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TECHNICAL APPENDIX II: HIVECON

**U.S. Department of Health and Human Services
Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases**

Division of Global Migration and Quarantine

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Technical Appendix II: HIVEcon

Additional notes and data on model inputs and outputs

Description of the Model

Our model considers the potential health care costs from admitting HIV-infected immigrants into the U.S. It compares such costs to the baseline (i.e. Alternative 1 above) which is no admittance, except pursuant to a waiver, of HIV-infected persons as immigrants or the adjustment of such individuals to permanent resident status within the U.S. We built the model, titled HIVEcon, using standard software (Microsoft Excel, Microsoft Corp, Redmond, WA¹). Essentially, the model estimates the number of potential HIV-infected immigrants that may arrive in the U.S. or be adjusted to permanent resident status within the U.S. (under the new proposed rule). The model then calculates the lifespan of such HIV-infected immigrants, building a survival curve (i.e., probability of survival to a given age), assuming that they receive the appropriate treatment in the U.S. that will extend their lifespan. Using the estimated number of HIV-infected immigrants and adjusted permanent residents and the estimated lifespan, the model

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then estimates the costs of treating those HIV-infected immigrants and adjusted permanent residents in the United States over their lifespan. For the economic analysis we established a primary (or base) case using the best science available for parameter estimates. Because data were not available for most of the parameters in our analysis we established lower and upper bounds for those parameters for which variation had the greatest impact on the results.

The model, HIVEcon, examines the health care costs associated with newly identified persons infected with HIV regardless of payer. The calculations reflect the total health care costs for HIV-infected immigrants arriving in the U.S. and persons who become infected due to onward transmission for appropriate treatment which extends the lifespan. The calculations further assume that all HIV-infected immigrants arriving in the U.S. and persons who become infected due to onward transmission would receive the current standard of care for the treatment of HIV.

We assumed that there would be no changes in the current standard of care for HIV treatment over time. That is, the treatment of HIV infection will remain in its current form and will not advance beyond the current level

of treatment. Additionally, in analyzing the longevity of persons infected with HIV, the analysis assumes no improvement in the treatment of HIV infections over time. Thus, the possibility that the life span of infected individuals will increase with improved treatment is not considered.

We used 30 years as the average age of HIV-infected immigrants. Because no data exist on this parameter we conducted sensitivity analyses using 20 years and 40 years as the lower and upper bound. The average age for persons with HIV infection in the U.S. is approximately 40 years (based on calculations from the table AIDS cases by age *HIV/AIDS Surveillance Report: Cases of HIV Infection and AIDS in the United States and Dependent Areas, 2006*) [1]. The median age of the lawful permanent resident in the U.S. is between 40 and 44 years [2]. The median age of the general U.S. population is between 25 and 30 years [3].

Model Inputs

The model, HIVEcon, consists of the following components or inputs: 1) prevalence of HIV in regions from which immigrants to the U.S. originate; 2) projected number of immigrants, by region, entering the U.S. annually; 2b)

annual percentage change in number of immigrants arriving in the U.S. compared with the baseline; 3) estimated onward transmission rates of HIV infection from HIV-infected immigrants to the U.S. population; 4) estimated survival analysis for the HIV-infected persons living in the U.S.; 5) annual discount rate (3% and 7%); 6) estimated average age of HIV-infected immigrant upon arrival in the U.S.; and 7) the projected annual cost of treating an HIV-infected patient in the U.S.

Table 1a: Summary of Model, HIVEcon, Inputs and Assumptions for Primary, Lower and Upper Bound Analyses*, ‡

Inputs and Assumptions	Values			Source
	Lower Bound	Primary	Upper Bound	
HIV-infection survival over time§ Average life expectancy at:	Age 20 years - 28.6 years	Age 30 years - 24.7 years	Age 40 years - 19.9 years	Calculated from Figure 2 in Harrison et al. (2008) [4]
Number of immigrants entering U.S. annually		1,052,415		DHS (2007) [2, 5]
Annual percent change in number of immigrants arriving in the U.S. †		0%		Analysis assumes that the number of immigrants will remain constant for the period of analysis
Weighted rate of HIV-infected immigrants (potential) per 1,000 applicants	1.02/1000 immigrants	4.06 /1000 immigrants	6.09/1000 immigrants	Calculated from [2, 6, 7](Assuming immigrant population HIV prevalence is equivalent to HIV prevalence of general population of region of origin)
Average age of HIV-infected immigrant upon entry into U.S.	20 years	30 years	40 years	Estimated from [1, 2]
Annual Transmission rate per 100 HIV-infected persons	0 cases induced annually per 100 HIV-	1.51 cases induced annually per 100 HIV-	4.53 cases induced annually per 100 HIV-	Pinkerton (2007)[8] (assuming rate per HIV-infected immigrants is half of

	infected immigrants	infected immigrants	infected immigrants	that of U.S. HIV- infected population for the primary case) Schackman et al. (2006) [9]
Annual cost of HIV therapy per HIV-infected person in the U.S. (2004\$)	\$19,466	\$25,200	\$30,954	
Annual discount rate	3%, 7%			

Notes:

* See the appropriate section of the main text for additional details and data sources.

†The model, HIVEcon, is available as a Technical Appendix [10], and a reader can determine the relative impact of altering almost any input value, individually or several simultaneously.

§ The model contains a complete survival-over-time curve. The numbers given in this table are samples of the life expectancy derived from the survival curve. See the appropriate section in the main text for the complete survival curve.

†HIVEcon allows, as with almost all inputs, the user to change this baseline estimate

Data sources; See the appropriate sections in the main text for data sources.

Table 1b. Regional population, immigration and HIV estimates used to calculate the weighted regional rate estimates.

Region of nationality	2007 HIV Estimates [6]**			2006 Population estimates [7]	HIV Rate per 1,000 population estimates			Legal Permanent Residents, 2007 [5]	Estimated number of HIV infected immigrants		
	Primary	Low	High		Primary	Low	High		Primary	Low	High
Africa*	22,880,000	21,170,000	24,800,00	1,267,495,00	18.05	16.70	19.57	96,105	1,735	1,605	1,880
Asia	4,800,000	3,920,000	6,060,000	3,727,145,00	1.29	1.05	1.63	383,508	494	403	624
Europe	2,360,000	1,800,000	3,200,000	731,284,000	3.23	2.46	4.38	120,821	390	297	529
N. America	1,300,000	480,000	1,900,000	338,831,000	3.84	1.42	5.61	339,355	1,302	481	1,903
Oceania	75,000	53,000	120,000	34,240,000	2.19	1.55	3.50	6,101	13	9	21
S. America	1,830,000	1,610,000	2,170,000	572,190,000	3.20	2.81	3.79	106,525	341	300	404
Global estimates	33,245,000	29,033,000	38,250,000	6,671,185,000							
					HIV Rate per 1,000 immigrants entering the U.S. based on regional weight estimates***			Regionally weighted number of Legal Permanent Residents	Total number of HIV infected immigrants		
U.S. Immigrant estimates					4.06	2.94	5.09	1,052,415	4,275	3,096	5,361

* In this case, Africa includes North Africa, the Middle East and Unknowns

** Total number of adults and children living with HIV in the region

*** Based on weighted regional estimates. The assumption is that prevalence of HIV amongst immigrants to the US mirrors that of the immigrant's native regions and is adjusted for the number of immigrants coming to the US from each region.

Number of HIV-infected cases

i) Data Input: Estimated prevalence of HIV in regions from which immigrants to the U.S. originate: In HIVEcon we assume that HIV prevalence among immigration applicants is the same as that of the populations in the regions in the world where the immigrants come from. HHS/CDC calculated HIV rates for each of the regions of the world using the World Population Estimates of the United Nations Population Division [7] and the UNAIDS 2007 AIDS Epidemic Update [6].

ii) Data Input: Number of immigrants, by origin, arriving annually in the U.S. HIVEcon uses data regarding immigrants into the U.S. from the 2007 Demographic and Health Surveillance Yearbook of Immigration Statistics [5]. HIVEcon divided immigrants into the U.S. as having come from one of six regions: Africa, Asia, Europe (East and West), North America, Oceania, and South America (including Central America and Caribbean).

iii) Calculation: Number of HIV-infected immigrants arriving annually in the U.S.

Equation 1: For a given region: Number of estimated HIV-infected immigrants arriving in the U.S = (number of adults

and children living with HIV / population of region) x
number of all immigrants from region.

Equation 2: Total Number of HIV-infected immigrants
arriving in the U.S. = Sum of numbers of estimated HIV-
infected immigrants from all 6 regions.

iib) Calculating upper and lower bounds for the number of
estimated HIV-infected immigrants from each region were
derived by taking the 5th and 95th percentiles (high and
low estimates) of the number of estimated HIV-infected
persons in each region but weighted by the number of lawful
permanent residents who entered the US in 2007. The
general equation, for each region, is as follows:

Equation 3: For a given region: Lower bound of number of
HIV-infected immigrants arriving in the U.S = (low estimate
of number of adults and children living with HIV /
population of region) x number of all immigrants from that
region in 2007.

Equation 4: Total, low estimate of number of HIV-infected
immigrants arriving in the U.S. = Sum of low estimates of
numbers of HIV-infected immigrants from all 6 regions.

We used a similar set of equations to calculate an upper bound of HIV-infected immigrants who will arrive in the U.S. under the new regulation.

iic) Data input: Annual change in the projected number of immigrants: An assumption was made, for the purposes of this model, that the number of immigrants to the US will remain constant for the period of analysis (50 years). Readers can change this assumption in HIVEcon (see Technical Appendix I [10]).

iii) Data input: Estimated onward transmission rate from HIV-infected immigrants to U.S. population. This calculation within HIVEcon estimates for the number of new infections among the existing U.S. population that might occur as a result of the arrival of HIV-infected immigrants. HIVEcon uses the following general equation to calculate estimated the number of new HIV cases caused by onward transmission from HIV-infected immigrants:

For a cohort of HIV-infected immigrants that arrive in the U.S. in Year Y:

Equation 5: Number of estimated HIV-infected cases due to onward transmission (in Year t) = (Number of HIV-infected immigrants + U.S. persons previously infected by onward transmission from HIV-infected immigrants that survive to Year t) x onward transmission rate.

Note that, for the purposes of calculating new HIV infections associated with HIV-infected immigrants in the U.S., HIVEcon adds persons infected by HIV-infected immigrants to the cohort of projected HIV-infected immigrants. This modeling technique represents the chain of onward transmission after initial transmission from an HIV-infected immigrant.

HIVEcon's value for the primary analysis for the rate of onward transmission is 1.51% to represent the annual estimated number of new infections caused by HIV-infected immigrants to the U.S., or caused by U.S. person infected by HIV-infected immigrants (i.e., annually every 100 HIV-infected persons infect an additional 1.51 persons). The most recent estimate of average onward transmission in the United States is 3.02 % [8]. However, multiple studies of HIV infection among immigrant populations indicate that these groups have less risky social behaviors and more

restricted and closed social networks than those in the general U.S. population. Thus, onward transmission rates are likely to be lower. For this analysis, we assumed that the onward transmission rate for immigrants would be fifty percent of the average U.S. rate (1.51%). Because data supporting this assumption are limited, this assumption was tested in sensitivity analysis. We used no transmission as our lower bound estimate and a transmission rate of 4.53 per 100 HIV-infected immigrants as our upper bound estimate. The upper bound transmission rate is a fifty percent increase in the average annual onward transmission rate of 3.02%. HIVEcon allows the user to change the assumed rate of onward transmission (See Technical Appendix I [10]). The results of further sensitivity analysis on the onward transmission rate are also provided in the Table 3. We are seeking comment on this assumption.

It should also be noted that, in HIVEcon, the estimate of the average annual transmission percent remains constant over the lifespan of an HIV-infected person. In fact, there is evidence that indicates that HIV prevalence, and thus possibly incidence, varies by age and population [6]. In effect, using a constant risk of onward transmission

implies that the risk of transmission used represents an age-weighted average risk based on the U.S. experience.

iv) Data input: Survival analysis for HIV-infected persons
Survival curves used in HIVEcon for both the general US population and those for HIV infected patients are presented in Technical Appendix II Figure II.1b.

Equation 6: Estimated number of HIV-infected person surviving in Year t = (Number from cohort in Year $t-1$) x probability of surviving from year $t-1$ to year t .

We calculated survival probabilities in 5 year increments (e.g., at age 5 years, at age 10 years, etc.). Thus, when calculating the probability of surviving from one year to the next, for those years between each 5 year estimate (e.g., year 6, year 11), we assumed that the annual survival probability remained constant until the next 5 year period (e.g., for age 10 years through 14 years, we used the same probability of surviving from year t to year $t+1$).

Note that, as described in the section on onward transmission rate (section iii, earlier), those in the U.S.

infected by HIV-infected immigrants are added, each year, to the HIV-infected cohort. We essentially assumed those so infected by onward transmission (directly from HIV-infected immigrants or from those US person previously infected by HIV-infected immigrants) are of a similar age as the HIV-infected immigrants, and thus join the survival curve at the same point as the HIV-infected immigrants.

iv) Data input: Sensitivity analysis: Impact on cumulative total of HIV cases in year 20.

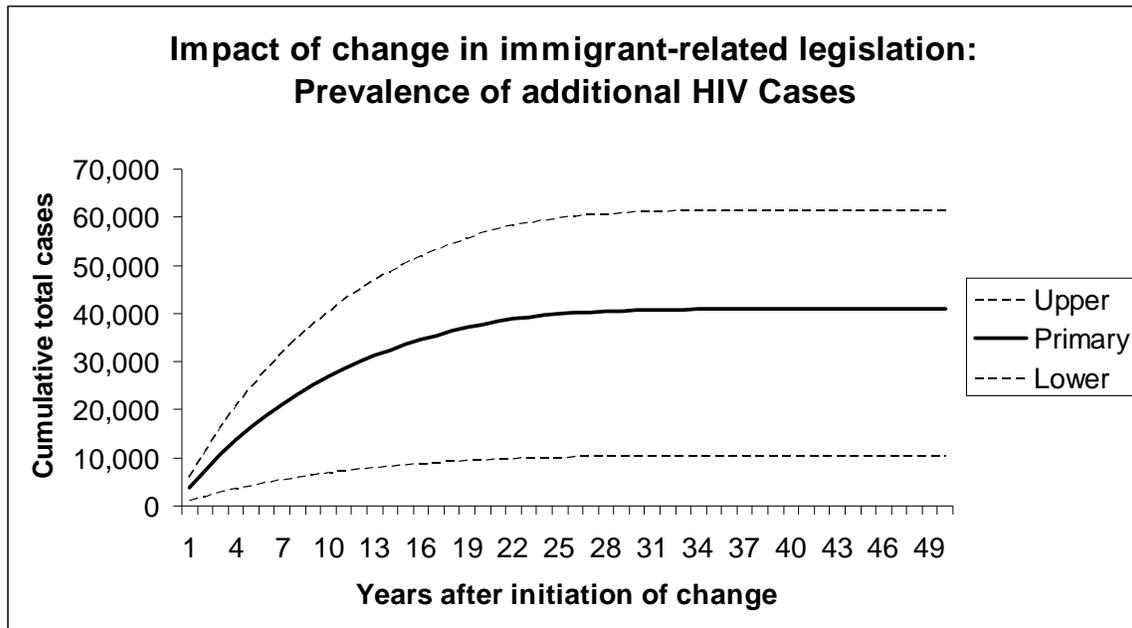
We conducted extensive sensitivity analyses to determine the relative importance of rate of HIV positive immigrants and the rate of onward transmission. We varied the rate of HIV positive immigrants from the primary estimate of 4.06/1,000 immigrants (Table 1a and Table 1b) in steps of +/- 25%. Simultaneously, we varied the rate of onward transmission from the primary estimate of 1.51% per year (Table 1a) in steps of +/- 25%. We also considered the impact of different average ages of entry, with 30 years as the primary case and 20 years and 40 years as the lower and upper limits, respectively.

Results: Number of HIV-infected cases

i) Number of estimated HIV-infected immigrants arriving each year in the U.S.: Using 2007 data, in our primary analysis (assuming average age of entry is 30 years) it is estimated that 4,275 HIV-infected persons would immigrate each year to the U.S.; the lower bound estimate is 966 and the upper bound estimate is 5,768 persons. This is equivalent to a rate of 4.06 infected persons per 1,000 immigrants (lower bound of 1.02 to upper bound of 6.09 HIV-infected persons per 1,000 immigrants).

ii) Results: Number of estimated total new HIV-infected cases in the U.S. (immigrants plus U.S. person infected due to onward transmission): Assuming an average age of arrival of 30 years, after the first 20 years post initiation of the new regulations, the cumulative number of estimated, additional HIV-infected persons in the U.S. will be 37,780 cases (lower bound 9,487; upper bound 56,645). This number includes both the arrival of HIV-infected immigrants and those infected in the U.S. due to onward transmission, assuming a rate of onward transmission of 1.51% per year (Figure 2).

Figure 1: Cumulative total estimated HIV-infected immigrants, plus those U.S. persons infected due to onward transmission, in the U.S. due to changes in immigration regulations: Primary, upper and lower bound estimates: Average age of arrival 30 years*§



Notes:

* Primary estimate calculated using a weighted average rate of 4.06 HIV-positive per 1,000 immigrants. Infection rates of 6.09/ 1,000 and 1.02/1,000 used to calculate the upper and lower bound estimates, respectively.

§ The rate of onward transmission was 1.51%. Those infected by onward transmission are included in the totals above.

Source: Calculated using HIVEcon. See main text for details, and Technical Appendix II, Table 11.3.

Figures 2a and 2b: Cumulative total HIV-infected immigrants, plus those U.S. persons infected due to onward transmission, in the U.S. due to proposed changes in immigration regulations: Base, high and low estimates: Average age of entry 20 years (2a) and 40 years (2b)*§

Figure 2a: Average age of entry 20 yrs

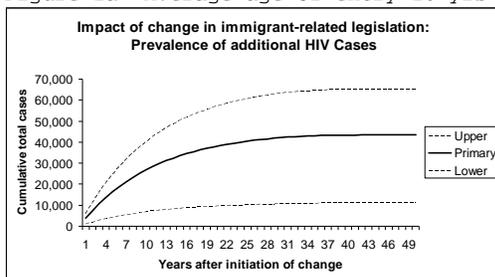
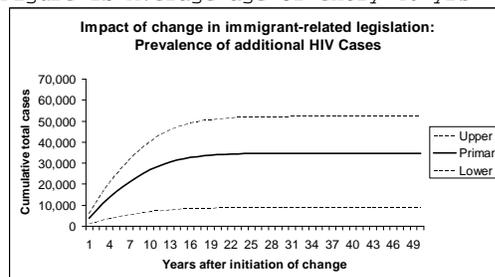


Figure 2b Average age of entry 40 yrs



Notes:

*Primary estimate calculated using a weighted average rate of 4.06 HIV-infected per 1,000 immigrants. Infection rates of 6.09/ 1,000 and 1.02/1,000 used to calculate the upper and lower bound estimates, respectively.

§ The rate of onward transmission was 1.51%. Those infected by onward transmission are included in the totals above.

Source: Calculated using HIVEcon. See main text for details.

Increasing the average age of entry of HIV-infected immigrants to 40 years, after the first 20 years post initiation of the new regulations, the number of additional

HIV-infected persons in the U.S. will be approximately 34,029 cases (lower bound: 8,545; upper bound 51,021). This number includes both the arrival of HIV-infected immigrants and those infected in the U.S. due to onward transmission (Figure 2b).

Decreasing the average age of entry of HIV-infected immigrants to 20 years, after the first 20 years post initiation of the new regulations, the number of estimated additional HIV-infected persons in the U.S. will be approximately 37,780 cases (lower bound: 9,487; upper bound: 56,645) This number includes both the arrival of HIV-infected immigrants and those infected in the U.S. due to onward transmission (Figure 2a).

Thus, given the other assumptions (Table 1a), the assumed average age upon entry of HIV-infected immigrants, particularly if the age of entry is assumed to be older than 30 years, can impact the estimated numbers of those living in the U.S. with HIV due to the arrival of HIV-infected immigrants.

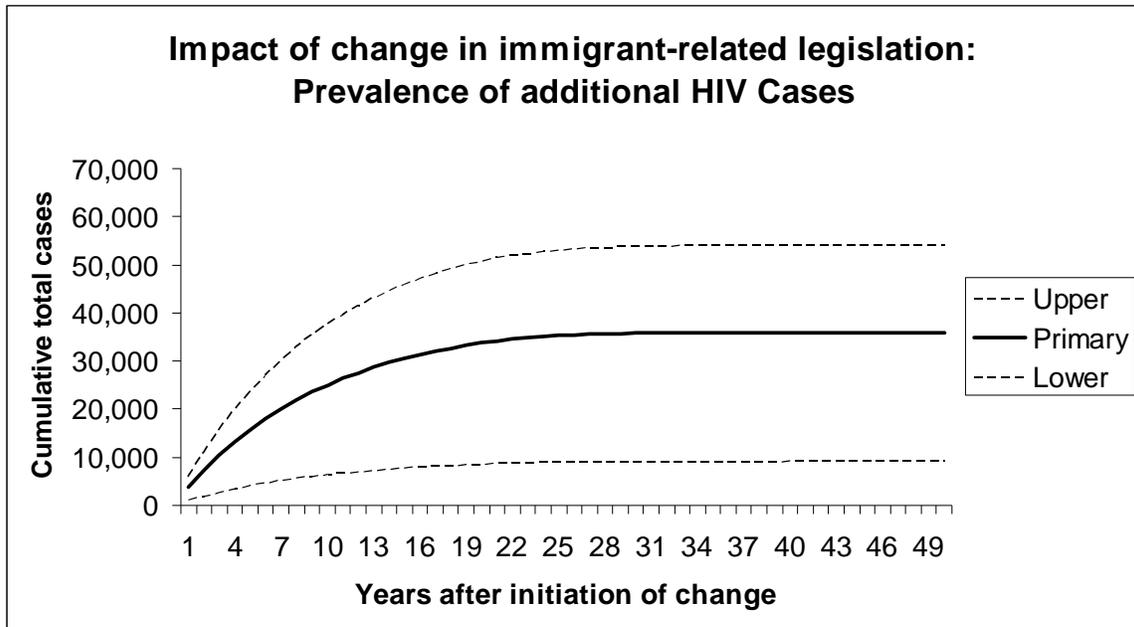
iii) Results: Number of total U.S. persons infected due to onward transmission: Removing the effects of onward transmission (done by simply setting, in HIVEcon, the rate of onward transmission to 0.0%), after 20 years from initiation of the new regulations, the number of HIV-infected immigrants in the U.S. will be approximately 33,795 persons (lower bound: 8,487; upper bound: 50,670) (Figure 3).

Subtracting the number of estimated HIV-infected immigrants in year 20 in the U.S. from the total number of HIV-positive cases in the U.S. (Figure 2) gives approximately 3,985 U.S. persons (lower bound: 1,000; upper bound: 5,975) living with HIV following the arrival of HIV-positive immigrants (in year 20, after enacting the new regulations) (Figure 4).

The number of HIV-infected immigrants using the lower and upper bound estimate of prevalence, transmission, and age upon entry into the U.S. are presented in the Technical Appendix II (Figures II.2a and II.2b, Tables II.4 and II.5). The numbers of U.S. persons with HIV following the arrival of HIV-infected immigrants are also presented in

the Technical Appendix II (Figures II.3a and II.3b, Tables II.4 and II.5).

Figure 3: Cumulative total HIV-infected immigrants, excluding those infected due to onward transmission, in the U.S. due to changes in immigration regulations: Primary, lower, and upper bound estimates: Average age of arrival 30 years*§



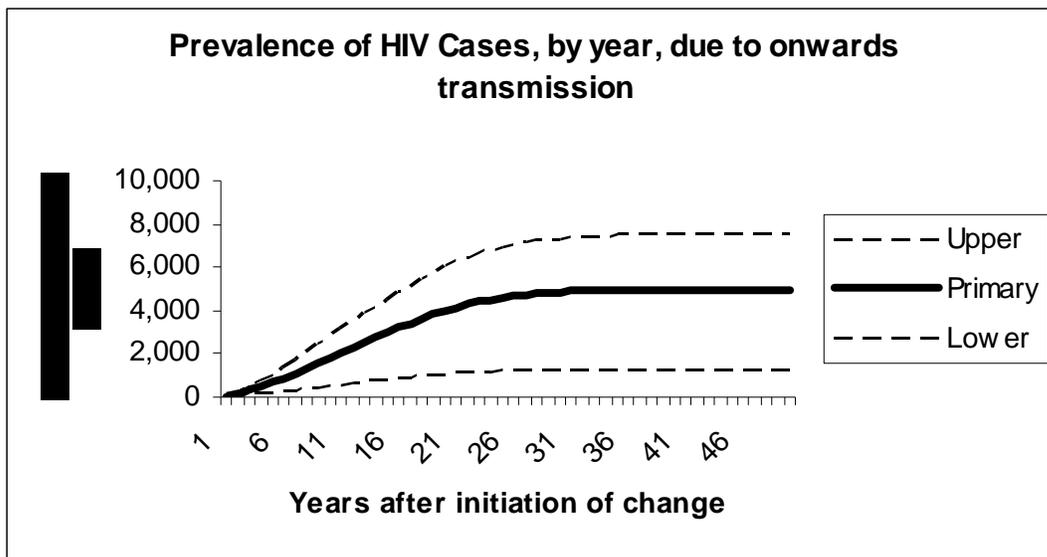
Notes:

* Primary estimate calculated using a weighted average rate of 4.06 HIV-positive per 1,000 immigrants. Infection rates of 6.09/ 1,000 and 1.02/1,000 used to calculate the upper and lower bound estimates, respectively.

§ For these estimates, no onward transmission is assumed.

Source: Calculated using HIVEcon. See main text for details, and Technical Appendix II, Table 11.3.

Figure 4: Cumulative estimated total HIV-infected U.S. persons (only), infected due to onward transmission (1.51% annual transmission rate), due to changes in immigration regulations: Primary, upper and lower bound estimates: Average age of arrival 30 years*§



Notes:

* Primary estimate calculated using a weighted average rate of 4.06 HIV-positive per 1,000 immigrants. Infection rates of 6.09/ 1,000 and 1.02/1,000 used to calculate the upper and lower bound estimates, respectively

§ For these estimates, onward transmission is assumed to be at a rate of 1.51%. For the purposes of calculating new HIV-infected U.S. persons due to HIV-infected immigrants,

HIVEcon adds those U.S. persons who are infected by HIV-infected immigrants to the HIV-infected immigrant cohort, and thus are able to onward transmit to other U.S. persons. Source: Calculated using HIVEcon. See main text for details, and Technical Appendix II, Table 11.3.

iv) Results: Numbers of new estimated HIV cases each year in the U.S. (incidence): the number of new projected HIV cases that could occur in the U.S. each year due to HIV-infected immigrants arriving comprises of two components: i) The number of projected HIV-infected immigrants newly arriving in the U.S.; and, ii) The number of persons infected by onward transmission either directly from the HIV-infected immigrants, or from persons who have previously been infected by HIV-infected immigrants.

The number of estimated persons infected by onward transmission: The estimated annual number of new HIV infections due to onward transmission by HIV-infected immigrants is presented in Table 2a-c. The number of new infections is impacted by the assumed average age upon entry of HIV-infected immigrants (Table 2). Detailed Tables of annual HIV incidence by years post enactment of the new regulation are provided in the Technical Appendix II (Tables II.6, II.7 and II.8).

Table 2a-c: Annual estimated numbers of new infections following arrival of HIV-infected immigrants: Annual estimated new infections by average age upon entry of HIV-infected immigrants.

Table 2a: Estimated new infections from onward transmission in the U.S.: Average age upon entry of HIV-infected immigrants: 20 years.

<i>Years post enactment</i>	<i>Numbers of new HIV infections due to onward transmission</i>		
	<i>Lower</i>	<i>Primary</i>	<i>Upper</i>
1	16	65	97
5	68	272	407
10	112	444	666
20	157	624	936
50	181	721	1082

Table 2b: Estimated new cases of onward transmission in the U.S.: Average age upon entry of HIV-infected immigrants: 30 years.

<i>Years post enactment</i>	<i>Numbers of new HIV infections due to onward transmission</i>		
	<i>Lower</i>	<i>Primary</i>	<i>Upper</i>
1	16	65	97
5	68	272	407
10	112	444	666
20	157	624	936
50	172	683	1024

Table 2c: Estimated new cases of onward transmission in the U.S.: Average age upon entry of HIV-infected immigrants: 40 years.

<i>Years post enactment</i>	<i>Numbers of new HIV infections due to onward transmission</i>		
	<i>Lower</i>	<i>Primary</i>	<i>Upper</i>
1	16	65	97
5	68	272	407
10	112	444	666
20	144	575	862
50	148	589	883

Notes: i) The primary case was estimated using a weighted average rate of 4.06 HIV-infected per 1,000 immigrants. Infection rates of 1.02/ 1,000 and 6.09/1,000 are used to calculate the lower and upper bound estimates, respectively.

ii) For these estimates, onward transmission is assumed to be at a rate of 1.51%. For the purposes of calculating new HIV-infections due to HIV-infected immigrants, HIVEcon adds those persons who are infected by HIV-infected immigrants to the HIV-infected immigrant cohort, and thus are able to onward transmit to other persons.

Source: Calculated using HIVEcon. See main text for details, and Technical Appendix II, Tables II.6, II.7 and II.8.

In year 20 post promulgation of the new regulation, assuming an average age of HIV-infected immigrants of 30 years, there will be approximately 4,899 new HIV infections in the U.S. This is calculated by using the primary estimate of 624 new infections among persons in the U.S. (only) due to arrival of HIV-infected immigrants (Table 2b, year 20 post enactment of the new regulations), and the primary estimate of 4,275 new HIV-infected immigrants who could be arriving each year (Results, part i).

For comparison, in 2006, an estimated 56,300 new HIV infections occurred in the U.S. [11]. Thus, the 4,899 new (annual) HIV infections estimated to be attributed to HIV-infected immigrants 20 years after the promulgation is equivalent to 8.7% of the annual HIV incidence that occurred in the U.S. in 2006.

v) Results: Sensitivity analysis: Impact on cumulative total of HIV cases in year 20. The sensitivity analysis (Table 3) illustrates that assumed rate of HIV positive immigrants per 1,000 immigrants is the most important variable determining the number of additional HIV cases in the U.S. (at year 20). For example, increasing the rate of

onward transmission from 0.75% to 4.53% (a 500% difference) will increase the number of HIV cases by approximately 34%. Yet increasing the rate of HIV positive immigrants per 1,000 immigrants from 1.02 to 6.09 (approximately a 500% difference) will increase the number of cases by approximately 500%.

Table 3. Sensitivity analysis: Cumulative total^a number of HIV+ immigrants and HIV cases due to onward transmission in year 20^b; Average age at entry 30 years (20 years; 40 years)^c

Cumulative total of HIV cases at year 20 due to immigration and onward transmission assuming:

Average age at entry: 30 years (20 years; 40 years)

Onward transmission rate (per 100 HIV+ immigrants)^d

		0	.75	1.51	2.27	3.02 ^e	3.78	4.53
Rate of HIV positive immigrants, per 1000 immigrants to the United States ^f	1.02	8,449	8,928	9,445	10,004	10,607	11,261	11,969
		(8,449; 7,714)	(8,928; 8,098)	(9,445; 8,507)	(10,004; 8,945)	(10,607; 9,413)	(11,261; 9,913)	(11,969; 10,449)
	2.03	16,898	17,856	18,890	20,007	21,215	22,522	23,937
		(16,898; 15,429)	(17,856; 16,196)	(18,890; 17,015)	(20,007; 17,890)	(21,215; 18,825)	(22,522; 19,813)	(23,937; 20,898)
	3.05	25,346	26,784	28,335	30,011	31,822	33,783	35,906
		(25,346; 23,143)	(26,784; 35,394)	(28,335; 25,522)	(30,011; 26,834)	(31,822; 28,238)	(33,783; 29,739)	(35,906; 31,348)
	4.06^g	33,795	35,712	37,780	40,014	42,430^h	45,044	47,874
		(33,795; 30,857)	(35,712; 32,391)	(37,780; 34,029)	(40,014; 35,779)	(42,430; 37,650)	(45,044; 39,653)	(47,874; 41,797)
	5.08	42,244	44,640	47,225	50,018	53,037	56,304	59,843
		(42,244; 38,572)	(44,640; 40,489)	(47,225; 42,536)	(50,018; 44,724)	(53,037; 47,063)	(56,304; 49,566)	(59,843; 52,246)
	6.09	50,693	53,568	56,670	60,022	63,645	67,565	71,811
		(50,693; 46,286)	(53,568; 48,587)	(56,670; 51,044)	(60,022; 53,669)	(63,645; 56,475)	(67,565; 59,479)	(71,811; 62,695)

^a The cumulative total represents the total number of HIV+ immigrants and those infected due to onward transmission living in the United States in year 20 due to the change of regulation. This number includes those immigrants who came in during year 20 as well as those living from previous years; this number also includes those cases due to onward transmission. This number excludes who died before year 20.

^b Year 20 represents the situation twenty years after the change in regulation, assuming that HIV+ immigrants seek treatment immediately upon arrival.

^c Average age of entry represents HIV+ immigrants' average age when entering the United States.

^d The onward transmission rate, per 100 HIV+ immigrants, is based on 0%, 25%, 50%, 75%, 100%, 125%, and 150% of the calculated onward transmission estimate (see note e).

^e This value is the weighted average of onward transmission cases due to sexual transmission in the United States (*Pinkerton SD. How many sexually-acquired HIV infections in the USA are due to acute-phase HIV transmission? AIDS. 2007 July 31; 21(12): 1625–1629.*)

^f The rate of HIV positive immigrants, per 100 immigrants to the United States is based on 25%, 50%, 75%, 100%, 125%, and 150% of the estimate for the prevalence all immigrants (see note g).

^g This is the calculated estimate for the rate of HIV positive immigrants; it is based on a weighted average of regional prevalence rates of HIV rates and estimates of immigration rates to the United States.

^h This is the result of using the calculated weighted average of prevalence of HIV (weighted by regional prevalence and immigration rate) and the weighted average of onward transmission in the United States (see notes e and g).

v) Limitations: The more prominent limitations of the HIVEcon model used to produce the results presented in this report are:

1) Estimated number and age of HIV-infected immigrants in the primary case analysis: Because we could not locate any data on the prevalence and demographic characteristics of HIV-infected applicants seeking entry into the U.S., the estimate of number of HIV-infected immigrants is calculated assuming that the number of HIV-infected immigrants from each region will be the same proportion of HIV-infected persons in that region. That is, if there are, for example, 5 HIV-infected persons per 1,000 persons in a region, then the proportion of HIV-infected immigrants among all immigrants from that region will be 5 HIV-infected persons per 1,000 immigrants.

There are several possible reasons as to why the proportion of HIV-infected immigrants could be less or more than the prevalence of HIV-infected persons in the region of origin. For example, the cost of adequate medical care in the U.S. may make HIV-infected individuals reluctant to immigrate to this country. With the increase in the availability of appropriate HIV treatments in many parts of

the world, adequate treatment is often cheaper outside of the U.S. Conversely, in regions or specific countries where appropriate treatment is less readily available, the portion of HIV-infected immigrants from those regions could be higher than the prevalence of HIV-infected persons in that region. We are seeking comments on these assumptions and data that would further allow us to refine our estimates.

We also do not have information on the number of HIV-infected immigrants who successfully obtained waivers, thus allowing us to estimate the number of HIV-infected immigrants in the baseline). We do know that the number is small. For example, in Fiscal Year 2007, Department of State reported that its consular officers found 746 immigrants ineligible for admission to the U.S. under the communicable disease grounds of INA 212(a)(1)(A)(i). Of those immigrants 327 overcame the initial finding. What portion of those who tested positive for HIV infection is unknown.

HIVEcon does show, with the lower and upper bound rates of HIV-infected immigrants per 1,000 immigrants, the impact of assuming different rates of HIV-infected immigrants to the U.S.

2) Estimated average age of HIV-infected immigrants upon their entry into the U.S.: As demonstrated in the results in Section 5, 6 and 7, the assumed average age of HIV-infected immigrants upon entry into the U.S. can greatly influence the calculated economic impact.

We do not know what the average age of HIV-infected immigrants upon entry (if the proposed regulation is enacted) would be. As stated earlier, a user can, with HIVEcon, readily explore the impact of different average age of entry of HIV-infected immigrants.

Cost analysis: Perspective: Due to data limitations, the model, HIVEcon, only examines the health care costs of the new regulations. We have only limited data on nonhealth care costs and utilization among immigrant groups in the U.S. We do not have data on health care payers and the proportion of HIV-infected immigrants receiving the appropriate standard of care. We conducted sensitivity analyses on the health care cost inputs and identified, but not quantified, other potential costs.

Cost Data

Annual cost of treating an HIV positive patient in the U.S.: In a model-based analysis, Schackman et al projected the lifetime cost of current treatment for HIV infection in the United States. Their model input data were derived from the HIV Research Network, a consortium of primary care sites that specialize in the treatment of HIV infection [12, 13]. Their analysis focused on a cohort of HIV-infected individuals with a mean CD4 cell count of 310 cells/mm³ and projected a mean survival of 24.2 years after cohort initiation. The undiscounted lifetime costs (of comprehensive treatment per HIV-infected person was \$618,900 [9]. Antiretroviral therapy accounted for 73% of the total cost, inpatient care accounted for 13%, and outpatient care accounted for 9%. The estimates also include an 8% additional cost for other medications related to antiretroviral therapy and opportunistic infection prophylaxis and therapy. We use their monthly estimate [9] of \$2,100, annualized to \$25,200. In our calculations, we discounted this annual cost at 3% and 7%. We have also varied this estimate in our sensitivity analysis. A user of HIVEcon can readily alter this estimate.

We did not include any other costs in our costs analysis. This is because, even if HIV-related health restrictions are removed as a barrier to admission for immigrants, all immigrants still must meet other admission requirements. In the United States, under the Federal Personal Responsibility Work and Opportunity Reconciliation Act (PRWORA) of 1996, most immigrants are not eligible to receive means-tested public benefits for 5 years after their entry into the U.S. [14, 15]. Federal means-tested public benefits include Supplemental Security Income (SSI), cash Temporary Assistance for Needy Families (TANF), Medicaid, and food stamps [14, 16]. State and local means-tested benefits are determined at the state or local level and vary by jurisdiction. We have no data to assume that HIV-infected immigrants will seek, 5 years after being admitted to the U.S., such benefits at rates different from non HIV-infected immigrants.

In addition, PRWORA placed other limitations on aliens' access to public benefits, making them more difficult for aliens to obtain such benefits in the first place. For example, the income and resources of the sponsor of a family-based immigrant or permanent resident are deemed to be available to that alien if he/she should

apply for certain means-tested public benefits. See 8 U.S.C. § 1631, 1632. Since a sponsor must first prove to DHS that he/ she is able to provide support to the sponsored alien at an annual income that is at least 125% above the federal poverty level before the alien's immigration application will be approved, it is unlikely that the alien will be able to show that his/ her available resources fall beneath the low income eligibility thresholds required for many means-tested public benefits. See INA, § 213A(a)(1)(A).

We also have not included costs associated with decreased productivity due to illness associated with HIV infection in immigrants and in the persons to whom they transmit the infection. We have only limited data on income and employment of immigrant populations but no data on the impact of HIV infection.

Thus, beyond the costs of treatment for HIV and related conditions (and we include the costs of treating those U.S. persons who are infected due to onward transmission), we have not quantified costs that HIV-infected immigrants will incur within the U.S. We are seeking comment and additional data on such costs.

Cost analysis: Sensitivity analyses on costs: In addition to calculating the impact of different discount rates (3% and 7%), we also examined the impact of altering the costs of treatment and, simultaneously, the impact of altering the rates of onward transmission. Schackman et al [9] estimated cost assuming a 30% reduction costs of drugs (for example, due to "additional manufacturers rebate"). To illustrate the impact of altering the annual cost of treatment, we decreased and increased the annual cost of \$25,200 by +/- 30% (lower estimate of \$19,466; upper estimate of \$30,954).

Cost Results

i) Assuming immigrants have an average age of entry of 30 years, the primary case undiscounted cost (costs of treating HIV cases, see earlier) in the first year would be approximately \$98,414,278 (lower bound: \$24,713,774; upper bound: \$147,555,771) (see Table 1a for definitions of primary, lower and upper bounded cases. Costs estimated assuming 1.51% annual onward transmission rate). Discounted at 7%, the equivalent values are \$91,975,961 (lower bound: \$23,096,985; upper bound: \$137,902,590)

By year 20, this amount increases to \$952,060,384 (lower bound: \$239,081,220; upper bound: \$1,427,415,519) (undiscounted) (see Technical Appendix Table II.9a). Discounted at 7%, the equivalent values are \$246,030,495 (lower bound: \$61,783,130; upper bound: \$368,881,632).

In comparison, immigrants who have an average age of entry at 40 years would also have the same costs in year 1 (\$98,414,278). By year 20 post enactment of the regulation, however, the undiscounted costs of the immigrants aged 40 years upon entry amounts to \$857,534,372 (lower bound: \$215,343,866; upper bound: \$1,285,729,553) (see Technical Appendix Table II.9b).

ii) If we exclude onward transmission from the analysis, and assuming immigrants have an average age of entry of 30 years, the primary case undiscounted cost in the first year would be approximately \$96,950,328 (lower bound: \$24,346,148; upper bound: \$145,360,823) (see Technical Appendix Tables II.10 a, b, c). Discounted at 7%, the equivalent values are \$90,607,783 (lower bound: \$,22,752,409; upper bound: \$135,851,236). These costs represent 98.5% of the costs that include those due to onward transmission.

By year 20, this amount increases to \$851,634,314 (lower bound: \$213,862,245; upper bound: \$1,276,883,402) (undiscounted). Discounted at 7%, the equivalent values are \$220,078,490 (lower bound: \$55,266,068; upper bound: \$329,970,985). These costs represent approximately 89.5% of the costs that include those due to onward transmission. That is, by year 20, the costs associated with cases generated due to onward transmission represent approximately 10.5% of total costs (undiscounted).

iii) Sensitivity analysis; Impact of discounting, altering rate of onward transmission and average annual medical costs. Costs at year 20. In Table 4 we present the results of a three-way sensitivity analysis showing the impact of varying discount rates (0%, 3%, 7%), varying rates of onward transmission (0%, 1.51% and 3.2%), and three different annual costs of treatment (primary estimate of \$25,200, and then +/- 30%). The results were calculated assuming an annual rate of HIV positive immigrants of 4.06/1,000 immigrants.

Changing the annual cost of treatment has an obvious impact on the total costs, but the chosen rate of discounting has

the largest impact (Table 4). In this sensitivity analysis, changing the rate of onward transmission has the smallest impact. For a given cost of treatment, moving from 0% onward transmission to 3.02% onward transmission caused an increase of approximately 25.6%. But, discounting costs by even 3% per year caused an approximately 55% in costs.

Table 4: Cost analysis: Sensitivity Analysis. A comparison of the impact on costs of HIV-infected immigrants due to varying discount rates and: Costs at year 20

<i>Onward transmission</i>	<i>Average annual medical costs per patient</i>	<i>Annual Cost (undiscounted)</i>	<i>Annual Cost (discounted at 3%)</i>	<i>Annual Cost (discounted at 7%)</i>
0	\$19,466	\$657,853,713	\$364,237,650	\$170,001,900
	\$25,200	\$851,634,314	\$471,529,271	\$220,078,490
	\$30,954	\$1,046,090,816	\$579,195,121	\$270,329,745
1.51	\$19,466	\$735,428,867	\$407,189,132	\$190,048,794
	\$25,200	\$952,060,384	\$527,132,751	\$246,030,495
	\$30,954	\$1,169,447,505	\$647,494,730	\$302,207,458
3.02	\$19,466	\$825,940,019	\$457,302,963	\$213,438,596
	\$25,200	\$1,069,232,943	\$592,008,356	\$276,310,111
	\$30,954	\$1,313,374,465	\$727,183,597	\$339,400,920

Notes:

Average age of entry of HIV+ Immigrants to the United States assumed to be 30 years.

Results calculated assuming primary case of rate of HIV positive immigrants at 4.06 per 1,000 immigrants.

iv) Cumulative total costs: In Table 5 we present the results of the cumulative total cost of treating HIV positive immigrants plus those cases generated due to onward transmission (assumed to be 1.51%). By year 20, the cumulative, undiscounted costs will be \$12,712,564,650 (\$5,695,373,827 discounted at 7%).

Table 5: Cumulative total costs of treating HIV positive immigrants.

Year	Cumulative present value (undiscounted)	Cumulative present value (discounted at 3%)	Cumulative present value (discounted at 7%)
1	\$98,414,278	\$95,547,843	\$91,975,961
5	\$1,316,781,552	\$1,184,735,214	\$1,036,058,444
10	\$4,225,172,011	\$3,470,925,628	\$2,716,672,394
20	\$12,712,564,650	\$8,817,948,745	\$5,695,373,827
25	\$17,653,167,533	\$11,322,037,845	\$6,740,956,908
50	\$43,372,996,582	\$19,869,994,895	\$8,944,933,304

Notes:

Average age of entry of HIV+ Immigrants to the United States assumed to be 30 years.

Results calculated assuming primary case of rate of HIV positive immigrants at 4.06 per 1,000 immigrants.

Average annual medical costs set at \$25,200 (before discounting).

These results include an assumed annual onward transmission rate of 1.51%

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