Erta Kalanxhi

Hello everyone and welcome to CDDEP's conversation series on global health. Today's topic is One Health and Antimicrobial Resistance. We are delighted to have here with us some of some scientists that have made significant contributions in the field, who are here to share with us some of their perspectives and research findings.

We have with us today Professor Mark Woolhouse, Chair of Infectious Disease Epidemiology at the Usher Institute at the University of Edinburgh. We have Professor Joakim Larsson, Director of the Center for Antibiotic Resistance Research at the University of Gothenburg. We have Professor Thomas Van Boeckel, assistant professor at the Department of Environmental Systems Science at the Swiss Federal Institute of Technology, and Professor Direk Limmathurotsakul, Head of Microbiology at Mahidol-Oxford Tropical Medicine Research Unit at Mahidol University.

In the first part of the webinar, we are going to have our speakers discuss some different topics on the One Health approach to antimicrobial resistance. Towards the end, we are going to answer some questions from the audience. If you do have any questions, please enter them in the Q&A section of your zoom platform. If you are following us live on Facebook, enter them under the comments section. We will start our webinar today with an introduction by CDDEP Director, Dr. Ramanan Laxminarayan. Ramanan, over to you.

Ramanan Laxminarayan

Thank you Erta, and good morning. Good afternoon. Good evening to all of you. I'm currently in India where it's obviously a tough time with respect to COVID.

I think that if there is anything positive to come out of COVID, it is this now shared understanding that one health is really something that we should all pay attention to and be mindful of: the idea that human animal and environmental health are closely connected, and what happens in one domain has repercussions in other domains. We're facing this now in the context of COVID.

The webinar is about one health and antimicrobial resistance, but that's a bit of a misnomer because antimicrobial resistance is one health, there is simply no other way to look at it. When we look forward to challenges such as climate change or global challenges that the world would like to face together, many of them will also deal with one health challenges:

- How to raise enough meat to feed a growing planet, while also not generating a greater risk of disease?
- How to be able to do agriculture sustainably in a way that doesn't unleash new viruses and bacteria from encroachment on forest lands?
- How do we really reduce the antibiotic footprint of how we conduct all of these activities, these economically important activities, including drawing fruit trees, or certainly raising animals or treating humans for infectious diseases?

In many ways, one health is really the underlying theme for nearly everything that CDDEP does, as a matter of fact. Just three weeks ago, the CDDEP board of directors in fact, voted to rename CDDEP as the

One Health Trust. Today is the informal announcement that this is what will now be named, but we'll have a formal announcement coming out soon. This is to recognize that one health is really going to be the frame for looking at many of the important health issues that face the planet today.

The set of speakers that we have today could not be a stronger set of experts who work on this issue, and at CDDEP and now the One Health Trust, we're delighted that they're all collaborators of ours and we work very closely with them. We're very happy to have their perspectives, which will be the ones that will then drive how we proceed in this particular area. With that, thank you all for joining and I'll hand it back to Erta.

Erta Kalanxhi

Thank you Ramanan for this very nice introduction to today's webinar. We will start with our first set of questions for today with Professor Mark Woolhouse. First of all, thank you very much for joining us today.

The first question we will explore is that about genomic epidemiology, and specifically, what can genomic epidemiology tell us about drug resistant infections attributed to animals?

Mark Woolhouse

Hello everyone, and thank you very much for inviting me to contribute to the seminar series. CDDEP being renamed this will be terribly difficult to get used to. We all love CDDEP, but we will get used to the new name and I very much welcome the inclusion of one health in your new title. I'm going to rephrase the question slightly, thank you for asking it.

What we'd like genomic epidemiology to do is help us to quantify the contribution that antimicrobial usage in animals makes to clinically relevant AMR in humans. That's a really hard question because it involves tracking resistance, right through the very complicated AMR ecosystem that we all know about. We all draw these lovely, complicated diagrams with many arrows on them. One of the reasons genomics keeps coming up is because genomics is very, very good for tracking. Of course, one of the things we're doing with it at the moment is tracking COVID-19 SARS-CoV-2, around the world.

How does it work with AMR? There's certainly been some considerable success, a lot of very high profile publications in tracking bacteria with AMR determinants on large spatial temporal scales, often globally over decades. That works especially well if you're dealing with bacteria that are clonal, so MRSA clonal complexes, for example, or salmonella typhimurium dt 104 would be good examples of really lovely studies that have been done of this kind. That's tracking the bacteria, and in the livestock human issue, we're probably more concerned about horizontal transfer and mobile genetic elements. Those are harder to track.

What we can say for sure is that some of those elements and some of the resistance genes are shared between human and animals, but the directionality is really difficult to get a handle on. There's actually a lot of studies of that kind going on. In my own group, we've been looking at data on resistance carrying plasmids and E. coli in the Netherlands. We can find shared plasmids, but actually, when they're shared, they're mostly not shared between humans and livestock - they are shared between one or the other.

On the other hand, rare events are going to be hard to detect because, let's face it, with the samples we've got, which are a few 100, maybe 1000 sequences, are a tiny, tiny fraction of the bacterial populations. One way we've tried to get round that is by building in much more structured sampling, and we've done that in a project in Nairobi, led by my colleague, Eric Fevre, the University of Liverpool. We found some, but not much, human livestock sharing of entire E. coli, so the whole bacterium.

On the other hand, we can find lots of shared resistance genes, but again, we can't determine this directionality question. How are we going to get firmer handles on these issues in the future? I think there's three things we need to do.

First of all, the genomics sequencing related to AMR has to be scaled up massively. Most studies that you'll see, sample hundreds, maybe 1000s of 1000 or so. We need to get up to 10 1000s maybe 100 1000s. I think that's actually going to happen. In the UK, Public Health England, led by Sharon Peacock, is going to do routine sampling of every single isolet that they get.

The other thing we want to do is introduce much more structured sampling. So far, we've been relying on scattergun and convenient sampling. It's the least efficient way possible at approaching this. When I say structured sampling, I mean structure sampling across multiple compartments, so clinical, community, animal, environment, food, all of them.

The third thing and this is important for the whole community that we're speaking to today, keep the AMR gene databases up to date and well created. Invest in those because those are what's going to allow you to track very easily.

Couple of closing comments, the general rule: the finer you type all the way down to genome sequencing, the less overlap you find. We are seeing plenty of examples of what looks to be, at the very least, exchange resistance between humans and animals, probably in both directions. Hard still to quantify the importance of that, but it's definitely there.

If it's there, my interpretation is that that makes it essential that we tackle AMR in both humans and livestock at the same time. If those two compartments are linked, in terms of the flow of AMR genes, then you have to do that. The best analogy I can give you is you don't try to solve the problem of your overflowing bath by just turning off one of the taps. Your instinct is to turn them both off. And I think your instincts are right about that. Thank you.

Erta Kalanxhi

Thank you Mark, that was a really good point that you raised. The next question is definitely fitting with the first one and I think you'll agree with me on this one. Whenever people think about AMR research, one of the main issues is the data and the type of data that is being used to analyze the AMR burden.

Has there been any progress in the scientific community, towards integrating the data or integrating interdisciplinary research from different aspects to address AMR, and what do you consider as one of the biggest challenges to do that?

Mark Woolhouse

Okay, thank you. I'll try and keep this answer brief, but it's a very interesting and important question.

I would say that the gold standard for integrating data is actually what I was talking about just now, the sequence databases. Sequence databases like NCBI, where you can find bacterial genomes for humans, from animals, from the environment, all in a single depository. That's a really good starting point.

The challenge for organizations like NCBI, which some of us have links with, is curation and quality control, and particularly of the metadata. In the era of mass sequencing, it's actually the metadata that is often the most valuable, the hardest to get, and also the hardest to assess for quality. For the older members of the audience like me, that is a complete reversal of what the position was 10, 15 years ago, when genomic data were rare and extraordinarily valuable. Now they're really easy to get, it's the metadata that's hard. That's the first step: better metadata to go with the sequence databases.

Lots of epidemiological projects nowadays are driven by a whole variety of widely available databases, livestock entities globally - I'm sure Thomas will talk about that in a moment - international air travel, astonishing array of databases out there. Our job is to link them. To give you one example of a project I know about, the Gram project, Institute of Health Metric Evaluation and the Oxford Big Data Institute, is trying to estimate global burdens of AMR and on their website, they have a list of 30 what they call critical data sources, data streams, they need to access and link in order to fulfill their task.

Closer to home, CDDEP has done some outstanding, really wonderful work on revealing global patterns of resistance levels and drug uses by exactly this sort of process. And you've made a really excellent contribution there.

But even so, as I've written about in the past and I'm sure Ramanan will acknowledge, the clinical resistance data for a start, nevermind the animal resistance data, is really very patchy. It's patchy in scope and scale and quality and purpose. That makes life difficult for all of us. You could ask anyone involved with WHO's GLASS network, for example, it's difficult.

As many of you will know, I've been working with Frank Aarestrup and his colleagues at Danish Technical University, on more systematic ways to collect, analyze and interpret resistance data. Our personal answer to this question is next generation sequencing of sewage samples.

This idea has actually turned out to be rather more controversial than I'd expected, but I think we're winning the argument slowly. It does seem to me to be a very potentially valuable shortcut to getting data across the board on AMR in human communities.

Now, the second part of your question was interdisciplinarity. I think the need for that is well accepted now, at least in principle. There are certainly national initiatives in the UK, there are international initiatives such as JPIMR and other EU programs that explicitly support interdisciplinary consortia. That's a very positive development. I regard the integrated approach as absolutely essential to tackling this problem.

What does that kind of interdisciplinary research require? Well, to me, it implies team science, which means team players - we're not all equally team players, I think - great leadership, the so-called T shaped scientists that can reach across disciplines, and crucially, from our funders, big budgets. Not just because

we want big budgets, but because we want breadth and depth, not research that is spread too thin to be useful.

We're not going to solve the AMR problem by sprinkling hundreds of small scale, standalone projects across dozens of different topics. We're looking at what most science funding colleagues call mission oriented research programs. I think it's fair to say that funders have started down this road, but there's a long way they could go and a valuable step, a really valuable step would be to have clear and compelling statements setting out precisely what those crucial missions are.

My understanding is that that is what this really excellent seminar series is all about doing. Thank you.

Erta Kalanxhi

Thank you for that. Now we are going to move on to our next speaker, Dr. Joakim Larsson from the University of Gothenburg, so thank you again for joining us here.

Our first question for you is why is environmental monitoring of AMR so important and how does it benefit human populations and animal populations?

Joakim Larsson

Thank you for the question and thank you both, Erta and Ramanan, for inviting me here and congratulations to the 10 year anniversary of CDDEP as well. I've prepared a couple of slides to try to address your question.

What objectives can this serve? Well, I think it's important to keep in mind that environmental monitoring and more can serve rather distinct objectives. These objectives often require that you measure different things, you measure different things in different places and you interpret these outputs in different ways.

The first apparent objective of environmental monitoring AMR is to assess transmission risks, often of fecal bacteria that spread through the environment and there is a risk that they colonize or infect us again. These events are rather common, and also in principle, quantifiable and predictable. However, the consequence of each of these individual transmission events is rather limited - it's incrementally adding to the problem of antibiotic resistance. These transmission rates can indeed be reduced with the right actions.

Another type of risk, it has to do with evolution of resistance with, in the worst case, the emergence of new forms of resistance that can be recruited from the vast environmental genetic reservoir of genes. These emergency events are probably much more rare than simple transmission events. In that way, they're also much more challenging to predict.

On the other hand, consequences of just a single transfer event to a pathogen can be lost and irreversible, as well. It's important to try to monitor and judge and do things about pollution risk as well.

A third objective could be to use the environment basically as a reflection of the local or regional resistance situation in humans or domestic animals. This can show you, for example, trends over time or in space. It may reveal new threats, depending on how you analyze the data: looking for new genes, for example.

You can use it to evaluate effective interventions and it can be used also potentially, if properly evaluated, there is a possibility that it can actually guide empiric therapy as well. In some parts of the world, there is basically no clinical surveillance to date. By looking at sewage, as Professor Woolhouse mentioned, that's basically looking at fecal bacteria from 1000s of people in the very same sample. You could get a picture of the resistance situation in that population, which could be very useful to the clinician.

You could also monitor it to estimate the use of antibiotics, which antibiotics and how much of them. It is a little bit more difficult to get quantitative data on this, particularly for our most common antibiotics, beta lactams, that are rather easily integrated, but it's possible.

All these four objectives are ultimately serving the protection for human and domestic animal health. Then there is also, of course, the possibility to assess ecological risks. AMR is perhaps not an ecological risk, but the exposure to antibiotics in the environment could potentially perturb ecosystem services, etc. Although, there is not as much evidence for that.

Now, I'll just quickly show one more slide on this. Here on the top, you see these different objectives and on the left, you see different things you can measure when you go out in the environment and sewage, for example. I'm not going to go through all this, but it's just there to illustrate that we think that these different end points reflect quite differently these different objectives.

That's very important to keep in mind when you design the monitoring system, what it is going to be used for, because it will decide where to monitor and what to measure. When it comes to risk of transmission, simple things like measuring fecal bacteria can be a rather good indicator. Thanks.

Erta Kalanxhi

Thank you Joakim. Now we're coming up to our next question.

Antibiotic use is one thing, but antibiotic production is an entirely different story, especially considering the emissions that come from that production.

You have shown in many studies that antibiotic emissions from manufacturing, in, for example, India, can be staggering. How do you think countries that buy these antibiotics like the USA or Sweden could contribute to reducing this type of pollution?

Joakim Larsson

Yes, it's a good question. I've prepared a couple of slides for that as well. You mentioned what we as consumers states can do. As a matter of fact, I think there's lots of different types of actors that can, in different ways, act to contribute to the reduction of antibiotic emissions from manufacturing.

In this paper, we have listed 33 different types of actors that in some way have the ability to make a change. I would argue that if you have the ability to make a change, you also have some level of moral responsibility to do so. However, all of these actors differ in terms of incentives and counter incentives. Often the incentive to act is money.

Sometimes there are other things that are more important that I think it's very important to think about the incentives for certain actions. If you want to affect the process, you also need to understand why they would do something in this direction or not. To analyze that a bit deeper could help to sometimes go forward from research into action.

Many of these types of actors have done many good things already. I should mention that in the antibiotic industry, they have voluntarily set up emission targets for antibiotics already a couple of years ago. That is, of course, very good, but bear in mind, none of these companies still reveal how large emissions of antibiotics they have and none of these companies reveal where or by whom their active ingredients are made. From that, I conclude that voluntary actions by industry are good, but they're not enough. Therefore, others need to contribute as well.

This includes consumer countries like the US or Sweden or other countries that have a particularly important role. I will mention three different types of actions.

One would be to award pollution control, when you procure drugs or when you buy drugs to hospitals or large organizations. Usually price is the most important factor, but you can award pollution control also and Norway and Sweden are actually doing that right now. I still think there is a lot more to do in terms of the criteria they're using, but they're on the way and they are awarding companies that are doing more in terms of controlling pollution.

Another relates to subsidies: when you go to the pharmacy, and you have a prescription you're subsidized by tax money or insurance companies in many countries, in the US and in Sweden, but then you often need to take the cheapest alternative otherwise you have to pay yourself. This effectively prevents companies from investing in pollution control because it may get their drugs a tiny bit more expensive at the end of the day.

In Sweden, there is now a proposal to actually also award pollution control, so that not necessarily the cheapest drug gets subsidized, but they also weigh in pollution control. There's a pilot project starting on this.

The very final thing is to ask for transparency from the pharma companies: where do they produce their drugs? And ideally, how much do they discharge? Without that, we cannot hold them responsible.

Just recently, we figured out that in New Zealand, they're doing this - not about how much we need, but where the API's are produced. The companies have to report where the API's are produced and where they formulate drugs to New Zealand, and it's open information on a website. If New Zealand can do it, I think everyone else could do it. The best thing is that it's completely free - doesn't cost anything.

Erta Kalanxhi

Thank you Joakim. These are very, very interesting points you've raised and some things that don't get spoken about that often. We are now going to move on to our next speaker. For the interest of time, we're doing this sort of chain question to question session, but it seems like everything ties in together very well.

Professor Thomas Van Boeckel, we have some questions for you. Having done some work on global comparisons on the trends in AMR in animals, in which region do you think we should concentrate future efforts for surveillance and intervention?

Thomas Van Boeckel

Thanks so much for the question Erta and thank you to Ramanan and CDDEP for inviting me to be part of this discussion today.

Simple question, where should we concentrate our efforts in the future? The answer is somewhat complex. What we try to do is to approach the question from the following angle. We started to amalgamate all the evidence we could find from event based surveillance across low and middle income countries. It's been quite a big data collection effort.

In essence, what we try to do is to extract a lot of information from studies that are done across different parts of the world, by hundreds of people. It's important to understand this is event based surveillance and not systematic surveillance can do to what exists in certain countries in Europe and North America.

What we tried to do is summarize trends across different drug-bug combinations across different species and identify hotspots of resistance using the customary metrics of resistance. What we try to use in this case, is sort of the proportion of drugs that have resistance higher than 50% in each of those individual surveys, and then we try to use some sophisticated statistical methods to interpolate that around the world. This is our result: it's a map of the degree to which drugs fail in animal parameters.

Now based on this map alone, what we can say is that there are hotspots of resistance in northeastern China and northeastern India, in South India, Iran, Anatolia, and in the Americas, it will be more in the southern regions of Brazil. Now, it's very important with this kind of exercise, based on event based surveillance, to acknowledge the knowns and the unknowns here.

I think that this map can potentially be useful in Asia to target stewardship efforts and biosecurity efforts in the known hotspots of AMR. What this type of work also tells us is about where we don't get much information from and here, much to our surprise, we found very little work coming from the Americas, although we looked for a lot of work in Spanish and Portuguese.

Here we have to think of potentially scaling up surveillance in the region where we don't know so much because we may be missing quite a bit of information, especially in regions like the Americas that have some of the major meat exporters in the world like Argentina and Brazil. It's a focus on what we know but not only on what we know for the future. Thank you.

Erta Kalanxhi

Thank you Thomas for that. Our next question is exactly that: the role of aquaculture. You've done a lot of work on AMR in aquaculture and how do you think that fits in the global picture in terms of both antimicrobial resistance and use?

Thomas Van Boeckel

I'll start with the point of view of, first, why we should look at aquaculture in general. What is very interesting about the world of aquaculture is that essentially, aquaculture is growing very fast.

If we have issues about antibiotic user resistance in aquaculture, those trends are likely to evolve quite fast. as well. Just to say a very simple statement here, aquaculture is growing faster than any other terrestrial livestock in terms of source of animal protein. I think it was about last year that production value in aquaculture overtook the fish that we capture in a traditional way.

Now, we look at antibiotic use. The story of antimicrobial use in aquaculture is typically pitched as a rather positive one, at least lately by the WHO. The quintessential example of that is really the case of salmon farming in the North Atlantic, which used to be associated with very high rates of antibiotic use. This has gone dramatically down in the last decades.

The reason for that is because there was a parasite causing furunculosis in salmon. This farm has been largely put under control now, thanks to the use of vaccines that are administered through highly performance machines. It's quite amazing to see and the problem has essentially disappeared.

The key problem with the salmon story, which has really dominated the narrative in high income countries, is that it's potentially misleading us on the global antibiotic use in aquaculture. The reason being, is that if you want to have a global idea of what's going on in terrestrial animals, all you need is to have three species to have 90% of the global biomass animals that we raised with. In the case of aquaculture, if you want to reach this 90% of the total biomass of fish that we're using, you need to have 27 species.

The world of aquaculture is incredibly diverse, different species are found in different parts of the world. In all of that, salmon only represents 4% of the biomass of the fish farm. Focusing on the salmon story is not quite enough.

What we tried to do with Dan Schar, who was co-supervised by me for his PhD work, is look at the evidence of what we had on not only salmon, but all across the different species of fish. Quite rapidly we ran into a problem because we realize we know very little. Essentially, out of 150 surveys or so, we found only two surveys that were discussing two of the most commonly found fish in the world, which are two species of carp, grass carp and the silver carp, which are predominantly found in China and together represent 60% of the aquaculture production.

If you take that into account in estimated antibiotic use inside some of the major aquaculture countries like India and China, you realize the weight of those things when trying to make an estimate of how much antibiotic is being used in fishes. We estimate the consumption of antibiotics in fish to be somewhere between 5 and 20%.

In essence, I think what we need to do about AMR in aquaculture is collect much, much more data, especially in Asia because this is where most of this increase is happening at the moment. I hope I can soon tell you more about trends in resistance, as we're also working on that. I hope I can tell you more about this in the future.

Erta Kalanxhi

Thank you, Thomas. This was very interesting. Since we're talking about data, and especially in certain parts of the world, it fits our next question that is for Professor Direk Limmathurotsakul.

Professor Direk, Thailand was one of the first middle income countries to publish on antimicrobial use in animals. Do you think other Asian member countries will follow suit? And if not, why?

Direk Limmathurotsakul

Thank you very much Erta. Thank you CDDEP and Ramanan for an invitation to join in this. My answer will be yes, it will come.

The question is when: it could be from one year to 10 years. Why? Because of the data: some of the countries already have the data, but they submitted to the FAO and FAO reported it as a regional consumption, which is quite difficult to understand in the country. We have a big momentum from the international organizations and the World Health Organization and the COVID that we understand the value of national statistics that you need to understand the total number by country so that you can compare between country and country.

I would ask everyone while you are listening, if you come from high income countries, how many tons of antibiotics are used in farm animals in your country? Do you know that? 10 tons, 100 tons, 1000 tons?

If you come from low and middle income countries, can you guess how many tons of antibiotics are used? For farm animals in Thailand? 40 tons, 400 tons, 4000 tons or 40,000 tons? You can think one ton is one cubic meter.

If you don't know the answer, I think it means that even whether you are policymakers, scientists or the NGO, I think that kind of quantitative number you might feel you can use it and make use of it further. The answer is 4700 tons and to move it forward, I would think whether it's short or long, it's up to three things: political will, population view and scientific view. Whether the politicians or the policymakers would like to push for it.

Whether the general people are the people who are aware about this issue, and would like to push to get it happen, or NGOs are supportive. And in the scientific communities, do research and stimulate that or not. No matter who you are, you can talk with policymakers, you can ask them how many tons we are using in our country.

Why have the US, UK, Japan and even Thailand had the data come out and where is the data in my country? You have to understand two things when you are talking about this: be careful about blame

games, everyone loves to blame the other. Don't talk about someone or something, go to fish that a fish doesn't talk about fish go to fish No no fish is good to chicken. The blame game is common.

When you talk with policymakers, you have to be calm and patient. Understand the drive, understand their issues, and try to work step by step. When you talk, try to think about quantitatively rather than qualitatively.

I think my answer is yes, whether it's short or long. Everyone can contribute to stimulate it, to make it available faster. To you Erta.

Erta Kalanxhi

Thank you very much Direk. We move from the level of policymakers and government to the community. Our next question addresses that.

Can you tell us something about the concept of antibiotic footprint and how it can help to convey the message of AMR burden to the community level?

Direk Limmathurotsakul

Thank you very much Erta. This is the website of antibiotic footprint. I hope that is present on your screen at the moment. Thank you.

The idea is that it's similar to carbon footprint, but it's not as in depth as a carbon footprint. This uses the concept of the consumption footprint. You have to understand that the consumption of antibiotics could be either directly to yourself as a human or indirect that you feed it to the farm animals and then you eat animals after that. By that, I will answer as a country-level first.

If you go to the antibiotic footprint, you can see how many tons of antibiotics are being consumed in your country. If you click each bubble, you can see how many are in humans, how many are in animals, and we only use official data that your government makes openly available, just to make it equitable and trackable. If you go to Thailand, available first in 2017, this is for both human and animal.

First is to make our data easy to communicate and then if you want to talk about it, community, I think that I will stop sharing and then come back to talk with you.I think about tons for the whole country that's fine when you talk with policymakers. When you talk with the individual or when you talk with the community, I think we have to learn from the communication skills that affect anything.

For example what I love is that this is a bucket of colistin, one kilogram of colistin, that you can use to feed animals, whether it's chicken, pigs, whatever. If you're a doctor, you will know that to get one ampule of colistin, which is considered as a last resort for the antibiotics available at the moment, it's so difficult, and it can be quite expensive in some countries. This one kilogram of colistin is just about $4. It's not that strange that we use it in Thailand.

Actually if you look into it, even in high income countries around the world, they use it. They still use colistin and some rare regions ban it already and they might use alternatives. You need something that is okay, tangible, touchable and then you have to talk about it.

When you think about it as a carbon footprint, we can think about the individual carbon footprint calculator. Now we make it as an antibiotic footprint as a country level in terms of tons. We are working on the individual calculator - we plan to pilot it.

You can try to simplify the communications question. For example, if you are listening to the broadcast or podcast at the moment, my common question is: when was the last time you took antibiotics?

You've never had it for your whole life, 10 years, more than 10 years ago, five years ago, more than two years ago, or within your last year you have just taken antibiotics. You can share it among your friends, people in your country and you compare with the people from the other countries that will use the need to learn, Dutch people as a champion.

If I ask the same questions to Dutch people, they will say that no, never in my whole life. More than 20 years. I never had antibiotics. When they ask a lot of experts who are British in my office, the last time was maybe when I was young, less than two years old, and I am 50 years old so I never took them since then.

But if you ask people in Thailand, most of the answer is six months. Most of the people just took antibiotics two times, up to four times a year. It can be appropriate, it can be inappropriate, but most of the time we use antibiotic footprint or calculator as a standpoint to ask, do you need that much? Is it always appropriate or inappropriate?

It could start that you are taking much more than the other people in the world or other firearms in the world. Could you do something or would you like to do something to reduce it a little bit? Then we can talk a bit about the demand and supply and the market, pricing, and further after that.

I think that would be in depth how the economy and pricing things can relate it to the antibiotic footprint. I think this is the concept: it could go to talk with the community, people.

Erta Kalanxhi

Thank you very much. We had some time to answer some questions from the audience. I also encourage our speakers to type some of the answers, if they can on the chat box.

We will start with a question for Dr. Joachim Larsson. It's a question on how we can reduce AMR from medical and hospital waste in low income countries.

Joakim Larsson

Yes, I think it's quite different if you talk about hospital waste. It's quite different from manufacturing waste where we have very few places and you can really pinpoint more to a certain company that has the direct responsibility for its action. Here it's very widespread.

We showed in the paper just a few months ago that indeed hospital wastewater even from Sweden, where we use very little antibiotics in an international perspective, is strongly selective for antibiotic resistant bacteria in the wastewater streets. There's something that needs to be done, but I think it's a huge challenge, because this is so much more widespread now and selection seems to occur already in the sewage systems. Given that you have water based sewage systems, in many parts of the world you don't because you don't have a water based toilet basically.

It's a big challenge that I cannot answer technically, how to do that. There are for sure technical ways to remove both the bacteria and the selected agent from wastewaters, but to do that you first basically need to have a rather good basic treatment.

Remove the organic material and then you could use more more specific methods that can remove antibiotics for example, etc, like ozone or, or such things. That costs money and it's a huge challenge to do this.

For low and middle income countries, I think basic treatment is probably the first step that will help sanitation issues, which will feed back to AMR in that if we reduce the spread of whatever pathogens to the environment, we will also reduce antibiotic use and in turn,reduce AMR.

Erta Kalanxhi

Thank you very much. That's a very good and practical answer to that question, though there is so much to be done. We have another question which I'm directing it to all of you and not to one specifically.

There's a question about a publication suggesting that the use of herbicides and antibiotics or fungicides in plants and crops have effects in AMR. However, the focus is mainly on human and animal antimicrobial consumption. When will it become a priority to look at agriculture in a holistic way and what needs to be done for that?

Thomas Van Boeckel

We did try to do some expiratory work about this in the same way that we try to review event based surveillance on AMR in animals.

For what we have found so far for three main classes antifungal, the evidence seems to be a little bit too thin in terms of surveys carried out to be able to do an exercise like the mapping that we have done for chickens, which is really a shame because it doesn't mean the question is not important. It just means that with the little evidence available we have, so far, it's really difficult to infer any sort of geographical trend. Perhaps that’s a scenario focus for future funders.

Erta Kalanxhi

Thank you, I'm just scanning through the questions and I had one directed to Professor Mark Woolhouse, if he's still available. From an academic point of view, all the activities using WGS mentioned by Professor Woolhouse have really good points.

How would it be possible to implement and perform all this Molecular EPI surveillance from a One Health perspective, particularly from an AMR microorganism, from environment and animals, in a continuous way and not just as individual studies? How can the government be involved to maintain these types of studies? What experience can be shared with us?

Apologies for the very long question, I did not know how to better summarize it, but basically it is one of the points that you emphasized in your talk.

Mark Woolhouse

Thanks Erta and I apologize for not answering the questions in the chat. My excuse is a very good one as I was listening to the other speakers because they had interesting things to say, so thank you for them.

I have to say that from the UK perspective, I think that sort of coordinated activity - just thinking very simply of humans and livestock, I take the comments we just heard about other forms of agriculture and particularly aquaculture - has to be centralized. I think the scale is too big.

What we're doing in the UK is actively trying to integrate human surveillance, just routine, laboratory surveillance, in humans and animals. It is difficult because the samples are not typically directly comparable. You get a certain level of resistance in food animals sent for slaughter.

How on earth do you compare that with a level of resistance even with the same drug-bug combination to children needing clinical care? There's not a direct one to one relationship between that.

We need the analytics, we need the modeling, and we need to understand those links that I was talking about when I was speaking better as well. There's a huge range of people on this meeting and maybe others will have different opinions, but I think in the UK that has to be a government led activity.

Erta Kalanxhi

Thank you. I have another question for you since we have you here online. The question is about looking at AMR in the One Health context, but acknowledging that there is an overall wider evidence globally that the problem is in human antibiotic use and poor infection prevention.

Is there a risk that in emphasizing One Health transmission, we distract from the need to prioritize what are probably the most important or effective interventions in the real world?

Mark Woolhouse

What a great question. That is a very important question.

The answer, the obvious one, is that we need to do both and it's very important that we do both. But I have seen, and this was particularly sort of five or six years ago in the UK, and even the WHO were doing this to some extent, it was a tendency to try and blame the problem in humans on agriculture. It was difficult to make that charge stick, while there was still clear evidence of extensive use and clinical and community settings in humans.

The question I posed during my talk, in which my groups had some efforts to answer, is exactly how strong is the link. This is the crucial bit. What we discovered is it doesn't have to be very strong.

If there is some flow of resistance from animals to humans, and this is very important from humans to animals back again, then the two systems are linked. It doesn't have to be tremendously strong. That's the basis for the comment I made: it is absolutely imperative that we tackle both at the same time, that we turn both taps off to our overflowing bath, and not just one of them.

I do take the point of the question, don't let the clinicians off the hook because we recognize the importance of One Health. I think that's right.

Erta Kalanxhi

The next question is open to all of you.

One of the members of our audience would like to know whether there is a concern for the increasing antimicrobial use in Sub-Saharan Africa and the need for foreign researchers to focus more on Africa.

Mark Woolhouse

We've done some work on this with Frank Aarestrup at DTU. The sewage surveillance is really interesting. There is a big problem with antimicrobial resistance in Africa, so let's not start from the point that there's less of a problem.

Personally, I happen to lead a research partnership, in which the research agenda is led by our colleagues in Africa. I think that's where the priority lies. I'd much rather the research priorities were set by my African colleagues than myself, but the most definitely is a problem - look at the sewage data. I'll stop because I was speaking already.

Direk Limmathurotsakul

From my point of view, I have to submit two concerns.

One, the burden of AMR in Africa is about treatment or whatever. If you're in high income countries, you might be able to have more expensive or more available new use in your country. If you're in low and middle income countries, especially in Africa, when you have third generation cephalosporin E. coli, you might stop and don't even have better drugs to treat in hospital. That’s the first concern.

The second, I don't do the research anymore in Africa myself, but from my colleagues: in the upper middle income countries like Thailand, although we have the data it means we use a lot, but most of the formula is used for the animals that we use to export to the EU and to Japan, so the formula is quite close to the EU.

The amount that you see is high because we follow the upper value, upper limit of what the EU allows. Even that, we measure antibiotics properly: when they say one kilogram, we measure one kilograms. From the hearsay, what I hear from the past in low income countries that had an entity is like this.

So the SEC and they put it into that. It tends to be overused more than underused, and it's from the local healers and people who have mouths to use it more than proper citation and even some kind of code or factory scale control. That's what I worry the most and often more and more studies will come out for that.

Erta Kalanxhi

I think we have time for one more question. Are there any ways in which the human, environment, and animal sector use of antibiotics and contribution to AMR can be quantitatively assessed? This is likely to be different for different countries and the data will be valuable for all implemented interventions. Does anybody have any thoughts on this?

Joakim Larsson

I may have a small comment on it. This is a huge question, I will just answer a very small part.

We have to think about the emergence question also: Where do resistance emerge? At the start of every type of new resistance problem, and to be honest we don't know where most resistances have emerged.

That makes it almost impossible to say that this is so much more important than this is so much more important than that, because we might be into surprises in the future, where resistance factors actually emerge and where efforts to try to reduce new emergences of resistance wouldn't be most effective.

Now when it comes to transmission risks, that's a big difference. I'll leave the floor open to other comments.

Thomas Van Boeckel

The question is imminently relevant that what we missed to provide an answer is okay, cancer is about huge in different parts of the world. I think Thailand has taken a super important step for the sub region.

What we really would like to see is those different sub regions for which WHO reports to be broken down at the country level and to follow that over time. I think then we might be in a position to answer the question asked and also regarding the last question, to finally bring an answer to what might be going on in middle income countries in Africa.

At the moment in terms of antibiotic use in animals, we know pretty much nothing between Morocco and South Africa.

Erta Kalanxhi

I see that we have reached our time limit for today. I'd like to thank all of you very much for joining us today. Thank you to our speakers and the audience for showing up to such an important discussion.

As Ramanan mentioned earlier today, it's a very timely discussion given that more than ever, we are aware that our health is just one piece of the One Health puzzle and that we are very much interconnected with the environment we live in and the species that we share it, such as the animals or plants. Thank you very much.

If you'd like to see a recording of this webinar, you can do that at CDDEP's webpage. Over there, you will also find links to previous webinars that we've had in this conversation series.

Thank you very much and have a good day. See you next time.