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ALEX MAIERSPERGER: I'm your host, Alex Maiersperger. And in season three of The Health Pulse podcast, we celebrate those changing health care and life sciences for the better. Previously, you've met Antonio De Castro as a guest. And in our continued globalization, we're so excited for this new phase where we get to have him as a special guest host for a few episodes focused on Asia-Pacific. And now I get to pass the mic over to Antonio.

ANTONIO DE CASTRO: Thank you for passing the mic, Alex. Hello, everyone. My name is Antonio De Castro. I will be your host in today's episode of The Health Pulse Podcast. I'm here to give a voice to health care and life science experts here in Asia.

Access and sharing of health data has always been a sensitive topic, whether it's electronic medical records, clinical research data, or genetic data. But creating secure platforms for exchange is a must if we want to move towards precision medicine. I'm delighted to introduce today's guest, Nino da Silva from BC Platforms.

Nino is the deputy managing director of BC Platforms, and he is based here in Singapore. He is an international leader in medical informatics and business strategy. Nino, thank you so much for taking time with us today.

NINO DA SILVA: Thank you, Antonio. It's a great pleasure to be here.

ANTONIO DE CASTRO: OK. Let's talk about these platforms. Can you give us an introduction about your company?

NINO DA SILVA: Absolutely. So BC Platforms spun out of the MIT Whitehead, the Eric Landers group, in the late '90s. Was quite a successful academic project that endeavored to merge geno and pheno data in one data construct, enabling advanced analytics on the combined data.

We still do it from that basis, that combining different data types in one environment in order to create possibilities for federated or centralized analytics, utilizing advanced analytical tools such as the SAS portfolio on top of it. And we do that for life science companies, discovery, clinical research, and for health care entities, precision medicine, and production of large scale biobanks and collections.

ANTONIO DE CASTRO: Excellent. A lot of our listeners are coming from clinical research space. Can you walk us through on how a company like BC Platforms help pharmaceutical companies in their drug development journey?

NINO DA SILVA: Well, still a large part of the development and discovery work for pharmaceutical companies based on an angle towards phenotypic data-- so longitudinal, clinical, and medical data. But since quite a lot of years, there's a growing field within genetics, using either genetics for discovery or combining genetics and phenotype picks for discovery work.

And this goes, on of course, all the way up to the clinical research side of the R&D and development spectrum for pharmaceutical companies, where we see an increasing need for having the genetic data as one of the components of the data set that you use.

This goes from everything from establishing synthetic control arms to the really pure discovery work, where you look at large cohorts in order to find patterns or markers that would indicate susceptibility or protection against certain disease or activity in relation to certain drug molecules that you want to explore.
ANTONIO DE CASTRO: I want to pick up on a specific subject there, synthetic control arms or external control arms. We've been hearing a lot about them together with the boom on real world evidence. How are synthetic controlled arms being used in clinical research?
NINO DA SILVA: Well, I'll give my view on this. And I want to make sure that it's understood that my expertise is in clinical informatics, more than in the side of application of synthetic control-- synthetic control arms or external control arms. But on a high level-- I think, if I'm not misremembering-- in 2017, there was issue the possibility to submit synthetic control arms as part of an approval for FDA in the US. And that kind of led the way to looking at how synthetic control arms could be deployed in this purpose, and for-- also for other purposes. And a large part of the rest of the world has followed on that track. What it really means is a possibility to avoid recruiting for clinical trials.
As an example, for when you want to deploy a certain drug, which is approved and submitted and approved in the US, as an example, in a European country, or basically anywhere in the world where there is a process for such submission and approvals. In reality, as you know, clinical trials has many difficult levels.
One of them is the fact that, in some cases, there might be even questionable ethics around them for the very reason that when you recruit these patients, some of these patients, even though very ill and in need of the drug, would be supposedly on placebo. Just giving a higher, coarse-grained example. And that is not the best motivator for participation. And you could also, of course ask if it's the right way.
But unfortunately, there are no other ways. And we have to find alternatives that still fulfills the demands and the necessity for validation accuracy. So synthetic control means that instead of recruiting for such a clinical trial, you can, based on the original submission, find an identical data set which matches the patients from the original clinical trial.
And then use that new data set and the original clinical data set as a reference to validate and approve the drug, for example, for a new market that has a different haplotype. So for example, a drug approved in the US might not apply to be approved in Germany without validating that it will have the same efficacy as it had in the original population.
ANTONIO DE CASTRO: Thanks for explaining some of the benefits of synthetic control arms. Clearly, it lightens the burden on recruitment, but does this mean that now I have a perfect study population? Well-represented, diverse, and perfectly stratified?
NINO DA SILVA: It's possible to get a better stratification. It's definitely-- because it's so much cheaper than actually recruiting for a clinical trial, you can afford, for example, to look for larger data sets. You can create a value out of the very fact that there is economical advantages as well as others. But there are also challenges.
Mind well that one of the challenges is that you need to find proper matches. And if it's a rare disease, this might involve engaging multiple data custodians in order to run the cohort needed because the number has to match the needs of the project. And as such, there is also, of course, the regulatory factors such as GDPR, and GDPR plus in countries like Israel and some of the Asian countries.
So I have to say that it all sounds like a dream when you talk about synthetic control arm, but we have worked quite extensively to find solutions that made us able to navigate the regulatory world in a

compliant and approved way. And also to combine cohorts that are separate without moving the data, necessarily. And in some times by moving the data into an environment, which can be approved in a GDPR Schrems context.

So everything looks perfect. And you are right, it could be what you are saying and implying here. But to get there, there are many components that you can't simply solve by just starting a project.

And I want to stress that this has to be done in a very accurate and professional way. You have to be able to engage multiple data partners from time to time. We do it regularly for these synthetic control arms. And then you have to harmonize between these in order to achieve the goals, and in order to be able to stratify in the way that you exemplified.

ANTONIO DE CASTRO: Now let's talk about sharing of health data. Can you tell us about BC Platforms's expertise in building trusted research environments.

NINO DA SILVA: Well, definitely. If you don't mind, I would like to touch two types of platforms. TRE, which is a Trusted Research Environment, and TCE, which is a Trusted Collaboration Environment. They are by nature similar, but have very different perspective.

The trusted research environment m in simplified context, it's a way for a data custodian to enable researchers within the country-- and potentially outside the country-- to access their data for specific research projects in a safe way without copying or moving the data. So it's protecting.

The intent is to enable research, highly dynamic research, with analytics. But without moving or quote, "selling" the citizens' data. Rather, to enable the citizens' data to build knowledge therapeutic treatments, drugs, and advances in precision and general medicine. Population medicine is a good example.

So TREs has come the last couple of years. And we have worked in several such projects. And they are still in a maturing process, but there are definitely ways of doing it that works well and is in use today, both from us and other entities.

When it comes to TCEs, that's something that we have started developing with a few of our pharmaceutical customers. And TCEs is a Trusted Collaboration Environment. So where a TRE aims to take one data custodian's data into the use of many researchers, a TCE aims to bring the possibility for one life science company, or several, to access multiple custodians in a same way.

Meaning regulatory approved without necessarily copying data, giving full dynamic access to analytics, bridging over multiple cohorts with different populations, or with the same population, depending on if it's a global or local project or a regional project. The TCE holds the promise of solving a lot of the challenges that you have in amassing enough data without necessarily having to colonize it.

So we are quite opposed to the general model of data copy, if it can be avoided. There are cases where you can't, but as much as possible to use true federation, to be able to use analytical tools on top of such platforms of true federation, is really that something we believe strongly in for the future.

ANTONIO DE CASTRO: I have a follow up question here regarding data protection and data quality for data protection. Could you please share with us the importance of granting data access in a secure manner, and how BC Platforms is at the forefront of data security?

NINO DA SILVA: So first of all, I want to say that I am not a regulatory expert. And that's important to underline. But I can give you a general view of this. So the basic principle is of course that whether you are under GDPR or not, we inherently believe that it is crucial, it's fundamental to protect the privacy of the data, the anonymity of the subjects that are participating in the data collections or in the health care as patients.

It is, of course, as fundamental that they are given the right to participate or not, so consent. And then, on top of that, each country has-- or many countries have-- either common laws like GDPR, which might still be interpreted a bit different between the GDPR countries, and even both more and/or less advanced regulatory protocols that needs to be followed and adhered to.

As an example, we are working in Israel that has one of the most stringent regulatory framework for utilizing patients' data. We are working with, actually, the health care entity that handles half of the population of Israel today. And we are working there with our system to build a satisfactory regulatory compliant environment for analytics of their data without moving it out of Israel. Actually, without moving it out of the firewalls of this health care entity.

And I think the proof points, really, that you can do that is the validations that has been done on the system in these environments. And remember, we can't build a system for every country. We have to build one system that fits the whole world. That means that we constantly are monitoring the changes. We are constantly making sure that we are compliant.

And I will tell you that this is one of the major challenges. Because if you do not do this, you can't provide the environment that is demanded. And you can't either manage the needs that are there, not only for the citizen and patients that are participating, which is primary, but also for the needs of the researchers that needs to access this data. Both needs to be kept happy, or else this will not work.

ANTONIO DE CASTRO: With regards to data quality, you can have data coming from multiple geographies with diversity in their practices. How is the variation in data quality assessed and treated?

NINO DA SILVA: Well if we talk about TCEs, and then a very good example of a large scale TCE is the BCRQUEST.com, our global data partner network with 33 million patient lives, where all 5 million are normalized and harmonized from five continents and more than 30 data partners around the world. It's a perfect example.

When we come to a potential data custodian that will once or are interested in becoming a data partner in our network, they all participate on their own conditions, on their own rules with the data they have. And what we do is we help them with the heavy lifting in curating normalizing, making that data harmonized with the other codes around the world. So that they can be properly compared.

And part of that is, of course, the quality validation. And the truth is this, that even the best data custodians on the planet today will have smaller or larger problems. You will find that some data partners, in some cases, might not even have electronic data formats when we start. And then part of that heavy lifting is to help them to get past that.

And in some cases, they have a very well-structured and very high quality data, but they might still have quirks and things that need to be corrected. , So in the role it's not only about the data quality inherently that they have. It's also about the work to harmonize and understand how to harmonize this data so it becomes comparable.

Because you can imagine that attrition-- meaning when you combine a data set, the number of subjects in the end that can be used for the specific research project-- attrition is always there. The matter is how high it is. And by using the methodology that we do-- we are OMOP-EHDEN certified and works with OMOP and multiple other data models-- the only way to do this is to do it over and over again.

Develop tools and automation and controls in order to have the lowest possible attrition. But still, there will be attrition in any research case as you come to the end point of creating the collection. And I think that is inevitable at this present point.

It's just a matter of how good you are at doing that, and how well you can cooperate with your data custodians and partners. And I find that we are very proud to say we are quite successful in that work, but we will still get better as we go forward, I'm sure.

ANTONIO DE CASTRO: Very insightful. Nino, we are both here in Singapore and both enjoy Asia very much. Can you tell me a little bit about why it is important for an organization like yours to be present and to grow here in Asia?

NINO DA SILVA: Hmm. Well, to start with, Asia is large. And the countries have substantially different cultures. But let's start with why we are here. I think that is a good start.

Well, we see that with the US being a leader in the genomics field, and Europe with some specific countries being about in the same position, and having a very good growth trajectory, we identified several years ago-- when we decided to put our new office and business organization, as well as R&D organization, now in Singapore-- that Asia has the potential of leapfrogging. Has the energy and the need to do that.

And, we determined that we believe in that the trajectory in Asia will be sharper than in Europe and the US, although they start from a lower baseline, so to speak. And in some countries like Singapore, there is a definite skill knowledge and ambition to be leaders. And I think Singapore is an excellent example, with the genomic-- the National Precision Medicine program, the SJ100K that they are running now.

And we see other countries around that are following this example, or building their own examples. We have been quite focused on Singapore, Japan, and South Korea. And I think it is easy to see in evidence that these countries are providing not only the market, which would be a reason for any company to come here, but they are providing skill sets and ideas and a different perspective that we can benefit from. And that we can also help and support locally.

And then, that knowledge, those ideas, those innovations can also be taken to the rest of the world, Europe and the US. And that is a fascinating prospect that we see clearly developing. Just right-- a few weeks ago, we moved our CTO to Singapore to build our second R&D office globally in Singapore, where we hope to have a full set of senior R&D individuals, and junior ones to learn and teach.

By the end of this year, beginning of next year, we hope to be a 10-man team there. And that's a good start, but it's not the end. So there are many reasons to be here. I want to state also, finally, that one reason is purely out of interest and supporting the science community. There is a lot of data custodians and there's a lot of research done on white Caucasian, if you pardon my phrasing. But that's the fact. And there is very little that is done on Asian haplotypes. And much too little because if you look at the number of population in Asia compared to the rest of the world, there should be a higher focus. And we believe strongly to be part of supporting that work. It will also benefit the whole world's population because we all come from the same root. So discovery is to be made here, we believe. And we want to be part of that.

ANTONIO DE CASTRO: Nino, it has been a pleasure to have this conversation with you today. We'd like to end The Health Pulse episodes with optimism. So I would like to ask you, with all that's going on in the world, and the difficult years we've had with the pandemic, what is it that you feel positive about the future?

NINO DA SILVA: Well, first of all, I've always believed in humanity. And I still do. And secondly, I'll say that what we have seen in the last few years in terms of initiatives and engagement to create cross-

border collaborations, to share data and work in true federation models to look at disease from multi-haplotypic perspective over country borders is just increasing.
And to me it's a significant sign that people recognize and are willing to compromise and find a way to do this. And I would say that that's a very positive thing.
ANTONIO DE CASTRO: Thank you, Nino, for teaching us many things today. To our viewers and listeners, thank you for spending time with us today. We can't wait to share more health care and life science content with everyone. We welcome you to the conversation, of course. Please reach out to us in the comments section below, or email us at thehealthpulsepodcast@sas.com. Thank you.