

PLOS Science Wednesday: Hi reddit, my name is Joel and I published a PLOS Pathogens study investigating whether viral genetic sequences of HIV-1 are similar between sexual and social networks in New York City – Ask Me Anything!

PLOSScienceWednesday ¹ and r/Science AMAs¹

¹Affiliation not available

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Abstract

Hi Reddit, My name is Joel Wertheim and I am an Assistant Professor of Medicine at the University of California, San Diego. My research focuses on the molecular evolution of RNA viruses, like HIV. In my lab, I am particularly interested in figuring out how to translate insights from HIV evolutionary biology into practical public health action. We recently published a study ‘Social and Genetic Networks of HIV-1 Transmission in New York City’ in PLOS Pathogens. In this study we asked HIV-infected individuals to name their sexual partners and injection drug-using partners. When these partners were also infected with HIV, we investigated whether their viruses were genetically similar enough to support a shared transmission history. Our findings suggest that incorporating HIV genetic sequence data can improve public health activities. I will be answering your questions at 1pm ET – Ask Me Anything!

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PLOSSCIENCEWEDNESDAY [R/SCIENCE](#)

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A question regarding your study design: how receptive was your study population to naming their sexual/drug-using partners? Based on your description, I imagine you couldn't just cross-reference given names with a list of HIV-positive patients to follow up with. Do you feel like the sensitivity associated with naming partners might have lowered your total number of subjects?

In conjunction with your main goal of improving public health activities, how far have you gotten in integrating with pharmacogenetics to better treat or prevent transmission of viruses with particular genetic traits?

[aflyboy](#)

This study was conducted on existing public health data collected by the NYC-Department of Health and Mental Hygiene (DOHMH). So my group was not involved in the elicitation of sexual/drug-using partner names. That being said, when people are asked for these names, they provide on average only 0.5 partners. Partner elicitation is certainly a sensitive topic, and based on that average, most people do not name any partners.

One important finding of our study is that, even in the absence of partner naming, we can use these genetic sequences to better understand transmission dynamics. And we can query someone's HIV genetic sequence against all other people in the database, looking for evidence of an epidemiological connection.

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To answer your second question, NYC and primary care provides use drug resistance profiles (captured in these genetic sequences) to modify treatment regimes. This was (and still is) the primary purpose of collecting these genotypes.

Hi Joe! When looking between the groups, how much variation do you observe in the HIV genome? Where in the genome do differences exist, and does this genetic variation have the potential to alter the infectivity or other activities of the virus? Thanks!

[anonymusmusculus](#)

There is an extraordinary amount of variation in the HIV genome. In fact, within a single person infected with HIV, there is typically more genetic variation than is found in influenza circulating the globe in a given year. This variation occurs across the entire genome, and is greatest in the envelope proteins, which evolve to avoid detection by the host's immune system.

There is quite a lively debate in the HIV research community right now about much this genetic variation affects infectivity potential (i.e. the concentration of virus in blood). It seems as if there is a relationship. However, it is an complicated relationship. And there aren't clear mutation-phenotype relationships when it comes to infectivity.

Other viral genetic features such as cell-tropism (which cells can HIV bind to and infect) and drug resistance have much clearer genetic underpinnings. And these types of mutations are often monitored quite closely.

Doesn't HIV mutate with fair regularity? Is enough of the sequence preserved to track it?

[happy_bever](#)

HIV is constantly mutating (about 1 mutation or so every time it replicates). By looking at a highly conserved region of the genome (where most mutations aren't tolerated because they render the virus non-functional), we can reconstruct the evolutionary history of the virus. If we only looked at a rapidly evolving part of the genome, we couldn't do this type of study.

Yesterday I read a post here about a correlation between plague survivors and HIV immunity in their descendants; does your research overlap with that at all?

[dude-O-rama](#)

I believe you're referring to the CCR5-delta32 mutation. In some people, a cell receptor (CCR5) on their CD4-helper T-cells is missing 32 nucleotides due to a deletion. HIV can use typically CCR5 to gain access to these cells, but not if these 32 nucleotides are missing.

There have been many theories as to why CCR5-delta32 exists at such high frequency in humans (particularly Northern Europeans): plague, smallpox, etc. I'm not convinced by any one theory yet. The timing and geography just doesn't fit.

And no, my research doesn't overlap with this topic. But I do find it fascinating.

Can you describe what concrete steps could be taken using this new knowledge to improve public health in this area?

Also could you describe the one or two outstanding scientific questions in this area that you would like to address next?

[alanson1809](#)

Yes, BC is doing some excellent work on incorporating these types of approaches into their surveillance activities. They are the leaders in the field.

Here in the US, we are already incorporating the findings from this study in public health practice: monitoring cluster growth and directing public health services to genetically linked people in clusters.

The questions I want to address next is can we use HIV genetic sequences to identify transmission clusters of greatest public concern? And can we direct resources (linkage to care, antiretroviral treatment support, partner notification services) towards these clusters to slow (stop) their growth?

My group is currently working on addressing both of these questions.

What made you choose NYC as opposed to LA, San Francisco, or any other West Coast city? Also how did you become interested/involved in this particular study?

[shinatree](#)

I do work for the CDC, consulting on their molecular HIV surveillance activities. As a part of this arrangement, I gave an online seminar to several state and city public health departments. NYC attended and approached me to start looking at their genetic data and how it could be used in public health applications.

What attracted me to this study in particular was the wealth of available data on partner services (names, etc.). It struck me as an important source of data that hadn't been addressed yet. Plus, this type of comparison gives us confidence in using HIV genetic sequences in other public health applications.

What sequences of the viral genome do you see the most conservation? Are most of the exons / packaging elements the same? Or are there large amounts of variation in essential elements of the viral genome?

[kitzdeathrow](#)

The polymerase region analyzed here (protease and reverse transcriptase) is the most highly conserved region in the HIV genome (at least for a region of comparable size). The HIV genome is incredibly compact, with regulatory elements imbedded within protein coding genes. And HIV doesn't have exons or introns like the human genome. In fact it has some overlapping genes that share sequence, sometimes in a different reading frame.

I'm fascinated by the privacy laws here - after participants gave you their contacts' details did any contact refuse to participate? Were there any legal or threatened legal issues?

[Samurai Pizza Catz](#)

Privacy laws here are of great importance. Any information provided to the NYC public health department is protected by New York State law. These data cannot be shared with law enforcement, etc. Even with this protection, many people still refuse to interact with the Department of Health for various reasons (including that of privacy).

Outside of New York, this issue becomes much thornier, since unintentional HIV transmission is still a crime in many jurisdictions. It is great concern among many researchers in this field that our work could be used to prosecute individuals. That being said, the type of data analyzed here are NOT sufficient to establish transmission between two people. All we can say using these genetic sequence data is that two people are infected with viruses that are similar enough to suggest a direct or indirect epidemiological connection. There could be intermediate or shared sources of infection that we cannot rule out using surveillance data.

Does publishing on PLOS not allow you to publish in a more traditional journal? How does publishing in PLOS vs a more traditional journal impact your credibility and considerations for tenure?

[CavalierEternals](#)

I don't think of PLOS as being different from a traditional journal in terms of credibility or promotion; they just have open access policies (which many 'traditional' journals are starting to employ as well). They have rigorous peer-review, etc. My department looks quite favorably on articles PLOS Pathogens in these regards.

What are future ideas to branching out this research?

The NYC TB folks have been at contact tracing for ever and given the high burden and common co-morbidity it seems like a natural progression.

What are your thoughts about WGS of HIV+ homeless populations?

[PHealthy](#)

Exactly! There is a big push in the HIV public health community right now to follow the path of TB. The next step is to use the genetic data to identify HIV transmission clusters of particular concern (i.e., potential for growth).

Speaking as a young physician who would love to be involved in more research, how did you get this past IRB? There's no way my institution would approve this study

[Henry Alden](#)

Our IRB at University of California, San Diego approved this study as 'Human Subjects Research - Exempt'. As previously mentioned, the data we collected through routine public health practices. The research portion (which IRB is concerned) was the analysis of de-identified data.

What mapping methods did you use?

[pteroso](#)

Are you asking about figure generation? I made the networks using graphviz (<http://www.graphviz.org/>) using the neato algorithm.

Hello, very interesting! I have two questions: 1) Did you find any instances of direct transmission, and

for those instances was there any evidence for a founder effect- are there similarities between viral strains that are founders? 2) Were there's differences in viral diversity based on type of social network? (I.e., injection drug users vs. Sexual partners?)

[dad386](#)

We cannot establish direct transmission with this type of sequence data.

Injection drug using partners were less likely than heterosexual partners to be genetically closely related.

How did you determine the social network of HIV-infected individuals? Was it strictly based on those who were newly diagnosed listing their sexual and IDU partners?

[LoriTrager](#)

People provided a list of their sexual and injection-drug using partners from the previous 12 months to the Department of Health.

Great work! However, I'm thinking about this legally and ethically. Say, you sequence all of the HIV from sexually active adults in a given community. You could potential trace the different lineages through to its originators. Since HIV mutates frequently, I assume you could tell if someone was infected by one person rather than another person.

Since you could definitively say if someone infected someone, is there an ethical or legal obligation to disclose that information to a person or agency?

[TheSecretNothingness](#)

The legal and ethical issues here are of great concern. Importantly, we cannot identify true transmission partners using this approach. All we can say is that people are infected with viruses that are so genetically similar as to imply a direct or indirect epidemiological connection. Importantly, we cannot rule out intermediate partners or a shared source of infection.

Any ideas on getting around the issue of convergent evolution with regard to drug resistance mutations?

[betterthanastick](#)

You can strip out all the drug resistance mutations from the analysis. We explored this, and it didn't make a difference. Convergence of resistance mutations are few and far between, relative to the total divergence between sequences. Drug resistance at one site, though important biologically, only changes the genetic distance in this region by 0.08%, and we looked at divergence thresholds between 1-2%.

A bit off topic perhaps, but i will shoot the question anyway. Do you think HIV vaccines can really work? I have seen a lot of under development HIV vaccines but do you think they can keep up with the ever mutating HIV virus and provide adequate immunity against HIV?

[floyd007](#)

HIV vaccination is outside my area of expertise. But we do not have an effective vaccine yet.

The next step this research is to employ treatment-as-prevention: providing antiretroviral drugs to HIV-infected people to reduce their likelihood of transmitted and providing drugs to HIV-uninfected people at high risk of acquiring HIV to prevent them from becoming infected.

I couldn't understand much from the title. Could you explain it to me in a ELI5 way.

[varishtg](#)

If you want to figure out HIV transmission patterns in NYC, use viral genetic similarity in addition to named partners.

Has a lot of other research tracking the same thing been done? If so, how does it compare to your results?

[xGiaMariex](#)

Other smaller studies (particularly among men who have sex with men; MSM) looking at this type concordance between named partners and genetic linkage have also found that named partners are not genetically linked.

I had to read your statement three times to get the slightest grasp of what it is that you do. When you tell peopel what you do is there usual reaction you get and can you tell the difference between those who are actually interested in what you do and those who are just being polite?

[quest47484748](#)

Most people are just being polite

Hi! I'm a freshman in college interested into going into epidemiology/public health!

So question: what public health initiatives do you actually plan on taking to raise awareness of this situation? I mean sure you can hold seminars or post flyers but how how do you actually get people to attend or catch their attention?

Also this will probably be buried deep, but what are the chances I could get an internship opportunity with you/your team to explore this research/field?!

[Romeooooow](#)

I'm working with NYC and CDC to initiate action on clusters of interest. If you're serious about research, follow the link to my lab at the top of the page and send me an email.