A Simulation-based Method for Efficient Resource Allocation of Combination HIV Prevention

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ABSTRACT
Over the past three decades there has been a wealth of operational research into effectively and efficiently combating human immunodeficiency virus (HIV). These interventions have had varying results. Condoms, for example, have been shown to decrease the probability of transmission per sexual act (PTSA) by 95%, but they tend to be used inconsistently. Male circumcision has been shown to reduce the PTSA by 50%, but provides consistent partial protection by design. Antiretroviral therapy (ART) is a medical treatment that slows the reproduction of HIV. ART has been associated with 96% reduction in PTSA, and has been shown to prolong the life of an infected individual. However, it is difficult to determine how to optimally distribute limited HIV prevention resources to prevention methods due to each method's different financial costs, levels of uptake and efficiency, and potential unintuitive interactions. In this paper we implement an individual-based model that simulates HIV transmission and prevention in a complex sexual network and use it to answer the question of combination prevention. Using optimization software, we find the best combination of prevention methods for given a given budget and sexual network structure.

General Terms
Simulation, HIV, individual-based modeling, agent-based modeling, stochastic modeling, combination prevention

1. INTRODUCTION
The severity of human immunodeficiency virus (HIV) epidemic is well-known, and is particularly prevalent in low-resource countries such as South Africa [27]. Many intervention strategies have been suggested to tackle the HIV epidemic including distributing condoms [18, 39], male circumcision [32], and behavioral change campaigns [37, 19, 17]. Most recently public health officials and epidemiologists have shown a lot of interest in treatment as prevention (TasP), as there is evidence that antiretroviral therapy (ART) reduces infectivity of HIV-positive individuals through decreased viral load [7, 11].

Many simulation models have been used to investigate the relative effectiveness of different intervention scenarios [4, 12, 16]. Van der Ploeg et al. developed the microsimulation STDSIM for decision support of sexually transmitted diseases [34]. It has been used to simulate the effect of mass treatment of sexual transmitted diseases [23], male circumcision campaigns [6], condom focusing strategies [36], and behavioral change campaigns [22]. For each they explore trade-offs and suggest implementation options for each independently. Sloot et al. have developed a complex agent network model and used it to investigate the benefits of TasP in the Amsterdam homosexual community [29, 28]. Rajaraman et al. described a network model which they used to explore the effectiveness of a prophylactic intervention [30]. Note that this is not an exhaustive list.

While the most intuitive solution is to spend at the point of maximal effect of each intervention, this is not possible in low-resource settings: in addition to the effectiveness of interventions, cost must be considered. In such settings the opportunity costs of allocating additional resources to one intervention over another might be great and so a greedy approach may not be appropriate. Differences in uptake, coverage, and consistency also support the notion that no single prevention method will be sufficient for disease eradication. Instead, a combination of interventions, known as combination prevention, is likely to be the most efficient use of public health funding [24].

Although combination prevention seems to be an obvious solution, the means by which we arrive at an optimal combination of preventions is not. The individual specific nature of HIV (age-disparity within relationships, concurrent sexual relations, and infectivity of individuals based on stage of infection and treatment status) make traditional compartmental and differential equation (DE) models overly simplistic [35]. For this reason stochastic individual-based models that consider more explicitly the dynamic nature of a population's sexual network are better suited to the modeling of HIV combination prevention interventions. However, stochasticity such as non-deterministic transmission, formation, and dissolution events, make a closed-form solution to

*Lucio Tolentino is a visiting research at SACEMA from the Computational Epidemiology research group in the Department of Computer Science at the University of Iowa the problem of combination prevention difficult. Additionally, the problem of optimal resource allocation becomes intractable when considering diminishing returns of scale of spending, and subtle interactions between interventions.

In this paper we present a method for finding a locally optimal combination of HIV prevention methods, and show that combination prevention performs better than any single intervention at reducing cumulative HIV incidence while working within a budget. Previous work has been focused on solving the resource allocation problem within the context of DE models [5, 40], or an exploration of the prevention allocation space within an individual-based model [25]. Our research is unique in that we consider the objective of minimizing cumulative incidence in addition to respecting some given budget within an individual-based model. Our method uses artificial intelligence algorithms to find the best possible allocation of resources to prevention methods. Specifically we use simulated annealing, and a genetic crossover algorithm [21] to determine the best achievable intervention starting times and spending amount for condom distribution, male circumcision, and TasP campaigns.

In the next section, we discuss our methods; the individual-based model we used to simulate the impact of intervention methods; the intervention methods and their implementation, and the cost and effect of each within the model. In Section 3 we analyze the results of our combination prevention and in Section 4 we conclude with a discussion of the implications for policy and the areas of future work.

2. METHODS

Our model is an event-driven individual-based model that uses the modified next reaction method (mNRM) algorithm [1], a derivative of the Gillespie Stochastic Simulation algorithm [13]. The algorithm schedules events to occur relative to the hazard of each event. The time till an event is the time required for the cumulative hazard of the event to reach a random number between one and infinity. Thus, events with high hazard are more likely to occur soon, and events with less hazard will occur further in the future. We keep track of the time till every event, and perform each event in series.

The main purpose of the model is to simulate the impact of HIV and HIV interventions. We conform to current recommendations for reporting of HIV modeling work [10], and follow the standard protocol suggested by Grimm et. al [15] to describe our model. This protocol, known as ODD (Overview, Design concepts, and Details), form the structure of our methods description.

For purposes of reproducibility, we include a table of parameters, values, and justification in Table 1. Parameters values are calibrated and validated in Section 2.8. Values are informed by the epidemic in South Africa, but can be changed to explore other contexts.

2.1 Purpose

The model was designed to explore the spread of HIV infections in complex and dynamic sexual networks. We built the model to address the question: which attributes contribute significantly to the diffusion of HIV, and what intervention can be most effective in interrupting this diffusion?

2.2 Entities, State Variables, and Scales

The model considers two kinds of agents: males and females. Both kinds of agents have a notion of who his or her:

1. Birth time (i.e. age)
2. Time since relationship change
3. Number of current relationships
4. Partnering value (described in 2.5 Initialization)
5. Time of infection
6. Exposure to a condom campaign
7. ART status (whether he or she has tarted taking ART)
8. Time of circumcision (males only)

2.3 Process Overview and Scheduling

Events occur one at a time according to the modified next reaction method. The events are:

1. Formation
2. Dissolution
3. HIV transmission

For purposes of simplicity mortality / replacement is not considered in our model.

As mentioned previously, events are scheduled to occur relative to the events specific hazard function (described in further detail in 2.7 Submodels). The order of events is significant since the firing of one event may enable or change another. The occurrence of some events affect the hazard of other events: the formation of a relationship between male i and female j may lower the hazard of formation of a relationship between male i and female k and thus the event will be scheduled to occur further into the future.

Additionally we have the notion of interventions which aim to interrupt disease spread by reducing HIV transmission probability. Interventions (described in more details in 2.7 Submodels) are implemented at a specific starting time, and their effect is relative to the amount of money spent.

2.4 Design Concepts

The model simulates the spread of HIV in complex sexual networks: events are specific to individuals (condom campaigns influence an individual, relationships among individuals consider individual level desirability of concurrency and age-disparity, HIV transmission considers time-since-infection), rather than to an aggregate sub-portion of the population. The individuality of events allows us to investigate the dynamics of an epidemic at a fine grain level. This in turn allows us to also model intervention methods and their potential effectiveness.

Parameters	Value	Justification
Population		
Population size	200 (100 male, 100 female)	This is the largest population we can run within a reasonable amount of time.
Initial infection	0.15	The approximate prevalence of HIV/AIDS in South Africa [27].
Age Distribution	70, 4	Scale, and shape parameters for Weibull [26].
Partnering Values	0.5, 0.5	α, β parameters for beta distribution. Set through experimental comparison to sexual behavior data [9].
Formation Event		
Baseline factor	2	See 2.8 Calibration and Validation
Current relations factor	0	
Mean age factor	-0.005	
Last change factor	0.014	
Age difference factor	0.1	
Mean age growth	0.4	
Mean age dispersion	0.154	
Preferred age difference factor	-0.18	
Dissolution Event		
Baseline factor	2.6	See 2.8 Calibration and Validation
Current relations factor	-0.23	
Mean age factor	-0.057	
Last change factor	-0.015	
Age difference factor	0.08	
Mean age growth	1.917	
Mean age dispersion	0.476	
Preferred age difference factor	-0.265	
HIV Transmission Event		
PTSA	0.032	[3]
Sex acts per week	2	[9]
Condom Distribution		
Risk reduction	0.80	This reduction incorporates inconsistent use [39]
Condom cost	$as = 2e^{cd/20} - 2$	We experimented with different cost curves, but found little difference.
Male Circumcision		
Risk reduction	0.50	Reduction for males only [38]
Circumcision cost	$cp = as/50$	[20]
Antiretroviral Therapy		
Risk reduction	0.96	[11]
ARV cost	$pa = as/500$	[31]

Table 1: Table of parameters, values, and justification used in the simulation model.

2.5 Initialization

At initialization 100 males and 100 females are created. The individuals are assigned ages from a Weibull distribution with scale 70 and shape 4 [26]. Each individual is assigned a random value from a beta distribution with $\alpha = 0.5, \beta = 0.5$. This value allows heterogeneity within our population so that some individuals with higher values are more likely to form relationships, and individuals with lower values are less likely to form relationships. Figure 1 shows the distribution ages and partnering values at initialization.

Relationships are allowed to form and dissolve until relationship dynamics are in a steady-state (two years). HIV is then introduced into the system through infecting 30 (15% of the population) randomly selected individuals [27].

2.6 Submodels

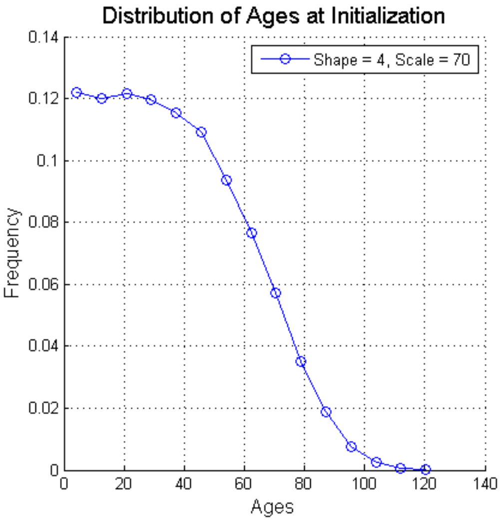
Our submodels are made up of the events that occur. Each event has a specific hazard function that determines the time till it occurs.

Formation. The event of relationship formation between male i and female j is based the hazard function

$$h_{ij} = exp(\alpha_1 u + \alpha_2 w + \alpha_3 (x - 15) + \alpha_4 y +$$

$$\alpha_5 \frac{1}{x\alpha_6\alpha_6''} |m - f - x\alpha_6\alpha_6'|).$$

Where u is the mean of the two individuals partnering values, w is the combined number of current relations, x is the mean age of the couple, y is the time since last change in



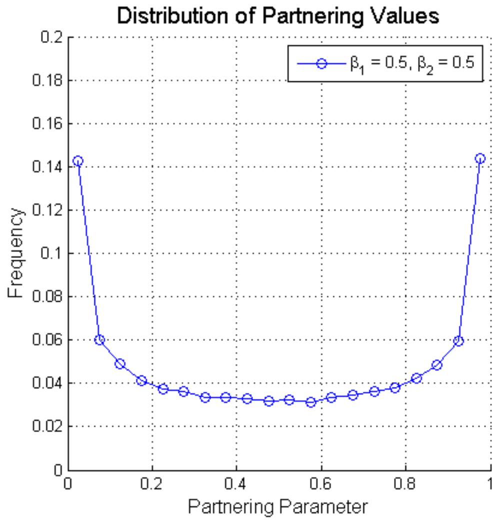


Figure 1: The distribution of ages (left) and partnering values (right) at initialization. Ages pulled from a Weibull distribution with scale 70, and shape 4, which is consistent with the age distribution of South Africa. Partnering values are pulled from a beta distribution with $\alpha = 0.5$ and $\beta = 0.5$, which produced a heterogeneous population similar to our observed sexual network (see Section 2.8 Calibration and Validation)

relationship status (the last time either the male or female was an actor in a formation or dissolution event), m is male age and f is the female age. All others (i.e. all α_i) are constants with values set during calibration. For example, α_5 is the age difference factor, and $\alpha_6, \alpha_6', \alpha_6''$ determine the preferred age difference. While HIV in men who have sex with men (MSM) is of concern, homosexual relationships are not considered in our model for simplicity. Relationships only formed between individuals older than 15 years. Figure 2 shows a graphical representation of some elements of the hazard function.

This means that every relationship between every pair of individuals has a baseline of hazard of forming of $e^2 = 7.39$. This hazard is decreased multiplicatively based on the above attributes. For example, consider a 22-year-old male (currently in one relationship, last ended a relationship 6 months [0.5 years] ago, and last started a relationship 1.2 months [0.1 years] ago) with a partnering value of 0.8, and a 19-year-old female (currently in no relationships, last ended a relationship 3 months [0.25 years] ago, and last started a relationship 2.4 months [0.2 years] ago) with a partnering value of 0.9. The hazard of a relationship forming is given by

$$exp((2.0 \times 0.8 \times 0.9) + (0.1 \times 1) + (-0.004 \times (20.5 - 15)) +$$

$$(0.01 \times 0.1) + (-0.1 \frac{|22 - 19 - (20.5 \times -0.181 \times 0.154)|}{20.5 \times -0.1812 \times 0.1544}))$$

$$= 8.51.$$

For random numbers 0.1, 1, 10, and 100 the time till relationship formation is 0.05, 0.43, 4.27, and 42.74 years respectively (random numbers are $(0, \inf)$ with expected value of 1). Note that even though the male is already in a relationship, there is a possibility of him forming another relationship with another female.

Dissolution. Once a formation event occurs, the event of the relationships dissolution becomes a possible event. The hazard of a relationship between male i and female j dissolving (breaking up) is based on a hazard function of the same form as the formation hazard function, but with different constants (see Table 1). Our sexual network then emerges from a series of formation and dissolution events.

HIV Transmission. Infection can occur in sero-discordant relations, i.e. relations in which one partner is infected and the other is not. The event is scheduled to occur relative to the hazard $-\log((1 - PTSA)^S)$. Where S is the number of sexual acts per week, and $PTSA$ is the probability of transmission per sexual act.

Condom Distribution. Unlike the random events, interventions are scheduled to occur at a specific time (e.g. five years into the simulation) and is therefore independent of a hazard. We consider different targeting schemes for condom distribution which leads to different individuals possessing condoms. The intervention targeting strategies we considered were

1. Individuals currently in multiple concurrent relationships
2. HIV positive individuals
3. Younger individuals (males and females between 15 and 25)

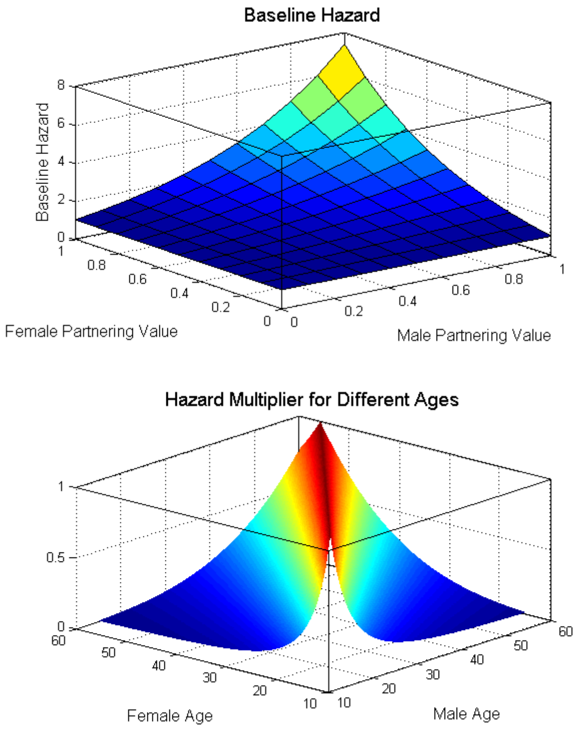


Figure 2: On the top, the baseline of a formation event is based on α_1 and the product of the two individuals partnering value. Individuals with higher partnering values will have a higher baseline for forming a relationship. On the bottom, the hazard is decreased multiplicatively as two individuals age difference moves further from the preferred age difference.

4. Individuals who have a high perceived risk (their partners are in more than one sexual relationship)

5. Random individuals (no targeting).

At the start time of an intervention, we find targeted individuals and mark them as influenced by the condom distribution campaign. One influenced individual consumes one distributed condom. Note that this means a "distributed condom" does not equate to using a single condom in a single sex act, but is instead analogous to a single individual being supplied with many condoms.

We make the assumption that we find targeted individuals with 0.8 probability (we account for the fact that finding specific individuals is difficult). Individuals influenced by a condom distribution campaign have their infectivity reduced by 80% [39]. While condoms are known to decrease infectivity by a significant amount [2], this lower number reflects the possible effects of inconsistent use.

We assumed a decreasing return to scale between condoms distributed and amount spent: $as = 2e^{cd/20} - 2$, where as is the amount spent in thousands of USD and cd is the condoms distributed by the campaign. This means that in order for a campaign to distribute 60 condoms it would need to spend $42,000.

Male Circumcision. Male circumcision (MC) is similar to condom use in that it reduces the PTSA, but has the added advantage of being used consistently [31]. While condoms reduce PTSA by nearly 100%, male circumcision can reduce PTSA by about half as compared to without circumcision [38]. We implemented a single MC campaign which does not target any group; at the start time of the intervention random males were chosen to have be circumcised. PTSA *to* males influenced by the MC campaign is reduced by 50%. Unfortunately, circumcision does not seem to hold any benefit to females other than their partners are less likely to become infected [14].

We assumed a linear relationship between circumcisions performed and amount spent: $cp = as/50$, where as is the amount spent in thousands of USD and cp is the circumcisions performed. This comes from the fact that a single circumcision costs about $50 to perform [20]. This means that in order for a campaign to reach 60 males it would need spend $3,000.

Antiretroviral Treatment. TasP as an intervention method not only reduces HIV related deaths, but also has the ability to reduce the infectivity of an individual by means of decreasing his or her viral load [33]. Therefore, treating a significant portion of the population with ARV can decrease HIV incidence. Our implementation of TasP finds HIV infected individuals with probability 0.8 and reduces their infectivity by 96%.

We assumed a linear relationship between patients on ARV and amount spend: $pa = as/500$, where as is the amount spent in thousands of dollars and pa is the number of patients on ARV. This comes from the fact that ARVs cost about $500 per person per year [31].

2.7 Search Heuristics

The optimization problem we aimed to solve had an objective of minimizing cumulative incidence with the constraint that amount spent could not exceed the prescribed budget of $1,000,000 (about $150 per person per year). Therefore a solution is a set of starting times and amount of money to spend on each intervention. The quality of a solution depends on cumulative incidence averaged over 10 runs. The cost depends on the two parameters "starting time" and "spending amount". The cost of a solution is determined by the number of years each campaign is implemented (calculated as the number of years between the start of the campaign and the end of the simulation) multiplied by the number of condoms distributed, or individuals on ARVs. Males circumcision does not incur a yearly cost – cost is calculated just once. A feasible solution spends less than the budget. The optimal solution has the minimal cumulative incidence possible.

The simulated annealing algorithm is a walk through the parameter space. Our implementation always accepts improving moves, and accepts unimproving moves with probability $exp(e - e_{new})/T$, where e is the quality of the current solution, e_{new} is the quality of the new solution, and T is the temperature of the system. Temperature decreased relative to the current time step k at a rate of $T(k) = 0.96^k$. Maximum number of steps was 100.

The genetic algorithm produces 10 random solutions, assesses their quality, then produces a new set of 10 solutions by performing a crossover of the best 5 solutions. This procedure is repeated for 20 generations. Crossing over two solutions means taking the first p values of the first solution, and the last $(n-p)$ values of the second solution, where n is the total number of start times and spending amounts, and p is a uniform random $[0, n]$.

We first applied the search heuristics to find the best combination of condom distributions, and then applied them to find the best combination of random condom distribution, male circumcision campaign, and a roll out of TasP.

2.8 Calibration and Validation

Inference of appropriate parameters values, or calibration, took part in three steps: (1) the simulation was run for a specific set of formation and dissolution parameters for 50 years (to ensure relationship equilibrium and to have a large number of individuals who became sexually mature within the simulation). (2) From the resulting sexual network we calculated the distribution of partner ages, age differences within relationships, total number of lifetime sexual partners, level of concurrency in the sexual network, and the duration of relationships of *males* in the simulations. (3) We then compared these summary statistics to the responses from *males* that took part in the Cape Town Sexual Network survey [9]. We compare to only male data because of possible gender-related sampling bias. The study took place from July 2011 to February 2012 and was located in three disadvantaged communities near Cape Town, South Africa.

Table 2 contains the actual values from the survey compared to simulated values from our model. With each is a chi-squared p-value, our proxy for similarity. P-value greater than 0.05 means that the values are statistically similar. Based on these statistics we believe that the produced population resemble a real population.

Figure 3 shows a graphical comparison of HIV prevalence in South Africa to the simulated prevalence. While the two curves are not identical we hold that the two are similar, and note that additional calibration may be necessary to achieve stronger results.

3. RESULTS AND DISCUSSION

3.1 Condom Distributions

Independent runs of the condom distribution strategies (Figure 4) show that all strategies have an effect on reducing cumulative incidence. The most effective strategy seems to be targeting HIV-positive individuals and individuals in concurrent relationships (high risk). Targeting the younger population seems to have less effect, likely because the number of targeted individuals is low. This results in unused condoms and higher cumulative incidence. Specific age group

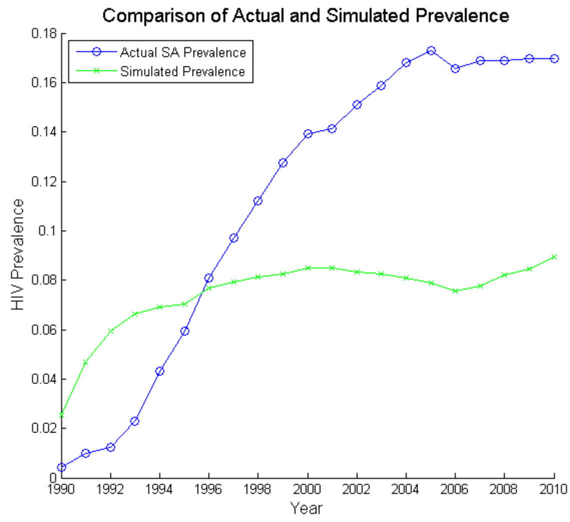


Figure 3: The actual HIV prevalence in South Africa and the simulated HIV prevalence are similar. For the validation, formation and dissolution parameters described in table 1 were used. Relationships were allowed to form and dissolve for 10 years before HIV was introduced and transmission events were allowed to occur. The above prevalence is the average over 10 runs with a population of 100 men and 100 females.

targeting was hypothesized to have an effect through protecting a large cohort and averting infections to the younger population (<15 years) reaching relationship formation age. This did not seem to play out however.

The fact that some condoms go unused implies that a better scheme would be a combination of condom targeting strategies in which each intervention spends at their maximal level of effectiveness and allocates the saved funds to other strategies. That is to say that it may be worthwhile to delay the start time of a certain intervention (and consequentially save some of the budget) since these individuals may not be infected for many years into the future. For example, it may be practical to delay the start of an intervention that targets individuals with a high perceived risk because they are unable to become infected until their risky partner becomes infected. This in turn reduces cost and allows more of the budget to be allocated to another condom distribution such as one that targets HIV positive individuals.

The optimization algorithms found a solution to the combination prevention problem for different prevention start times and amount spent as seen in Table 3. The total cost is $987,385, about the same as the independent runs of condom interventions, but the cumulative incidence of combination prevention (Figure 5) is lower than targeting high risk individuals and much lower than no interventions.

The combination prevention has a lower cumulative incidence because it is able to fund each intervention at it's locally optimal cost-effect point and therefore distribute more condoms to more people with less waste. Additionally the

Summary Statistics	Survey Value	Simulated Values
Age of Partner (years)		
Median	26	27.8
Lower Quartile	21	21.3
Upper Quartile	39	34.9
Age of Partner (%)		
≤24 years old	35.6	34.7
25-34 years old	24.9	38.7
35-44 years old	14.3	12.7
≥45 years old	25.2	12.1
Age Differences (years)		
Median	3	4.2
Lower Quartile	0.5	1.7
Upper Quartile	6	8.6
Age Disparate (%)		
≤5 year age difference	65	49.5
5-9 year age difference	17.8	28.4
≥10 year age difference	17.2	22.1
Total Lifetime Sex Partners (%)		
1	8.7	14.5
2-5	42	62.4
6-14	22.1	22.4
15+	27.2	0.7
Cumulative Concurrency (%)		
Yes	50.9	12.4
No	49.1	87.6
Duration of Relations (weeks)		
Median	17	27.1
Lower Quartile	1	8.6
Upper Quartile	43	95.7
Duration of Relations (%)		
1	26.6	8.0
2-39	48.5	52.1
40+	25.1	39.9

Table 2: A comparison of sexual network statistics from survey data and simulation. Since the data about the sexual relationship network is imperfect it is not of much consequence that simulated values and data values are not exact. We instead note that values are similar and take this as evidence that our model is similar to the actual sexual network.

Intervention	Start Time	Condoms
Random	17	42
High Risk	10	10
HIV Positive	2	40
Age Specific	12	1
High Perceived Risk	4	42

Table 3: The starting time and amount to spend on each intervention for our condom combination prevention strategy. The cost for this combination of condom distributions interventions is $994,971.

susceptible or infected population is not a single group but a combination of groups. Therefore the intervention that targets many different groups in combination is likely to be the most effective. This is perhaps why the random strategy performed well in independent runs: It was able to reach many different groups. However this intervention is not implemented until later in the combination prevention solution. This is likely because combination prevention allows us to target these groups specifically through the other interventions, diminishing the necessity of a random distribution campaign.

3.2 Combination Prevention

Figure 6 shows the cumulative incidence male circumcision, TasP, the random targeting condom distributions, and a combination of prevention strategies. Table 4 shows the values of the combination prevention solution. These values additionally indicate the values for each intervention run independently.

The solution to combination prevention performs many male circumcisions, likely because each is relatively cheap. It also spends heavily on TasP, which is comparatively expensive, but also has the most dramatic effect on HIV cumulative incidence within our model. However, combination prevention achieves the best reduction in cumulative HIV incidence.

4. CONCLUSIONS AND FUTURE WORK

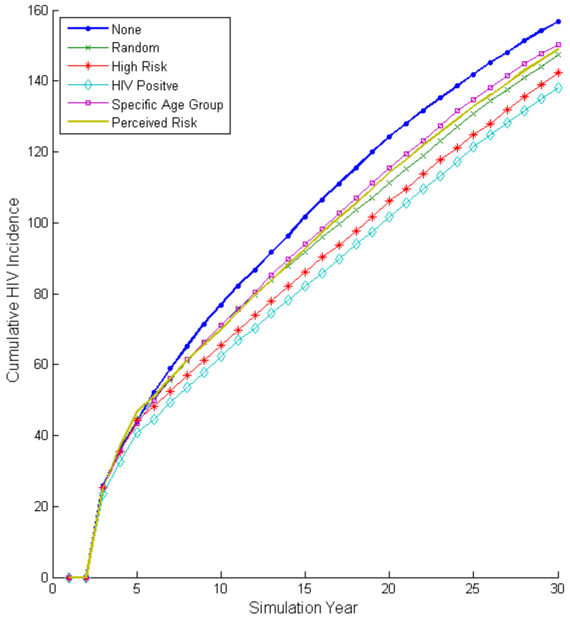


Figure 4: The cumulative incidence for the five described targeting strategies and the "no interventions" strategy averaged over 50 runs. The cumulative incidence shows that all interventions reduce the cumulative incidence, although targeting HIV-positive and those with high risk seem to be the most effective. The other interventions reduce cumulative incidence from doing nothing, but not much difference can be seen between random, high perceived risk, or age-specific targeting. However, all of the interventions are wasteful as none use all the allocated condoms. Each intervention was started in year five, and was allowed to distribute 54 condoms. The cost was the same for all interventions at $996,000 which is within our $1,000,000 budget.

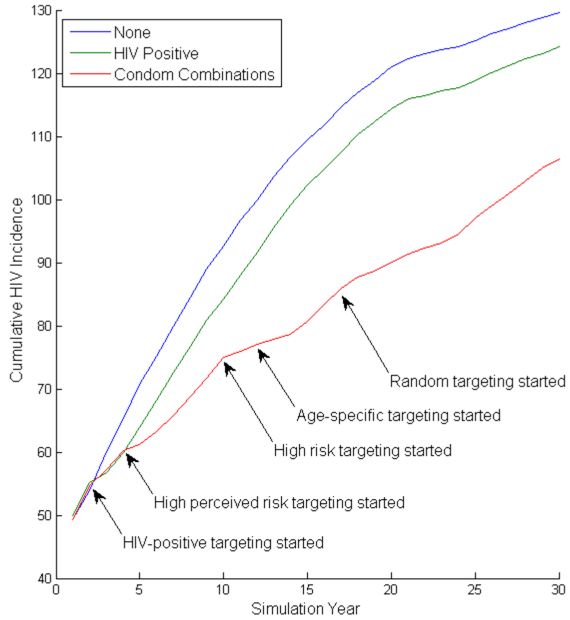


Figure 5: The cumulative incidence for no interventions, for targeting HIV-positive individuals, and for a combination of condom targeting strategies averaged over 50 runs. The figure shows the overall trend that condom combination prevention has a lower cumulative incidence than high risk targeting, which has a lower cumulative incidence than no intervention at all. The reason for this is that the condom combination prevention accounts for diminishing return and allows each intervention to be funded at the best level and is able to redirect unused resources to other interventions.

No current intervention is likely to be a silver bullet to the HIV epidemic, and none is likely to be found. Therefore a combination of prevention methods is likely the most effective solution. While the most intuitive strategy is to spend maximally on each intervention, this is not always possible due to limited resources. In this paper, we have shown that combination of prevention can be more effective at minimizing cumulative HIV incidence than any single strategy, and described a method for finding the best possible combination prevention.

Other metrics of the quality of interventions should also be considered: cumulative incidence only tells one story. Additional consideration should be given to more time sensitive outcomes like the number of AIDS orphans averted or number of orphan years averted. These other metrics may provide greater support for the life-prolonging ART treatment intervention and yield a different combination of preventions. Future work will consider multi-component objectives.

While we have many every effort to make informed parameter choices, we acknowledge the fact that there may be a disconnect between our simulation and the real world. While we have validated our model, the way at which HIV diffuses through the network relies greatly on the relationship model we have chosen. We believe this work is nonetheless important since it provides evidence for combination prevention and suggests methods for determining the most efficacious allocation of resources.

While we maintain that an initial population of 200 suffices as a proxy for a larger population, simulations run with a more realistic population size could lend more credit to the study. However, due to the precise nature of the algorithm large populations can take a significant amount of time, even when run on a cluster. For this reason steps to speed up the simulation such as tau-leaping or distributed computing may be helpful in future investigations.

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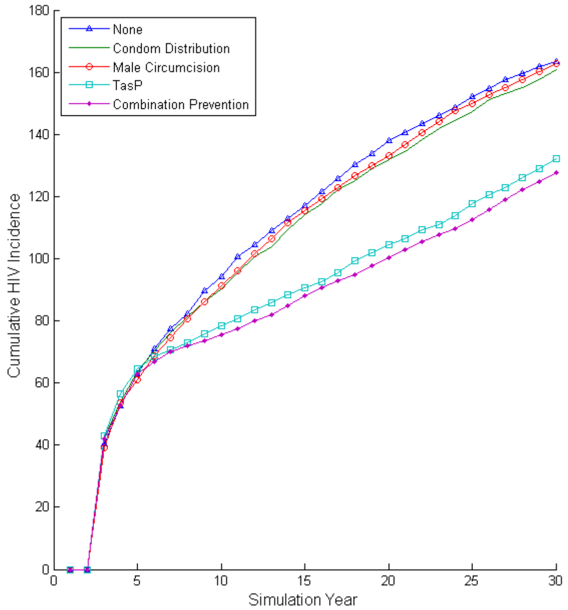

Figure 6: The cumulative incidence for no interventions, random targeting condom distribution intervention, male circumcision, TasP, and combination prevention. Our combination spends heavily on TasP, but also relies on condom distributions and male circumcision to achieve an even lower cumulative incidence. This shows that funds may be better allocated to a combination of prevention methods instead of any single interventions. The total cost was $995,870 for the combination prevention scheme.

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Intervention	Start Time	Spend Variable
Condom Distribution	5	28
Male Circumcision	5	100
ARV Treatment	5	64

Table 4: The starting time and amount to spend on each intervention for our combination prevention strategy. All preventions start early, but have different levels of implementations as indicated by the spend variable. The spend variable is determines the condoms distributed, circumcisions performed, or patients on ARV respectively.

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