PLOS Science Wednesday: Hi Reddit, we're Jessie Abbate, Carmen Lia Murall and Christian Althaus, and we developed a mathematical model showing the sexual transmission of Ebola could prolong the epidemic in West Africa – Ask Us Anything!

PLOSScienceWednesday [1] and r/Science AMAs[1]

[1]Affiliation not available

April 17, 2023

Abstract

Hi Reddit, We are Jessie Abbate, Carmen Lia Murall, and Christian Althaus, infectious disease researchers collaborating between France (Research Institute for Development), Switzerland (University of Bern), and Germany (Max Planck Institute). Collectively, our work focuses on the epidemiology, ecology, and evolution of pathogens, including human viral infections. We recently published a study entitled "Potential Impact of Sexual Transmission on Ebola Virus Epidemiology: Sierra Leone as a Case Study" in PLOS Neglected Tropical Diseases. Recent observations show that Ebola virus can remain active and transmissible in sperm for up to 9 months, meaning patients can remain infectious after they recover from the initial symptomatic phase of the disease. We developed a mathematical model to study the potential impact of sexual transmission on the size and duration of Ebola outbreaks such as the 2013-2016 epidemic in West Africa. Using the epidemiological data from Sierra Leone as an example, we found that despite very few additional cases, sexual transmission from survivors could extend the duration of the epidemic substantially, allowing cases to continue popping up throughout 2016 and highlighting the need for care providers to stay alert for this possibility. We will be responding to questions from 1pm EDT (10 am PDT) – Ask Us Anything! Don't forget to follow us on Twitter @jessieabbate @cl_murall @c_althaus.

the WINNOWER

REDDIT

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PLOSSCIENCEWEDNESDAY R/SCIENCE

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Hi, I wanted to ask how you go about the process of modelling something like a disease. An organic phenomenon seems rather difficult to model so I wanted to know what techniques did you utilise or what steps did you follow ?

How did you determine which approach was the best one ? What were some alternate methodologies you could have pursued ?

OmegawOw

(Christian Althaus): The transmission of an infectious disease can be considered as an ecological system where different sub-populations of individuals interact with each other. There are so-called susceptible individuals who can get infected, infected individuals who are in a latent phase and do not transmit the disease yet, symptomatically infected individuals who do transmit, and those individuals who recovered from the disease or died. With sexual transmission, we assume that a certain proportion of those individuals who recovered from symptoms remain infectious through sexual transmission for a

mathematical model showing the sexual transmission of Ebola could prolong the epidemic in West Africa -- Ask Us Anything!, *The Winnower* 3:e146901.19041 , 2016 , DOI: 10.15200/winn.146901.19041

certain amount of time. The dynamic interactions of all these sub-populations and the movement from individuals from one sub-population to the other (e.g., from latently infected to symptomatically infected) can be described by a set of ordinary differential equations. Often, such models are fit to data (e.g., the reported number of incident cases/infections) in order to estimate the rates at which individuals move from one sub-population to the other (e.g., the transmission rate). Ordinary differential equation models are typically deterministic and describe the average behavior of a population but cannot take into account chance effects (stochasticity). These effects can be particularly important when population sizes (e.g., the number of remaining infectious individuals) are small. This is why we also performed stochastic simulations of our model that allowed us to study the expected variation in the size and duration of an epidemic. Alternative methods are, for example, individual-based models that allow for a much more detailed description of the interaction between individuals, households and communities. However, these type of models are often difficult to parameterize due to a lack of the relevant data.

How big of a factor is rape?

Detaineee

(Jessie) I think the best way to answer this is that in our model, we have a parameter that accounts for the number of sexual contacts per individual (well, in this case, males), and this is generated from studies on the sexual behavior of people in similar communities. This is an important thing to measure, but the importance would simply be equivalent to the proportion of sexual contacts that are non-consensual. There is no difference between a consensual versus non-consensual sexual contact - particularly because we specifically are concerned with UNPROTECTED contact, which one would imagine would comprise most non-consensual events.

What can we do in the United States to help in Africa with this problem and other similar problems? What is the best use of our time and resources?

acphil

(Jessie) This is a great question. I think we will have to answer this in stages, and probably with multiple opinions, as there's clearly not one correct answer. For sure, IMO, our time and resources are best spent on pre-emptive measures: (establishing where needed and) securing health care infrastructure in countries at risk, funding basic research of both natural disease emergence and epidemiological processes, and public funding of vaccines and treatments for those diseases we already know about. One of the biggest challenges is that companies who currently foot the bill for this type of research & development are less willing - and financially able - to do so for rare pathogens especially those that currently only affect poor countries. In any way, preventing and increasing the efficiency of response to crises no matter where they emerge is much less costly in time and money than having to deal with something that has gotten out of control (a great example at the moment being the Zika virus).

Do y'all for see Ebola eventually becoming a disease like measles or chicken pox that will have a vaccine and be under reasonable control or do you think it will potentials mutate and become even more deadly and easily spread?

InkSpiller333

(Jessie & Carmen Lia & Christian) Thanks for your question. While the likelihood of something like an "MMRE"-type routine vaccine is not likely, given it is essentially not a sustained human disease (the

West Africa epidemic, arising from a single cross-species transmission event, was successfully brought under control), now that we do have human trials of the vaccine(s) for Ebola, as well as some effective treatments, it will likely only be necessary to vaccinate when new events arise. It is anyone's guess, however, as to how likely it would be for a mutant to easily spread despite those resources. Adequate surveillance and study of circulating viruses, such as those found in populations of reservoir hosts, is the best method we have to protect ourselves from that possibility. This is precisely the type of work that has just been published in another PLOS Neglected Tropical Diseases paper recently by colleague Barbara Han and co-authors, which can be found here: http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004815 (edited: grammar! sorry for the long sentences!)

If you could rename Ebola into anything you wanted, what would you name it?

acouvis

(Jessie) This is actually a really good question. There is a problem with naming viruses or diseases by recognizable places or animals (e.g., Mexican flu or Swine Flu), as it can be bad for the place (one might think twice about going on a ride down the Ebola River?) and also may be incorrect as far as descriptions go (e.g., not actually from Swine, or Mexico). So, we have scientific names (like the family Filovirus), followed by a number, for that. But it can sometimes be hard to place a virus or a bacterium, due to an ever-changing tree of life!

Are you guys mathematicians or biologists?

blbrd30

[In response to a question we can no longer find, asking what training one would need to do this kind of work](Carmen Lia): I would first suggest basic math and stats training, such as calculus, linear algebra, probability and statistical methods used in sciences. More advanced maths like inference methods, dynamical systems and biomath courses (which use ODEs and PDEs) are very useful. Competency in a major programming language, such as C++, Matlab, python, etc. will really help speed up your learning and ability to perform new tasks. Biologists use R a lot for data analysis and statistics (it helps that it's free!). For our paper we used R because it was the common language between the authors. If you are a biology major then I suggest you take at least a minor in math but if you are a math major then I suggest taking some biology courses. Sometimes just sitting in a biology class that you otherwise can't take helps. For example, during my PhD I sat in more advanced virology and immunology courses to learn more about the systems I am modeling. Also, during your training ask yourself if you like (are better at) analyzing data and statistics or if you like building and analyzing mathematical models, because these are different kinds of computational biology approaches.

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blbrd30

Jessie is a biologist (evolution/ecology) with epidemiology training. Carmen Lia is a biologist (evolution/ecology) with math training (PhD in theoretical biology). Christian is a theoretical epidemiologist with biology (molecular biology/biochemistry/evolution) training.

Hey, thank you for hosting this AMA! There are many people who have drawn comparisons between the outbreak and spread of Ebola and of Zika. What similarities actually exist between the two

diseases? Are the preventative methods we've recognized as effective in dealing with Zika (from both a social and scientific standpoint) useful when considering how to best deal with the current Zika crisis?

wdennis22

(Jessie) Great question. The two biggest differences between Zika and Ebola are (1) Zika Virus is thought to be, and probably actually is, mostly transmitted by mosquito vectors which do not require the close contact with bodily fluids that Ebola Virus needs for both sexual as well as non-sexual transmission, and (2) Ebola Virus has a much higher rate of symptomatic expression of the virus, which can slow down its spread because of behavioral resistance mechanisms and simply because killing or immobilizing the host means transmission also ends (except where cultural funeral practices are involved).

For similarities, however, there is the fact that for both diseases, a symptomatic patient has the potential to spread the virus during their asymptomatic convalescent period. There was a recent report that this may have occurred with an asymptomatic couple (published in Eurosurveillance : http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=22500), but it is unknown how common that could be.

For certain, knowing that a symptomatic patient has the potential to spread the virus during their asymptomatic convalescent period - something that was rarely given much importance before the West Africa outbreak of Ebola Virus - allows people to take precautions to help stem its spread through both testing as well as practicing safe sex for a recommended period of time following known or potential exposure. Scientifically, it's hard to say this in humans (case-controlled studies are difficult if not unethical), but education is a huge part of achieving public health goals.

This is for Christian, and a bit off topic. In 2007 you did some work on looking at CD8+ T cell dynamics during both chronic and acute infection by LCMV in mice. A big question in the paper that wasn't really addressed was what causes the radical change in dynamics from immune expansion to tolerance. Do you know if there has been a better description since then of the reason for this switching?

The_DrPark

(Christian Althaus): Thanks for your interest in my LCMV paper! We certainly could not address the change from proliferation to tolerance in detail with the data we had at that time. Unfortunately, I have not been up-to-date with the recent literature on CD8+ T cell dynamics for acute and chronic infections and do not know of a better description of this process. I expect, however, that the research groups from Miles Davenport in Australia and/or Rustom Antia from the US might have addressed this question in more detail.

¿How possible is a global epidemic of any viruses in the future?

ma_x_power

(Christian Althaus): Every year, there is a global epidemic (or pandemic) of the flu virus. Other recent viruses, such as HIV, have also spread globally. Whether a virus really has the potential to spread globally will depend on its transmissibility, transmission route and virulence (how sick people get).

This is really cool work! Very interesting.

I'm sorry, but I had to skim (no insult intended, pressed for time), so I apologize if I misread the description of your model, or if you addressed my question in the paper and I blew past it. It would be

great if you could direct me to the relevant sections of your paper if that's what happened.

My question:

While you talk about "sex-acts" in general in the early part of your paper, in the description of your model it appears you only consider transmission events from convalescent men to unaffected individuals ("η is the per sex act transmission probability of Ebola virus from convalescent men, and q is the daily rate at which they engage in sexual intercourse"). While you cite evidence which "suggest that sexual transmission from convalescent men can and does occur," you do not appear to explicitly describe your reasons for excluding convalescent, sexually active women from your model, despite observing that "active virus has been documented in...vaginal fluids." I would love for you to expand on your reasoning for making this exclusion. Is it simply that there have been no case reports of F-M or F-F transmission, or data are too limited to assign a probability of transmission with any confidence? Do you have a physiological basis for making this exclusion? Was it a simplifying choice? Whatever the reason, why did you not choose to directly address your reasons for making the exclusion in your paper? (We are talking about a large potential viral reservoir here, aren't we? Given the exploratory nature of your model, and the fact that M-F transmission data are limited as well, I found it surprising that you didn't explain your exclusion of potential F-M transmission, no matter how justified, reasonable, and perhaps obvious to you that choice may have been.)

Again, apologies if I missed something.

ranstopolis

(Jessie) Great question. For parameterizing the model, we tried to limit it to documented evidence. While virus in vaginal fluids has been well-documented, it does not appear occur to the same extent as in the seminal fluids (as yet documented) as no active replication of virus from vagnial fluids post-acute recovery, and no F -> M sexual convalescent transmission, has ever been documented. We grappled with this though, given that such little was truly known, and this is why we made this set of parameters (eta and p, the proportion of survivors who are infectious and sexually active) flexible.

EDIT: In the string below, you will see that [ranstopolis] pointed to a mistake we made in the article: replicating virus, to our knowledge, has only been documented for seminal and ocular fluids. This mistake is essentially a typo that occurred in the shortening of the article from its original format published to bioRxiv in November last year (which can be found here: http://biorxiv.org/content/early/2015/11/25/031880.full.pdf+html).

It should be noted however, at least for vaginal secretions, this lack of evidence is more due to very limited testing rather than sufficient evidence that it does not occur.

What kind of software tools do you guys use for modelling?

ninedecibels

(Christian Althaus): For this particular project, we used the R software environment for statistical computing. R is frequently used for modeling in ecology or epidemiology as it allows to perform model simulations, data analyses and plotting. Another frequently used programming language is Python which shares similar characteristics with R. For computational expensive simulations, researchers often stick to C or C++. Commercial software tools such as Mathematica or Matlab are also used.

Does the spreading of diseases often prolong epidemics? This seems like it would be a big issue all over the poorer parts of the world

Collinnn7

(Christian Althaus): How fast an epidemic ends will depend on the number of remaining individuals that can get infected, and the control measures that are implemented.

Wondering whether you have any thoughts on the political failures that led to the West African outbreak spiralling so far - errors at WHO (and perhaps particularly WHO Africa), the relative inaction of the African Union.

Do you see ways these problems can be, or are being, overcome?

(if that's too far from your field, sorry - just ignore me :)

genericmutant

(Jessie) While this is certainly beyond our scope, I think by far the best way to overcome these problems is to build the public health infrastructure and have systems for response in place, rather than trying to do it in crisis-mode. Not to mention more internationally-funded teams that can be deployed when and where they are needed couldn't hurt.

Hello! Thank you for taking the time to do an AMA.

I'm wondering about your work with other scientists. To collect data or review it, do you work with anthropologists (of any specialty) in the area? I saw a response to a deleted question referencing courses of study and I'm curious if social sciences play any (weighted) part in how you work.

Thank you all!

neckbeardProblems

(Christian Althaus): Thanks for your question. We do not directly collaborate with anthropologists or other social scientists. However, specialists in these fields were certainly involved in the collection and processing of data that we used in our study, such as sexual behavior or epidemiological data. There is definitely an overlap between social scientists and epidemiologists in their interests about contact networks between people.

Have you read **The Hot Zone** by Dan Brown? If yes, what is your collective opinion of that book and the claims it makes?

Edit: format

balfrey

(Jessie): I'm assuming you mean The Hot Zone by Richard Preston. I'll first say that that book recounted the experiences, mostly, of the people whose shoulders our work absolutely stands on: the brave men and women in the field. The health care workers in these communities are those who do the real work, caring for those infected and stopping the chains of transmission; also those at the CDC labs where samples are sent and analyzed, those sent to the field from the CDC. I haven't read it since I was 13 years old, so I can't say that after all of my lab and field experience, and now our collective understanding of the epidemiology, what those claims were and thus my opinion on them. However, I can say that reading that book when I was 13, along with Laurie Garrett's The Coming Plague, is why I went into this line of work. The threats of disease emergence are as real as they are natural, but our resilience (what we call 'behavioral resistance': science, medicine, quarantine) as a species is not to be

underestimated. On a lighter note: I was so taken by the descriptions of Dr. CJ Peters from the hot zone that I dressed up as him for halloween on multiple occasions as a teenager. And no, I didn't mind that no one else got it.

Very interesting work!

Years ago, when Ebola first entered popular awareness, it seemed that the high mortality rate and the speed with which it affected people meant that it couldn't spread too widely. It wasn't a virus like HIV that could remain hidden for a long-time. It was as though Ebola had evolved to be too deadly to humans for its own good. But now it seems that Ebola has all of its bases covered. Is there any indication if this ability to persist in bodily fluids and be transmitted sexually after the acute phase is something new that the virus developed? Have we helped Ebola evolve this ability by helping people survive it? Or has it always been possible but we didn't know because we weren't able to help many survive previous epidemics?

I'm asking this question for a friend. I don't have to worry because, after reading the paper, I'm never leaving my bunker again (at least for the next 9 months).

mark_freeman

(Jessie) Hi, and thanks for the question. The quick answer is that it is very unlikely that this is something new for the virus. There is no evidence yet published as to whether this strain of Ebola virus behaves any differently to those that came before it with respect to mortality rates (outside of interventions) nor to sexual transmission (as the number of people who recovered in past epidemics was so limited, as was funding for the intense job of following patients, I can imagine). Though we can't say for sure, it is thought to have taken off simply due to the circumstances and location of random events that occurred after the single cross-species transmission (including the heavily criticized slow response, but also one notably important funeral and proximity to dense populations and health care centers). There's a great paper on the natural history of Ebola virus, if you are interested, by Xavier Pourrut et al. 2005 (http://www.ncbi.nlm.nih.gov/pubmed/16002313).

While it's necessary to seriously consider the possibility of sexual transmission from asymptomatic convalescent survivors from a public health point of view (remaining poised to respond to an event), we hope one also takes away the point that these events are likely to be very very rare. No need for bunkering!

I noticed in the paper that you model sexual transmission as B(s) = n*q . The q of 8.27 coital acts per month and then p for proportion of men.

You note that you assumed that the transmission probability is frequency dependent and the probability the partner is susceptible is S/N.

My question, given a proclivity towards monogamous pairings, is the S/N really a safe assumption for the susceptibility of the partner? I'd guess that it'd probably be reduced by an elevated number of both exposed couples.

That proportion could substantially reduce the epidemic time? Am I off-the-rails in my thinking here?

AspiringInsomniac

(Jessie) You are certainly not off-the-rails. This is actually one of the initial interests I had in doing this work, as spatial/contact network considerations are important for epidemiology of sexual transmission in particular. However, given such little data on this aspect, we decided not to include it. While there

are likely to be some things that drive down susceptibility of partners, particularly in smaller communities where exposure rates were high, there are also social aspects of such perturbation in contact networks due to death or stigma which could drive partner susceptibility up. To me, this is the logical next question that needs to be asked. I'd love to spearhead it, but am currently committed to other research.

Thank you for doing this AMA, with the Olympics coming up how detrimental do you think the spread might be? Also have you seen direct links to the deformities and the virus being prolonged in women or just if they are pregnant?

allycatastrophie

This question is about Zika virus, please see above.