Tracey: [00:01](https://www.rev.com/transcript-editor/Edit?token=LX4ovjpNysJP_slj0rSDhUMJFNeUtVJuiMuMG5cuL6oQa69d2SFvFNBFWmcq0g4TPUFziDz3kNXgzh-FZufX3ThidH4&loadFrom=DocumentDeeplink&ts=1.28) Hello, and welcome to NC State's Audio Abstract. I'm your host, Tracey Peake. Dengue fever is one of several serious viruses transmitted by the Aedes aegypti mosquito. Although dengue occurs most commonly in the tropical and subtropical environments of Southeast Asia, South America, and parts of Africa, lately cases of the virus have appeared in Florida. We're speaking today with mathematical biologist, Alun Lloyd on the spread of mosquito borne illnesses in the US and the methods we can use to stop them. Welcome, Alun.

Alun: [00:35](https://www.rev.com/transcript-editor/Edit?token=IpJzAiLhfb6oJPSVYFCsbzoRANkN8s80I66k5SmKyIOjX9rIuV47k8UfGP9Gi5W23qoEat9Hj6zBuLGRQNg3kvbzCKs&loadFrom=DocumentDeeplink&ts=35.48) Hi there.

Tracey: [00:37](https://www.rev.com/transcript-editor/Edit?token=kBDMsGvdytpF5FUJBJMx5QqrdTSZaRaVuCBNeC32YlCcONtgNXWFNuh7cRLdRZ-YGx312RdxXmFYPHfOi-SJS9gBp48&loadFrom=DocumentDeeplink&ts=37.01) So how does a virus get into a mosquito population to start with? Why are certain viruses associated with certain mosquito species?

Alun: [00:48](https://www.rev.com/transcript-editor/Edit?token=5RwYwp5DrkR7zcO_05YiNcsgVw9_AGQPycyVdgvekHQ8iTpMhmPEwCtxN1UdV4acPkNGvUIH8NdQvvQBWt7FvhAumkU&loadFrom=DocumentDeeplink&ts=48.91) Viruses can't reproduce by themselves. In order to reproduce, they need to use the cellular machinery of a host species. This process is often fairly specific, both in terms of the host species and even the type of cell within that host that's involved. So for instance, HIV uses a particular type of white blood cell, a CD4 cell, within humans in order to replicate. So this specificity of this replication process is why certain viruses that are associated with certain mosquito species.

Tracey: [01:24](https://www.rev.com/transcript-editor/Edit?token=mCwngvcsHHVKxUSz4pPUI2VepkWjU2jcrU2FtZnyC80FfLtCH6Gidi7FUgWhZ0VmPPNm_Oj4vku-TvnpBQfq7iXsalk&loadFrom=DocumentDeeplink&ts=84.02) In the case of dengue fever and the Aedes aegypti, then there's another subspecies that carries it as well, are they born with the virus in them, or do they pick it up from a host and then, because of their internal biology, they are uniquely suited to carry this thing around and transmit it?

Alun: [01:52](https://www.rev.com/transcript-editor/Edit?token=td0hlVKaGquA3jAPFuAwzajZPIwlO7AlZnBYCqE368dLK9c95now0qlobbhElAlu7RLm8hOqJYE_eLcpHobuOGClorU&loadFrom=DocumentDeeplink&ts=112.76) Mosquito borne infections of viruses that infect humans generally have a two step life cycle. They have to be in the mosquito and then they get transmitted to a person and then they get transmitted back to the mosquito. There can be some exceptions to that, but generally the infection is going backwards and forwards between the mosquito and the human. Of course, where it originally comes from is a bit like chicken and egg. Is it in the mosquito first? Is it in the human first? So when I said there's this specificity for viruses, sometimes the virus can work in in more than one species. So a classic example is influenza that can be spread by pigs, we get swine flu, bird flu, so on, and it can replicate in people. So that gives the opportunity for the virus to jump from species to species.

 Presumably at some point, the virus jumped into the human population and it must able to spread backwards and forwards between the mosquito and the human. Often these jumps are associated with the genetic changes in the virus's genetic code. So for instance, you mentioned aedes aegypti is the primary mosquito that transmits things like Zika and dengue, and there's another virus called chikungunya that it transmits. But at some point, there was a mutation in the chikungunya virus that allowed it to be more effectively spread by, or as effectively spread, by another mosquito species, Aedes albopictus, which happens to be one that we have here in Raleigh, North Carolina. So it certainly is prevalent in my backyard. So those sort of jumps between species of particular interest and concern.

Tracey: [03:55](https://www.rev.com/transcript-editor/Edit?token=D-y4iokcyeVOJj1yhpwg-0rpXVb328s2H2FiQBfPb4Ijz_HG5uMXRr_k6YLffXNR4xKc9w2H9bEy4QwTN00RXszn6D8&loadFrom=DocumentDeeplink&ts=235.92) You are a mathematical biologist and your job, is to use math to give a mosquito a disease forecast for a given area to figure out how these diseases spread through a population. How exactly do you guys do that?

Alun: [04:17](https://www.rev.com/transcript-editor/Edit?token=Dtl_tyBCJymSwQ3HfpWczV_mjW9eoGv517Zv_hT8KE_9kznhh28kcriPNtZJJm1Loic4qDTaC0wZuDdjLhjE1ndn6kw&loadFrom=DocumentDeeplink&ts=257.28) One approach, we make mathematical models that actually describes how transmission happens back and forth between humans and mosquitoes. So for instance, if we know, or if we can predict, how many mosquitoes there are, what fraction of the human population has infection, and what the probability of transmission is when a mosquito bites a person, then we can figure out how many mosquitoes are going to catch infection. Then we asked the question the other direction. We can figure out how many people are going to have the infection and we can figure out how the virus moves through this transmission chain.

 Now, there's another type of way of modeling or predicting as well. It's maybe a more of a statistical approach. You might just look at the distribution of mosquitoes across some region. It's natural that transmission is more likely to happen where there are more mosquitoes than in places where there are fewer mosquitoes. So you can create a risk map. Maybe there are other variables that you can use and to go into that prediction, like some measure of socioeconomic status, for example, might impact disease transmission. They're not as mechanistic as the sort of models that I make, but then they're more statistical models.

Alun: [05:56](https://www.rev.com/transcript-editor/Edit?token=RhjOQqUuge9JmLBl5SUuwaaBdWKyw6LpF0GIBt718XY6yw2gieUN_XGDYS-D8hP3lW6BH8_QC1a9hPr8Fb3S4jmAphM&loadFrom=DocumentDeeplink&ts=356.06) One advantage of the mechanistic models that I make is that, we can not only predict what's happening under the current situation, we can make tweaks. We can say, what would be the impact doing a control measure? So I could say, for example, what happens if we halve the number of mosquitoes? What happens if people use DEET and so repel mosquitoes? What happens if you use, for other mosquito borne infections, bed nets, or if you have a vaccine, for instance? Those are the sorts of questions you can ask with a mechanistic model that maybe you can't ask so easily with a statistical model.

Tracey: [06:39](https://www.rev.com/transcript-editor/Edit?token=Pt5dLNpleLqURI9leBtUpGGvyyhDMwVYVpEbUa4uyrYRqqUQm4sRi68vA93KS81mGSeV5FLdT1L_YghVi2JxIdKc12Q&loadFrom=DocumentDeeplink&ts=399.77) Okay. So it's more like being able to game out different scenarios during an infection.

Alun: [06:52](https://www.rev.com/transcript-editor/Edit?token=PFs0g0wXQVgUtMV91MC-cuHbeQGAWH79V3EEoA2v9wv9CIGmcYQwbxRq2eQAppSgrGJqZP4GdYncQy8WRBZu_AJijE4&loadFrom=DocumentDeeplink&ts=412.77) But one thing to say, of course, our ability to make forecasts always depends on how much data we have. So if we don't have a good idea of how many mosquitoes there are or where the mosquitoes live, or if we don't have very good idea of how people or mosquitoes interact, that makes it difficult for any sort of approach to make forecasts.

Tracey: [07:53](https://www.rev.com/transcript-editor/Edit?token=J2TJDjNHtOu0UJXPxZcbz3F_1KUktNZ9FhJdskjZxUco-rWzAG0PcCcAWqiD1j4dAbZjUweo8g-GsDeWwj5ZOjdTY3I&loadFrom=DocumentDeeplink&ts=473.81) Okay. Now, once a mosquito species gains a toehold in a new area, can we using your mechanistic models? Can we predict how many cases of, say, in Florida dengue fever, we may see in a year?

Alun: [08:23](https://www.rev.com/transcript-editor/Edit?token=l3m8VfHs2Z-4r-cnyAO6aUYHvlrtilc1BPZLkky7E6NcQ80_HifgPUG6cJ8z-3a9F8-6MjpyfXPy8yHVJTVb5V6AkJs&loadFrom=DocumentDeeplink&ts=503.77) So we can certainly make predictions, but then the question is how good are those predictions? So when we do modeling, it's very much an iterative, step by step process. We typically make predictions compared to what we see happening. Usually that means that we have to improve our models to do a better job of forecasting or predicting. Now, in places where a dengue transmission, for instance, has been going on for a long time, we have historical data that we can use to calibrate and check our models. But when dengue emerges in a new location, we don't have that luxury, so it's a lot more difficult. An important thing to keep in mind is the transmission patterns can be quite location dependent. So mosquito is a cold blooded creature. So they're highly impacted by weather and climates, temperature, rainfall, so on. Also, the transmission is impacted to quite a great degree by lifestyle differences for people.

 So how often we encounter mosquitoes. So transmission in, for example, a Texas city or a Florida city might be quite different to the pattern of transmission in a nearby Mexican city. So this lifestyle thing is really important when we think about the risk of disease transmission in the US. Because we live in screened houses and we spend most of our time in air conditioned spaces, we really don't encounter mosquitoes as often as people in other locations do. Houses elsewhere often rely on natural airflow to cool them rather than artificial air conditioning, so they're more free for mosquitoes to come in and out of houses, and hence interact with people. In that situation, you'd have a much higher risk of transmission of infection.

Tracey: [10:13](https://www.rev.com/transcript-editor/Edit?token=6veuOaEMPgvXSFUl3v8vboMDRnLMa7EssbOxVTrL1dfsC-6W0Lh7660GUOJ6MEcm2YHsQ4Ff8fsy9uyuci1XWFTxEvE&loadFrom=DocumentDeeplink&ts=613.61) On a related note, once we see this particular species appearing in the US, once they get their little six legs on the ground in Florida, how long would it take, or what is the likelihood that they're going to spread throughout the Southeastern United States?

Alun: [10:42](https://www.rev.com/transcript-editor/Edit?token=nRDDR-4lTfvRFafkLxiShb6mcnSAHQPqdUpje_VUUA9_-fY_1wFkoO6VNTcZDBUTMbGJCAOTVLOfR4mGofInI4U43g8&loadFrom=DocumentDeeplink&ts=642.23) Both Aedes aegypti and Aedes albopictus are invasive species. Albopictus, the one that we have here in Raleigh, is a more recent arrival in the US but seems to be better able to spread. It's already pretty widespread throughout the Southeast of the US, whereas Aedes aegypti seems to be more restricted to the Southern most edges of that region. So Southern Florida, Texas, Louisiana, and so on. Also, I should say Aedes aegypti also present in California.

Alun: [11:22](https://www.rev.com/transcript-editor/Edit?token=2ZCEKcEl4iPkXozOi2djzFMUeFanFSOyvpN9ERwvYADi0mlb3zF3RMb1wr4fJHp3T2D6--3akpWsU5pNlUAXIulSTWo&loadFrom=DocumentDeeplink&ts=682.5) Dengue and Zika are more effectively transmitted by aedes aegypti, the one that's rather limited range. The one that is rather limited say, to places like Florida. More effectively spread by Aedes aegypti than Aedes albopictus. So we would have a slightly lower risk here right now. But as I mentioned before, you can have mutations happening in the virus. The example of chikungunya that was able to spread through Aedes albopictus after a pretty simple mutation is rather worrying and concern in terms of the wider spread of these infections.

Tracey: [12:07](https://www.rev.com/transcript-editor/Edit?token=0YSGCh86uYgZ2O7p6OeaS3HPfQFnwbR8kc5WrtzvBCDy9-1Mpq-vXqo1PpdkHHPwms9KhQucnh4qlM3Yi9JQ7OnQNPI&loadFrom=DocumentDeeplink&ts=727.53) Realistically, just controlling mosquito populations is the best way to get a handle on this so that tropical or subtropical diseases do not then spread through the US. Florida recently permitted the release of some genetically modified mosquitoes to try to stop the spread of disease or control it. Can you give me a little bit of information as to how that process works? What are we doing to these genetically modified mosquitoes and what happens when they enter a population? Do you have models that could explain their effect?

Alun: [12:46](https://www.rev.com/transcript-editor/Edit?token=qelMF5bkDAnAmawYz3PrhE_5bdSmAHjsHJmzBqk_laMd4wimYpg3Nom5r1YUEMe8zryTbWoWj10bLj0QmOaL_MeIUgw&loadFrom=DocumentDeeplink&ts=766.92) The modified mosquitoes, these are aedes aegypti mosquitoes that have been modified to carry a gene that prevents their offspring from surviving to adulthood. The idea is you release lots of these altered mosquitoes, so that many or most of the native Aedes aegypti mosquitoes mate with these modified mosquitoes. Then the offspring from all those matings will be doomed. They won't survive to adulthood. As a result, this approach, if you continue to release these modified mosquitoes, will reduce the number of mosquitoes in a region. I should say, ideally, you only want to release male mosquitoes because, one thing we haven't talked about, it's only female mosquitoes that bite people. We haven't talked about why mosquitoes bite people and why they're a threat. Female mosquitoes need blood in order to produce that eggs, so it's only female mosquitoes that bite.

 If you released both male and female mosquitoes, you'd be increasing the overall number of mosquitoes while you're doing the releases. Then those female mosquitoes that you release would be biting. So that would both be a nuisance for local residents, but also that that would pose a disease risk. The idea is you just release male mosquitoes, and it turns out there's ways of separating male and female mosquitoes, so then the males obviously will pass on their genetic material, but the male mosquitoes don't bite. So you neither increase the nuisance nor the disease risk.

Tracey: [14:21](https://www.rev.com/transcript-editor/Edit?token=NWNCb-7zMhmzWaM1FDPn0Jmci_JGgP9xCVgMeAAduj6PHumnh72RU-WoguNm0UC0fYT_rk3RnvC_8Gg7uVUwQWuQ8gA&loadFrom=DocumentDeeplink&ts=861.89) That's very clever. Has this been tried on a large scale in other places in the world? I'm thinking probably.

Alun: [14:33](https://www.rev.com/transcript-editor/Edit?token=atmIBNSy9oI6BORkJ4Jb6TB0qTIM3lPWkS-2D9Y8KeXc4UTILMbZlc5wFeyYlriOiDMbEZAPEX3PANfF3KucQc44W74&loadFrom=DocumentDeeplink&ts=873.07) Good question. The first thing to say is the approach requires the release of lots of mosquitoes, because you need to make sure that those native mosquitoes have quite a high chance of mating with your modified mosquitoes. So you want to outnumber the local population. There have been small scale trials of this approach in various places over the years. It has been shown to work at the small scale in reducing local mosquito populations. People do worry whether the approach is one that can successfully be scaled up to a larger area because of the number of mosquitoes that have to be released in order to do it. So far, my understanding is that it's been shown that you can reduce the number of mosquitoes. Showing that it has an impact on disease spread is a lot more difficult, in part because these infections often happen in sporadic outbreaks.

 So it could just be that the year you happen to do your release and you reduce the mosquito population, that might just be in a year when you wouldn't have had a disease outbreak in the first place. People want to do large scale, randomized cluster trials, the gold standard medical trial thing, and these could show that these control measures have an impact. The only problem is these sorts of trials are very expensive and difficult to carry out. There is an example of such a trial for a related genetic approach currently underway, but these are challenging to do.

Alun: [16:48](https://www.rev.com/transcript-editor/Edit?token=Oq2dRMSP-U-GS0ulFfdsRH7kGYDfvqMtfBr7A_tV8mON3Osr8GCum7bcEwoBV3SyQtzfoQFD3j-oiKVXub5EJVhdq0g&loadFrom=DocumentDeeplink&ts=1008.18) So you asked whether we model these sorts of releases of genetically modified mosquitoes. I've been here at NC State for about 17 years and, during my first year at NC State, Fred Gould from the entomology department showed up in my office and mentioned this idea of genetic control of mosquito born diseases to me. We've been working together ever since. So we've been developing mathematical and simulation models to look at this sort of approach and a bunch of related approaches using genetic techniques for the control of mosquito populations and the infections that they carry.

Tracey: [17:29](https://www.rev.com/transcript-editor/Edit?token=8DmoLw_MLCcJABI_V48anrGelE9Cr-QzS6QwoJMK9L3DcrygsnyhunJQqtRTiCVNhJBkMOKG1ZEmeguNy6Fhj37i_sQ&loadFrom=DocumentDeeplink&ts=1049.84) Well, that brings me to my final question, which is, what is the coolest thing about being a mathematical biologist? What is the most interesting thing that you do and the coolest thing? Why you do what you do.

Alun: [17:47](https://www.rev.com/transcript-editor/Edit?token=rq1AkKIjdcuLs_bv4reNhYLf61Ssv8RUp1FcXccaPC8XLepcexhyxVCl4hQET6p989fCIfcgPplZKwVP6WNAA9kselI&loadFrom=DocumentDeeplink&ts=1067.15) One of the cool things for me is that my undergrad degree was in mathematics and math is often a very inward-looking, insular discipline. The fact that you can apply mathematics to real world problems that people care about, and you can describe the sorts of approaches you do in fairly simple terms. So I teach, basically, the fundamentals of my disease modeling in my undergraduate calculus classes aimed at biology students. So for me, it's great to see the power of mathematics in moving to describe real world systems. Then there's lots of things about mosquitoes is that I just find fascinating. I'm always staggered by the amount of press that say, for example, shark attacks get, and if you look up the numbers, there are something like around the world, 10 human deaths from shark attacks every year.

 But if you look at mosquitoes and of course the infections they carry, those mosquitoes and their infections kill about 750,000 people every year still.

Tracey: [19:00](https://www.rev.com/transcript-editor/Edit?token=70KewICGlsKujl88pwory9QFGGZ1WCGu8Nq3pMNPnMu67E82yRJ7UIx-prnNNw-niK8YbJA7IphL_tdf7eBFQGIKh1o&loadFrom=DocumentDeeplink&ts=1140.55) Good grief.

Alun: [19:01](https://www.rev.com/transcript-editor/Edit?token=-8djs94fnzfRoL5sTcmKG2JbhHGno9GcnglNln6qVbJ8jjA31JIu4nIyIho84xEEyTQDZC9jjy048kEMKqKuW-ZvDvg&loadFrom=DocumentDeeplink&ts=1141.03) Despite all the work that's gone on in trying to control mosquitoes, trying to research vaccines and treatments and so on. So the sheer scale of the impact and burden that mosquito borne infections place on humans is staggering. Then for the mosquitoes themselves, I'm always amazed by and disgusted by their ability to find humans to bite. I'm a keen gardener and I like to go outside, mow my lawn, and so on. But those mosquitoes, those Aedes albopictus mosquitoes, they find me within a few minutes when I'm outside. They're buzzing around my arms and legs and I'm suffering from their bites for a long time afterwards.

Tracey: [19:50](https://www.rev.com/transcript-editor/Edit?token=SF6trxLTaXNYDMlGi9VoEwNjkzZXI13CBo5rxw_F2aCV5SkE0aa52rVwhOvHKhZVWunNTLx6m9RfUWc_qsWdKWWXW2o&loadFrom=DocumentDeeplink&ts=1190.38) Not my most favorite thing in the world for sure. Well, thank you Alun, for being here today. It's been an extremely interesting conversation.

Alun: [20:04](https://www.rev.com/transcript-editor/Edit?token=t7XhmdHWJAeVk90a000er-AIZsCN2ABEfxIRIahRKIKZqcj_sch8KNEQcMseavu6a8i2WEs626XpgRDDhEweL-AtAtU&loadFrom=DocumentDeeplink&ts=1204.61) Well, thank you for having me.

Tracey: [20:05](https://www.rev.com/transcript-editor/Edit?token=0O-o9dMj99f8GYrYWUenIVYsp7Ap5RBN_Wy6mNKQYc0d1dlaoCyYK3m4Ko7XqVDF8ESNup36aD9Re4S3GZUSX3SdWPU&loadFrom=DocumentDeeplink&ts=1205.03) We have been speaking today with Alun Lloyd, mathematical biologist here at NC State. This has been Audio Abstract. I'm your host, Tracey Peake. Thank you so much for listening.