

## Reevaluation of HIV transmission modes: A systematic analysis

Jiman He <sup>1, 2, \*</sup>

<sup>1</sup> Liver Research Center, Brown University, Providence, United States.

<sup>2</sup> Hongli Women Health, Guangdong, China.

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### Abstract

**Background:** Before the widespread use of antiretroviral therapy, data on the age-specific distribution of AIDS diagnoses and deaths due to HIV/AIDS indicated that HIV transmission was high or highest among children aged a few to 14 in Africa, Asia, and parts of Southern Europe/Latin America. These data contradict the theory of sexual transmission. Similarly, there are many contradictions between the current transmission theory and other epidemiological data. Currently, there are no animal research data that support any existing transmission theories.

**Methods:** The present study compares two existing transmission theories by systematically analyzing high-risk populations, infection rates between regions with high and low mosquito abundance in each country globally, and progress in HIV preventive practices.

**Results:** A wide range of epidemiological data and evidence in preventive practices can consistently be explained by the theory of mosquito transmission, but not by the sexual transmission theory.

**Conclusion:** These solid and consistent data strongly indicate that mistakes may have occurred in our understanding of HIV transmission, and further research is urgently needed.

**Keywords:** Human immunodeficiency virus; AIDS; Sex; Mosquitoes; Risk factors; Vector

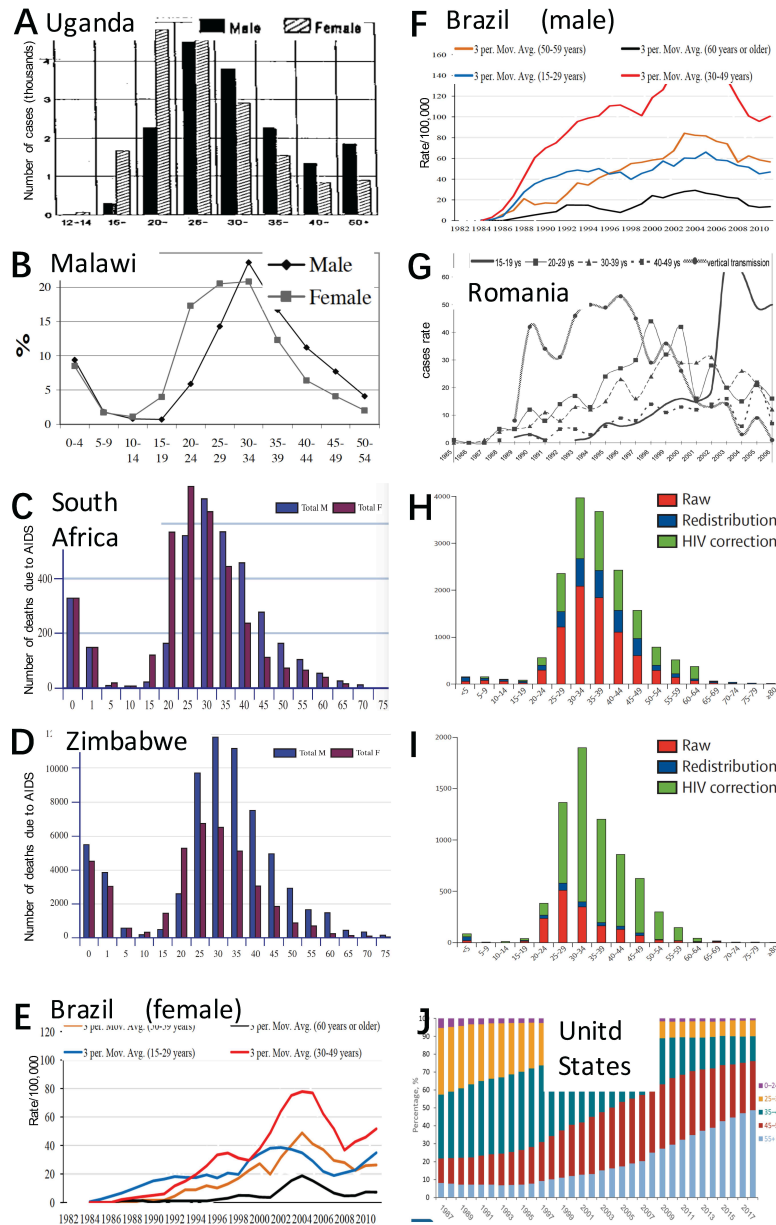
### 1. Introduction

According to guidelines, the time between HIV transmission and an AIDS diagnosis is usually 10–15 years, and without treatment, people with AIDS usually survive for three years.<sup>1,2</sup> Therefore, individuals diagnosed with AIDS or who died from AIDS between the ages of 15 to 29 should have mostly acquired HIV between the ages of a few to 14. In other words, before the widespread use of antiretroviral therapy (ART), data on AIDS diagnosis or mortality from countries in Africa, Asia, and parts of Southern Europe/Latin America (Fig. 1A–1I) indicate that rates of HIV infections were high or highest among children.<sup>3–8</sup> However, in Western developed countries, rates of HIV infection among children were low (Fig. 1J).<sup>9–11</sup>

Before ART became available in clinics, few studies examined HIV transmission among children aged between several years old and 14. Moreover, parents, especially those who were HIV positive, were often unwilling to have their children tested due to stigma and discrimination, making it impossible to obtain objective results. However, individuals with AIDS who became ill would seek medical assistance. Therefore, there was plenty of data on AIDS diagnosis and mortality before the widespread use of ART. These early data are useful for our understanding of disease transmission.

\* Corresponding author: Jiman He

The highest rate of infections among children clearly contradicts the current transmission theory asserting that sex is the primary mode of transmission. As discussed below, contradictions commonly exist between the current transmission theory and a wide range of data. Currently, there are no animal research data that support any existing transmission theories. To explore these issues, we compare two existing transmission theories using common sense: a valid theory should be able to consistently explain the data in the given field.



**Figure 1** A) Adult AIDS cases stratified by sex, 1992, Uganda. Source.<sup>3</sup> B) AIDS cases by age and sex, 2000, Malawi. Source.<sup>4</sup> C) Reported AIDS deaths, 1996, South Africa. Source.<sup>5</sup> D) Certified AIDS deaths, 1995, Zimbabwe. Source.<sup>5</sup> E) Trends of AIDS incidence, per 100,000 females, Niteroi/Rio de Janeiro, 1982–2010, Brazil. Source.<sup>6</sup> F) Trends of AIDS incidence, per 100,000 males, Niteroi/Rio de Janeiro, 1982–2010, Brazil. Source.<sup>6</sup> G) Trends of AIDS cases in women, 1986–2006, Romania. Source.<sup>7</sup> H) HIV deaths, 2005, Thailand. Registration deaths assigned to HIV (red), deaths coded to garbage codes redistributed to HIV (blue), and misclassified deaths reassigned to HIV (green). Source.<sup>8</sup> I) HIV deaths, 2005, Russia. Registration deaths assigned to HIV (red), deaths coded to garbage codes redistributed to HIV (blue), and misclassified deaths reassigned to HIV (green). Source.<sup>8</sup> J) Persons with AIDS. United States. Source.<sup>9</sup>

## 2. Methods

### 2.1. Research strategy

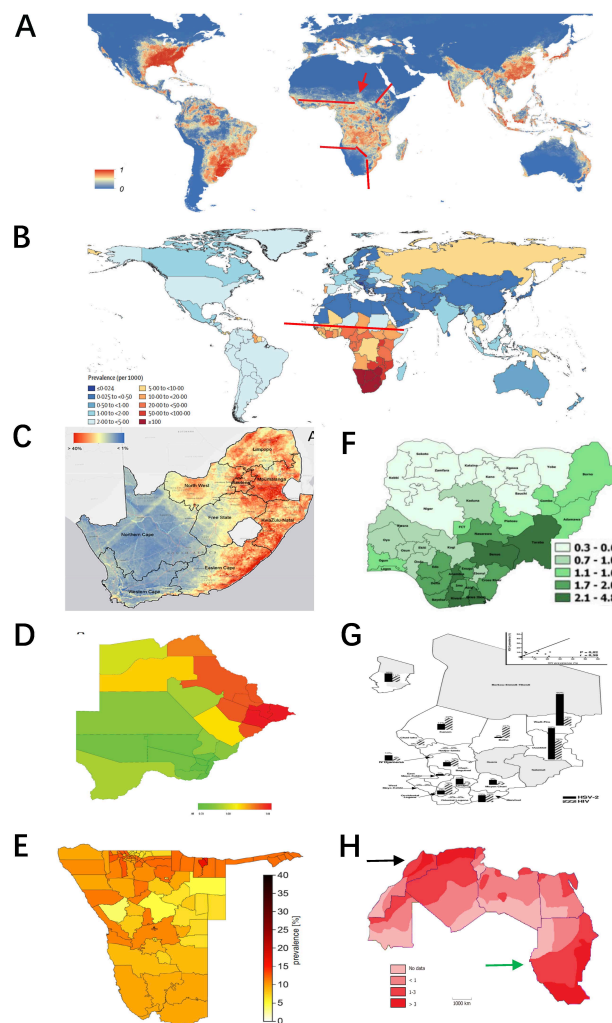
We systematically analyze high-risk populations based on lists stated in clinical guidelines, track progress in HIV preventive practices based on the UNAIDS global report, and compare HIV infection rates between regions with higher and lower *Ae. albopictus* mosquitoes based on a map of the global geographic distribution of *Ae. albopictus* mosquitoes.

The time for HIV to spread to different countries varied. Domestic factors may also impact HIV transmission. Therefore, we compare HIV infection rates in different regions within each country rather than comparing between countries.

## 3. Analysis

### 3.1 Distribution of HIV infections in high-endemic regions

Sub-Saharan Africa (SSA) accounts for 70% of global HIV infections.<sup>12</sup> This extreme case is in line with another striking observation: about 90% of global malaria cases, a mosquito-borne disease, occur in the WHO African region.<sup>13</sup>



**Figure 2** A) Predicted distribution of *Ae. albopictus*. Source.<sup>14</sup> B) Age-standardised HIV prevalence for both sexes, 2017. Source.<sup>15</sup> C) HIV prevalence, male, 2016, South Africa. Source.<sup>16</sup> D) Risk of HIV infection, Botswana. Source.<sup>17</sup> E) HIV prevalence among men (15–49 years old), Namibia, 2013. Source.<sup>18</sup> F) HIV prevalence, Nigeria, 2014. Source.<sup>19</sup> G) HIV prevalence, Chad, 2007. Source.<sup>20</sup> H) Incidence of HIV, North African Countries from 2008 to 2017. Source.<sup>21</sup>

Fig. 2A shows the global distribution of *Ae. albopictus* mosquitoes,<sup>14</sup> and Fig. 2B displays the global distribution of the average HIV infection rate for each country.<sup>15</sup>

HIV prevalence is much higher in the east of South Africa (Fig. 2C),<sup>16</sup> northeast of Botswana (Fig. 2D),<sup>17</sup> and north of Namibia (Fig. 2E).<sup>18</sup> These patterns are similar to the pattern of mosquito distribution in the region as shown in Fig. 2A.

The abundance of *Ae. albopictus* mosquitoes is decreasing from central Africa to North Africa (Fig. 2A). HIV prevalence is also decreasing to the north in parallel (Fig. 2B). Ghana, Togo, Liberia, Sierra Leone, and Côte d'Ivoire have small land sizes and are located in regions with high mosquito abundance, making them unsuitable for exploring our issue. In Nigeria, there is a much higher abundance of mosquitoes on the coast (Fig. 2A). Consistently, HIV is also higher on the coast (Fig. 2F).<sup>19</sup>

In Chad, the highest rate of HIV infections occurs in the eastern provinces of Darfur (Fig. 2G).<sup>20</sup> The region seems to be the site with the highest abundance of mosquitoes in Chad (red arrow in Fig. 2A). The southeast of Sudan has a higher abundance of mosquitoes (Fig. 2A). Consistently, HIV infection rates are also higher (as indicated by the green arrow in Fig. 2H).<sup>21</sup> However, there are deserts in the northern parts of Chad and Sudan, which complicates the analysis. Similar issues exist for Niger and Mali.

Kenya has a higher rate of *Ae. albopictus* mosquitoes in the Southwest (Fig. 2A). The rate of HIV infection is also higher in this region.<sup>22</sup>

### 3.2 In low-endemic regions

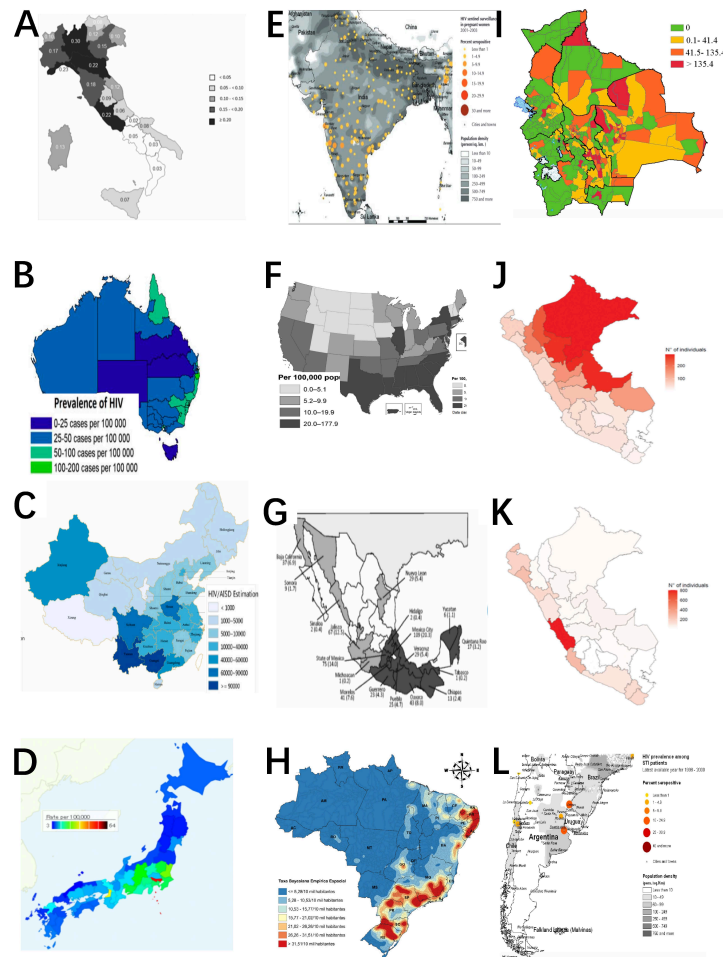
Northern coastal African countries are a low-endemic region. As shown in Fig. 2A, there is a much higher rate of mosquitoes on the northeasternmost coast connecting to Europe and on the north coast of Algeria. Consistently, there are also high rates of HIV infections (as indicated by the black arrow in Fig. 2H).<sup>21</sup>

Fig. 2A shows that *Ae. albopictus* mosquitoes are substantially more abundant on the south coast and northeast coast of Spain, the south coast of France, the north of Italy, the west of Turkey, and the coast of Georgia. Consistently, these regions have a higher prevalence of HIV infections.<sup>23-27</sup> Fig. 3A shows example data from Italy.<sup>25</sup> Greece has a high abundance of *Ae. albopictus* mosquitoes on the peninsula, with lower abundance in the narrow north border region (Fig. 2A). We have not found reported data on the national distribution of HIV in Greece. There is a high abundance of mosquitoes on some Black Sea coast in Russia (Fig. 2A). Russia has a vast land size, and the reported data we have found on HIV distribution is collected based on sub-country settings (average data of each sub-country) and does not show data from small sites.

In Australia, *Ae. albopictus* mosquitoes are most prevalent along the east/northeast coasts (Fig. 2A), where HIV infections are also highest (Fig. 3B).<sup>28</sup> In China, *Ae. albopictus* mosquitoes are most prevalent in the south, southeast, and central regions (Fig. 2A). Consistently, HIV prevalence in these regions is generally high (Fig. 2C).<sup>29</sup> The question of why HIV prevalence is also high in the westernmost part where the abundance of mosquitoes is low will be discussed in the following section. Mosquitoes are less abundant on the North Island in Japan compared to other territories (Fig. 2A). This trend is generally in line with the data on HIV infections (Fig. 3D).<sup>30</sup>

However, in India, the distribution of HIV (Fig. 2E)<sup>31</sup> does not seem to match well with the distribution of mosquitoes (Fig. 2A). The highest abundance of mosquitoes is located in a region in northern Pakistan (Fig. 2A). Although two outbreaks reportedly occurred in this site, one occurred in the mid-south side.<sup>32</sup>

In the United States, the prevalence of *Ae. albopictus* mosquitoes is highest in the Southeast (Fig. 2A). Consistently, the rate of HIV infection is highest in the Southeast (Fig. 3F).<sup>33</sup> In Mexico, *Ae. albopictus* mosquitoes are prevalent along the coasts. HIV-infected patients are usually from the coastal regions (Fig. 3G).<sup>34</sup>



**Figure 3** A) People living with HIV diagnosed, 2012, Italy. Source.<sup>25</sup> B) HIV prevalence, Australia. Source.<sup>28</sup> C) People living with HIV/AIDS, 2014, China. Source.<sup>29</sup> D) HIV carrier rate (per 100,000), 1985-2015, Japan. Source.<sup>30</sup> E) HIV sentinel surveillance in pregnant women, 2001–2003, India. Source.<sup>31</sup> F) Rates of diagnoses of HIV infection among adults and adolescents, 2011, United States. Source.<sup>33</sup> G) Geographical distribution of HIV infected Mexican Mestizo individuals, Mexico. Source.<sup>34</sup> H) People living with AIDS, Brazil, 2005–2020. Source.<sup>35</sup> I) Average annual HIV incidence, 2014–2017, Bolivia. Source.<sup>36</sup> J) Spatial projection of infection rate (cluster 3), Peru. Source.<sup>37</sup> K) Spatial projection of infection rate (cluster 4), Peru. Source.<sup>37</sup> L) New Cases of HIV infection, Argentina, 2010–2018. Source.<sup>38</sup>

In Brazil, *Ae. albopictus* mosquitoes are most prevalent in the southeast regions (Fig. 2A), where HIV prevalence is also highest (Fig. 3H).<sup>35</sup> Bolivia has high rates of mosquitoes in its east region (Fig. 2A), where HIV infections are higher (Fig. 3I).<sup>36</sup> In Peru, the abundance of mosquitoes is higher in the east and central regions than on the west coast (Fig. 2A). Consistently, HIV infections in clusters are higher in these regions (Fig. 3J),<sup>37</sup> but much lower on the west coast (Fig. 3K).<sup>37</sup> There are substantial mosquitoes in the northern and central parts of Argentina (Fig. 2A) where HIV prevalence is also higher (Fig. 3L).<sup>38</sup>

### 3.3 High risk populations

According to the guidelines,<sup>39,40</sup> the following populations are at high risk of infection: 1) homeless individuals; 2) fishermen; 3) truck drivers; 4) prisoners; 5) sex workers; 6) clients of sex workers; 7) individuals having sex with many partners; 8) men who have sex with men (MSM). —and their sexual partners; 9) people who inject drugs; and 10) transgender people.

Homeless people are often exposed to mosquitoes. Fishermen are also frequently exposed to mosquitoes because they live in high humidity environments where mosquitoes thrive. Some truck drivers often work through the night; some times they sleep in simple conditions, exposing them to mosquitoes.

Mosquitoes are active at night. Sleeping in the same room or in a crowded space close to each other allows mosquitoes to easily bite two people within a short interval (e.g. minutes). The fresh blood left on a mosquito's mouthparts from one person will immediately be transferred to the bloodstream of another person during subsequent bites. Some prisoners sleep in crowded spaces. Sexual partners often sleep in the same room.

Based on the characteristics of mosquito biting, it can be explained why MSM and their partners have a high rate of HIV infections: 1) Men are more likely than women to attract mosquitoes.<sup>41</sup> Therefore, two men staying together are more likely to attract mosquitoes than a man and a woman together, followed by two women together. 2) For two persons in a room, mosquitoes usually bite the more attractive one. If their bite is interrupted, they either come back to bite or fly away, but are less likely to bite the other person. However, if two persons have similar attractiveness to mosquitoes, mosquitoes are likely to bite either one after an interrupted bite, potentially leading to disease transmission. Two men are more likely to have similar attractiveness to mosquitoes than a man and a woman. Consistently, as reported in various mosquito-borne diseases, men usually have much higher rates of infection than women.<sup>42</sup>

High rates of HIV infections among injecting drug users involve a different story – sharing needles. The situation for transgender people is complex (e.g. having high rates of drug consumption).

### 3.4 Rapid progress after 2000

Fig. 4A shows that new HIV infections among children in SSA decreased rapidly from 2002 to 2007, while there was only a slight increase in the number of pregnant women receiving ART for the prevention of mother-to-child transmission.<sup>43</sup> Therefore, ART alone is not sufficient to explain the rapid decrease in new HIV infections among children before 2007.

Similarly, before 2006, although new HIV infections among adults decreased rapidly in Eastern/Southern Africa (Fig. 4B) and Western/Central Africa (Fig. 4C),<sup>44</sup> there was only a slight increase in coverage of ART (Fig. 4D & 4E).<sup>44</sup>

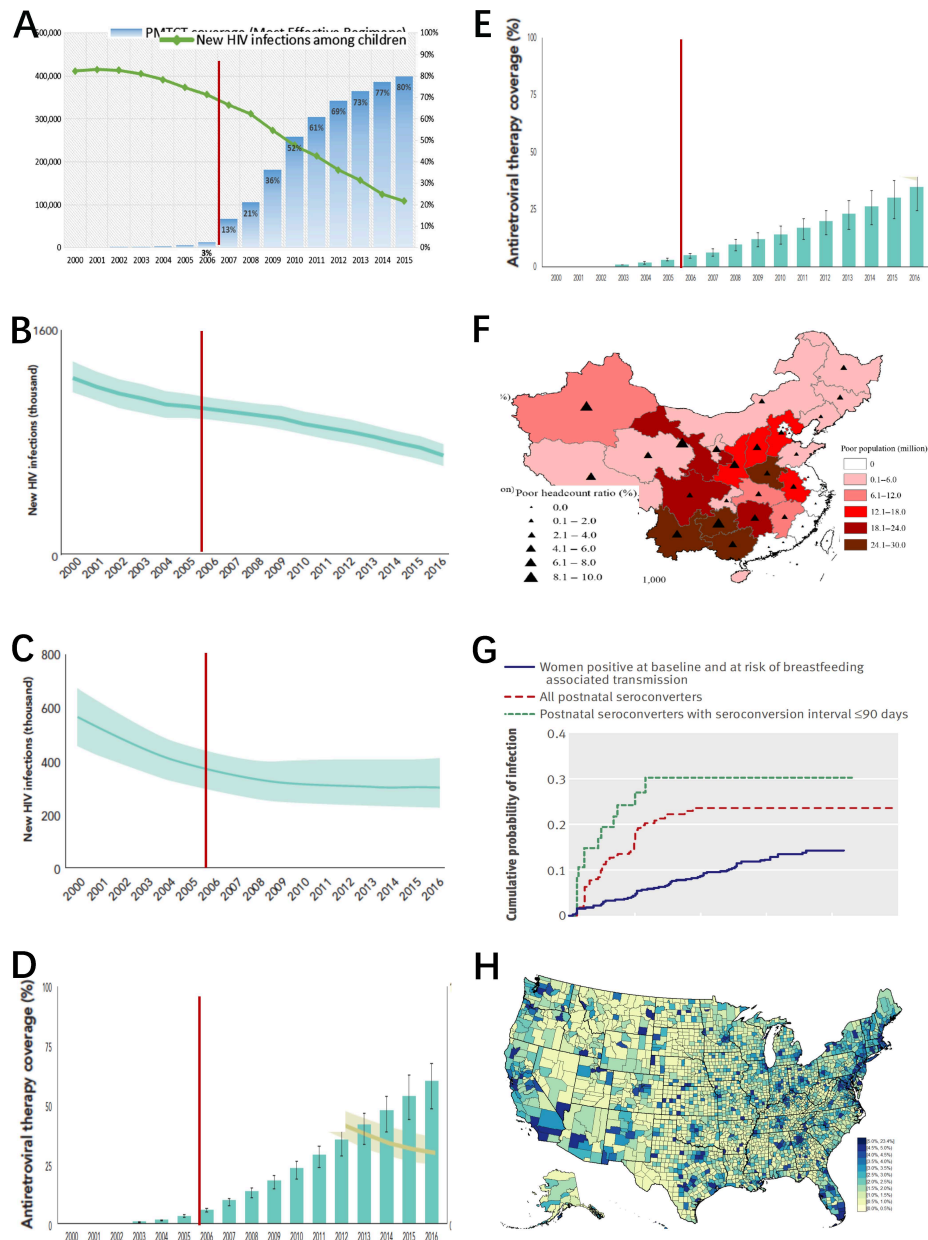
According to the UNAIDS Data 2017, there was a rapid decrease in new HIV infections in all malaria-endemic regions (eastern/southern Africa, western/central Africa, Asia/the Pacific, and the Caribbean) from 2000 to 2016, with a greater decline in children (aged 0–14) than in adults (aged 15+).<sup>44</sup> Latin America, a region with a low level of endemic malaria,<sup>45</sup> exhibited a rapid decline in new HIV infections among children, but not among adults.<sup>44</sup>

In contrast, a rapid decrease in new HIV infections did not occur in non-endemic malaria regions.<sup>44</sup> New HIV infections among children slightly increased during 2000–2016 in the Middle East and North Africa.<sup>44</sup> There was no data on children in Europe and North America in the UNAIDS 2017 report. Among adults, new HIV infections during 2000–2016 increased substantially in Eastern Europe/Central Asia, did not change in the Middle East/North Africa, and declined slightly in Western/Central Europe and North America.<sup>44</sup>

The theory of mosquito transmission can help explain the above data. Unprecedented efforts were made to prevent malaria in globally endemic regions after 2000, starting first in Africa in 1998.<sup>46</sup> For example, more than half of the population in SSA slept under insecticide-treated mosquito nets in 2015, compared to only 2% in 2000.<sup>47</sup> Children were prioritized in the distribution of mosquito nets because they accounted for 90% of the total deaths caused by malaria.<sup>46</sup> This helps explain why a rapid decline in new HIV infections occurred in malaria endemic regions but not in non-malaria endemic regions, and why the progress is so striking among children in malaria endemic regions.

If HIV is transmitted by mosquitoes, poverty would be an important factor. Poverty often leads to families living in a small house. Therefore, many family members have to share a sleeping room, increasing the risk of disease transmission by mosquitoes. Fig. 4F displays the distribution of poor populations in China.<sup>48</sup> When considering both this poverty data and mosquito distribution (Fig. 2A), it becomes clear why HIV is distributed in China as depicted in Fig. 3C. The first HIV case was reported in China in 1985. The southeast coasts became the richest region in China after 1980 (Fig. 4F). Therefore, HIV infections in these coasts are high but not the highest.





**Figure 4** A) Trends in percentage of pregnant women living with HIV receiving ART for the prevent of mother-to-child transmission and new HIV infections among children aged 0–14 in 21 sub-Saharan African Global Plan countries, 2000–2015. Source.<sup>43</sup> B) New HIV infections, Adults ( $\geq 15$ ), Eastern/Southern Africa, 2000–2016. Source.<sup>44</sup> C) New HIV infections, Adults ( $\geq 15$ ), Western/Central Africa, 2000–2016. Source.<sup>44</sup> D) ART coverage, Eastern/Southern Africa, 2000–2016. Source.<sup>44</sup> E) ART coverage, Western/Central Africa, 2000–2016. Source.<sup>44</sup> F) The poverty headcount ratio and rural poor population, 2017, China. Source.<sup>48</sup> G) Cumulative probability of mother-to-child transmission for mothers infected at different time. Source.<sup>55</sup> H) Estimated percentage of MSM, 2009–2013, United States. Source.<sup>57</sup>

### 3.5 Highest infections among children before the use of ART

Now, let's turn to Fig. 1: why did the highest infections occur among children in Africa, Asia, and parts of Southern Europe/Latin America?

In Asia, Africa, and parts of Southern Europe/Latin America, it is common for infants and children to share a bed with their parents,<sup>49,50</sup> while this practice is much less common in Western populations.<sup>49,50</sup> Mosquitoes are active at night. If mosquitoes transmit HIV, this difference in sleeping culture will cause a high difference in HIV infections among children. This helps explain why HIV infection rates are high or highest among children in Africa and Asia but low among children in developed Western countries.

Similar observations occur for other mosquito-borne diseases. US national survey of some mosquito borne diseases shows that, infection rates among children were low.<sup>42</sup> For example, among 1,132 people infected with West Nile, children aged 1 to 17 years accounted for only 2%.<sup>42</sup> In contrast, in Nigeria and India, infection rates among children aged 1 to 17 were 22.9% and 33%, respectively.<sup>51,52</sup>

If mosquitoes bite young children, feeding is less likely to be interrupted due to children's deep sleep. In contrast, mosquito feeding on adults is more easily interrupted. After being interrupted, the mosquito will then search for the next person to feed on, leading to potential disease transmission. Therefore, when family members are sleeping in a room, mosquito-borne diseases are easier to spread from adults to children, rather than among adults or from children to adults.

In the United States, HIV infections are more than 10 times higher among Black infants than white infants, despite there being little difference in mothers receiving ART before pregnancy to prevent perinatal transmission.<sup>53</sup> Consistently, a US survey shows that bed-sharing with mothers among black infants is several times higher than among white infants.<sup>54</sup> Moreover, black people have a several times higher rate of homelessness - another high risk factor related to mosquitoes.

HIV infection rates among infants born to mothers who seroconverted postnatally are several times higher than among infants born to mothers who seroconverted at the time of birth (Fig. 4G).<sup>55</sup> These data suggest that whether mothers know their positive status is an important factor. To protect their children, mothers who are aware of their positive status at birth will have less close contact with their infants (e.g. sleeping, or others). In contrast, mothers who seroconverted postnatally may not change their behaviors until their seroconversion.

In a study involving 31,239 individuals in a poor region in Pakistan, HIV prevalence was found to be 6%–7% among tested children aged 0–5, 2% among children aged 6–15, 1% among adults aged 16–49, and 1% among older people ( $\geq 50$ ).<sup>56</sup> Researchers suggested that infections mainly occurred due to contaminated needles and blood products in hospitals, as well as mother-to-child transmission.<sup>56</sup> However, why was the positivity rate only 1% among older people ( $> 50$ ) who often visit hospitals? Why were 90% of the tested mothers negative?<sup>56</sup> In impoverished regions, children also often share sleeping rooms with other family members. Researchers should test HIV among fathers, grand parents, and other family members.

### 3.6 How does the sexual transmission theory explain?

Obviously, the sexual transmission theory cannot explain the highest infections among children in Africa, Asia and other regions before the widespread use of ART, the much higher infections in regions with mosquitoes worldwide, and the rapid decline in new HIV infections in malaria endemic regions but not in non-endemic regions after 2000.

Let's examine high risk populations. Prisoners are less likely to engage in sexual activity and drug use due to their controlled living conditions. Unlike business people, some factory workers, and those who have opportunities to meet new people during their work, fishermen and truck drivers have limited opportunities to socialize due to the nature of their jobs. Therefore, the high rates of infections among these three populations are difficult to explain by the theory of sexual transmission.

Homeless people live a hard life and have a low social status, making it difficult for them to attract sexual partners. However, some argue that these individuals are less likely to use condoms.

One may argue that the sexual transmission theory can explain the high HIV infections among sexual partners (Populations 5, 6, 7, and 8). This is not true. Let's discuss data from a specific country. Sexual behavior is similar nationwide in the United States, and the distribution of MSM, who account for 67% of new cases of HIV infections, is also similar nationwide (Fig. 4H).<sup>57</sup> However, why is the rate of HIV prevalence several to 10 times higher in the Southeast than in other regions? Contradictory.

Guidelines state that testing HIV status and using condoms are important for preventing HIV transmission. The rates of condom use and HIV status testing among Black women are substantially higher than those among White people in the United States.<sup>58,59</sup> Why is the rate of HIV infection among Blacks 8 times higher than that among Whites?<sup>58</sup> Contradictory.

Logic is always a rule for determining the truth, regardless of whether it is in court, everyday life, or scientific research. Contradictions in the last several paragraphs can be consistently explained by the theory of mosquito transmission. The highest abundance of mosquitoes in the US Southeast helps explain the highest HIV infections in this region. MSM are



at a high risk of HIV transmission by mosquitoes, and the risk is higher in regions with a higher abundance of mosquitoes (e.g. the US Southeast). Rates of homelessness and bed sharing among Blacks are much higher than among whites,<sup>54,60</sup> explaining why Blacks have much higher rates of HIV infections.

### 3.7 The theory of mosquito transmission

As stated in a review paper,<sup>62</sup> the three most frequent explanations for why mosquitoes do not transmit HIV include: 1) HIV concentrations in the blood are too low to permit vector transmission; 2) HIV is unable to survive long enough outside of humans for vector transmission; 3) HIV is not able to replicate within vectors.

However, some patients have high viral concentrations ( $\geq 10^7$  copies/ml).<sup>63</sup> Importantly, when a mosquito feeding is interrupted, it can move to bite others in the room to continue feeding within minutes. Therefore, the blood on the mosquito's mouthparts is transferred almost immediately into others' bloodstream. This immediate mechanical transmission does not require a long survival of the virus outside of the human. No literature has addressed this issue.

The currently recognized mosquito borne pathogens (e.g. ZIKA) are usually those that can survive in mosquitoes for a long period. These pathogens can enter the salivary glands and are transmitted through saliva between people (known as biological transmission). However, HIV cannot enter mosquito salivary glands. Animal studies should examine mechanical transmission of HIV and mimic a scenario: mosquitoes bite two people within minutes.

### 3.8 The theory of sexual transmission

There is a wealth of data reporting high rates of HIV infections among sexual partners, sex workers, etc. This kind of data supports different transmission theories (sexual contact, vectors, fomites, air, etc.). For example, COVID-19 also spreads easily among sexual partners.

The effectiveness of condoms in preventing HIV transmission closely relates to the question of whether HIV is transmitted through sex. However, the effectiveness of condoms in HIV prevention has been a controversial topic.<sup>64-66</sup> Some researchers have reported that condoms are effective, while others have proposed different opinions.<sup>64</sup>

The results showing a lower prevalence of HIV infections among people who consistently use condoms were obtained from retrospective studies. If these results had come from prospective randomized studies, they would provide convincing data supporting the sexual transmission of HIV. Due to ethical reasons, this kind of study is not allowed.

Our question regarding these retrospective studies is: why do some people consistently use condoms, while others do not? Clearly, the former population is more concerned about HIV transmission and more cautious in their behaviors. This difference means a lot. For example, they may reduce their sexual activity or avoid having sex with individuals whose HIV status is unknown, ultimately leading to a decrease in exposure to various risk factors (e.g. sleeping with others).

In the 1990s, the biggest global effort to fight against HIV was the strategy of using condoms. However, the rate of HIV infection remained stable or increased in the 1990s.

Uganda achieved a historic success in reducing HIV infections in the 1990s.<sup>65,66</sup> The Ugandan government did not believe that condoms can prevent HIV transmission. In fact, they restricted the importation of condoms.<sup>66</sup>

In South Africa, 20% of the black population is infected with HIV, while only 0.2% to 0.5% of the white population is infected.<sup>67</sup> The black population often experiences the loss of family members and relatives to HIV. Everyone fears death. They hate sex and drugs. They are extremely cautious with sexual activities and drug use. It is hard to imagine that they acquired HIV due to their risky sexual activities and drug use. The theory of mosquito transmission can easily explain these data. Only 4% of white families live in a house with 1 to 2 rooms, compared to 31% for black families.<sup>68</sup> This means that many black family members sleep in a single room, making it easy for mosquitoes to transmit diseases.

In the United States, the prevalence of HIV infection is several to 10 times higher in the Southeast than in other regions (Fig. 3F). No data has shown that the rates of condom use are significantly lower in the Southeast. Black women have higher rates of condom use than white women, but their HIV infection rates are much higher than those of white women.<sup>58</sup>

We believe that condoms are effective in preventing the spread of pathogens through sex. However, they have a limited effect on HIV prevention because HIV is mainly transmitted through routes other than sex.

#### 4 Discussion

The theory of sexual transmission of HIV was developed several decades ago in a Western developed country setting. If developed in developing countries, it would be very different. For example, in South Africa, sexual behaviors are similar between the east and west, so why are the rates of HIV infections in the east 50 times higher than in the west (Fig. 2C)? Sexual behaviors are similar between blacks and whites, so why are infection rates among blacks 50 times higher than among whites?<sup>67</sup> Moreover, why are infection rates highest among children before the widespread use of ART? Researchers in South Africa may consider any potential transmission modes rather than sex.

For researchers in developed countries who adhere to the theory of sexual transmission due to the high rates of HIV infection in Western developed countries occurring among individuals entering adulthood, MSM, sex workers, and men who have multiple sexual partners, I would suggest that they examine data on West Nile, Zika, and other mosquito-borne diseases in Western developed countries.

One may argue that there is no animal research data showing mosquitoes can transmit HIV. However, is there animal research data showing HIV can spread through sex? No. There are various reasons why animal research may not yield positive results. For example, animals have a much lower susceptibility to HIV compared to humans.

Close proximity (e.g. sleeping together) is a critical factor for the transmission of pathogens, regardless of whether they are spread through the air, vectors, fomites, etc. Since there is no data pin pointing transmission occurring through this route but not another route, a systematic analysis of all types of data must be applied.

A valid theory should be able to consistently explain the phenomena in the given field. Since a wide range of data can be consistently explained by the theory of mosquito transmission but not sexual transmission and there is also no animal research data supporting sexual transmission, how can we be sure that HIV is transmitted through sex and not mosquitoes? The present systematic analysis of global data has alarmed us: a mistake may have occurred in our fight against HIV, and calls for urgent research into this issue.

To explore this issue, we suggest two simple epidemiological studies for global researchers: 1) comparing HIV transmission rates among children who sleep in the same room as their parents or others, versus those who sleep alone in a room; 2) comparing transmission rates between people who consistently use mosquito nets and those who do not.

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#### Compliance with ethical standards

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The author declare no conflict interests.

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