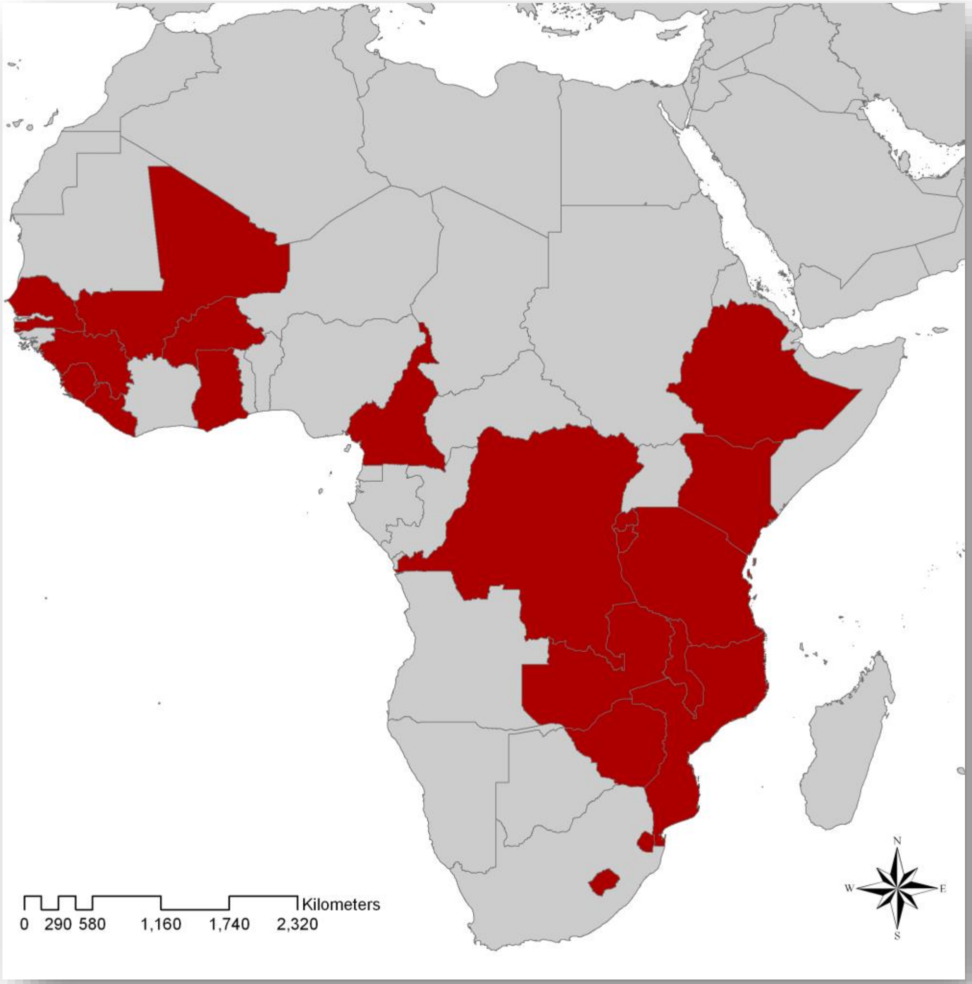
Sexually transmitted infections (STI)

Infected → **Susceptible**

Research question:

Is the spatial distribution of HIV random? Clustered?

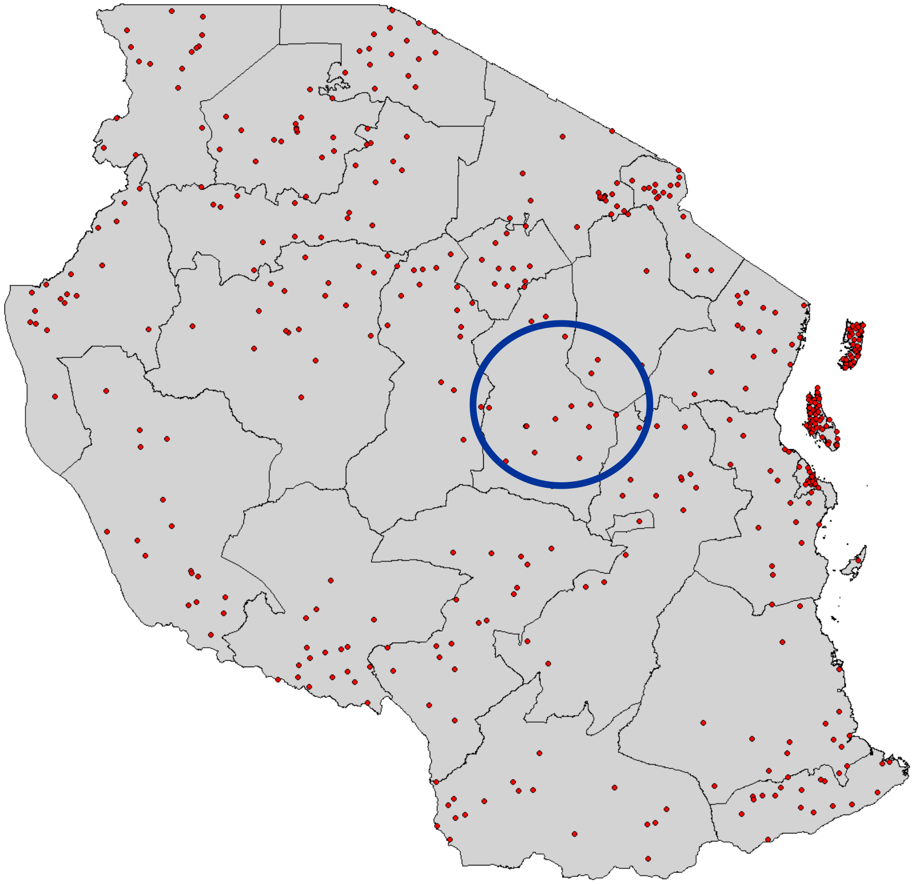
- For each country, we only considered the most recent Demographic Health Survey where HIV data were collected. As a result, a total of **20 countries in SSA were included**



Methods: Clustering analysis

- **Spatial scan statistics** is a cluster detection test able to find the location of areas with **higher or lower numbers of cases** (for instance HIV infections) than expected

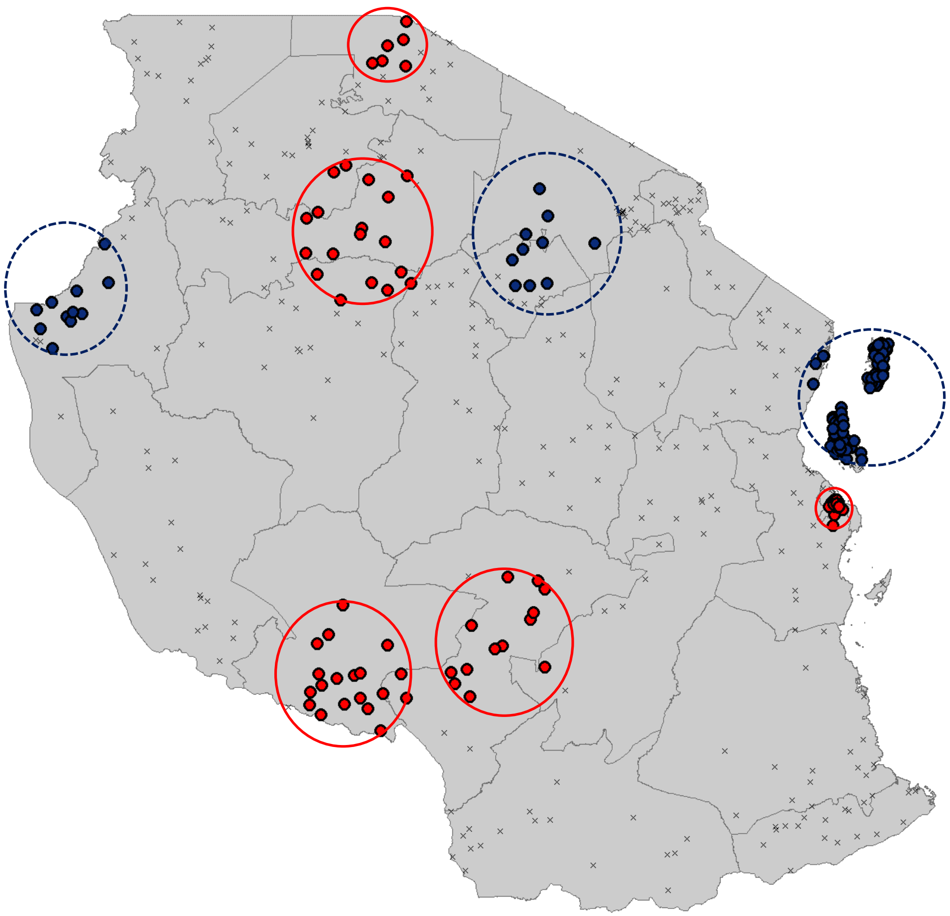
- For each potential cluster, a likelihood ratio test was computed. The numbers of observed and expected HIV infections within and outside the circular window were then compared to test the **null hypothesis of spatial randomness**



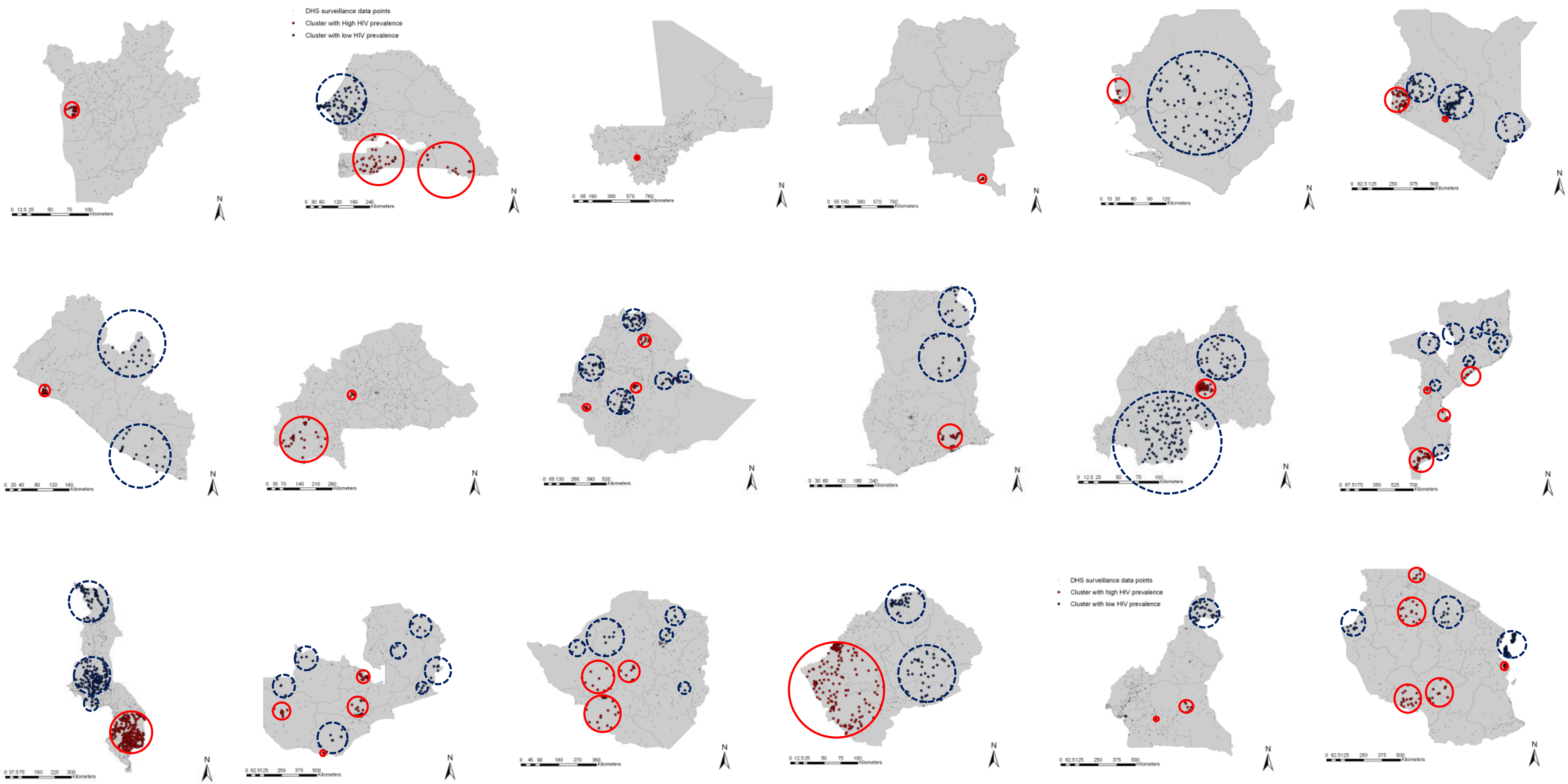
Hot and cold spots

- We identified **38** clusters with high HIV prevalence (**hot spots; red circles**), and **45** clusters with low HIV prevalence (**cold spots; blue circles**)

- The HIV seroprevalence within the clusters with high HIV seroprevalence ranged from 1.9% in a cluster in Senegal to 30.8% in a cluster in Zimbabwe, with a **median of 11.5%**

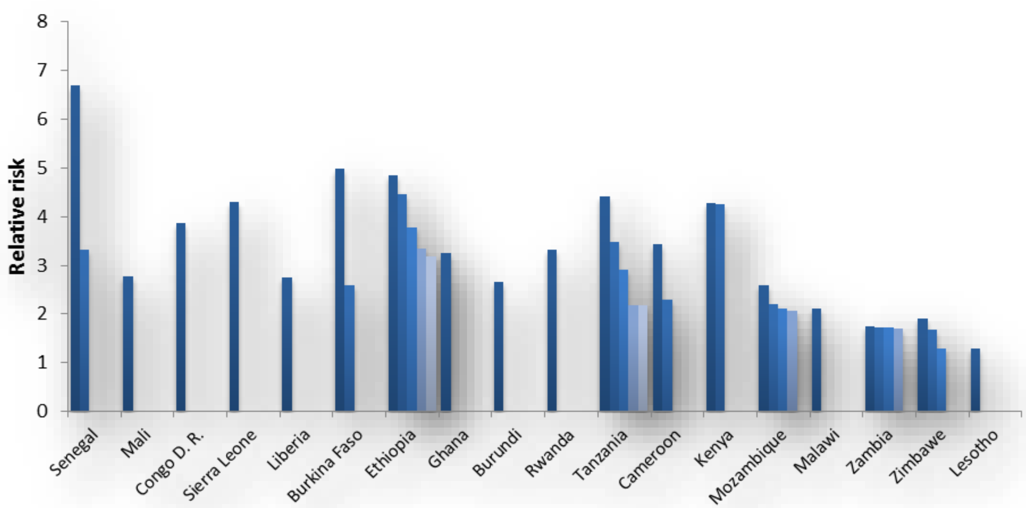


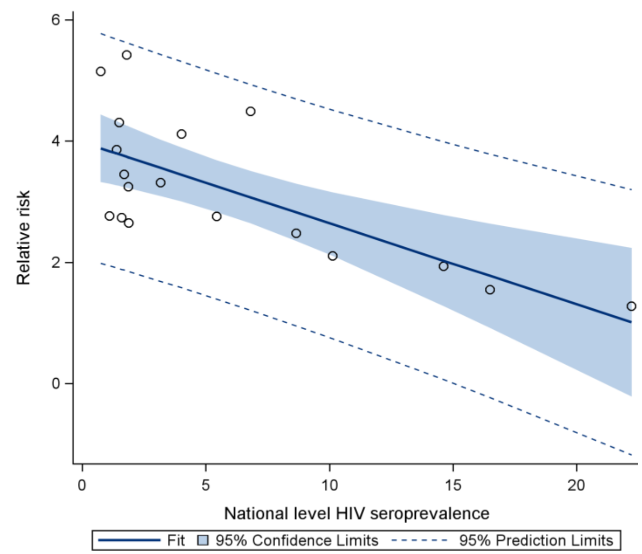
HIV clustering



Cuadros, Diego F., Susanne F. Awad, and Laith J. Abu-Raddad. "Mapping HIV clustering: a strategy for identifying populations at high risk ofHIV infection in sub-Saharan Africa." International journal of health geographics (2013)

Results: HIV clustering

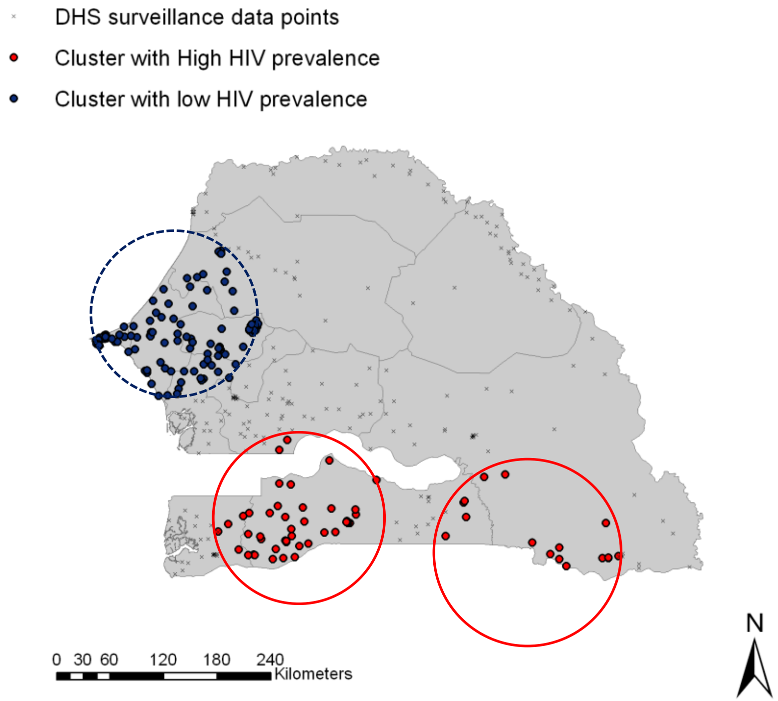


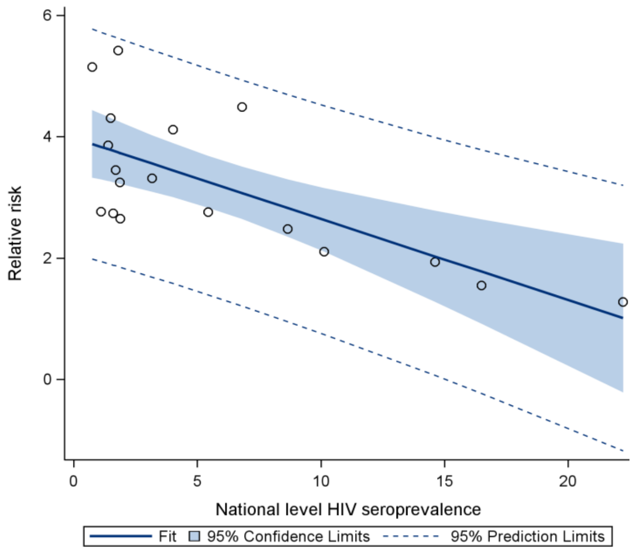


The relative risk of HIV infection for individuals within clusters with high HIV seroprevalence was **negatively associated with HIV prevalence** of the corresponding country ($p < 0.001$)

Cuadros, Diego F., Susanne F. Awad, and Laith J. Abu-Raddad. "Mapping HIV clustering: a strategy for identifying populations at high risk ofHIV infection in sub-Saharan Africa." International journal of health geographics (2013)

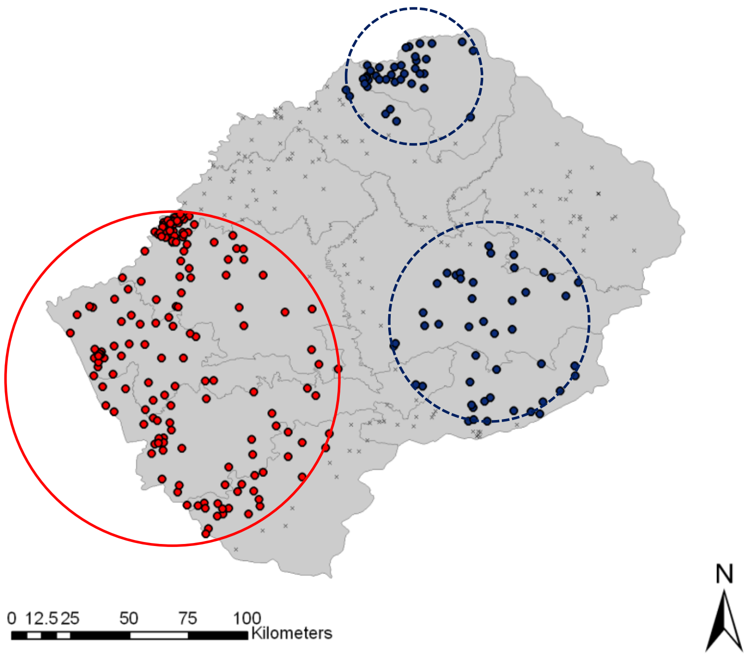
Results: HIV clustering in Senegal

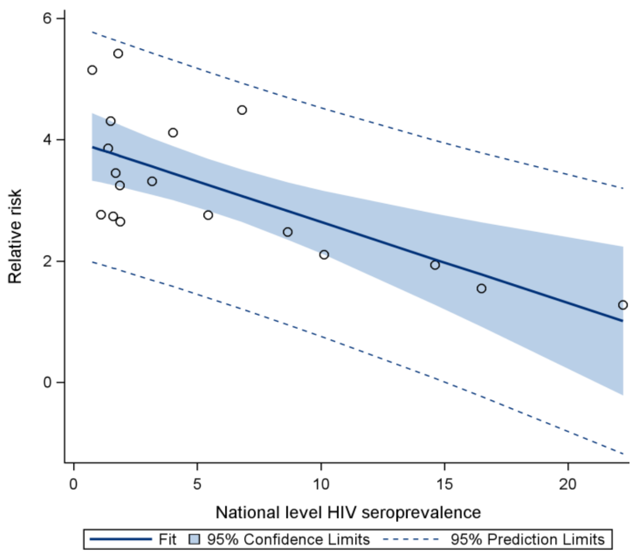




The strength of the clustering was **higher in countries with low HIV prevalence**. The highest RR of HIV infection was estimated in a cluster in **Senegal** (RR = 6.69, HIV seroprevalence = 4.3%), the country with the lowest HIV prevalence (0.7%)

Results: HIV clustering in Lesotho



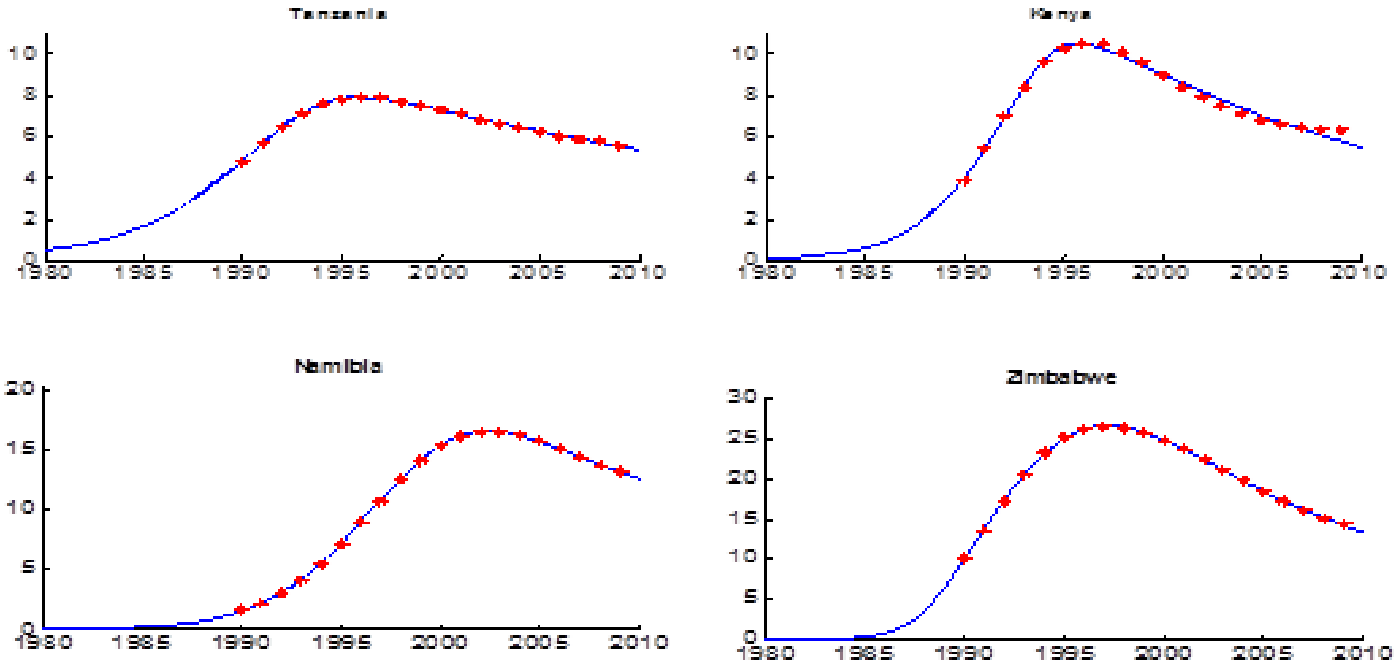


The strength of the clustering was **smaller in countries with higher HIV prevalece**. In **Lesotho**, the strength of the clustering was fairly small (RR = 1.28, HIV prevalence = 25.4), the country with the highest HIV prevalence (22.2%)

- The results of our analysis indicate **stark geographical variation in HIV prevalence** in most of the countries. The observed spatial variation in HIV prevalence highlights **a clustered HIV transmission across SSA** within micro-epidemics of different scales

Rationale: HIV prevalence decline

- **HIV prevalence is declining** in parts of West, Southern and East Africa



Research question:

Is the geographical clustering structure of HIV affecting the temporal dynamics of the epidemic?

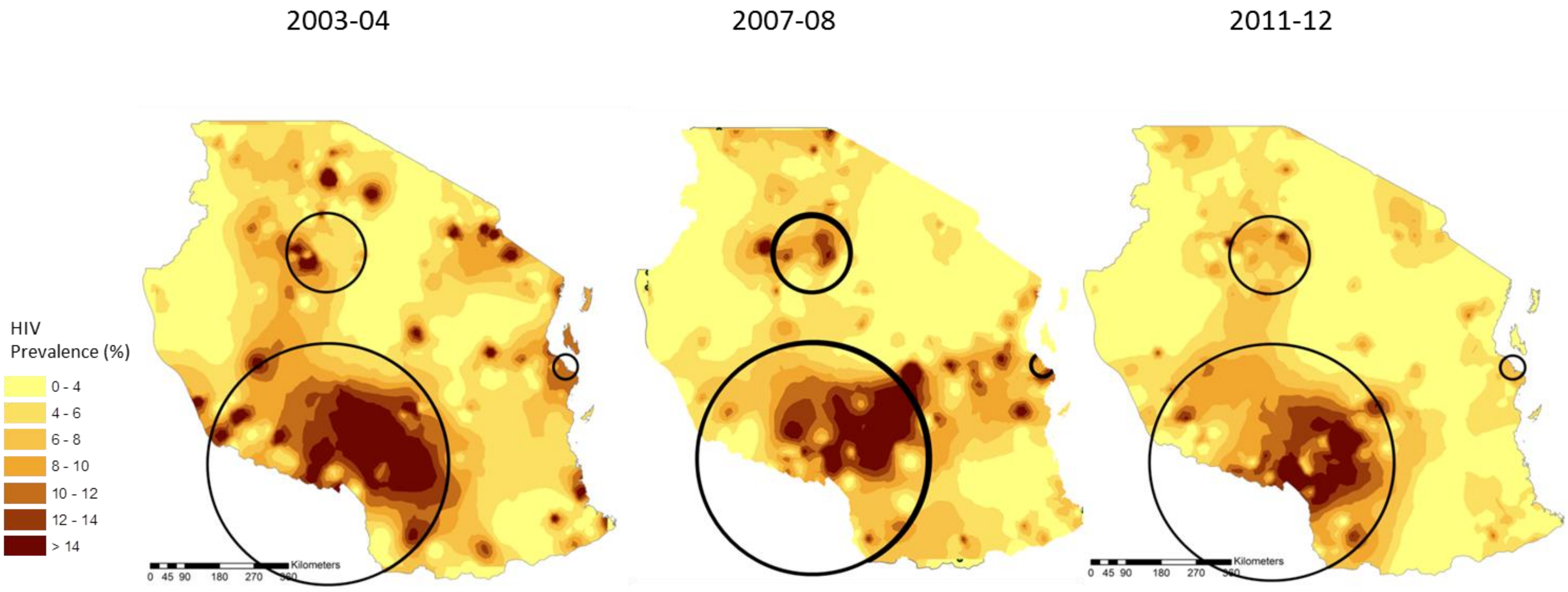
Methods: Spatiotemporal HIV clustering

- Data were obtained from **Demographic and Health Surveys (DHS)** conducted at different times in Tanzania

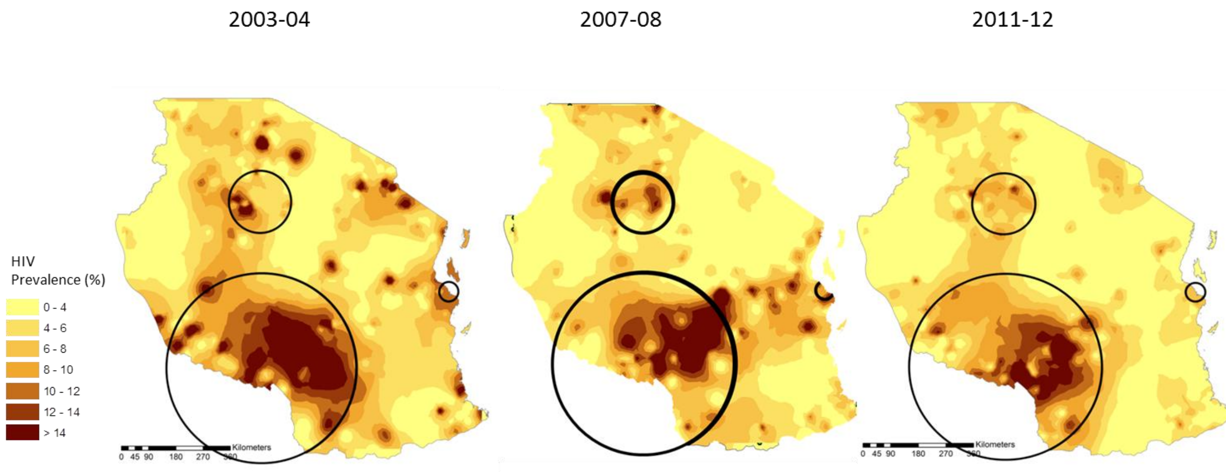
- We used **spatial scan statistics** to identify the geographical clusters with high numbers of HIV infections in each country

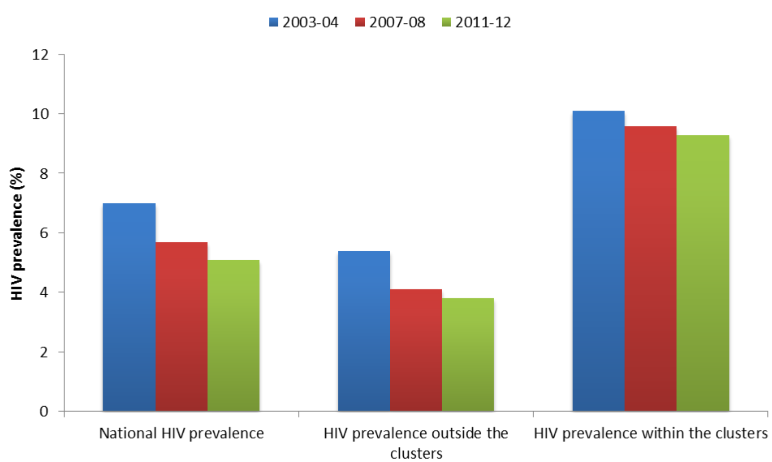
- The trend in HIV prevalence was assessed for the clusters with high HIV prevalence and outside these clusters using the chi-square test for trend for Tanzania (as three DHS rounds are available)

Results: Spatiotemporal HIV clustering



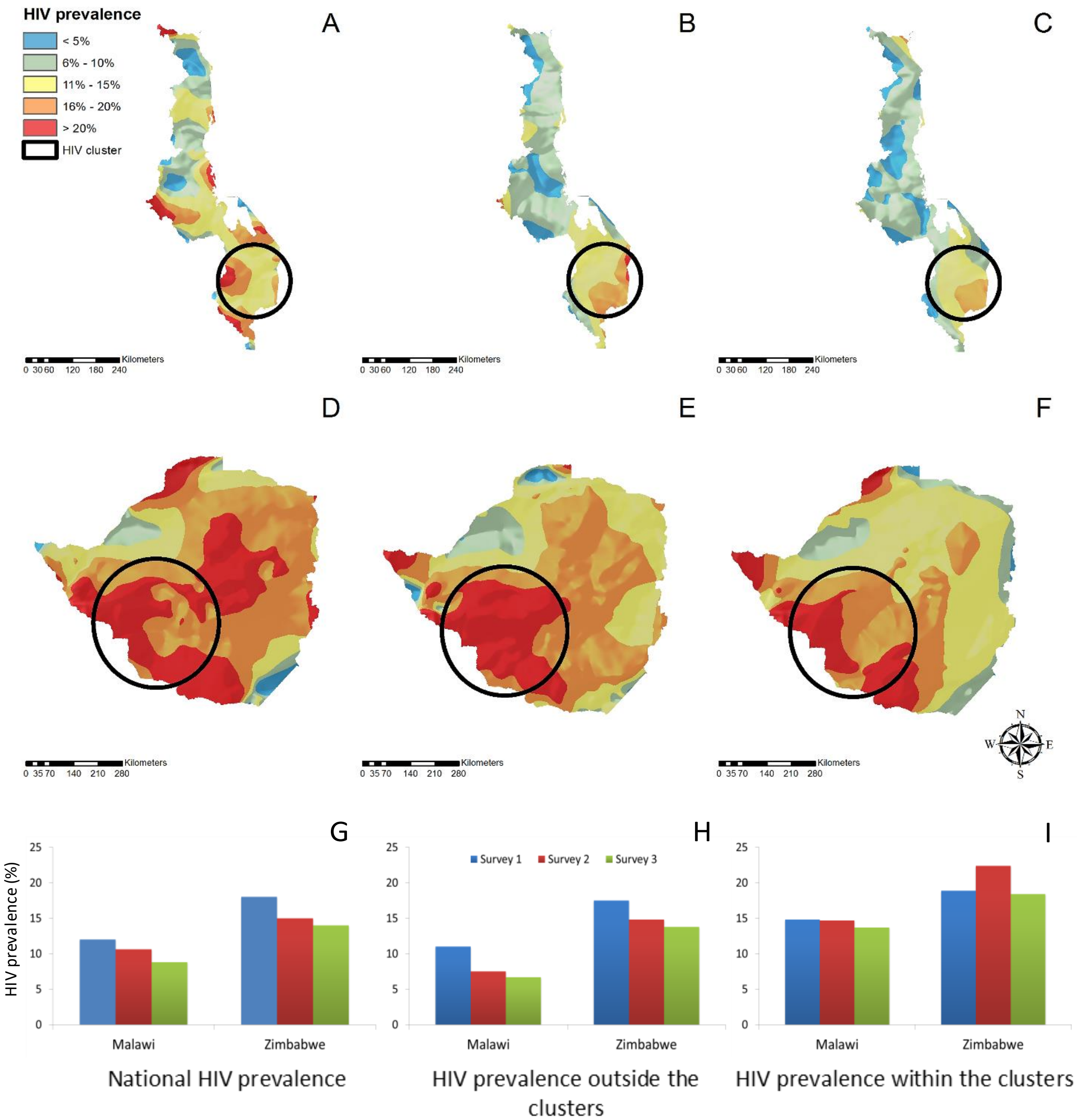
Results: Spatiotemporal HIV clustering





- The national HIV prevalence in Tanzania declined by 27% from 2003 to 2011 ($P < 0.001$)
- No decline was observed within the clusters with high HIV prevalence collectively ($P = 0.14$)
- HIV prevalence outside the high HIV prevalence clusters declined by 30% ($P < 0.001$)

Results: Spatiotemporal HIV clustering



Temporal trends in the clustering of HIV infection in Malawi and Zimbabwe. Spatial locations of the high HIV prevalence cluster in Malawi 2004 (A), 2010 (B), and 2015-16 (C). Spatial locations of the high HIV prevalence cluster in Zimbabwe 2005-06 (D), 2010-11 (E), and 2015 (F). Continuous surfaces of HIV prevalence within a country were generated using a kernel density mapping algorithm. Bar charts illustrate the temporal trend in national HIV prevalence (G), HIV prevalence outside the high HIV prevalence clusters (H), and HIV prevalence within the high HIV prevalence clusters (I)

Conclusions: Spatiotemporal HIV clustering

- Our study suggests that the national HIV prevalence declines in SSA may not be representative of broad declines in prevalence within countries, as much as reflecting **sharp declines in prevalence in areas of already lower HIV prevalence**

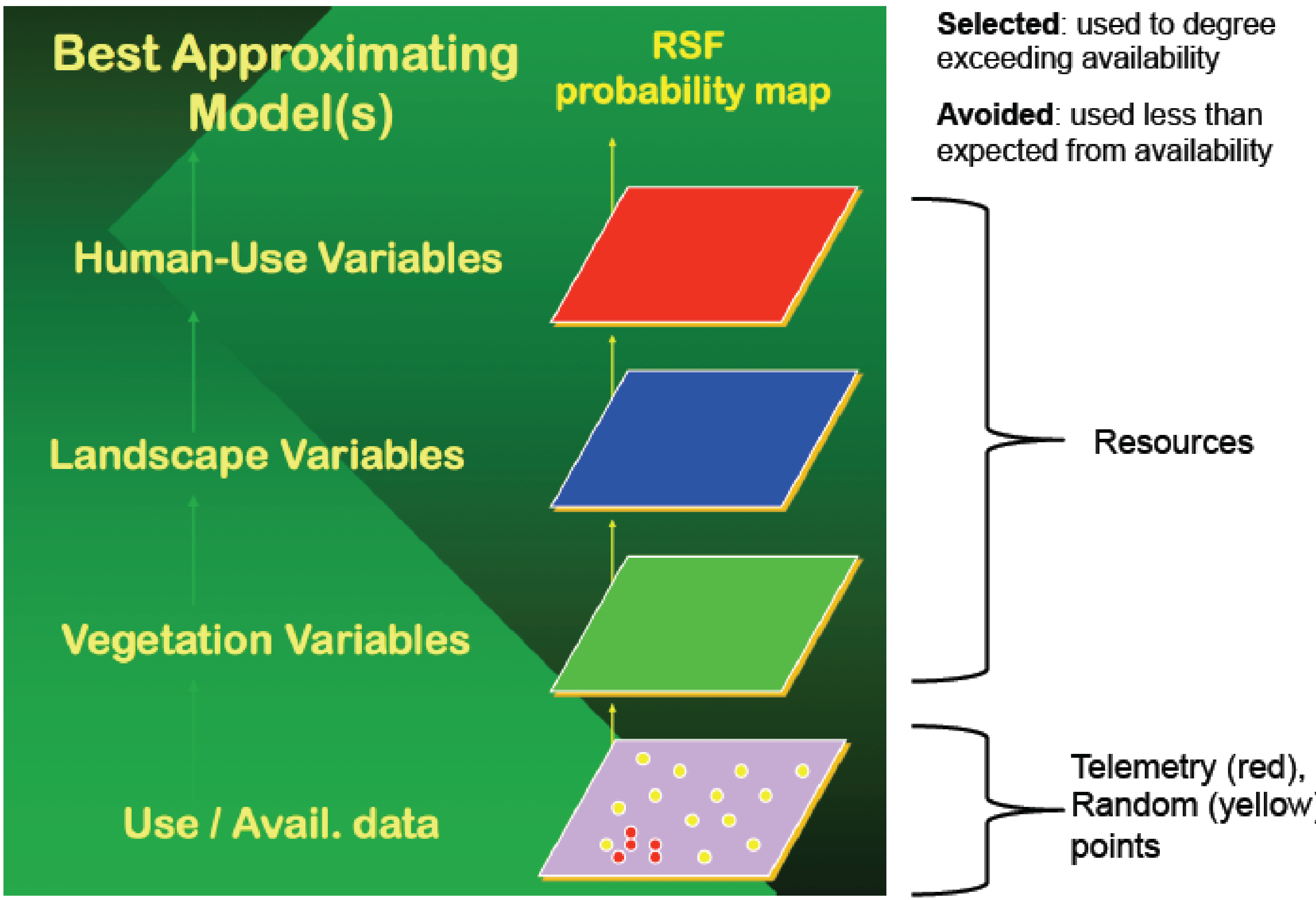
- HIV prevalence declines in Tanzania, Malawi and Zimbabwe were **driven by rapid changes in prevalence outside of the core areas** of intense HIV transmission

- The temporal evolution of the epidemics appears to be that of “contraction” towards somewhat isolated “cores” of high HIV prevalence

Research question:

Could environmental and socio-economic and behavioral factors be used to generate high resolution maps of HIV prevalence in SSA?

Ecological Niche Modeling



HIV factors

Four countries

Tanzania, Kenya, Malawi and Mozambique

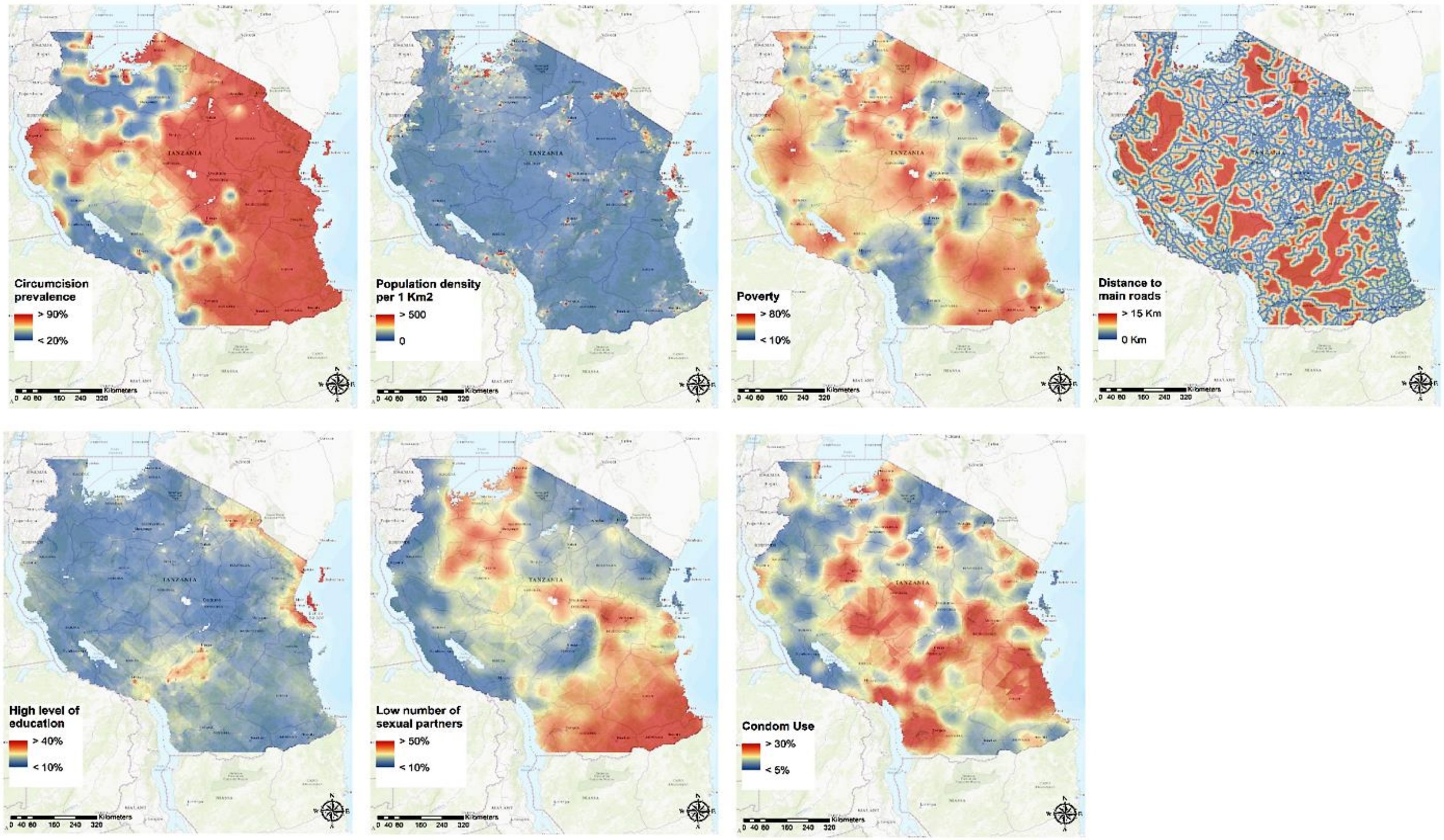
Environmental (geographical) factors:

- Normalized Difference Vegetation Index (NDVI)
- Population
- Distance to main roads

Socio-economic and behavioral factors:

- Wealth index
- Male circumcision
- Lifetime sexual partners
- Education
- Ever been tested for HIV
- Condom use

Maps of cofactors



Cuadros, Diego F., et al. "Mapping the spatial variability of HIV infection in Sub-Saharan Africa: Effective information for localized HIV prevention and control." Scientific reports (2017)

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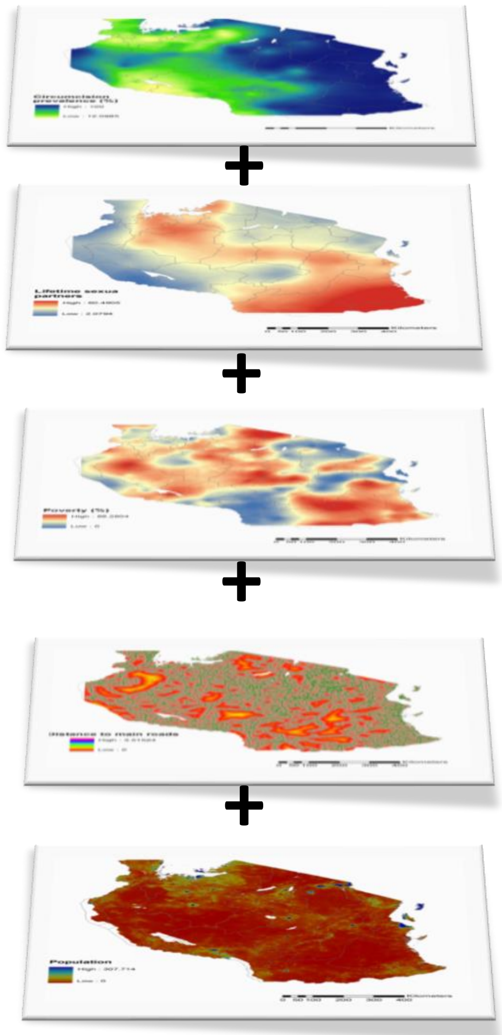
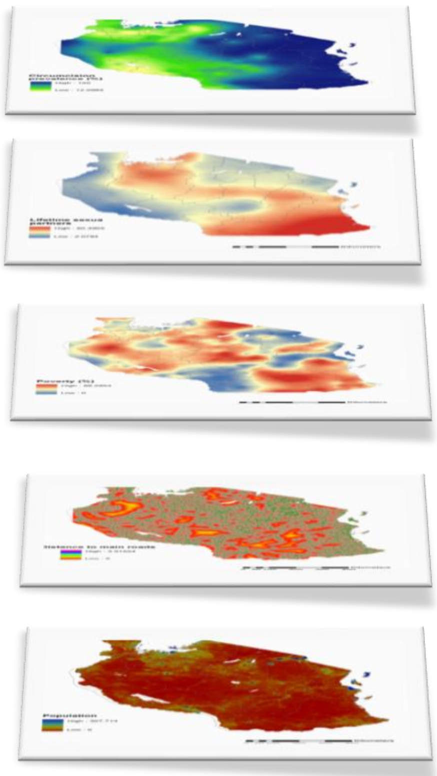
Maps of cofactors



= High Resolution HIV prevalence map

High resolution map of HIV in Tanzania



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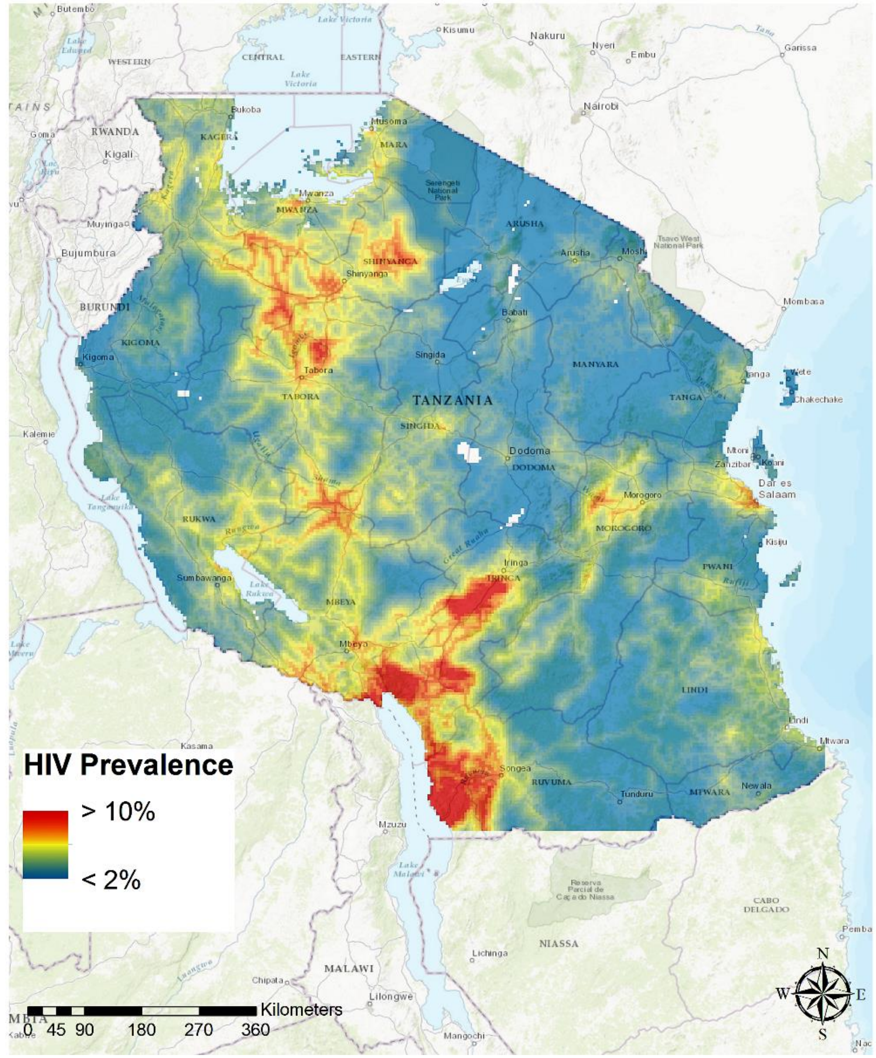

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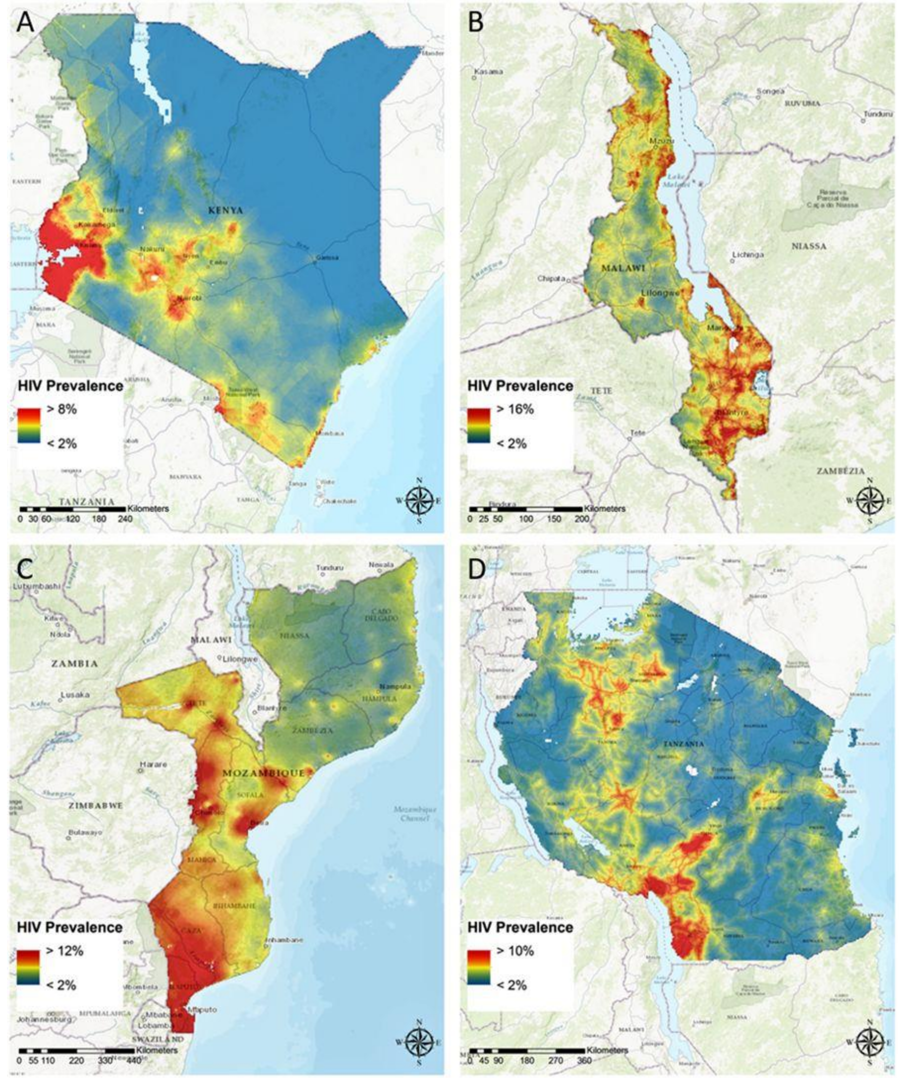
High resolution maps for HIV prevalence in East Africa

High resolution maps for HIV prevalence in (**A**) Kenya; (**B**) Malawi; (**C**) Mozambique; and (**D**) Tanzania.



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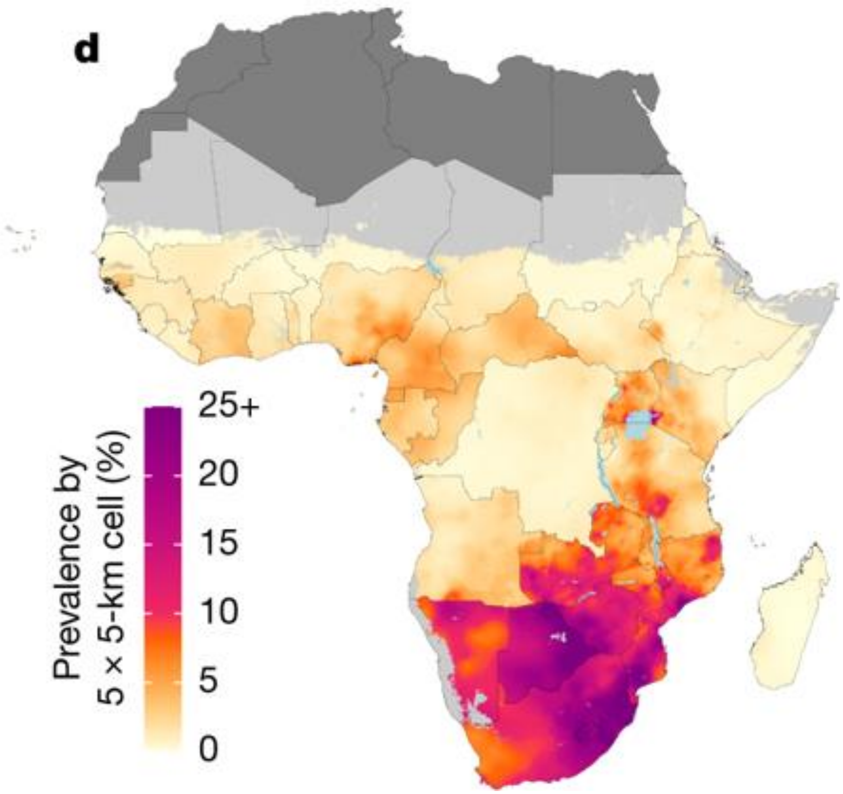
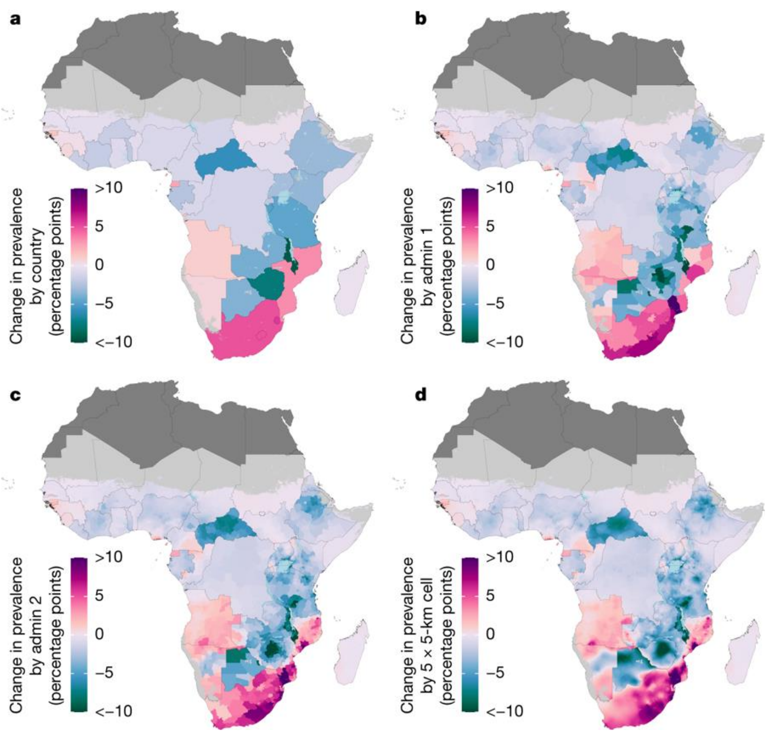
HIV prevalence distribution in Africa



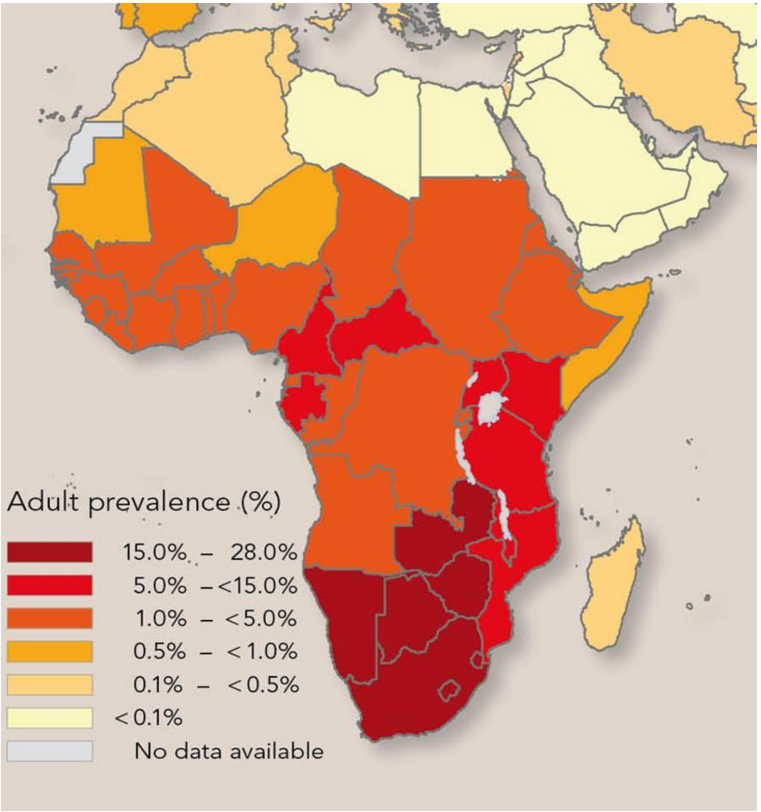
Institute for Health Metrics and Evaluation, University of Washington

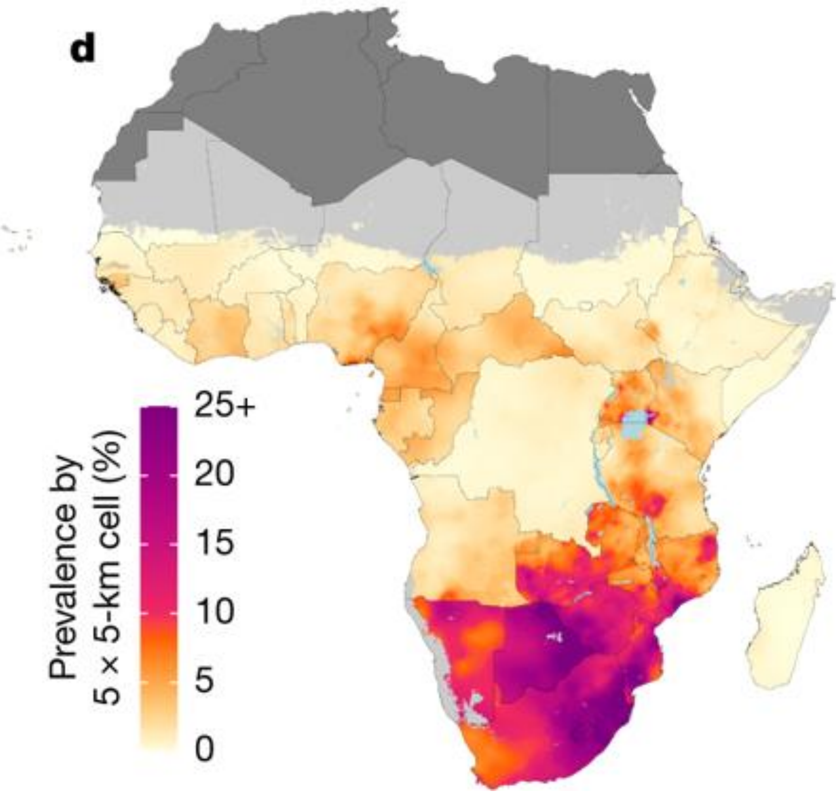
Dwyer-Lindgren, Laura, et al. "Mapping HIV prevalence in sub-Saharan Africa between 2000 and 2017." Nature (2019)



Absolute change in HIV prevalence among adults aged 15–49 between 2000 and 2017 at the country level (**a**), first administrative subdivision level (**b**), second administrative subdivision level (**c**) and 5 × 5-km grid-cell level (**d**).

HIV prevalence distribution in Africa



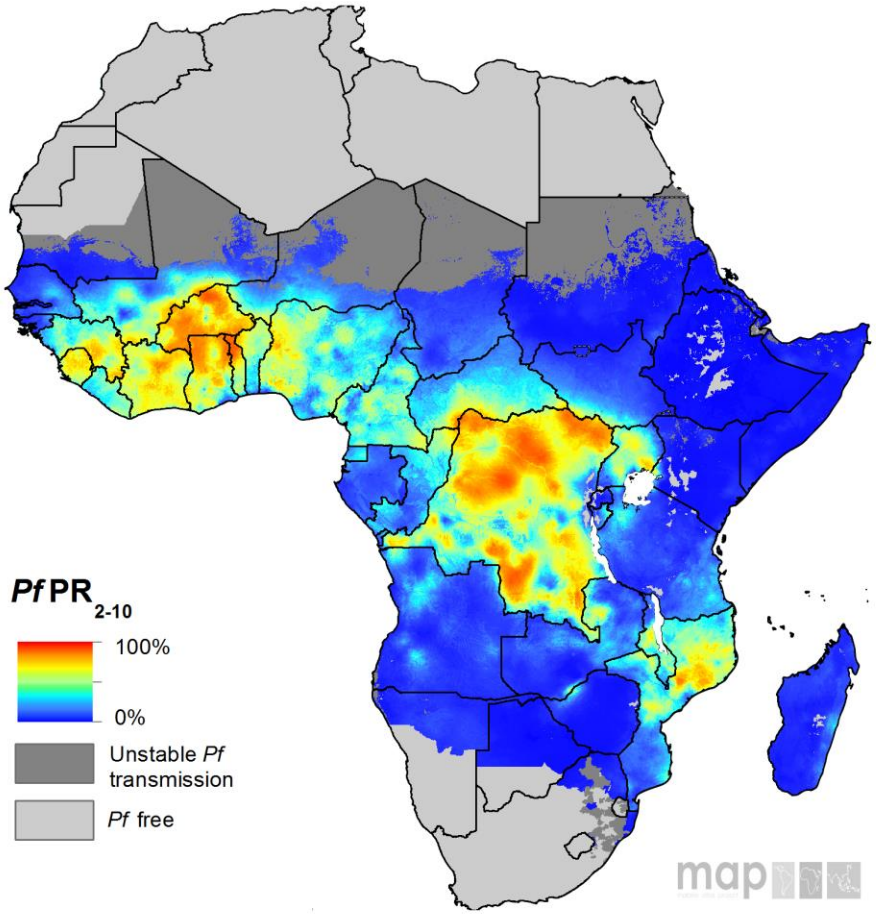


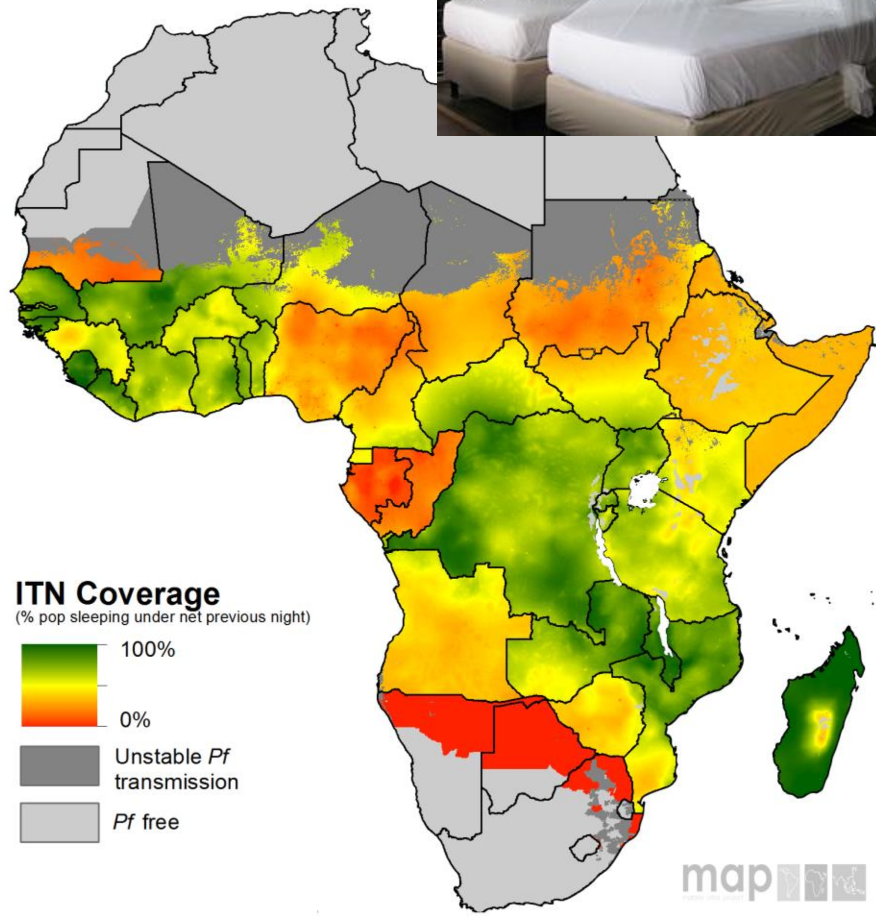
Dwyer-Lindgren, Laura, et al. "Mapping HIV prevalence in sub-Saharan Africa between 2000 and 2017." Nature (2019)

Why mapping diseases?

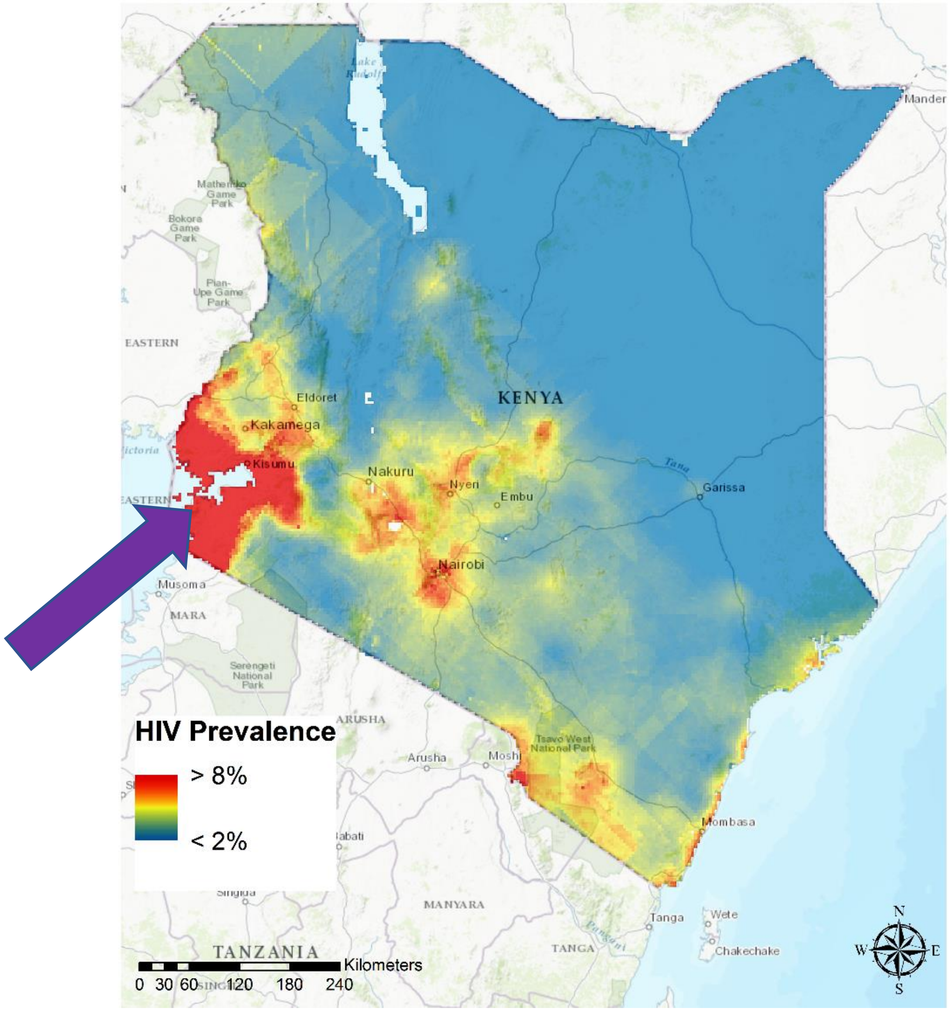
- Maps of disease distribution and intensity allow an immediate visualization of the extent and magnitude of the public health problem

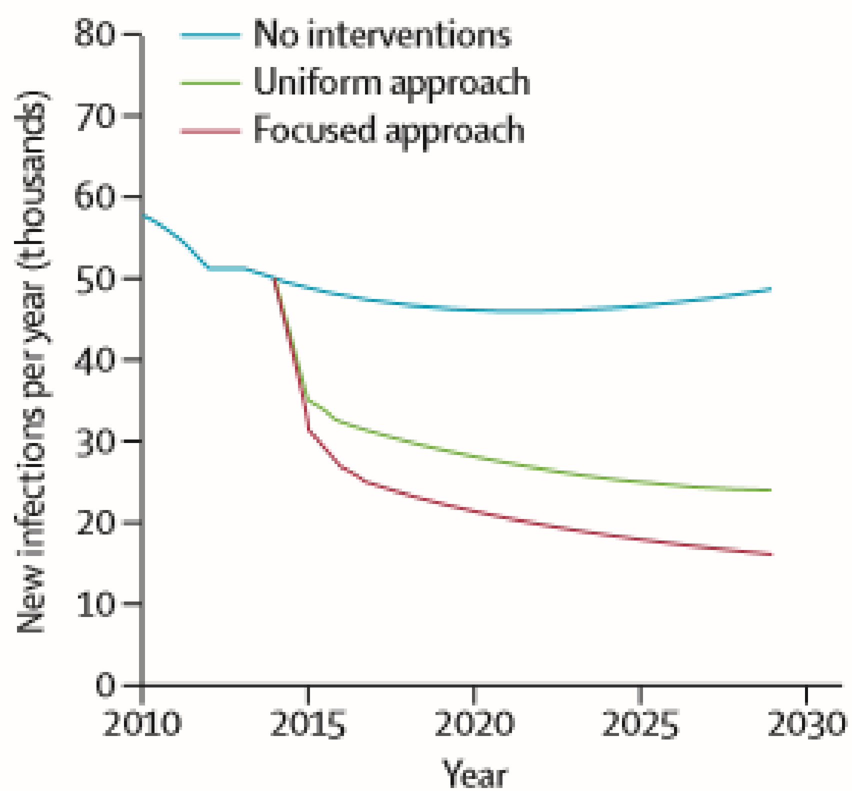
- The identification of the settings where both the burden of disease and the drivers of the disease are concentrated could play an important role for **optimization of resource allocation based on geographically targeted interventions**


Pf PR 2-10
100%
0%
Unstable *Pf* transmission
Pf free
map


ITN Coverage
(% pop sleeping under net previous night)
100%
0%
Unstable *Pf* transmission
Pf free
map

Resource allocation

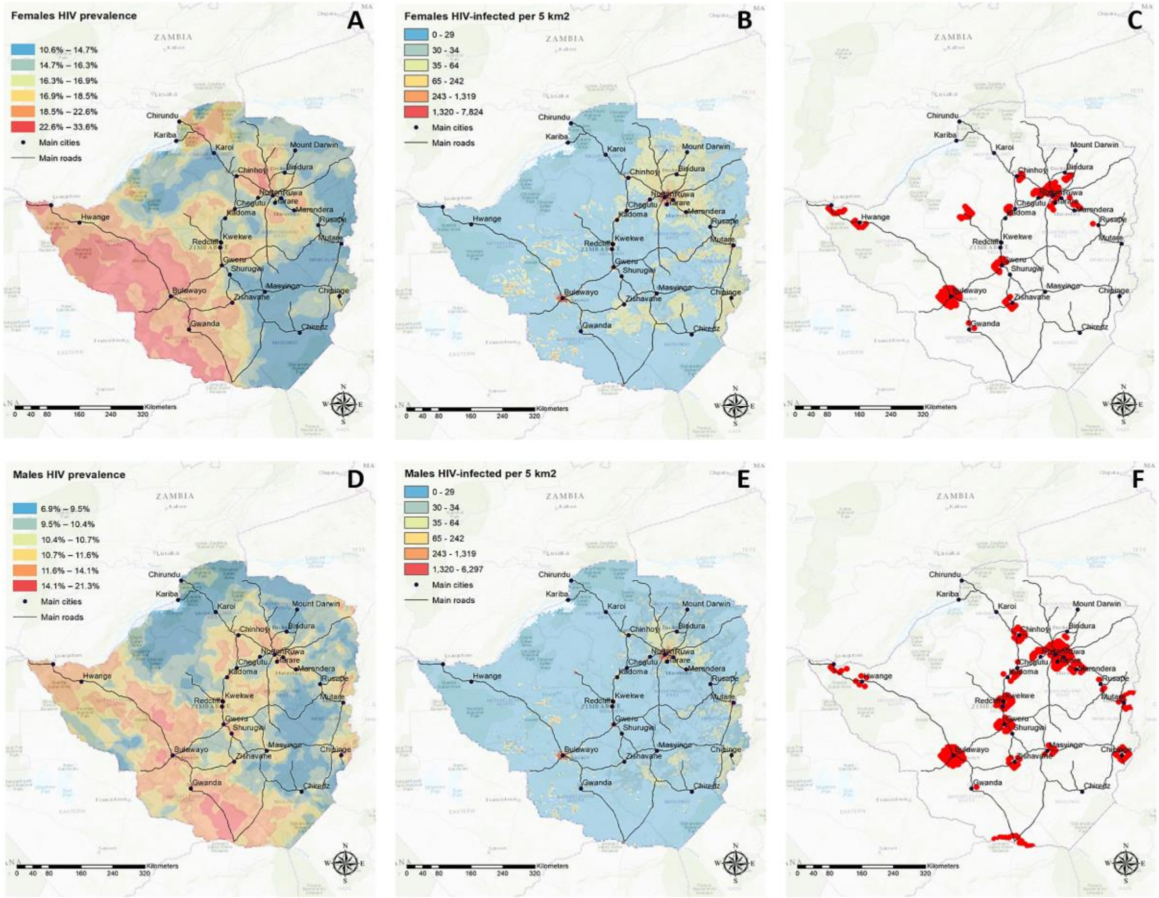




Difference in health gains between the uniform and focused approaches
Anderson et al. *Lancet HIV* 2014

HIV prevention and care in Zimbabwe

High resolution maps of HIV prevalence in Zimbabwe for (A) Females and (D) Males; geographic dispersion of HIV-infected (B) females and (E) males in Zimbabwe. High HIV burden areas are illustrated in red for (C) females and (F) males.



Cuadros, Diego F., et al. "Towards UNAIDS Fast-Track goals: targeting priority geographic areas for HIV prevention and care in Zimbabwe." Aids (2019)

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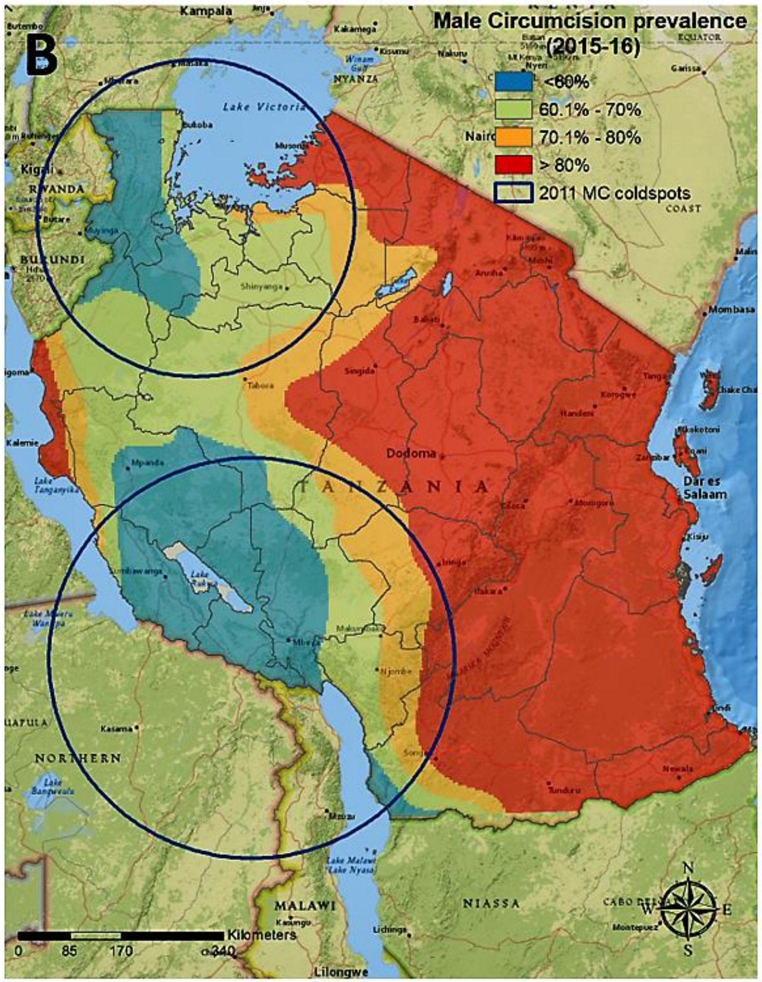
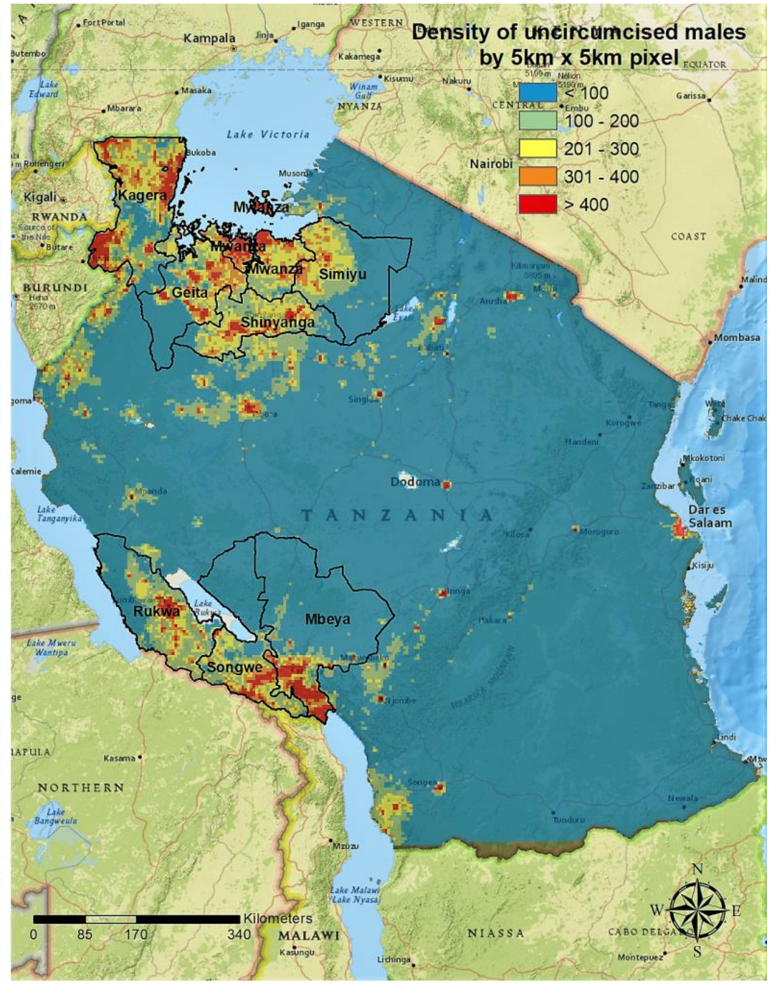
Density distribution of uncircumcised males in Tanzania





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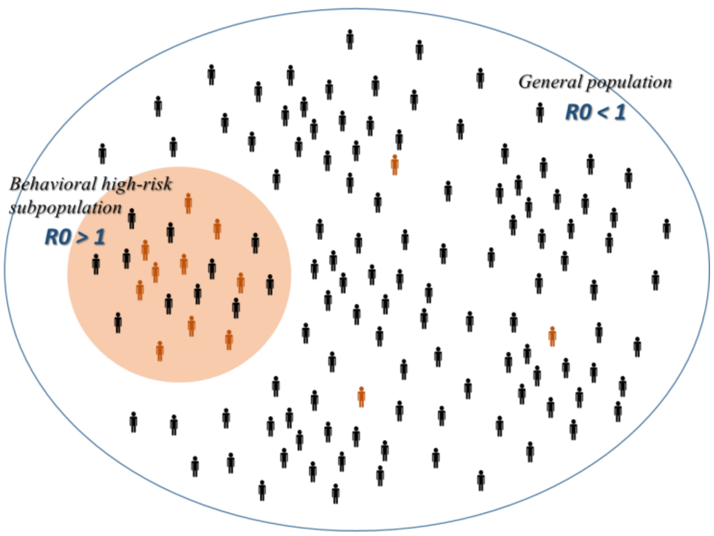
Research question:

What is the contribution of HIV hot-spots in the overall HIV transmission network?

Concentrated epidemic



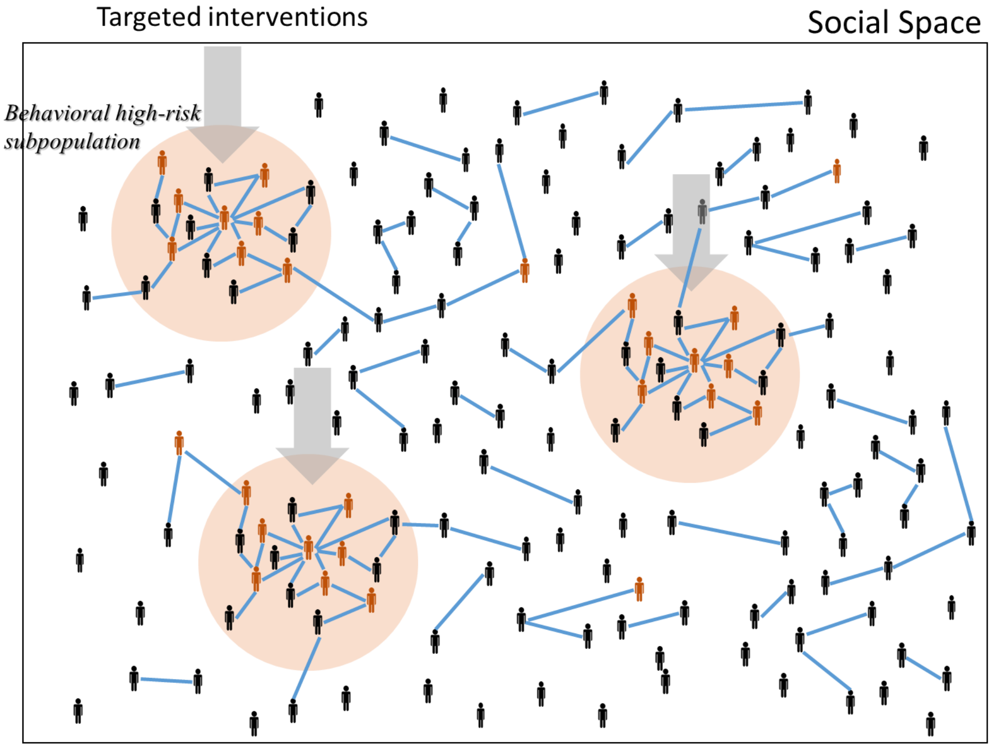
Social space

The study of sexually transmitted infections such as HIV has focused on **social space**

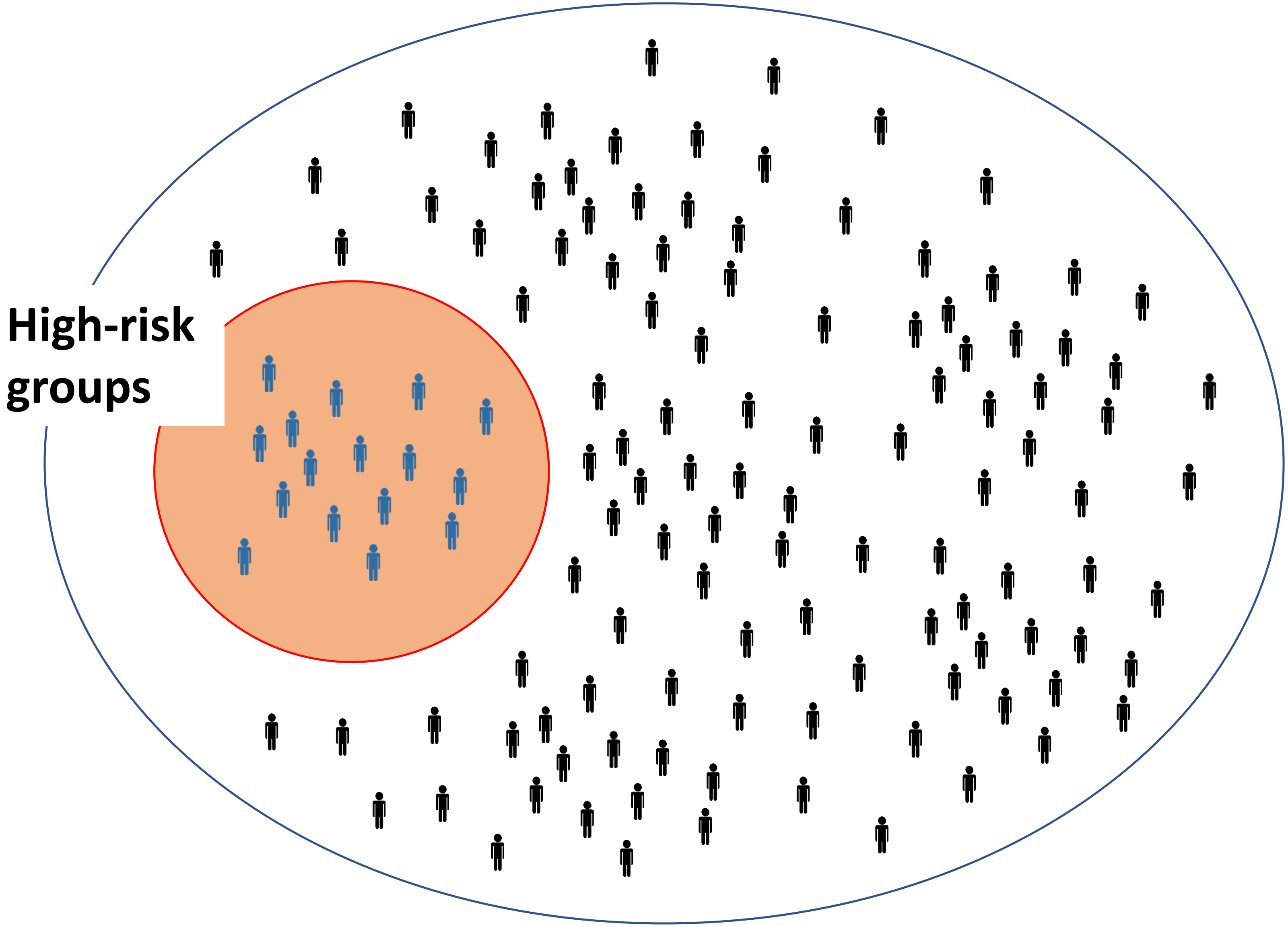
Sexual networks: groups of persons Connected to one another sexually

Characteristics:
-Number of partners (links)
-Serial monogamy
-Concurrent relationships

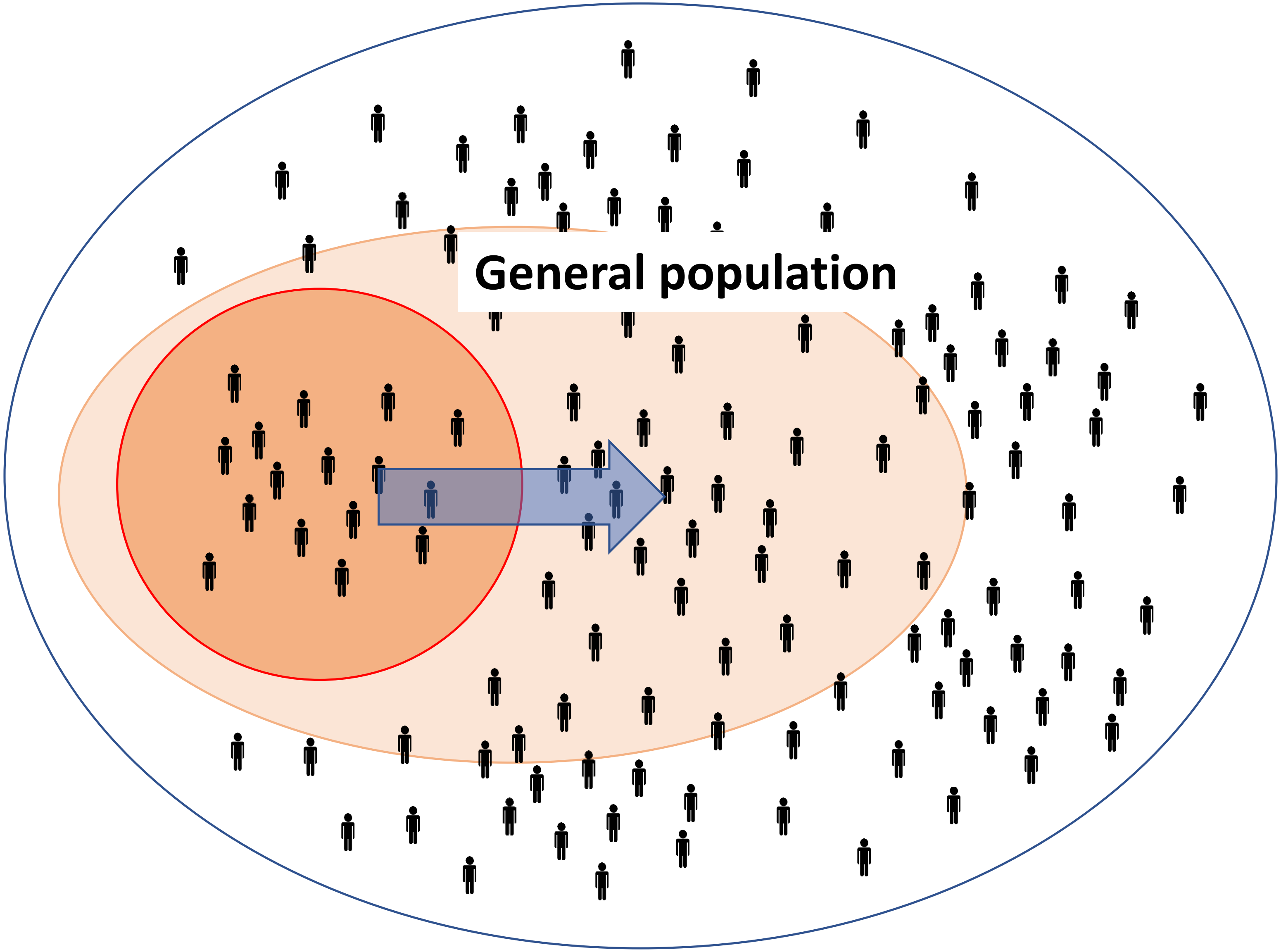
Core groups: members that have high levels of risk behavior and can fuel sustained transmission.



Concentrated epidemic

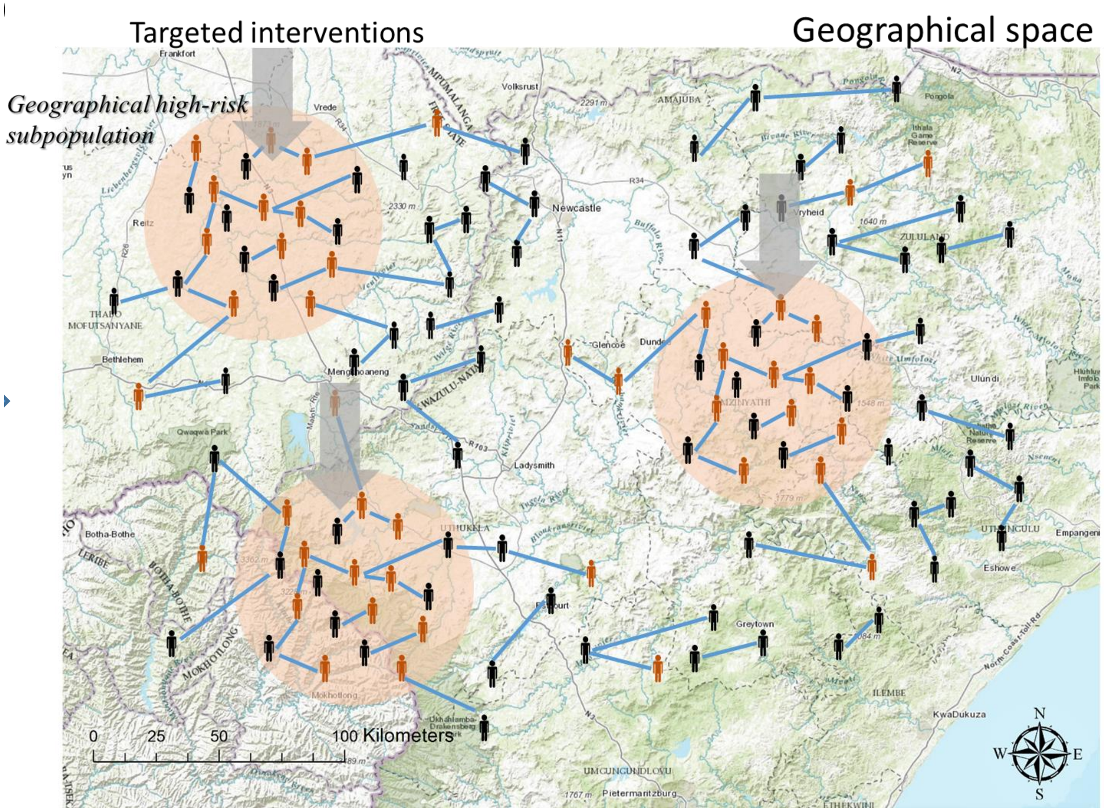


Generalized epidemic

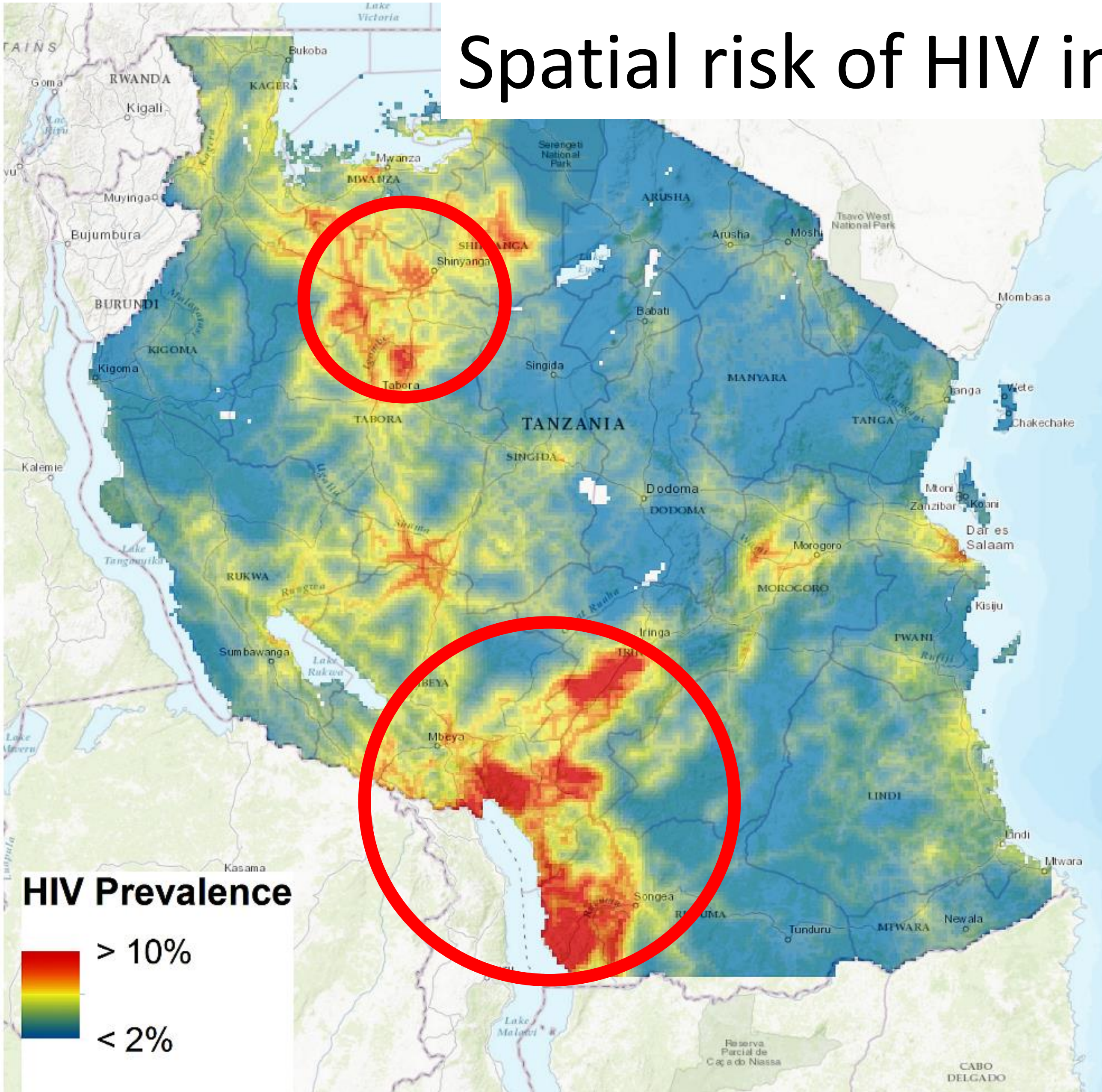


Geographical space

- HIV ‘hot-spots’ can behave as the highly connected nodes of in the transmission network



Spatial risk of HIV infection



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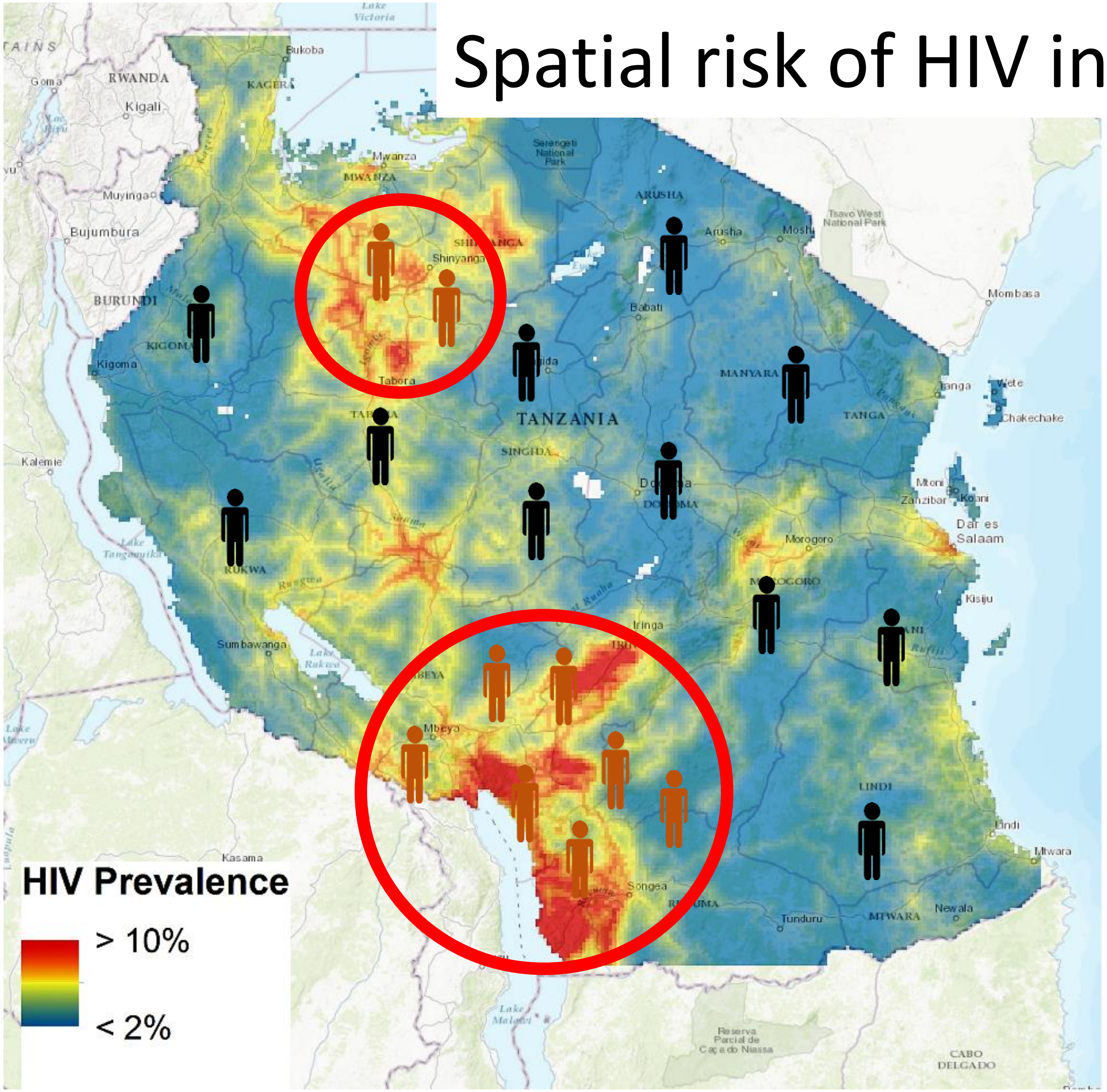
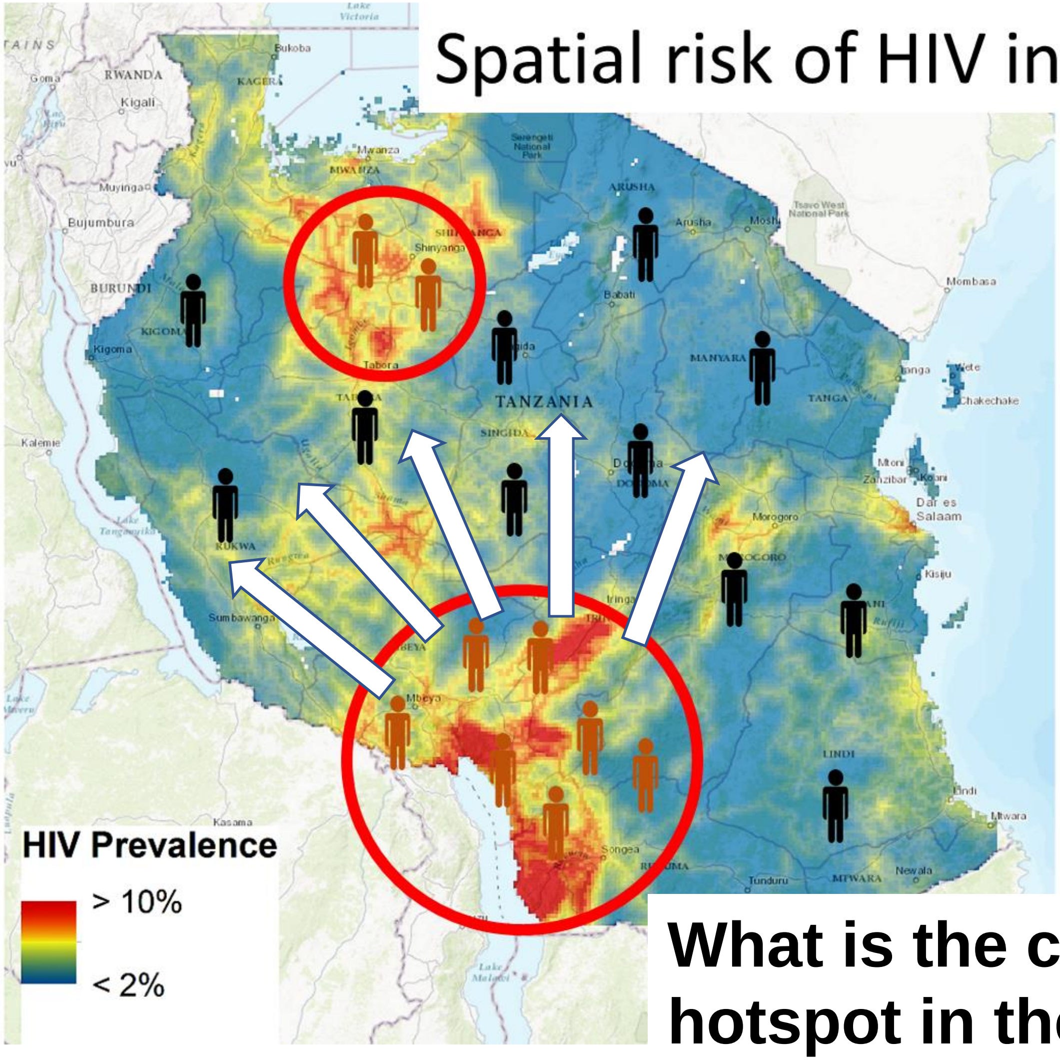
Spatial risk of HIV infection

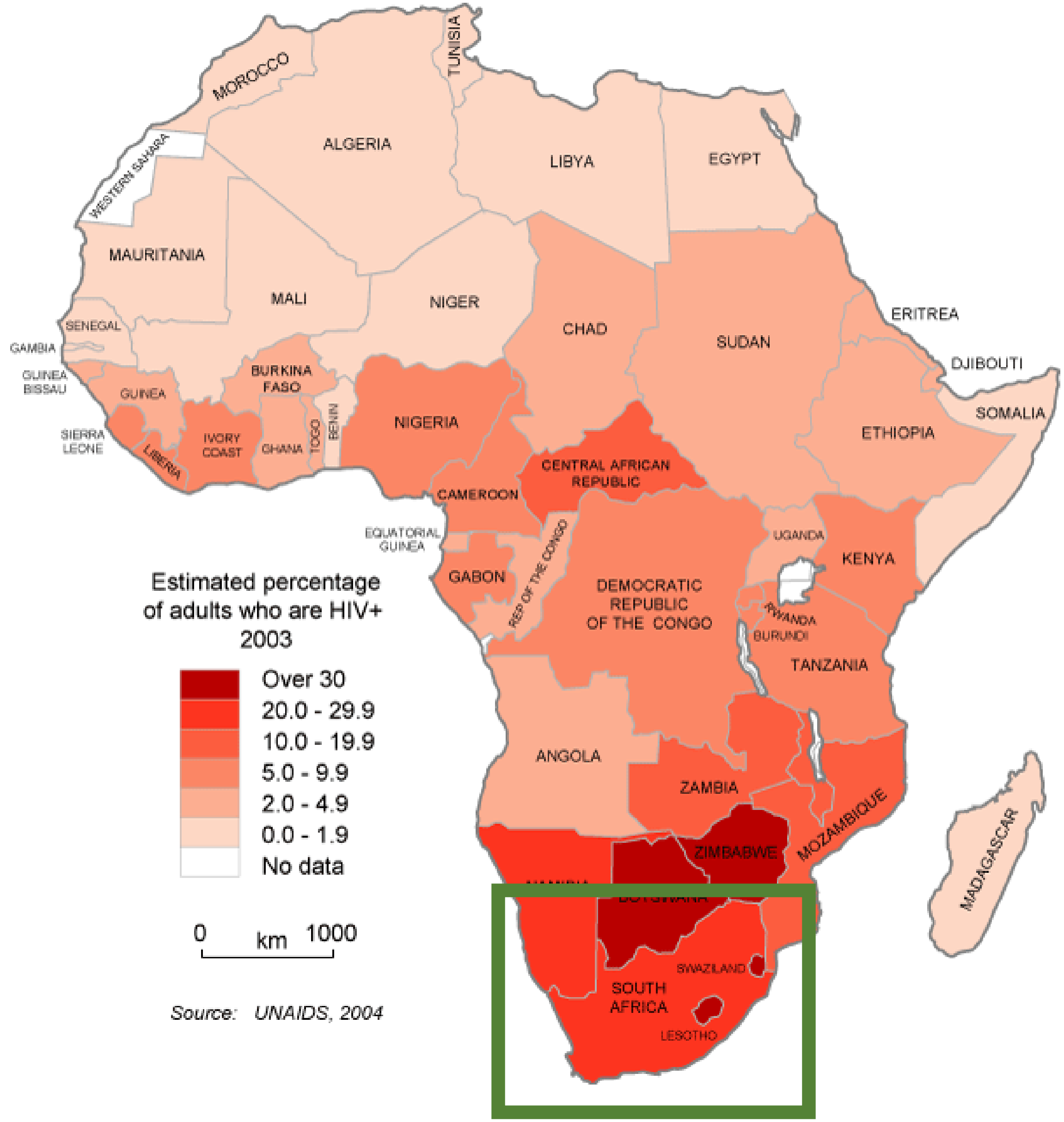


Spatial risk of HIV infection



- The spatial connectivity of the transmission network of an entire community has never been studied before, and the contribution of geographical clusters of HIV infections, or ‘hot-spots’ on the spread of the infection in the entire population is virtually unknown

What is the contribution of the HIV hotspot in the transmission network?



Source: UNAIDS, 2004

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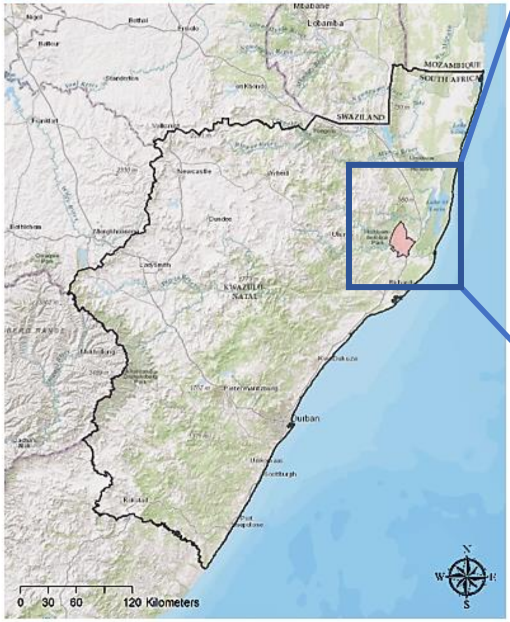
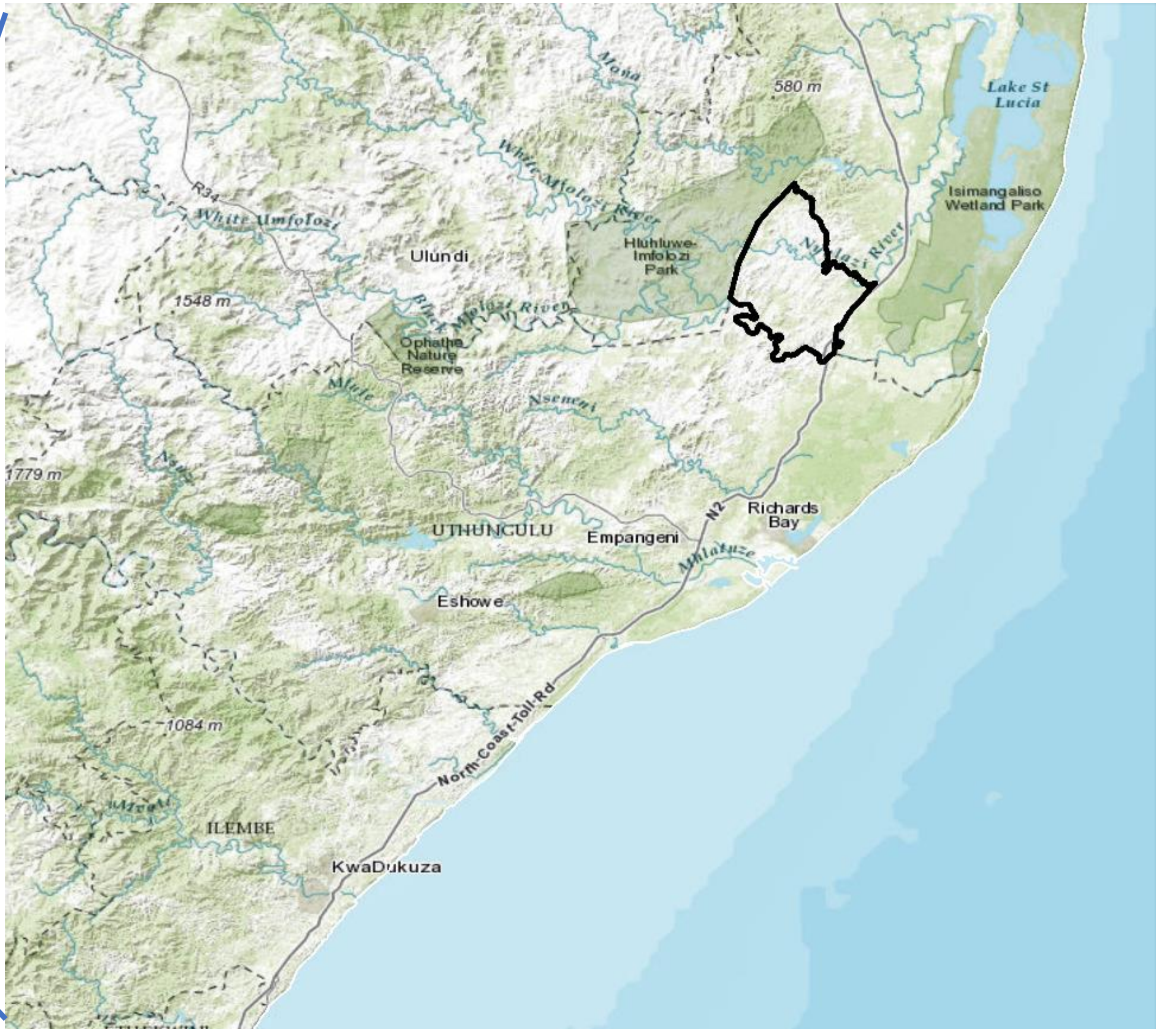
About AHRI.

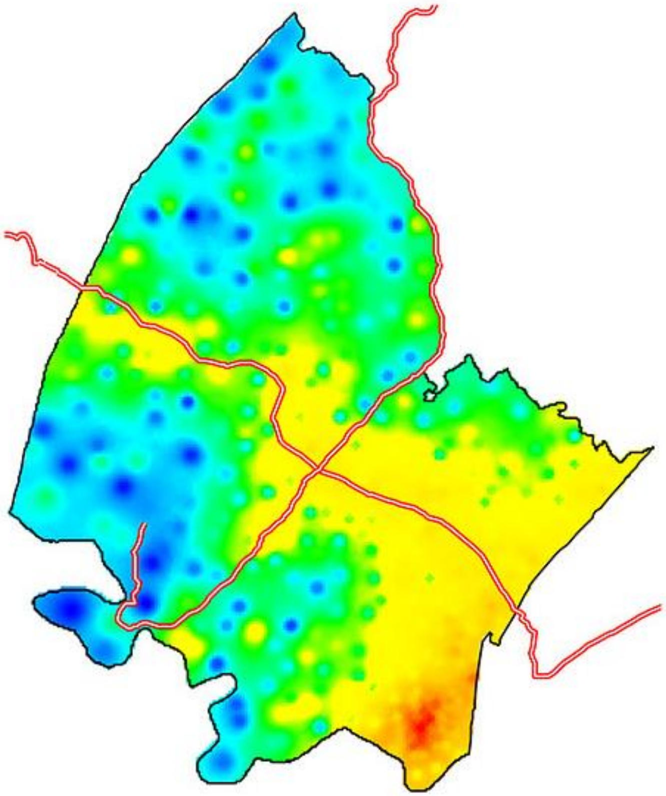
The **Africa Health Research Institute** is committed to working towards the elimination of HIV and TB disease.

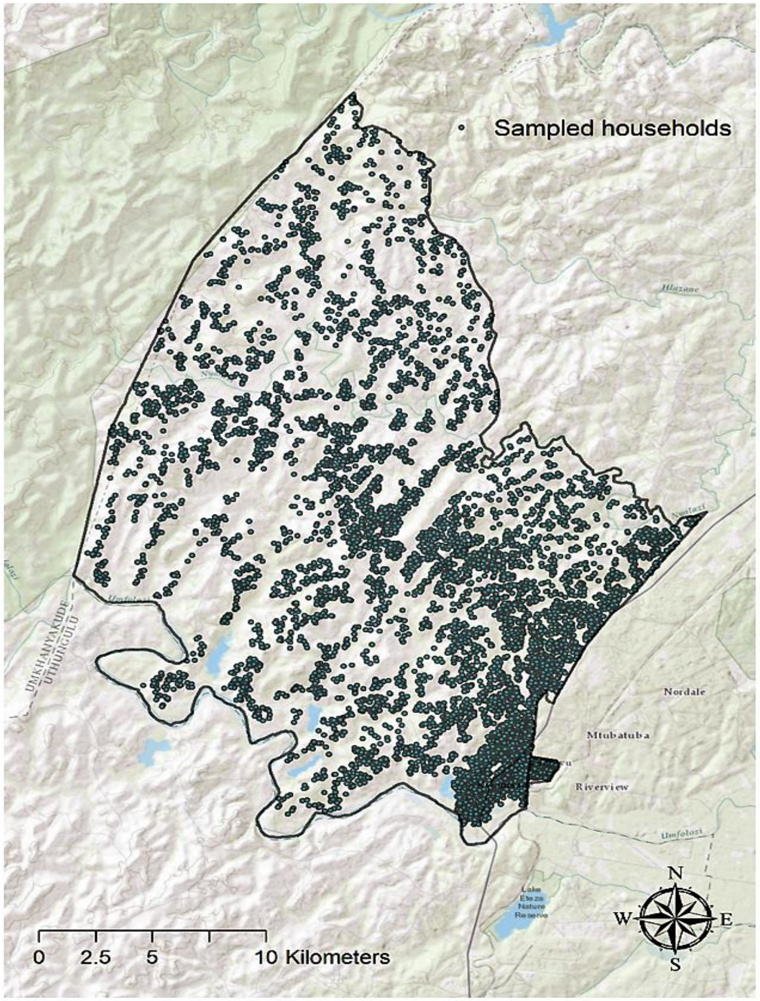
Africa Centre Demographic Information System Surveillance





Africa Centre Demographic Information System Surveillance





- All participants under surveillance are geo-located to their respective homesteads of residence (accuracy <2m)

Methods

- Geographical description of the HIV epidemic and hotspot identification
- Spatially explicit transmission network construction

Methods

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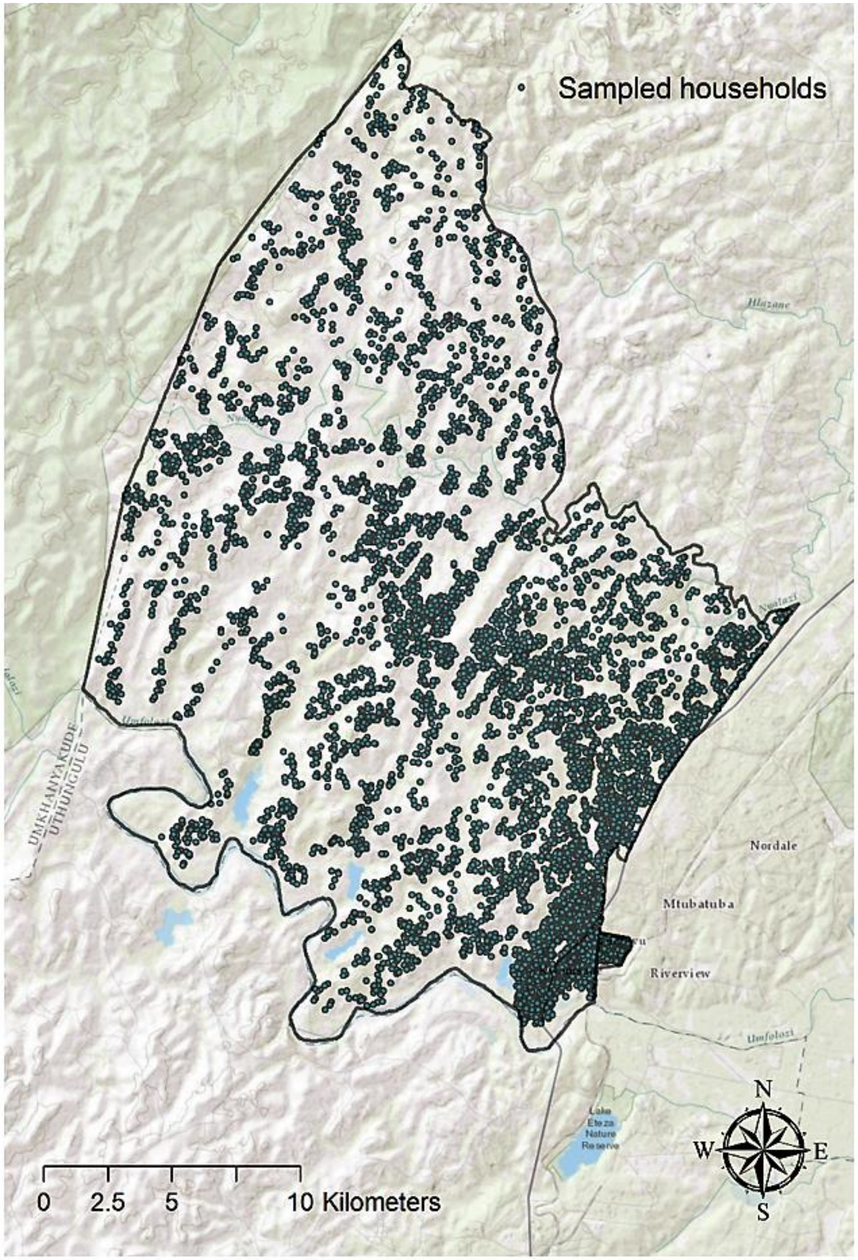
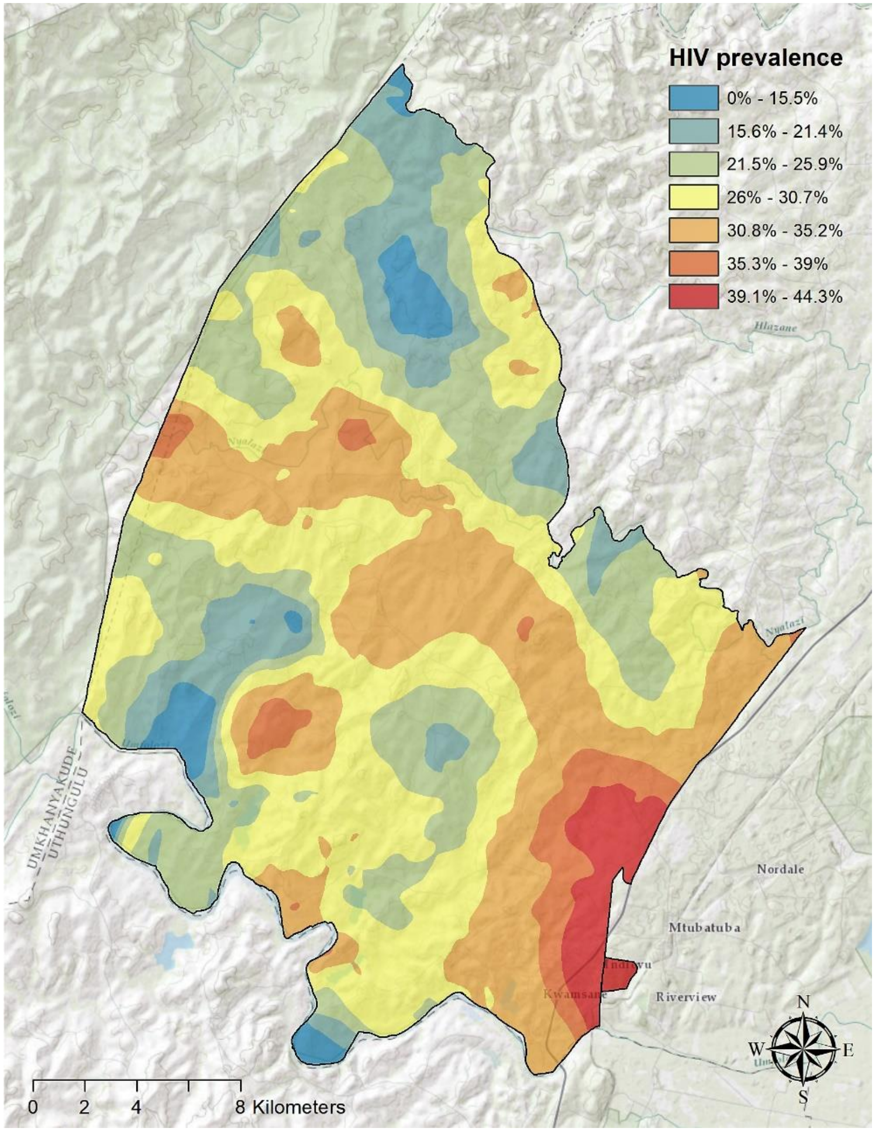


- We examined a sample of 18,294 individuals located in a hyper-endemic rural community of South Africa from 2011 to 2014 from which 5,624 tested positive for HIV



- We examined a sample of 18,294 individuals located in a hyper-endemic rural community of South Africa from 2011 to 2014 from which 5,624 tested positive for HIV

- We generate continuous surface map of HIV prevalence using kernel interpolation techniques

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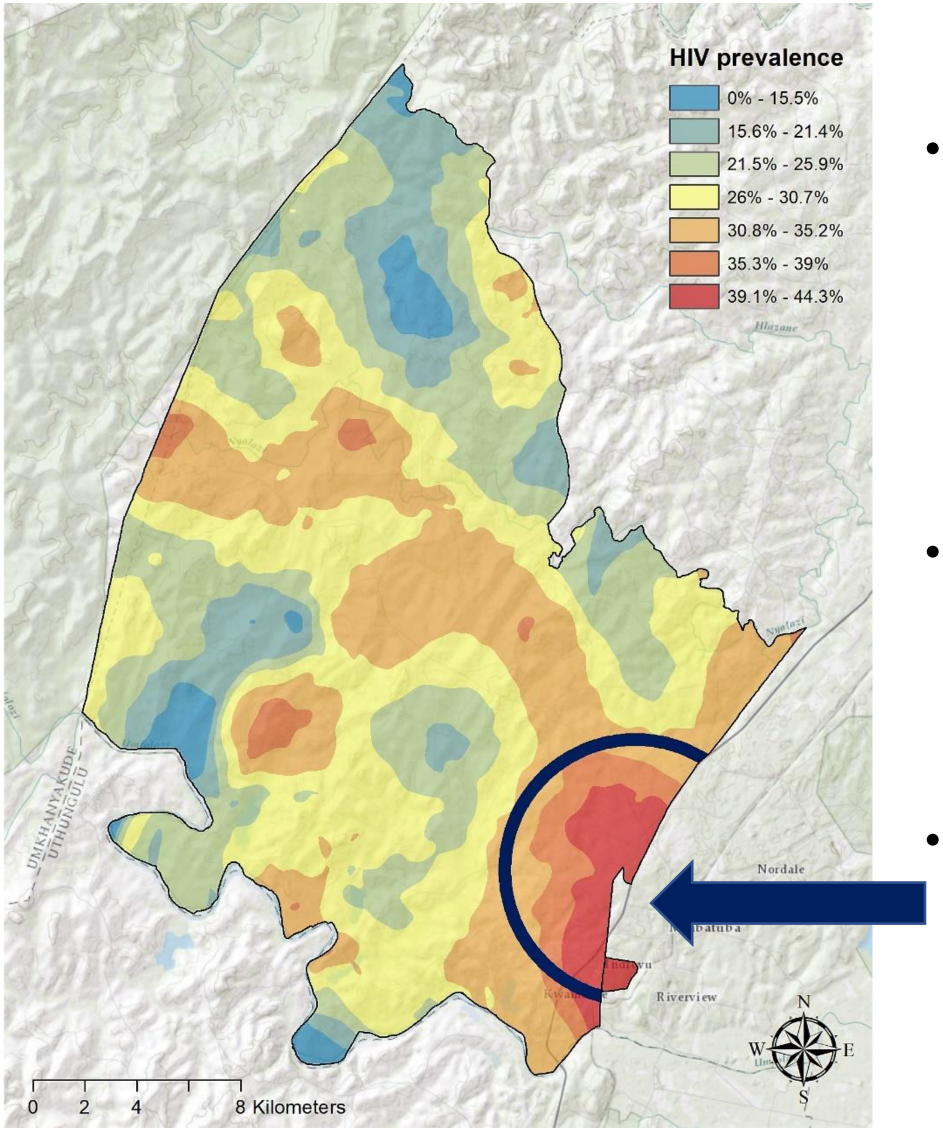
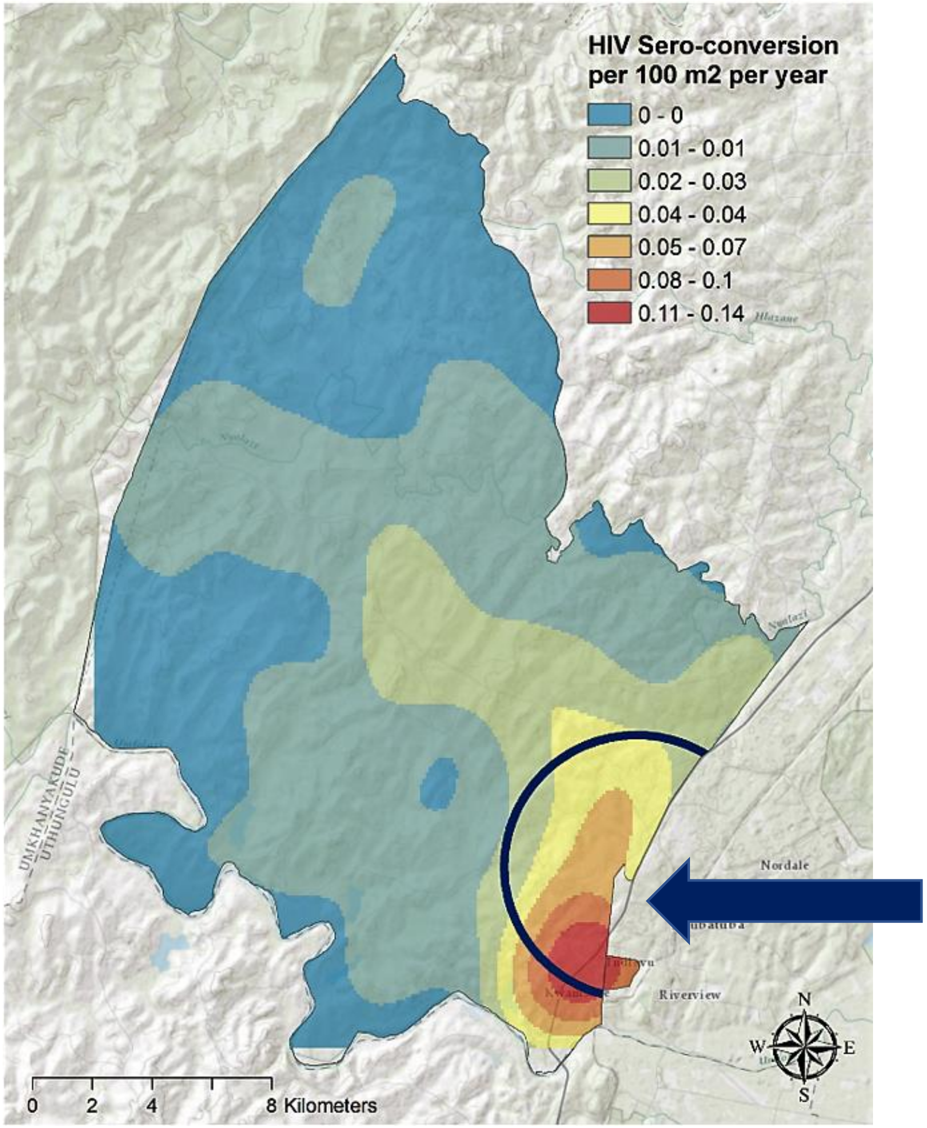


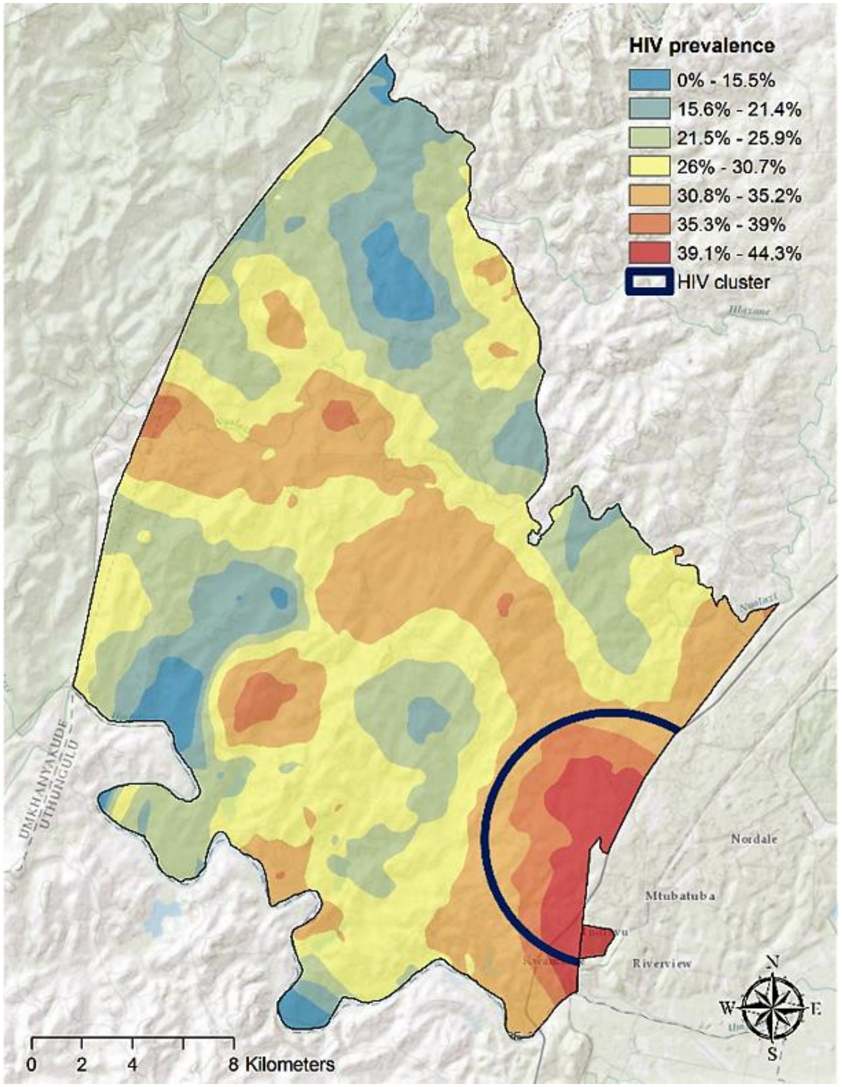
- We examined a sample of 18,294 individuals located in a hyper-endemic rural community of South Africa from 2011 to 2014 from which 5,624 tested positive for HIV

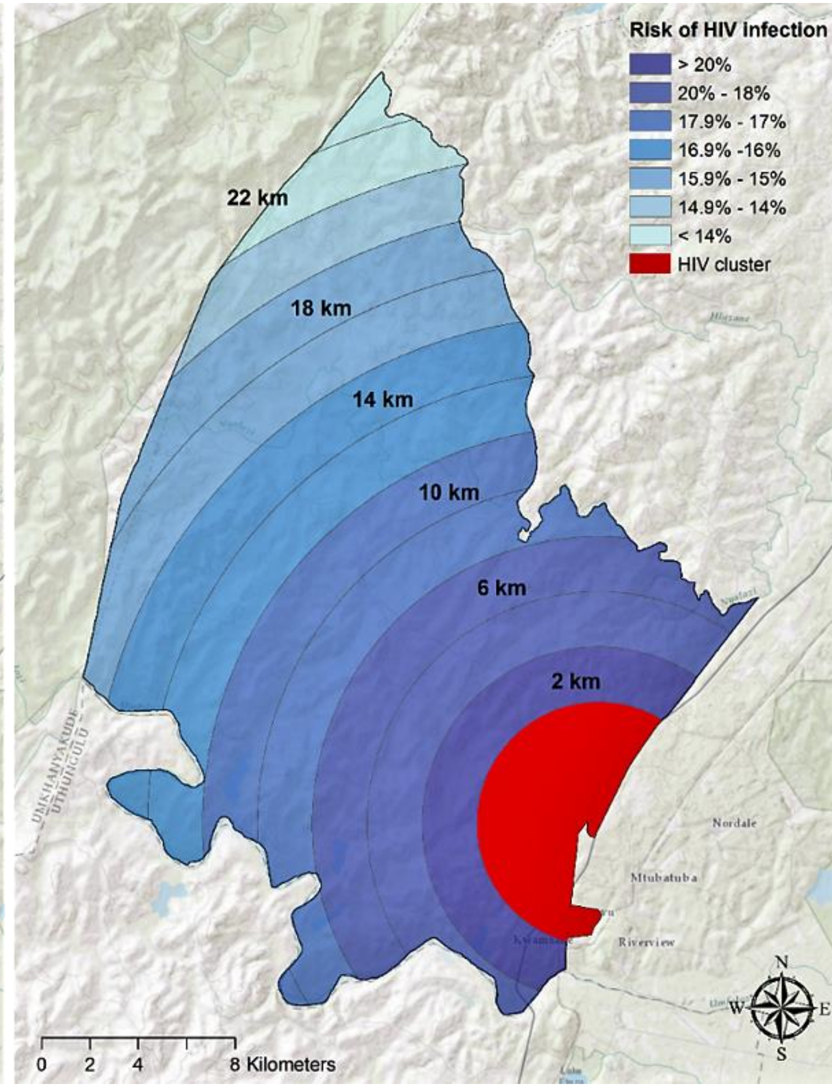
- We generate continuous surface map of HIV prevalence using kernel interpolation techniques

- We identified a geographical cluster with high numbers of HIV infections (HIV 'hotspot') using spatial statistical analysis



- Estimated HIV seroconversions per year were highly concentrated within the HIV hotspot with and an average of 0.04 seroconversions per year per 100 m2, compared to 0.01 seroconversions per year per 100 m2 in the area outside of the HIV hot-spot





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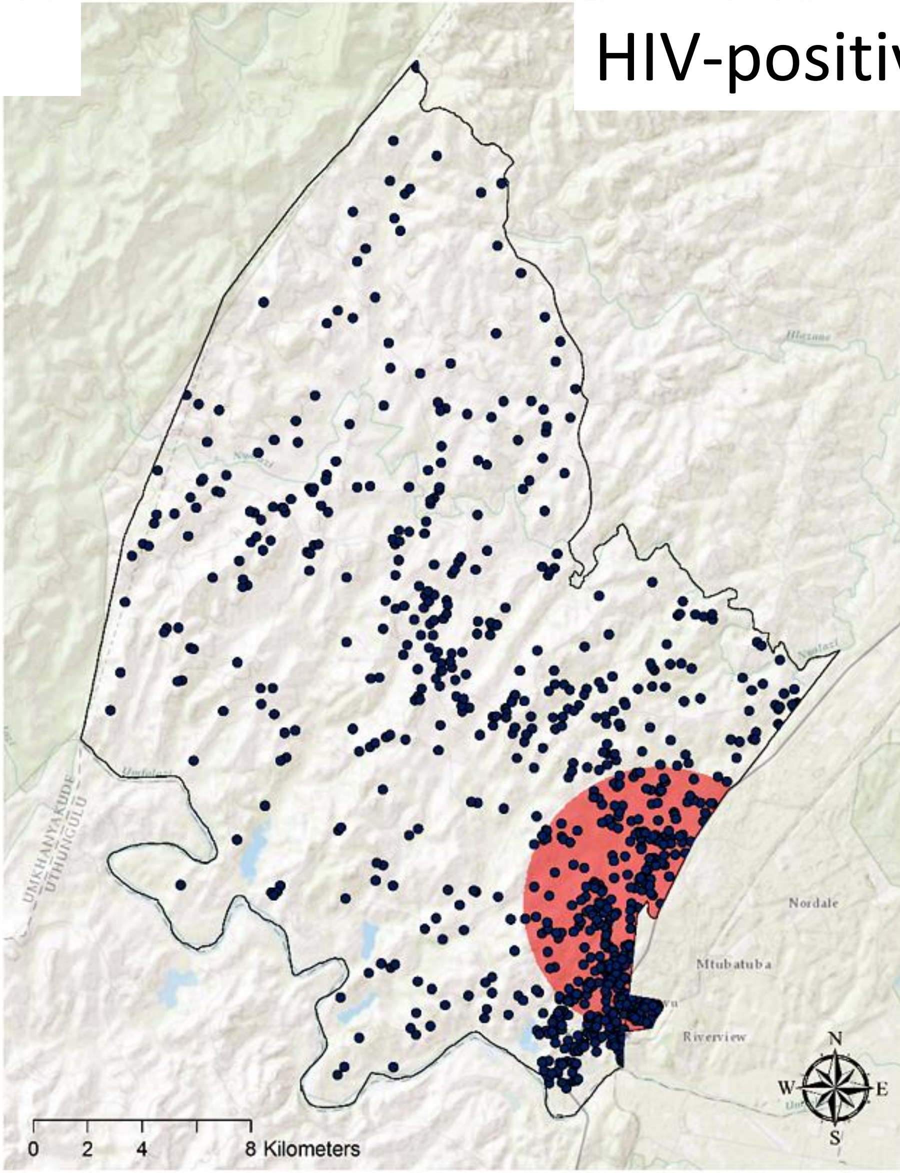
Methods

- Geographical description of the HIV epidemic and hotspot identification
- Spatially explicit transmission network construction

HIV-positive individuals



- We geo-located and genetically sequenced 1,222 HIV-positive individuals, from whom phylogenetic transmission clusters were identified

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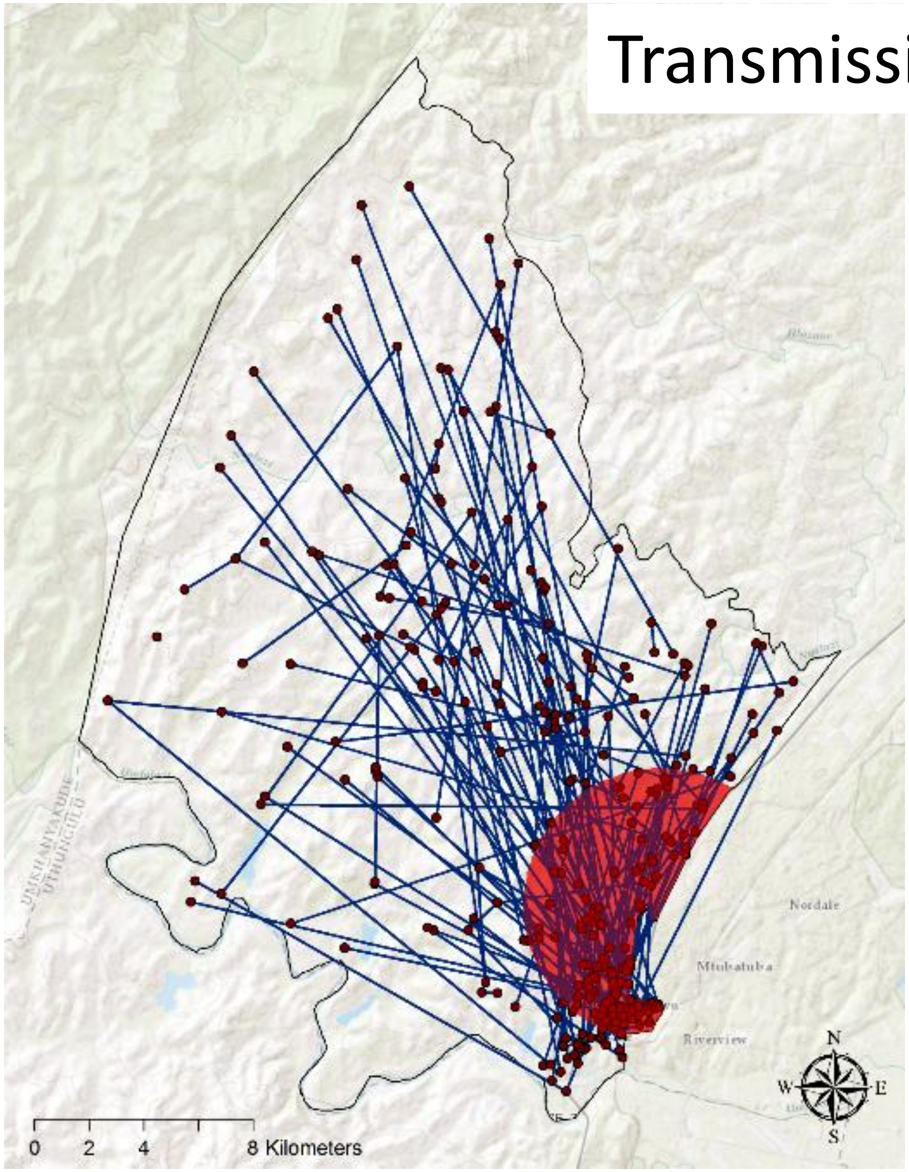
Transmission links



- We geo-located and genetically sequenced 1,222 HIV-positive individuals, from whom phylogenetic transmission clusters were identified
- We constructed the spatially explicit transmission network with 350 transmission links identified

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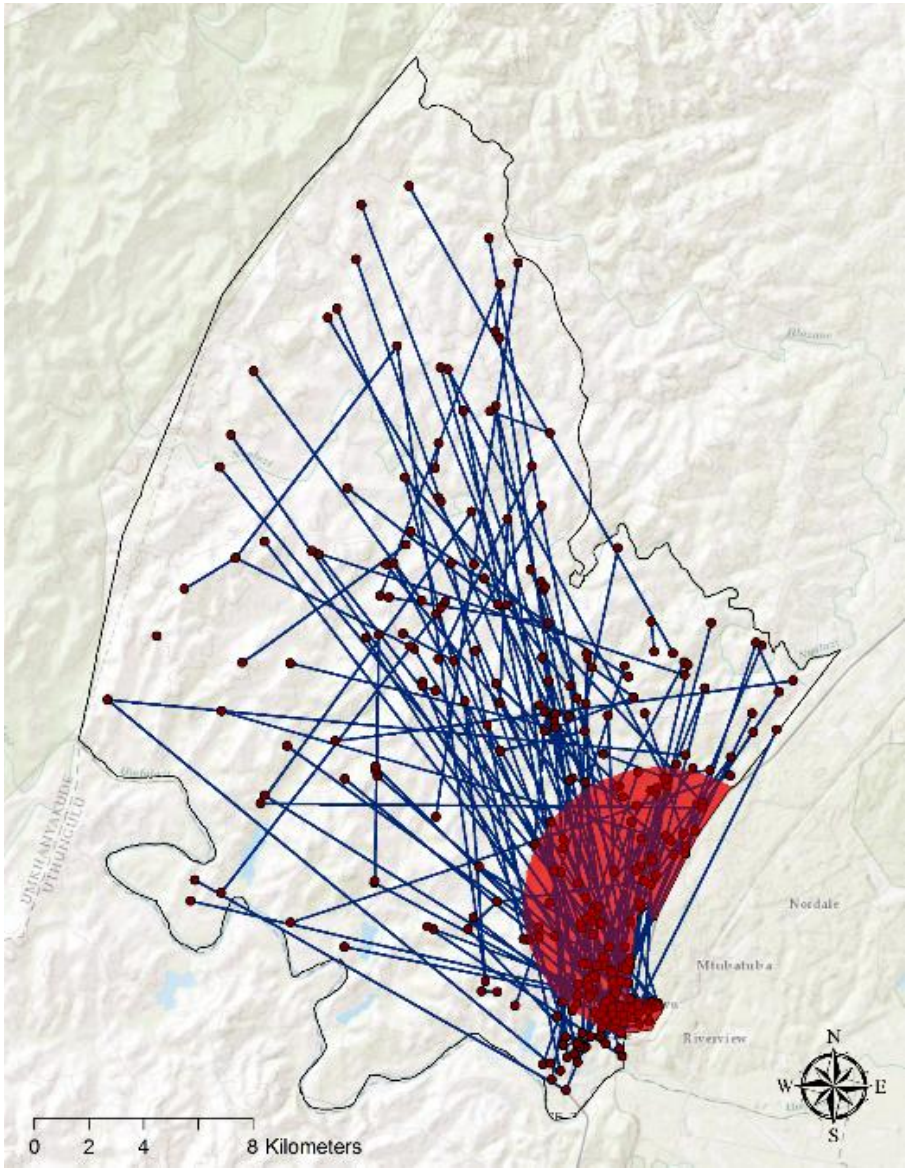

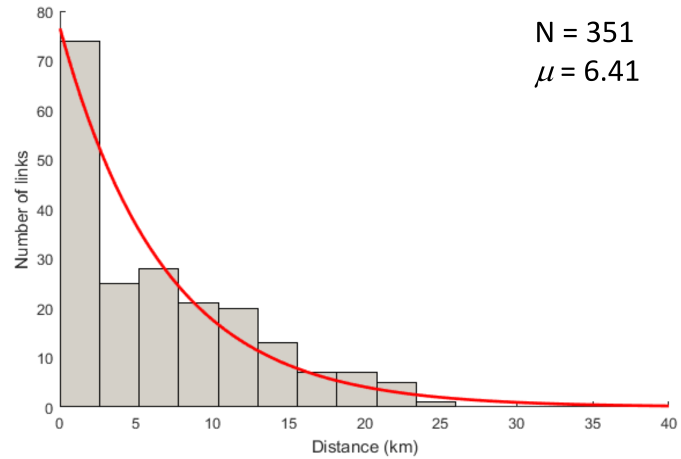

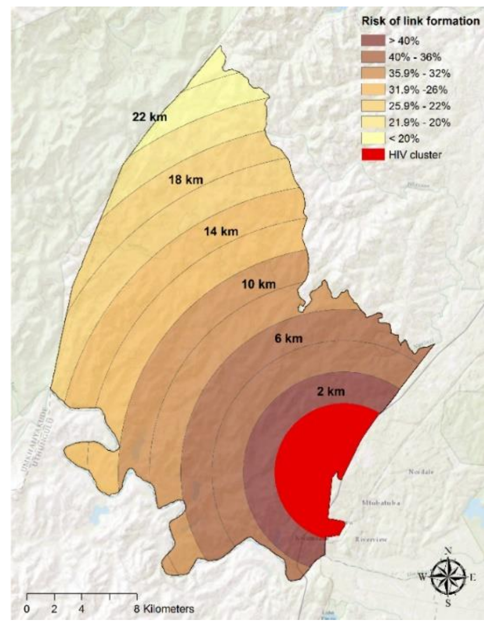

- The risk of link formation between individuals located inside and outside of the HIV hot-spot was reduced in 5.8% for each km distant to the hot-spot

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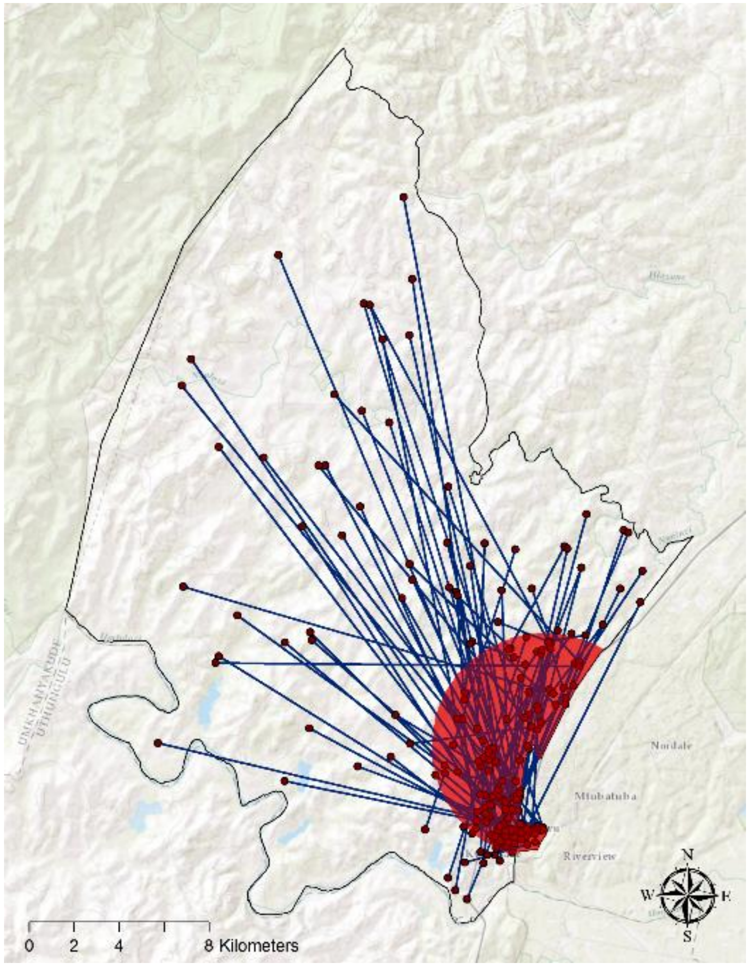
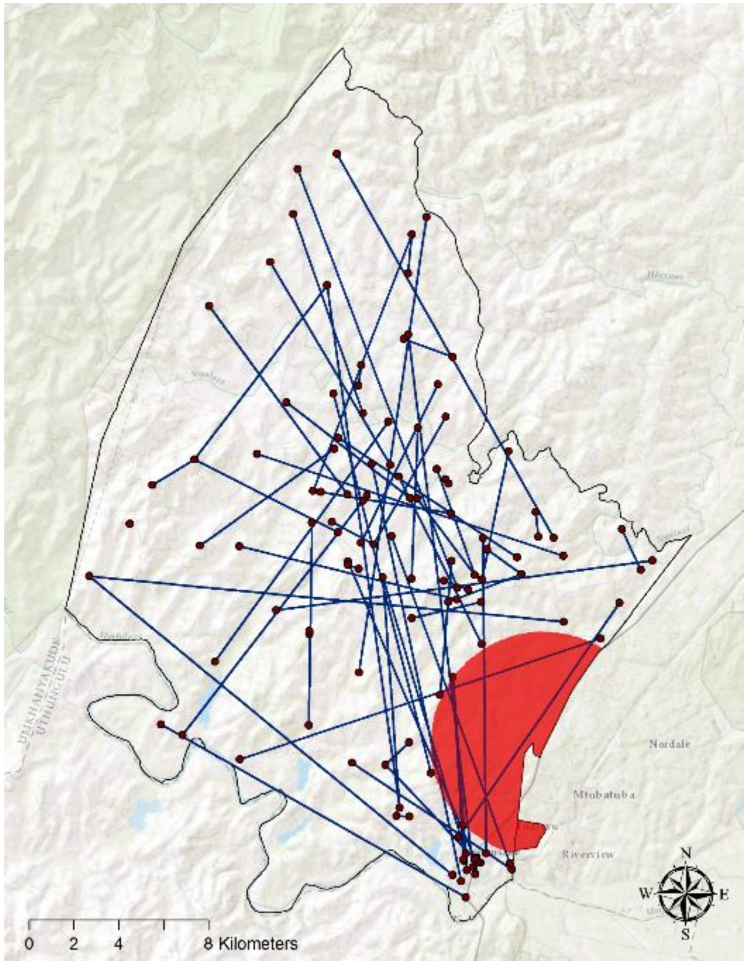




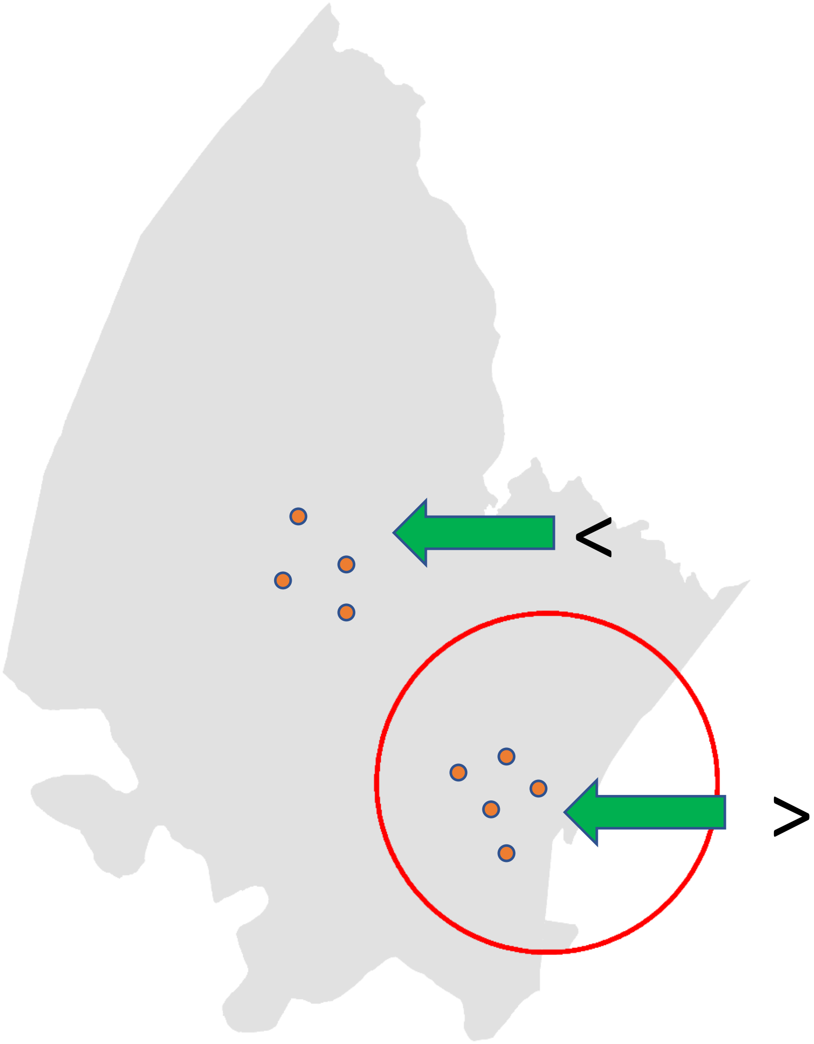
- 72% of the links included at least one individual located within the HIV hot-spot
- 28% of the links included individuals located outside the HIV hot-spot

Microsimulation models

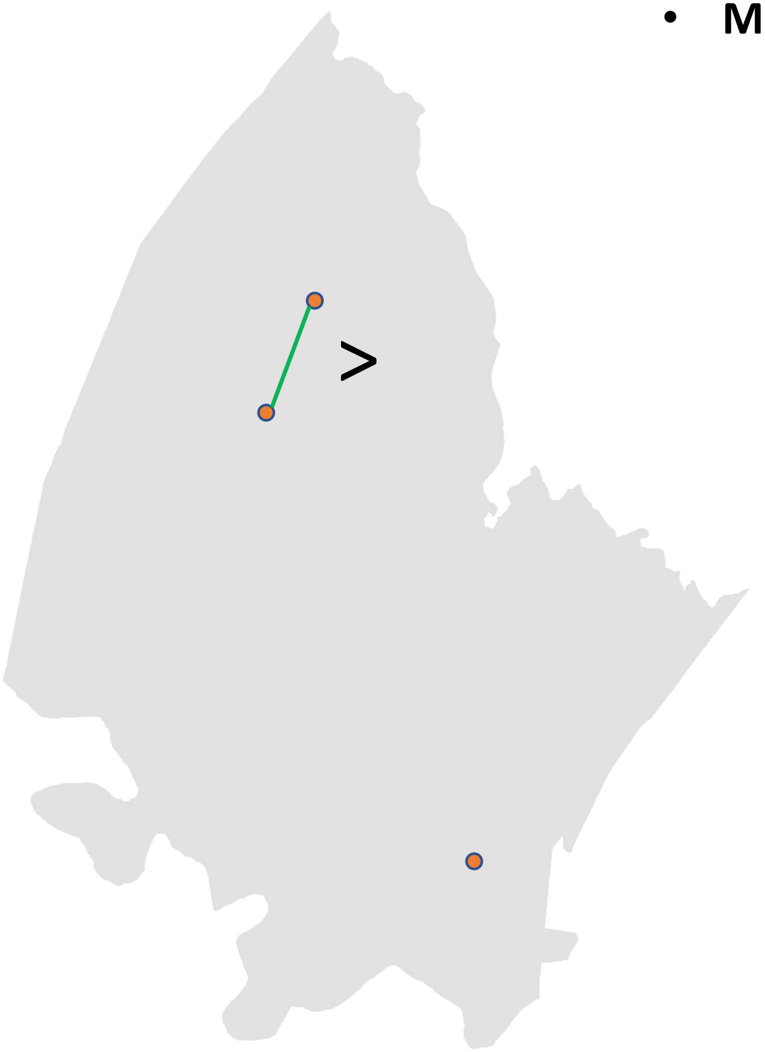
Three microsimulation models were generated to assess the association between the HIV hotspot and HIV transmission links

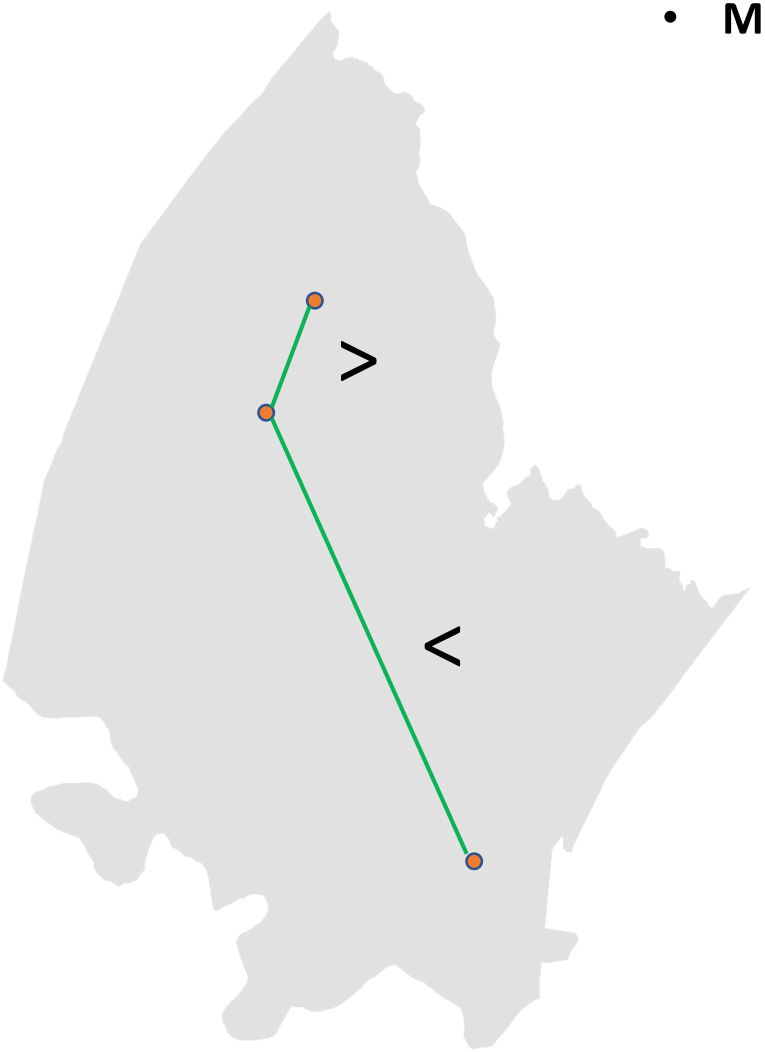
- **Model 1.** Epicenter model
- **Model 2.** Distance decay link formation model
- **Model 3.** Random links formation model

- **Model 1.** Epicenter model



- **Model 2.** Distance decay link formation model





- **Model 2.** Distance decay link formation model

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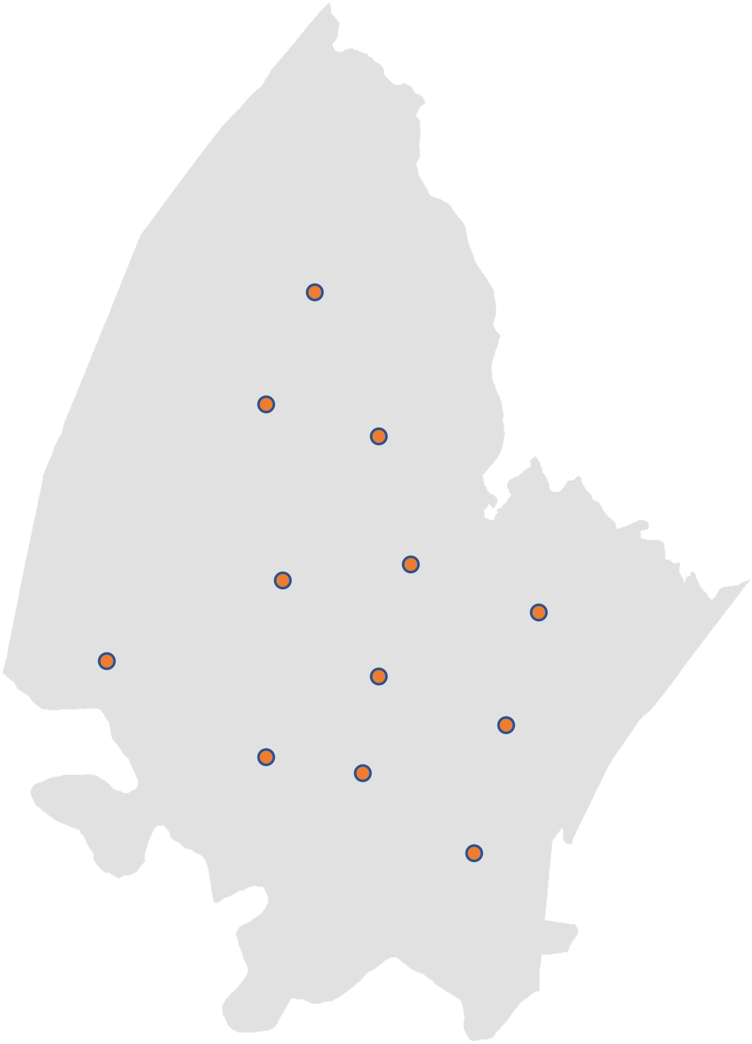
- **Model 3.** Random links formation model



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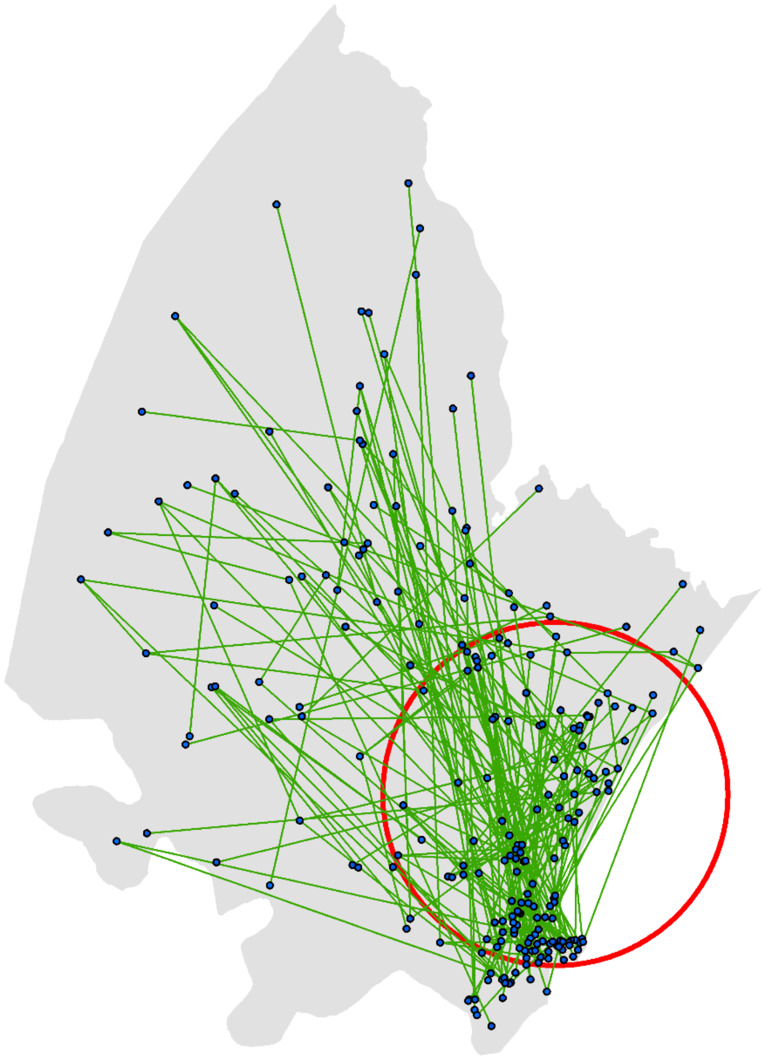
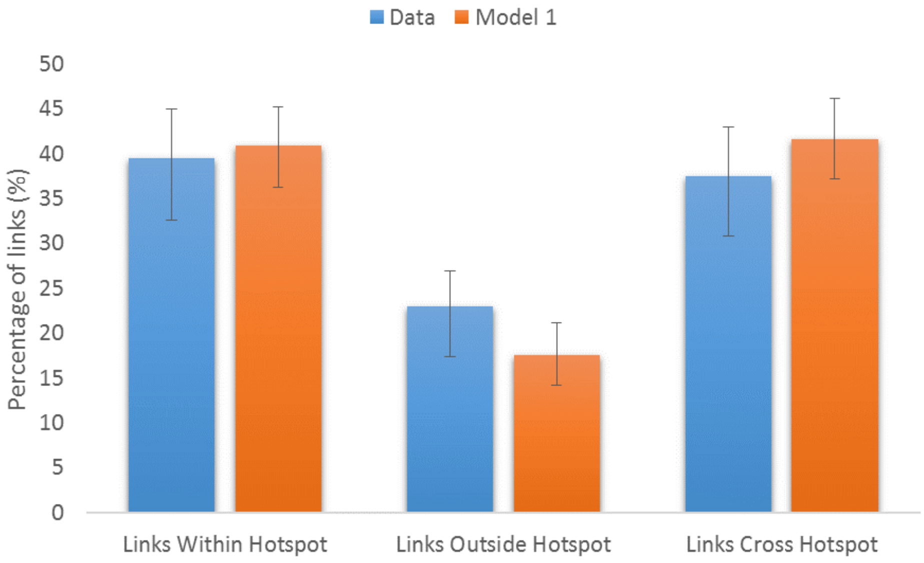
- **Model 1.** Epicenter model





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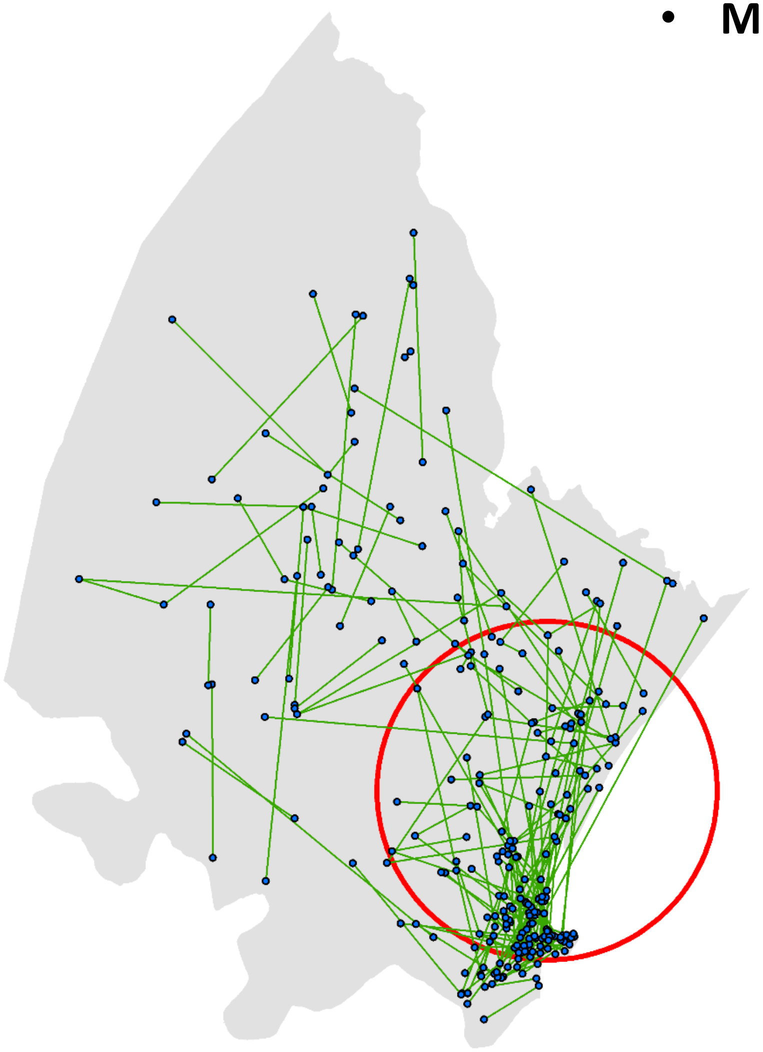

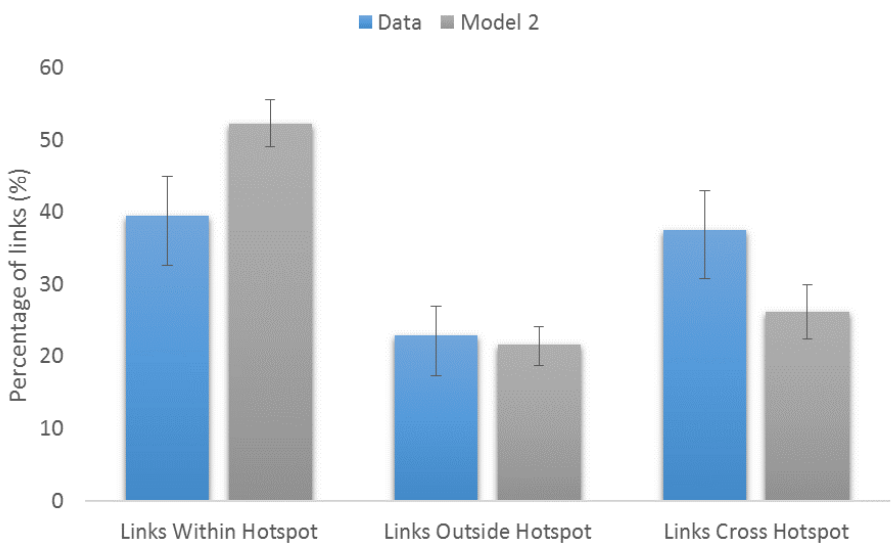

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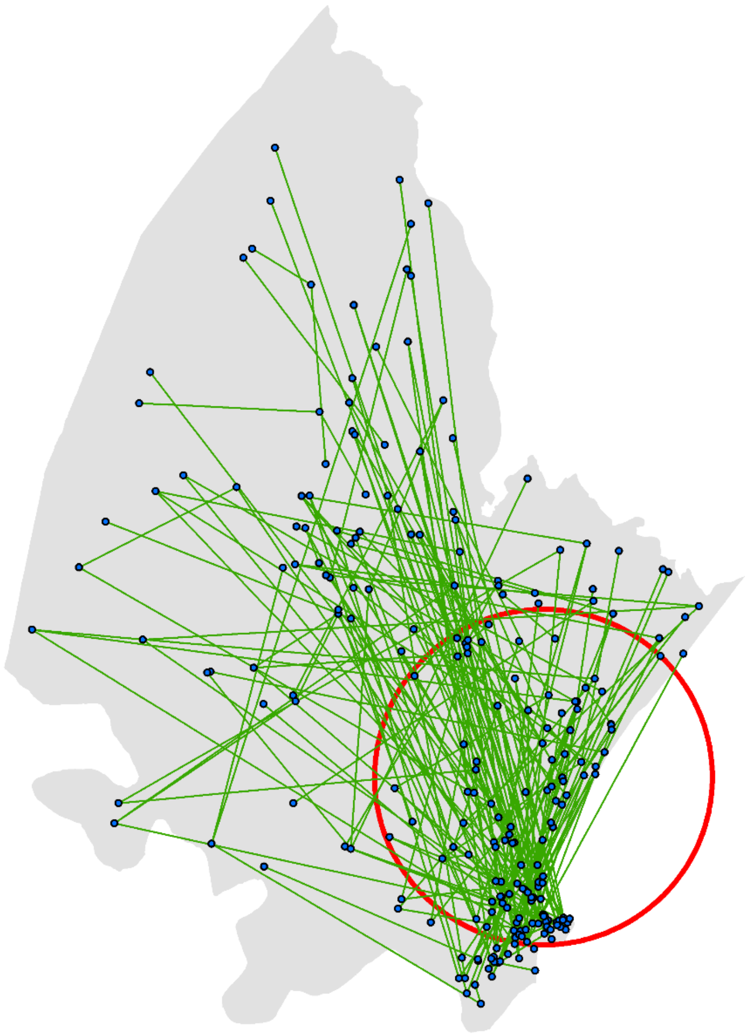
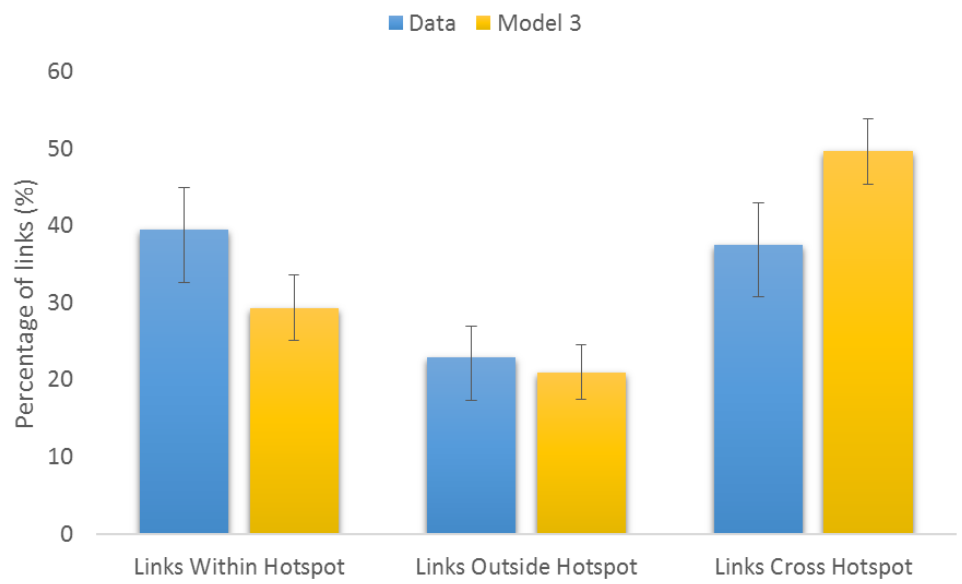
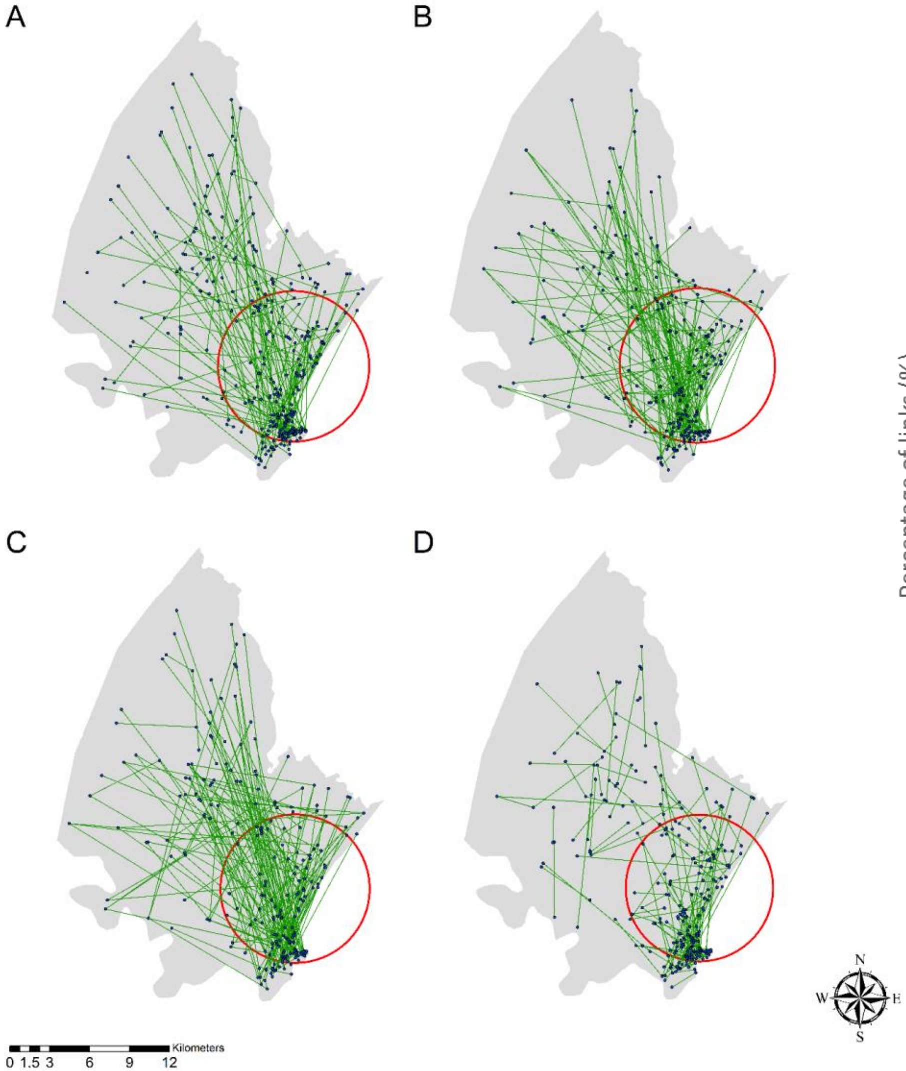
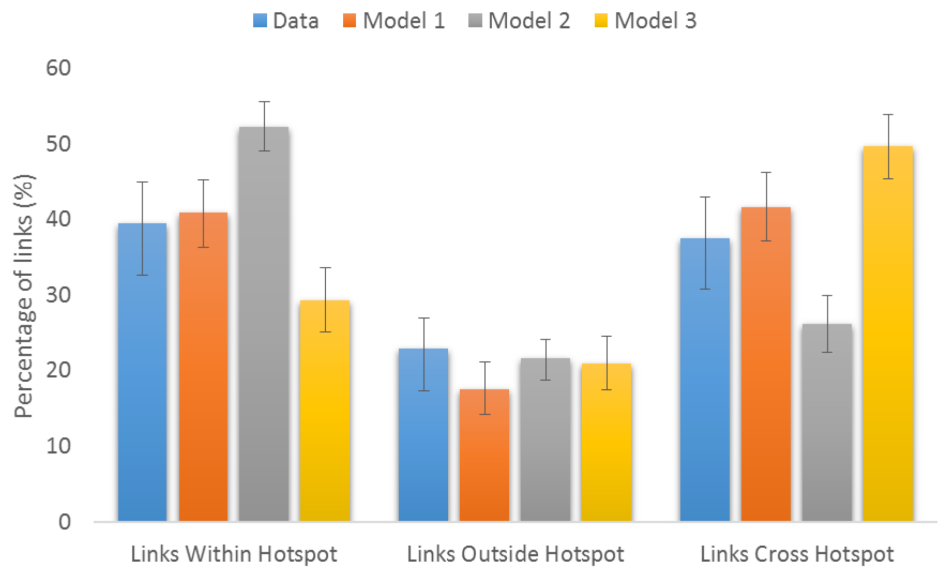
- **Model 3.** Random links formation model







Geographical representation of HIV transmission links from model simulations. In **A)** Distribution of HIV transmission links from the data; **B)** Results from Model 1; **C)** Model 2; and **D)** Model 3. Green circle illustrates the location of the HIV incidence hotspot



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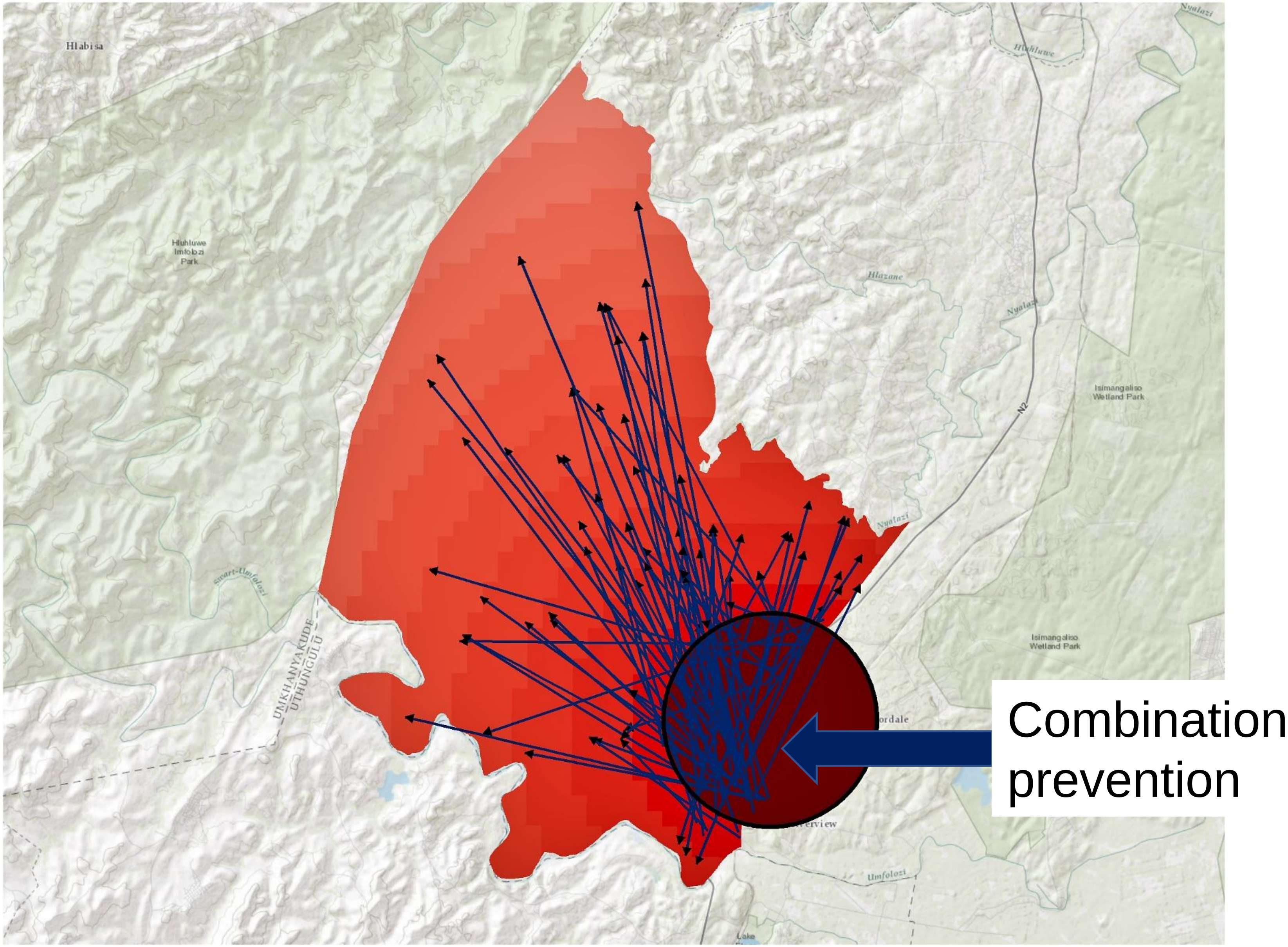
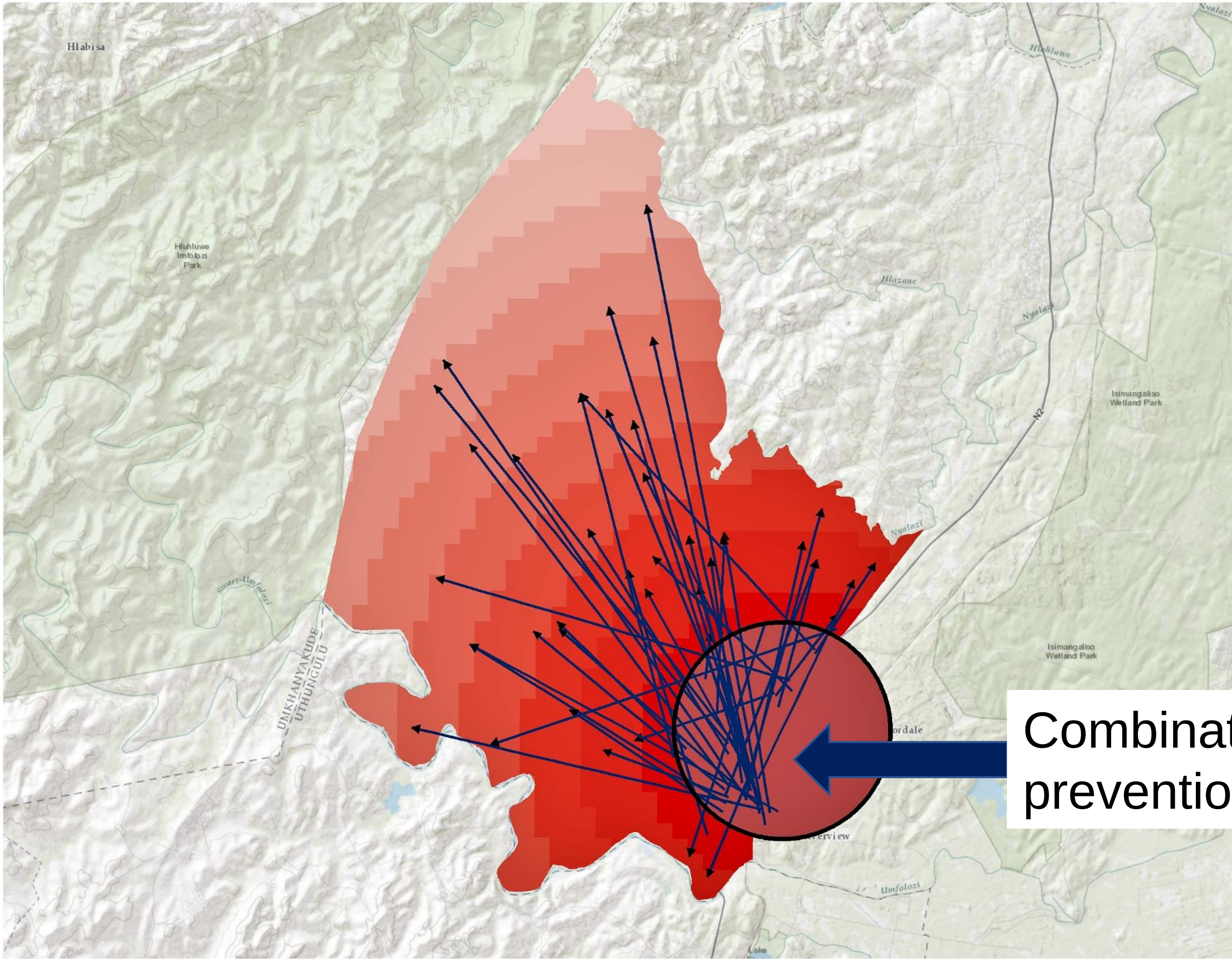
- We found that more than 70% of the HIV transmission links identified were directly connected to an HIV hot-spot, illustrating the **high connectivity between the hot-spots and the general community**

- The HIV hotspots might play a key role in the HIV transmission network and could substantially contribute to the dispersion of the infection

- We hypothesize that HIV hot-spots behave as core groups in the transmission network, and **interventions targeting these hot-spots could not only reduce the levels of new infections in these geographical core groups, but also disrupt the transmission of the infection in the entire community**


Hlabisa
Hluhluwe Imfolozi Park
Hlazane
Nyalazi
Hluhluwe
Isimangaliso Wetland Park
Isimangaliso Wetland Park
N2
UMKHANYAKUDE
UTHUNGULU
Umfolozi
Lake
Combination prevention



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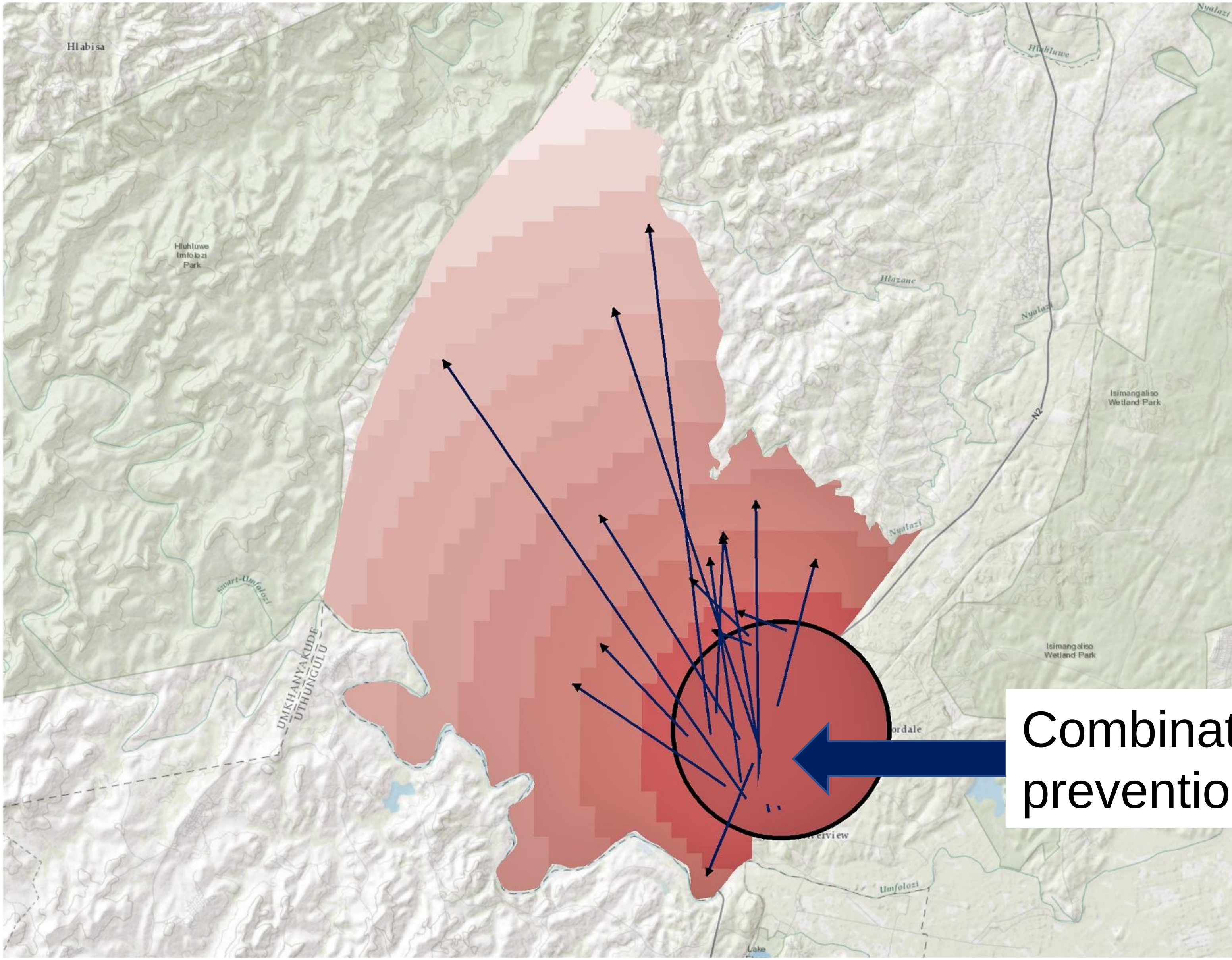
Hlabisa
Hluhluwe Imfolozi Park
Hlazane
Nyalazi
Isimangaliso Wetland Park
Isimangaliso Wetland Park
N2
UMKHANYAKUDE
UTHUNGULU
Umfolozi
Lake
Combination prevention

General Conclusions

- If the level of connectivity between the ‘hot-spot’ and the entire community is high, then a successful intervention approach in these geographical high-risk populations could generate a marked impact on reversing the overall epidemic

- Disrupting the transmission network using geographically targeted interventions could be an effective strategy aimed to optimize resources and maximize the impact on the epidemic in SSA

Acknowledgements

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Newton Fund

Acknowledgements

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Andrew Tomita

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Thank you!