보건학석사학위논문

Effect of Voluntary Rapid Testing on HIV and AIDS Transmission: Mathematical Modelling

신속검사가 HIV와 AIDS에 미치는 영향: 수학적모델링

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이 논문을 보건학석사학위논문으로 제출함

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2016년 8월

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ABSTRACT

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In Korea, the cumulative number of infected cases is 9,615 by 2014, according to World Health Organization (WHO), it is, however, underestimated. To prevent this problem, testing is critical for individual to be aware of their serostatus. To enhance the effect of testing, rapid testing pilot testing started in 2014 in Seoul, Korea, it is, and however, due to the voluntary and anonymous characteristic of the testing, the effect of it has not been studied. The result has shown that when the rapid testing is only conducted in Seoul with national wide conventional testing will lead to 35% and 25% in HIV and AIDS cases in 5 years, respectively. When the rapid testing is conducted throughout Korea with national conventional testing, reduction rate for HIV and AIDS cases are 50% and 39%, respectively. Therefore, the rapid testing can be a critical factor to detect HIV/AIDS cases and proceed into reducing HIV/AIDS underestimation in Korea.

Keywords: rapid test, mathematical modelling, HIV, AIDS

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Chapter 1. Introduction

1.1 Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome

After the initial case of the human immunodeficiency virus (HIV) infection was first introduced in 1959, there are currently 36.9 million people living with HIV/acquired immune deficiency syndrome (AIDS) and every year about 2 million new cases arise worldwide (1). Although the vast majority of newly infected cases occur in Africa, Asia contributes to the worldwide cases increasingly every year. In Asia and the Pacific regions, 4.3 million cases live with HIV and 350,000 new cases are diagnosed every year (2). In Korea, the cumulative number of infected cases is 9,615 by 2014, according to World Health Organization (WHO), it is, however, underestimated. The estimated number of cases in Korea is between 12,000 and 20,000 (1). This underestimation is under several reasons, however, the most critical method to overcome this problem is testing.

1.2 Case Detection Methods

Several testing methods are available for HIV/AIDS testing: HIV antibody tests and rapid tests. HIV antibody test is the most commonly used HIV infection detection method and is generally referred to enzyme-linked immunosorbent assay (ELISA) or enzyme immunoassay (EIA). It detects HIV antibodies in the body which is produced after the infection. The test can be performed as early as 3 weeks after the infection and it requires a lab facility. HIV antibody count can be detected by blood, oral fluid, and urine. It gives 99.5-99.8% accurate results. The results from the test can be available after 2-14 days of the test.

Another available test is the rapid test. It is similar to ELISA for its ability to detect the HIV antibody, however, the results can be produced in 20 minutes. In the United States, the testing kit is available for anyone with a low cost, thus convenience is one advantage of the test. Drawback of this test is the relatively lower accurate (96-99%) result, therefore, once a person is positive, another test, ELISA or the second rapid test, should be performed to reconfirm the test results. However, by its convenience, low cost, and short result producing time, rapid test is being used in many parts of the world.

In Korea, a pilot test incorporating HIV/AIDS rapid test kit is being conducted since 2014. In 2014, five public health centers (PHCs) were included in the study and in 2015, it was expanded to 25 PHCs throughout Seoul(3). The test is conducted anonymously in order to reduce the fear of identification exposure. However, there is insufficient studies on the effect of rapid testing on HIV/AIDS status and because of differences in culture, environment, behavior, lifestyle, physical factors, and social factors, different testing results can be produced distinct from the foreign researches. Therefore, there is a need of a research considering customized factors that comply with Korea.

1.3 Effect of Awareness on HIV/AIDS Infection

Globally, about 156,300 (12%) of the HIV/AIDS infected persons are unaware of their infection status. HIV/AIDS is a sexually transmitted disease (STD) and is directly correlated with the behavior of the population at risk (4). A mathematical analysis performed in the United States has estimated that the serostatus-unaware group is 3.5 times more likely to transmit the disease in comparison to the aware group (5). Another study estimated that 49% of the transmission occurred from the 20% of persons unaware of their infection and suggested that eight transmission of 100 persons newly aware of their infection can be averted (6). Thus, it is critical for infected persons to be aware of their infection to reduce the occurrence of newly infected cases.

In public health centers (PHCs), approximately 20 percent of the infected persons are diagnosed. HIV seroprevalence research suggested that the proportion of positively tested subjects from the voluntary testing in public health centers in Korea were high, therefore, there is a need of methods that encourage people to take voluntary testing (7). The strategy is to implement the rapid testing in the diagnose process. The effectivity of the rapid testing has been studied and in a controlled trial research, sexually transmitted disease (STD) incidence was high in rapid testing group than the EIA testing group among men (8, 9). Tested individuals was found to prefer the rapid testing than the EIA testing mainly for its same day result. The rapid testing also showed the same return rate with the EIA testing (9). The purpose of this research is based on the assumption that the immediate knowledge of HIV/AIDS test result can be a critical modifier of subsequent risk behavior change and ultimately lead to reduction in incidence of the new HIV/AIDS cases. To confirm this assumption, a dynamic mathematical compartment model will be used to estimate the effect of rapid testing on HIV/AIDS incidence with several scenarios.

1.4 Mathematical Model

Different fields of the study have been combined to develop various technologies of researching and analyzing the effect of infectious diseases. Mathematical model is one of such technologies widely used recently to evaluate and analyze the infection and possibly lead to public health intervention.

Mathematical model for HIV is widely used to find the effect of various interventions throughout the world. World Health Organization (WHO) has developed a mathematical model to evaluate the immediate antiretroviral therapy as prevention with voluntary HIV testing on case reproductive number (10). Based on the test case data from southern Africa, the mathematical model was built in two different ways: deterministic and stochastic model. Deterministic model was divided into susceptible, 4 natural phages of HIV development, and death compartments. With different stages of HIV development phages, they were able to evaluate the effect of the involuntary testing with antiretroviral therapy in different phages. However, in this research, by lack of data, the behavior change was not included in the study.

A mathematical model on the effect of the circumcision was developed targeting sub-Saharan Africa as a prevention strategy intervention (11). Where the heterosexual transmission is common, the intervention from a country where homosexual activity is the majority cause of transmission may not provide significant change. Therefore, male circumcision was considered in the mathematical model and they assumed that male and female have different infectivity. Therefore, two sex model was built to evaluate the effect and they concluded that with full coverage of male circumcision can lead to 2 million new HIV infection aversion. The study was limited in accuracy for not able to obtain the current practice of male circumcision.

Testing was considered as an intervention in several researches (10, 12-14). A mathematical model was built to evaluate the effect of HIV infection awareness on infection transmission (12). The model included the four compartments of the population: susceptible, aware infectives, unaware infectives, and AIDS patients. The model was first analyzed using analytic and numeric studies to conduct a stability analysis including local and global equilibria of the model and reproductive number equation. Every scenario was analyzed to obtain new equilibrium and reproductive number equation and numerically calculated for results. The results has shown that the screening effect reduces the infection transmission among susceptible when the aware infectives changes their sexual behavior and do not take part in sexual activities.

The mathematical models introduced in this study proposed the new mathematical models, however, none of the studies found included the effect of rapid testing and different range of sexual behavior and majority of them used foreign data. Therefore, a model from a previous research was modified to fit the Korean situation to evaluate the scenarios.

Chapter 2. Methods

2.1 Methodological Overview

According to the research question of the study, “is the rapid testing effective as a preventive strategy”, the research was constructed with a dynamic mathematical compartment model, assumptions, parameter collection and estimation, validation, and analysis. By the lack of public data of HIV/AIDS, verifying the effect of rapid testing is difficult in Korea. Therefore, a dynamic mathematical compartment model was considered in the study. The model was based on the model developed in a previously published article and was modified to fit the study purpose (15). During the modification, treatment compartment was added to the model because the standard model did not have a population with infection that do not actually infect others who are not AIDS population. This will increase number of population without infectivity.

The subject population was divided into five compartments: susceptible (S), unaware infectives (I_1), aware infectives (I_2), treatment group (T), and AIDS patients (A). In Republic of Korea, 83.9% of the HIV/AIDS cases were infected by sexual activity, in which, the heterosexual sexual contact comprise 58.0% of all infections due to sexual activity (16). Therefore, the sexually active subjects aged 15-49 were considered as susceptible population. Other causes of infection (mother-child infection, blood transfusion, needle sharing) were not considered in this model. The data was collected through Population and Housing Census Report and calculated to identify the proportion of the sexually active population to identify the immigration rate into the sexually active population.

Serostatus unaware population is assumed to be more infectious because of their unwillingness to change their sexual behavior; therefore, an assumption considered in this compartments were the aware population would reduce their hazardous sexual behavior. To be aware of their serostatus, the testing is critical. Since the study focuses on the effect of a testing method, the infective population was divided into two compartments: unaware infectives and aware infectives. With these compartments, the effect of testing can be evaluated.

Assumption were made in the process of model building. Because the numerous unexpected events occur in reality, portraying every aspect of a disease nature in a mathematical model is unrealistic. Therefore, during the mathematical model building process, several factors are constraint to simplify the model and to interpret the results from the model. In this model several assumptions were made and introduced in the mathematical model section.

The parameters were collected through the previously published articles (15)-(17) and except for several parameters, most of the values are imported from internationally published article due to lack of research in such area. Non-HIV related death rate was estimated by the reverse of the life expectancy (1/life expectancy).

To evaluate the model for its validity on current Korean situation, with the initial value given, the reproductive number was estimated to compare with the actual reproductive number. The overall methodological overview is portrayed in Figure 1.

The model is evaluated by three scenarios followed by the validation of the model to test the effect of sexual behavior and rapid testing. The scenario 1 and 2 were built to evaluate the effect of sexual behavior when there is no test conducted, furthermore, the overall scenario assumes the sexual behavior of aware and unaware infectives are different and the testing methods varies. The result of this scenario will allow the best strategy to control the HIV/AIDS cases and evaluate whether the rapid testing is a good method for prevention of HIV/AIDS.

2.2 Mathematical Model

In the total population N(t) consists of 5 subclasses of HIV-negative population, susceptible with constant immigration rate, α, and proportion of the population become infected at the rate of force of infection, λ, calculated with $\lambda = \frac{\beta_1 S I_1}{N} + \frac{\beta_2 S I_2}{N}$. The parameter β is the effective contact rate and 'i' stands for the awareness of the serostatus (i=1, unaware of serostatus; i=2, aware of serostatus); HIV-positive populations with ability to infect other with HIV are divided into two compartments: serostatus unaware infectives, I_1 and serostatus aware infectives, I_2. When the test is conducted the unaware infectives become aware of their serostatus at the rate, θ.

Being aware of their HIV/AIDS serostatus allow aware population to receive treatments at the rate, ψ. When the cell count of white blood cell, CD4+ drops to less than 200 $cells/mm^3$ then this population is immigrated to AIDS compartment at the rate γ. Every compartment, non-HIV/AIDS death rate was expressed as τ. When immunity decreased as an AIDS level, complications occur and lead to death. Thus, rate of AIDS-related death is noted as μ. To express the change of each compartments, differential model was developed and summarized in Figure 2 with graphical structure of the model and the differential model. Parameter and its value is shown in Table 1.

When the population is only composed of the compartments shown in the above mathematical model, then, non-negative total population $(\mathrm{N}(0) = \mathrm{N}_0 > 0)$ can be expressed as

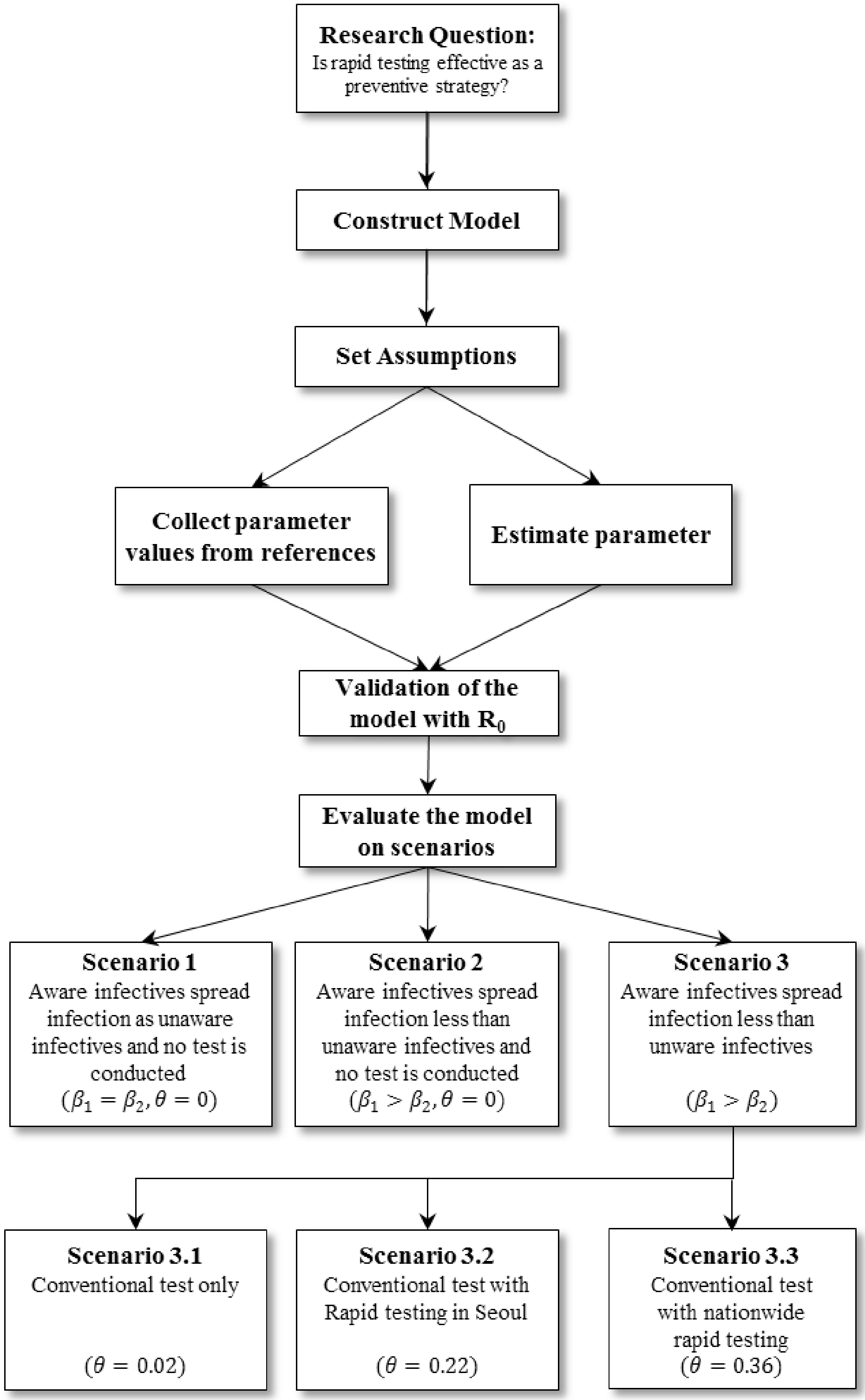


Figure 1. Methodological overview

$N = S + I_1 + I_2 + T + A,$ then the equation can be rewritten as below:

$$\frac{dN}{dt} = \alpha - \tau N - \mu A$$

$$\frac{dI_1}{dt} = \frac{\beta_1(N - I_1 + I_2 + T + A)I_1}{N} + \frac{\beta_2(N - I_1 + I_2 + T + A)I_2}{N} - I_1(\theta + \gamma + \tau)$$

$$\frac{dI_2}{dt} = \theta I_1 - I_2(\psi + \gamma + \tau)$$

$$\frac{dT}{dt} = \psi I_2 - T(\gamma + \tau)$$

$$\frac{dA}{dt} = \gamma(I_1 + I_2 + T) - \tau A - \mu A$$

The variables $(\mathrm{S}, \mathrm{I}_1, I_2, T, A)$ shown on the models above are greater or equal to 0. The model is under assumptions below:

1) The transition rate of aware and unaware infective and treatment group to AIDS is equal;

2) Serostatus aware infectives are less infectious than serostatus unaware group;

3) AIDS and treatment group is not infectious;

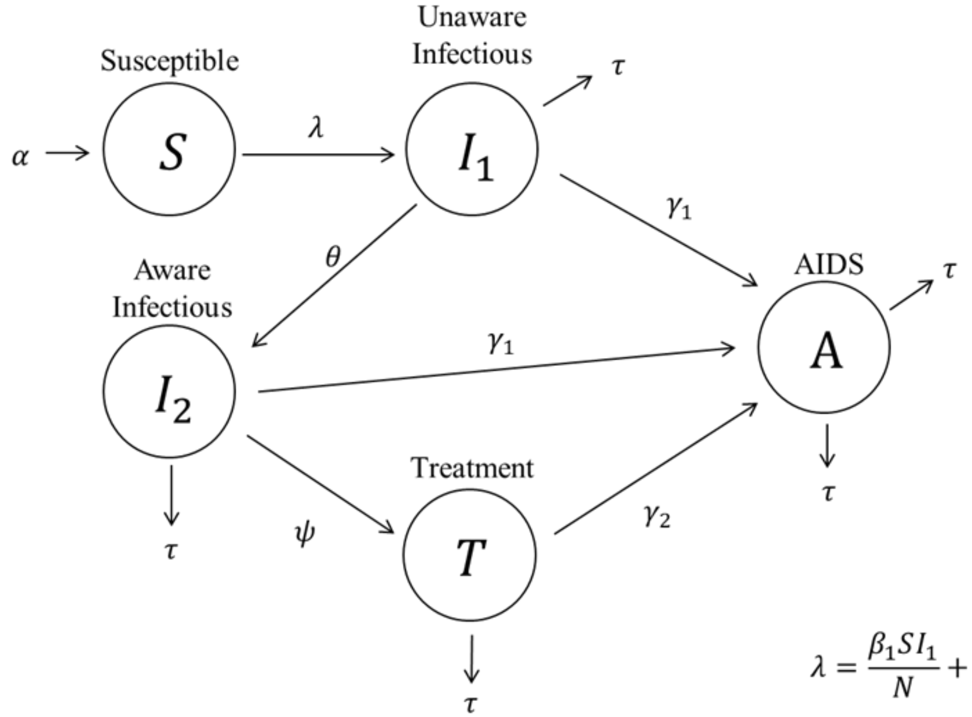
4) All the immigration between the compartments occur simultaneously without delay;

5) HIV/AIDS symptoms are shown as soon as the susceptible infected and infectivity follows the value of unaware infective parameter unless

tested

2.3 Parameter stability

Model stability needs to be evaluated in every model to obtain accurate prediction of the infectious diseases. Since the model is composed of mainly parameters, the stability of the parameter is stability of the model. Therefore, it is necessary to conduct parameter stability analysis in a constructed model. To evaluate the model's stability, every parameter was evaluated through sensitivity test. When the parameters are stable, the results of susceptible, aware infectives, unaware infectives, treatment group, and AIDS group will sustain at the similar level. Every parameter was given with different range of sensitivity test to evaluate which parameter is stable in the model. The parameters included in the sensitivity test were: transmission rate (β_1 and β_2), non-HIV/AIDS-related death rate (τ), progression rate (γ_1 and γ_2), and treatment rate (ψ). Screening rate is excluded in the parameter stability test because it is evaluated through three scenarios in this study. All of the parameters were evaluated in the range 0.0 to 0.5 with 0.05 steps except for non-HIV/AIDS-related death rate because it is unrealistic to set the mortality rate to 20-50% of the whole population. When the parameter do not show the large fluctuation through sensitivity test, it is a stable one, therefore, the parameter do not affect the model through its value.



$$\lambda = \frac{\beta_1 S I_1}{N} + \frac{\beta_2 S I_2}{N}$$

$$\frac{dS}{dt} = \alpha - \tau S - \lambda$$

$$\frac{dI_1}{dt} = \lambda - I_1(\theta + \gamma_1 + \tau)$$

$$\frac{dI_2}{dt} = \theta I_1 - I_2(\psi + \gamma_1 + \tau)$$

$$\frac{dT}{dt} = \psi I_2 - T(\gamma_2 + \tau)$$

$$\frac{dA}{dt} = \gamma_1(I_1 + I_2) + \gamma_2 T - \tau A - \mu A$$

$Where\ \ S(0) = S_0 \geq 0,\ I_1(0) \geq 0,\ I_2\,(0) \geq 0,\ T(0) \geq 0,\ A(0) \geq 0$

* See text for detailed description of the parameters

Figure 2. HIV/AIDS proposed model

2.4 Scenarios

The effect of rapid testing was evaluated through several scenarios. For the scenarios, equal parameters used to validate the model is used. The scenarios are as follows:

1. As emphasized in the introduction, the test plays critical role to suppress the new incident cases of HIV-positive, thus the model will be evaluated on a condition of neither conventional test nor rapid is conducted assuming unaware infectives and aware infectives have equal infectivity ($\beta_1 = \beta_2,\ \theta = 0$);
2. To evaluate the effect of the aware infectives on the infective population, Serostatus aware infectives are less infectious than unaware infectives, and test is not conducted($\beta_1 \neq \beta_2,\ \theta = 0$);
3. The testing is being conducted as the part of the National Health Plan, several scenarios with the effect of the rapid testing are evaluated as follows:

   i. Only conventional test is conducted assuming that infectivity of aware infectives are less than unaware infectives; ($\beta_1 \neq \beta_2,\ \theta = 0.02$)

Table 1. Description and values of the parameters used in the model

Parameters	Description	Baseline Value	Source
α	Recruitment rate of population aged between 15-49	0.49	Reference (15)
β1	Transmission rate of unscreened	108/1000	Reference (18)
β2	Transmission rate of screened	3/100	Reference (18)
τ	Non-HIV/AIDS-related death rate	10/824	Estimated*
γ	Progression rate to AIDS	0.279	Reference (19)
θ	Screening rate	0.02	Reference (19)
Ψ	Treatment rate	0.00	Reference(17)
μ	AIDS-related death rate	48/1000	Reference (19)

* Non-HIV/AIDS-related death rate=1/life expectancy

** See the text for details

Table 2. Summarized description of scenarios

Scenario		Description	Parameter Values
1		Aware infectives spread infection equally as unaware infectives and no test is conducted	$\beta_1 = \beta_2,\ \theta = 0$
2		Infectivity of aware infectives is less than that of unaware infectives and no test is conducted	$\beta_1 \neq \beta_2,\ \theta = 0$
3		Infectivity of aware infectives is less than that of unaware infectives and:	$\beta_1 \neq \beta_2$
	1	Only Conventional test is conducted	$\theta = 0.02$
	2	Conventional test is incorporated with rapid testing in Seoul	$\theta = 0.20$
	3	Conventional test is incorporated with Nationwide rapid testing	$\theta = 0.345$

ii. Conventional test is conducted nationwide and rapid test is only conducted in Seoul; $(\beta_1 \neq \beta_2,\ \theta = 0.20)$

iii. Serostatus aware infectives are less infectious than unaware infectives and the rapid testing is conducted nationally. $(\beta_2 \neq 0,\ \theta \neq 0)$. The number of national test cases (T_{NR}) were estimated with total number of rapid testing cases of Seoul in 2013 (r_{sb}) and 2015 (r_{sa}), number of positive result cases from rapid testing (r_{sp}), and regions population (P_k), and health center numbers distributed through the regions (H_k) where k indicates the regions (1= Seoul, 2=Busan, 3=Daegu, 4=Incheon, 5=Gwangju, 6=Daejun, and 7=Ulsan). The equation for the national rapid test estimation is as follows:

$$T_{NR} = r_{sa} + \sum_{k=2}^{6} \frac{H_k(r_{sa} - r_{sb})}{r_{sa}H_1}$$

The actual number of tested population in 2013 was not publically opened, thus, the number (T_{NP}) is calculated and estimated as follows:

$$T_{NP} = \sum_{k=2}^{6} \frac{r_{sa}P_1}{P_k}$$

Then, the overall test rates (T_R) were calculated with the equation below:

$$T_R = \frac{T_{NR} - T_{NP}}{T_{NP}}$$

2.5 Analysis

We simulated the model with annual testing rates of the conventional and rapid testing, treatment, and AIDS immigration rates to project the trends based on scenarios for the duration of 50 years from current practice. The number of infectives and AIDS patients were projected according to the scenarios to compare with the initial value with no tests and no sexual behavior intervention to determine if the proposed rapid testing strategy will reduce the number of infectives and AIDS patient population in Korea. The sensitivity analysis was included in the scenarios to determine if changing sexual behavior after receiving the test is effective in reducing the number of infectives and AIDS population. Scenario 1 and 2 evaluates the effect of sexual behavior by assuming that the aware population and unaware population have some infectivity towards susceptible population; the projections were resulted in the number of infectives and AIDS population.

Intervention of rapid testing was evaluated in scenario 3 by comparing it to conventional testing under an assumption that the aware infectives are less infectious than unaware infectives. The number of infectives are projected to show the effect of the rapid testing for 50 years of intervention. The projected number of the infectives and AIDS population was recorded divided into short-term (1, 2,3,4,5 years), mid-term (10, 15, 20 years), and long-term (30, 40, 50 years). The analysis was done using R 3.3.0 with *deSolve* package to evaluate the dynamic model built in this study.

Table 3. Parameters used to estimate the nationwide rapid testing rates

Parameters	Description	Baseline Value	Source
T_{NR}	Nationwide number of test cases	15,271	Reference(16)
r_{sb}	total number of rapid tested cases of Seoul in 2013	3,045	Reference(11)
r_{sa}	total number of rapid tested cases of Seoul in 2015	20,987	Reference(11)
r_{sp}	number of positive result cases from rapid testing	386	Reference(3)
P_k	Regional population	Varies*	Reference(15)
H_k	Number of health centers distributed throughout the region	Varies*	Reference(15)

* k=1, Seoul; k=2, Busan; k=3, Daegu; k=4 Incheon; k=5, Gwangju; k=6, Daejeon; and k=7, Ulsan

Chapter 3. Results

Under the estimation of the current practice with only conventional testing by a dynamic mathematical compartment model with initial values given in the method section, the initial value of the model of HIV infectives at year 0 was 10,800 cases and after 50 years. The initial infective case number was decreased to 3,971 cases (63.2% reduction) after 50 years of intervention. The AIDS cases were initially 200 cases, however, after 50 years, the population increased to 393 cases (196.5% increase). This initial result will be evaluated and compared by the scenarios proposed and will project the number of infectives and AIDS population.

3.1 Parameter stability

The results of the parameter stability were expressed in different graphs to show the fluctuation of the parameters through sensitivity test. Transmission rate of aware infectives, AIDS progression rate of aware infectives, and treatment rate are the stable parameters in the study, and transmission of unaware infectives, AIDS progression rate of unaware infectives, and non-HIV/AIDS-related death rate were not stable parameters.

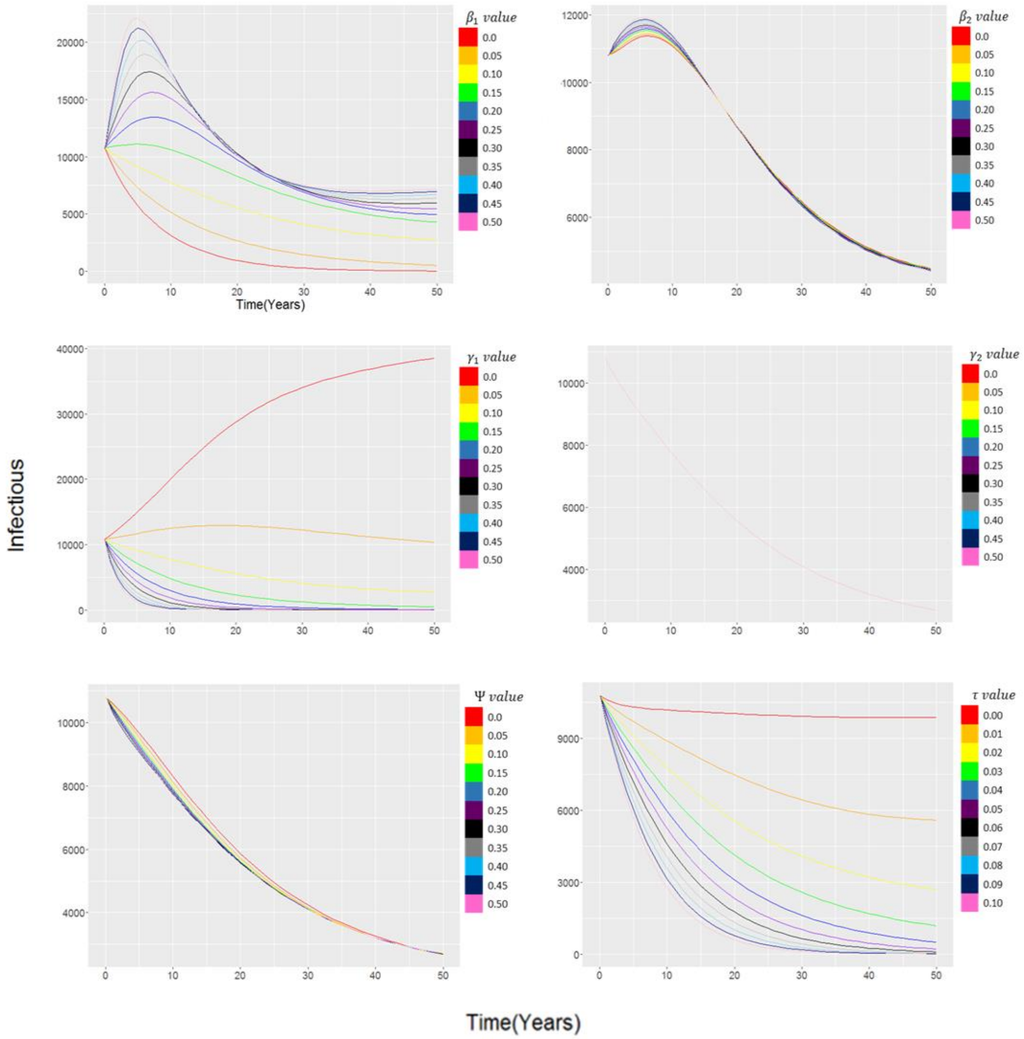


Figure 3. Parameter sensitivity analysis

This results have shown that the parameters with large fluctuation are important ones to consider and necessary in the study. However, through this evaluation, it is difficult to conclude that the model is stable, because of half unstable parameters.

3.2 Scenario 1: Equal infectivity and no test conducted ($\boldsymbol{\beta_1 = \beta_2,\ \theta = 0}$)

Scenario 1 evaluated the situation where the aware infectives do not change their hazardous sexual behavior and infectivity is equal to that of unaware infectives. In addition, no tests including conventional and rapid testing is conducted throughout Korea. In a short-term, the cumulative projected number of infective over 5 years was 11,544 and compared to the initial condition, it was 596 (5%) cases higher (Table 4). Among the AIDS population over 5 years without any intervention, the number of projected AIDS cases was 1,115 which is 7%(33) increase compared to the initial condition. For mid-term, the difference in the HIV and AIDS population of no intervention and initial condition is significantly increase (Table 5). The total number of estimated HIV cases was 8,683 and 17%(1,289) difference was shown. In the long term the difference became greater and resulted in 33%(1,110). AIDS population over 50 years, the cases were 442 and 1.2 times higher than the initial condition (332 cases).

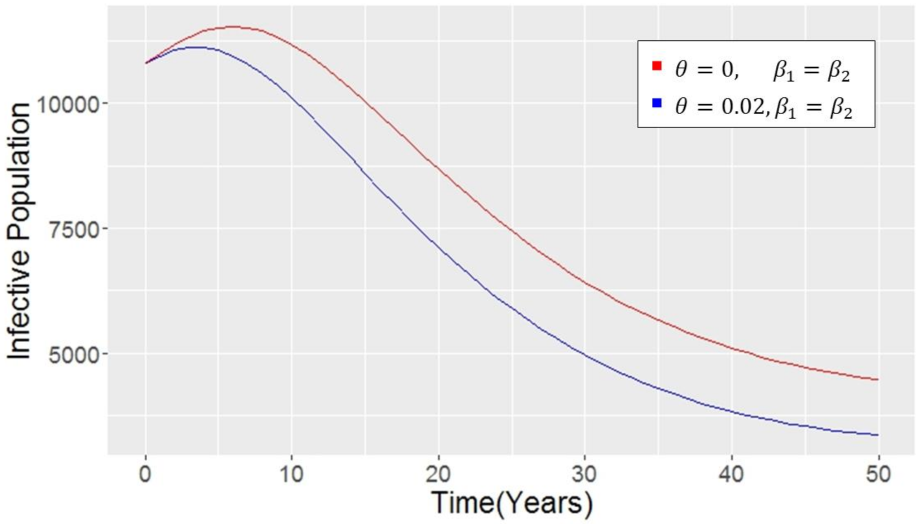


Figure 4. HIV population under scenario 1[1)]

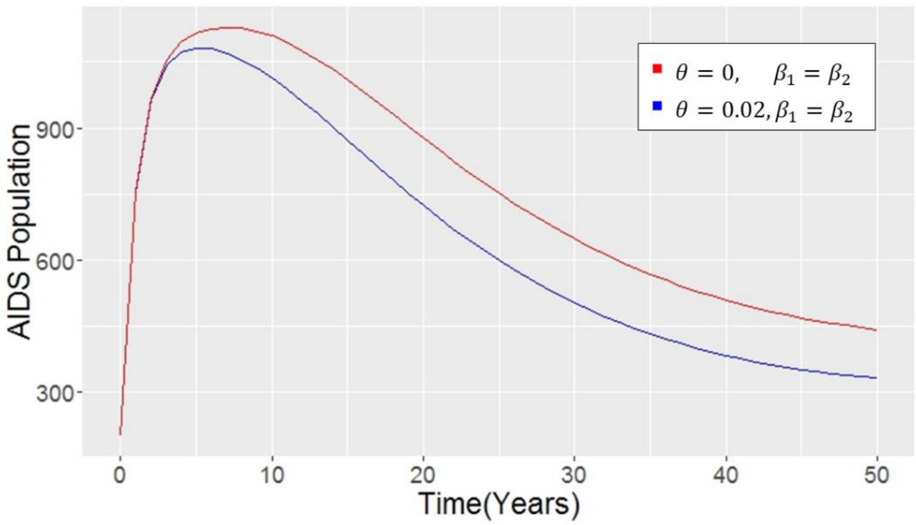


Figure 5. AIDS population under scenario 1[1)]

[1)] Scenario 1(the aware infectives do not change their hazardous sexual behavior and infectivity is equal to that of unaware infectives) is compare with the initial condition

3.3 Scenario 2: Different infectivity and no test conducted ($\beta_1 \neq \beta_2$, $\theta = 0$)

Assuming that the aware infectives engage less in hazardous sexual behavior with no test conducted ($\theta = 0$), the effect of the different sexual behavior of aware and unaware infectives on overall infective population of the model was projected. As shown in the Figure 5 and 6, overall implemented projected results were similar to the initial condition population number.

In the short-term projection over 5 years, the behavior change has displayed the lower number of HIV/AIDS population. The infective cases were reduced by 1.3 %(154). Although the projected number of infectious cases decrease in a mid and long-term intervention, the overall population difference was only 20 cases and the implemented cases were 8,694 over 20 years and slightly larger (0.1%) than that of initial number of cases (8,683) (Table 5). In the 50-year projection, the difference was slightly greater than that of 20 years, however, the difference was still negligible (Table 6). AIDS population projection portrayed no significant difference. Its projected number were at the approximate of the initial condition.

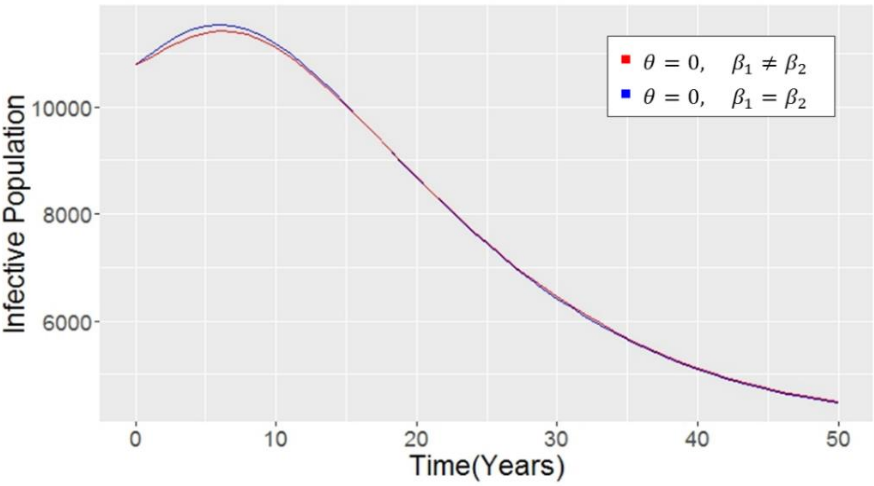


Figure 6. HIV population under scenario 2[2)]

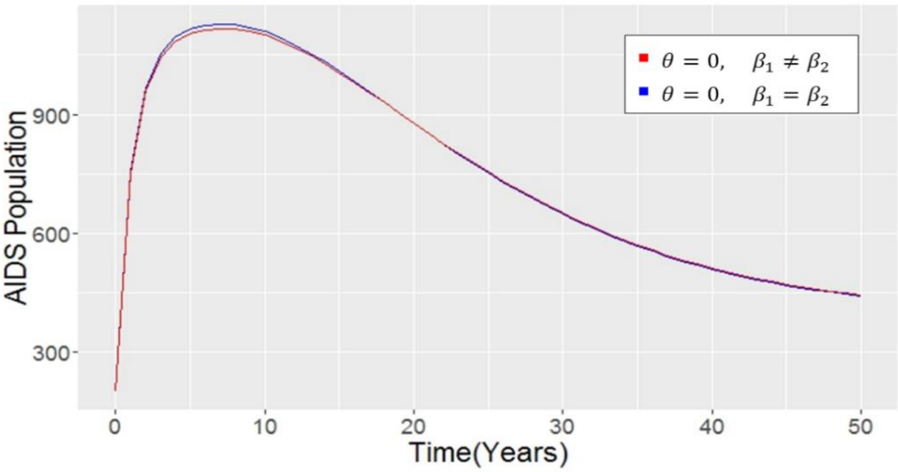


Figure 7. AIDS population under scenario 2[2)]

3.4 Scenario 3.1: Conventional tests only ($\boldsymbol{\beta_1 \neq \beta_2}$, $\boldsymbol{\theta = 0.02}$)

Scenario 1 and 2 evaluated the number of infective and AIDS

[2)] Scenario 2 (the aware infectives engage less in hazardous sexual behavior with no test conducted) is compared with the initial condition population depending on the difference in sexual behavior. From Scenario 3, effect of two methods of testing is projected: conventional testing and rapid testing. On Scenario 3.1, only conventional test is compared to the test-absent condition. In a short term, no significant change (11,816) was shown over 5-year period compared to the test-absent condition (10,948). However, in the mid-term, the projected number of infective population was reduced by 6%(453) and 2%(75) in the long-term. The AIDS population was increased after a short-term, however, reduced by 2%(7) in the long term.

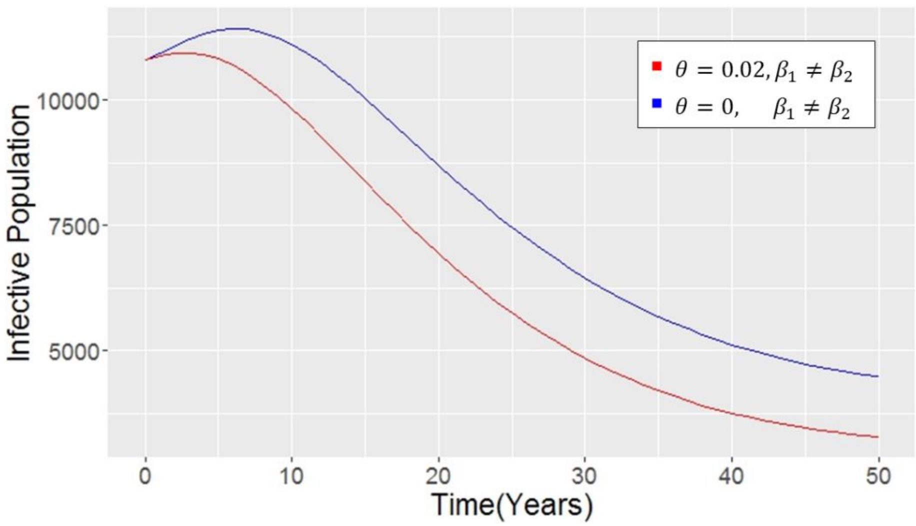


Figure 8. HIV population under scenario 3.1[3)]

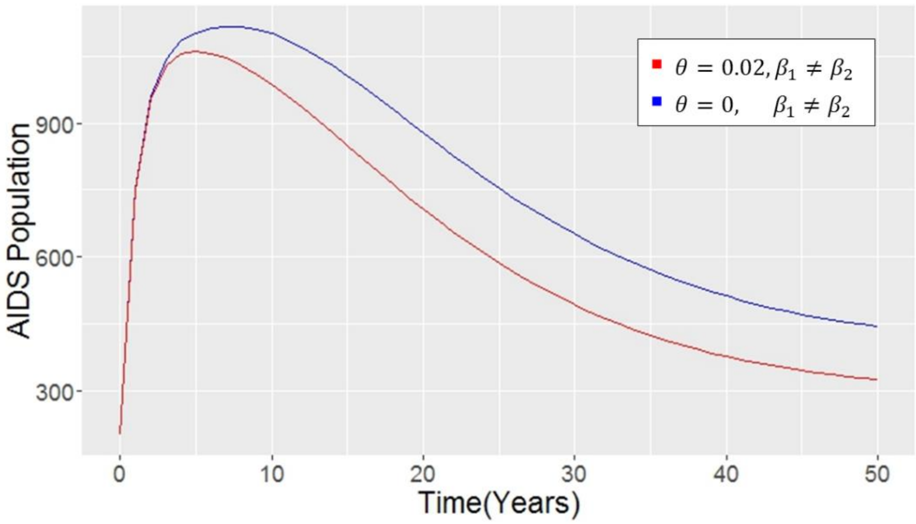


Figure 9. AIDS population under scenario 3.1[3)]

3.5 Scenario 3.2 and 3.3: Rapid test in Seoul and Nationwide ($\beta_1 \neq \beta_2$, $\theta \neq 0$)

When the rapid testing was incorporated in the intervention, the projected results indicated a large reduction of infective and AIDS population. Based on the previously published study, the rapid testing was tested as an intervention as a method of detection in 2014 and 2015 in Seoul, Korea (3). With the data given in the study, the rapid testing participation rates were calculated to be included in the model. The assumption was that the testing rates are 10 times higher than the conventional testing, thus, the parameter used for testing rate was 0.20. Also, if the rapid testing was expanded to every

[3)] Scenario 3(conventional testing) is compared with no test condition health centers throughout the major cities in Korea (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan), the testing rate was 0.345. The projected results had displayed the significant difference in the infective and AIDS population. The immediate reduction in the infected population was significant compared to other scenarios, and the reduction effect was clearly shown in the results. Five years of implementation has shown 34%(3,468) decrease in number of infectives and comparing to the test-absent condition, 35%(3,864) of infective population was reduced. Reduction after 20 years was 92%(9,929) and after 50 years was 98%(10,741). AIDS population also have portrayed a large reduction in numbers. In year 2 and 3, the number was increased and still was higher than the value at year 0 by 2.89%(35), however, in the mid and long-term, the number dropped quickly.

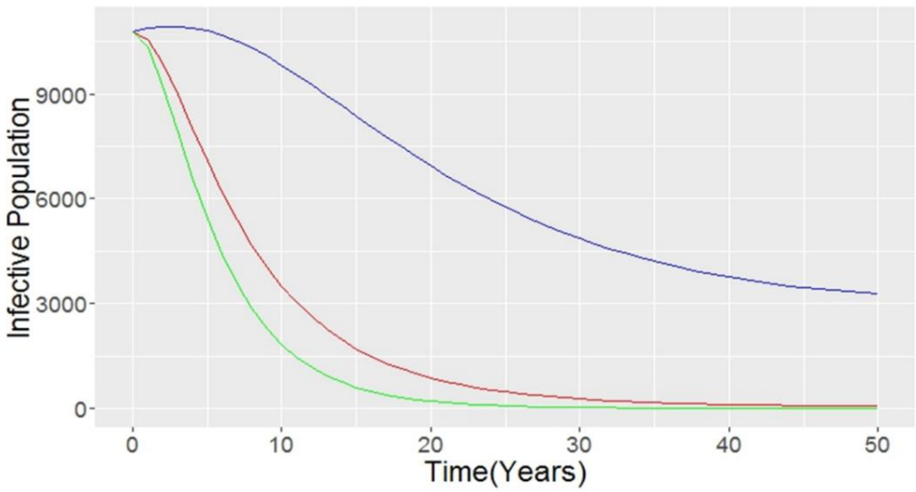


Figure 10. HIV population under scenario 3.2 (Seoul) and 3.3 (Nationwide) **4)**

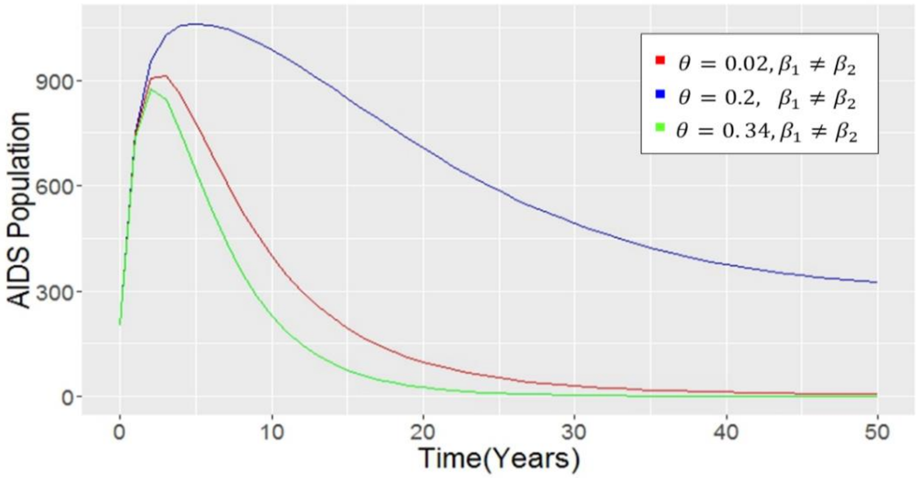


Figure 11. AIDS population under scenario 3.2 and 3.3[4)]

Implementation after 20 years showed the 51% reduction in AIDS population and 85%, 94%, and 97% reduction in 30, 40, and 50 years, respectively. With the nationwide implementation of rapid testing displayed faster reduction in both infective and AIDS populations. Five years after the intervention initiation, 50% reduction was shown in the infective population, however, the AIDS population was still higher than the year-0 population (Table 4). AIDS population was decreased rapidly to 87% and approximately to 100% in the mid-term and long-term, respectively.

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4) Scenario 3.2(rapid test is conducted only in Seoul) is compared with scenario 3.3(rapid test is conducted nationwide)

Table 4. Short-term results from the mathematical model analysis of different scenarios proposed

Condition	Scenario		Duration of Implementation											Difference with initial condition	Difference with conventional testing
			0	1		2		3		4		5			
HIV	Initial condition		10800	10952	(0.01)	11060	(0.02)	11116	(0.03)	11058	(0.02)	10948	(0.01)	-	-
		1	10800	10981	(0.02)	11164	(0.03)	11324	(0.05)	11445	(0.06)	11544	(0.07)	0.05	-
		2	10800	10912	(0.01)	11058	(0.02)	11199	(0.04)	11314	(0.05)	11390	(0.05)	0.04	-
		3.1	10800	10874	(0.01)	10924	(0.01)	10934	(0.01)	10899	(0.01)	10816	(0.00)	-0.03	-
		3.2	10800	10552	(-0.02)	9868	(-0.09)	8979	(-0.17)	8024	(-0.26)	7084	(-0.34)	-0.35	-0.35
		3.3	10800	10333	(-0.04)	9224	(-0.15)	7907	(-0.27)	6608	(-0.39)	5430	(-0.50)	-0.50	-0.49
AIDS	Initial condition		200	755	(2.78)	963	(3.82)	1043	(4.22)	1073	(4.37)	1082	(4.41)	-	-
		1	200	756	(2.78)	967	(3.84)	1055	(4.28)	1095	(4.48)	1115	(4.58)	0.07	-
		2	200	753	(2.77)	961	(3.81)	1045	(4.23)	1083	(4.42)	1103	(4.52)	0.06	-
	Initial condition	3.1	200	751	(2.76)	954	(3.77)	1030	(4.15)	1056	(4.28)	1045	(4.23)	0.00	-
		3.2	200	743	(2.72)	906	(3.53)	913	(3.57)	857	(3.29)	778	(2.89)	-0.25	-0.24
		3.3	200	736	(2.68)	874	(3.37)	845	(3.23)	752	(2.76)	641	(2.21)	-0.39	-0.38

Table 5. Mid-term results from the mathematical model analysis of different scenarios proposed

		Duration of Implementation								
Condition	**Scenario**	**0**	**10**		**15**		**20**		**Difference with initial condition**	**Difference with conventional testing**
HIV	**Initial condition**	10800	11180	(0.04)	8597	(-0.20)	7394	(-0.32)	-	-
	1	10800	11180	(0.04)	10042	(-0.07)	8683	(-0.20)	0.17	-
	2	10800	11180	(0.04)	10020	(-0.07)	8694	(-0.20)	0.18	-
	3.1	10800	9827	(-0.09)	8367	(-0.23)	6941	(-0.36)	-0.06	-
	3.2	10800	3506	(-0.68)	1708	(-0.84)	871	(-0.92)	-0.88	-0.87
	3.3	10800	1830	(-0.83)	604	(-0.94)	210	(-0.98)	-0.97	-0.97
AIDS	**Initial condition**	200	1013	(4.07)	903	(3.52)	725	(2.63)	-	-
	1	200	1109	(4.55)	1009	(4.05)	877	(3.39)	0.21	-
	2	200	1100	(4.50)	1006	(4.03)	878	(3.39)	0.21	-
	3.1	200	987	(3.94)	849	(3.25)	707	(2.54)	-0.02	-
	3.2	200	400	(1.00)	194	(-0.03)	98	(-0.51)	-0.86	-0.86
	3.3	200	229	(0.15)	75	(-0.63)	26	(-0.87)	-0.96	-0.96

Table 6. Long-term results from the mathematical model analysis of different scenarios proposed

Condition	Scenario		Duration of Implementation							Difference with initial condition	Difference with conventional testing
			0	30		40		50			
HIV	**Initial condition**		10800	5122	(-0.53)	3830	(-0.65)	3361	(-0.69)	-	-
		1	10800	6424	(-0.41)	5190	(-0.52)	4471	(-0.59)	0.33	-
		2	10800	6454	(-0.40)	5121	(-0.53)	4491	(-0.58)	0.34	-
		3.1	10800	5019	(-0.54)	3756	(-0.65)	3286	(-0.70)	-0.02	-
		3.2	10800	306	(-0.02)	113	(-0.09)	59	(-0.17)	-0.98	-0.98
		3.3	10800	31	(-0.04)	6	(-0.15)	1	(-0.27)	-1.00	-0.99
AIDS	**Initial condition**		200	502	(1.51)	383	(0.92)	332	(0.66)	-	-
		1	200	648	(2.24)	509	(1.55)	442	(1.21)	0.33	-
		2	200	651	(2.26)	511	(1.56)	444	(1.22)	0.34	-
	Initial condition	**3.1**	200	492	(1.46)	376	(0.88)	325	(0.63)	-0.02	-
		3.2	200	30	(-0.85)	12	(-0.94)	6	(-0.97)	-0.98	-0.98
		3.3	200	31	(-0.85)	6	(-0.97)	1	(-0.99)	-0.99	-0.99

Chapter 4. Discussion

By evaluating the dynamic mathematical model, the analysis on the 50-year period indicated the testing incorporating the rapid test has a significant effect on the number of HIV/AIDS population.

In this study, the first baseline assumption was that when more proportion of population is tested, more infected population was found to be HIV-positive or an AIDS patient and they will engage less in hazardous sexual activities. Thus, the transmission rate of an aware infected person is less than that of unaware infected person, which lead to a reduction of overall infected population. Additionally, in preliminary researches, the behavioral change is critical and effective method to prevent the spread of the disease (15-17). The overall model evaluation with scenarios has demonstrated that the disease will eventually decrease even in an initial condition with no test and no behavioral change. Evaluation of behavioral change is assumed to further decrease the number of infected cases. However, he projected value of infected population has indicated that there is no significant difference before and after the behavioral change. Instead, when behavioral change is followed by testing, the effectiveness can be shown and be used as a preventive strategy for HIV/AIDS. Without testing, number of aware population decreases by the population immigrating into the non-infectious treatment group or progression to AIDS. Reducing number of people will practice the safe sexual activity, therefore, leading to limited effect of behavioral change. The method to enhance the results of behavioral change is testing.

The projection of the model indicated that the rates of infected population reduction is more rapid when testing is included in the intervention. Conventional test is determined to be effective method to detect and for its high sensitivity that leads to accurate test results, the conventional test has been used throughout Korea. However, the projection of the parameters estimated from Seoul rapid testing results has indicated that the effect of rapid testing is greater in detecting the HIV/AIDS population and it can even lead to eradication of the disease over longer period of time. When every health centers in major cities participated in the rapid testing, the results are more rapid and 10 years will be saved to reach the close range of eradication.

This study proposes the possible HIV/AIDS control strategy by evaluating the effect of rapid testing. Current world health HIV/AIDS goals are focused on the short-term reduction of HIV/AIDS (19). However, the health centers and medical centers currently offer the conventional tests and which in the short-term (up to 5 years) will lead to increase of infective population.

For the immediate results to achieve the short-term goals, the rapid testing is a sufficient way. A preliminary research has determined that rapid testing with counseling increase the follow-up rate and return for second test to identify the false positive (8). To enhance the effect of the rapid testing, the immediate counselling session can be used to increase awareness of the disease information and to educate the infected person with safe sex guidelines to further decrease the infectivity of aware infective population.

The limitations of the study are: first, the rapid testing was conducted voluntarily and anonymously, therefore, although we were able to find the data of the total surveyed and number of population taken the test, it is difficult to ensure the test taken population has not taken the test elsewhere in Seoul. Therefore, the number of tested population may have been overestimated and it may lead to overestimated infected and AIDS population. Second, the parameters were imported from preliminary published international articles by the lack of researches using Korea-originated data. To predict the accurate number, more Korean data-based research needs to be conducted. Third, not all the natural history of HIV/AIDS were not included in the study. The latent period of 2-3 weeks or months is the first basic natural history of the disease, however, when the mathematical model include every aspect of reality, the model will grow larger and the calculating such complex model, the processing would take long period of time. Mathematical model is the simple representation of the real world, therefore, it is unnecessary to include all the aspects. However, by its simplicity, the capacity of accurately calculate the reality may be a challenge. Through parameter stability analysis through sensitivity test of the parameters, it is hard to ensure the stability of the model. Model, however, is significant for inclusion of actual Korea data and being the first model to combine rapid testing and mathematical model in Korea. When the model is further refined to gain more stability, this study can be another evidence for establish a rapid testing policy.

Chapter 5. Conclusion

Proposed dynamic mathematical model in this study has shown the effect of behavior change, conventional testing, and rapid testing on prevalence of HIV/AIDS cases. The maximum number of infectious and AIDS population can be achieved through scenario 3.3 where the aware infective population change their behavior after the test results, and conventional and rapid testing is simultaneously. However, the behavioral change may not be used as an intervention alone because of its insignificant results. The implementation of the strategies included in this research may benefit in reducing the HIV/AIDS cases in the future.

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국문초록

신속검사가 HIV와 AIDS에 미치는 영향: 수학적 모델링

이 연구의 목적은 신속검사와 검사결과에 따른 행동 양상의 변화로 인해서 한국의 감염자수가 얼마나 변화하는지를 수학적 모델링으로 검증하는 것이다. 한국의 전체 HIV/AIDS 감염자는 2014년에 9,615명으로 나타났지만 세계보건기구의 의하면 한국의 감염자 수는 과소평가 되었다는 결과가 있었다. 환자수가 정확히 보고 될 수 있는 중요한 방법은 검사의 변화이다. 본 연구는 2014년 서울에서 시작한 신속검사 시범사업을 기반으로 하여서 수학적 모델링을 구축하였고, 그 모델링으로 신속검사와 위험행동의 변화로 인한 감염자수의 감소를 측정하였다. 이 연구의 주요 결과는 다음과 같다. 첫째, 기존의 검사를 유지하고 신속검사를 서울에서만 진행하였을 때 5년 후에는 HIV 감염자는 35%, AIDS 환자는 25% 감소하였다. 둘째, 신속검사가 한국 전체로 확장되었을 때 총 HIV 감염자는 50%, AIDS 환자는 39% 감소하였다. 종합하자면, 신속검사의 효과로 검사가 확대될수록 HIV/AIDS 환자가 감소할 수 있으며, 나아가 신속검사가 예방을 위한 전략을 수립하는 데 있어서 지침을 제공할 수 있을 것이라 기대한다.

주요어: 신속검사, 수학적 모델링, HIV, AIDS

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