

Shiga Toxin–Producing *E. coli*, Ireland, 2013–2017

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Paul Hynds, a researcher at the Technological University Dublin in Ireland. We'll be discussing patterns of Shiga toxin-producing *E. coli* enteritis infection in Ireland.

Welcome, Dr. Hynds.

[Paul Hynds] Thank you very much and thank you for having me.

[Sarah Gregory] Your study looked at Shiga toxin–producing *E. coli*, or S-T-E-C. What makes S-T-E-C different from, say, regular *E. coli*? And is there a regular *E. coli*?

[Paul Hynds] That's a good question. So the simple answer is no. There's really no regular *E. coli* in which the same way there's no such thing as a regular human, although there is a common ancestor, and we tend to refer to those common ancestors as "wild type". But no, there is no regular *E. coli*. There are two main types of *E. coli* and that's what we do a lot in...within epidemiology and particularly in environmental epidemiology is we tend to look at classification systems a lot. So in terms of *E. coli*, there are two main types. So one is pathogenic, and essentially anything that is capable of forming or starting an infection in a host is known as being pathogenic—a lot of people would refer to them as germs, essentially. And non-pathogenic, so non-pathogenic are essentially those *E. coli* that can't or don't produce infections in humans or other hosts.

In terms of what....and I'll probably refer to it—don't tend to refer to it as S-T-E-C, we tend to refer to it as STEC, or in Europe we actually refer to it as VTEC, and actually improperly so. So what is STEC? Well it stands for Shiga toxin-producing *E. coli*, and what that essentially is, it's based on its mode of actions. So as I mentioned, there is the pathogens and the non-pathogens. Within the pathogens, we further classify them into five different types of pathogens and it's based on the mode of actions. So essentially when it enters the human system or any mammalian system, they essentially do one of five things and that's how we classify them. So STEC (or S-T-E-C), they get into the human system, into the digestive track to the gut. They produce Shiga toxin, and that's why we call them STEC (so Shiga toxin-producing *E. coli*).

[Sarah Gregory] Okay. And STEC comes in different serogroups. Could you explain what a serogroup is?

[Paul Hynds] Like I said before, we're always constantly trying to classify and further classify. Again, in much the same way as we try to do with people, because of machine-learning algorithms and things like this. So the serogroups are essentially another way of classifying bacteria or viruses into similar groups based on what we call a phenotype. What a phenotype would be is something like, say, in humans, you can have Norwegian people, Irish people, English people; but you can have Norwegian people with green eyes, blue eyes, brown eyes. So this is essentially what we mean by serogroups in *E. coli*. So we use a serogroup to further classify the pathogen. The serogroups, in terms of *E. coli*, it's all based on the presence or absence of antigens.

So antigens—and people will probably be very, very familiar now with the word "antigen"—but essentially an antigen...it's just a molecule, and it's a molecule on the surface of the bacterial cell. And in terms of *E. coli*, we tend to classify them based on the presence or absence or the type of

two different antigens: there's an "O" antigen and there's an "H" antigen. And it's actually a really good classification system for us because then when we look at human infection, we can refer to the specific type of *E. coli* that has caused that infection. So in epidemiology, we're not just looking at *E. coli*, we're looking at specific types of *E. coli*. So there's 700, actually, serotypes of *E. coli*. So people may have heard of (I'm not sure), but one we would look at quite a bit here in Ireland is O157. And the specific strain of that would be O157:H7. So it has the "O" antigen 157 and "H" antigen 7. And that's what's a serogroup. So all of those *E. coli* that have the 157 antigen present are members of the O157 serogroup.

[Sarah Gregory] Okay, interesting. Yes, for listeners I have done several podcasts on that specific serogroup.

So how is this pathogen spread?

[Paul Hynds] *E. coli* can be spread in a multitude of ways. *E. coli* can pretty much be spread in any of the ways that any infectious bacteria or virus can be spread. And that's at most why we work a lot in *E. coli* here in Ireland is that we typically tend to see it spread via water a lot, particularly water that is consumed. But in North America—so I spent a year...year and a half working in Canada as my second postdoc (or postdoctoral contract)—in North America, *E. coli* (and particularly *E. coli* 157 that I've just mentioned) is often called the "burger bug" because typically in North America, *E. coli* O157 is foodborne. So the main routes of transmission tend to be water, food—often salad leaves, actually because of washing with contaminated water or irrigating the crops with contaminated water. In other countries, we sometimes see outbreaks because of ice (the use of contaminated water for making ice). And then, like a lot of the enteric pathogens (so *E. coli* is an enteric pathogen) and so far as this causes a gastrointestinal infection. It can be spread via person to person, which we call secondary transmission; it can be spread via direct animal contact, in particularly cattle and sheep (in Ireland, anyways); recreational waters (so beaches, swimming pools, and things like that). So they're essentially the main sources of transmission.

[Sarah Gregory] How would it be spread person to person? Is it like droplets or fecal matter?

[Paul Hynds] Yeah, both of those—we don't want to mention the "c" word, I presume—but, it can be spread exactly as you just said. It can be aerosolized (so coughing and sneezing) and also fecal matter. And we see that particularly in crash outbreaks and things where you may have younger people whose hygiene may not be the best and it's then spread person to person.

[Sarah Gregory] Yeah, that's really interesting. I guess because I live in North America, but I've done so many podcasts I didn't ever really register that it could be spread person to person.

Your study looked at the Republic of Ireland. Any particular geographic locations there?

[Paul Hynds] Essentially. Actually the objective to the study itself was to identify specific locations. We've typically—we've known for quite a long time that Ireland is a little bit of a hot spot. We tend to have a lot more of this infection than a lot of other places. So in order to start to get some appreciation or understanding around why that might be, we wanted to try to figure out are there hot spots within the country itself, and then what are the characteristics of those particular areas if we find them (so it was unknown, essentially). We looked at all of Ireland with the aim to specifically identify locations within Ireland

[Sarah Gregory] You also looked at the crude incidence of STEC in Ireland. Is there a difference between incidence and crude incidence?

[Paul Hynds] There is. So as like any scientific field, we tend to have a lot of terminology, we use a lot of different...like I was saying about *E. coli*, we really don't refer to *E. coli* very much. We tend to refer to the individual strain's serogroup serotype. And we also have a lot of terminology around numbers. So how exactly do you say that there's a lot of *E. coli* here? How exactly do you say that there's not a lot of *E. coli* here? So we have things like crude incidence rates, incidence, cumulative incidence, prevalence. So essentially what the crude incidence rate is, it's the number of new infections—let's say, *E. coli* enteritis (or STEC) infections—that occur across a specific population or specified population over the course of one calendar year.

So our specific population, as you just asked, was it certain locations or the whole of Ireland? So the population we looked at, that was all of Ireland. And then we looked at it year on year on year on year. So we expressed the crude incidence rate as the number of infections per 100,000 population. And what that allows us to do is we can calculate and express the crude incidence rates for Ireland, and we can compare it to Denmark and the U.K. and France, and the U.S. and Canada. So it allows us to try to get an appreciation for where is it high and where is it low.

The crude incidence rate typically looks year on year on year, whereas the incidence (what we would call the incidence proportion or the proportion) normally is...it takes perspective of what is happening over in accumulation of time. So we don't split it out year on year on year on year. We look at essentially the entire data set that we have for the entire study period that we have. And that's why we call it the cumulative incidence. So we don't break up the time, we look at the entire time that we have and we figure out an incidence rate across the entire time. But there are lots and lots of different incidence rates and different crude incidence rates. For example, we have an age adjusted incidence rate where we would look at, let's say, what is the incidence rate among children in Ireland between the ages of 0 and 5, and we would do it in exactly the same way. We'd figure out how many people (or how many children) in Ireland are aged between 0 and 5, and we have a total population. And then we look at the number of infections within that population over this specific timeframe, and then we express it in the same way. Therefore it's a crude incidence rate per 100,000 population between the ages of 0 and 5.

And then the other ones that we use quite a bit (the other rate that we use quite a bit) is the prevalence rate. It's a separate one to calculate, but we cannot use it so much because it's very current. So essentially the prevalence rate will change day to day and week to week. And the prevalence rate is essentially how many people (let's say, in Ireland) are infected with a Shiga toxin-producing *E. coli* right now. Well, obviously that may be different tomorrow and it will be different next week. So we don't tend to use the prevalence rate so much.

[Sarah Gregory] So apparently this crude incidence is 10 times the EU average. That's obviously a big difference. Why is it so much higher?

[Paul Hynds] Every student asks me that question every time I go to a conference. Because anytime you see something like that (10x), why is Ireland so much higher? Are people dropping like flies all over Ireland? And no, we're not. I guess...number one, typically the problem with the crude incidence rate is it can be exaggerated if you have a smaller population—well, typically the crude incidence rate for STEC across the state are much, much smaller. But essentially there are two reasons why we're 10 times the EU average. One is a good reason, on one hand, and one is a bad reason. Typically in Ireland, because we became aware of this problem or issue with STEC (or what we refer to often as VTEC), I'll try to keep remembering to say STEC. But because we recognize this issue in Ireland, I will say probably 10 to 12 years ago

(maybe a little bit more)—so what we essentially have now in Ireland is one of the best surveillance systems for STEC in Europe. Which means that the better you are at looking for something, the better you are at finding it. So typically, we tend to have...a lot of the time, we have higher VTEC incidence rates than other countries because sometimes other countries are simply not looking for it.

So it's sometimes unfair and often times in papers maybe it's a little bit of a dramatic thing to say that it's 10 times the EU average, because the EU average is kind of biased because typically there's a lot of countries that don't surveil for it so well or so often. And therefore, that drives the overall mean down. So it's kind of a case of comparing apples and oranges. And that's often the case, actually if you look at the EU, we have a lot of countries. We have some high-income countries, and we have some low-income countries, and typically in the higher-income countries we tend to have a better surveillance network. Now with that being said, if you take a lot of the lower-income countries out of the EU mean...let's say the high-income EU mean is still around about 20-30% the Irish mean (this is the bad side of the equation), so typically in Ireland—and we've written this and I've written in many papers over the last four, five, six years—we kind of represent the perfect storm for this one specific infection for a number of reasons. We have a very, very high number of cattle. Between 60-70% of all the entire landmass of Ireland is grazing land, and the vast majority of that is grazed by cattle and cattle are the main source for the STEC pathogen. We also have a very high reliance on groundwater in Ireland, over 25% of all of our water comes from ground water (so that's water for consumption). But of that, or not of that but around about 15-16% of our population drinks from private wells, and they're entirely unregulated. So they have no regulation, you can dig it where you want, as deep as you want. You can finish it well or you can finish it poorly, etcetera, etcetera. So often times those systems are not treated, they're not tested very often. And also we have a very high reliance on septic tanks. So these kind of one house, domestic wastewater treatment systems...we have around about a half million. Which may not sound like a lot in the American context, but in a country of just about 5 million, to have a half million septic tanks is a huge, huge number of septic tanks. And then again, we have a very, very....I'm not sure if many of your listeners have been to Ireland, we have this joke, we say there's a very high hydraulic turnover in Ireland which essentially means—if I come from a hydrological backend, it essentially means we have a huge amount of rain in Ireland and we have a very diverse geology. We have a lot of characteristic geology which is quite susceptible to contamination. So there are kind of....on one hand, we have very good surveillance—so we're good at looking so we're good at finding. On the other hand, we just have a lot of STEC in the country and it moves around the environment very quickly due to the rain and the geology and the private wells.

[Sarah Gregory] What is the timespan of your study?

[Paul Hynds] We looked at five years, and we did that for a very specific reason. A lot of our models we're using, they're basically AI algorithms (artificial intelligence) but we would call them machine-learning algorithms. There's a lot of data involved. We started the study in 2013 because before 2013, there was a geographical bias within the country in terms of where we know we were looking in very specific places. And also because of where our labs were based, there was a geographic bias, and we didn't want to introduce that into this study. So we looked at five years (2013-2017) and we've held back two years (so we have 2018 and 2019), and we've held them back for a couple of reasons. Number one, we want to use those as an independent data set to essentially test all of our models. And number two, we had what the Irish would

consider quite a significant drought—so essentially once in a lifetime drought. And I know a drought in Ireland looks very, very different to a drought in the U.S., but we didn't want to introduce (in terms of climate) very extreme years. So we kept the study to five years.

[Sarah Gregory] Your study looked at spatiotemporal dynamics of incidence. Explain that to us.

[Paul Hynds] Spatiotemporal dynamics, they're very simple things. So it comes from spatial and temporal. What the spatial is, is trying to figure out what are, let's say, the hot spots and cold spots of this infection. Because we want to figure out well, where do we have lots and where do we have a little. And then in terms of the temporal, well temporal is just another word essentially for a time series. So I often try to explain it to students in terms of, you'll see in epidemiology and environmental epidemiology a lot that we do this hot spot analysis where you put in 10 years of data and you get kind of a picture back, a visual back, and it will say, "this place is a hot spot and this place is a cold spot, and in between them is neither a hot nor a cold spot".

So I often think of a lake, ok? You take a big rock and you throw it out in the middle of the lake and just after it splashes down, that is essentially your hot spot map. So it says, "this is where the rocks hit this lake". It's quite crude. I often then try to explain this idea of spatiotemporal dynamics. If you took the same weight as your big rock, but you split it up into lots and lots and lots of small pebbles and gravel and you flung it across that lake, they will hit different places at different times and it will create different ripples at different times. So we can figure where and when (that is your spatiotemporal) and how that moves from season to season and year to year. And then what we do is we overlay that with things like the geology and the rainfall, etcetera, etcetera. That's what I mean by spatiotemporal dynamics—so how this infection essentially from season to season and year to year, how it moves. How the incidence rate goes up and down in different places, be that counties or provinces or local regions, etcetera. So that's what we mean by spatiotemporal dynamics.

[Sarah Gregory] And why is it important to analyze spatiotemporal dynamics?

[Paul Hynds] Because essentially—so I kind of come from an engineering, hydrological background, and we have this saying, "what you cannot measure, you cannot improve". And essentially because this had been done before, we knew that let's say, in the west of Ireland we tended to have more STEC infection than in the east of Ireland. But we didn't really know when we would get it in the west, and did it stay the same year on year on year on year? So I've kind of changed that motto to not what you can't measure, but what you can't understand, you can't improve. So the overarching sort of aim of analyzing the spatiotemporal dynamics were to understand the mechanisms of infection. Do similar *E. coli* serotype hit similar places—and not just similar places—but similar people within those similar places year after year after year? Or is it changing? So we're trying to account for things like climate change, dietary change, and things like that. So do serotypes peaks occur at different times? Do urban/rural peaks occur at different times? And when we start to put all of that together, we start to get a picture for how this infection and how this organism moves around the country. And once we do that, we can start to help further improve surveillance. And our hope would be to start to educate and increase awareness among clinicians, GP's, farmers, laboratories, and even politicians. That's kind of the overarching why we've done what we've done.

[Sarah Gregory] So you also looked at sporadic cases of STEC. And what does that mean compared to the other ways we've talked about?

[Paul Hynds] Essentially there are four main terms we use to describe the distribution of an infection. There's sporadic, endemic, epidemic, and pandemic. And I'm not going to go into epidemic or pandemic because I'm presuming everyone in the entire—

[Sarah Gregory] We those.

[Paul Hynds] —everyone in the entire world knows what they are. And if you don't, you should look it up actually because there is a very, very distinct difference between epidemic and pandemic. There are different boxes we tick. A sporadic infection is an infection that occurs either infrequently or irregularly. And those are actually two different things. So infrequently and irregularly—so irregularly means that you can't predict when it's going to occur, or infrequently means it occurs very, very rarely. And then what we mean by endemic is this is where we have a constant presence of a disease or an agent or a microorganism or pathogen in a population (a distinct population) within a geographic area. So we have things like, malaria would be endemic within particular areas or particular regions. Essentially, diseases that we only see occasionally or we see irregularly...so we see STEC pretty regularly in Ireland, across the entire country we would say that STEC is essentially endemic (it's always there), but it is also sporadic. And so far it's very, very hard to predict that it will be there next Tuesday.

Why we did this is, again, that's kind of data scientists with the epidemiologists would be constantly using data, and with every year, it seems like our data sets are just getting bigger and bigger and now we're receiving things like parallel computings, and we run a lot of our models on remote servers. But what we're always trying to do is have the cleanest, most unbiased dataset we possibly can. So why we've chosen to look only at sporadic cases of STEC are because essentially outbreaks create a bias. So if you have a large outbreak of STEC, let's say in County Kildare, if you have a very large outbreak there and you include that in your dataset, it creates a very, very large bias which would say Kildare (this county just outside Dublin) is a hot spot for STEC (for this infection). What might have actually happened there is that a couple maybe went on holiday and they ate some salad, and they drank some drinks then they managed to pick up STEC enteritis, and then they brought it home and then essentially all the rest of the infections were by person to person. So they're what we call secondary infections. So actually, that area is not a hot spot. It's certainly not a hot spot for what we would call domestic infection, and that's what we're interested in, is to look at the domestic infection. So that's what I mean by sporadic, and that's why we've used only sporadic cases.

[Sarah Gregory] Do cases vary seasonally, and if so, why? Does it have to do with the rain that's always there? Then that would make it seasonal...I don't know.

[Paul Hynds] Yes. There's a very, kind of marked, notable seasonality for VTEC infection in Ireland. And it typically occurs in July and August. So every July and August, we tend to— unless it's a very remarkable year—we tend to have a peak of infections during that year. But we've actually found in the current study that when you split the serotypes, that we actually have two different peaks. So O157, the peak occurs during September/October and O26 which is another serotype—so they're the two most prevalent serotypes in Ireland, O157 and O26—that tends to occur...the peaks of that occurs in June. And that essentially comes back to all types of things like different sources, different pathways, different receptors, etcetera, etcetera. And we tend to use—because we're environmental epidemiologists, we use...there's a model for environmental contamination called the source pathway receptor model. I suppose you could call it like the fireman's triangle. Without a source of your pathogen and a pathway for that pathogen

to get to the eventual receptor, without all of those three things being in place you cannot have an infection. So that's what we're always trying to figure out is what is the source, what is the pathway, what is the receptor? So in terms of, let's say, like I just spoke about those two serotypes that peak at different times, well they're down to different sources and different pathways. The pathway—one of the pathways is rainfall. We've always tended to see a higher incidence of STEC infection in Ireland approximately two to three weeks after very, very heavy rain. We think that the O157 peak occurs later in the summer (or actually into the fall) because of the return to school and international travel, and then we think that the O26 peak occurs due to things like....so, waterborne infection via wells because you have animals out on the land, and we do get—if you've been to Ireland, then you know we get rainfall all year round. But it's different types of rain during the year. But we also have things like barbeques. So there's a very distinct seasonality of when you actually start to split it out via serotype and look at the different seasons, and you can actually do.....we've looked at, let's say, elderly cases versus childhood cases of STEC. And they're actually very, very different as well. Which kind of...what we're trying to do is stack, not evidence but stack inference on top of inference on top of inference. So we've done a lot of that type of work, and we think that, let's say, that O157 peak is due to kids returning to school after summer holidays and also kind of late summer international travel.

[Sarah Gregory] Did you say barbeque?

[Paul Hynds] Barbeques, yeah. Cooking outside. Irish men are not very good at barbequing because essentially, they don't get much experience. We only really get two, three, four weeks of very good weather here a year. And every time we get a spell of good weather—I spoke about this, our so-called our hydrological drought during the summer of 2018—that had the highest number of STEC enteritis notifications over the past 10 years in Ireland. And we're doing modeling at the moment and we're looking at it at the moment, and what we think is that the main source of the infection is normally water in Ireland. But we think that due to the really good weather, etcetera, etcetera, that the main transmission route changed over to food. And it was primarily because of things like barbeque—people undercooking meat. So normally O157, for example, is not considered the "burger bug" in Ireland. But during summer 2018, our transmission rate and our sources of transmission became essentially more American (it became more North American). So it changes from year to year and season to season.

[Sarah Gregory] That's very interesting. So undercooking the food and probably cross-contamination where putting raw meat on.....

So in general, cases increased during the study period. Do you know why that is?

[Paul Hynds] We don't. We don't know exactly why that is. We always have hypotheses. We do know that over the past five, six, seven years, as I've already alluded to, our surveillance is improving all of the time. We are constantly getting better at looking for it, and the better you are at looking, the better you are at finding. So we think that the better surveillance is at least one reason for that. As I've already mentioned, it's typically considered a waterborne infection in Ireland. So we think that shifting weather patterns—so essentially, very, very, very short-term...not climate change, but weather change is causing an increase in infections. And then we also have things like urbanization. There's a lot of...we find that in Ireland, we have urban and we have rural and then we have these transitional zones. And these transitional zones are really not suburbs, they're...and if you've been to Ireland, you'll notice that when you drive out of a town or city, it goes from being pretty urban to very rural very, very quickly. So we call these the

transitional zones. And we have a lot of movement now in Ireland. Dublin is one of the most expensive cities in Europe to live in. So people are starting to move out to these transitional zones. So you have a lot of people moving out of the cities, but they still want to be close to the city. So you have a lot of people starting to use new wells, there are an increased number of septic tanks. So you have a lot of wells and a lot of septic tanks and a lot of cattle in quite small areas. And you also have an increasing national herd—so you have more and more and more cattle because we are intensifying our agriculture here. So we think that those two or three of four things are probably all coming together to create this increasing trend. But we're not 100% sure yet.

[Sarah Gregory] Many of the patients were children and you mentioned that there's a spike when children go back to school. Are they particularly at more high risk?

[Paul Hynds] Yep. My group tends to...we look at essentially, almost exclusively up until 18 months ago, up until March 2020 we looked almost exclusively at enteric pathogens. So any enteric pathogen—as I've already said, a pathogen is any microorganism that can cause disease and an enteric pathogen is essentially where the disease is—it's essentially gastroenteritis. So a virus protozoa (or parasite) or a bacteria that causes some kind of gastroenteric illness. And essentially amongst all of the enteric infections, they all are essentially higher in kids than adults. And then you see a small spike again in the older population. Why is this? Well, there's certainly...I mean, we know they have a much lower immunity (so they have decreased levels of acquired immunity). They have been on the planet far less long, so they don't have that level of developed immunity that adults have. They haven't drank very, very small amounts of contaminated water, they haven't eaten very small amounts of contaminated food very often. So they have just a lower immunological status. And they also have a lower threshold than adults. They travel to a grandparent who lives in the country, they drink a glass of water or whatever the case may be, and they can become very, very sick. But we also think we're pretty sure (and we're starting to do a lot of work on this now), but we're looking at essentially what we call social epidemiology. So it's this whole idea of how behaviors—of how human behavior feeds into the likelihood of infection via exposure. But like I mentioned earlier, kids have different behaviors. They tend to be more tactile; they tend to probably not wash their hands so much, they have a lower threshold for infection and they also have a higher exposure.

[Sarah Gregory] You talked already about the role of population and rural areas and urban areas. Do you have anything more to say about that?

[Paul Hynds] Yeah, I suppose we've published quite a bit this year and what we've found that—I mean, there is no doubt that STEC in Ireland is primarily a rural infection. We see different peaks, actually, from urban to rural areas as well. But like I say, it is essentially a rural infection in Ireland. So if you look at all of Ireland, you could say, well, it's associated with population density but it's actually associated with the higher likelihood of infection in areas of lower population density. But that's because population density is essentially an indicator of rurality, which is quite obvious (it's logical). But what we've also found when we looked at—it kind of carried on nicely from, as I was saying about social epidemiology—we just very recently looked at the sociodemographics of these cases and what we've actually found in Ireland is that in urban areas, STEC tends to be—and this is a little bit of a generalization—but STEC tends to be a quote on quote, "high-income disease". So we tend to see it in urban areas, in areas that have higher sociodemographics—so higher employment rates, higher mean income, higher mean levels of education attainment, etcetera, etcetera. Once you go out into rural areas, it doesn't care.

It's neither high income nor low income. It's kind of all bets are off; anyone can become infected. But in urban areas, for some reason (and we kind of have ideas around this too) but it tends to be a higher income infection and we think it's things that play into it like more international travel and particularly more fresh produce, and so a different diet. So you're more likely to go to a butcher to get your meat and it's less likely to be highly, highly UV treated, etcetera, etcetera. Things like that.

[Sarah Gregory] Boy, that is so counterintuitive, the higher income...

[Paul Hynds] Yeah, it's a strange one.

[Sarah Gregory] Yeah. And the eating fresh vegetables that we all need so desperately is actually hazardous. I've gotten to the point where I won't order a salad in a restaurant anymore.

[Paul Hynds] Really?

[Sarah Gregory] If I haven't...you know, if I haven't washed it thoroughly, sprayed it with vinegar, washed it again myself I don't eat it.

So what was the goal of your study?

[Paul Hynds] I think the goal (I think it's pretty simple really) to really improve and further understanding of STEC in Ireland, to figure out why do we have such high rates. And I know it sounds a little bit "holier than thou" but I really would...we would like to improve Irish people's health and the efficiency of surveillance and healthcare. But genuinely what I was doing—my first PhD actually came from an environmental engineering background, PhD was four years, but I spent a good two years at that (or two and a half years even) out, as we would say, in the field on site. I was collecting huge numbers of ground water samples and I was measuring, you know, the setback distance from wells, the septic tanks, and the setback distance from wells to roads and wells to grazing animals and all this kind of good stuff. But over the course of my PhD, some of the wells I would sample one off because I was trying to get that spatial element, but then I chose, I think it was 25 wells where I asked the well owners (these were all private wells), I asked the well owners would it be ok if I came back every month because I want to get a time series, I want to see how your well changes from month to month to month to month. And country Irish people, of which I am one myself, are pretty nice, I think. And once I told, you know, that it would be confidential, and I would obviously...I would give you the results of your tests and all that kind of stuff.

But what occurred over the course of that 21-month period that I was testing these wells every month, is that a child got very, very sick. And they rang me—was it they rang me or texted me, I think?—and asked me could it possibly be the well water. Now I was a student, far from being an expert. I'm far from an expert now, but certainly back then I had absolutely no confidence in my kind of understanding or so-called expertise. So I said I really don't know, I'm not a doctor. You should definitely get the well tested, if in doubt. I mean, you shouldn't have to ask me to get your well tested, you should definitely get it tested. This is the person's grandson. And they did get their well tested and it was full of STEC (or what we would refer to it as VTEC). But that child had what we call STEC enteritis, which is essentially bacterial gastroenteritis, but it turned into a condition called hemolytic uremic syndrome (which we refer to as HUS). It led to total renal failure in the child, and the child ended up, I think, having a 4 or 5x blood transfusion over one night. So they had to pour blood into this child, and this child was (I think) six at the time (five or six). Now the child survives, everything was fine in the end but I was amazed by how shocked I was at the whole thing. I'd never met the child, but I had met the child's grandfather.

I'd met him every month for 20 months (21 months). And I was just blown away by the fact that—and at the time, we were talking about, you know, the Irish Celtic tiger and we have one of the highest in CDPs in all of Europe. We're a very small income country but we're actually quite a small rich little country. And the fact that a child could almost die from a waterborne infection kind of shocked me. So that's kind of the underlying goal to all of this, is I don't feel like that should happen. I don't feel like it should be let happen. And I think if we had more understanding and more data, it wouldn't happen. That's kind of why we're doing all of this stuff.

[Sarah Gregory] Altruistic and very public health minded.

Is there anything else you'd like to tell us about what you found from your study?

[Paul Hynds] I mean, one thing we know (we knew this beforehand), VTEC or STEC...it's an extremely complicated pathogen, and perhaps even more complicated in Ireland. But we do know more now than we did then, let's say. One thing we found—and it's not necessarily, I suppose it's something I'm interested in because the first degree was applied science and I very much went down the kind of mathematical and statistical route—is we used a lot of different spatiotemporal techniques. And funnily enough, some of the simpler ones were the best. So the choice of algorithm or modeling approach is extremely important because different algorithms point to different things and that's quite dangerous, because you could end up making recommendations, be it to policy makers or doctors. Better to—you might make them with the best intentions, thinking you have a firm evidence base for them. But they could point you in the right direction, essentially. And it's quite dangerous in terms of, you know, when you're dealing with public health.

So we ended up—and in the paper itself, we've kind of developed our own space-time index which seems (for the time being) to be kind of one of the more clearer to have in terms of finding these particular spots over time. To reiterate the interesting stuff, kind of in urban areas we found it's a rich disease, and rural areas...it doesn't discern between rich and poor. It just goes for any host it can find.

[Sarah Gregory] Other than that, were there any other surprises?

[Paul Hynds] Yeah, I mean we've been looking at maps and we've been looking at these data for years and years and years. And the HSE, which is essentially the Irish version of the CDC, they report every season, they report every year. But in using our index, this ST index—what we're calling a....ST is space-time (spatiotemporal) recurrence index, we've pinpointed...we've managed to find these three specific areas in Ireland that have these space-time clusters or these space-time incidences that are way above everywhere else. If you just looked at one page from the entire article, look at this—it's the first large map of Ireland. And these three areas...so we've colored them from blue is very low to red is very high. But there's so much red in these three areas that they are almost black. And that surprised us, that it was so extremely discernable, and it just jumped out of the page. And I was reading all of the reports down through the years from our own CDC (the HSE), they had never really pinpointed any of these three areas. They'd always said that, you know, essentially STEC tends to be more prevalent in the West of Ireland, but they'd never really focused in on these three areas. So that was a bit of a surprise. And kind of, I guess, a happy surprise. And that none of our cities were located in any of these high incidence areas. Which is important in Ireland, because much of our healthcare here is centralized. So that's important to know that these three really, really kind of dark areas (in terms

of space-time incidence), none of them...there are no very, very large towns or cities within them.

[Sarah Gregory] And what were the three very large areas for those not looking at the map?

[Paul Hynds] There was one that is just northeast of Galway, it's about 20-30 square miles. There's one southwest of Limerick city, and another that is in the southern midland, let's say. So there are three, very kind of very, very distinct areas in the country. We were surprised that they were so distinct.

[Sarah Gregory] So what were your biggest challenges?

[Paul Hynds] Probably a lot of epidemiologists will say the same thing—acquiring the data. Getting these data, it's pretty tough because in Europe we have GDPR, you know, in terms of ethics, ethical approval, peoples or individuals right to privacy, etcetera, etcetera. So we essentially had to design our own method for geocoding the data themselves. And we've published that, actually, in an Irish medical journal because we want other people to be able to use the same protocol. But that was by far the biggest challenge. It took us months and months to get the data. And then once you get the data...because all of these studies are of what's known as—the study design is what's known as an ecological study. So we don't study people. The study unit is an area, so it's essentially the area that the person lives in. But we cannot use—under GDPR, under our own, kind of privacy legislation here in Europe—we can't use the person's address. So we had to come up with mapping protocols and coding protocols that we could use a very small area around that person's address, but it couldn't be so small that you could actually figure out who the person or the household was. So we're trying to balance between being very accurate geographically but also kind of respecting the person's or the household or the community's right to privacy.

[Sarah Gregory] Sure, yes.

So your article also discusses the role of infrastructure in preventing STEC infections. What can be done to protect local populations against this pathogen?

[Paul Hynds] So essentially from—there's two ways of attacking any problem of this nature: there's top down or bottom up. Top down is essentially where you legislate or regulate. But because these systems in rural Ireland are entirely unregulated, that option is really not open to local government or the national government. So essentially what you would have to do is go bottom up, and you can do that via education and communication. I know that might seem like a trite answer that's been kind of carted out a thousand times. But you have to kind of, in a way, help people help themselves because the county councils or the Irish government cannot walk in onto that person's property and make them maintain their well. They can't make them take a sample and have it tested. They can't make them treat their water because there's no regulation there to do that. So you have to try to (as best you can) educate people by showing, "okay, well you live in a hot spot. You live in a place that you need to be mindful of this kind of thing. So maybe you should get your well tested every now and then". So typically, in terms of infrastructure, there's no real answer there. You can't—because we have no...there's no legislative tool by which we can improve infrastructure. You can only encourage people to maintain their own infrastructure.

[Sarah Gregory] Well, as a 25-year CDC health communicator, I can definitely say that it doesn't seem small to me to use education and communication as a tool to change and enact public change.

[Paul Hynds] Absolutely. But it does work. I was just talking (I'm an adjunct faculty member in Queen's University, Ontario), and we were looking at...for the average in terms of *E. coli* detection rate. Now this is not pathogenic, I don't want to scare anyone. This is a non-pathogenic *E. coli* that we use as an environmental indicator. But the average detection rate in Ireland when you go out and you randomly sample up wells is around about 25%. So essentially one in four wells will have *E. coli* present. And like I said, that could be...it's often times non-pathogenic, so people don't need to worry so much. But it is evidence of recent fecal ingress (so the recent presence of some kind of fecal material).

In Ontario, that figure is around about two, so around about one in 50. In both jurisdictions these are private wells. These are entirely private wells, so there is no legislative tool. There are no different laws, essentially. But in one area, in Ireland, is 25%. In the other area (i.e. Ontario) it's 2%. And we think that the main difference between the two is that in Ontario, Public Health Ontario offers free well testing, and we think that that in itself is probably the biggest reason that there's 25% on this side of the Atlantic and 2% on the North American side of the Atlantic. And that's not just communication, but that's kind of a...it's a lovely scheme, but it's risk management and risk communication, and in that way it's risk assessment as well. But, I mean, that's a huge, huge difference.

[Sarah Gregory] Yeah, I would say so.

[Paul Hynds] And in terms of kind of governments, you think well, why don't we do it in Ireland? And the government would probably say, "well, it will cost us a lot of money". But you kind of think, well, how much is gastrointestinal infection costing you? You reckon in Ireland per year, it's costing the healthcare system between one and two hundred million Euro.

[Sarah Gregory] Oh goodness.

[Paul Hynds] Yeah. Which I know, again, it doesn't seem like a lot of money in a North American context. But because Ireland is so much smaller, that's quite a chunk of change. You would test a lot of wells for a hundred million Euros.

[Sarah Gregory] Seems like a lot of money to me.

What do you think is the most important public health message in what you discovered?

[Paul Hynds] I think here, there's this very serious health inequity associated with many of the infections we study, yeah? STEC being one, cryptosporidiosis being another, norovirus being another. But it's not high-income, low-income. It's not rich versus poor, which whenever you mention inequity in terms of health, often times the first thing you think of is...tends to be rich and poor. In Ireland, it's country versus city. It's urban versus rural, which in Ireland is very, very important because we're a very small nation. We have these small cities and they just stop extremely, extremely quickly. But if you look at all of our large hospitals, all of our large—all of our ICUs, all of our consultants are based in the city, which is a ways from where these infections are occurring. And I think that's a health message that's not just for, let's say, policy makers and clinicians, but also rural people. It's good to know that, yeah there is this susceptibility there and you need to be mindful of it.

[Sarah Gregory] Are there ways that clinicians can impact positive outcomes?

[Paul Hynds] Yeah, I think so. In terms of—and again, it comes back to almost the exact same thing as, let's say, the rural residents and policy makers, I think it's just simply awareness what relates to the rich versus poor or urban versus rural to date. Because I think in high-income countries, like I was saying...like I told you earlier from my own, kind of, PhD field work, we simply don't expect to encounter serious illness or death from waterborne diseases in a high-income country (in a rich little country). But it's there. I think that's the message, it is there. And I think from what we've found, where a person lives and when they're living there is extremely important. So when, let's say a patient has come into a clinician's with, you know, those normal symptoms of gastroenteritis or hematochezia, nausea, vomiting, etcetera, etcetera, to think about where exactly do you live? You live close to cattle. Do you use a private well? Has there been a lot of rainfall—not yesterday, but was there a lot of rainfall two weeks ago? And if the answers to some of these questions are yes, what they should probably do is take a stool sample and send it to our STEC, kind of national reference lab because—and this also speaks to, I suppose, the importance of data. So without notification and lab confirmation of these infections...this is really important because if we don't have high-quality data, we can't study it. And what you often see—and this is why we couldn't go right back to, say, the year 2000, year 2002 (2000 is when notifications started) because they were picked up in a very, very patchy way. You could see where there's one doctor in this area that is doing lots and lots of stool samples and he or she is sending it and they're getting lots of lab-confirmed infections. But the problem is is that, that one really good doctor who is extremely aware is creating this bias. He's creating (or she is creating) a hot spot. So what we need is kind of for everyone to be aware that if you're dealing particularly with rural residents, that you may ask questions like have you, you know, has there been flooding in your area? Do you use a well? Do you have a septic tank? And be aware of the time of year as well, you know. Like when are the cattle being overwintered? When are they out on pasture? Etcetera, etcetera. Just being aware of the sources, the pathways, and the receptors for the infection I think would help clinicians ask the right questions, and if they ask the right questions they can then make the right decisions.

[Sarah Gregory] Okay. So how can listeners protect themselves, especially in Ireland, themselves and their families? Regular testing of their wells, right? Anything else?

[Paul Hynds] I think for me, it's all about—and it's like I was saying with the GPs (the clinicians), it's about kind of being vigilant. Because we're not saying for a second we think that around about between 60 and 75% of STEC infection in Ireland is probably waterborne. By waterborne, we mean that either the primary infection or...let's say, either the sporadic infections are waterborne or where you have these household clusters that that first infection (which we call the primary infection) is a waterborne infection. But that's not to say maybe 6 in 10 are kind of derived from waterborne transmission. But I think a lot of—and it's not just Ireland, but everywhere. It's kind of...don't presume that systems—so it's kind of be vigilant. Don't presume that systems are operating perfectly. Be aware of things like changes in weather, roadworks around your home, or kind of people digging around the home, changes in diet, changes in kind of social contact, changes in the places you visit. And kind of don't hesitate to ask experts, actually, if you think that...or when you do go visit a doctor, tell the doctor all of these things. So it's kind of more of vigilance than anything else. But yes, I would say (and I say to every well owner and well user) get your water tested. It's crazy to think that it's a hole in the ground and anything can happen, you know?

[Sarah Gregory] Yes, yes.

Tell us about your job (you've mentioned aspects of it), how it relates to *E.coli*, and what you enjoy most about it.

[Paul Hynds] I'm a jack of all trades, and master of none. This means I'm not very good at any one thing, but I understand just about enough of quite a few things that I can kind of put things together. Essentially, I would normally describe myself as an infectious disease epidemiologist or an environmental epidemiologist. My background is in ground water (or water in general). I've done a lot of hydrological modeling and groundwater sampling and quantum microbial risk assessment. So I've always used *E. coli* as an indicator for potential contamination, but now we're—and we always think of the receptors, so for years and years I studied wells and now we're just studying people instead, essentially. So I did a masters at one stage in kind of data science and statistics, but I just love datasets and I love finding patterns in large datasets and then trying to use whatever little bit of expertise I have or whatever expertise is within my group—so that's climate, hydrogeology and hydrology, and microbial ecology and human behavior—to try and provide kind of logical reasons for these pathogens and then hopefully design new projects to prove or disprove these. It's a wonderful job, I essentially get paid to answer my own questions, which not everyone can say.

[Sarah Gregory] Like my job.

[Paul Hynds] Yeah, well there you go. You know, it's really, really interesting and when we see...ok, well it's a strange job, I guess because when we have really bad weather here (you know, two, three, four weeks of rainfall) on one hand, I'm kind of...I'm like everyone. I'm not happy, it's a bit grim. But then I'm thinking, "I can't wait to get out and start sampling groundwater to see what change this has made to ground water". And I wonder in next year's stats, will we see a small peak or a small rise of some infection somewhere in the country due to these three or four weeks of wet weather. So, I don't know. It's like, kind of like being an environmental Sherlock Holmes, except I'm far less smart. Yeah, we just—we start with the event, we start with the infection. So we start at the end and we work backward. And it's all pretty logical, really.

[Sarah Gregory] Well, you're real and Sherlock Holmes was fictional. So, doing good.

Have you discovered new ways to spend free time since the pandemic began?

[Paul Hynds] No. I haven't.

[Sarah Gregory] No?

[Paul Hynds] No. In the first lockdown, I spent a lot of time walking in the local parks and listening to podcasts. Then, I almost kind of forgot I'm an epidemiologist and then we just got involved in a lot of COVID projects. I'm part of three COVID projects now, so my group (STEER) has one of its own called COSMID and then I'm on two large European COVID projects, and one of them will go on for another two years. So I'm tired of that word.

[Sarah Gregory] Yes, well aren't we all?

[Paul Hynds] Yep.

[Sarah Gregory] But I'm glad you're doing work on it because, boy, there's so many unanswered questions yet.

[Paul Hynds] Yep. There's a lot to do, there's a lot to do.

[Sarah Gregory] Well thank you so much for taking the time to talk with me today, Dr. Hynds.

[Paul Hynds] You're very welcome.

[Sarah Gregory] And thanks for joining me out there. You can read the September 2021 article, Spatiotemporal Dynamics of Sporadic Shiga Toxin–Producing *Escherichia coli* Enteritis, Ireland, 2013–2017, online at cdc.gov/eid.

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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