Is the Elimination of HIV Infection Within Reach in the United States? Lessons from an Epidemiologic Transmission Model

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SYNOPSIS

Recent estimates show that the transmission rate of human immunodeficiency virus (HIV) in the U.S. has substantially decreased. This raises the question, is elimination of HIV infection in the nation feasible in the foreseeable future? We demonstrate that if the HIV transmission rate were reduced by 50%, then the reproductive rate of HIV infection would drop below unity and lead to eventual elimination of infection. In recent congressional testimony, the director of the Centers for Disease Control and Prevention and others asserted that the HIV transmission rate can be halved by 2020, if not earlier, provided sufficient investment is made toward achieving this goal. We assert that if adequate investment is made and the transmission rate is in fact lowered by 50%, then the HIV reproductive rate would fall below unity, setting the stage for eventual elimination of HIV infection in the U.S.

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On September 16, 2008, both the director of the U.S. Centers for Disease Control and Prevention (CDC) and this author testified under oath before the House of Representative's Committee on Oversight and Government Reform that the transmission rate of human immunodeficiency virus (HIV) in the U.S. could be reduced by 50% in the foreseeable future. The transmission rate [T(x)] is defined as the number of HIV transmissions to HIV-seronegative partners of 100 people living with HIV in a given year x, and is calculated as 100 times the HIV incidence in year x divided by prevalence in that year.[1–4] The two sets of testimony differed slightly in terms of the financial and temporal resources needed to achieve the reduction of 50% in T(x), but both agreed that halving the transmission rate was possible at least by 2020.[1–3]

CDC's testimony listed a wide variety of HIV-prevention interventions, research and evaluation projects, and surveillance activities needed to achieve a reduction of one-half in the transmission rate. CDC's assertion that this level of reduction could occur was based on expert judgment, but was not based on a quantitative model linking investment levels to service delivery to anticipated outcomes.[2,3] This author's own testimony asserted that a reduction of 50% in the transmission rate could occur in five years. This estimate was based on a mathematical model that estimated reductions in transmission rates and incidence, given specified investment levels and intervention effect sizes published in the scientific literature for a variety of HIV-prevention interventions.[1] This modeling exercise emphasized the need for an HIV information and awareness campaign coupled with very substantial HIV counseling and testing expansion as soon as possible. These earliest efforts would be followed by major expansions of evidence-based HIV-prevention interventions for people living with HIV, and science-based prevention programs for people who are seronegative but at heightened risk of infection.[1]

POLICY QUESTION: IS ELIMINATION OF HIV INFECTION FEASIBLE?

The HIV transmission rate in the U.S. in 2006 was a little less than 5.0 (meaning there were approximately five HIV transmissions that year for every 100 individuals living with HIV, and at least 95% of people living with HIV in that year did not transmit HIV to a seronegative partner).[4] If indeed the transmission rate were reduced to 2.5 in the coming years (with appropriate investment),[1–3] then the next question is, could such a 50% reduction in the transmission rate lead to the elimination of HIV infection in the U.S.? A well-recognized definition of "elimination of infection" is as follows: "reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts; continued measures to prevent reestablishment of transmission are required."[5]

TRANSMISSION RATE, REPRODUCTIVE RATE, AND INFECTION ELIMINATION

Of course, if the transmission rate could be reduced to zero, then this definition of elimination of infection obviously would be met in the short term. However, a non-zero transmission rate in the present could eventually lead to elimination of infection if the reproductive rate were to drop below one. May and Anderson have defined the basic HIV reproductive rate (R_0) as follows: the number of HIV transmissions from one person living with HIV to HIV-seronegative partners over the HIV-seropositive person's lifetime. The reproductive rate is the product of three main factors: the number of HIV-seronegative partners that someone living with HIV has in a given time period, the probability of passing the virus to a given partner in that time period, and the duration (number of time periods) of infectiousness. May and Anderson rightly note that if the reproductive rate eventually drops below one—meaning there is less than one infection per every person living with HIV over the course of that person's lifetime—then eventually (perhaps over a very long time period) the epidemic will cease, as new infections become more and more rare.[6,7]

As defined previously, the transmission rate, T(x), functions as an annualized reproductive rate. In other words, T(x) captures the numbers of partnerships and probability of transmission within a given partnership in the incidence numerator. However, because T(x) is focused on a given year x, it does not incorporate consideration of duration of infectiousness (D). The relationship between T(x) and R_0 may be expressed as follows:

$$R_0 = (T(x)/100) * D$$

T(x)/100 is the expected number of HIV transmissions from each individual living with HIV in year x. The statistical expectation is that if this level of transmission would continue for D years, there would be (T(x)/100) * D transmissions; and this is the very definition of R_0. For instance, if T(x) is 5.0, and the average survival with HIV post-infection was, for example, 15 years, then R_0 would be 0.75; if the average survival, D, were 30 years, R_0 would be 1.5. Of course, there is the complicating factor that the duration of infectiousness may be less

than life expectancy, depending on the course of the disease and treatment. In this model, we assume that any variation in transmissibility due to natural history of disease or treatment is captured in T(x), and D is the number of time periods at the T(x) level of transmissibility.

REPRODUCTIVE RATE ESTIMATION FOR THE U.S.

Because we have available estimates of T(x) in the U.S.,[4] we only need to identify a plausible estimate of D to calculate R_0 for the U.S. and determine if it is more or less than unity (again, if R_0 is less than one, eventually the epidemic will contract toward elimination). CDC has provided estimates of the number of new HIV infections that occur among broad age groups in the U.S.[8] If we accept these estimates, assume that very few infections occur beyond 85 years of age, and take the midpoint of CDC's age ranges, we can calculate a mean age of infection in the U.S. of about 34.2 years. A major study of survival of people with HIV and on treatment in high-income countries estimated that at age 35, life expectancy is approximately 37.3 years.[9] A study of two HIV-seropositive cohorts in British Columbia estimated that for injection drug users living with HIV and not on treatment, life expectancy is about 19.1 years.[10]

CDC has estimated that approximately 21% of people living with HIV are unaware of their serostatus.[11] It has also been estimated that among people living with HIV who are aware of their serostatus, roughly a third are not on treatment.[12] This implies an effective percentage (52.9%) of people living with HIV who are on treatment. We, therefore, estimate the life expectancy after infection in the U.S. to be roughly 28.73 years [(37.3 * 0.529) + (19.1 * 0.471)]. If everyone were on treatment, we would estimate the life expectancy to be simply 37.30 years.

In its 2001–2005 strategic HIV-prevention plan, CDC aimed to achieve a treatment level of 80%; in its interim plan through 2010, CDC has lowered its expectations to a target treatment level of 65%. These two target treatment levels would imply life expectancies of 33.66 and 30.93 years, respectively. As noted previously, we make the simplifying assumption that life expectancy with HIV is an estimate of D because we assume that any variation in transmissibility due to natural history of disease or treatment is captured in T(x), and D is the number of time periods at the T(x) level of transmissibility.

The Table displays calculated values for R_0 at a variety of T(x) levels and four levels of life expectancy: 28.73, 30.93, 33.66, and 37.30 years. The Table also includes several other levels of life expectancy so one can readily see how R_0 changes from a low life expectancy of 15.00 years up to 40.00 years. Indeed, if T(x) could be driven down to 2.5 (as may be feasible with the proper investment according to the September 2008 congressional hearing testimony), then R_0 would drop below one and eventually the epidemic would move toward elimination of infection.

The Table also displays the threshold values for T(x) at which R_0 equals unity at any of the scenarios for D.

Table. Calculated HIV reproductive rate at various transmission rates and levels of years of post-infection life expectancy, United States

	D							
T(x)	*15.00*	*20.00*	*25.00*	*28.73*	*30.93*	*33.66*	*37.30*	*40.00*
5.0	0.75	1.00	1.25	1.44	1.55	1.68	1.87	2.00
4.5	0.68	0.90	1.13	1.29	1.39	1.51	1.68	1.80
4.0	0.60	0.80	1.00	1.15	1.24	1.35	1.49	1.60
3.5	0.53	0.70	0.88	1.01	1.08	1.18	1.31	1.40
3.0	0.45	0.60	0.75	0.86	0.93	1.01	1.12	1.20
2.5	0.38	0.50	0.63	0.72	0.77	0.84	0.93	1.00
2.0	0.30	0.40	0.50	0.57	0.62	0.67	0.75	0.80
1.5	0.23	0.30	0.38	0.43	0.46	0.50	0.56	0.60
1.0	0.15	0.20	0.25	0.29	0.31	0.34	0.37	0.40
Threshold T(x) for R_0 = 1	6.67	5.00	4.00	3.48	3.23	2.97	2.68	2.50

HIV = human immunodeficiency virus

D = duration of infectiousness (levels of years of post-infection life expectancy)

T(x) = transmission rate

R_0 = reproductive rate

The thresholds for T(x) were calculated by using the Goal Seek function in Microsoft® Excel.[13] We see that the necessary level of T(x) to achieve an R_0 of unity is never more than 3.5 and never less than 2.6 under the four main scenario levels for D.

DISCUSSION

The primary point of this analysis is that if R_0 drops below unity, elimination of infection will eventually follow (though elimination might occur quite some distant years in the future). For the U.S., if the transmission rate can be reduced by 50% from 2006 levels, then R_0 would appear to fall below unity. Two independent estimates have suggested that achieving a reduction of one-half in the transmission rate is possible with currently available types of interventions by 2020, if not earlier, provided that the investment in HIV prevention in the U.S. is suitable.[1–3] Therefore, using this logic, elimination of HIV infection in the U.S. could well be in our future (even if a rather distant future), provided that we as a nation make the choice to invest the requisite resources recently described to Congress.

Limitations

Of course, these analyses were subject to some limitations, as are any mathematical modeling exercises. As an example, Granich et al. recently used a complex mathematical model to examine the potential impact of universal HIV testing with immediate antiretroviral therapy (ART) on an exclusively heterosexual epidemic in South Africa[14] (of course, the major mode of transmission in the U.S. epidemic is same-sex contact, and the transmission rate actually rose initially when highly active ART [HAART] became available in the U.S.[4]); eight editorials, as well as the authors' reply, were subsequently published pointing out limitations and controversies in the Granich et al. model.[15–23] Therefore, transparency regarding model limitations is important.

As to the analysis presented in this article, we note that the level of uncertainty in the calculation of T(x) is the same as that uncertainty inherent in CDC's recent extended back-calculation estimates of HIV incidence in the U.S.[8] Further, experience with the natural history of HIV disease in the era of HAART is still unfolding, and current life expectancy estimates (D) contain uncertainty and may well need to be revised in the future.[9,10]

Additionally, as more is known about how HIV treatment impacts transmissibility of the virus to seronegative partners,[24] it may be that our assumption that duration of transmissibility at the T(x) level is equal to life expectancy is somehow false, and D should be set at less than life expectancy. However, employing this assumption in this model is conservative because as D becomes progressively less than life expectancy, the amount of reduction in T(x) from current levels needed to achieve an R_0 of unity is accordingly lessened.

CONCLUSION

These analyses are not meant to imply that we as a nation should be patient and wait for a lengthy period of time for HIV infection to be eliminated in the U.S. Rather, these analyses are meant to suggest that if a seemingly feasible level of reduction in the HIV transmission rate can be achieved in the foreseeable future using existing prevention strategies, then in the long term, eventual elimination of HIV infection in the U.S. should follow. The speed at which this will occur is within the control of those who influence and make funding and programmatic decisions surrounding HIV and acquired immunodeficiency syndrome programs.

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