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Different Patterns of HIV Expansion Between High-income and Non-rich Countries and the Potential Drivers during the 1980s

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Abstract

Disease dynamics theory predicts that after the introduction of an infected individual into a susceptible population, the number of infected individuals will grow exponentially until a point at which the depletion of the susceptible class starts to affect the rate of increase of the infectious class. The disease then starts to self-limit its own rate of increase towards an equilibrium with the size of the infectious population. Here, we explored whether the HIV dynamics described exponential growth as theoretically predicted during the 1980s decade for 64 countries. We focused on the HIV population rate of change per infectious individual (*RHIV*) of the infectious class. We used nonlinear regression between HIV infectious class size and *RHIV* to determine the dynamic behavior of HIV. The prevalence of HIV increased exponentially in most countries, except for high-income countries. The world during the 1980s could be separated into two groups based on HIV dynamics at the country scale.

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We performed a multivariate analysis with variables mentioned in the HIV literature to explore the preexisting scenarios that could influence this global separation with regard to HIV dynamics. Poverty levels, malaria burden, the prevalence of men who have sex with men, the prevalence of sex workers, the modes of transmission (HIV subtypes) and the urbanization process could interact to explain the differences among countries with regard to HIV dynamics. The results suggest that during the 1980s, we could divide the world into two groups based on the HIV exponential (non-rich countries) and logistic growth patterns (high-income countries).

Keywords: Poverty; HIV; global patterns; dynamics; HIV subtypes; urbanization; malaria.

1. Introduction

Human immunodeficiency virus (HIV) is a lentivirus that attacks the immune system [1], removing millennia of selective pressures and decades of medical advances. HIV freed many diseases from governmental control; the prevalence of these diseases started to rise again after decades of decline, including tuberculosis, malaria and hepatitis. HIV affected the world at many levels [2-17]. It changed social behaviors, disease burdens, investments in health care and education, life expectancy, and household and country income levels [2,18-22]. There are no doubts that HIV changed everything. Here, we look to the recent past of the HIV expansion phase (the 1980s) and ask if there were any dynamic differences in HIV among countries, and if so, which variables could explain those differences.

HIV subgroups 1 and 2 emerged in Democratic Republic of the Congo (old Zaire, in Kinshasa district); the virus transmitted from monkeys to humans in approximately 1930 [1]. Infectious travelers have initiated the global dispersion of HIV inside and beyond Africa, and this dispersion intensified during the 1970s and 1980s. The HIV 1 Group M subgroups A, B and C accounted for most disease cases around the world [9].

Epidemiology theory and HIV natural history suggest that after the introduction of an infectious individual into a naïve population, the HIV infectious class would grow exponentially [23-29], independently of the socioeconomic scenario in which HIV dynamics take place. During this initial period, HIV mortality rates are low, and the new infection rate is high, resulting in maximum transmission rates. With the increase in the HIV infectious class and the depletion of the susceptible pool, the rate of new infections declines. The disease is then expected to limit itself towards a theoretical equilibrium population size (i.e., following logistic growth), a process known in epidemiology as self-limiting [10].

During the 1980s, the lack of knowledge about the HIV life cycle and its modes of transmission (hetero- and homosexual intercourse, blood transfusion and needle sharing among drug users) allowed the virus to spread within risk groups in every country where it was introduced. Based on disease dynamic theory and the lack of knowledge about HIV during the 1980s, we can speculate that the HIV burden increased in each country following the exponential type of growth.

From WHO reports and related literature, one can observe that many global patterns currently overlap [1,2,9-17]. Today, we can observe an unequal distribution of the HIV burden globally, which suggests that even

though HIV grew exponentially, distinct scenarios composed of distinct drivers inside each country could affect distinct rates of HIV growth. We took a retrospective approach to select an initial scenario during the 1980s. HIV may be related to poverty levels, the number of risk groups, the type of HIV circulating, the malaria burden and the urbanization process.

The HIV burden is higher in African countries than in the rest of the world [7-9]. HIV 1 subgroups A and C can be transmitted through heterosexual intercourse and are the most common strains circulating in Africa, which has a high density of low-income countries. The Americas and Western Europe contain a higher number of middle- and high-income countries, and HIV 1 subgroup B (transmitted mainly via male homosexual intercourse) is the most common strain. All subgroups can be transmitted via needle sharing among drug users. Hence, in the African region, there was an additional risk group (via heterosexual transmission) where HIV spread [3, 7, 8, 9].

HIV/AIDS is a disease related to poverty. Sex work is one of the last options before an individual faces extreme poverty. Poverty could facilitate a higher inflow of susceptibility to risk groups (sex workers and injected drug users), and poor areas and poor countries may have a higher prevalence of sex workers and drug users and a higher burden of HIV [14-19]. These global patterns suggest that income levels and risk groups could be involved in the first years of HIV global dispersion.

Another global phenomenon is the urbanization process, which could be related to income levels. In general, immigrants have settled in high-density and poor areas. Urbanization intensified during the second half of the 20^{th} century, principally in low- and middle-income countries [30-33]. The poor economic environment could enhance the probability of individuals engaging in HIV risk behaviors. Interestingly, malaria global endemicity overlaps with the distribution of low- and middle-income countries at low latitudes, which have environmental conditions (temperature and rain regimes) for malaria to complete its life cycle. The interaction between malaria and HIV is synergistic. Malaria could favor HIV spread at the population level because malaria increases CD4 cell counts, which are HIV host cells, thus favoring HIV replication [34-38]. Hence, malaria burden could enhance the susceptibility of individuals to HIV, extending the HIV acute phase and increasing an individual's infectivity. The malaria burden could also influence HIV dynamics during the 1980s.

Here, we evaluate whether the theoretical prediction about HIV exponential growth is applicable to the first ten years of HIV spread (1979 to 1989) in 64 countries. We used exponential growth as a null hypothesis from which any population can dynamically deviate (i.e., self-limiting). The specific null hypothesis is that all countries will display exponential growth independent of their income level, HIV subgroup status, malaria burden and urbanization.

2. Methods

Disease dynamics and trends are either analyzed at the city scale by epidemiological studies or at the country scale by WHO reports [4-9]. Here, we follow WHO reports by using the country scale. We are looking for global patterns, and there is no large HIV data set for the 1980s available at the city scale. Human populations

are concentrated in cities, and HIV dynamics at the country scale may well reflect the HIV dynamics observed in cities. Hence, this study may be interpreted as an extension of WHO reports with an epidemiological approach [10].

We concentrated on the HIV infectious class (the number of HIV cases) from 1979 to 1989 using data obtained from the Gapminder Foundation in 2010 (n = 64 countries). We focused on the HIV population rate of change per infectious individual (R). R can be estimated by the per capita differences between new infections and mortality or by the natural log ratio between past and current population sizes:

$R_{HIV} = Ln(HIV_t / HIV_{t-1})$. We used the latter approach [10].

R can be affected by exogenous and endogenous processes [10]. An exogenous process occurs when there is no feedback loop between at least two variables. One may affect the other, but this effect does not provide feedback on the former. One example is the introduction of many vaccines during the last century, reducing the burden of many diseases. HIV may also be considered an exogenous force for other diseases, such as tuberculosis [10]. An endogenous process occurs when *R* is dependent on its own past population sizes, as in the self-limiting process. Moreover, in a constant and favorable environment, without positive or negative feedback, the population may grow in an unbounded manner and exponentially, as suggested by the theory [23-28, 39-43].

We used nonlinear regressions between HIV infectious class size and *RHIV* , with graphical inspections to determine the dynamical behavior of HIV. When R was independent of population size, the dynamics were classified as exponential growth. When *R* was negatively correlated with HIV population size, the dynamics were classified as self-limited growth, captured by the nonlinear form of the logistic model:

$$R_{HIV} = R_{max} - b \times HIV_{t-1}{}^{q} \qquad \text{Eq. 1}$$

where R_{HIV}, the HIV infection per capita population rate of change, is estimated by the natural log ratio between *HIVt* and $HIVt_{-1}$. *R*max is the maximum difference between new per capita infections and per capita mortality rates during the introduction and initial spread of HIV and is analogous to R_0, the basic reproductive number (Lima 2009). The parameter *b* measures the impact of the introduction of one infectious individual on R_{max}. $HIVt_{-1}$ is the HIV population size in the previous year. q is the nonlinear parameter. Nonsignificant parameter results and low R^2 (coefficient of determination) values from Eq. 1 will suggest that R_{HIV} is independent of HIV infectious class (exponential growth), thus corroborating the null hypothesis. Significant parameter results and high R^2 values (which measures the endogenous contribution to HIV dynamics) will suggest that the HIV dynamics displayed logistic growth.

We also explored the distinct scenarios in which HIV spread took place during the 1980s. We performed a partial least squares regression (PLSR) with a cross-sectional approach to explore the effects of the potential exogenous variables on R^2 (which measures the effect of HIV infectious class size on R_{HIV}) and R_{max}. PLSR indicates the variables with the highest weight on orthogonal components and the proportional contribution (%) of each component to the variance in the response variables [44]. Each component can be interpreted as a latent (unmeasured) variable. We established an initial scenario (latent variable) composed of economic, social, and

public health potential drivers mentioned in the HIV literature. The analysis will allow us to infer how the change in scenarios (latent variable) between countries influenced the differences in the response variables (R^2 and R_{max}) and HIV dynamics.

The explanatory variables were poverty (the average per capita GNI and life expectancy of 1980s), urbanization (the average ratio between the urban and rural population), the malaria burden (average malaria incidence rate, per 100,000), the number of risk groups and the prevalence of MSM and sex workers. We used the most important HIV subtype circulating in a country as a proxy of the number of risk groups. Hence, subtypes A and C (also transmitted by heterosexual intercourse) received a higher value than countries with subtype B. There are no estimations for the prevalence of men who have sex with men (MSM) and sex workers at the country level in the 1980s. We used recent estimations, assuming that risk size prevalence remained relatively stable throughout the decades.

We took two approaches. We performed the PLSR including all countries and another using only non-rich countries because of the dynamical differences observed between countries (see results). We repeated the two approaches with and without the estimates of MSM and sex worker prevalence because of data quality. First, both are illegal in many countries, which could influence the estimations. Second, only one highincome country estimated the sex worker prevalence. Hence, we removed this variable from the all-countries approach and included it in the PLSR for the non-rich group. The data were gathered from the World Bank, World Health Organization, United Nations and Gapminder websites. We fitted Eq. 1 using the nls library in R through non-linear regression analysis. All statistical analyses were performed in the R environment [45].

3. Results

The HIV infectious class grew exponentially in the majority of countries (Figures 1 and 2, Table 1). The countries where it grew logistically were Canada, the United States of America, Australia, the United Kingdom, Ireland, Belgium, the Netherlands, France, Norway, Sweden, Finland, Denmark and Germany (Figure 3, Table 1). All of these are high-income countries with subtype B as the main HIV strain circulating in the population. The exceptions among these high-income countries were Iceland and Luxembourg, which displayed an exponential growth pattern (Figure 3).

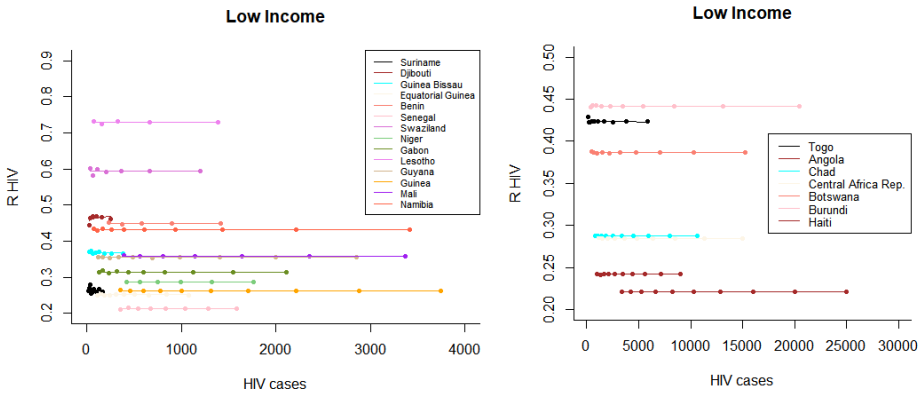

Figure 1: The HIV population per capita rate of change (R HIV) in function of the HIV infectious class size from 1979 to 1989 for the low-income countries.

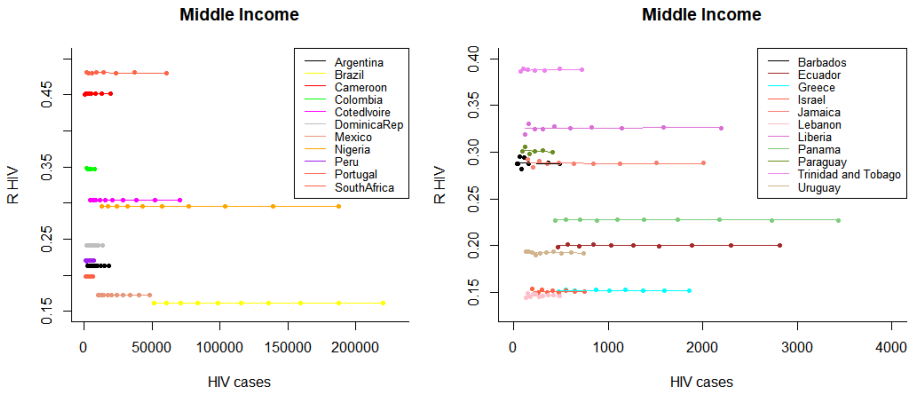

Figure 2: The HIV population per capita rate of change (R HIV) in function of the HIV infectious class size from 1979 to 1989 for the middle-income countries.

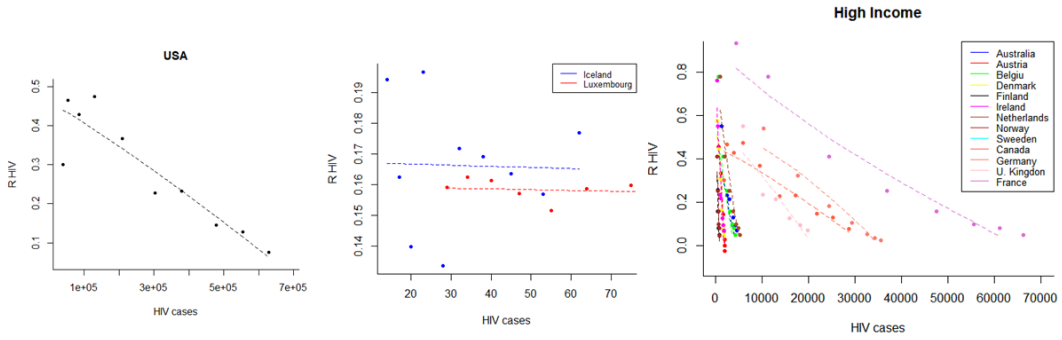

Figure 3: The HIV population per capita rate of change (R HIV) in function of the HIV infectious class size from 1979 to 1989 for the high-income countries.

Table 1: Non-linear logistic model results between R and HIV_{t-1} infectious class size for some high- (H) and low (L) and middle-income (M) countries classified based on income levels during the 1980 decade (per capita Gross National Income, GNI, calculated using the World Bank Atlas method). Rmax is the RHIV maximum per capita rate of change and was fixed. In the case of high-income countries Rmax is the mean of the first three years of RHIV. And, the mean of the ten years of the RHIV levels for low and middle-income countries. b is the linear pendent and q the non-linear parameter. Bold faces depict statistically significant results. The results were organized in ascending order in regards of the R^2, which is the coefficient of determination and measures the endogenous (HIV population size) contribution to HIV dynamics. Luxembourg and Iceland are examples of high-income countries with exponential growth (low R^2).

		Parameters			
Country	Income level 1980	Rmax	b	q	R^2
Australia	H	0.649	0.00025	0.921	0.936
Austria	H	0.729	3.42E-05	1.012	0.998
Belgium	H	0.793	0.00048	0.885	0.962
Canada	H	0.458	2.54E-06	1.163	0.912
Denmark	H	0.575	0.000026	1.348	0.979
Finland	H	0.38	-8.3E-07	1.951	0.954
France	H	0.934	0.00017	0.772	0.979
Germany	H	0.539	1.1E-07	1.465	0.976
Iceland	H	0.168	0.0001	0.682	0.079
Ireland	H	0.773	0.0008	0.903	0.958

Luxembourg	H	0.1597	0.000071	0.75	0.218
Netherlands	H	0.793	0.0003	0.9111	0.96
Norway	H	0.59	3.53E-06	1.723	0.961
Sweden	H	0.589	0.00004	0.87	0.986
United Kingdom	H	0.55	4.2E-06	1.184	0.923
United States	H	0.458	1.4E-07	1.11	0.911
Angola	L	0.242	0.00009	-0.0681	0.077
Benin	L	0.449	6E-07	1	0.276
Botswana	L	0.365	-0.0077	-0.022	0.202
Burundi	L	0.441	-0.0012	0.0518	0.269
Central African Republic	L	0.285	1.2E-07	0.678	0.262
Chad	L	0.288	-1E-08	0.937	0.216
Djibouti	L	0.44	-0.0086	0.213	0.518
Equatorial Guinea	L	0.25	-0.0006	0.082	0.039
Ethiopia	L	0.389	-0.139	0.000001	0.079
Gabon	L	0.314	9E-09	1.374	0.138
Guinea	L	0.262	-0.0005	0.0579	0.069
Guinea-Bissau	L	0.37	-2.59	-1.971	0.596
Guyana	L	0.354	-0.0017	-0.128	0.033
Haiti	L	0.221	-0.0008	0.0232	0.371
Kenya	L	0.391	-0.0006	0.011	0.256
Lesotho	L	0.729	-4.4E-10	1.798	0.034
Malawi	L	0.525	-4E-09	1.25	0.185
Mali	L	0.358	-0.001	-0.0435	0.048
Mozambique	L	0.292	-0.001	-0.017	0.164
Namibia	L	0.432	6.4E-06	0.525	0.138
Niger	L	0.287	3E-08	0.9732	0.345
Senegal	L	0.213	-1E-06	0.874	0.173
Sudan	L	0.269	-0.00005	-0.0088	0.173
Suriname	L	0.266	0.00002	1.06	0.077
Swaziland	L	0.593	-0.0058	-0.097	0.062
Togo	L	0.424	6.5E-06	0.564	0.258
Argentina	M	0.212	-0.0008	0.017	0.072
Barbados	M	0.289	0.000001	0.791	0.113
Brazil	M	0.161	-0.00004	-0.006	0.365
Cameroon	M	0.451	-0.001	0.0646	0.392
Colombia	M	0.347	-0.00173	-0.129	0.367
Côte d'Ivoire	M	0.304	-0.0044	-0.0036	0.287
Dominica	M	0.241	-0.0004	-0.111	0.085
Ecuador	M	0.2	-1.2E-06	0.69	0.215

Greece	M	0.151	-0.0005	0.204	0.307
Israel	M	0.151	-0.0208	-0.483	0.139
Jamaica	M	0.288	-0.0124	-0.064	0.203
Lebanon	M	0.146	-0.0004	0.063	0.013
Liberia	M	0.325	-0.00002	0.553	0.204
Mexico	M	0.171	-0.00071	0.0129	0.291
Nigeria	M	0.295	-0.00018	0.019	0.05
Panama	M	0.227	-0.0002	0.068	0.013
Paraguay	M	0.302	4.3E-07	1.366	0.269
Peru	M	0.22	2.3E-07	0.641	0.104
Portugal	M	0.198	-0.00203	-0.188	0.262
South Africa	M	0.48	-0.00061	-0.033	0.15
Trinidad and Tobago	M	0.387	-6.4E-05	0.46	0.321
Uruguay	M	0.193	2.7E-06	0.853	0.202

The PLSR analysis suggested distinct latent variables on R^2 and R_{max}. Using the entire data set, PLSR pointed out that income levels (per capita GNI) followed by urbanization comprised the first component, explaining more than 50% of the R^2 differences between countries. When both MSM and sex work data were removed, income levels appeared again with the highest weight on the first component, followed by life expectancy (which is collinear with per capita GNI) and the number of risk groups (Table 2). With regard to R_{max} as the response variable, the income levels appeared to show the highest weight on the first component and MSM and the number of risk groups on the second component, which explains approximately 24% of the variance in Rmax total. After removing MSM and sex worker data, income levels presented the highest weight on the first component (Table 2).

For the non-rich group, the malaria incidence had the highest weight on the first component and in the second component, the prevalence of MSM on R^2 variance (with sex worker and MSM data). Without the data of MSM and sex workers, malaria, followed by the number of risk groups, appeared to have the highest weight on the first component, with malaria incidence rate followed by life expectancy on the second component. Income levels (with MSM and sex worker data) and urbanization (without MSM and sex worker data) appeared with the highest weight on the first component of R_{max} variance. In both approaches (with and without sex work and MSM data), the number of risk groups followed the income levels and urbanization with regard to their weight contribution to the first component (Table 2).

Table 2: Partial least square regression analysis (PLSR); results of the exploratory variables on R^2 (linear coefficient of determination) and R_{max} (the maximum per capita rate of change). Explanatory variables: GNI (per capita gross national income, atlas method); life (life expectancy at birth); ratio (the ratio between urban and rural populations); MSM (the prevalence of men who have sex with men); sex (the prevalence of sex workers); risk (size of risk group based on the most important subtype circulating); and malaria (malaria incidence rate per 100,000 individuals). We performed the PLSR including all countries and another PLSR using only non-rich countries because of the dynamical differences observed among countries (see results). We repeated the two approaches with and without the estimates of MSM and sex worker prevalence because of data quality. W1, W2 and W3 represent the loading weights of each variable in the first, second and third PLS regression components. R^2 % is the proportion of the variance in the response variable accounted for by each component of the PLS regression. All predictor variables were standardized.

R^2							
All counttries without sex workers				All counttries without sex workers and MSM			
	Loadings weights				Loadings weights		
Variables	Comp 1	Comp2	Comp 3	Variables	Comp 1	Comp2	Comp 3
GNI	**0.693**	0.604	0.366	GNI	**0.698**	0.616	0.358
Life	0.365	-0.324	-0.447	Life	0.472	-0.249	-0.45
Ratio	0.43	-0.1	-0.481	Ratio	0.328	-0.241	-0.378
Malaria		0.533	-0.643	Malaria	-0.15	0.612	-0.724
MSM	0.31	-0.33	0.106	Risk	-0.399	0.356	
Risk	-0.314	0.357	-0.101				
R^2	**65.208**	12.665	7.740		**61.989**	12.968	10.743

Rmax							
All countries without sex workers				All counttries without sex workers and MSM			
	Loadings weights				Loadings weights		
Variables	Comp 1	Comp2	Comp 3	Variables	Comp 1	Comp2	Comp 3
GNI	**0.92**	0.169	0.316	GNI	**0.777**	0.513	0.347
Life	0.246	-0.394		Life	0.426	-0.331	-0.352
Ratio	0.258	-0.381	-0.61	Ratio	0.35	-0.182	-0.388
Malaria	0.156	0.419	-0.721	Malaria		0.575	-0.765
MSM		-0.49		Risk	-0.295	0.513	0.144

Risk		0.506					
R^2	**52.52**	**24.85**	8.90		**60.73**	14.24	10.82

R^2

Non-rich countries: with MSM and sex workers

	Loadings weights		
Variables	Comp 1	Comp2	Comp 3
GNI	-0.308	0.371	0.217
Life	-0.225	0.324	-0.337
Ratio		0.427	
Malaria	**0.737**		-0.162
Sex	0.281	0.168	-0.633
MSM	0.304	0.702	0.325
Risk	0.362	-0.222	0.547
R^2	42.643	30.349	11.245

Non-rich countries: without MSM and sex workers

	Loadings weights		
Variables	Comp 1	Comp2	Comp 3
GNI	-0.256	0.381	-0.367
Life	-0.285	0.545	0.736
Ratio	-0.263	0.410	-0.567
Malaria	**0.796**	0.574	
Risk	0.389	-0.245	
R^2	55.864	19.315	8.002

Rmax

Non-rich countries: with MSM and sex workers

	Loadings weights		
Variables	Comp 1	Comp2	Comp 3
GNI	**-0.511**	-0.209	-0.135
Life	-0.343	0.443	0.441
Ratio	-0.441		0.194
Malaria	0.336	0.163	
Sex		0.698	-0.525
MSM	-0.291	0.485	0.264
Risk	**0.469**		0.636
R^2	59.951	17.467	3.969

Non-rich countries: without MSM and sex workers

	Loadings weights		
Variables	Comp 1	Comp2	Comp 3
GNI	-0.346	0.472	-0.554
Life	-0.414	0.599	0.305
Ratio	**-0.593**	-0.644	-0.176
Malaria	0.350		0.399
Risk	**0.484**		-0.640
R^2	59.954	10.118	11.56

4. Discussion

The results suggest that during the 1980s, we could divide the world into two groups based on the HIV exponential and logistic growth patterns.

In light of our findings regarding HIV dynamics, the PLSR results confirmed that poverty levels (and to a lesser degree, urbanization and the number of risk groups) could explain the dichotomy between high-income and non-rich countries based on R^2 and R_{max}. Among the non-rich countries, PLSR results suggest that the malaria incidence rate could influence the endogenous HIV process (R^2) and that income levels and urbanization could explain the differences with regard to R_{max} levels among countries. Although we did not find statistical evidence of the prevalence of sex workers and MSM effects (probably because of data quality), we will also discuss the importance of these variables on the global dichotomy because there is a general consensus sustained by empirical evidence that they are important to HIV dynamics [46-50].

HIV dynamics at the population level are the product of the interaction between the pools of infectious and susceptible individuals, the recruitment of susceptible individuals, seroprevalence status and exogenous variables [39-43, 46-54]. After infection, the virus spreads quickly in host cells (acute phase), and the immunological system reacts, leading to a period of low virus burden (chronic phase). Individuals in the acute phase are more likely to recruit susceptible individuals than are individuals in the chronic phase of the disease [53, 54]. After the introduction of an infected individual in a naïve risk group, most of the infected individuals are in the acute phase in a large pool of susceptible individuals. AIDS mortality is low, and per capita new infections are high, resulting in high levels of R_{max}. The prevalence of individuals progressing from the acute to chronic phase, together with the depletion of the susceptible pool size, limits the HIV rate of increase (self-limiting) [53]. This is a combination of a time effect (progression rate from acute to chronic phase) and the sizes of the infectious and susceptible classes (the endogenous component). Self-limiting growth suggests a reduction in the difference between the two rates as a function of time and infectious class size. We believe that the HIV dynamics observed in high-income countries described this phenomenon.

After the chronic phase, the viral load increases again (AIDS stage), increasing one's susceptibility and morbidity to other diseases such as tuberculosis. During the 1980s, knowledge of viral status and changes in risk behavior increased over time, after a long period of recruitment of susceptible individuals [53, 54]. This produced a period of higher levels of per capita new infections (recruitment) than the removal of individuals from the infectious class (morbidity). The exponential growth suggests that the differences between the two rates remained constant during the 1980s for the non-rich countries.

The HIV dynamical differences between high-income and non-rich countries may rely on the distinct environments in regards to the risk group pool size and the inflow of individuals to it. In high-income countries, low poverty levels could restrict the inflow and the size of risk groups (MSM and drug users). These features may allow the increase of the infectious class (individuals at chronic phase in risk groups) to drive the reduction

of per capita new infections, thus depleting the R HIV.

In non-rich countries, low- and middle -poverty levels, together with urbanization and malaria incidence rates, could favor high inflow and high-risk group sizes, thus avoiding the self-limiting process observed for high-income countries. In middle- and low-income countries, urbanization was and is an unplanned process, occurring mainly in high-density poor areas [55-57]. The city's inability to absorb this incoming labor force could facilitate the inflow of individuals into HIV risk groups. Moreover, the non-rich countries are located throughout tropical latitudes, where the Anopheles mosquito and malaria Plasmodium may prosper. Cities expand over natural mosquito habitats, reducing natural predators and increasing urban Anopheles habitats [55-57]. The agglomeration of individuals increases the contact rate, favoring malaria epidemics. The Plasmodium increase the replication of host cells (CD4 cells), which may increase the period of the acute phase of HIV, potentially sustaining a more prolonged period of recruitment. An additional hypothesis is that the effects of malaria on HIV replication may also increase the infectiveness of an individual at the chronic phase, which could also sustain the exponential growth period. A chronic individual in non-rich countries may be more infectious than chronic individuals in high-income countries because of the potentially higher HIV viral load during the chronic phase product of the effects of malaria on HIV replication. These characteristics could also explain a lower but constant level of R HIV (the difference between per capita new infections and mortality rates) than that observed in high-income countries. Poverty, urbanization and malaria incidence could interact to favor high inflow and risk group sizes, resulting in a longer period of exponential growth.

The average R_{max} for African countries is 1.9 times higher than that for non-rich and non-African countries. The exponential HIV spread in Africa was almost twice the exponential growth outside non-rich countries. High poverty levels, high malaria burden and an additional mode of transmission (HIV 1 type A and C) could be involved in explaining the R_{max} differences among non-rich countries.

Some studies have suggested that the concurrent sexual partnership (as opposed to serial monogamy) is higher in Africa than in the rest of the world, while others have suggested that there are no differences among regions in this respect [58-63]. If concurrent partnership is indeed higher in Africa, we can suggest that the African risk group sizes were even higher than those of the rest of the world, and during the 1980s, the high sexual contact rate between individuals may also have fueled the exponential spread of HIV at higher levels in Africa than in other non-rich countries.

If poverty disparity was the major driver of HIV dynamics during the 1980s among countries, which variables and/or processes explained countries' poverty levels? There is another global distribution that almost overlaps with on the distribution of High-Middle and Low income [2]. Most of the middle- and low-income countries were European exploitation colonies until the end of 19th (outside Africa) and after the second half of the 20th centuries (Africa) [64, 65].

Colonialism and neo-colonialism removed resources from colonies for centuries. Independence was usually followed by the emigration of investments and institutions, resulting in a period of economic retraction that has extended until the present. After independence, many countries passed through a period of social instability,

which in many cases escalated to civil wars, as in Africa, negatively impacting many services such as food production and distribution and health care, which intensified the poverty burden [64-73]**.** Colonialism could influence the global income distribution and ultimately the HIV dynamical differences among countries during the 1980s (Appendix 1, Figure A1 and Table A1). Centuries of exploitation settled a favorable scenario for the exponential growth of HIV in the late XX century.

Here, we applied population ecology theory to explore HIV dynamics at the country level and explored the potential drivers that could explain the global dichotomy we found. The framework employed is based on the realized per capita population rate of change (R_I), which is supported by plausible ecological principles and is hence an advantageous starting point to explore disease dynamics. Any country interested in its HIV epidemics may use our results as hypotheses and expand on this research. For example, governments and health agencies may use the framework on a finer scale (region and cities) using national data with regard to the changes in HIV burden within risk groups, the effects of interventions, the changes in risk behavior activities, knowledge of modes of HIV transmission, condom use and other potential drivers. Any government may disentangle R_I in its components (new per capita infections and per capita mortality), explore which of them are most important for R_I trends and explore the contributions of endogenous and exogenous processes. Hence, we suggest that this approach, based on simple principles from population ecology theory, could be included as a supplement to WHO reports with minimal cost- and time-demanding efforts, which could provide insights and hypotheses and may facilitate the testing and estimation of the drivers of HIV dynamics.

5. Conclusion

The HIV dynamics during the 1980s decade showed a clear separation between high-income and non-rich countries. The ecological principles and the simple approach used in this study allowed to discover this global pattern.

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7. Authors' contributions

All authors contributed equally to the manuscript.

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9. Ethics Declarations

Ethical Approval and Consent to participate:

Not applicable.

Consent for publication:

Not applicable.

The authors declare no conflicts of interest.

10. Appendix

A 1. Relationship between independence date and the economic (GNI per capita, Atlas method) performance of high-income and non-rich (low- and middle-income) countries during the 1980s.

Countries that were already states during the discovery of the new world (and the beginning of colonialism) received an independence date of 1500 A.D. This is not the real date of the formation of many of the European countries and neglects geo-political changes (i.e., Iberic Union between Spain and Portugal) for the last 500 years. By setting the 1500 A.D. date, we made a conservative estimation of state formation and independence. We used data on high-income and non-rich GNI per capita from the World Bank website, which includes more countries than the present study does. Independence data were taken from the World Population Review website.

We used a linear regression between per capita GNI and time to explore the economic levels and performance during the 1980s between high-income and non-rich countries.

We can observe higher per capita GNI levels in high-income countries than in non-rich countries. We can observe an increase in per capita GNI for high-income countries (principally from 1984 on) and a modest increase in low- and middle-income countries (Figure S1, Table S1) during the 1980s. We also found that the high-income countries presented an average older independence date (mean= 1765 (95% confidence interval: $1699.2<\mu<1830.7$)) than the non-rich countries (mean=1932.045 (95% confidence interval: $1919.8<\mu<1944.2$)). Note that the date (mean) for high-income countries is almost 200 years older than for non-rich countries, and the ICs do not overlap, suggesting two separate groups.

These results suggest a correlation between economic performance during the 1980s and the period since the end of colonization of the non-rich countries. These results suggest that the hypothesis that poverty level and HIV dynamics could be explained by the historical exploitation of new-world African and Asian colonies.

Table S1: The linear regressions between the average per capita GNI and time (year) for non-rich and high-income countries during the 1980s. All estimations (intercept and the linear pendent with time) are significant (P-value < 0.05). Note that the pendent of high-income countries is 51.88 times that of non-rich countries.

Economic status	Coefficients	Estimate	Std. error	t-value	P-value
High income	(Intercept)	-1.579.189.2	320.606.0	-4.926	0.000818
	Year	801.9	161.6	4.962	0.000778
Non-rich	(Intercept)	-29.975.142	7415.887	-4.042	0.00292
	Year	15.455	3.738	4.135	0.00254

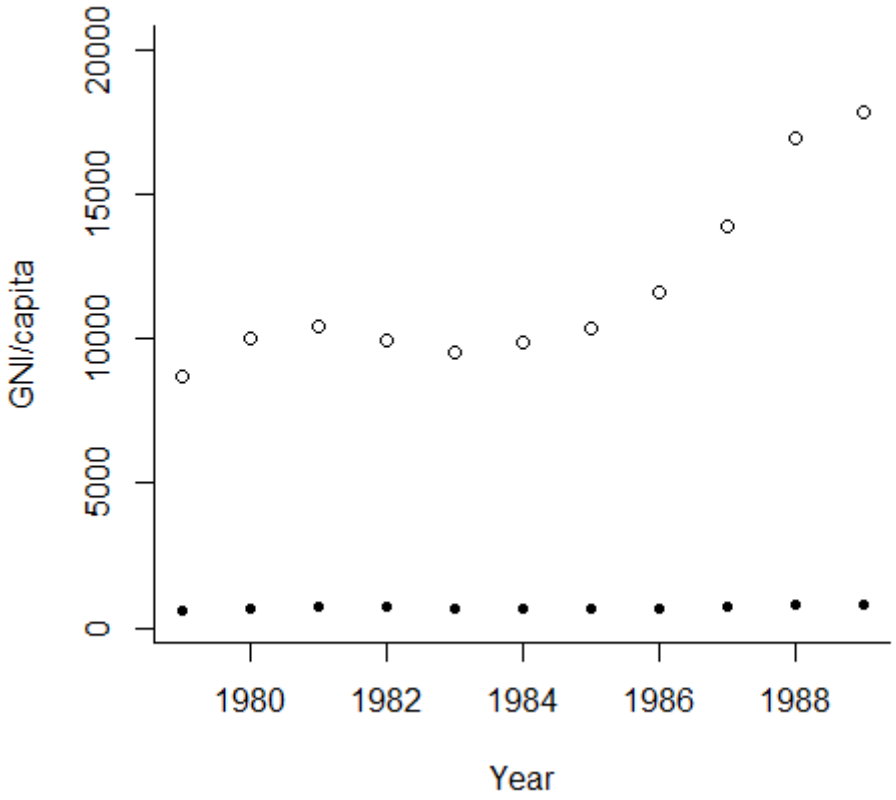

Figure S1: The average per capita GNI per year during the 1980s for high-income countries (open circles) and non-rich countries (close circles).