Pharmafile

Therapeutic areas in focus

Volume 72 Autumn 2021

Antimicrobial resistance

Governments and global organisations continue to play a pivotal role in developing and enforcing plans against AMR

In affiliation with

Pharmafocus

The rare disease spectrum

People suffering from rare and ultra-rare diseases must be better supported to overcome their unique daily obstacles

Approaching eczema in 2022

Patients with skin conditions face significant challenges in their personal and professional lives, but what can be done to address these?

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VOLUME 72
AUTUMN
2021

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Executive Director – PMGroup Ltd
Karl Equi
kequi@pmlive.com

Sales Manager
Eliot Haynes
eliot@pharmafile.com

Editorial Coordinator
Will Brown
will@samedanltd.com

Designer
Peter May
designer@samedanltd.com

Journalist & Editorial Assistant
Lina Adams
lina@pharmafile.com

Subscriptions & Data Management
Beeline Data Services Ltd
T: +44 (0) 333 0124514
samedan@beelinedata.co.uk

Journalist & Editorial Assistant
Ana Ovey
ana@pharmafile.com

Pharmafile is published each Spring and Autumn. For subscription information, please contact us.

ISSN 0959-8758. All rights reserved. © 2021 Samedan Ltd

Cover image: © Unsplash | CDC

Contact us:

Pharmafile, Samedan Ltd,
Suite E, 11 Bell Yard Mews,
175 Bermondsey Street,
London SE1 3TN,
United Kingdom

T: +44 (0)20 7724 3456
W: www.pharmafile.com

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Charting the

Welcome to the Autumn 2021 edition of *Pharmafile*. 2021. What began a year of great hope for us all has seen plenty of challenges, not least the pharmaceutical and healthcare industries. They've faced a rapidly changing and evolving virus, a rise in antimicrobial resistance across infectious diseases, and the necessity of engaging increasingly via remote channels, with all the associated limitations. All the while, rare, chronic, and infectious diseases have needed addressing through innovative treatments and therapies. Kate Pain, Associate Director of Digital Strategy and Capabilities at Astellas, and Sebastien Noel, Director of Multichannel Strategy at Veeva, gave us insight into healthcare professional (HCP) engagement at a time when our relationship with health is constantly changing, and the needs of patients are both precarious and increasing.

Nine out of ten HCPs are claiming they would prefer either all virtual, or a mix of virtual and in-person meetings. Sebastien Noel, Veeva, shares: "The long-term implications for the industry with the dramatic shift to virtual, or hybrid, engagement are huge. I believe that the quality of relationships between reps and HCPs is the one big positive that has come out of this enforced shift to virtual. The ability to have more one-on-one facetime with HCPs is now enabling reps to present more content in a more streamlined way, in a way that works and is convenient for both parties."

Kate Pain, Astellas, shared that the shift "requires an exponential revision in the way that pharma companies deliver their services. We need to ensure that our field colleagues have the tools and capabilities to be equally confident in hosting virtual or in-person meetings."

It is not always easy to meet these demands, however: "We need to be proactive, not just reactive, so that we are primed for change and can pivot in accordance with environmental shifts and/or customer preferences. One size won't fit all, which will add further complexity, but it also adds colour and opportunity for pharma companies to differentiate themselves from the maelstrom, and shine."

"In 2021, almost 70% of HCPs are digital natives," Sebastien elaborated, "so providing a personalised, hybrid engagement model is needed to support meaningful interactions. With 87% of HCPs now wanting either a fully virtual or a hybrid meeting experience post-COVID-19, it is important that life sciences companies personalise their engagement channels to meet different HCP needs."

But how might a company do this? Kate gave us some insight into how Astellas addressed the challenge of a rapid change in HCP needs: "When the pandemic hit, we jumped from first to fifth gear in terms of our digital deployment. We prioritised our focus on three core channels – Veeva Engage, our HCP portal Astellas-Pro, and rep-triggered e-mail. Stripping these three must-have channels out from the nice-to-haves enabled us to narrow our focus and maximise our impact. We were able to preserve a line of communication with our customers, and ultimately with our patients." So, organising communication is key: "Between March and April 2020,

Astellas deployed Veeva Engage to 44 countries in just six weeks. Segmentation was key to the speed of the roll-out. We separated the 44 countries into 4 waves, split by their size and digital maturity, so that we were rarely managing more than 10-11 affiliates at one time.

"For our first release, we set our sights on mastering the basics. We enabled only the basic functionality within Veeva Engage. Now, on our fifth release, our offering has evolved into something significantly more sophisticated. As a business, we were able to differentiate between the immediate need versus a longer-term aspiration.

course to 2022

We also adopted standardised modular templates, a single source playbook, and maintained strong communication among project teams and affiliates throughout.

This activity, paired with our deployment of the other must-have channels, kickstarted a progressive digital mindset that was to continue for the next 18 months, and has left an indelible imprint on our commercial model moving forward, with a commitment to delivering omnichannel excellence."

There are significant benefits to remote engagement, Kate argues: "One of the greatest advantages of remote engagement is that meetings are typically longer than in-person calls. The average face-to-face call is 6 minutes and the Astellas average for a virtual call is 26 minutes. It's essential to provide soft skills training to support these longer interactions and to increase confidence levels with the technology also." These benefits exist alongside hurdles, however: "we experienced access issues in select healthcare organisations, which deterred customers from connecting with us via Veeva Engage. This was experienced in Germany, Spain, and the Adriatics and Baltics. In this case, personalising our invites to include Zoom meeting links overcame the issue, and since then more than 8,000 HCPs have connected using these links."

Further difficulties do seem to arise in relation to geography: "Challenges may also arise when operating across different countries, as the adoption of remote technology and response to COVID-19 has not been consistent around the world. Some reps and medical scientific liaisons have viewed it as a temporary fix until face-to-face interaction resumes,

Foreword

while others have been quicker to welcome it as a long-term solution."

So, what is the future of HCP engagement, in such an uncertain landscape? Is the virtual solution temporary, or the new way of liaising with healthcare professionals? "It's too early to predict what the pattern will be post-pandemic," Kate told us. "From April 2021 onwards, we've seen in-person interactions increasing, however the numbers fluctuate monthly, and the face-to-face/virtual frequency has yet to find its balance." With the emergence of the Omicron variant, and winter approaching, the status of face-to-face meeting is again looking uncertain. "The critical point is that we need to deliver according to our customers' preferences," says Kate. "We need to get better at listening to them while also learning from early adopters outside our sector to provide effective solutions."

Sebastien believes it likely that "over the next five years, face-to-face meetings will undergo a gradual resurgence across Europe, but virtual meetings will stay. This is because virtual meetings facilitate longer, more meaningful HCP interactions and deliver greater flexibility when scheduling several appointments in the same day. They also provide an alternative means to interact when face-to-face meetings are cancelled or disrupted last minute.

"With the life sciences industry now acutely aware of these benefits, I predict that an omnichannel approach to HCP engagement will become increasingly popular over the next five years."

The pandemic has highlighted the growing need for DNA vaccines, in multiple areas including infectious diseases and cancer. Looking ahead to the future of healthcare during the precariousness of a pandemic, we spoke to Professor Lindy Durrant, CEO of Scancell, which develops immunotherapies simulating the body's own immune system response. Scancell believe that DNA vaccines are one component of tackling diseases, believing the vaccines "give more sustained production of antigen which should lead to longer term protection than RNA vaccines." This vaccination form is significant for the increasing demands and needs of global healthcare: "Dendritic cell-targeting DNA vaccines are cheap and easy to manufacture, and have long term stability at -20°C. They can be rapidly adapted to give protection against both infectious disease and cancer. They can be used for repeated injections or for injections for other viruses, whereas viral vector-based vaccines can only be used twice before the immunity to the vector overwhelms the response to the inserted virus." For the many and varied needs presented by patients of infectious disease, this is significant.

Scancell uses a human monoclonal antibody to target cells that stimulate immune system response. This vaccine can be customised against a specific disease – a promising feature considering the changing nature of disease we have witnessed over the past year, and even the past month. This has the potential to change the current impact of vaccination. "A vaccine encoding both nucleocapsid protein linked to a modified Fc and receptor-binding domain should stimulate long-term memory B and T cells, and should give sustained protection over several years. This will give less opportunities for variants to arise and prevent people from having to be vaccinated every six months.

Scancell shared that its vaccine "targets antigens to dendritic cells to give more potent T cell responses that lead to long-term memory, and still give high titre neutralising antibody responses. The nucleocapsid protein is more highly conserved, giving better protection against variants."

As for the future, Professor Durrant looks forward to "simpler delivery systems for DNA vaccines. Currently we use a mechanical needle free device which is acceptable, but a simple injection would be more reasonable". Durrant also hopes for "better investment in vaccines that give broad protection (i.e. all coronaviruses – not just COVID-19), and sustained protection for 5-10 years should be developed now so they can be rapidly adapted when the next pandemic hits."

Ana Ovey – Pharmafile
Journalist & Editorial Assistant

With thanks to Veeva, Astellas, and Scancell for their contributions.

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Q&A

PHARMAFILE SPEAKS TO

DeepDrug

Deep down inside: How AI is supporting new therapeutic combinations

Dr Kishor Wasan, Dr Supratik Mukhopadhyay, and Dr Bruce Weng are a part of the DeepDrug journey, which aims to develop new drugs for neglected and infectious diseases. In the first of these, Skymount Medical's Chief Medical & Scientific Officer, Dr Wasan, explores how AI can help to bring drugs to the people who need it most

Pharmafile: **How can AI help us adjust to new strains of the virus?**

Dr Kishor Wasan: Artificial intelligence (AI) is like a child where you're feeding it new information, and as it processes new information it develops an evolved algorithm based on that new information. As we get information about the variant strains, the AI algorithm can adjust to virus strains and spit out new compounds, or new molecular targets, to address it. But there's a key point here: many people look at viral proteins to determine as potential targets, DeepDrug looks at human proteins. In other words, what are the proteins that the virus uses, so that it can enter, replicate, and transmit itself. And so many of the variant strains use the same human protein to do its business. That's how we adjust to the new strains of the virus.

DeepDrug also examines the potential toxicity of proposed treatments – how far does this increase patient safety during clinical trials?

For greater than 50% of all drugs made to the market, the toxicity profile kills a product in drug development, because of nonspecific dose dependent toxicity. We can, early on, understand and identify which drugs are going to be too toxic for animal studies and ultimately human studies early on. AI not only predicts efficacy and drugs that might be very effective against the virus, but we can also predict what drugs at concentrations and doses that we want to see efficacy might actually be toxic to patients *in vivo*, and will lead to drug interactions. We have to confirm this work with wet lab pharmacology, we don't jump straight from AI into patients. But what we do is eliminate early on what drugs are going to be toxic, what drugs we think will be toxic at the doses that we need to show efficacy.

The drug combination may reduce 'long haul' syndrome, the long-term consequences reported after COVID-19 recovery. How do you hope the drug will impact mental health issues following COVID-19 in some patients?

Long haul syndrome is becoming a bigger and bigger issue, and we're still gathering data about it: we're only 18 months into the pandemic, but we're seeing that around 30% of patients might have some kind of long-haul syndrome, lingering effects, long after they've recovered from the virus. A lot of it has to do with the effects on their cardiovascular health, their mental health, as well as other things. We think if our drug combination can decrease the length and severity of the symptoms – once you get COVID-19, instead of having to suffer for 10 to 15 days and then afterwards have these lingering effects – if we can cut the symptoms of severity down to a few days, as opposed to a few weeks, it will have a long-term impact on organ damage and mental health. When you have long, lingering effects of a disease weeks or months after you've resolved the disease, I think that's what taxes your mental health, because you're still suffering. The direct effect on organ damage, and the indirect effect of the lingering effects on your mental health, is why we think this could help with mental health issues in the long run.

How can AI speed up the response to outbreaks of previously unknown diseases?

DeepDrug was working in emerging infectious diseases for a number of years, and we pivoted to COVID-19 eight months ago. But the whole idea and the premise is if we understand how viruses work, we actually know how many of these viruses utilise human proteins to replicate entry, transmit, etc. With that fundamental knowledge already in our back pocket, we're going to be able to be ahead of the curve when a new emerging disease comes out. When a new disease emerges, we look at how the disease works, compare it to what we have in our algorithm, input into the AI any new features about that virus or disease that we don't know about. From that already built algorithm, which is evolving and growing, we can then make predictions to deal with those emerging infectious diseases and viruses.

What developments in drug discovery do you anticipate in the next five years?

I've been involved in systemic fungal infections for 30 years. Many of us in the infectious disease community have said that the cupboard has been bare: we have not had a new set of drugs or drug compounds to treat a variety of infectious diseases for a very long time. In the field of systemic fungal infections, we've actually not had any new drugs, with new mechanisms of action, to deal with some of the new emerging systemic fungal infections, ones that have drug resistance, in the last 20 years. Looking into the future, if the pandemic has done anything else, it has really woken everybody else to the fact we need to fill that cupboard up with new drug therapies with new mechanisms of action. Moving forward, there will be a reemergence of research and development of new infectious disease drugs, using AI and other routes, so that we don't get caught with what has happened in the last 20 years in infectious disease.

What are your hopes for AI and neglected diseases?

I'm the co-founder and co-director of the neglected global diseases initiative at the University of British Columbia, which we formed 10 years ago. For us, the idea was to develop drugs at a low cost for developing world indications. The definition of neglected diseases is that they have a huge number of patients or people that are infected with the disease, but there's very few resources to treat the disease. What I hope will happen is that with AI, we can develop new drug molecules more effectively, more efficiently, that are cost effective, that we can then go after many of these neglected global diseases that we really haven't spent the time on. Unfortunately, many companies are trying to make a profit, and for neglected diseases, you're working in countries that don't have the economics that pay for those high dollars. I think that's where AI comes in. Because we can develop cost effective drugs that can get to millions of people for these neglected diseases. In fact, it's emerging out of what we're trying to do with the neglected global disease world, and what we're trying to do with more efficient drug development through AI.

Dr Kishor Wasan is Chief Medical & Scientific Officer at **Skymount Medical**. He has published over 240 peer-reviewed articles and 280 abstracts in the area of lipid-based drug delivery and lipoprotein-drug interactions. Dr Wasan has won many prestigious awards and is a fellow of the American Association of Pharmaceutical Scientists and the Canadian Academy of Health Sciences. He is currently an Adjunct Professor and Distinguished University Scholar in the Department of Urologic Sciences, Faculty of Medicine at the University of British Columbia, and is the co-founder of the Neglected Global Diseases Initiative at UBC. Dr Wasan led the research team at the Wasan lab at the University of British Columbia in the development of an oral formulation of amphotericin B, which has successfully completed Phase I human clinical trials. He heads the pharmacology programme at Skymount Medical.

Dr Supratik Mukhopadhyay is the lead researcher who developed the LSU DeepDrug AI platform. He is a computer scientist and professor at LSU

The DeepDrug team has been working on the AI for drug-resistant pathogens for eight years – what have the biggest milestones been over this time?

Dr Supratik Mukhopadhyay: I first had the idea of using AI to accelerate drug discovery around 2007. However, at that time, AI was not really as mature as it is today – the AI revolution had not started. Also, I didn't have access to high-performance supercomputers. So I let the idea germinate. In 2009, I joined LSU and had access to LSU supercomputers (that was one of the reasons why I joined LSU). By 2012, the AI revolution had started. I also found a fantastic collaborator in Professor Michal Brylinski who had just arrived at LSU. At this point I decided to act, starting the DeepDrug project.

There have been several accomplishments along the way. We broke up four adenosine receptor antagonists into their molecular fragments and then recombined them to create an adenosine receptor molecule. Adenosine receptor paired with various G proteins have effect on inflammation, pain, and immune responses. By 2016, we entered the IBM Watson Artificial Intelligence XPRIZE and by 2020, we had reached the semi-final of the Artificial Intelligence XPRIZE (among 142 teams worldwide). In February 2020, I gave the semi-final presentation at the TED World Headquarters at New York City. After we came back, we saw the first COVID-19 wave hit the US. Soon, there was a lockdown in Baton Rouge. At this point, we decided to pivot our engine towards therapeutics discovery for COVID-19. Today, a combination therapy is undergoing human trials both at the Riverside University Health System Medical Center in California and in Europe.

What is the potential of AI in drug discovery and research? What will it change?

I will give an analogy here. If you see the time period between 200 BC and 1500 AD, science and technology progressed at a very slow pace. For example, all through this period our mode of transportation was horse-drawn carriages/horses and sail-driven ships.

However, in the last 300 years, suddenly you see rapid progress in science and technology. We went from horse-drawn carriages/ horses and sail-driven ships to high speed locomotives, cars, aeroplanes, and rockets. What changed?

Let us look at physics. Before the 17th century, physics was mostly descriptive (it was called Natural Philosophy). All that changed when Sir Isaac Newton invented calculus that brought in the quantitative aspect in physics. Now you could compute and predict.

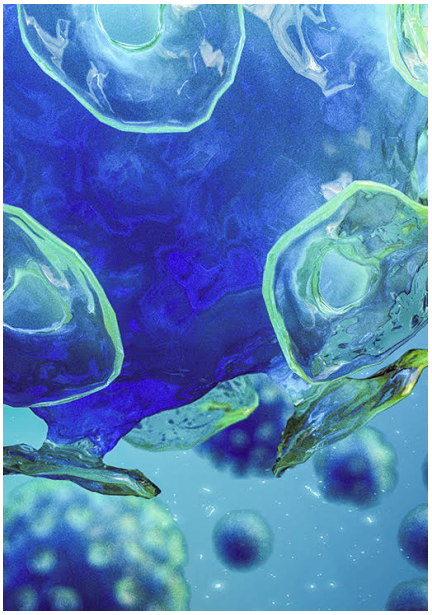
I believe that biology and pharmaceutical sciences, have been, for a long time, like physics before 17th century, largely descriptive. What AI brings is the quantitative aspect. You can now compute and predict. This can change the nature of drug discovery.

Today the time and cost needed to take a new drug to the market from scratch is 10 years and $2.5 billion. A lot of this time and cost required is due to the fact that only 12% of the drugs developed by pharmaceutical companies succeed. As a result, pharmaceutical companies were reluctant to develop new drugs for sectors that had low profit margin, e.g., infectious diseases. In fact, the last new antibiotic was developed by the pharmaceutical industry in 1987. AI can not only accelerate the identification of hits but also improve the success rate drastically. You will now be able to take new drugs to the market at a fraction of the time and cost.

In what ways will AI impact future drug discovery?

I think AI will be tightly integrated into the drug discovery pipeline. There will be renewed focus on drug discovery for infectious diseases and other neglected global diseases. AI-enabled drug discovery pipelines should be able to handle pandemics in a much better way. In addition, given the ubiquity of genomics datasets as well as EHR data, I anticipate the rise of personalised therapeutics.

We will see pandemics, this pandemic and even the next ones, getting rapidly addressed. We'll see new types of medicines and vaccines, for things like Dengue, cancer, and lung damage, for which we have hardly any medicine to treat. Treatment for these kinds of diseases, neglected diseases, will see a rapid



advancement. Moreover, we will see a rapid advancement in our understanding of biology.

How can AI help us improve global health and access to therapeutics?

AI can help repurpose generic drugs and their combinations towards emerging diseases, providing affordable therapeutics for the world as opposed to expensive treatments like monoclonal antibodies. AI can help develop environmentally friendly drug manufacturing processes. In addition, AI can help discover lipid nanoparticles with certain properties that make them suitable for drug delivery. AI can find therapeutics based on generic drugs: there are thousands of generic drugs on the market today, and it can see if any of these generic drugs can help us treat diseases, or in combination can. And that immediately changes the potential cost of pharmaceuticals, because generic drugs are cheap.

Another thing is nutraceuticals: there are plant extracts, natural products, plant extracts and other minerals, that may be suitable for prophylactic, immune, purposes for different diseases. COVID-19 may be one of them, and maybe other diseases, like flu, and so on. Advantages here are an environmentally friendly manufacturing process, and price – these plants can be grown in mass in different parts of the world.

AI can revolutionise global health, and it can revolutionise disease diagnosis. Combining the two potentially gives patients access to personal therapeutics.

DeepDrug can reduce the time and cost of drug discovery by as much as 90%. How will this huge reduction in resource allocation change things, and how will it allow the focus of drug development to shift?

There are two modes of operation, one is creating new molecules completely from scratch, the other is repurposing existing FDA approved drugs. For new drug development, DeepDrug can save 30% of the time. However, through drug repurposing, DeepDrug can save 90% of the time. Because DeepDrug can already filter out candidates that are likely to fail, you will need less *in vitro* testing, and less *in vivo* testing. It helps rapidly take a drug to human trials. Because of the drastic reduction in time and cost, pharmaceutical companies can now attend to neglected global diseases that have so far received very little attention.

Professor Supratik Mukhopadhyay is a faculty member at Louisiana State University. He led the DeepDrug team on artificial intelligence for automated drug discovery to the semifinal of the IBM Watson Artificial Intelligence XPrize. His team was one of only 142 teams to compete worldwide. The DeepDrug Artificial Intelligence Platform's combination therapy for COVID-19 is in the process of undergoing human studies in Ukraine and at the Riverside University Health System Medical Center, California. It took 13 months from inception to human studies, which is one of the fastest in the pharmaceutical world for a combination therapy. The DeepDrug technology developed by Dr Mukhopadhyay has been licenced by Skymount Medical. Dr Mukhopadhyay has been awarded three US patents and has another eight patents pending. He cofounded Ailectric LLC, an AI startup focusing on sound, text, and image analytics.

Dr Bruce Weng is an infectious disease specialist and physician at Riverside University Health System Medical Center, partnering with Skymount Medical to facilitate human clinical trials demonstrating the safety of SM-19

Now that this drug combination is in clinical trials, what do you think its potential will be?

Dr Bruce Weng: This is intervention post-infection, so it doesn't replace preventative therapy, which I think is the most crucial intervention. I think a lot of people may look at interventions that are now available and say 'Oh, I don't need vaccination,' and I do want to emphasise that one of the most, if not the most effective therapy, is getting vaccinated.

But we know that nothing's perfect, and there will be breakthroughs, or maybe some people make a personal choice that they don't want to be vaccinated, and they can potentially get COVID-19. What we're trying to look at is a combination therapy to see the safety and efficacy in potentially reducing the side effects and complications of COVID-19 infection. Right now, it's a small trial, so safety and efficacy are the most important. We've seen in the pipelines that potential oral therapies are coming out, you've probably all seen it in the news. Availability of more options would be great, especially if they're generic options, not just in the US or the UK but anywhere in the world.

How does this compare to other COVID treatments that are available?

Outside of the highly effective vaccines that we know are already available, the current treatments are primarily IV therapy, at least here in the US. There's been a big push to use that, especially for people who are high risk and are not hospitalised, but we know that IV therapy can be really difficult to set up. Having a therapy where you could just go to the pharmacy, or have somebody else go to the pharmacy and pick up for you, really would improve accessibility. The key is having something that's easy to give and easily accessible, potentially at a lower cost, too.

What changes do you think have proven most significant to our approaches in medicine, in recent years?

Technology is a big part of everything we do now. Computer technology is in almost everything. Having this rapid technology, being able to create these new interventions and bring them to the public – through potential interventions and then therapeutics – is huge.

But, technology is a double-edged sword. If I'm looking at something online, and I'm not a mechanic, I don't know about a lot of other stuff which isn't in my field, and I can't separate what's real and what's not, it can get very confusing, because you can read something which looks like it's coming from a reliable source. And how do you differentiate if that's factual information versus false information? Just looking at the vaccination issues, it's very easy to get things confused.

How might AI help us in future pandemics?

I think that as people use AI, and as AI technology improves over time, it can potentially even identify pandemics before they start. So maybe you can see a certain pattern or scenario in the world and identify something that's going to happen, target it and hopefully cut off the next COVID-19 outbreak, or at least be able to contain it a lot more rapidly. That might be a wonderful use for AI just with regards to tackling future pandemics; obviously the evolution of AI is going to continue, it could help with other new innovations and therapeutics, especially with other outbreaks. This is something that's been talked about over here, at least theoretically, but it doesn't even have to be restricted to infectious disease: the thought of using AI for therapeutics and intervention, all sorts of medicine, is tremendous. Just extrapolating the use of AI into other spheres of humankind, for example education: it's really just waiting for people to come up with an innovative way to use it. But I think with regards to pandemic, potentially just identifying them much earlier, that might be one way that we really utilise the technology. Within medicine, the biggest area it may be used is for new therapeutics down the road. If you're looking at the world of endocrinology, cardiology, or cancer research, for example, the ability to identify existing and approved medications, repurpose them is vital. AI may be able to understand certain patterns and know whether these medications might actually be applicable and useful in a different area or need. That's really where AI could help in the field of medicine.

Several organisations have studied which therapeutics might prove successful against COVID-19. What brought about this undertaking between RUHS and other organisations?

When RUHS first heard about this potential study from our partner group, Skymount Medical, the idea of a potential oral therapy that might be much more easily accessible to the public was very appealing. Our hospital and healthcare system serves a really underrepresented and underserved area. The thought of having something that's easily accessible to them was a huge plus, and the somewhat novel idea of using AI-based technology to be able to identify and repurpose medications was really interesting too. The thought was, if it could be used for something like infection, it could be used in other fields of medicine. That novel approach was very appealing, and that's what got RUHS jumping on board. Obviously first and foremost is what we're doing with this particular study, making sure it's safe, more than anything. But the initial appeal was number one, this novel approach, and number two, being able to find a potentially accessible and affordable therapeutic for the general population, not only here but across the US and the rest of the world.

Bruce Weng is an infectious disease physician, practicing at Riverside University Health System Medical Center (RUHS) in Moreno Valley, California, which serves as the primary safety-net hospital for Riverside County residents. He is serving as an assistant clinical professor at the University of California, Riverside and Loma Linda University Medical Center. His primary focus of practice involves serving as co-chair of the antimicrobial stewardship programme, in addition to general infectious disease practice. Dr Weng and his team are assisting in the clinical study investigating the safety and efficacy of a DeepDrug formulation at RUHS.

Resisting change: The pathway to better AMR planning

The latest global survey on antimicrobial resistance has seen a global plan initiated by WHO. ICON's Caroline Forkin talks us through the various actions that should be taken to improve AMR planning

Antimicrobial resistance (AMR) is an urgent and growing public health threat. Since the transformative global adoption of antimicrobials in the last century, pervasive misuse and overuse has driven widespread AMR in pathogens, and rendered once reliable treatments ineffective. The drivers of AMR are multifaceted, with far-reaching consequences. Meanwhile, the development of alternative antimicrobials and interventions has been slow. With so many forces accelerating a problem that spans the globe, mitigation will require unprecedented social support, and coordinated, holistic action is needed to help combat the growing global public health crisis of AMR.

Reinforce understanding of AMR

Many antimicrobial drugs already have an ancient history of use and evolved resistance by microbes. Understanding the evolutionary relationship between antimicrobials and microbial resistance helps explain why acquired AMR can emerge so quickly following intensive antimicrobial use.

Microbial resistance is the result of a random genetic mutation or a combination of mutations impairing an antimicrobial's utility. In the absence of an antimicrobial, resistance mutations tend to be disadvantageous because they are costly. However, when a population is exposed to antimicrobials, resistance mutations are often necessary for survival, and are likely to be passed from one generation to the next. Resistance genes can also be spread between unrelated microbes through horizontal gene transfer (HGT).[1]

Because the presence of antimicrobials determines whether resistance mutations provide a competitive advantage or disadvantage, AMR prevalence is tightly correlated to the likelihood of antimicrobial exposure. Before widespread antimicrobial use by humans, AMR was generally contained to a small population of microbes that had natural, sustained exposure to an antimicrobial. However, when an antimicrobial is intensively applied by humans, the advantage of acquiring resistance becomes widespread.[2]

Following sustained antimicrobial use in a clinical or agricultural setting, pre-existing resistance genes – which took generations of antimicrobial exposure to first evolve – can be rapidly and ubiquitously acquired through HGT by microbes in a shared environment. Microbes transported to other environments may then bring resistance with them.

Understanding AMR mechanisms is key to developing intervention strategies to disrupt AMR emergence and spread. In addition, comprehending why AMR occurs, and the risks it poses to public health, will support personal investment in initiatives to combat it.

Optimise antimicrobial use

The utility of antimicrobials in preventing infectious disease has transformed medicine and agriculture. Preventative antibiotics drastically reduced the risk of surgery, and common deadly diseases, including pneumonia and tuberculosis, suddenly became treatable. Moreover, antibiotics in agriculture made it possible to raise faster-growing livestock at higher densities.

Initially, the application of antimicrobials in these settings was indiscriminate.[3] However, the subsequent body of evidence linking antimicrobials to AMR motivated private initiatives and governmental regulations to temper antimicrobial use. Still, substantial progress must be made before antimicrobial application is optimised in healthcare and food production.

Healthcare:

Up to 50% of all antimicrobials may be being used inappropriately in human healthcare.[4] Appropriate and restricted use of antimicrobials will require the implementation of diagnostics able to indicate which treatment is most likely to be effective, and reduce the number of antimicrobials prescribed. Diagnostics that can monitor a patient's response to treatment may also help to prevent continued use of an ineffective treatment. Eventually, the adoption of treatment alternatives to existing antimicrobials may help ensure treatment efficacy when the risk of AMR is high. Optimised antimicrobial use also depends on patient compliance. Suspending treatment before an infection is entirely cleared can lead to a recurrence that is more resistant than an initial infection, and can increase the risk of AMR outbreaks. Here, clinicians play a critical role in educating patients about the importance of following an antimicrobial regimen.

Food production:

Agriculture accounts for more than 75% of annual antimicrobial consumption in the EU and the US, and has been directly linked to AMR disease in humans.[5] Addressing overuse and misuse of antimicrobials in agriculture will involve three strategies:

1. Abolition of trace antibiotics used in feed to promote growth

2. Abolition of continuous low-dose antibiotics for disease prevention

3. Using alternative antimicrobial treatments wherever possible

Antimicrobials also enable unhealthy agricultural practises promoting disease acquisition and transmission, such as overcrowding and inbreeding. Reintroducing practises that promote the health of livestock and crops could help reduce the number of infections, and help to minimise the need for preventative antimicrobials.

Governmental policies and initiatives supporting more sustainable food production practises can have a profound effect on optimising antimicrobial use in agriculture. For example, Vietnam's National Action Plan for addressing AMR prompted the ViParc (Vietnamese Platform for Antimicrobial Reductions in Chicken Production) project. ViParc became the first large-scale intervention tackling antimicrobial overuse in Southeast Asian animal production systems.[6] ViParc offered small-scale poultry farms in Vietnam's Mekong Delta veterinary care as an alternative to antimicrobials. The project determined that access to trained veterinarians reduced antimicrobial use by 66%, in a region where food production accounted for 72% of use overall.[7]

Prioritise disease prevention

The risk of AMR emergence and transmission is especially acute in low-income countries and disadvantaged communities. Social and economic issues, especially overcrowded living conditions, unsanitary water, and limited healthcare access, increase the risk of acquiring and spreading AMR disease.[8] Reducing the incidence and spread of infectious disease in communities most vulnerable to AMR infection will be critical to combatting AMR.

Investments in public health resources may be even more effective with appropriate communication, awareness, and training, to promote understanding of AMR prevention. Informing healthcare and food production workers about the risk of antimicrobial overuse, and training them in measures to prevent contracting and spreading AMR disease, will help to prevent transmission from AMR hotspots to surrounding communities. Campaigns that engage a public audience, such as World Antimicrobial Awareness Week, are also key to encouraging awareness and best practises among the general public, health workers, and policy makers.

Establish funding for AMR research and development

While the problem of AMR has snowballed, the development of new antimicrobials has slowed. The incentive for pharmaceutical companies to develop new antibiotics is especially low, because antibiotic efficacy declines over time, and the upfront cost of drug development has risen to 1.5 billion dollars.[9] Implementation of financial incentives for pharmaceuticals may facilitate reduced reliance on traditional antimicrobials. The recent European Commission strategy document includes a programme to develop incentives for drug and diagnostic development, and marks the first time a major governing body has codified this approach.

Existing programmes for the funding of AMR research and development include the Global AMR Innovation Fund (GAMRIF), a UK-based group with the goal of reducing the threat of AMR in low- and middle-income countries. GAMRIF has a goal of funding the development of two to four novel antibiotics and making them available to patients by 2030. State and local initiatives to combat AMR may be further supported by national efforts, such as the Antibiotic Resistance Solutions Initiative funded by the Centers for Disease Control (CDC).

Development of cheap, effective, and accessible diagnostics

The development of rapid, accessible, and low-cost diagnostics would enable the timely use of targeted therapeutics, and allow clinicians to better monitor treatment effectiveness over time. One diagnostic method uses polymerase chain reaction (PCR) to identify pathogens by their genetic fingerprint to diagnose disease. This method is substantially faster than traditional culturing methods. PCR diagnostics enable clinicians to diagnose tuberculosis within hours instead of weeks following the collection of a clinical sample.[10] However, PCR techniques require laboratory equipment and conditions that limit the technique's application.

Adaptations of PCR technology, such as PCR Loop Mediated Isothermal Amplification (PCR LAMP), improve the practicality of PCR-based diagnostics by making them cheaper and transportable. The minimal equipment and speed of LAMP made it an ideal tool for rapid COVID-19 testing.[11]

Improving AMR diagnostics will require simplifying diagnostic workflows, taking advantage of technologies such as next-generation sequencing (NGS) and artificial intelligence (AI). Researchers at the Oxford Biomedical Research Centre (OxBRC) are working on a modern diagnostic platform using whole genome sequencing analysis that is scalable and open-source.[12] The diagnostics platform aims to assist in outbreak response, infection control, and direct patient care on a global scale. Another global support system, the CDC's AR Lab Network, helps laboratories enhance detection of AMR using DNA sequencing technologies.[13]

Developing alternatives to antimicrobials

Alternative treatment methods to antimicrobials include bacteriophages, probiotics, and

vaccines. While all of these treatments have promise, vaccines may be especially impactful in the prevention of community disease spread and reduction of antimicrobial use in agricultural settings.[14]

Unlike response-based treatments that can select for the most resistant microbes in an exposed population, vaccines facilitate an immune response that is early, targeted, and varied between individuals. Microbes are less likely to develop resistance to vaccines than to other targeted treatments.[15]

However, until the COVID-19 vaccines, vaccine development was expected to take more than a decade. Now, vaccine development for AMR may be expedited by genetic sequencing technology, COVID-19-informed models for accelerated clinical trials, and fast-tracked regulatory approval processes.[16]

Research into antimicrobial alternatives will benefit from establishing combination treatments and treatment cycling, helping antimicrobials maintain efficacy, especially when AMR spread is likely. Determining the real-world efficacy and optimal use of diagnostics and treatments requires organised monitoring and surveillance of AMR by dedicated organisations.

Coordinate surveillance and monitoring of AMR

Coordinating observations of AMR emergence and spread helps identify key drivers of AMR and effective prevention strategies that can inform preventative action plans. The Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) started the development of WHO guidelines on the use of antimicrobials in food production, and contributed a guidance document on integrated surveillance of AMR.[17] The Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) was chartered by the EU and the US in 2009 to improve peer collaboration, information exchange, and understanding of best practises for contending with AMR.[18] The Global Antimicrobial Resistance and Use Surveillance System (GLASS) outlines and facilitates standardised collection, analysis, interpretation, and sharing of AMR data to inform research. In 2021, 64,000 surveillance sites in 66 countries contributed data. Participation has grown exponentially since the system's initiation in 2015.[19]

Implement action plans

Governments and international groups have a pivotal role in developing and enforcing holistic action plans to combat AMR. The tripartite partnership of global organisations – WHO, the Food and Agriculture Organisation and the World Organisation for Animal Health – coordinated The Global Action Plan (GAP) to combat AMR in 2015, and encouraged countries to develop their own national plans.[20] The plan jumpstarted global initiatives such as GLASS, and the Interagency Coordination Group.[21]

GAP has supported the development of national action plans to combat AMR in 144 countries. These national plans are well positioned to use insights from global AMR monitoring, and research efforts for locally tailored enforcement and multifaceted engagement strategies.[22]

Conclusion

AMR is a problem of daunting scope, and we need to be prepared for the next disease-X type global threat. However, the evolutionary mechanisms and consequences of AMR are well characterised and understood. There are concrete actions that individuals, institutions, and governments can take to address the drivers of AMR and treat AMR infection. Working in concert, actions from diverse players will make it harder for microbes to evolve and sustain resistance to life-saving treatments.

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Dr Caroline Forkin brings 26 years' experience in clinical, pharmaceutical and global health settings, including extensive experience in Africa.

With a clinical background in Infectious Diseases, Caroline's experience in Africa included senior roles as HIV/AIDS Advisor for both the World Bank and the Irish Government. These roles involved working with the Mozambican Ministry of Health, National AIDS Council, together with other global health entities such as the Clinton Foundation HIV/AIDS Initiative, the Global Fund for AIDS, TB, and Malaria, the President's Emergency Plan for AIDS Relief. Dr Forkin's pharma experience prior to joining ICON includes country medical lead for two biotech companies. Her role at **ICON** is Vice President for Clinical Research Services, with responsibility for all our studies in Africa and the Middle East.

A bold and ambitious plan: Harnessing data and improving health and care continuity for the next decade

The NHSX and DHSC draft strategy aims to improve patient outcomes, by placing them at the centre of the care journey. Dr Dipesh Hindocha at Doctor Care Anywhere explores how health data systems can be used to help patients directly engage with their care experience, and build trust in their providers

As the UK emerges from COVID-19 restrictions, some of the old debates are beginning to reassert themselves, and now the minds of politicians and the public are returning to long-term public health issues. In June, the publication of a draft strategy paper from NHSX and the Department of Health and Social Care (DHSC) was scarcely noticed by many. The paper threw into sharp relief the debate about where patient privacy should end, and where joining up NHS data across the NHS estate and beyond can be expected to drive better outcomes for patients and clinicians alike.

There will surely be many across the private and public sectors in healthcare and technology who will feel the publication of *Data Saves Lives: Reshaping Health and Social Care with Data* marks a significant and welcome step. Harnessing the relatively untapped potential of joined-up patient data use brings closer the prospect of delivering significant health, social care, and services improvement across the NHS and elsewhere in the wider health system. The national public health emergency caused by COVID-19 has highlighted how effective data analytics can simultaneously save lives while driving efficiencies – both of significant value to the NHS. This has played a huge role in tracking the virus and infection hotspots, prioritising the distribution of critical resources, mapping regions and groups for mass vaccination and, most importantly, in the case of this latest initiative, accelerating the ease of access and sharing of patient care records.

It is therefore encouraging to see the importance that DHSC and NHSX is attaching to placing the patient at the centre of the care pathway. People should be closer to their own data, which will enable healthcare professionals to review the entire clinical journey from GP surgery through to patient aftercare, and ultimately improve outcomes.

This concept is something the private sector is rapidly innovating. We therefore feel well placed to provide our perspective and to assess this initiative through the lens of both a primary care clinician and a thought leader in the private, digital health space. We seek to strike a balance between someone embedded within the NHS, and an innovator outside it.

Putting patients at the centre of the care journey

The crucial point, from a patient perspective, is about building a system that can maintain trust, confidentiality, and transparency. It is also about building and maintaining the highest standards in data processing, which will be critical to building trust amongst patients, clinicians, and wider organisations.

The rapid rise of data use over the last ten years, and digitalisation of many aspects of our lives, has led, somewhat understandably, to concerns about the scope for data leaks, and the fear of inappropriate use being made of individuals' data. To this end, developing and enabling a transparent health data system that allows users to see how and when their data is being used, is to be warmly welcomed.

Another question that needs resolving is how we come to a shared understanding of what 'data' mean to those using the system, ie the patient, and the care giver. Given the complex nature of health data, data privacy, data handling, and legalities surrounding data, if patients are going to 'buy-in' to the concept, they need to be persuaded of its value and indispensability for their own wellbeing. The Wellcome Trust's Understanding Patient Data, a health data initiative working in partnership with the NHS, which seeks to bring transparency, accountability, and, crucially, understanding, will be an important tool in delivering this. However, further initiatives will be needed to bring all stakeholders onboard, such as clinicians and healthcare managers. Patients will increasingly engage with their data in the future. This is inevitable. But if participants, such as those clinical and care staff delivering healthcare, are not well positioned clearly or openly to explain or discuss this with their patients, then full acceptance cannot be guaranteed.

> **The ability to review such information in innovative and more efficient ways, can help clinicians, researchers, and healthcare managers make transformative differences to patient and public health outcomes**

From a technical perspective, personal data stores, in whatever form they take, will only work if all the moving parts of the system are speaking the same health language and information can be contextualised by the person receiving or reviewing the information. The mass consolidation of data, and the joining up of all the constituent parts will require a unified governing framework and terminology system. Universally accepted clinical vocabulary systems, digital platforms and frameworks, such as SNOMED CT, will of course help ensure there is ubiquitous language across all systems. But we would suggest more still needs to be done.

Access to patient data

Access to relevant patient data is hardly a new or groundbreaking concept. However, as witnessed acutely during the pandemic, access to substantially enhanced data sets and the ability to review such information in innovative and more efficient ways, can help clinicians, researchers, and healthcare managers make transformative differences to patient and public health outcomes.

However, such innovative analytics will only be as good as the data being supplied. Transposing raw data, some high quality, some low quality, which will come from various sources including digital platforms and apps, will need extensive health analytics capabilities. And as patients are increasingly

Building the right architectures and standards to allow third parties readily to innovate and share those learning with the NHS, and supporting this with a clearer pathway to achieving effective whole-of-market strategies, is exactly what the proverbial doctor ordered

likely to add their own data to the system, it is imperative that proper governance and validation frameworks are put in place to best inform the decision-making process, and provide clarity and reassurance both to patients and clinicians.

We may see this when linking digital and remote assessment tech with real-time patient data collection, such as through home monitoring systems, which really could revolutionise care delivery to the most vulnerable patients in society. However, this will need to be supported by innovative analytics and thoughtful consideration of how and when this information flows back to healthcare workers. There would obviously be little value in having a set of data delivered that had not been through a considered process of analysis to ensure that information was being used effectively. Indeed, it would be possible to imagine poor outcomes being the result of a failure to achieve this.

Shared care records

Shared care records, i.e., the various constituent parts of the health and care system seamlessly sharing information about patients, has the potential dramatically to reduce errors being made from a clinician's perspective. However, patients will in due course be likely to expect all parts of their health and care experience to be included in this process, both within the NHS as well as any private or third-party healthcare companies and providers. They will want all of their health data to sit within their central shared care record, and so naturally this needs to be underpinned by clear and well understood structures about how this data is used, in order to maintain transparency, honesty, and trust with our patients.

There will also be inevitable questions about what constitutes appropriate stewardship and curation of shared care records. And there will also be challenges. For example, how can this all be done coherently and effectively in the context of a shared record that intersects with different parts of the health system, some of which speak different 'health' languages? Who will be responsible and accountable for the overall curation of these records? Who will ensure critical information is kept up to date and made consistent with information previously data inputted? We would hope that, as a part of the consultative process on initiatives like Understanding Patient Data, the mobilisation and inputs of private and third sector groups are brought in to play in order to provide complete and compelling answers to these questions and create the best possible, and most sustainable, solutions and systems for the future.

Supporting local and national decision makers

We don't believe this needs to be limited to public sector healthcare leaders. Where there is a legitimate reason, underpinned by the right consents, confidentiality, and governance systems and processes, organisations providing care beyond the NHS, but still critically important parts of the UK healthcare ecosystem, should have access to shared cared records. This is necessary to ensure clinical and social care continuity, especially as the delivery of services via digital platforms and operators continue to increase. In the event of a further lockdown or emergence of a new COVID-19 variant, this will be vital.

A good example would be patients attending private hospitals, referred to by their private health insurer but via an NHS GP, for surgical procedures. Of course, they, and their physician, would benefit medically from shared access to this information. As per the draft guidance, "where access to data is granted, having met these high thresholds, it must always have the explicit aim to improve the health and care of our citizens, or to support the improvements to the broader system."

Next steps

The plans included in this draft strategy are bold, ambitious, and necessary. But questions do arise. Are they achievable in the timeframes stated? How will the big propriety systems that are already contracted and providing services throughout the NHS come onboard? How will public and private sector organisations work together, without ever compromising or impairing the objective of improving patient outcomes?

The commitment to help innovators and health technology providers to work with health and care organisations is very much to be welcomed. Building the right architectures and standards to allow third parties readily to innovate and share those learning with the NHS, and supporting this with a clearer pathway to achieving effective whole-of-market strategies, is exactly what the proverbial doctor ordered.

We all want to achieve brilliant outcomes for patients and their care. Patients deserve no less. But those outcomes must be the right ones, as well as achievable and sustainable ones. As always, the devil is in the detail. So, we await with eager anticipation the next iteration of NHSX's proposals.

Dr Dipesh Hindocha, Clinical Innovation Director at **Doctor Care Anywhere,** started his career as a locum GP following his Master's in Medical Sciences and Clinical Practice. In 2018 he began working with Doctor Care Anywhere as a Clinical Lead, moving on to become Head of Clinical Product Development, before being promoted to Clinical Innovation Director in 2021.

Redbow Consulting Group

A UNIQUELY PLACED HEALTHCARE STRATEGY CONSULTANCY. Dedicated to healthcare, we work hand in hand with our clients across many areas of organisational strategy worldwide. Our assignments span Long Range Planning, Portfolio and Brand Strategy, Marketing Academies, and individual mentoring. We have wide ranging experience in the use of business simulation and gamification in Learning & Development and strategy creation using our innovative workshop-based methodologies. These are designed to help our clients maximise the knowledge and expertise within their cross-functional teams. In every project, we work to create and enhance the value that our clients bring to their customers and the patients they serve.

OUR ORGANISATION

We use an associate-based model to assemble the very best team for each and every project. Each project is led by Jonathan Dancer who has 30 years' experience in the Pharmaceutical Industry in a wide range of sales, marketing, market access and consulting roles across the world. Jonathan has led strategic healthcare consulting businesses for just over half his career, having founded two consultancies in 1999 and 2013.

OUR APPROACH

Jonathan is a firm believer in the power of teams, and whilst many projects do focus on the concrete end of strategy and implementation, even more revolve around the creation and maintenance of healthy teams that can take the organisation forward.

STRATEGIC CONSULTANCY

Redbow has worked with a number of organisations in the development of organisational and brand strategy and Jonathan has extensive experience working with many Leadership Teams over the past 20 years.

Redbow has developed and run bespoke strategic planning processes for many clients and also uses its unique gaming methodologies to enhance strategy development and organisational engagement.

LEARNING & DEVELOPMENT

Jonathan is training lead for PriMe, the Pharmaceutical Marketing Society's L&D organisation and has trained marketing organisations all over the world. He is also a visiting lecturer in Marketing at Kings College London.

Jonathan Dancer, Managing Director

Redbow has set up and run a number of Marketing Academies for clients as well as training sales leaders and other members of the cross-functional team.

ORGANISATIONAL HEALTH

It has been said that "culture eats strategy for breakfast, lunch and dinner". It is observably true that most teams are usually able to resolve intellectual challenges. However, teams that are capable in this way are not always able to create the healthy environment needed for teams to thrive.

For this reason, Redbow works with Patrick Lencioni's model of teams and Jonathan is an experienced and accredited practitioner in The Five Behaviors of a Cohesive Team™ supported by EverythingDiSC™.

This adaptive personality assessment model helps to create the cohesive team environment needed for organisations not only to be good, but to achieve greatness. Many Redbow clients have already benefitted from the Five Behaviors model, which Jonathan runs as part of a two or three-day programme.

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It is not possible to market any offering competently without creating the successful "exchange of value" described by Kotler, and yet so many marketing teams fail to focus on the creation of value that not only builds loyal customers who keep coming back, but gives their organisation a sustainable competitive advantage. It is Redbow's mission to help our clients to do just that.

redbow
consulting group

Redbow Consulting Group
8 Avebury Close
Horsham
West Sussex
RH12 5JY
United Kingdom

+44 1403 289318
www.redbowconsulting.com

KEY CONTACTS
Jonathan Dancer
Managing Director
jonathan@redbowconsulting.com

Delivering transformational data analysis for infectious disease drug discovery

Artificial intelligence and the insights it can provide offer a route for infectious diseases to stay in the spotlight and draw interest from R&D investors worldwide. Liam Tremble at Poolbeg Pharma explores how this technology can be applied to data analysis

Pharmaceutical R&D is becoming increasingly expensive, and returns on investment (ROIs) have been falling over the last several decades, with static levels of new drug approvals since the 1980s. It is estimated to cost over $2 billion to develop a single product and over 90% of products which have a filed investigational new drug application (IND) go on to fail. ROI from the pharma sector has fallen from 10% in 2010 to just 2% in 2018 but has recently started to recover.[1-2]

No sector has been as severely impacted as the infectious disease market. Before COVID-19, almost two decades had passed without substantial improvement in treatment options for a range of viral illnesses, such as influenza.

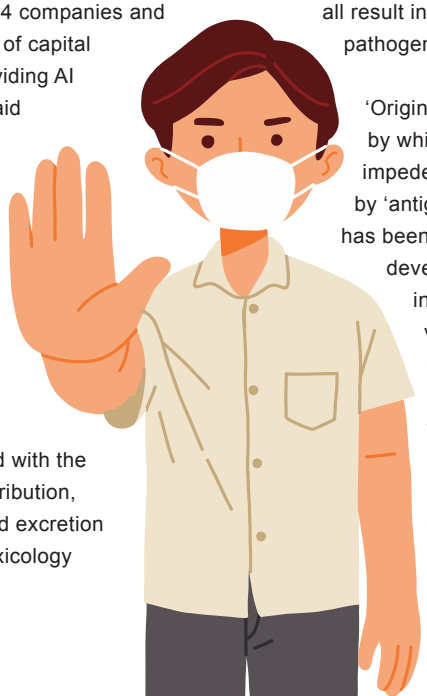
Part of the dilemma of diminished returns is thought to be related to the consistent improvement of each new drug. Subsequently, making incremental improvements in new drug candidates has become more difficult, especially when coupled with the probability that the majority of intuitive drugs, considered likely to succeed, have already been discovered. Now, more than ever, there is a need to look beyond conventional drug development approaches to discover the next generation of therapeutics.

In recent years, researchers have been battling against reduced returns by using artificial intelligence (AI) to help guide drug discovery and development within the pharma sector. AI is designed to deal with big datasets from a variety of sources and formats, making it ideally equipped to deal with modern cutting-edge analysis techniques. These range from single-cell transcriptomic sequencing and proteomic analysis, which produce Big Data, to the diverse data types that together describe a disease phenotype.

AI is a high-power computing technique, which uses iterative 'learning' algorithms to interpret, learn, and discover from underlying patterns in 'Big' Data. In addition to traditional Big Data, modern AI providers incorporate machine reading comprehension (MRC) to allow algorithms to learn from unstructured text-based publications, creating formidable 'intelligent' machines, which are up to date with the latest literature.

The US is the undoubted leader in pharma AI, with over 184 companies and over $12 billion of capital invested in providing AI based tools to aid drug discovery, development, and medical treatment. *In silico* AI tools exist to identify disease specific targets, interventions against those targets, coupled with the absorption, distribution, metabolism, and excretion (ADME) and toxicology profiles of them, can determine their probability of success in the clinic. Pharma companies are using AI to expand their pipelines and to prioritise existing assets, with many major pharma companies refraining from commercial decisions on their pipelines without the input of AI-based predictive outcomes.

The role of AI in infectious disease is particularly pertinent due to the diverse range of factors that can impact the trajectory of infection and immunity. Although conserved responses have been identified in infectious disease, such as the decoupled interferon responses, which distinguish severe and mild viral infections, a multitude of factors such as age, human leukocyte antigen (HLA) type, immunological history, immunological status, volume of pathogen initially experienced, and host comorbidities, can all result in varied responses to a single pathogen.



'Original antigenic sin,' the process by which immunological history can impede antigen specific responses by 'antigen trapping' early in infection, has been identified by vaccine developers as a major obstacle in the design of universal vaccines. Particularly in elderly or immunocompromised individuals, it can be difficult to stimulate a durable vaccine response in a consistent manner due to the multitude of underlying factors. It is likely that elements of

personalisation will be needed to drive the effector mechanisms for lasting immunity.

The non-biased ability of AI to integrate multi-omic data makes it an ideal platform to deal with these wide-ranging factors that affect and predict immunity, host response, and recovery in the face of a plethora of infectious diseases. It also makes it the ideal partner in helping to identify the next generation of pharmaceutical products to prevent and treat disease.

One of the significant challenges for AI-based discovery is the quality of the data input and the presence of high-powered comprehensive datasets that can be used to validate its findings. Commercial grade platforms often overcome this issue by the integration of gargantuan datasets taken from publicly available information. However, these datasets are often incomplete due to limited publishing of original datasets and data protection legislation, which regulate clinical data.

Despite the large-scale support for AI-driven improvement of healthcare delivery, progressive improvements in AI have largely outpaced the development of the regulatory framework surrounding it. Data protection legislation, designed over the past decade to counter the exploitation of personal data by corporate interests, often finds itself at odds with the principles of AI-based learning.

AI is beginning to revolutionise the delivery of healthcare. Its ability to integrate and infer from diverse data types, (such as imaging data, clinical notes, demographics, and lab results in real time to produce tools for diagnoses and prognosis), can aid clinical decision-making. The ethical implications of rapidly advancing AI-based contributions to medical treatments have stirred global bodies to develop guidelines and principles for the integration of AI in medical settings.

Integration of AI in the drug discovery and drug development process is impacted less by these ethical concerns. However, issues still exist, such as the propagation of ethnic bias in medical treatments due to underlying bias in datasets, which may manifest further differences in healthcare outcomes across underserved minorities and developing nations.

Global initiatives, such as the Human Vaccines Project, have been engaged in sustained efforts to characterise the immune system in exquisite detail, with the underlying belief that integration of diverse high depth datasets will produce prognostic and interventional products to improve health outcomes. Single-cell next-generation sequencing, full length protein microarrays, phage display, and cell phenotyping arrays produce Big Data, which can be layered onto host biology.

The power of AI will advance exponentially over the coming years. However, in order to accelerate insights, there is the opportunity to progress beyond the gradual accumulation of data snippets and to input bespoke high depth data from infectious disease. High depth analysis of clinical data is cost prohibitive, particularly when the insights of AI may be only the first step in the development of a new product.

In light of the COVID-19 pandemic, it is vital that national bodies recognise the potential of AI to prepare for and respond to future challenges. There has been a unique opportunity to provide bespoke data for AI-driven infectious disease research through human challenge trials, in which volunteers are inoculated with an infectious agent in carefully controlled conditions and monitored through health, sickness, and recovery. During this time, daily biological samples can be obtained, revealing local and systemic responses to the challenge on a real-time basis, which can then be coupled to an intervention.

Academic institutions such as Imperial College London and Oxford University have championed the technique in recent years, including challenge of healthy volunteers with SARS-CoV-2. A beneficial impact of the high depth data analysis of modern immunological techniques has been the reduction in the number of subjects required for powered and meaningful interpretations.

Recent evidence in COVID-19 has shown that germline mutations and HLA types can profoundly influence susceptibility to severe disease. The data highlight the importance of matched genetic, transcriptome, and immunology datasets for training AI algorithms. In the absence of matched HLA data, immunological trends can be misattributed to other mechanisms or signals that may not be detectable behind the background variability that these factors create. The noise of biology will always be present, but it is the responsibility of those using AI for research to produce clean data, which minimise confounding factors and facilitate the next generation of insights.

As a scientific community, we have great confidence in the ability of AI to lead the next generation of interventions in the war on infectious disease. However, while AI will not replace the requirement for basic research, our ability to integrate AI cutting-edge analyses into clinical datasets will speed up the development of novel interventions which can improve patient outcomes.

The potential for using AI analysis of biological data to quickly and cost effectively identify many more interesting and efficacious drug candidates for infectious diseases with serious unmet needs, is both very real and very exciting.

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2. *Visit: www.thepharmaletter.com/article/r-d-return-on-pharma-investment-picks-up-for-the-first-time-in-six-years-despite-pandemic*

Liam Tremble PhD, Project Manager, R&D Operations at **Poolbeg Pharma plc** (London AIM: POLB) – a clinical stage infectious disease pharmaceutical company, which aims to develop multiple products faster and more cost effectively than the conventional biotech model. Liam, an immunologist, has worked at hVIVO, part of Open Orphan PLC, the provider of human challenge trials with a focus on strategic engagement to enhance recruitment for clinical trials. Prior to that, he was a researcher at the Cork Cancer Centre, Republic of Ireland. He completed his doctoral degree at University College Cork on the role of tumour associated macrophages in melanoma.

liam.tremble@poolbegpharma.com

Q&A

PHARMAFILE SPEAKS TO

The Brain Charity

Supporting rare neurological disease patients during COVID-19

The pandemic presented numerous challenges for those living with rare neurological diseases. Nanette Mellor, CEO of The Brain Charity, delves into the numerous ways in which the charity is continuing to provide assistance to patients, in areas extending from mental health to logistical support

Pharmafile: **What are some of the ways in which The Brain Charity supports those with rare diseases?**

Nanette Mellor: If you Google your very rare neurological disease, most likely The Brain Charity will be the listing that appears first.

One of the key things we do for clients is find them more information about their condition and what a diagnosis means for their life – from research papers, health documents, other charities etc. If your condition is very rare, there may not be a lot of information out there, so this might be difficult to find for yourself.

We also put people with rare diseases in touch with others with the same condition through social activities and support groups. Being around others in a similar situation means clients can offer each other practical advice on how they've coped with different challenges. Each understand what the other is going through, and can offer a non-judgemental space for sharing.

What are some of the biggest challenges faced by patients with rare neurological diseases?

While the diseases themselves are very different, we find there are several overarching themes in terms of the challenges people tend to face.

> **If their disability is invisible, they can also feel stigma attached to that in terms of how they are treated, particularly when applying for welfare benefits**

The first problem is that it's very difficult for people to get a diagnosis, in some cases it takes years, and in that time frame, they may be given various misdiagnoses or even mistreatments. For this reason, The Brain Charity does offer expert legal advice for any clients who have struggled with misdiagnosis or medical negligence.

A lot of people struggle to get a diagnosis if their GP hasn't come across someone with that very rare condition before. This can be very difficult for them to join the dots. If their symptoms seem confusing, they can be mistaken for being psychosomatic.

Another challenge is actually getting information. If they have a rare condition, the likelihood is less research happening into the treatment of their condition as less people are affected. There can also be very little available factual information about causes, symptoms, how it will affect them, which leads to feelings of bewilderment. If their disability is invisible, they can also feel stigma attached to that in terms of how they are treated, particularly when applying for welfare benefits.

It can also be difficult for people with rare neurological diseases to find someone to talk to, who understands completely what they are going through. They may never meet someone with the same condition as them, face to face.

How was The Brain Charity impacted by the pandemic? What changes did this period bring about?

2020 was the most challenging year in The Brain Charity's history for our clients. Throughout the pandemic, people with neurological conditions have remained some of the most vulnerable in our society, and in desperate need of support.

The Brain Charity finished 2020 having seen a rise of more than 50% in demand for our services compared to 2019. Long COVID-19, the rise in mental health problems due to the social isolation caused by the pandemic, and mass unemployment, means this is likely to increase further.

At the beginning of lockdown, the charity reached out to its most vulnerable service users to ask how they felt, how they were coping, and if they needed any extra assistance. Many people were shielding and unable to leave the house, and were struggling to access online food deliveries, which led to further anxiety. Others were worried about running out of money.

When our centre in Liverpool closed last March, we acted quickly to divert our resources to offer a new food delivery service. We then introduced a broader community service to help people shielding at home. This involved making trips to the shops, picking up prescriptions, keeping gas meters topped up, and even helping with vet visits for pets. Between March and August 2020, a team of 21 staff and volunteers delivered 1,104 food packs across Merseyside, helping an average of 58 people per week.

The Brain Charity also launched a telephone befriending service to combat loneliness, to ensure anyone left socially isolated by coronavirus could hear a friendly voice at the end of the phone, or via video call, each week. This is still running, and currently makes more than 50 hour-long calls per week.

The number of people coming to our counselling service at the point of suicidal thoughts has also risen by more than half over the last 12 months. We extended provision for our free counselling appointments so more people could be seen, giving clients the option to have a video or telephone appointment if they would prefer, and ensuring our building was COVID-19 safe for face-to-face appointments, too.

For many of our service users, The Brain Charity's regular social events and activities were the highlight of their week, the chance to meet in a safe, welcoming space, free from judgement and discrimination. Moving these online allowed us to open classes and workshops which may previously have only happened in our centre to people as far afield as Newcastle, Scotland, and Cornwall.

Our two innovative community-based projects also pivoted to online video-based alternatives: 'Music Makes Us!' provides speech and language therapy via song, and physiotherapy via dance to people living with dementia, and The Brain Changer Arts Project provides physiotherapy via dance, and occupational therapy via arts and crafts to children with neurological conditions. This meant more people from across the UK were able to participate. Throughout the pandemic, all our practical help services offering advocacy, info, advice, and welfare benefits support, continued running remotely.

Nanette Mellor, CEO of **The Brain Charity** has dedicated her career to working for disabled people for over twenty years, and has experience in the field spanning the public, private, and third sector. Her previous role included national responsibility for the design and implementation of Mencap's grassroots campaigning activity. In 2014, Nanette took up her first CEO role with The Brain Charity. She has recently been voted Social Leader of the Year at the English Woman of the Year Awards (North) 2018.

www.thebraincharity.org.uk

Treatable, untreatable, undetermined: Overcoming rare disease

Manjinder Bains, Country Medical Director UK & Ireland at Ipsen, illuminates the underestimated impacts of rare and ultra-rare conditions

Pharmafile: **What are some of the obstacles many patients face in the diagnosis of rare diseases?**

Manjinder Bains: Many rare diseases will never be encountered by a clinician in their whole career. Because of this, awareness and understanding of specific rare diseases is generally low amongst the majority of healthcare professionals (HCPs). With as many as 7,000 known rare diseases, diverse and often-complex in nature, reaching a correct diagnosis can be a long and arduous journey. It is not uncommon for a diagnosis to take over five years, with some patients experiencing delays significantly longer.

Within this period of uncertainty, patients often face a myriad physical, practical, and mental health challenges. While clinicians will do their best to understand and manage the unexplained symptoms their patient is experiencing, a reality is that the person in question may not be receiving the treatment they need. The consequences of this can range from the worsening of their disease and symptoms to an increased likelihood of irreversible damage or even shorter life expectancy.

When an HCP does not see an improvement and the diagnosis remains elusive, the common solution is to seek greater expertise and refer patients elsewhere. In fact, in the UK, patients with a rare disease see, on average, eight clinicians, including four specialists, before a diagnosis. The patient and their family will have to deal with numerous appointments, tests, and misdiagnoses, which can severely impact the patient's life – from missing school or time off work to being unable to cope with much else beyond their condition – often with no end point in sight.

We believe in the importance of supporting HCPs, and most importantly patients, to help overcome obstacles to rare disease diagnosis.

For the patient at the centre of these diagnostic pathways, the journey begins at symptom onset where their first port of call is most often their GP. While it is not feasible to expect a clinician to be familiar with even a fraction of the possible rare diseases, novel technological approaches can support GPs by flagging risk factors and symptom combinations that might be indicative of ultra-rare diseases. By partnering with health technology companies providing these services, Ipsen hopes to improve intervention at the earliest possible point in the diagnostic pathway.

Moving forward, the industry must work closely with the NHS, patient advocacy groups (PAGs), and patients to better define diagnostic pathways, leveraging research, real world data, and patient experience to optimise these processes.

The cause of many rare diseases is often unknown or not fully understood, as is the case for neuroendocrine tumours (NETs). What changes would research into identifying causes be able to bring about?

While the specific causes of many rare diseases remain undetermined, a significant number are known to result from genetic abnormalities. Over the past 20 years, huge advances in genomics and health technology have opened the door to new research possibilities, helping us to better understand risk factors associated with certain rare diseases and how their early presentation differs from patient to patient. We now need to bridge the gap between research and clinics, and support HCPs in spotting early manifestations of these conditions.

As a step towards this, Ipsen is working with health technology company Mendelian to equip clinicians with a tool to assist in the early detection of NETs. Mendelian's MendelScan tool can flag patients that are suspected of having a rare disease, including suggesting investigation into NETs. The scanning algorithm does this by searching electronic health records for indicators of rare diseases and associated clinical patterns.

Genetic testing is also important, and not only plays a role in understanding the causes of rare disease, but can also be utilised in diagnostics. Last September, the UK Government set out a 10-year strategy to create the most advanced genomic healthcare system in the world, building on the success of the 100,000 Genome Project and the ongoing UK Biobank, amongst other genomic research programmes. As part of their plan, the government will aim to roll-out whole genome sequencing to patients with a suspected rare disease, which could be instrumental in achieving earlier diagnosis of these conditions.

What are the next steps to improve the standard of care given to patients with rare diseases, and what are some of the most significant hurdles on the way to meeting their needs?

Historically, small patient populations have presented cross-sectional challenges when it comes to rare disease, from difficulties in recruiting for clinical trials, to a lack of investment and limited patient voice. There have also been significant challenges in showing the value of therapies using conventional models of cost-effectiveness. However, changes to the way in which new drugs are tested and evaluated means the pharmaceutical industry has been able to better utilise real-world data and patient insight. This has helped to remove some of the barriers to bringing new therapies to market, and allowed us to generate important debate about the provision of care for those impacted by rare conditions.

While rare individually, collectively, rare diseases affect 1 in 17 people, meaning there is a massive community of people that could benefit from improved standard of care. This can often be achieved in a realistic and practical way: creating more specialist centres, increasing homecare provision, and providing more support for caregivers.

As with all disease areas, patient organisations play a crucial role in providing information and support to patients and their surrounding networks. At Ipsen, whenever possible, we partner with these dedicated groups to help raise vital awareness, and provide information and support to rare disease communities.

The effects of suffering a rare disease are far-reaching, extending beyond initial symptoms of a condition. What are some of the consequences of rare diseases often neglected in discussions of their impact?

While there are the obvious physical impacts of living with either a diagnosed or undiagnosed rare disease, there is also a huge psychological toll on the patient and their support network. Dealing with a disease diagnosis can be a confusing and daunting time, and while this is true for many conditions, emotions can be heightened with rare diseases. Unfortunately, due to the limited awareness of these conditions, there are often fewer resources and support services available to both the patient and their loved ones. Sadly, this has been exacerbated by COVID-19, which made people less able to connect with those around them and access external support.

Ultimately, the most important factor to consider is the quality of life attained by the patient living with the rare disease. Too often, the focus is only on whether treatment is reducing symptoms and prolonging life. However, the impact of treatment on the overall quality of life (QoL), and the ability for a patient to participate in work, socialising, and other aspects of their lives, should be considered as equally, if not more, important.

The changes being implemented by National Institute of Health and Care Excellence (NICE) to their health technology appraisals, following their recent methods review, are a positive step towards better factoring in QoL, when considering the value proposition of novel or innovative therapeutics.

How might certain rare diseases help us better understand medicine as a whole?

Rare diseases as a whole encompass a broad spectrum of therapy areas and affect a multitude of bodily systems, so there are often learnings from our research into rare diseases that can be applied more generally, providing insight on disease drivers, genetic predispositions, disease pathology and inheritance patterns. In particular, genomics is a fantastic tool for understanding disease and medicine, and we are now able to utilise the capabilities of technology to store this data and build an increasingly clearer picture of health and disease. While health technology software is currently being utilised to scan for rare diseases, as this bank of genomic data, along with stored clinical patterns and symptom presentations expands, it may become possible for these approaches to aid clinicians in the earlier diagnosis of more common diseases.

2021 marks the 15th Anniversary of the announcement of discovering the mutation ALK2/ACVR1 gene, which causes fibrodysplasia ossificans progressiva (FOP). Since 2006, what has changed in the management of the disease as a result of this?

The most important change is that there has simply been a much greater focus in the last 15 years on FOP as a disease. Prior to this, awareness and understanding of FOP was relatively low. This change is, of course, positive in terms of the impact on those patients living with FOP – ultimately more understanding of the disease and burden of illness leads to greater drive to investigate and develop treatments to improve outcomes.

The other key change that has happened is that the importance of early diagnosis has been brought to the forefront of FOP management. The fact that we now have a genetic marker to support that all-important diagnosis is crucial for many patients and their families.

There is currently no definitive treatment for FOP. Is this often the case with rare diseases, and what is needed to address it?

As with other therapy areas (and especially in the case of rare diseases) patient-centricity needs to be kept front of mind. It is understandable that rare disease patients may sometimes feel 'forgotten about' or 'left behind'. A feeling of being alone is understandable when a patient may have never met anyone else with their condition.

There is also merit in mentioning the importance of creating a focus on rare diseases for policy makers. Any approval and reimbursement processes need to be agile and adaptable as, simply put, it is a challenge to demonstrate the value of rare disease therapies using conventional models of cost-effectiveness. I am pleased to say that these processes are adapting and making better use of real-world evidence and patient insights to demonstrate value.

The most important takeaway is the plight of truly understanding rare diseases, and the importance of improving outcomes for those that live with them – be that treatments, homecare, support with mental health, or anything else that affects their overall QoL.

Dr Manjinder Bains, is Medical Director at **Ipsen** for UK & Ireland.

Passionate for science, innovation, and making a difference. Before devoting his fulltime work to Ipsen, Manjinder has over 12 years pharmaceutical experience in both the UK and Switzerland, across four organisations in a range of roles within medical and commercial functions. Prior to joining the pharmaceutical industry, Manjinder spent almost nine years in the NHS as a trainee surgeon across a range of geographies.

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Rare disease and orphan medicines – Will government policy change the paradigm?

Angela McFarlane, Vice President, Strategic Planning, North Europe, IQVIA talks about orphan and ultra-orphan diseases, and the diagnostic odyssey which many are forced to undertake

There is nothing rare about rare diseases, and 3.5 million people in the UK will be impacted by one at some point in their lives. The diagnostic odyssey for patients in the UK is 4-7 years.[1,2]

Having received a diagnosis, what is unfortunately still rare are treatments for the condition – of the 7,000 rare diseases identified, only 400 have a licensed treatment.[3] However, obtaining a license is only the start of the challenge – approved medicines must navigate the daunting barriers of access and adoption to realise their promise for patients. Could the Innovative Medicines Fund (IMF) be that catalyst for improving access to innovative orphan medicines, just as the Cancer Drugs Fund (CDF) has been for cancer treatments?[4]

Before we explore that question, let's look at how issues are improving for people with rare disease, namely the global leadership the UK is showing, in respect of accelerating diagnosis of rare disease.

In 2015, the National Disease Registration Service (NDRS) was set up to develop and run a comprehensive population-based registration service, collecting and quality-assuring data on congenital anomalies and rare diseases across the whole population in England.[5] Since 2015, it has realised national coverage of over 1,400 congenital anomaly or rare disease datasets out of over 6,000 collected.

In 2013, the UK Government launched the 100,000 Genomes Project to investigate whether whole genome sequencing (which involves reading through 3 billion pairs of letters in the human genome) could help improve diagnosis and accelerate the discovery of precision medicines.[6] Five years later, the UK became the first national health system in the world to offer WGS to people with undiagnosed rare diseases and cancer as part of routine care. The 100,000 Genomes Project has transformed the diagnosis of the 8-in-10 rare diseases with genetic causes, and the creation of the NHS's Genomic Medicines Service – as well as the 50-fold goal of achieving five million sequences, offering further new hope to people with a rare disease.[7]

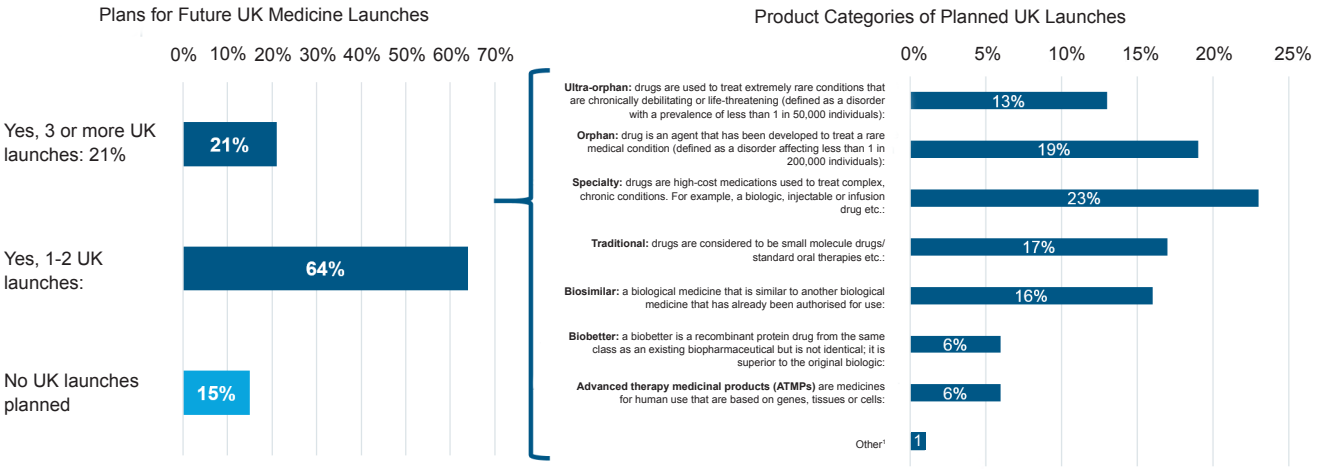
Earlier this year, Genomics England announced the Newborn Genomes Programme (NGP) in which up to 200,000 babies' genomes will be sequenced and analysed for a set of actionable genetic conditions which may affect their health in early years.[8] The programme aims to ensure timely diagnosis, access to treatment pathways, and enable better outcomes and quality of life for babies and their families. The NGP will co-design and run an ethics-approved research pilot embedded in the NHS to explore how, and whether, to offer whole genome sequencing (WGS) to all newborns, to accelerate diagnosis and access to treatments for rare genetic conditions.

On the 11th November 2021, a study published in *The New England Journal of Medicine,* led by Professor Mark Caulfield and Professor Damian Smedley, analysed the diagnostic and clinical impact of genetic sequencing within the NHS.[9] Analysing the genomes of 4,660 people from 2,183 families led to a new diagnosis in 25% of patients. Many of these patients have spent years enduring the diagnostic odyssey. One such patient in the study is a 10-year-old girl who endured multiple hospital visits during her seven-year journey to diagnosis at an estimated cost to the NHS of £375,000. Once the WGS had identified her underlying problem, she went on to have a bone marrow transplant which cured her disease, costing £70,000.

As a result of Caulfield and Smedley's work, 25% patients received more focussed care, such as family screening and therapies to help manage the condition. For patients with conditions such as intellectual disability, vision, and hearing disorders, the diagnostic yield was even higher at 40-55%. This will pave the way for accelerating the discovery of precision medicines, and attract even more clinical research to the UK for paediatric and rare disease.

Findings indicate a healthy launch pipeline for UK patients, with strong focus on specialty medicines and rare conditions

A large proportion (85%) of respondents indicate that their organisations plan to launch at least one new medicine (including new indications) in the UK over the next three years



Question: At present, is your organisation planning on launching new medicines (including new indications) in the UK during the next three years, and if so, how many?

Base: All respondents *(n=152)*.

Question: Which of the following categories apply to these planned UK product launches? (Please select all that apply)

Base: All responses from respondents who indicate plans to launch new medicines in the UK *(n=353)*; multiple responses per respondent allowed.

[1]**Other include:** Added Value Formulations; Specifically offering traditional that offer disruptive price points for prevalent diseases.

Figure 1: Over one third of planned UK launches in the next three years will be dedicated to orphan or ultra-orphan medicines[10]

The orphan medicines discovery landscape is transforming

In August 2021, IQVIA conducted primary market research amongst global C-Suite pharma and biotech leaders regarding the overall attractiveness of the UK for conducting clinical trials and launching new medicines, following the UK's exit from the EU Bloc.[10] Over 200 global industry leaders participated in the survey, and the results were a vote of confidence in the UK. Respondents called out the UK's performance in respect of research and discovery of COVID-19 vaccines and treatments, and the impactful new UK Government Life Sciences Policies, from the MHRA, NICE and the Office for Life Sciences. 79% confirmed that the UK will remain a priority launch country for their company, with 74% stating that the UK would be a Tier 1 early launch country over the next three years.

The promise for people with rare diseases was even more exciting, with over one-third of the new medicines launches planned in the UK being for orphan or ultra-orphan medicines.

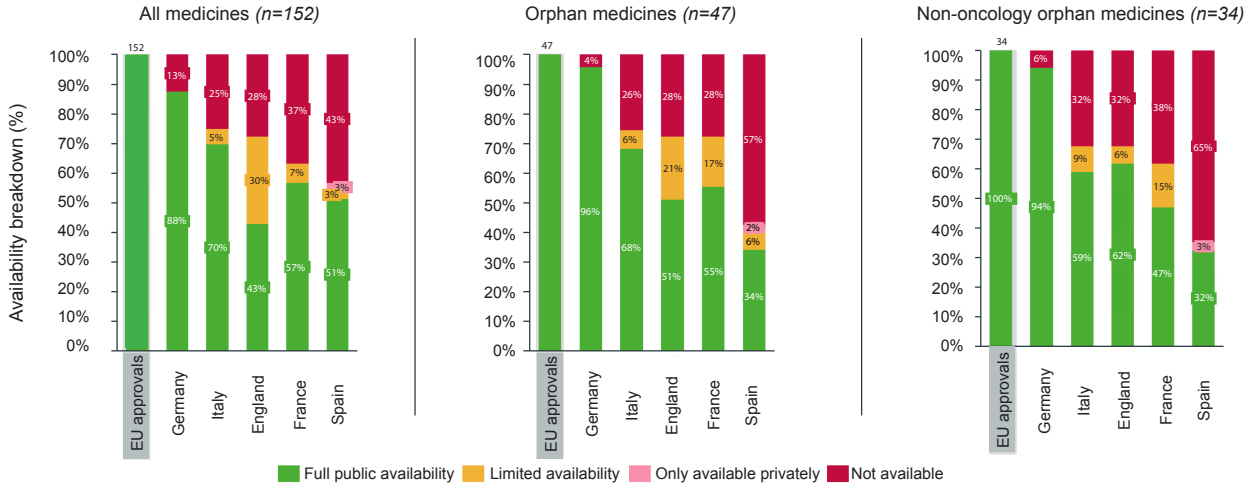
Changes to the approval landscape and the advent of the IMF

Headlines for breakthrough rare disease medicines, such as the triple therapy for the cystic fibrosis gene therapy, Zolgensma, which NICE ruled had an 'exceptional impact' for babies with severe spinal muscular atrophy (SMA), majored on deals and list price.[11,12] Little was reported about the time the negotiations took, and the number of other promising orphan medicines that didn't make it over the line with either NICE or NHS England, due to the unique challenges orphan medicines face in research and data generation. Consequently, over the last five years, patients living with rare diseases in the UK and their carers have been dissatisfied with the medicines approval processes for rare disease treatments, according to a survey of this community by the Genetic Alliance and Alexion.[13] Typically, patients believe the UK processes are unfair on those living with a rare disease, and the system is both too slow, and not resourced for rare diseases.

> **As a result of Caulfield and Smedley's work, 25% patients received more focused care, such as family screening and therapies to help manage the condition**

Rate of availability (%, 2016 – 2019)

The 'rate of availability' is the number of medicines available to patients in European countries (for most countries this is the point at which the product gains access to the reimbursement list*). This includes all medicines' status to provide a complete picture of the availability of the cohort of medicines studied.



Source: The Patient W.A.I.T. indicator 2020; *Please refer to the Patient W.A.I.T. indicator for country-specific definitions of availability and limited availability

Narrow eligibility requirements for the Highly Specialised Technology (HST) programme means that many treatments can struggle to secure approval from NICE for routine use on the NHS. In most cases, those that do secure approval often see their use restricted to certain subpopulations of their licence. The result is that patients in the top five European countries, such as Germany, Italy, and France, have better access to medicines than counterparts in England. Yet, England is ahead of most European countries, including Scotland, and restrictions to medicines might be valid given the evidence available.[14]

However, steps are being taken by Government and the NHS to reduce these inequalities, through initiatives such as the review of NICE's methods and processes, the implementation of the Rare Disease Framework, and development of the Innovative Licensing and Access Pathway (ILAP). Former Minister for Innovation, Baroness Nicola Blackwood – who herself suffers from a rare disease and endured her own diagnostic odyssey – set up the Accelerated Access Collaborative and launched the NICE methods review and the Commercial Framework, announcing the new £500m Innovative Medicines Fund as part of the 2019 Conservative manifesto.

The IMF will seek to expand on the existing Cancer Drugs Fund (CDF) for the purpose of improving access to rare disease treatments, among others. This is an important step. No single initiative can solve the access to treatment challenges facing patients and their carers in England, but the IMF can address the fundamental issue of data uncertainty for rare disease treatments at the time of their first assessment by NICE.

The IMF could be a catalyst for improving access to orphan medicines. However, it is important to note that it should not be seen as a bypass for improvements to these medicines being approved for routine commissioning. IMF should ensure that system challenges, such as biomarker testing at the seven regional Genomic Laboratory hubs, do not further delay patients with life threatening diseases with access at a local level to these nationally approved innovations.

In March 2021, Alexion and AstraZeneca rare disease commissioned IQVIA to work with the rare disease community and thought leaders in the UK medicines access policy, on the development of a white paper. This was launched in September 2021 – *The Innovative Medicines fund – a catalyst for access to rare disease treatments.*[15]

The paper is designed to:

- Support the rare disease community response to the public engagement exercise on the IMF, to be led by NHS England during 2021

No single initiative can solve the access to treatment challenges facing patients and their carers in England, but the IMF can address the fundamental issue of data uncertainty for rare disease treatments

> **To drive access for patients, rare disease medicines must have the same opportunity for IMF-funded access as a medicine for any other disease**

- Support the wider efforts of the rare disease community to improve outcomes for those with rare diseases and their families
- Shape future policy for the IMF, and provide recommendations for NHS England and NICE to optimise design and implementation
- Support all stakeholders who contributed to the much-anticipated consultation on the forthcoming IMF, by providing an evidence-based narrative from leaders in the rare community, and benchmark data from IQVIA.

The paper makes a series of recommendations for consideration by those finalising the IMF, to ensure that orphan medicines take their rightful place in it.

Recommendation 1: Ambition
To drive access for patients, rare disease medicines must have the same opportunity for IMF-funded access as a medicine for any other disease.

Recommendation 2: Entry and exit criteria
The IMF must have clear but flexible entry and exit criteria that can accommodate rare disease medicines, as well as other medicines.

Recommendation 3: Funding
IMF funding should not be ringfenced by disease area or medicine type, and must not operate on a 'first-come, first-served' basis.

Recommendation 4:
The IMF should have a flexible budget linked to horizon scanning.

Recommendation 5:
Funding for the IMF should be tabled as part of negotiations on the 2024 Voluntary Scheme for Branded Medicines Pricing and Access (VPAS).

Recommendation 6: **Data collection**
The IMF should allow for bespoke data collection, taking a medicine-by-medicine approach to outcomes, data sources and the time required. The IMF must recognise the complexity and difficulty of evidence generation in rare diseases.

Recommendation 7: **Governance**
An external IMF multi-stakeholder group should be formed, reporting annually on IMF performance using Key Performance Indicators (KPIs) broken down by disease and orphan status.

Alignment with other initiatives

Recommendation 8:
The IMF must be aligned with the evolving access landscape, including initiatives such as the ILAP, NICE Methods and Processes Review and UK Rare Diseases Framework.

UK collaboration

Recommendation 9:

The four UK nations should hold discussions to leverage lessons from the IMF – and their own funds – and explore the scope to increase the value of the evidence generated. The four UK nations should also work together to ensure access to innovative medicines, including rare disease medicines, is equitable across the UK.

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Angela McFarlane, Vice President, Strategic Planning Northern Europe, **IQVIA**, works with the UK Government, NHS, Pharmaceutical and Biotech Industry and Patient Organisations on pioneering collaborations that will improve NHS patient access to clinical trials, RWE studies and innovative medicines. She founded the Clinical Research Coalition to embed learnings from the pandemic, the output of which became Lord Bethell's Clinical Trial Transformation programme.

In 2018, she was nominated by Pharmaceutical Marketing Europe as one of the 30 most influential women in UK Healthcare and in September 2019 appointed by the UK's CSO as an Ambassador for Women in Science and Engineering.

Every number has a face: Are you valuing the patient voice?

Considering the needs of patients during drug development is a crucial step to guaranteeing the most inclusive treatments possible for them. Many pharma companies lose sight of the patient experience when developing treatments so, how can they improve?

Imagine having to choose which risk you are willing to take to slow the progression of your disease. Could you give up the freedom to have children in opposition to when you and your partner want? Could you risk a potentially fatal rare brain infection as a potential cost of care? Could you risk kidney or thyroid disease just for the sake of a treatment?

These are the life-changing decisions that people living with multiple sclerosis (MS) are forced to make when choosing to begin the most aggressive form of treatment. Like many living with a rare condition, these patients rely on a drug to improve their health and quality of life. MS patients who do require the most aggressive treatment place their hopes in ocrelizumab, natalizumab, and alemtuzumab.

A patient's drug regimen is the most promising gateway back to a normal life. Patients with aggressive MS often find they must sacrifice their body and dreams to avoid disability.

My question is: why are MS patients forced to make these life-altering decisions when most are diagnosed in their 20s, 30s, and 40s? Those living with MS may have been consulted at the time, but viewed the substantial risk as one worth taking until a better treatment was developed. If so, was their voice heard throughout the drug development process when creating the new drugs for the future? I wish I had the answers.

Involving patients from the beginning of drug development may prevent treatments, such as for MS from being developed without consideration of the patients' needs and wants. Patients and patient advocacy groups are the true experts in their condition; these individuals understand the patient experience and can shed light on the reality of living with MS. Not involving patients in the R&D process devalues their expertise and hinders the effectiveness of a treatment. To develop, manufacture, and sell a treatment to a population successfully, the voice of the patient is critical.

Understanding a disease goes beyond the science. While pharmaceutical companies must ensure that a drug is both safe and effective for patients, they need to understand how a patient population will perceive the treatment being offered. By hosting focus groups with patients and patient group leaders who are affected by the condition, pharma companies can learn exactly what the community wants, needs and expects from a treatment. That information can be used to ensure that a product or drug is delivered in a way that best suits the targeted patient population. This point rings true, whether you are developing the first treatment for a rare disease or creating a new treatment for a condition that already has a current therapeutic on the market.

'Social listening' is one way to gain insight into a particular patient experience. Joining an open patient support group on Facebook to see which conversations are being had by those living with the condition can prove enlightening. You'll uncover truths that you may have never contemplated before. You'll learn the good, the bad, and the ugly in an authentic, unfiltered, and raw way. Whether you want to learn more about what it's like to live with that condition, or which treatments are currently available (if any) for it, these communities provide the insight you need to develop a drug that addresses their unmet needs.

To illustrate this point, a senior executive involved in the development of a treatment for progressive MS told me that her company initially wanted to use bottles with safety caps. She insisted that she needed to first sit down with a group of progressive MS patients to test the prototype bottles

> **It is easy to get bogged down in the science of a drug and forget about the patient experience of those who are relying on your research. Rare disease patient populations may be small, but each number is a human being**

before proceeding with the design. It was during this focus group that she realised that progressive MS patients didn't have the manual dexterity to open the bottles. Had she not insisted on speaking with those who would be taking the treatment, her company never would have been aware of this significant insight.

I encourage you to explore a rare disease patient group's website for your specific condition of interest, as the insights from patient forums can be invaluable. You will find an array of first-hand information about a condition's cause, symptoms, and quality of life. The questions, answers, concerns, and lived experiences are all there. This is particularly important for those who are developing treatments in the rare disease space.

Jason Colquitt, CEO of Across Healthcare, emphasises this critical need when he asks, "How can we appropriately help care for rare disease patients without giving them an appropriate voice? Co-production, a non-healthcare concept first described in the 1970s, has proven that those who are affected by a service are the best ones to help design it. Input from the patient should be a top priority when delivering care and facilitating research in the rare disease space."

I am delighted that rare diseases are beginning to gather more interest from the pharma industry. Through drug repurposing and adopting a co-production, collaborative approach, the pharma industry is giving hope to rare patients who were previously overlooked due to low patient population numbers and a high cost of drug development. The pharma industry alongside the healthcare and academia sectors are now investing in rare research, and are placing a higher value on the patient voice. These sectors are actively collaborating with rare disease patients and support groups to deliver treatments that are better targeted to the patient populations they serve.

Rare disease patient groups have more than earned their seat at the table. Their efforts have proven the value of putting patients at the heart of rare disease research and care. Despite having limited time, funding, and resources, rare disease patient groups have successfully organised patient consultations at NICE, supported the delivery of highly specialised services for ultra-rare diseases, and launched their own rare disease patient registry to aid in research. Rare disease support groups have shown why it is crucial for the pharma industry to value the patient voice. They have lobbied tirelessly for patients and their loved ones to gain access to the treatments needed to improve their lives.

I agree with Donovan Quill, President and CEO of Optime Care, when he says, 'Patient-first' has become a buzzword for many specialty pharmacy organisations that merely focus on profits. A true patient-first approach can enable pharma companies, pharmacists, physicians and other members of the care team to better address compliance and adherence to treatment, improve outcomes and enhance quality of life for patients. From day one, patient-first experts provide ongoing support and are available to answer questions. For many with rare diseases, and especially for those starting a new medication, this level of support is comforting and effective."

Patient-first cannot become a buzzword, nor can it be a box to check half-heartedly. Rare disease patients and their support groups are watching. They will hold you accountable and demand equitable, inclusive treatment that meets their needs. The pharma industry, rare disease patient groups and rare patients all have the same goal: to create tailored treatments that are safe, effective, and designed with patients' needs in mind.

My challenge to the pharma industry is to never lose sight of the patient experience when developing rare disease treatments. It is easy to get bogged down in the science of a drug and forget about the patient experience of those who are relying on your research. Rare disease patient populations may be small, but each number is a human being who has dreams, hopes and fears. Rare diseases are cruel, unfair and overwhelming. Living with one can challenge, devastate and isolate. The treatments you create are what keep the fire and hope alive for rare patients and their families.

If you only remember one message from this article, I would like it to be this:

See the people, not the profits. Every number has a face. Every number has those who love them. Every number has a life to live. Every number depends on you. Listen to those you serve. Listen to the patient voice.

Blayne Baker is the Marketing and Engagement Manager at **Findacure**, a UK rare disease charity that is building a united rare disease community driven by patient groups. Findacure envisions a world in which all rare diseases have treatments made together with patients, for patients. If you'd like to learn more about Findacure's work and how you can partner with them, please email Blayne:

blayne@findacure.org.uk

Not so rare diseases: The cumulative burden of underdiagnosis

Dr Anne Pariser from the NCATS illuminates the impact of under-research, underfunding and underrepresentation in the sphere of rare diseases, and looks ahead at the future of therapies and innovations for rare disease care

Pharmafile: **What are the significant changes we've seen in drug development for rare diseases in the past 10 years?**

Dr Anne Pariser: The overwhelming majority of rare diseases are single gene disorders – or monogenic disorders – where there's a mutation in just one gene and sometimes as little as one base pair within the gene. If you can find the mutation in the gene, and then work backwards to find out what that gene does, what it transcribes, that gives us a target (to work towards). If we have a target to go after, we can design drugs, or genetic or other advanced therapeutics with considerable precision to go right after whatever that problem is. The vast majority of modern drug development is using this targeting strategy, so in addition to changing how we approach drug development, it also opens up the possibility of personalised medicine, and we're starting to see some examples of this.[1]

What role does genetic research play in advancing the standard of treatment available for rare disease patients?

A lot of rare disease patients go through what we call the diagnostic odyssey; it often takes years to get an appropriate diagnosis. Now it's a lot easier and less expensive to do genomic analysis.

In England, for example, with the 100,000 Genomes Project, they're trying to move more rapidly towards characterising young children and sick babies in the NICU to try to make these diagnoses earlier. Once you know what's wrong, it opens the possibility of trying to develop targeted therapies that could be both highly efficacious, but also improve the safety of the drugs, because now you're only treating a selected subset of patients who are likely to respond.

Previously, you have outlined the 'large and growing medical footprint of rare diseases in society'. What are the effects of this footprint, and how has the footprint changed over the past five years?

It is hard to find rare disease patients and it can be very hard to diagnose patients. We know there are a lot of people out there who aren't diagnosed. This is probably an underestimation, but here in the US we estimate about 25 to 30 million patients have a rare disease. That's about one in 10 people, but it may actually be higher than that because there's so many people that haven't been diagnosed, and that percentage should be similar pretty much anywhere you would look around the world. These estimates are derived from some genomic studies based on what we know about diseases. We just published a paper on a project called 'The Ideas Initiative', where we were trying to do a pilot to estimate the cost burden of rare diseases, with cost being a surrogate for illness. People who are high users of a medical system tend to have serious illnesses. That's not a huge surprise, but you can quantify costs, and it's a lot more difficult to quantify pain and suffering. It is very difficult to even find rare disease patients in medical records or health system databases. The majority of rare diseases – probably about 75% – don't have a specific medical record code. About 50% don't even have a general code, so they're often lumped into these very high level terms like 'congenital anomaly unspecified', 'seizure disorder', or 'unspecified motor delay'. About one in ten people have rare diseases illnesses, and that's a large public health problem which hasn't really been identified. It also hasn't been prioritised, and this leads to all kinds of downstream effects: difficulty getting appropriate care, and difficulty even telling people what they have. And 95% of rare diseases don't have a treatment. Has this footprint changed over the past five years? Probably not, because these patients have always been there. I think our ability

to recognise this now and try to call attention to it has been increasing.

How does suffering from a rare disease multiply the existing difficulties in access to healthcare?

I can only really speak from the US perspective; we have a very fragmented healthcare system. You add a serious illness – for which there are a few disease experts or expert centres to care for these patients – to the existing problems with fragmented care, lack of coverage, out of pocket expenses. People who don't live in urban centres will need to be treated at a tertiary care centre or a super specialist, and there may only be a couple for each disease in the country, so they're often having to travel long distance to access care. We suspect that it may take longer to get a diagnosis if you're in a rural area, or in a place that does not have access to a medical expert. Think of any problem in a healthcare system, and then throw a rare disease on top of that, and it just makes it worse.

What changes are needed in the next two years to better meet the needs of patients with rare diseases, and which should be prioritised?

First and foremost, we must recognise rare diseases for the serious public health problem that they are. We have the rare diseases as a misnomer; collectively, they're not rare at all. We are trying to educate people that rare diseases are rather common – not the individual diseases, but the patients with rare diseases. They have serious illnesses and need better care, and are as entitled to research and medical care and efficacious therapies as anyone else. That's a real priority. We have the tools to improve this diagnostic odyssey, and we have the capability to do it now. What we're trying to do, through education, is move on that faster. A lot of these diseases are slow, chronic, and progressive. For example, a child may have a delay, maybe not quite meeting their milestones. The tendency is to check again in six months, check again in a year, and this really starts to add up to years and multiple referrals. What we're trying to do is try to escalate, particularly, our younger patients faster to get genetic testing, and preferably at an expert centre, or children's hospital that is used to handling these diseases. Most of our diseases don't have approved treatments, we know there are 1000s of diseases right now – we know the gene, and we know how to at least potentially treat that patient (a gene replacement, a gene silencing, or something that modulates the gene expression). We have the technology to do a lot of this for many more diseases; we now face more operational, logistical issues.

How can translational science help advance therapies for rare diseases?

This is predominantly now a translational problem. Once a person is appropriately diagnosed, it's then trying to string all the pieces together to use some of the things we already know how to do. That can mean trying to speed up gene therapy development, for example. It's the same for newer technologies, such as antisense oligonucleotides and gene editing. We estimate that it's going to take about 2,000 years to get everybody an effective therapy at the rate we are going now. Can we approach this by looking at many diseases at the same time?

We've started a programme at NCATS called Platform Vector Gene Therapy (PaVe-GT) where we're trying to develop four gene therapies at the same time.[2] The AAV gene therapy is a natural platform; you have the capsid of the virus, hollow out the virus DNA, and put in the human gene of interest. This hopefully will save time, money, and resources, and we can learn from one programme to another. Hopefully, that could set us up well enough that we wouldn't have to keep repeating a lot of these steps, but we could just move a lot faster. The NIH also just stood up what they're calling the Bespoke Gene Therapy Consortium, which is examining the commonalities around gene therapy development in the preclinical area and the clinical areas.[3] We can do these one at a time or share the knowledge from one programme to another. Gene editing and antisense oligonucleotides also have that potential as well. Oncology has done quite well in advancing therapeutics through platform approaches, and we're trying to borrow from their experience with platforms, as well as treating multiple diseases or multiple drugs within a single protocol. We think translational science is the answer to this, so we just need more of it.

'Rare disease' encompasses a spectrum of up to 10,000 different disorders. Are there some diseases which are more neglected than others?

Almost all of them are neglected to some degree. We only have therapies for about 5% of rare diseases, so there are 95% to go. Most of these diseases are sometimes referred to as the 'Ultra-rare Disorders'. That's not a real definition; it's rare or it's not, and in this country, it's less than 200,000 people with the disease in the US. In Europe, it's a prevalence estimate of five per 10,000 people with the disease.[4] For most rare diseases, they will be classified as rare in either region, because 90% of the rare diseases are what would fall into this ultra-rare category (approximately one in a million or so people with the disease or less). We have lots of diseases, where there's 100 or fewer patients, or a few thousand or fewer. The real distinction is it's very hard, even with available financial incentives, to make a business case to develop a drug for 50 people or so. Even when we know what's wrong, it is trying to harness resources to bring it through a drug development programme, so we really need better solutions.

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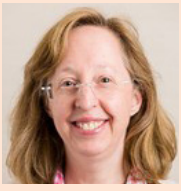

Dr Anne Pariser, MD is the Director of the Office of Rare Diseases Research (ORDR) at the **National Center for Advancing Translational Sciences (NCATS) NIH**. ORDR is dedicated to accelerating rare diseases research to benefit patients, through rare diseases programs such as the Rare Diseases Clinical Research Network, Genetic and Rare Diseases Information Center (GARD), and the NCATS Toolkit for Patient-focused Therapy Development. Dr. Pariser came to NCATS in 2017, and before this, she worked for 16 years at the FDA Center for Drug Evaluation and Research, where she founded the Rare Diseases Program in FDA CDER's Office of New Drugs in 2010 and served as a Medical Officer and Team Leader for rare diseases drug and biologics product development, review and regulation. Dr. Pariser has 20 years of experience in rare diseases research, and her current research interests include "many diseases at a time" research approaches, such as platforms for gene therapies and other rare disease product development, and informatics approaches to diagnosis.

Q&A

PHARMAFILE SPEAKS TO

Allergy UK

Scratching the surface of eczema care in the UK

In light of a recent report by Allergy UK about treatments for eczema patients, we spoke to Head of Clinical Services, Amena Warner, about the future of diagnosis, treatment, and support for this prevalent condition

Pharmafile: **In the new Allergy UK report, you reported 30 out of 30 healthcare professionals felt there was not adequate mental health support provided for patients with eczema – what measures do you believe are needed to combat this?**

Amena Warner: There is a need for more awareness of the very significant impact on quality of life, mental health and a person's lived experience that living with eczema can bring. We believe that psychodermatology services should be commissioned and made more widely available within the new integrated care system/primary care network infrastructure, and attached to secondary/tertiary dermatology/allergy services to address this need. There are support groups and organisations that can also help, such as Allergy UK, and there is a need for healthcare professionals to direct patients to these sources for ongoing support.

Waiting times for diagnosis, and access to effective treatments, are often lengthy (sometimes even over a year) for eczema patients. How can the healthcare system effectively respond to this statistic?

Prioritisation within the healthcare infrastructure of eczema as a disease area that can be treated and managed effectively, if a correct and timely diagnosis is made with accurate assessment, is key. There is a need for early interventional services and investment into this

area. Service provision needs to be addressed and increased to bring down long waiting times.

How does Allergy UK support those living with eczema?

We are the leading patient support and information charity for people living with all kinds of allergies. We have a helpline and webchat with a response team supported by our own clinical team. Our website is also a source of free information, factsheets and leaflets to help support people living with allergic conditions. At the same time, we run masterclasses, and produce videos and podcasts aimed at healthcare professionals on all aspects of allergy, including eczema.

Our work is focused on improving the lives of people impacted by allergic conditions.

What are some of the greatest challenges experienced by people living with eczema, and how have these been exacerbated by COVID-19?

Eczema is a very visual skin condition which can flare and can become very problematic at the most inconvenient times. People often say the itch is the worst aspect, and this often leads to sleepless nights, infection, and scarring of the skin. The huge impact this can have on the individual should not be underestimated, and this is backed up with data from many research studies, as well as what we hear on our helpline. Imagine this on a regular or daily basis and you can begin to understand why so many people affected have difficulty with work/school, with relationships, with concentration, with social situations, etc. Getting an accurate and timely diagnosis can be a challenge for many; as can gaining treatment to control and manage their condition without giving them serious long-term side effects. While COVID-19 has been unkind to everyone, having a condition like eczema can be isolating in itself, causing psychological, as well as physical, distress. The changes in our daily lives caused by COVID-19 are inevitably going to exacerbate those issues. Online consultations are challenging because they do not give a full picture of the condition, and many people are reluctant or embarrassed to expose the full extent of how eczema affects them.

What guidelines would you like to see implemented for better patient outcomes?

We would like to see the prioritisation of the development of NICE guidelines for children, young people, and adults. Also, creating patient pathways for people affected by atopic eczema, with a standardised approach to diagnosis, treatment and management of eczema across the whole of the UK in order to put the patient at the heart of the decision-making process for best practice care.

What are your hopes and visions for the future of eczema care and support?

That best practice care, treatment and support be received by those who need it. No one with eczema should feel alone with their condition and the impact it has on their lives. Finally, of course, that a cure will mean that eczema will be eradicated as a health condition.

Amena Warner is Head of Clinical Services at **Allergy UK**, a national charity that works to raise awareness of allergic disease both nationally and internationally. She took up this appointment after working as a Clinical Nurse Specialist in Immunology and Allergy at an NHS Hospital Trust. She trained at University College Hospital, followed by paediatric training at Great Ormond Street Hospital in London. She also holds a Public Health and Specialist Practice in School Nursing qualification gained in 1994. Visiting schools and carrying out health assessments made Amena very aware of the rising incidence of allergy in the UK and was instrumental in developing her interest in the field.

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‘Cumulative life course impairment’: The unforeseen burdens of severe eczema

AbbVie’s Rachael Millward takes a deep dive into dermatitis, patient impact, and patient expectations – and how a healthcare professional might meet them

Pharmafile: **What are some of the unexpected complexities of skin conditions such as atopic dermatitis?**

Rachael Millward: Atopic dermatitis (AD) is a common chronic inflammatory skin disease with a complex pathogenesis. The severity of the disease varies widely but AD can affect multiple aspects of a patient’s life from the skin manifestations such as the characteristic rash and itching, to less visible impact; such as depression, anxiety, and lack of sleep. AD is what is known as an atopic disease, and is commonly related to other atopic disease such as asthma, allergic rhinitis and in some cases food allergies. Interestingly, Abbvie has conducted a database analysis to further characterise potential comorbidities associated with AD using two distinct databases, CPRD and HES. This analysis has revealed some interesting insights such as observing an increase in the reporting of inflammatory bowel disease as the severity of AD increases. We need to do more research to understand the overlapping immune pathways across the immune mediated diseases to deepen our understanding of such diseases.

AbbVie focuses on dermatological areas with high unmet medical need – which areas within dermatology have you identified on these lines, and why do they qualify?

AbbVie has had long heritage in immunology, but with a dermatology focus for around 20 years. As mentioned AD can have a significant burden on patients lives, added with the complexity of the AD pathogenesis and limited treatment options, there has been a high unmet need for these patients. Some AD patients can be incredibly unwell, with 60% of patients with severe AD talk about their symptoms as unbearable or unrelenting. You can imagine the onward impact of that in terms of things like sleeping, work productivity. For me, focusing on AD and the high unmet need is key and fundamental.

AbbVie also work in delivering treatment areas where current options do not meet patient expectations – can you speak a little on the importance of meeting these expectations, and the current difficulties in delivering on them?

Centrally we need to listen to our patients and understand what they need to do be able to manage their disease. We can assume patients want to be completely free of their disease, however what they actually want could be a good night’s sleep; to wear a dress to go to a wedding or a birthday party; to wake up and feel refreshed and take their kids to school. Small things that can mean a lot to patients. When we look at the patient research we’ve conducted in AD, we often hear patients talk about their desire for freedom from the relentless itching, not being able to sleep, not being able to be productive at work, not being able to concentrate. Patient often talk about feeling embarrassed by their condition, particularly if the rash is on a highly visible areas – on your hands, your face, your legs, skin clearance, for example, could be an ambition we should be aiming towards. At AbbVie, we set out to make a remarkable impact on patients’ lives, and as we innovate and understand immune mediate disease better, we should be asking ourselves: are we meeting the needs of our patients?

What are some of the most serious implications for those who suffer serious chronic skin conditions? How can healthcare professionals work to decrease their severity?

The serious implications are that skin conditions are often dismissed quite early on. One of the biggest barriers for patients, especially for patients with severe skin disease, is being referred to a specialist. Patients can spend a significant period of time in a primary care setting and not receiving the care they require. Sadly some patients may never get to see a specialist, and can drop out of the care system all together, and then we hear of patients self-managing the condition. We need to work in partnership, to allow patients access to a specialist when they need it, and not allow the fact it’s a skin condition to prevent that from happening.

Those patients who do enter into the secondary care system, it’s vital they’re given time with their healthcare professional to talk about how best to manage their conditions as each patient is different and the impact of the disease can vary from patient to patient. Small, but effective, steps, such as educating patients on how to optimise their topical

treatments can be vital. For example, patients are often not given any instruction of how much emollient to use on or how much of the affected skin. Simple steps can really help patients gain control of their disease, however time and resource constraints make this difficult in practice.

But, beyond the healthcare system, certainly the symptomatic relief of the condition itself, and always reminding ourselves that some of these patients have been living with this condition for a very long time and have adapted to cope with the condition. When aiming for holistic care, there are many factors that need to be considered, such as the age of the patient, visible signs and symptoms, and emotional wellbeing. It is well documented that AD can have huge psychological impact on patients, but it is not often part of the management plan. Access to psycho-dermatology clinics for complex patients have demonstrated significant improvements and have provided patients coping mechanisms to support the management of their disease. Unfortunately, this service is not widely available to the patients who need it. Budget cuts have made it particularly hard for departments to offer this valuable service.

We strive to support patients and healthcare stakeholders to access the Future of Better Care, Quicker; focusing on the need to secure better outcomes for patients by working in partnership with healthcare stakeholders.

Between 11-20% of children in the UK suffer from AD, and 2% of these cases are severe. How are AbbVie working to address this long-term condition, and what are its impacts?

AD has quite a high prevalence in adolescents and children and can manifests itself very early in a patient's life and the effects of AD on children can have lifelong implications. The concept of cumulative life course impairment is interesting, whereby children with AD may not achieve certain milestones when compared to patients of the same age without AD, because of the profound negative impact of the disease. Educating on this concept and managing the disease early and effectively could reduce the overall impact the disease has on children over the long term.

What recent innovations in the treatments of long-term skin conditions have you been particularly excited by?

It is fantastic to see significant investment being made to advance innovation and management of skin diseases in general, there are myriad skin conditions now being investigated and prioritised, many with significant patient burden and with an associated high unmet need, AD is just one of such conditions.

UK-ABBV-211014
December 2021

Rachael Millward is currently head of medical affairs for immunology at **AbbVie UK**, where the team are working on a wide range of immune mediated inflammatory diseases. Rachael has held various roles, across multiple organisations, ranging from clinical research, pharmacovigilance, medical information, and latterly medical affairs. Rachael's academic background and research interests are in biotechnology and molecular genetics with a particular focus on pluripotent stem cells.
For more information, contact: **UKMediaRelations@abbvie.com**

Dermatologically speaking: Finding new treatments for women

Pharmafile sat down with the team at Organon to unearth the different ways that women's dermatological conditions can be successfully supported and managed

Pharmafile: **What is the future plan for expanding the range of treatments available to women with dermatological conditions?**

Simon Nicholson, Managing Director UK&ENI Cluster: Essentially, we are a women's health company built on three pillars: women's health, biosimilars and established medications. We have a strong foundation of more than 60 medicines across a range of areas including contraception, reproductive health, menopause, cardiovascular disease, dermatology, allergy and asthma, to name a few.

Our mission is to deliver impactful medicines and solutions every day for every woman. Our focus for the future is not limited, but our commitment remains to listen to women and identify areas of unmet need. This will drive our investment and our future portfolio.

How does dermatitis and other skin conditions affect those suffering from them?

Manjit Aujla, Lead Established Brands & Biosimilars UK-ENI: Dermatitis and other skin inflammatory conditions can have a real impact on self-esteem and confidence, and in extreme cases the psychological impact can be far reaching with some people experiencing depression and anxiety.[1] A person's long-term well-being can be impaired by skin conditions. These can have a profound effect on all aspects of people's lives, including personal relationships and social engagement. Improvements in awareness of skin conditions, and access to specialist services including psychological interventions, can be helpful in both treating and coping with many skin conditions.[2]

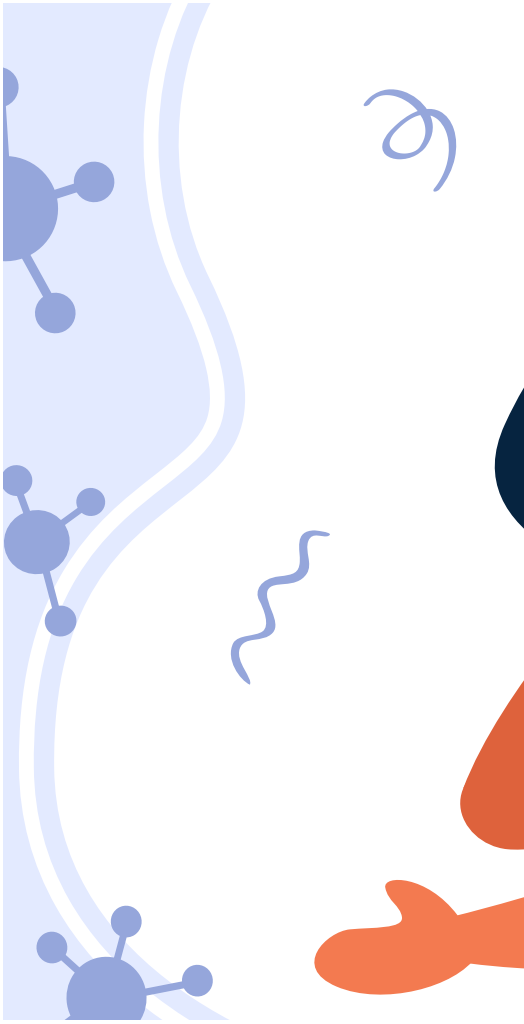
What would you say is the greatest challenge faced by women suffering from skin conditions?

Faye Sheen, Brand and Customer Manager UK and Ireland: It is very difficult to talk about one single challenge that women with skin conditions face as every part of their life can be affected – including relationships, careers, self-confidence, mental health, and in some cases, this could have an indirect impact on wider family members quality of life.[3]

Depression and anxiety are probably the greatest challenge for women suffering from skin conditions as this can affect women's ability to work and study, and can have a major impact on family and social life. Women with skin conditions may want to cover up or shy away from social interactions.[1]

What are the priorities in this area?

Simon Nicholson: It is now five months since we launched Organon, and we launched with a commitment to identify the unmet needs in the women's health space, by really listening to women and all our key stakeholders. We have continually sought the views of women through many channels, and it is clear there are a number of significant areas of unmet need in both the provision of solutions to treat conditions which specifically affect women, but also those which have a disproportionate effect on women. The biggest challenge for us moving forward will be to prioritise our efforts and ensure we are supporting women in the areas of greatest need, at the right time and in the right way. An example



The biggest challenge for us moving forward will be to prioritise our efforts and ensure we are supporting women in the areas of greatest need, at the right time and in the right way

of this is the impact of COVID-19 on sexual health services, which in turn impacted access to contraception and resulted in a substantial increase in unplanned pregnancies across the world.

On World Contraception Day, we partnered with The Faculty of Sexual and Reproductive Health to shine a light on the challenges that women have faced through this disruption, and as part of a major initiative to improve access to LARCs, we have been pioneering the development of a new treatment pathway in Liverpool. By igniting the conversation around contraception, we hope to empower women with the knowledge that they need to understand the contraceptive options that are available to them.

More recently, on World Menopause Day, we listened to women between the ages of 40-60 – undoubtedly a time in a woman's life that can be really challenging. Our survey results confirmed that although there is still need for further education, when women feel supported, it can also be a time of real empowerment and a milestone that positively opens the door to the next chapter of their lives.

Our next major milestone is International Women's Day on March 8. We will be continuing to give women a voice, and continuing to listen so that we can make a material difference and create a better, and healthier, every day for every woman. This is just the beginning for us as a women's health company. There is much more to come.

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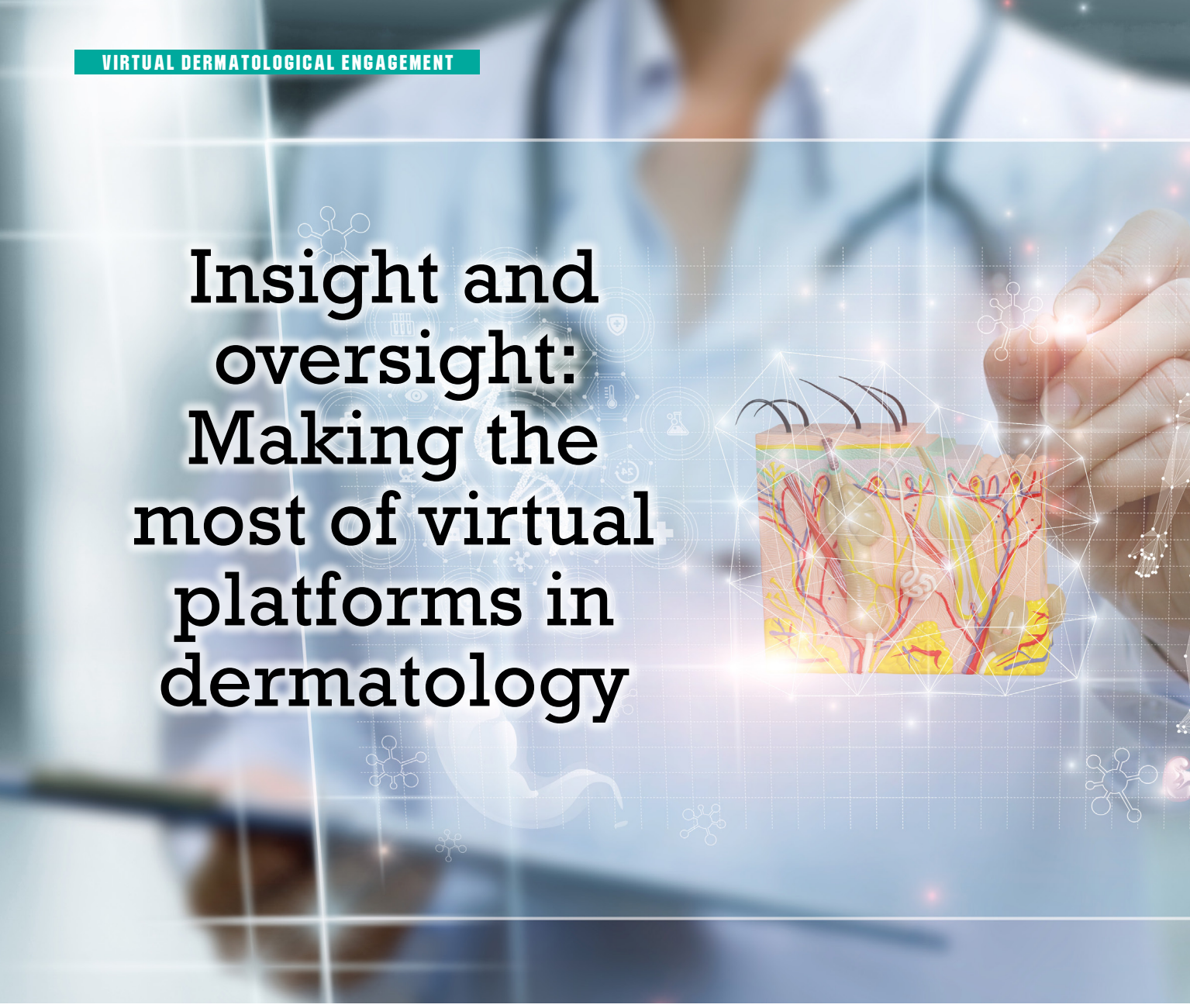
Simon Nicholson is the Managing Director of the UK & ENI Cluster at **Organon**, with over 14 years of experience in the pharmaceutical industry. Simon is committed to making life better for each and every woman.

Faye Sheen is the Brand and Customer Manager UK and Ireland at **Organon**. Faye has a strong focus on supporting women, ensuring that women's voices are heard, and is keen to make sure that Organon reflects what women want.

Manjit Aujla is the Lead of Established Brands and Biosimilars UK & ENI at Organon, with over 13 years of experience in the pharmaceutical industry. Manjit has a particular interest in multi-channel marketing and integration.

Insight and oversight: Making the most of virtual platforms in dermatology



FIDE is an independent expert-led consultancy, specialising in providing insight into inflammatory skin conditions. Dr Bruce E Strober, Executive Director, takes a look at virtual communication with HCPs and patients, and offers insight into how to make the most out of virtual communications with dermatologists, HCPs, and patients

Pharmafile: **What has the impact of restricted one-to-one healthcare professional (HCP) access engagement been on dermatological patient care?**

Dr Bruce Stober: We have observed minimal effect – our practice has functioned mostly normally (with appropriate COVID-19 precautions in place) for the past 18 months.

Some restrictions have been placed on the number of pharma reps to keep density down. We're actually busier than ever with patient care, and allow in-person interaction with pharmaceutical representatives. Truth be told, some restriction on pharmaceutical interaction is positive, as it can be overwhelming to a busy HCP trying to conduct patient care.

COVID-19 restrictions have also limited knowledge transfer – what effect has this had on dermatological R&D and patient care?

The lack of in-person meetings has necessitated virtual learning, which isn't vastly inferior. However, in-person learning likely fosters more Q&A and discussion that is somewhat blunted by the virtual medium. Patient care likely hasn't been impacted significantly. The real issue is how COVID-19 has delayed the FDA review process, inhibiting the approval of important new medications for patients in need.

Dermatology is an area with significant unmet patient needs. What is needed to provide access to expert insight, and how do you work to ensure it?

To really get to the bottom of unmet patient needs efficiently, it is vital for biopharmaceutical companies to develop relationships with a variety of HCPs who can provide unbiased insights on the market

landscape. These insights are crucial for uncovering real challenges across the patient and healthcare professional journey. It is only by truly listening that organisations can develop solutions that can improve the lives of patients.

As a consultant I regularly interact with pharmaceutical companies of all types and sizes to help ensure more sensible product development and commercialisation. I also participate in numerous virtual continuous medical education (CME) and promotional activities that foster education and discussion.

Which areas of dermatology are neglected in terms of research and development, and patient care?

Some rare skin conditions, such as lichen planus, scarring alopecia, granuloma annulare, and hypersenstivity dermatitis (that primarily affects older individuals), are overlooked. These conditions are often tough to treat and require a lot of trial and error approaches. They also often face treatment failure. Further, medications that might be effective, without FDA approval for these uses, are hard to deliver to patients.

What have the most interesting developments in dermatology been over this time period, and what changes do you anticipate in the next ten years?

Without a doubt, the advancement of psoriasis therapeutics, which are now very effective and safe, and the incipient development of effective therapies for atopic dermatitis. The next 10 years will see further advancements in atopic dermatitis, hidradenitis suppurativa, alopecia areata, and vitiligo. Further, there appears to be a revolution brewing in the development of novel topical drugs with safe and effective mechanisms of action and can treat inflammatory dermatitis.

What are some of the ways dermatologists can adjust to the challenges presented to them in patient care through the COVID-19 pandemic?

In the US, COVID-19 has not recently impacted dermatology, with many practices quite busy. It appears that business has returned to normal. In essence, we are learning to live with COVID-19, instituting the correct precautions along the way.

What difficulties have arisen in educating HCPs in managing skin conditions over the past few years?

While allowing learning in the comfort of one's own home or office, the movement to virtual media, due to lack of good engagement, is an inferior approach to in-person conferences and symposia. It is a mixed bag, as the lack of travel is, on balance, easier on lifestyle and happiness. HCPs who are disciplined and engaged can still learn a lot from the current virtual educational offerings.

What is your number one piece of advice for biopharmaceutical companies looking to enhance their relationship with dermatologists today?

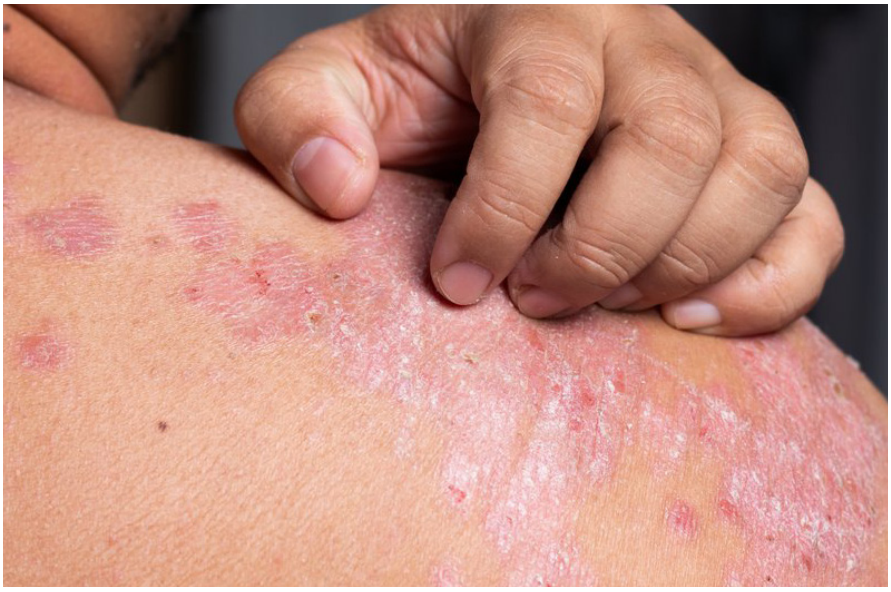
Keep the interaction data driven, with honest presentations of your drug/agent – no tricks and over-commercialised approaches that don't jibe well with reality. Also, focus on patients who have comorbidities – work with registries and other repositories of real-world data to get an idea of how the drug really works when used in clinical practice.

Dr Bruce E Strober, Executive Director at **FIDE**, is Clinical Professor of Dermatology at Yale University School of Medicine, and practices at Central Connecticut Dermatology. He is also co-Scientific Director of the CorEvitas psoriasis registry, Treasurer of the International Psoriasis Council, and Editor in chief of the *Journal of Psoriasis and Psoriatic Arthritis*. Dr Strober earned both his medical degree and his doctorate from Columbia University College of Physicians and Surgeons in New York. He completed his residency in dermatology at the Department of Dermatology, New York University School of Medicine. He is certified by the American Board of Dermatology and is a Fellow of the American Academy of Dermatology.

To find out more about FIDE, contact: **steve.annels@fide.net**

"The pain keeps me awake at night. I can't cope with this anymore"

The therapeutic agents of the past decade have revolutionised dermatological treatments, improving the quality of life of patients with psoriasis. Dr Susanne Farwer at UCB shares her extensive clinical experience in the area



Pharmafile: **What have been the most significant advancements in dermatology and psoriasis management over the past decade?**

Dr Susanne Farwer: The past decade of dermatology has seen the development and launch of novel therapeutic agents with differentiated modes of action, enabling more targeted treatment approaches with a range of effective and well-tolerated therapies. The introduction of these therapies revolutionised dermatology and I have been very privileged to witness first-hand how these drugs have transformed the lives of patients living with chronic inflammatory dermatoses, such as psoriasis or atopic dermatitis.

Despite these scientific advancements, psoriasis remains a challenge to treat, with a substantial proportion of patients not achieving optimal disease control with the current therapeutic options.

My clinical years exposed me to countless patients desperately seeking that 'magic pill', with hopes and expectations for a treatment that will relieve them of the disease burden they have been carrying both mentally and physically. It is these experiences which inspire my passion for improving patient outcomes, and I am excited to be working at the forefront of these advancements.

What challenges and barriers still exist and prevent patients from reaching their treatment goals and living their lives to the fullest?

More than 50% of the UK population are affected by skin disease at some point in their lifetime, with over 13 million people (24%) visiting their GP with a skin condition.[1] In comparison to other chronic conditions such as diabetes, chronic obstructive pulmonary disease (COPD) or cardiovascular disease, dermatological conditions still rank low on the government and health policy makers' agenda.

The high disease burden and wide-ranging impact of psoriasis on people's daily lives is still underestimated. Furthermore, the high prevalence of co-morbidities affecting joints, psychosocial well-being, and the metabolic system, are often not well understood or acknowledged across the various stakeholders in the healthcare system. Reports show that nearly 60% of people with psoriasis say the disease causes problems in their everyday lives.[2] What vividly remains in my memory are the many patient struggles I heard during my clinical years.

Patients consistently report a lack of understanding and awareness of the treatment options available to them, and so they fail to

> "My skin looks like a mess and people are staring at me; I am itching all over, and the pain keeps me awake at night. I can't cope with this anymore, I don't think anyone will ever find me attractive being covered in all these red patches from top to toe. I've not worn a sleeveless top in years and have lost all my confidence showing off my skin," anonymous patient, aged 35, from South Yorkshire.

understand what they can and should expect from their treatment. This therefore limits their influence in shared decision making about their treatment pathway, in partnership with their dermatologist.

Currently, the system isn't working well enough for people with psoriasis, so we are dedicated to working with healthcare professionals and the NHS to find new ways to overcome the systemic challenges that stand between people with skin diseases and access to innovative treatments, and holistic, integrated patient care.

How is UCB Pharma challenging the status quo and how do you hope to impact the space going forward?

Collaboration is fundamental to delivering transformative solutions to those who need it. While those involved in dermatology – patients, clinicians, payors, patient groups, or the scientists working to unlock the treatments of the future – face different challenges, ultimately, we are all working towards the same goal.

This goal is to ensure better lives for those living with skin disease, and faster access to innovative treatments. By working together as partners, we believe we can significantly reduce the time from diagnosis to effective treatment and ultimately, find ways for everyone to feel comfortable in their own skin and live fulfilled lives, free of physical and emotional burden.

We aim to not just listen to stakeholders and gather their insights, but to also involve them in the co-creation of insight-driven solutions. The recent pan-European EPICENSUS Project showcases our collaborative approach to improving outcomes for people living with psoriasis.[3] Initiated in December 2020 by UCB, this integrated consensus programme involves key stakeholders (clinicians, payors and patient advocacy groups representatives) from across eight European countries, and focuses on generating engagement, gathering insights and enabling a multi-disciplinary conversation. It will critically evaluate the current standard of care with regards to diagnosis, monitoring, access, and patient-reported outcomes in psoriasis, with results due to be published later this year. We hope that EPICENSUS will ultimately deliver a paradigm shift in outcomes for people with psoriasis, reducing the significant burden on the health care system and enhancing the delivery of future psoriasis care.

How will new technology such as machine learning and AI influence the dermatology space in the coming years?

New technologies such as machine learning have been successful in predicting the trajectory of patients' health in various fields such as cancer, diabetic complications, and cardiovascular mortality. Recent studies have shown that although ample data exists on the efficacy of biologics in psoriasis, decision making on treatments is still often based on a trial-and-error approach. In a real-world setting, over 50% of patients required dose adjustment during therapy and 20-50% of patients experienced a relapse, resulting in a switch to another medication.[4]

The application of such modelling algorithm methods for psoriasis treatment could help to predict long-term responses to biologics. Combining patient variables such as demographic data with disease and therapy specifics has shown promising results in this space.

To make the use of these impressive technologies a common practice, further studies and analyses on a larger and more diverse dataset are needed to identify universally applicable criteria.

What further advancements are needed in the dermatology space to achieve better health outcomes for patients, and enable an improved patient experience?

The introduction of integrated care systems (ICSs) provides an opportunity to acknowledge the impact of skin conditions on wider society and the healthcare system. It is important that these ICSs are gathering these insights and using them to implement decisions that strive towards integrated approaches to care.

It is also important that we are leveraging the range of data and the latest innovations in digital technologies to accelerate the identification of genetic, tissue and serum markers, to better predict treatment response and drug survival. This will help to optimise data-driven decision-making to personalise treatment and ultimately improve patient outcomes.

Above all, we won't stop searching for the best solutions so that everyone has the opportunity to feel completely comfortable in their own skin, to leave the burden of skin disease behind, and to lead a healthy and happy life free of embarrassment, stigma, and judgement.

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Dr Susanne Farwer joined **UCB** in August 2020 as the Medical Solutions Lead for Dermatology in the UK and Ireland. Prior to this move, she spent over 20 years as a healthcare professional including time as a GP and a Specialty and Associate Specialist (SAS) doctor in dermatology for the NHS.

Susanne's extensive clinical experience combined with her deep passion for advancing and implementing solutions that reduce the disease burden and improve patients' quality of life, makes her an asset to UCB whose own philosophies include bringing innovative therapies to those with severe chronic diseases.

On a personal level, Susanne prides herself on being adaptable, determined, and inspiring those around her, all while having a great sense of humour.

Supporting dermatology and oncology services to build back better post-COVID-19

The coronavirus pandemic has challenged the NHS across multiple disciplines, contributing to a growing backlog of patients, and increasing pressure on its staff. Caitriona Walsh, UK Regional Business Unit Head at Novartis, believes that the pharmaceutical industry can play an important role in supporting both patients and NHS beyond the provision of medicines

We are in the midst of a 'silent pandemic'; a healthcare crisis in which millions of people are waiting for treatment. The NHS faces a challenge in managing the unprecedented backlog which has emerged in services, like dermatology, that were deemed 'non-urgent' during the pandemic. This is a challenge that requires bold solutions, close collaboration, and exciting innovation.

COVID-19 has taught us that if we are to bring about real change, we must all collaborate like never before. Recognising this, at Novartis, we partner with the NHS and the wider health ecosystem to identify and implement healthcare solutions for patients most in need, no matter where they are, or what their background. This has meant transforming the way we operate in the UK to be a better partner for the NHS. At a regional and national level, we are attempting to better address the needs of the NHS and UK patients. As a result, we are currently involved in 288 collaborations with the NHS across the UK, and we work extensively with world-leading academic institutions, such as Imperial College London.

Even before the current global health crisis, there was a growing need for all players in the UK's healthcare landscape to improve cooperation, to grow efficiencies, and ultimately improve patient outcomes. During my career, I've seen treatments revolutionise patient care. In psoriasis, for example, treatments are now assessed using a PASI 100 score (completely clear skin) – a major improvement on the PASI 75 score which used to be our benchmark. We are currently living through a golden age of medicines development. Novartis, and others, have contributed to this improvement by introducing a highly effective new generation of biologic medicines. Nevertheless, challenges remain.

Many people with psoriasis face delays in accessing newer biologic treatments, largely due to existing backlogs in the system. The commitment to a 'two-week wait' for assessment of possible skin cancer is commendable, but despite this, melanoma diagnosis has fallen by 17% during the pandemic. This, in turn, could lead to workload implications for other areas of dermatology – patients with psoriasis, chronic spontaneous urticaria, or paediatric dermatology, may see further delays in accessing the most effective treatments.

Our oncology division has initiated a joint working project with Velindre University NHS Trust to redesign the South East of Wales referral pathway for all stage 3 melanoma patients, treated in an adjuvant setting, and for stage 4 metastatic melanoma patients (new and progressive). Driven by a new specialist multidisciplinary team, the project aims to provide equitable patient access, and improved quality of care.

Immuno-dermatology is a major area of interest for Novartis; we continue to invest in research resources, growing our understanding of the underlying science, developing new treatments, and expanding the applications of our existing medicines portfolio. This is a normal approach to a therapy area by a major pharmaceutical company, and is perhaps to be expected. More recently, however, we have felt the need to expand and diversify our engagement with the UK healthcare ecosystem. We have begun to examine our wider role in improving care provision, starting with digital innovation.

Data can save lives, so we are seeking to harness this potential through a digital innovation lab (Novartis BIOME).[1] The lab develops digital and data-led solutions to combat health inequalities, digitise patient pathways, and to advance remote care. In 2018, we created the global BIOME network of innovation hubs. We aim to help our partners to become an extension of our own teams, able to work with us as easily and productively as possible.

We're currently facing some of the biggest healthcare challenges – something we can't, and don't want to, do on our own. We intend to combine our existing scientific insight with the expertise of the tech world to develop digital solutions that have the potential to improve and extend patients' lives. To do this, we realise that we need to make it easier for companies, big and small, to partner with us. The healthcare

industry is notoriously complicated – highly regulated and often behind the curve in terms of digital disruption.

In March 2020 we began a digital innovation partnership with Cievert Limited, a UK provider of innovative digital healthcare solutions, aimed at developing a tool to help streamline the management of rheumatological and dermatological diseases.[2] The new tool will allow patients to become more active in their own disease management by inputting data into a central platform which will, in turn, help clinicians more closely monitor disease status and manage care. By allowing remote monitoring of patient-reported outcomes, the platform could help clinicians to prioritise appointments based on patient need, potentially saving time, addressing the current backlog, and supporting the NHS' recovery. Ultimately, we believe that a digital solution has the potential to offer faster, safer, and more convenient care, in line with the NHS Long Term Plan.

When it comes to oncology, another partnership that has emerged from the BIOME is with Vine Health – a technology innovator that has created a compliant AI-based app, designed to better manage a patient's journey through their cancer treatment.[3] The app supports patients by monitoring and reporting their symptoms, medications, and activity levels, and by managing their appointments, improving their quality of life. A professional version of the app delivers predictive analysis and allows care teams to view real-time data and personalised patient information, leading to better clinical decision-making, remote care, and greater service efficiency. The accessibility of the app has led to it becoming the top-rated cancer tool globally, with particularly high levels of uptake by the over 65s.

Technology is only one part of our holistic approach to care, however. We also increasingly appreciate the need to treat the 'whole patient', taking into account potential co-morbidities, as well as remaining mindful of the psychological burden that illnesses can impose. One of the ways we do this is through 'You First' – our nurse-led patient support programme which has been tailored to meet the individual demands of patients, and is designed to work alongside the expertise of the NHS healthcare team.[4]

The service is implemented by a team of dedicated nurses who offer routine clinical assessment, phone calls and texts, direction to local and national services and support groups, and phlebotomy service at home. They also offer motivational interviewing and mentoring, injection training, and administration of medicine if required. The programme is offered for up to three years to dermatology patients on specific medicines, and is aligned to the individual needs of both patients and participating NHS Trusts.

When the pandemic began, we knew we would have to adapt our patient care, so we worked with patient groups to help us understand the challenges that patients were facing. We adapted our support programme accordingly to address these needs – our nurses offered additional precautions (e.g., PPE and video-only visits), implemented a remote enrolment process, offered collection and delivery of medicine, and streamlined the sign-up process for NHS Trusts. We are continuing to work with patient groups to ensure we can keep patients' needs in mind when developing our services, and to make sure that they are not overlooked or left behind during the pandemic. Our intention is that patients receive a more complete and considerate package of care that extends beyond their prescription, complementing and supporting NHS services.

Our commitment to keep patients front of mind has led us to develop medicines that serve unmet needs in dermatology – most recently for paediatric patients, which I am particularly proud of. Within our pipeline, we are continuing to look at other dermatological diseases with high unmet need, through which we hope to support many more patients in the future.

Outside of drug development, we continue our efforts to support patients more directly. To increase awareness of melanoma, we are working in partnership with Melanoma UK on the 'Melanoma: Let's Get Under The Skin Of It' campaign, which aims to encourage people diagnosed with melanoma, their loved ones, and their partners and carers, to learn more about melanoma. We hope that this campaign will give people the confidence and support they need to speak to their doctor about their skin cancer.

Finally, we recognise that all of these efforts would mean nothing without our incredible UK healthcare service. Our healthcare inequalities pledge reflects our commitment to help the NHS build back better, and address the health inequalities and underlying healthcare conditions exposed by COVID-19. We will collaborate with policymakers and healthcare systems, to enable solutions that provide faster diagnosis and earlier interventions for those population groups which are at the highest risk of ill health and poor health outcomes.

I believe that all of us who work within or around the UK's healthcare system must look beyond our traditional roles. We need to identify new ways to add value and to work collaboratively towards improved outcomes in the new, post-COVID-19 healthcare environment.

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Caitriona Walsh, UK Regional Business Unit Head at **Novartis**. Caitriona Walsh is Regional Partnership Business Unit Head at Novartis UK. She has been with Novartis for over 15 years, covering country and regional leadership roles in medical, marketing and sales across different therapy areas, including immunology, hepatology, and dermatology, neuroscience, ophthalmology, respiratory and cardiovascular. Caitriona has a PhD in immunology and a background in biotechnology with a focus on marketing and management.

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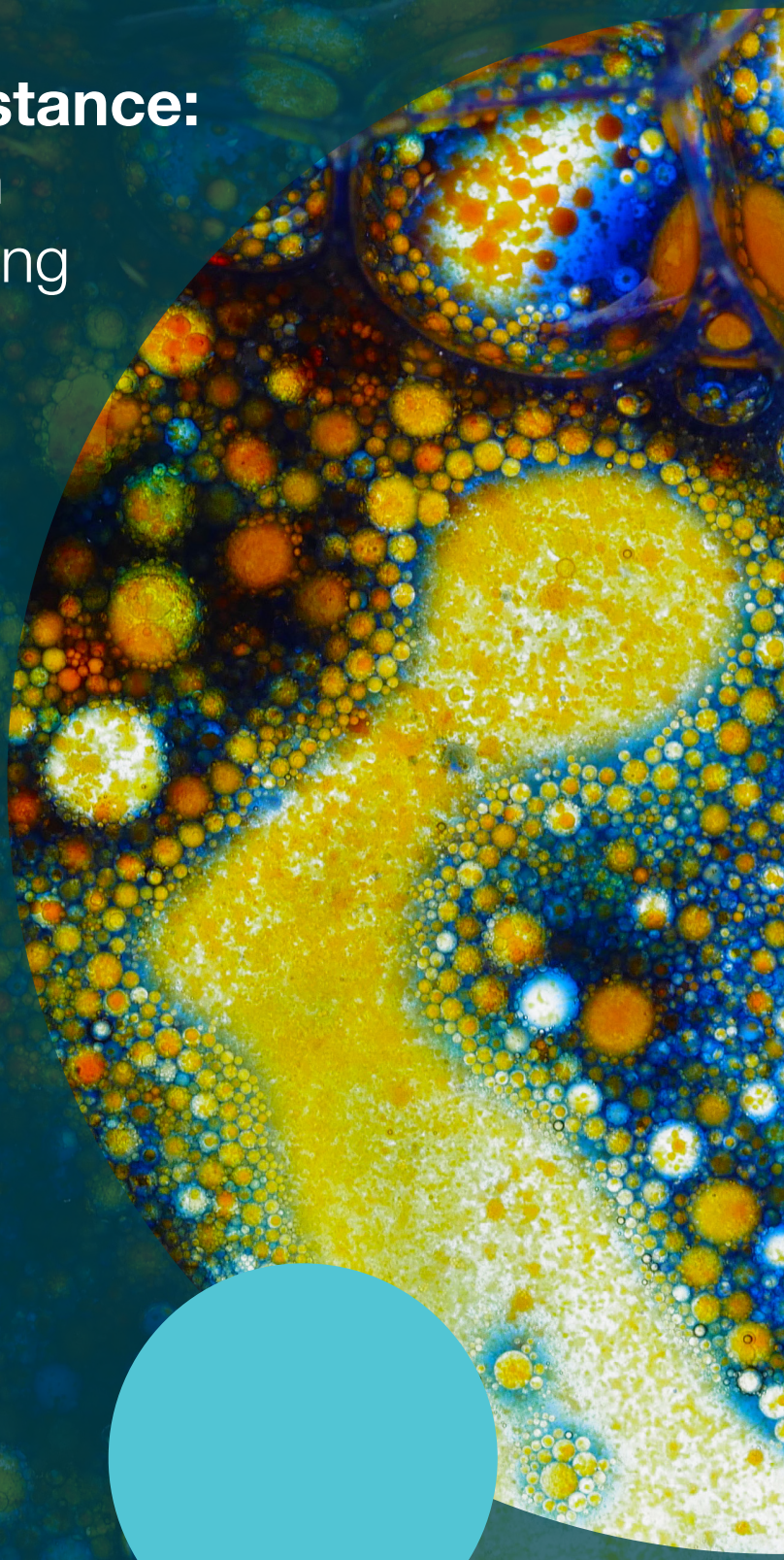
Antimicrobial Resistance:
How clinical research can combat an ensuing global crisis



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