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The Interaction of Risk Network Structures and Virus Natural History in the *non-Spreading* of HIV among People Who Inject Drugs in the Early Stages of the Epidemic

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Abstract

This article explores how social network dynamics may have reduced the spread of HIV-1 infection among people who inject drugs during the early years of the epidemic. Stochastic, discrete event, agent-based simulations are used to test whether a “firewall effect” can arise out of self-organizing processes at the actor level, and whether such an effect can account for stable HIV prevalence rates below population saturation. Repeated simulation experiments show that, in the presence of recurring, acute, and highly infectious outbreaks, micro-network structures combine with the HIV virus’s natural history to reduce the spread of the disease. These results indicate that network factors likely played a significant role in the prevention of HIV infection within injection risk networks during periods of peak prevalence. They also suggest that social forces that disturb network connections may diminish the natural firewall effect and result in higher rates of HIV.

Resumen

Este artículo explora cómo las dinámicas de redes sociales pueden haber reducido la propagación de la infección por VIH-1 entre las personas que se inyectan drogas durante los primeros años de la epidemia. Estocásticas, eventos discretos, las simulaciones basadas en agentes se utilizan para probar la de si un "efecto cortafuegos" puede surgir de los procesos de auto-organización, al nivel

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Compliance with Ethical Standards

The authors declare that they have no conflicts of interest. All original data collection with human subjects was carried out under Institutional Review Board supervisions, and informed consent was obtained from all individual participants included in the study. The current study involves secondary data analysis using only de-identified data. This article does not contain any studies with animals performed by any of the authors. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

de actor, y si este efecto puede dar cuenta de las tasas estables de la prevalencia del VIH por debajo de la saturación de la población. Repetidos experimentos de simulación muestran que, en la presencia de brotes recurrentes, agudos, y altamente infecciosos, las estructuras micro-red se combinan con la historia natural del virus del VIH para reducir la propagación de la enfermedad. Estos resultados indican que los factores de la red probablemente jugaron un papel importante en la prevención de la infección por el VIH dentro de las redes de riesgo de inyección durante los períodos de pico de prevalencia. Además, sugieren que las fuerzas sociales que perturban las conexiones de red pueden disminuir el efecto cortafuegos natural y resultan en tasas más altas de VIH.

Keywords

Risk Networks; PWID; Firewall Effect; Simulation

Introduction

The interaction of human social dynamics and disease spread lies at the roots of epidemiology. The use of computer simulation to investigate this interaction is new, (1,2); newer still is the inclusion of specific social network models to capture dimensions of human interaction that go beyond random or spatial mixing (3–5). Such approaches hold out the promise of more realistic understanding of the actual spread of disease and the potential to discover the source of epidemic differences between epidemics even where the pathogens at the heart of the epidemic are the same. As Bauch and Galvani point out, “[t]he role of disease-behavior interactions in outbreak heterogeneity has received little attention because of the difficulty of quantifying social feedbacks…” (6). Here we propose one such a quantification and a system of social-network feedback to help explain known but as yet unexplained patterns of HIV prevalence in people who inject drugs (PWID).

Globally, populations of PWID in the early stages of the epidemic demonstrated HIV+ rates that stabilized at levels well below population saturation (7). More so, sub-saturation stabilization takes place despite the presence of ostensibly “small world” social dynamics (8–10), and ongoing risk-intensive behaviors (such as needle and equipment sharing or sex in the context of drug use (11,12)) that combined highly infectious, early-stage HIV outbreaks (13,14) with highly-connected risk networks (12) and significant populations of uninfected individuals. These levels of high connectivity and concurrency go well beyond what is seen in sexual risk networks. All of these factors would seem to point toward infection prevalence rates that would, in the absence of testing, behavior change, or intervention strategies, continue to climb to near-saturation levels. Why this did not happen remains an open question.

Wide-scale, direct evidence for prevalence levels in the early stages of HIV epidemic are limited because prevention interventions often preceded accurate prevalence measurement (15). Reconstructions point to an interesting contrast with other pathogens circulating in same population at the same time, however. While HIV+ rates among PWID in New York stabilized around 50% (7), Hepatitis C (HCV) infection in the same population stabilized at

80% (16). Further, such high prevalence levels for HCV are not limited to PWID in New York; world-wide samples of PWID regularly show HCV prevalence rates of 70-80% (17). While there are significant differences between the epidemiology of the two viruses, the contrasting prevalence levels raise the question of why HIV rates remained lower even prior to testing and drug user awareness of their own HIV status. Put another way, high levels of HCV side-by-side with lower, stable rates prevalence of HIV suggest that PWID risk dynamics were, in the early 1970s through 1980s, capable of producing near saturation prevalence rates for blood-borne infections passed through needle, equipment, and sexual risk behaviors (18,19). Given this, the question remains why HIV infection among PWID did not, during these same years, achieve similar prevalence levels as HCV in these same networks.

To address this question—how stable prevalence rates of HIV well below population saturation might arise and be maintained in the absence of prevention and individual knowledge of infection—we describe the results of an agent-based, network-actor simulation experiment that addresses this question at the scale of a large and concentrated PWID population such as that found in New York City in the early days of the epidemic. The goal of this research was to use the earliest network data available from the HIV epidemic to parameterize a transmission model that in turn matched historic prevalence and incidence rates for the epidemic in that location at the endpoint of the period under consideration. While such data necessarily post-date the start of the epidemic by nearly two decades, they represent risk interaction at roughly the peak of infection prevalence, at a time when efforts to stem the spread of HIV remained small compared to the years that would follow (15). When our simulation is parameterized with agent network behaviors drawn from data collected prior to widespread testing and infection prevention/treatment, the resulting simulations can be investigated for social/risk network effects on virus-transmission dynamics that potentially explain the macro-level disease dynamics from this same time period (including, especially, stable sub-saturation prevalence rates). Further, by employing “zero intelligence” agents (20), we also indirectly test the hypothesis that HIV rates can stabilize below saturation in the absence of individual knowledge of infection, ongoing behavior changes on the part of drug users, or intervention programs aimed at infection prevention, all of which have subsequently reduced HIV rates among PWID to levels well below their peak in the early 1990s (13). In this way, our aim is to determine whether risk network properties *alone* are capable of producing the observed population level prevalence dynamics based solely upon the behavioral dynamics observed among PWID and their networks in New York City between 1990 and 1993. As such, we seek to mimic a situation where community education was still in its early stages and interventions were rare, and then simulate how the epidemic spreads in these conditions.

At an abstract level, this strategy aims to uncover “emergent” epidemiological phenomena—disease dynamics that result from the aggregate behaviors/effects of a population, but which are not reducible to those behaviors/effects. Examples of emergent phenomenon from the natural world have been known for some time, and are now recognized as relatively common. In public health, these phenomenon have only lately begun to receive widespread scholarly attention (21,22).

In this investigation we were guided by a hypothesized network mechanism for stable sub-saturation prevalence: the “firewall effect” proposed by Friedman et al (23). More than 15 years ago, these authors proposed that structural features of PWID risk networks alone could combine with the specific epidemiological natural history of HIV-1 virus to insulate uninfected segments of the network from highly transmissible, early stage infections. This is possible because of a feature of HIV infection and its interaction with the human immune system that sees viral loads of newly infected individuals spike in the first 6 weeks of infection, then moderate to relatively much lower levels. Chronic viral loads then remain low relative to peak levels for an extended length of time, often for many years, even in the absence of treatment.

This period of acute, highly infectious and asymptomatic infection represents a major challenge to stemming the spread of HIV (24). Yet as Friedman et al pointed out at the time, to the extent that individuals with lower, chronic infections were immune from reinfection and the recurrence of extremely high viral loads, it is possible that their location at key breakpoints in a risk network could potentially slow the spread of new, highly infectious outbreaks arising in one area from spreading to other non-infected segments of the network: hence the concept of a network “firewall” (23). The research design of the study from which those authors were working limited what the paper could show, however, because the data were cross-sectional and lacked data on viral loads or time since infection. As such, the question remained whether individual-level network attachment dynamics such as those hypothesized by Friedman and colleagues could result in placing older infections at key network locations even while some of those around them remained uninfected.

To pursue this hypothesis, we developed a succinct measure of network firewalling, and here demonstrate that, in simulation, a firewall effect similar to that described by Friedman et al can arise out of the self-organizing processes seen in real-world PWID networks, absent individual knowledge of infection, changes in pre-/post-infection behavioral profile, and any outside interventions aimed at reducing viral load or agent risk behaviors. From these results, we conclude that the firewall effect likely played a role in the sub-saturation prevalence seen in New York City by Des Jarlais et al (7), and perhaps elsewhere as well.

Methods

Methodological and Data Background

This research is possible due to significant advances in two areas: the availability of high-quality risk network data from the early stages of the epidemic, and significant gains in network simulation strategies developed in the last several years. To date, risk network research among PWID has produced considerable data on HIV-1 infection profiles and equally detailed data on the broad demographic and behavioral profiles of injecting communities and their risk behaviors. Risk networks are now widely recognized as a critical construct in understanding infection patterns, as they, as much as the human bodies in which infection happens, represent the natural environment in which transmission takes place and through which infection propagates (25).

Here we draw on data collected by Friedman and colleagues for the Social Factors for HIV Risk study (SFHR) (26). Conducted between 1990 and 1993, SFHR was a large cross-sectional, mixed methods data collection project that asked 767 PWID recruited in out-of-treatment settings about their risk networks and HIV risk behaviors in the prior 30 days. Interested in both individuals' network composition (namely, the presence of high-risk partners) and sociometric risk position, the SFHR study produced several major findings relevant to risk populations with high HIV prevalence and low secondary incidence (12,27). In all, SFHR documented 662 connections between study participants that were sorted into 92 connected components, including a large connected component of 230 individuals that contained a 105-member core exhibiting notably higher HIV prevalence (12). Prevalence data from the earliest stages of the epidemic are not available, as considerable self-organization and changes in risk behavior had taken place prior to even the earliest network research (28,29) . However, the SFHR data used here represents a "best available" strategy. A full description of the SFHR factors used in this study is published elsewhere along with the derivation of the actor model (11). Agent-level behavioral factors included connection preferences that weighted known tendencies toward "homophily"; i.e. clustering on the basis of age, ethnicity, and individual network size (such that those with high numbers of partners were likely to have risk partners with a similarly number of partners, and vice versa. The model also included "heterophily" for female genders (where female injectors were disproportionately connected to male injectors), and network structural factors that include a preference for "network transitivity" (the tendency of individuals to choose among the partners of their current partners when expanding their risk networks).

Modeling risk networks as (stochastic) discrete dynamical systems provides an opportunity to understand the long-term behavior of PWID risk networks themselves—well beyond what can be seen by considering their constituent individuals in isolation or at a single time (30). Toward this end, epidemiology has taken advantage of breakthroughs in two somewhat distinct simulation areas: agent-based stochastic modeling (ABM) (1) and social network models based on exponential random graph methodologies (ERGM) (31). Both have their advantages. ABMs can contain multiple types of agents and derive macro-level characteristics entirely from the behaviors of agents themselves. These models have shown success in public health research (32–35), spawning a range of useful platforms such as EpiSimS (36). The resulting models have one significant drawback, however, that limits their applicability to real world populations of PWID: social interaction in ABM is normally modeled as a process of random, spatial mixing. In contrast, ERGM-based simulation produces models of *networks* whose link structure follows stochastic, dyadic probabilities that can incorporate the influence of network structure on actor pair likelihoods (37). Here the loss of actor-level agency and absence of multiple actor types obeying distinct attachment rules is balanced by avoiding the problem of fitting degree distributions under conditions of network change. The result is that ERGM maintains the structured, network framework missing from random mixing ABM approaches. Current ERGM platforms include RSIENA (38) and Statnet/EpiModel, both of which have been used to successfully model HIV infection (39,40).

Recognizing that aspects of both of these approaches contain features necessary for the modeling of large risk networks (41), we developed a simulation platform that contains

features of both. This platform, and its mathematical/computational basis are described elsewhere (42). In brief, the simulation strategy was to represent network participants as finite state agents defined by a list of risk partners, rates of risk interaction, rates of partner "churn", and a number of fixed and variable attributes that conditioned attachment transitions and risk probabilities. These agents then acted in a discreet event framework where a master scheduler tracked agent requests for actions according to a detailed timeline, and agents scheduled events and determined event outcomes according to stochastic throws against probabilities conditioned on their own traits and on the state of their network neighborhood. The overall simulation strategy conforms to protocols described by Guizani et al (41) and employed in large scale, stochastic, discrete event frameworks more generally.

Simulation and Analytic Approach

This platform was used to simulate large, dynamic networks of PWID ranging from 1000 to 100,000 network actors for periods of 15 years. The simulations were parameterized for actor attributes and connection tendencies listed above (age, ethnicity, and network size homophily; gender heterophily; and network transitivity) according to the values found in the SFHR data (11). Per risk act HIV transmission rates were tuned to match observed HIV incidence rates for New York City during the early 1990's. Large simulations of 25,000 actors entailed more than 15 million risk events, more than 350,000 partner changes, and the inclusion of more than 75,000 distinct agents (as agent migrated into and out of the network over simulation time). Each simulation began with a HIV prevalence rate of 0.01%, which generally grew quickly to roughly 50-60% before stabilizing within that range. The simulation algorithm is presented elsewhere in greater detail (43).

The primary outcome of interest in this paper is the firewall effect proposed by Friedman et al. To quantify the firewall effect, a measurement protocol is introduced that allows researchers to calculate the extent to which a network, frozen at a given point in time, exhibits firewalled characteristics. This measure is calculated in a series of steps. First, by sampling a simulated network at a single point in time, we extract for analysis purposes a static "firewall analysis" network. For purposes of calculating the firewall measure, we remove from the analysis network all of the chronically infected nodes (i.e. those simulation actors with a positive status and whose infections are older than 3 simulation months). Removing these individuals produces a "risk-centric" view of the network containing only uninfected (highly susceptible) and newly infected/acute (highly infectious) nodes and their connections to each other. Figure 1 shows two different examples of analysis network scenarios (A & B) and how an analysis network is viewed before (socio-centric) and after (risk-centric) the removal of all chronically infected nodes. In general, the effect of this step is to produce an analysis network where the formerly well-connected simulation network becomes a new network that is often fragmented into a range of distinct components (now containing only acute and uninfected nodes and their mutual connections) drawn from an actual simulation snapshot. Obviously, some of these components will contain recently infected (acute) individuals and some will not.

It is important to note that the extraction of the analysis networks, and our removal of chronic nodes from them, are only used to calculate the extent of network firewalling, and

do not interrupt or alter the simulation. The actual dynamic simulation continues in the background with all nodes and edges that existed prior to the analysis “snapshot”. In the simulation, all nodes (chronic, acute, and uninfected) still engage in risk acts with their network neighbors, change risk partners, and eventually leave the network due to age, late-stage illness, or migration. Thus, in the simulation infection can take place between chronically infected nodes and uninfected nodes, though in keeping with the existing literature the odds of this event are smaller than the likelihood of transmission in acute/uninfected pairs. The removal of chronic nodes in the firewall analysis networks is thus only for purposes of measuring the firewall effect in the ongoing simulations, not to take the place of those simulations, nor to ignore the risk of infection from chronic nodes to uninfected neighbors in the simulation process. Rather, given that chronic nodes’ transmission risk to their neighbors is considerably lower (as a result of lower viral loads) than nodes in an acute infection state, the firewall measure is meant to quantify the effects of that difference at the level of the network as a whole.

Using the analysis graphs, a firewall measure can then be calculated as the proportion of those uninfected nodes found in components without an acutely infected node, as a proportion of the total number of uninfected individuals in the entire network. The example networks in Figure 1 demonstrate two calculations of this measure on networks with identical structures, and equivalent incidence (acute), and prevalence (overall) rates of HIV infection. The example is meant to demonstrate how the different placement of chronic versus acute infections in the network can results in very different future infection scenarios. In Scenario A, there is a greater likelihood of future infections than in Scenario B due to the direct exposure of uninfected nodes to highly infectious acute nodes. This is shown by the distribution of acute nodes across four network clusters in Scenario A while they are restricted to two components in Scenario B. In Scenario B, the chronically infected nodes in the socio-centric network work as “firewalls” to shield uninfected clusters from acute, highly infectious outbreaks, as can be seen in the risk-centric view of this same configuration. This difference between the two scenarios is captured in the different firewall measures for Scenario A (0.474) versus Scenario B (0.947).

Calculated in this way, the firewall measure has a lower bound of zero and an upper bound of one. A value of zero would occur in a network where all uninfected nodes, after a hypothetical removal of chronically infected nodes, would be found in a component that also contains an acutely infected individual. Something approaching this situation occurs at the beginning of each simulation, as the hypothetical removal of the small number of chronic nodes does little to fragment the network into separate components because so few of those infected have reached a chronic state, and acute infections are widespread and thus found in many components. At the other extreme, a measure of 1 would indicate that all uninfected nodes share connections only with chronically infected nodes or with other uninfected nodes. We note that the simulated networks never achieved a firewall value of 1, as would be the case in a network where only chronically infected and non-infected individuals are found. The reason for this is clear: even after the network reaches a steady prevalence rate, new (acute) infections continued to appear. In addition, the firewall measure is not meant to indicate full protection from infection for uninfected nodes. Rather, the measure indicates the extent to which uninfected portions of the network are removed from risk of infection by

acutely infected nodes, whose high levels of infectiousness might otherwise raise both prevalence and incidence rates above stable levels. As originally postulated, the firewall hypothesis does not discount the ongoing possibility of infection from chronic to uninfected nodes. Its sole concern was to explain why acute outbreaks did not spread. The firewall measure proposed here is meant to quantify the extent to which self-organizing network structures provide this sort of protection.

As noted above, in the simulation scenario used here, there is no change in agent behavior. That is, sub-saturation stabilization does not occur because chronically infected nodes change or are "trying" to prevent others from becoming infected as in serosorting or negotiated safety (44). Rather, in the case explored here, both risk and attachment behavior are held constant for all agent throughout the simulation. As such, any demonstrable firewalling (as indicated by a high firewall value) discovered in the simulation networks can only be attributed to an emergent "firewall effect" such as that hypothesized by Friedman and colleagues, whereby emergent network properties alone account for both the spreading and non-spreading of HIV seen in the simulations. In this way, we test a case where effective intervention strategies have not taken place at a large scale but where risk reduction efforts by the actors has taken part to some degree autonomously or due to small-scale interventions, though far less than would take place beginning in the mid-1990s.

Results

Multiple simulation trials across a range of network sizes showed that, in networks of more than 1000 actors, the sub-saturation stabilization noted by Friedman, Des Jarlais, and others (7,15) for the early years of the epidemic regularly appeared (Figure 2a). In all simulations, the prevalence of HIV in the simulated networks increased sharply before stabilizing between ~40% (at 60 months: mean 0.418, std 0.019) and ~55% (at 180 months: mean 0.516, std 0.098). This stabilization occurred while agent behavior and risk profiles were held constant and while new infections were consistently occurring in the networks. At the macro-network level, the combination of non-zero incidence amid a high percentage of uninfected nodes fits well with the observed phenomena that inspired the original firewall hypothesis (23).

When the firewall measure derived in these simulations is calculated at monthly intervals, the results show the presence of high levels of firewalling in networks of varying sizes (Figure 2b). For populations of PWID larger than 1000 actors, a relatively stable firewall value between ~65% (at 60 months: mean 0.684, std 0.029) and ~80% (at 180 months: mean 0.812, std 0.026) appeared a few months after the beginning of the period of stable prevalence rates. This would indicate that, of all the uninfected nodes in the network, 65-80% could potentially attribute their negative disease status to the presence of network firewalling. As such, we conclude that emergence of this sort of network firewall effect is likely, and at least in simulation, that it plays a large role in stabilizing HIV prevalence at levels well below saturation.

Given these results, and the emergence of both sub-saturation stabilization and high levels of firewalling, the question becomes whether and to what extent risk partner attachment

tendencies and local network dynamics can be seen to account for these macro-network phenomena. These questions are particularly important since the overall infection dynamics present in the population prior to stabilization contrast strongly with those occurring after the first two years, despite the fact that aggregate actor risk behaviors do not change.

An examination of the early simulation periods (months 1-20 in Figure 2a) shows that the number of infections rises quickly during the first months after the virus is introduced to the network. Here, it would seem, high infectiousness takes advantage of the small world nature of PWID networks (43,45), where a low network distance between clusters creates short paths between any two randomly chosen nodes. This small world character is partly due to the presence of network hubs: individuals with high numbers of partners.

The early infection of network hubs can be seen in the simulations. As shown in Figure 3a, acutely infected nodes had an average number of uninfected risk partners between 2 and 4 in the early stages of the simulated epidemic. Figure 3a also shows that, following an initial peak, new infections take place in nodes with decreasing numbers of uninfected partners. This is an indication that the network hubs—key connectors in the network because of their high number of partners—were infected early in the epidemic. After two years of simulation time, however, virtually all hubs have transitioned to a state of chronic infection. The new infections, after this time, are taking place among network agents with fewer and fewer partners. This can be seen in Figure 3b, which shows the total number of uninfected nodes connected to agents in a state of acute infection. After the initial, high incidence period, the number of uninfected nodes at high risk because of a risk network connection with a highly infectious acute node is much lower.

This makes intuitive sense in ordinary epidemiological terms. The more risk partners one has, the more likely one is to encounter a risk partner who is infected, particularly during periods of high incidence. As a result, outbreaks tend to spread quickly at first via highly connected individuals. Yet the two stage viral load dynamics—marked by very different levels of infectiousness in the acute and chronic phases—means that, as these hubs transition to low infectious chronic states, the number of uninfected agents who are exposed to highly infectious node drops rapidly. Of interest is the fact that, in simulation, this exposure remains low even as both infected and uninfected agents change risk partners, and new (uninfected) agents enter the network.

The latter point is critical. These results suggest a complex pattern of infection pathogenesis interacting with network structure which results entirely from regular patterns of making and unmaking risk connections among network members. Here, even as the network continues to “churn” (42), local level clustering continues to occur as agents carry out well-known rules of risk partner attachment that favor homophily and risk partners who are connected to one’s current partners (11,46–48). Interestingly, even in a dynamic situation in which risk relationships are frequently “rewired”, this rewiring does not result in the aggregation of large clusters of uninfected nodes. This is important as such a cluster would run the risk of a rapidly spreading outbreak once the virus is introduced within it.

Evidence of this can be seen in the simulations as well. When we examine “at risk” components (i.e. those that contain an acutely infected node; Figure 4a) we see that they diminish in size significantly after the first two years of the simulated outbreak. Initially, the number of at risk nodes in a single component is very large, on the order of the size of the simulated population. After the initial period of peak incidence (simulation months 0-20), the size of at risk components diminishes dramatically to an average level of 10 or lower. Relatedly, though at a much less dramatic scale, we see in Figure 4b that the average size of a firewalled component (a network component of uninfected nodes which does not contain an acutely infected agent) stabilizes after the first 24 months at a relatively small average size. The implication is that chronically infected nodes are in effect segmenting the network into very small, firewalled clusters.

This is important, since network churn ensures that all nodes continue to find new risk partners over time. Yet because the number of acute infections drops off significantly after the first wave of rapid spread, the number of components containing an acute infection is relatively low, and the likelihood that an uninfected node comes into risk contact with an acutely infected node is small. As such, despite uninfected nodes seeking out and finding new risk relationships, this does little to change their overall risk of infection. The bulk of their new connections will be nodes with chronic infections and uninfected nodes. This is true despite a high number of risk partner changes. In the simulations shown in Figures 2-4, the network contains approximately 5000 nodes at any point in simulation time, with an average participation rate of 7 years, an average degree of 2.5 risk partners, with whom they engage in an average of 2.5 risky events over a 30 day period. Churn rates were set such that each agent replaced (stochastically) his/her entire network twice during his/her scheduled participation in the network. In all, this means that, on average, the simulations shown in Figures 2-4 contained roughly 10,000 total agents, more than 2.25 million risk events, and 50,000 churn events (where agents remove a risk partner and chose a new one from their extended network neighborhood (42)).

Limitations

Tests of significance for stochastic simulation differ from ordinary statistical models. Each simulation works via a series of stochastic decisions—where a random number is generated and compared to a statistical distribution of possible outcomes. Such “rolls of the dice” alter the course of the simulation such that no two simulation runs are identical. Repeated simulations from the same empirical starting points thus produce different outcomes. The results of a high number of runs produce a distribution of possible “futures” from a given starting point. This distribution (represented in Figures 2-4 by a mean and standard deviation) constitute the results of the simulation experiments. In effect, the mean represents the center of the most likely outcomes of the disease process over a long simulation period, while the standard deviation represents the level of uncertainty around that center. As above, the empirical basis for all of the simulations in this paper can be found in prior research (11), and are based on currently accepted network statistical methods (49). In interpreting these results, we note that means with wide standard deviations indicate non-convergent simulation results, while low standard deviations indicate that, despite the stochastic nature of the simulation, the results converge on a “highly likely” set of results. In the simulations

discussed here, strong convergence is indicated by the low standard deviations shown in the later stages of the simulations (Figures 2-4). Such interpretations conform to current standards in stochastic simulation (41). Nevertheless, simulation results represent forward projections from current starting points and need to be approached with caution. Historical events, changes in actor behavior, and the actual serendipity of human social interaction necessarily complicate future disease dynamics in ways that limit the usefulness of simulation for actual future projection.

In addition, it is possible that during the early stages of the HIV epidemic, death due to AIDS played a role in the stabilization of HIV prevalence. In the current simulations, considerable population turnover is included, such that any real world effects of removal would be captured. To test whether such turnover contributed to or detracted from stabilization effects and firewalling, we performed a number of simulations with low (and very low) levels of population turnover (results not shown). In these simulations, both the stability of HIV prevalence over time, and level of the firewall effect were higher, indicating that population turnover mitigated (rather than exaggerated) the stabilization effects found here. To what extent this was true of the early stages of the epidemic remain speculative. Along these same lines, we emphasize here that our purpose is to demonstrate that firewalling effects could have contributed to subsaturation stabilization. We are not arguing that they were the sole cause. Other factors, such as an increasing awareness by PWID of unknown dangers associated with syringe sharing, education, early syringe exchange programs, risk-based interventions, and population turnover likely played a significant role in the actual historical trajectories mimicked here. Our argument is limited to the question of whether firewalling could also have played a role.

Discussion

The key finding of this paper is that the sub-saturation levels of HIV prevalence which have been previously observed in populations of PWID may be highly associated with and attributable to firewall effects arising from the self-organizing risk network behaviors of drug users themselves. In such a situation chronically infected individuals with lower viral loads and significantly lower risks of infection act as firewalls, which halt or delay the spread of HIV from acutely infected individuals to clusters of uninfected individuals across the larger network. This is possible due to the period of lower viral loads associated with chronic HIV infection, which represent lower likelihood of infection during a risk event when compared to periods of early, acute infection. We show that, in simulation, the average firewall score increases substantially by the 20 month mark just as the HIV prevalence rate stabilizes. These simulation results suggest that local level attachment dynamics combine with HIV viral natural history to counter the small-world character that might be suggested by looking at the degree distribution of PWID risk networks alone (10,45). These findings are important at a time when emerging variants on traditional SIR epidemiology models continue to speculate on the source of stabilization in HIV levels (17) by pointing to interventions that occurred much later in time. Our results would suggest that, for HIV, this is not necessarily the case, and that stable sub-saturation prevalence can emerge from attachment dynamics themselves (in interaction with the natural history of HIV in the human body), without the introduction of behavior change interventions or knowledge of infection.

And importantly these results remained true despite high levels of both risk and dynamism in the simulation model.

Importantly, the firewall effects observed in these simulations occur in an environment where actor behavior remained constant across the entirety of the simulation

This means that the stabilization of HIV prevalence below saturation levels, the increase of the average firewall measure, and the changes seen in the number of firewalled components over time are all independent of changes in agent action. In saying this we do not dispute the importance of individual or group intervention strategies in reducing HIV transmission. Instead we are interested in the puzzle of why sub-saturation levels of HIV have been repeatedly observed in situations where such interventions are relatively rare, and where other diseases such as HCV have seen far greater saturation. By holding agent behavior constant at the observed levels from New York City in the early 1990s, a period when community education was largely the only type of intervention available, this paper demonstrates the feasibility of the firewall hypotheses to explain sub-saturation levels of HIV prevalence among PWID *prior to* medical and behavioral interventions.

All of this takes place in simulations within which infection from chronically infected nodes remains possible, but (much) less likely than would be the case for infection from acutely infected nodes (42,43). To the extent that these two infection probabilities equalize, the firewall effect dissipates, and sub-saturation stabilization disappears. Such a scenario—where infectiousness/viral load remains more consistent from the acute to the chronic phase and overall prevalence rates climb to 80% or more—would seem to match the real world example of HCV (50), where such dramatic differences in viral load/infectiousness are not the case.

We note, however, that the effects discussed here may not be permanent. As the original authors of the firewall hypothesis made clear, a firewall effect also implies that as prevalence rates decrease due to the deaths of the infected individuals or due to infected people leaving the city or neighborhood drug scene, changes in network structure and risk partner patterning can potentially increase overall vulnerability to a renewed outbreak (23). For this reason, we agree that maintaining prevention programs remains critically important. In addition, antiretroviral treatment of HIV infections can prevent or delay chronically-infected people from developing high viral load late-stage infection, which should prolong the effects seen here and potentially reduce the late stage upswing seen in Figures 2-4. We would add that to the extent to which patients maintain low viral loads, the increased prevalence of antibody positive, low viral load people on ART should increase the firewall effect and further restrain new outbursts of transmission.

In locating the source of the firewall effect in the clustering tendencies of network actors, these results are potentially important to public health officials. The presence of natural network barriers to HIV spreading in a high risk population offers the possibility of intervention strategies that work to enhance such naturally occurring phenomena. Conversely, programs aimed at radically disrupting network structures, such as mass arrests of PWID or urban renewal projects that disperse them into other neighborhoods—which in turn require that those who remain in the network must radically reorder their network

connections—represent potentially significant public health risks by reducing the effectiveness of these naturally occurring barriers. Put another way, to the extent that network dynamics are capable of producing emergent constraints on overall prevalence of HIV among people who inject drugs, these structures must be carefully considered when designing and implementing disease, harm reduction, and interdiction strategies. This advice should not be limited to HIV, as the firewall effects described here are likely to be true for infections characterized by a large divergence of infectivity between initial and latency stages which are spread via risk network interactions.

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Glossary of Network Terms

agent/actor
simulation objects that act as PWID; each is characterized by a range of individual characteristics (gender, risk propensity…) that condition their risk interactions with other agents/actors

churn
the effect of network agents changing partners over time; a measure or approximation of overall change of network connections

clusters
parts of a network characterized by a high number of mutual connections; dense parts of a network

component
a part of a network that is not connected to other parts of network; an isolated cluster of agents

core
a highly connected section of a network where those with high numbers of connections are linked to others with high numbers of connections

degree distribution
a histogram of how many people or agents have how many connections (i.e. this network contains 5 people with 1 connection, 8 people with 2 connections, etc)

network transitivity
the process where agents tend to make connections with the connections of their current connections

node
general term for the objects that are connected

partner/network neighbor
in a PWID risk network, an agent with whom an agent often shares a risk behavior; on the street, a “running partner”

risk network
a network where the agents are meant to simulate people and the connections show potential avenues of infection due to risk behaviors

small world
a network configuration where even large numbers of actors are connected by a small number of intermediaries—similar to “six degrees of separation”

stochastic
a simulation strategy where random “rolls of the dice” determine situational outcomes

sociometric
a formal network rendering of human social interaction

Cited

1. Huang C-Y, Tsai Y-S, Wen T-H. Simulations for epidemiology and public health education. J Simul. Mar; 2010 4(1):68–80.
2. Marshall BD, Galea S. Marshall and Galea Respond to “Data Theory in Epidemiology.”. Am J Epidemiol. Dec; 2015 181(2):106–7. [PubMed: 25480819]
3. Goodreau SM. Assessing the Effects of Human Mixing Patterns on Human Immunodeficiency Virus-1 Interhost Phylogenetics Through Social Network Simulation. Genetics. Apr; 2006 172(4): 2033–45. [PubMed: 16636112]
4. Hsieh J-L, Huang C-Y, Sun C-T, Tsai Y-S. Learning to build network-oriented epidemic simulation models in epidemiology education. Int J Simul Process Model. 2009; 5(1):31–41.
5. Sloot PMA, Ivanov SV, Boukhanovsky AV, van de Vijver DAMC, Boucher CAB. Stochastic simulation of HIV population dynamics through complex network modelling. Int J Comput Math. Aug; 2008 85(8):1175–87.
6. Bauch CT, Galvani AP. Social Factors in Epidemiology. Science. Oct 3; 2013 342(6154):47–9. [PubMed: 24092718]
7. Des Jarlais DC, Friedman SR, Novick DM, Sotheran JL, Thomas P, Yancovitz SR, et al. HIV-1 Infection Among Intravenous Drug Users in Manhattan, New York City, From 1977 Through 1987. JAMA J Am Med Assoc. Feb 17; 1989 261(7):1008–12.
8. Brown AJL, Lycett SJ, Weinert L, Hughes GJ, Fearnhill E, Dunn DT. Transmission Network Parameters Estimated From HIV Sequences for a Nationwide Epidemic. J Infect Dis. Nov 1; 2011 204(9):1463–9. [PubMed: 21921202]
9. Dombrowski K, Curtis R, Friedman S, Khan B. Topological and Historical Considerations for Infectious Disease Transmission among Injecting Drug Users in Bushwick, Brooklyn (USA). World J AIDS. Mar 1; 2013 3(1):1–9. [PubMed: 24672745]

10. Vieira, et al. Small world network models of the dynamics of HIV infection. Ann Oper Res. Jul; 2010 178(1):173–200.
11. Dombrowski K, Khan B, McLean K, Curtis R, Wendel T, Misshula E, et al. A Reexamination of Connectivity Trends via Exponential Random Graph Modeling in Two IDU Risk Networks. Subst Use Misuse. Jul 2.2013 48:1485–97. [PubMed: 23819740]
12. Friedman SR, Neaigus A, Jose B, Curtis R, Goldstein M, Ildefonso G, et al. Sociometric risk networks and risk for HIV infection. Am J Public Health. Aug; 1997 87(8):1289–96. [PubMed: 9279263]
13. Des Jarlais DC, Perlis T, Arasteh K, Torian LV, Beatrice S, Milliken J, et al. HIV incidence among injection drug users in New York City, 1990 to 2002: use of serologic test algorithm to assess expansion of HIV prevention services. Am J Public Health. Aug; 2005 95(8):1439–44. [PubMed: 15985649]
14. Des Jarlais DC, Perlis T, Friedman SR, Deren S, Chapman T, Sotheran JL, et al. Declining seroprevalence in a very large HIV epidemic: injecting drug users in New York City, 1991 to 1996. Am J Public Health. Dec; 1998 88(12):1801–6. [PubMed: 9842377]
15. Friedman SR, Des Jarlais DC. HIV among drug injectors: the epidemic and the response. AIDS Care. 1991; 3(3):239–250. [PubMed: 1932186]
16. Des Jarlais DC, Perlis T, Arasteh K, Torian LV, Hagan H, Beatrice S, et al. Reductions in hepatitis C virus and HIV infections among injecting drug users in New York City, 1990-2001. AIDS Lond Engl. Oct; 2005 19(Suppl 3):S20–25.
17. Stadler T, Kühnert D, Bonhoeffer S, Drummond AJ. Birth–death skyline plot reveals temporal changes of epidemic spread in HIV and hepatitis C virus (HCV). Proc Natl Acad Sci. Jan 2; 2013 110(1):228–33. [PubMed: 23248286]
18. Hagan H, Pouget ER, Jarlais DCD, Lelutiu-Weinberger C. Meta-Regression of Hepatitis C Virus Infection in Relation to Time Since Onset of Illicit Drug Injection: The Influence of Time and Place. Am J Epidemiol. Nov 15; 2008 168(10):1099–109. [PubMed: 18849303]
19. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. The Lancet. Aug 19; 2011 378(9791):571–83.
20. Farmer JD, Patelli P, Zovko II. The predictive power of zero intelligence in financial markets. Proc Natl Acad Sci U S A. 2005; 102(6):2254–2259. [PubMed: 15687505]
21. Galea S, Riddle M, Kaplan GA. Causal thinking and complex system approaches in epidemiology. Int J Epidemiol. 2010; 39(1):97–106. [PubMed: 19820105]
22. Philippe P, Mansi O. Nonlinearity in the Epidemiology of Complex Health and Disease Processes. Theor Med Bioeth. Dec; 1998 19(6):591–607. [PubMed: 10051792]
23. Friedman SR, Kottiri BJ, Neaigus A, Curtis R, Vermund SH, Des Jarlais DC. Network-related Mechanisms May Help Explain Long-term HIV-1 Seroprevalence Levels That Remain High but Do Not Approach Population-Group Saturation. Am J Epidemiol. Nov 15; 2000 152(10):913–22. [PubMed: 11092433]
24. Friedman SR, Sandoval M, Mateu-Gelabert P, Rossi D, Gwadz M, Dombrowski K, et al. Theory, measurement and hard times: some issues for HIV/AIDS research. AIDS Behav. 2013; 17(6): 1915–1925. [PubMed: 23564029]
25. Valente, TW. Social Networks and Health: Models, Methods, and Applications: Models, Methods, and Applications [Internet]. Oxford University Press; USA: 2010.
26. Friedman, SR., Curtis, R., Neaigus, A., Jose, B., Jarlais, DCD. Social Networks, Drug Injectors' Lives, and HIV/AIDS. 1st. Springer; 1999. 2010. Softcover of ed
27. Friedman SR, Neaigus A, Jose B, Curtis R, Des Jarlais D. Networks and HIV risk: an introduction to social network analysis for harm reductionists. Int J Drug Policy. 1998; 9(6):461–9.
28. Friedman SR, de Jong W, Rossi D, Touzé G, Rockwell R, Des Jarlais DC, et al. Harm reduction theory: Users' culture, micro-social indigenous harm reduction, and the self-organization and outside-organizing of users' groups. Int J Drug Policy. 2007; 18(2):107–117. [PubMed: 17689353]
29. Friedman SR, Des Jarlais DC, Sotheran JL, Garber J, Cohen H, Smith D. AIDS and self-organization among intravenous drug users. Int J Addictions. 1987; 22(3):201–219.

30. Koopman J. Modeling infection transmission. Annu Rev Public Health. 2004; 25:303–326. [PubMed: 15015922]
31. Goodreau SM. A decade of modelling research yields considerable evidence for the importance of concurrency: a response to Sawers and Stillwaggon. J Int AIDS Soc. 2011; 14:12–12. [PubMed: 21406079]
32. Kumar S, Grefenstette JJ, Galloway D, Albert SM, Burke DS. Policies to reduce influenza in the workplace: impact assessments using an agent-based model. Am J Public Health. 2013; 103(8): 1406–1411. [PubMed: 23763426]
33. Marshall BDL, Paczkowski MM, Seemann L, Tempalski B, Pouget ER, Galea S, et al. A Complex Systems Approach to Evaluate HIV Prevention in Metropolitan Areas: Preliminary Implications for Combination Intervention Strategies. PLoS ONE. Sep 13.2012 7(9):e44833. [PubMed: 23028637]
34. Marshall BDL, Friedman SR, Monteiro JFG, Paczkowski M, Tempalski B, Pouget ER, et al. Prevention And Treatment Produced Large Decreases In HIV Incidence In A Model Of People Who Inject Drugs. Health Aff (Millwood). Mar 1; 2014 33(3):401–9. [PubMed: 24590937]
35. Monteiro JFG, Galea S, Flanigan T, de Monteiro M, Friedman SR, Marshall BDL. Evaluating HIV prevention strategies for populations in key affected groups: the example of Cabo Verde. Int J Public Health. Apr 3; 2015 60(4):457–66. L. [PubMed: 25838121]
36. Mniszewski, SM., Del Valle, SY., Stroud, PD., Riese, JM., Sydoriak, SJ. EpiSimS simulation of a multi-component strategy for pandemic influenza; Proceedings of the 2008 Spring simulation multiconference [Internet]; 2008. p. 556-563.[cited 2013 Apr 3]Available from: http://dl.acm.org/citation.cfm?id=1400636
37. Snijders TAB, van de Bunt GG, Steglich CEG. Introduction to stochastic actor-based models for network dynamics☆. Soc Netw. Jan; 2010 32(1):44–60.
38. Ripley, RM., Snijders, TA., Preciado, P. Manual for RSiena. University of Oxford: Department of Statistics; Nuffield College: 2012.
39. Handcock MS, Hunter DR, Butts CT, Goodreau SM, Morris M. statnet: Software Tools for the Representation, Visualization, Analysis and Simulation of Network Data. J Stat Softw. 2007 1548--7660.
40. Jenness, S., Goodreau, SM., Morris, M., Beylerian, E., Wang, L., Bender-deMoll, S. Package 'EpiModel'. 2016. Package "EpiModel." 2016Available from: http://star-www.st-andrews.ac.uk/cran/web/packages/EpiModel/EpiModel.pdf
41. Guizani, M., Rayes, A., Khan, B., Al-Fuqaha, A. Network Modeling and Simulation: A Practical Perspective. 1st. Wiley-Interscience; 2010.
42. Khan B, Dombrowski K, Saad M. A stochastic agent-based model of pathogen propagation in dynamic multi-relational social networks. Simul Trans Soc Model Simul Int. 2014; 90(4):460–84.
43. Khan B, Dombrowski K, Saad M, McLean K, Friedman S. Network Firewall Dynamics and the Subsaturation Stabilization of HIV. Discrete Dyn Nat Soc. Jun 4.2013 2013:1–16.
44. Yang C, Tobin K, Latkin C. Perceived Serosorting of Injection Paraphernalia Sharing Networks among Injection Drug users in Baltimore, MD. AIDS Behav. May 20; 2010 15(1):16–21.
45. Jiayu, L., Guihong, B., Hairui, W. A cave small world network model for HIV transmission among intravenous drug users; IEEE: 31st Chinese Control Conference (CCC); 2012. p. 7475-80.
46. Costenbader EC, Astone NM, Latkin CA. The dynamics of injection drug users' personal networks and HIV risk behaviors. Addict Abingdon Engl. Jul; 2006 101(7):1003–13.
47. Curtis R, Friedman SR, Neaigus A, Jose B, Goldstein M, Ildefonso G. Street-level drug markets: Network structure and HIV risk. Soc Netw. 1995; 17(3–4):229–49.
48. Latkin CA, Kuramoto SJ, Davey-Rothwell MA, Tobin KE. Social norms, social networks, and HIV risk behavior among injection drug users. AIDS Behav. Oct; 2010 14(5):1159–68. [PubMed: 19466537]
49. Snijders TAB, Pattison PE, Robins GL, Handcock MS. New specifications for exponential random graph models. Sociol Methodol. Dec 1; 2006 36(1):99–153.
50. Dahari H, Shudo E, Ribeiro RM, Perelson AS. Mathematical modeling of HCV infection and treatment. Methods Mol Biol Clifton NJ. 2009; 510:439–53.

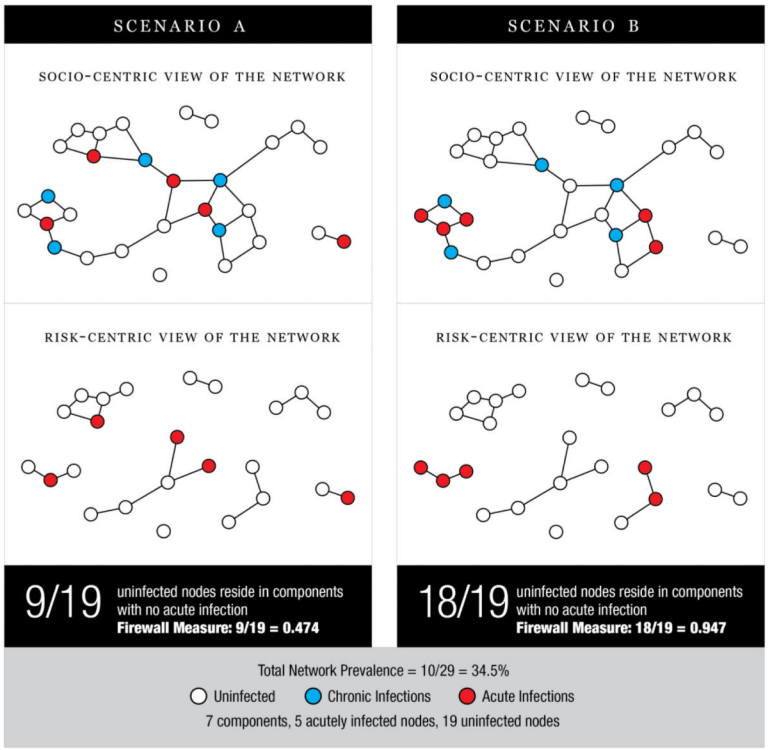

Figure 1.

Calculation of the "Firewall Measure" across two scenarios of equivalent prevalence and incidence but different locations of infections in the network. Here we see that, in a risk network scenario, different infection locations can have important implications for the future of the epidemic.

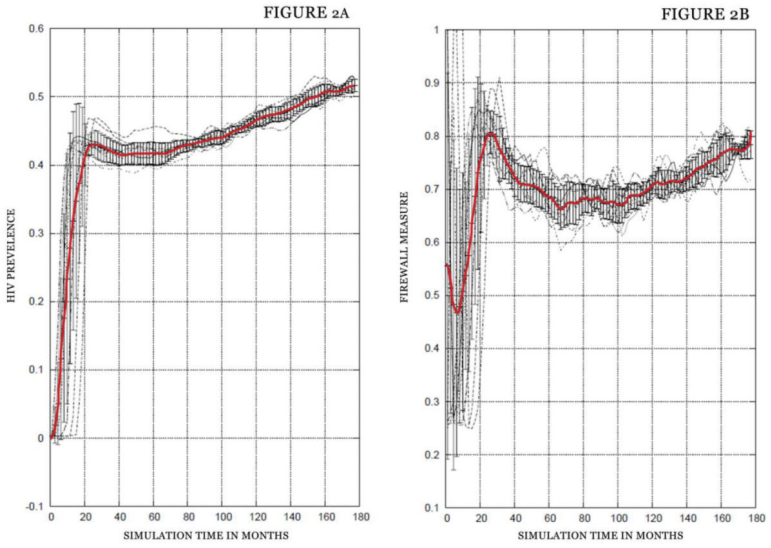

Figure 2.

HIV prevalence (a) and Firewall Measure (b) in repeated simulations of 5000 PWID across 180 months. The red line indicates the mean across 10 independent simulations.

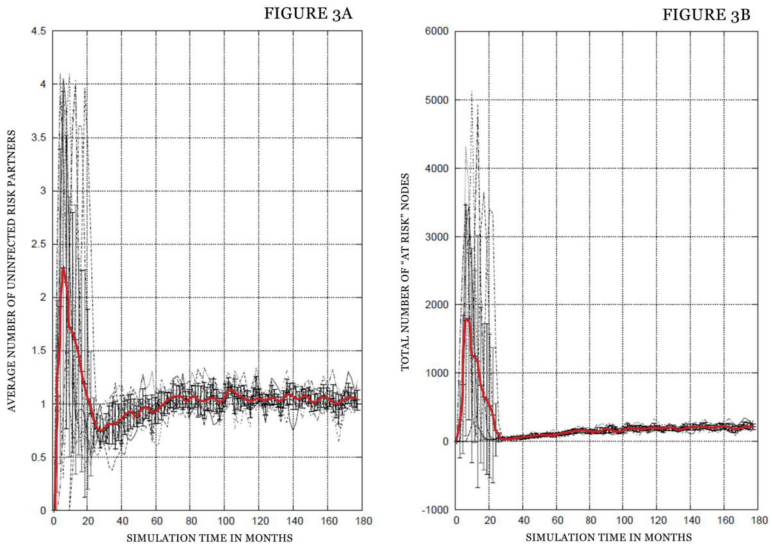

Figure 3.

Average number of uninfected risk partners per acutely infected node (a) and total number of unifected nodes exposed to a highly infectious agent (b) in repeated simulations of 5000 PWID across 180 months. The red line indicates the mean across 10 independent simulations.

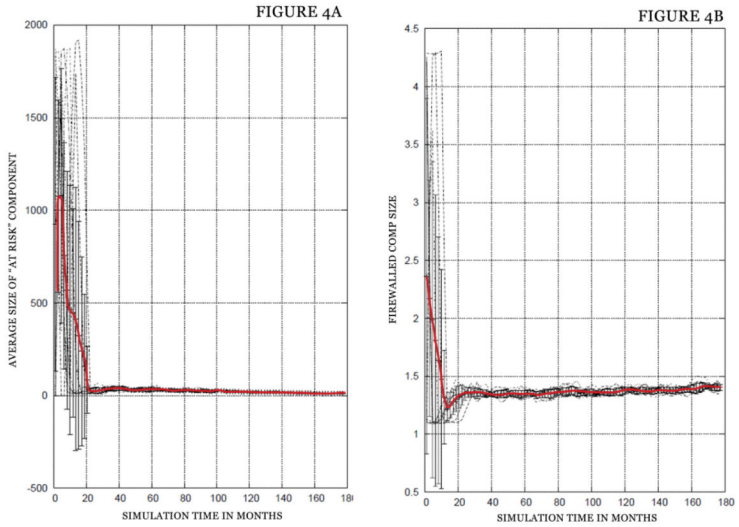

Figure 4.

Showing the average size of (a) “at risk” components (i.e. those that include an acutely infected node) versus (b) “firewalled” component over time in repeated simulations of 5000 PWID across 180 months. The red line indicates the mean across 10 independent simulations.