Can we achieve epidemic control in hyper-endemic HIV settings?

CAPRISA 021: Controlling HIV with Everyone on Anti-retrovirals - The CHEVA study

Principal Investigator : Quarraisha Abdool Karim

To End AIDS, we need...

…a HIV vaccine

…and a cure for AIDS.

Until then, we need to do our best to control the spread of HIV.
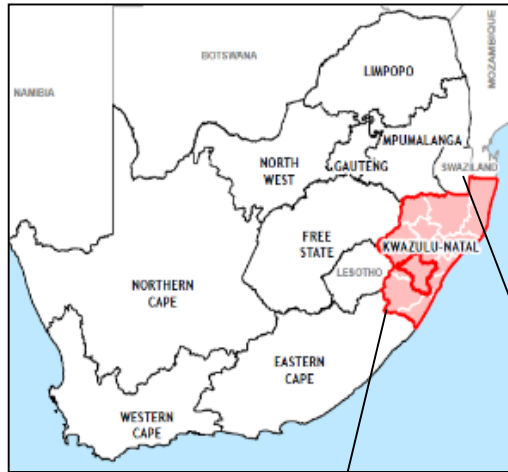
Epidemic control - UNAIDS 2030 goal

- **The United Nations Declaration 2030 target is 90% decline in HIV incidence from 2010**

- UNAIDS goal is to reach "The End of AIDS as a Public Health Threat" (Epidemic control) by 2030

- Epidemic control is the reduction of disease incidence, prevalence, morbidity or mortality to a locally acceptable level as a result of deliberate intervention measures. Mathematically defined as the reproductive rate of infection (R_0) below 1

- Some suggest - incidence rate of 1/1000 p.a. is a marker of control

The world is embarking on a Fast-Track strategy to end AIDS epidemic by 2030.

To reach this visionary goal…countries will need to use the powerful tools available, hold one another accountable for results and make sure that no one is left behind.

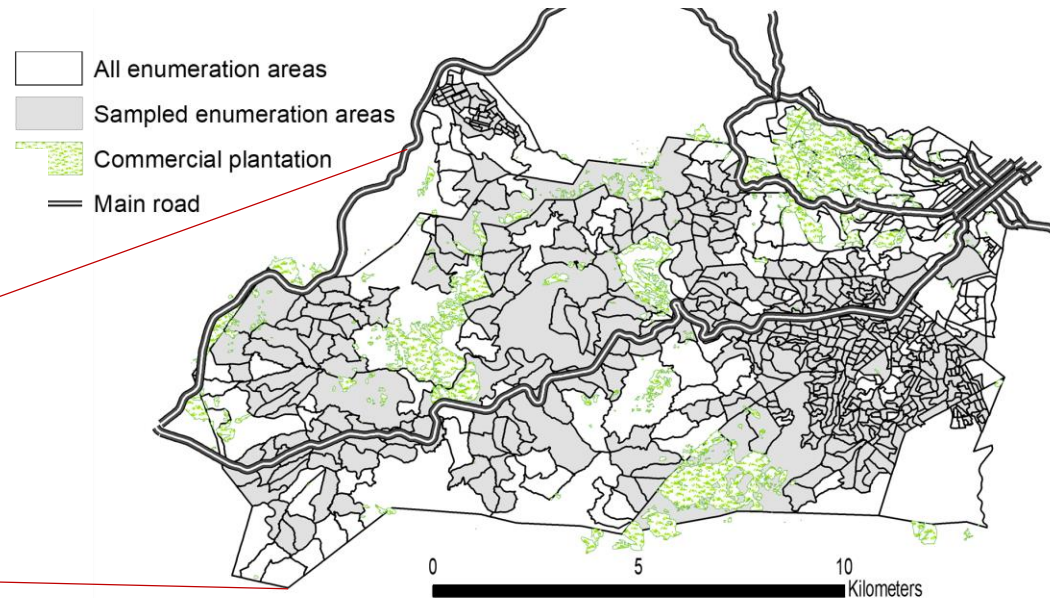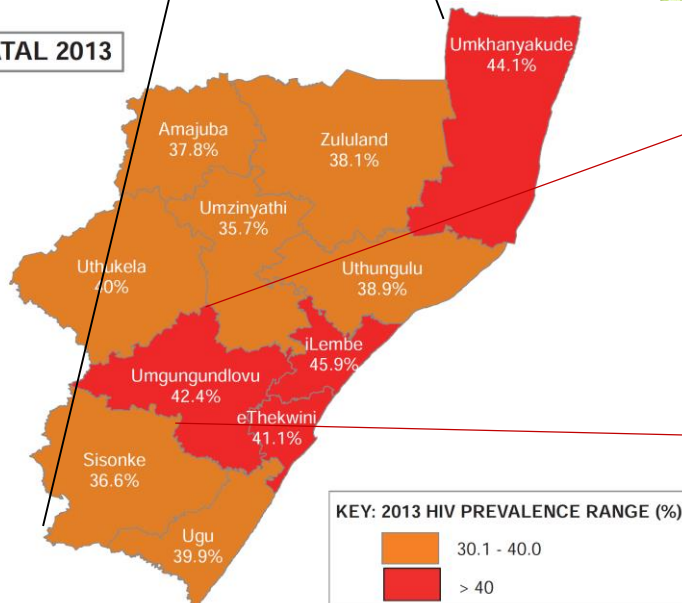UNAIDS

FAST-TRACK

ENDING THE AIDS EPIDEMIC BY 2030

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# Hyper-endemic HIV in uMgungundlovu – one of SA's worst-affected districts

- **HIV prevalence 36.3% in general community**

- **Population of ~370 000**
  - Males ~176 418
 - Females ~191 515

KWAZULU-NATAL 2013

Umkhanyakude 44.1%

Amajuba 37.8%

Zululand 38.1%

Umzinyathi 35.7%

Uthukela 40%

Uthungulu 38.9%

iLembe 45.9%

Umgungundlovu 42.4%

eThekwini 41.1%

Sisonke 36.6%

Ugu 39.9%

KEY: 2013 HIV PREVALENCE RANGE (%)

	30.1 - 40.0
	> 40

All enumeration areas
Sampled enumeration areas
Commercial plantation
Main road

0   5   10 Kilometers

Source: *HIV Incidence Provincial Surveillance System 2014-2017*

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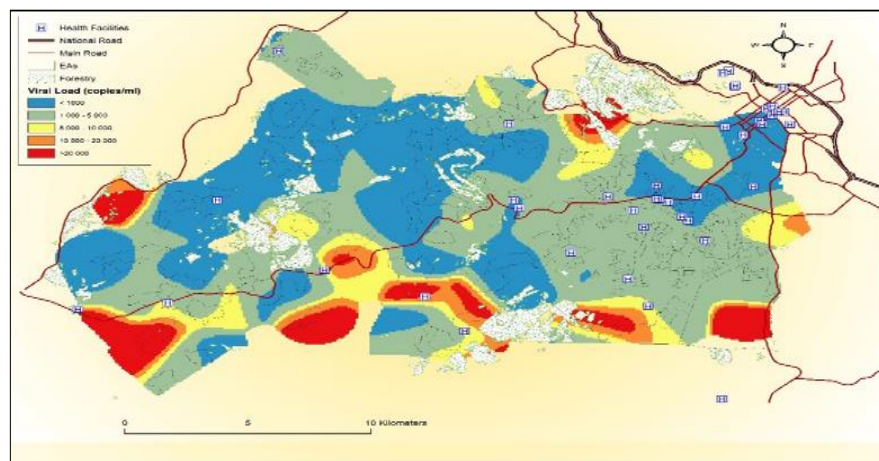CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

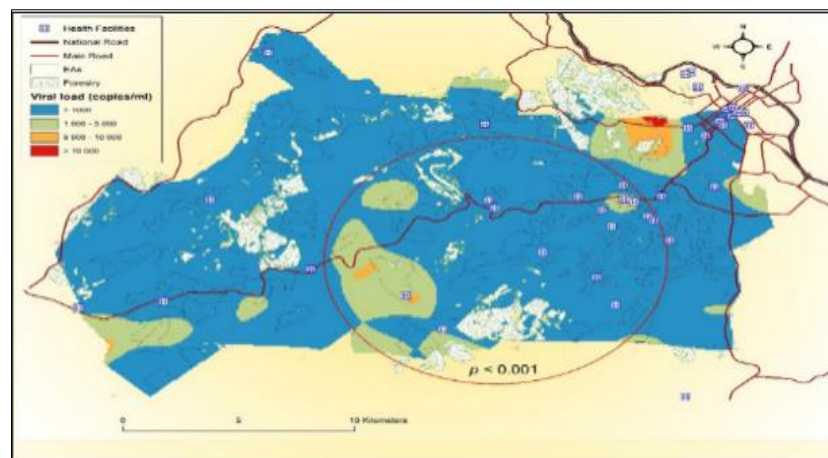# Geospatial mapping of HIV prevalence & viral load
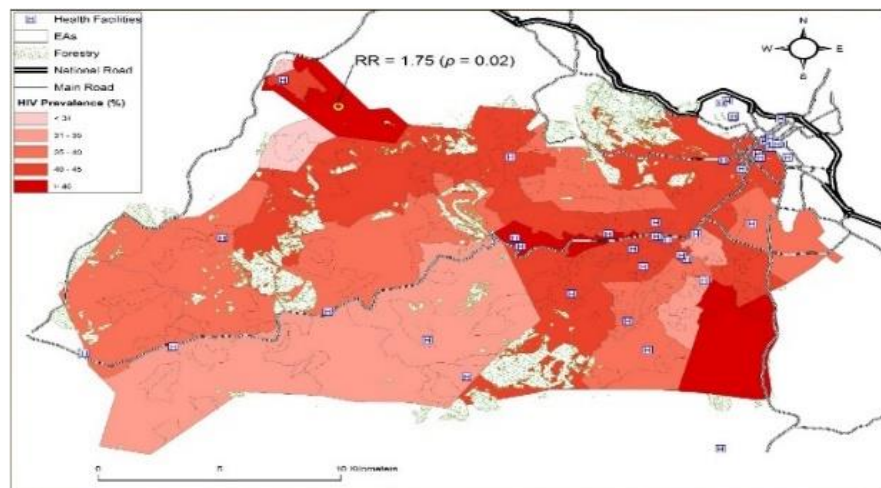
HIV Prevalence by ward
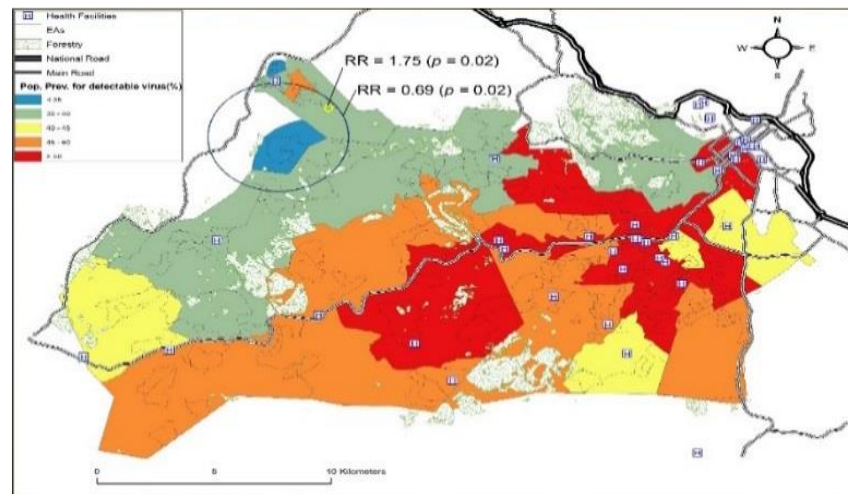
Detectable viral load

Viral load distribution in men

Viral load distribution in women

Phylogenetic analysis shows: "Cycle of HIV transmission"

90 phylogenetic clusters from 1,589 viruses from 9,812 people

Men
Mean age: 31.5 years (n=79)
Knew HIV status: 22%

Community HIV prevalence in men aged 25-40 years: 40%* (N=1548)

Most young women <25 years acquire HIV from older men (Mean age difference = **8.7 years**, CI: 6.8-10.6)

39% of the men linked to a woman < 25 are simultaneously also linked to a woman 25-40 years

Most men & women 25-40 years acquire HIV from similarly aged partners (Mean age difference = **1.1 years**, CI: -0.6-2.8)

Young women <25 years
Knew HIV status: 23%
62% of male partners are 25-40 years

Community HIV prevalence: 22%* (N=2224)

Women 25-40 years
Knew HIV status: 43%
63% of male partners are 25-40 years

Community HIV prevalence: 60%* (N=2680)

When young women reach >25 years they continue the cycle

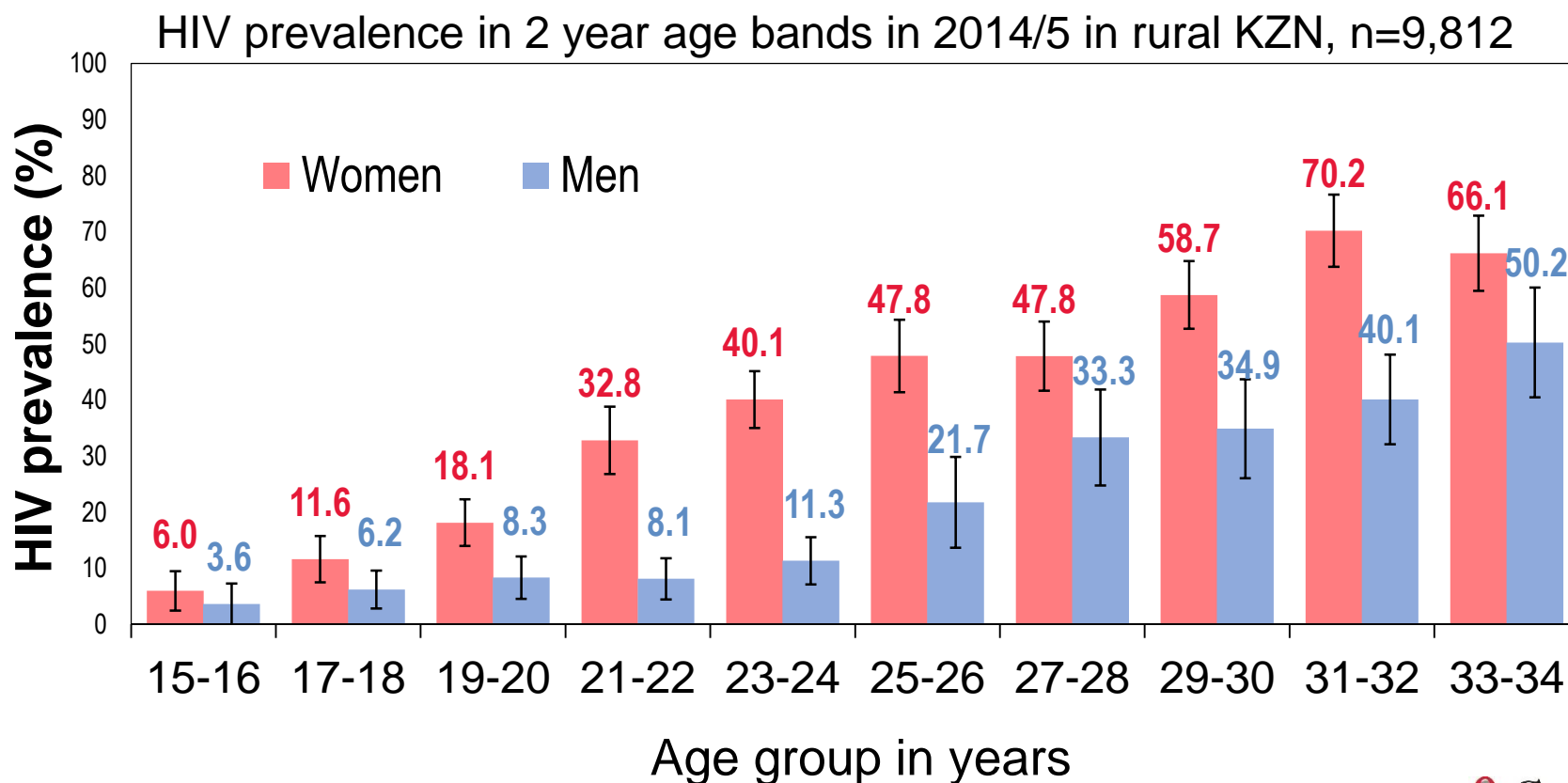| Women age group	Age difference with male partners
16-20	11.5 yrs
21-25	7.0 yrs
26-30	1.5 yrs
31-35	1.7 yrs
36-40	0.7 yrs

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HIV incidence in this KZN community

	< 25 years incidence rate (95% CI)	≥ 25 years incidence rate (95% CI)	Incidence rate by sex (95% CI)
Male	**0.9** (0.6 - 1.6) (n=1055)	**2.3** (1.3 - 4.6) (n=518)	**1.4** (1.0 - 2.3) (n=1573)
Female	**4.3** (3.4 - 5.7) (n=1299)	**1.6** (1.1 - 2.5) (n=664)	**3.4** (2.8 - 4.4) (n=1963)
Incidence rate by age (95% CI)	**2.5** (2.0 - 3.1) (n=2354)	**2.0** (1.3 - 3.2) (n=1182)	**2.3** (1.9 - 2.9) (n=3536)

HIV rates in adolescent girls & young women: biggest challenge to prevention

Overall HIV prevalence: 36.3%, Men = 28.0%, Women 44.1%

HIV prevalence in 2 year age bands in 2014/5 in rural KZN, n=9,812

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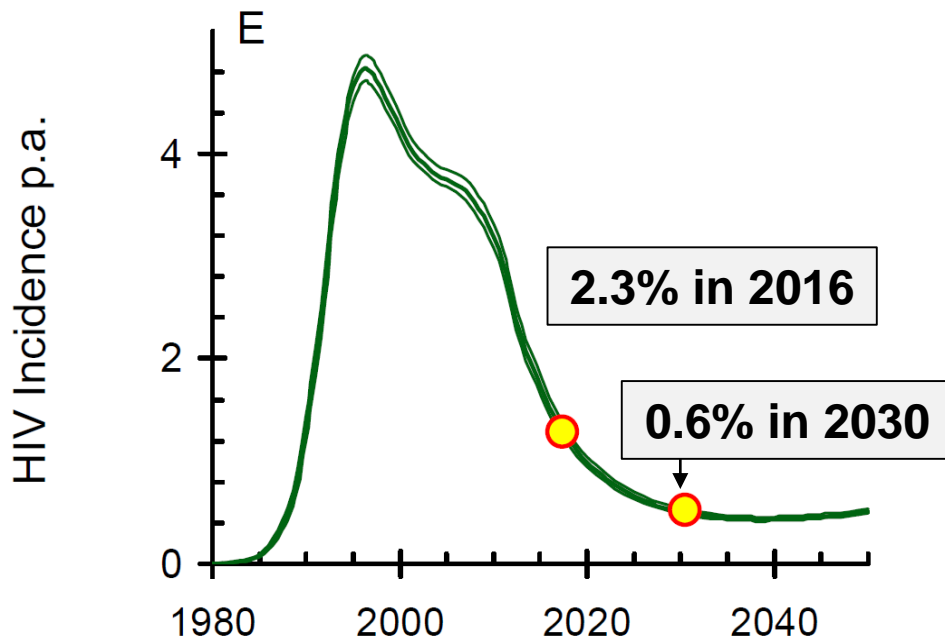CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

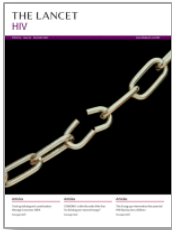# No prospect of epidemic control with current rate of ART scale up
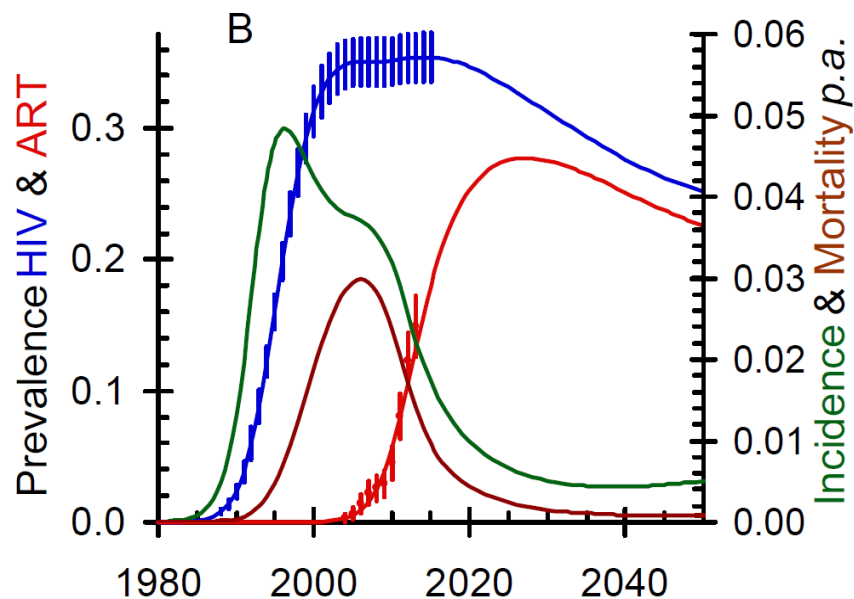
Under the present rates of implementation the incidence should fall from about 2.3% *p.a.* now to 0.6 – 1.0% *p.a.* in 2030

Projections assuming current rate of scale up of ART continues

2.3% in 2016

0.6% in 2030

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Test & treat did not lower incidence in KwaZulu-Natal & Botswana

Universal test and treat and the HIV epidemic in rural South Africa: a phase 4, open-label, community cluster randomised trial

Collins C Iwuji*, Joanna Orne-Gliemann*, Joseph Larmarange, Eric Balestre, Rodolphe Thiebaut, Frank Tanser, Nonhlanhla Okesola, Thembisa Makowa, Jaco Dreyer, Kobus Herbst, Nuala McGrath, Till Bärnighausen, Sylvie Boyer, Tulio De Oliveira, Claire Rekacewicz, Brigitte Bazin, Marie-Louise Newell, Deenan Pillay*, François Dabis*, for the ANRS 12249 TasP Study Group†

- Adjusted HR = 1.01 (Incidence: 2.11 vs 2.27 per 100pys; p=0.89)
- Poor linkage to care likely explanation – clinic-related stigma

Is the UNAIDS target sufficient for HIV control in Botswana?

Salim Abdool Karim

Centre of AIDS Programme of Research in South Africa, Durban,

Botswana's progress toward achieving the 2020 UNAIDS 90-90-90 antiretroviral therapy and virological suppression goals: a population-based survey

Tendani Gaolathe, Kathleen E Wirth, Molly Pretorius Holme, Joseph Makhema, Sikhulile Moyo, Unoda Chakalisa, Etienne Kadima Yankinda,

UK: Mathematical modeling - viral-load suppression has to reach 90% to bring the U.K. HIV epidemic under control

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Bold new approach:

Mass drug administration to treat & prevent HIV

Everyone on Antiretrovirals (EvA)

What is EvA?

1. ARVs to treat HIV positive   ($\pm$ 45% of community)
2. ARVs for PrEP in HIV negative   ($\pm$ 45% of community)
3. ARVs for those who do not test   ($\pm$ 10% of community)

...but with a difference:

- ❖ Everyone on the same pill (TDF/3TC/DTG)
- ❖ Strategy is a pill-a-day for everyone for 1 year
- ❖ Everyone gets their pills by community distribution to each household (linkage to home care)
- ❖ Each person's adherence to pill-a-day is supported and monitored through home visits

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Examples - mass drug administration

Mass drug administration of azithromycin for trachoma reduces the prevalence of genital *Chlamydia trachomatis* infection in the Solomon Islands

M Marks,[1,2] C Bottomley,[3] H Tome,[4] R Pitakaka,[5] R Butcher,[1] O Sokana,[6] H Kako,[7] A W Solomon,[1,2] D C Mabey[1,2]

40% ↓ in prevalence of genital *C. trachomatis* infection following azithromycin MDA for trachoma elimination

Short-term Impact of Mass Drug Administration With Dihydroartemisinin Plus Piperaquine on Malaria in Southern Province Zambia: A Cluster-Randomized Controlled Trial

Thomas P. Eisele,[1,a] Adam Bennett,[2,a] Kafula Silumbe,[4] Timothy P. Finn,[1] Victor Chalwe,[5] Mulakwa Kamuliwo,[6] Busiku Hamainza,[6] Hawela Moonga,[6] Emmanuel Kooma,[7] Elizabeth Chizema Kawesha,[6] Joshua Yukich,[1] Joseph Keating,[1] Travis Porter,[1] Ruben O. Conner,[3] Duncan Earle,[4] Richard W. Steketee,[3] and John M. Miller[4]

Two rounds of MDA with DHAp rapidly reduced infection prevalence, infection incidence

Mass administration of DEC-medicated salt for filariasis control in the endemic population of Karaikal, South India: implementation and impact assessment

G. Subramanyam Reddy[1] & N. Venkateswaralu[2]

prevalence of microfilaraemia declined significantly from 4.5% in 1982 to 0.14% in 1985 and 0.4% in 1993

Targets for EvA implementation

1. **HIV testing:**   **90%** of community members tested
2. **ART for HIV +ve: 81%** coverage
3. **PrEP for HIV -ve: 50%** coverage
4. **ARVs for those who do not test: 33%**
5. **Overall >60%** (81% of 45% + 50% of 45% + 33% of 10%) **of everyone in the community to take a pill-a-day**
6. **When EvA ends at 1 year, then focus is on maintaining 80% - 90% ART coverage of PLHIV & 25% HIV –ve on PrEP**
7. **Continue VMMC, condoms, etc as usual**

Plan to intervene in cycle of transmission by stopping transmission by treating HIV +ve and stopping new HIV acquisitions through PrEP in HIV -ve


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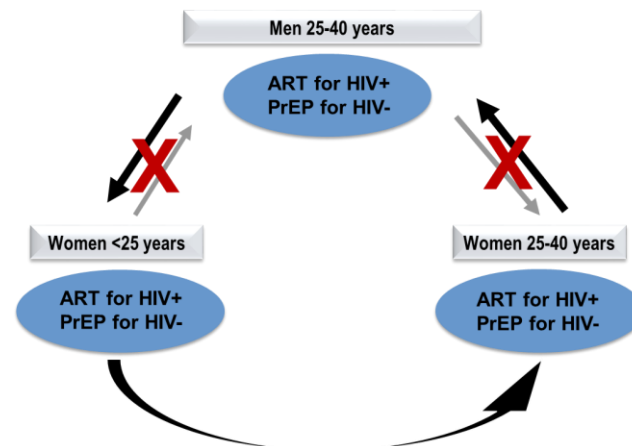
CHEVA: A study assessing EvA

- **CHEVA – Controlling HIV with Everyone on Antiretrovirals**

- **The name CHEVA means you have a natural interest in the welfare of your fellow man, and a desire to help and serve others in a humanitarian way***

- **CHEVA - acronym title for the CAPRISA 021 study in which the EvA intervention will be implemented in all those aged 15-50 year in 2 Umgungundlovu communities (n = ~46,000)**

- **Impact of EvA on preventing HIV assessed by comparing HIV incidence in these 2 areas with 2 nearby communities**

- **A cohort of 6,000 in each of the 4 communities has >90% power for >66% reduction in HIV incidence - 2-sided α=0.05**

- **2° Outcomes: drug levels for adherence, viral load, drug resistance, impact of pill-a-day on stigma & discrimination**

Source: https://www.kabalarians.com/Male/cheva.htm

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Intervention Population 1: 25,732
HIV prevalence: 40%
HIV incidence: 2.1

Intervention Population 2: 21,612
HIV prevalence: 40%
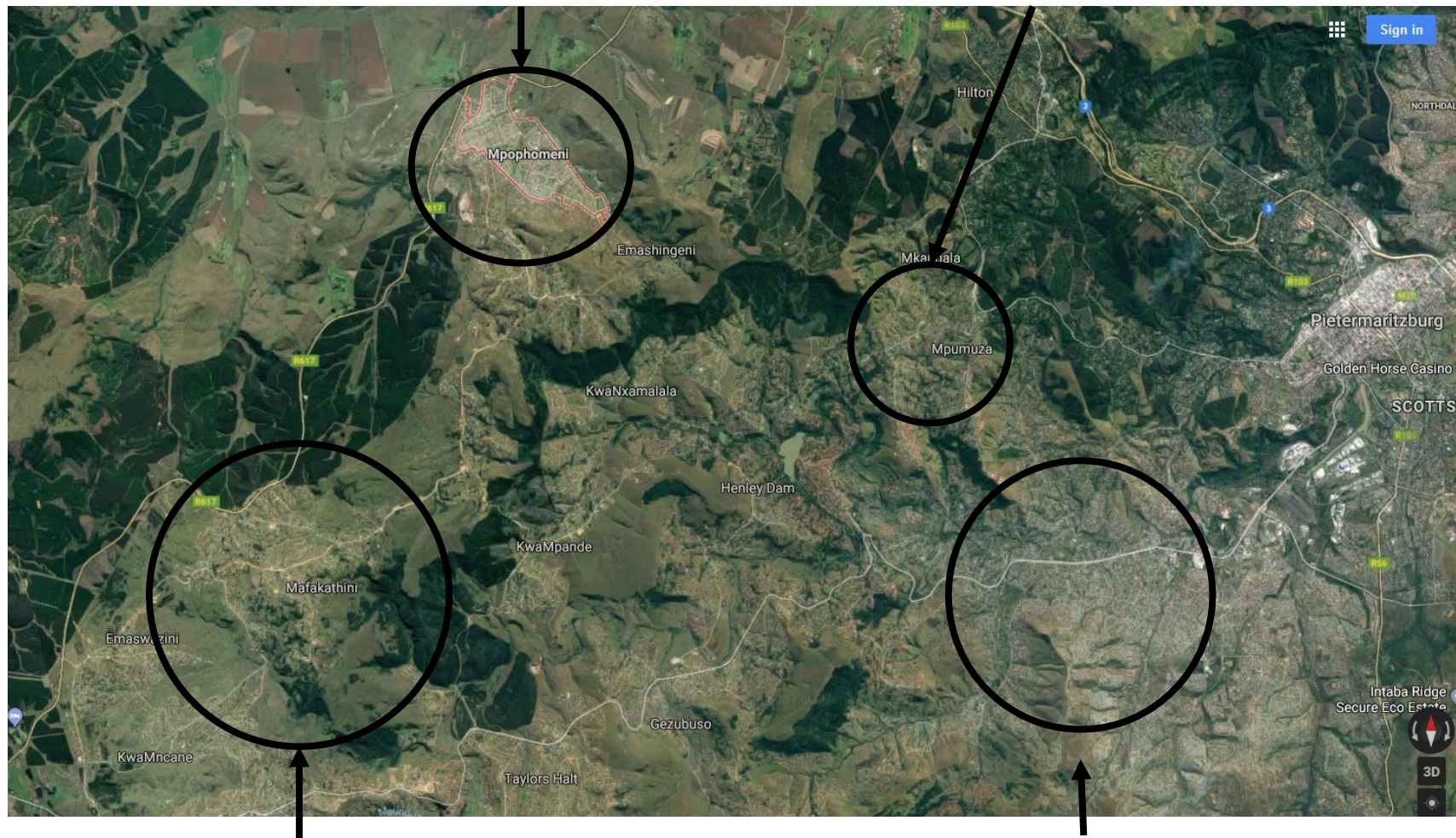HIV incidence: 2.0%
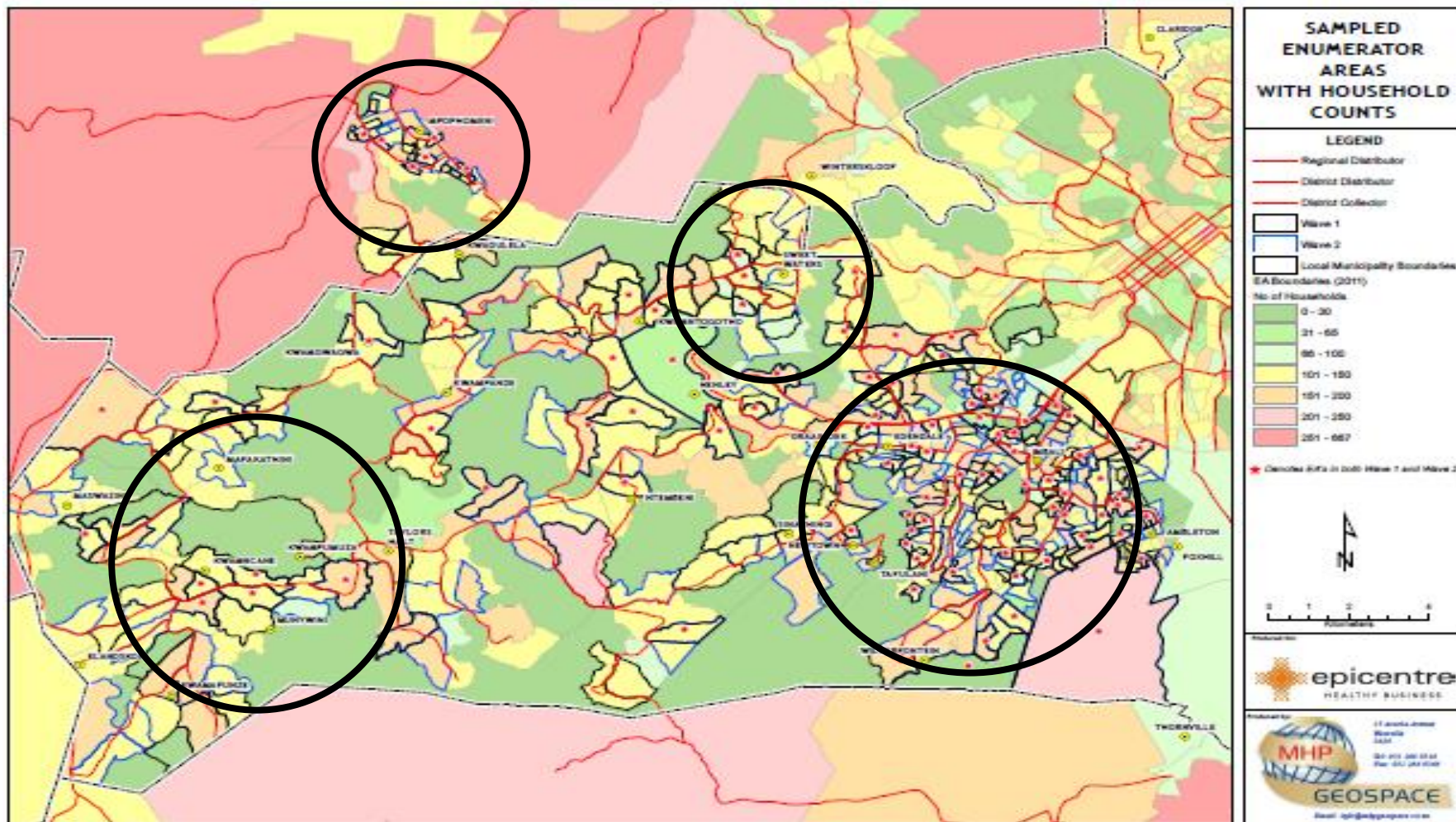
Control Population 2: 157,233
HIV prevalence: 35%
HIV incidence: 1.9

Control Population 1: 210,700
HIV prevalence: 37%
HIV incidence: 2.7

Intervention Population 1: 25,732
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Considerations & Challenges

1. Justification for adding DTG to TDF/3TC for PrEP

2. Risks & benefits of ART to people with no HIV status

3. Logistical feasibility of implementing EvA for 1 year

4. Potential contamination of control communities

5. Limitations of a cohort comparison – not an RCT

6. Will the EvA intervention increase drug resistance?

7. How long will the impact of EvA, if any, be sustained beyond the EvA intervention period?

Modelling the impact of EvA in the study population
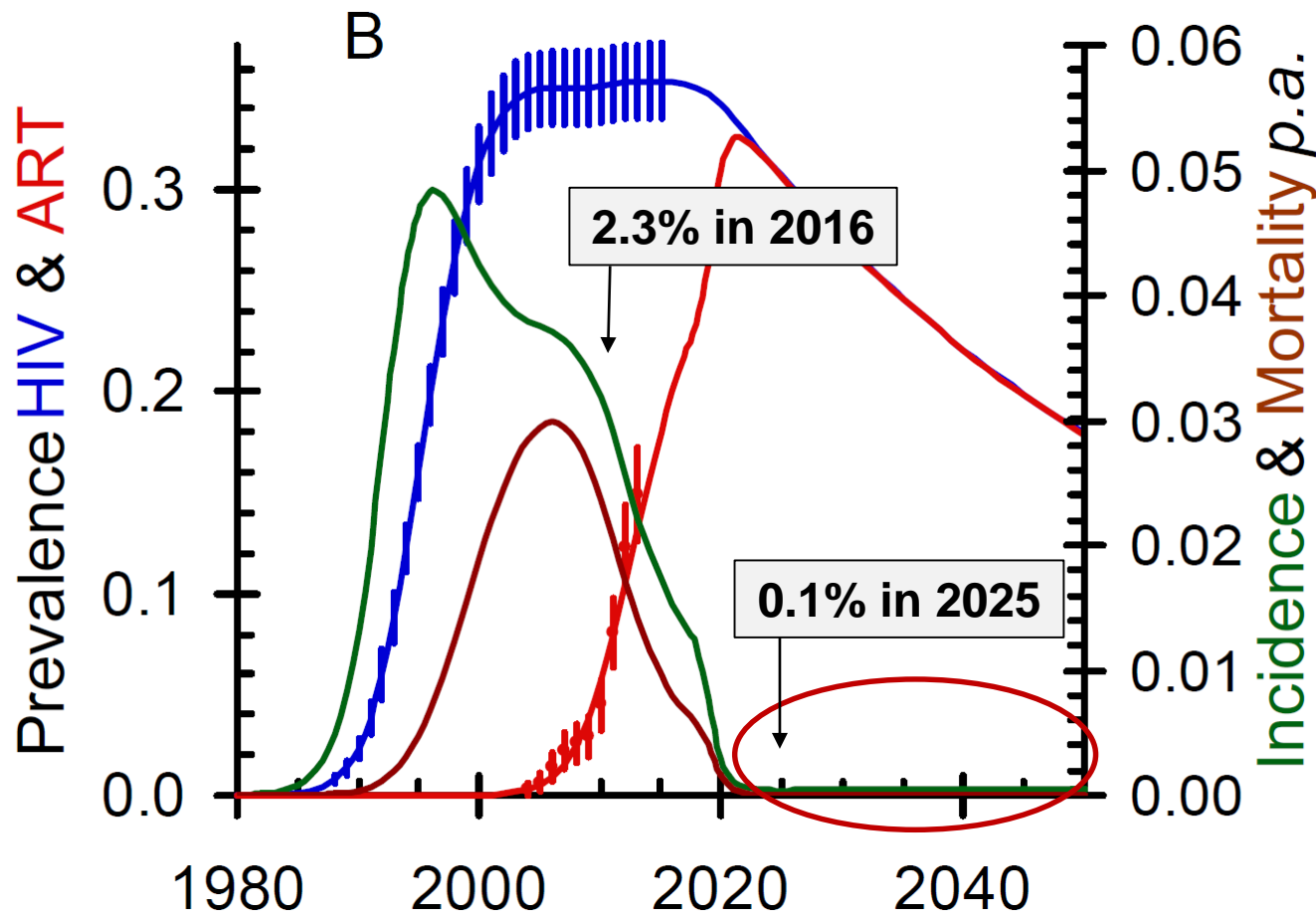
Projected rate of scale up of treatment and prevention