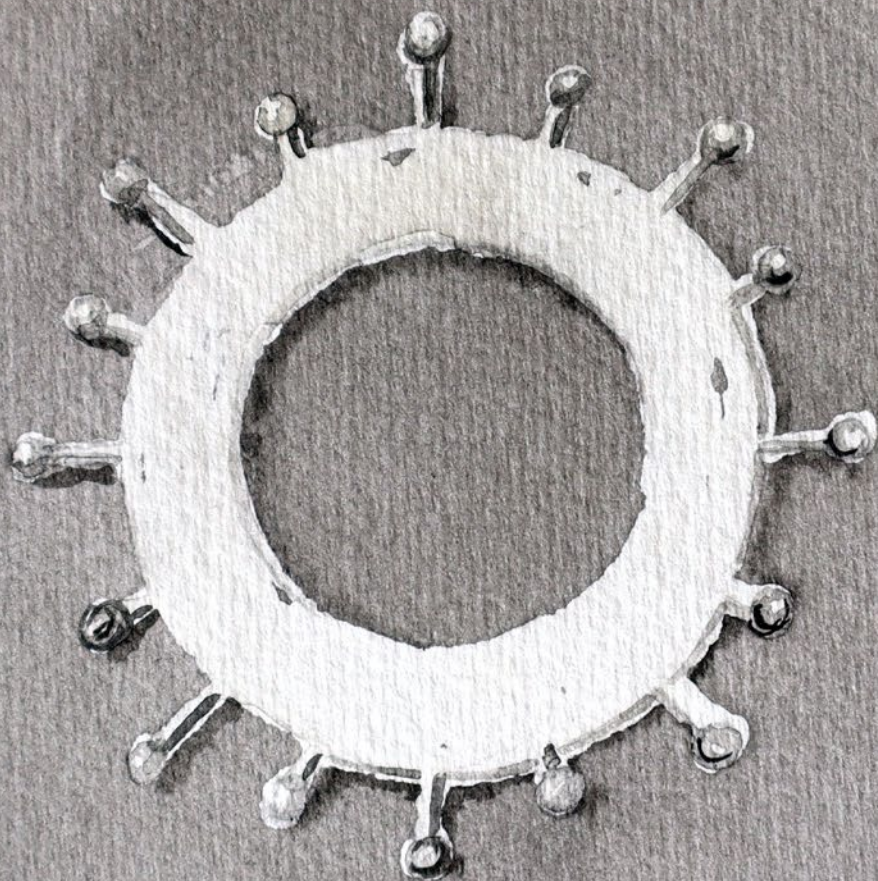


THE PANORAMIC PRINCIPLE



Tanya Poole

2024

Professor Christopher Butler

Co-Chief Investigator, with Richard Hobbs and Paul Little
Nuffield Department of Primary Care Health Sciences
University of Oxford

PRINCIPLE and PANORAMIC

In open competition, we won funding for the *Platform Randomised trial of treatments in the Community for epidemic and Pandemic influenza* (PRINCIPLE) of repurposed medicines for COVID-19, and for the *Platform Adaptive trial of Novel antivirals for early treatment of COVID-19 in the Community* (PANORAMIC). The tiny minority of COVID-19 trials have been done in the community. Fewer still produced clinically useful findings. Funded by UKRI / National Institute of Health and Care Research, with Urgent Public Health prioritisation and the support of the UK's clinical research infrastructure and the NHS, PRINCIPLE and PANORAMIC randomised over 40,000 people, evaluating nine medicines, and have transformed guidelines and impacted on policy and care around the world. It was people who made all of this possible, and this Trials Unit and Trials Artist in Residence **Panoramic Principle** exhibition celebrates all of them.

Inverse care and inverse research participation laws

In 1971, Julian Tudor Hart, a general practitioner and clinical researcher who practiced in Glyncoed in South Wales coal field, articulated the concept of the Inverse Care Law, which states that the 'availability of quality medical care tends to vary inversely to the need for it in the population served.' Those living in socially deprived areas experience higher burdens of illness. For example, people living in the most deprived areas of Wales can expect to live nearly ten fewer years than those living in the least deprived areas. The COVID-19 pandemic further highlighted these health inequalities: as with deprivation generally, the most deprived regions in South Wales experienced the highest mortality rates from COVID-19.

During the early stages of the SARS-CoV-2 pandemic, while working clinically as a GP at the

Cynon Vale Medical Practice, also in Wales, I managed one of the first patients in the practice with probable COVID-19. This consultation emphasised not only the lack of evidence-based treatments then available for this person, but also an absence of clinical trials available to the patient to contribute to addressing this gap. The focus of treatment research, political, and media attention at that time was almost entirely on severe, already hospitalised cases of COVID-19, with limited attention given to community-based therapeutic trials. This led us to formulate the Inverse Research Participation Law, which holds that 'access to research is often inversely proportional to a participant's potential contribution, and to where the research findings should be most applicable.' This drove thinking around how the PRINCIPLE and PANORAMIC trials were shaped.

Epidemic and pandemic trials

Not a single person was randomised in the community during the Swine Flu (H1N1) pandemic. We therefore still don't know if the medicine that was widely used for that infection, oseltamivir (Tamiflu), did more good than harm. As part of the European Union PREPARE Project, we did the 14 country ALIC4E randomised controlled trial of Oseltamivir for influenza-like illness. The trial was designed to be able to test more than one treatment at a time, and to add in new treatments even once the trial was underway.

When the COVID-19 pandemic broke, we applied for funding to a similar kind of trial for treatments for COVID-19 in the community. It is in primary care where finding out what works, and what does not work, can have the greatest reach and impact. Early, safe, cost-effective, scalable treatments that stop people from deteriorating, so that they do not need hospital treatment, is a major priority for patients and the substantiality of the health services and society.

Tragically, there was no research-ready, Europe-wide infrastructure that could rapidly initiate international trails of therapeutics for COVID-19. But the far-sighted vision of the UK's Chief Medical Officers, especially Jonathan van Tam, led the UK to only deploy drugs once they were proven to work, rather than follow assumption-based medicine, or politically-motivated, evidence-free opinion.

So - we took what we had learned from the ALIC4E trial and rapidly set up a platform adaptive trial of repurposed medicines, PRINCIPLE, which went on to evaluate seven different treatments within under three years. Perhaps the finding from PRINCIPLE that we are most proud of was the early demonstration that the antibiotics, azithromycin and doxycycline, should *not* be used to treat COVID-19. These precious antibiotics were being widely used around the world for COVID-19, as they have anti-inflammatory properties and some antiviral activity in-vitro. Unnecessary use of antimicrobial drugs wastes resources, puts people at pointless risk of side effects, and drives antibiotic resistance, the 'global warming' of medicine. These findings from PRINCIPLE informed guidelines, changed practice world-wide and are enhancing antimicrobial stewardship.

The UK governments, and governments around the world, then procured large stocks of two novel antiviral drugs (Molnupiravir and Nirmatrelvir/Ritonavir), which help keep unvaccinated people with COVID-19 out of hospital in efficacy, company-sponsored trials. Jonathan van Tam, our Deputy CMO at the time, and other key decision makers, resisted calls to immediately deploy these drugs at scale, insisting that they should first be trialled in their intended-use, UK, now vaccinated population. In open competition once again, we won a grant for PANORAMIC, which became the fastest-recruiting, and largest trial of any medicine in acute community care, regarded by some as the UK's first truly *democratic trial*.

Taking trials research to the people

Both PRINCIPLE and PANORAMIC relied heavily on the Clinical Research Network Infrastructures embedded in the NHS in all four UK nations, supporting GPs, nurses, and pharmacists in all devolved administrations to achieve remarkable recruitment and generate clinically actionable, policy -relevant findings. This model relies on recruiting patients who are registered to receive care at those GP practices set up for a research project, which limits participation according to where one lives

and receives health care. Over time, we worked out ways and got necessary permissions to complement this site-based recruitment model to enable people sick with COVID-19 to contribute their experiences to the trials without having to leave their sick beds, irrespective of where they lived, or received their healthcare.

Our commitment to research inclusivity paved the way for novel engagement initiatives to enhance participation from minority ethnic populations and people living in areas of high deprivation to further advance research inclusivity, and the University of Oxford established the Centre for Research Equity.

Influencing the future

Often in 'efficacy', tightly-controlled regulatory trials, participants are highly selected and so are very similar to each other. This maximises internal validity. But clinicians often ask whether findings from such, usually small, homogeneous study populations apply to the complex patients they see in their everyday clinical practice, because their patients are not necessarily like the ones in regulatory trials, and so might not respond in the same way to the treatments in question.

The World Health Assembly (WHA) recently passed resolution 75.8 on strengthening clinical trials. Their main point was that we need bigger and better trials that include more diverse people, to ensure that those who interventions are intended for are included in the trials, and so can properly benefit from the findings. PRINCIPLE and PANORAMIC, in a sense, are a beacon response to the WHA call; these trials demonstrate the importance of large scale, effectiveness trials that address practical questions, such as, 'If I prescribe this medication, will a patient like the one I am caring for right now benefit, compared to if I do not prescribe the treatment for them and go with current usual care alone?' By having large numbers in these 'pragmatic' trials, and by maximising diversity in the study populations, trials like PRINCIPLE and PANORAMIC not only reveal the average effects of treatments, but can also tell whether people benefit if they have different characteristics, such as being older, being sicker, and having other illnesses.

We did not include placebo drugs in these trials for many reasons, perhaps the most important of which is that they compare care with a new medicine to current practice without the new medicine. We don't use placebos in general practice, so comparing the care people would receive without the drug, and

not to the artificial situation of care with a placebo, was the urgent imperative. This kind of pragmatic policy and care-relevant research is generally under-appreciated by medical journals and bodies such as the National Institute of Health and Care Excellence. When we submitted a paper from PRINCIPLE to the New England Journal of Medicine, for example, they replied, 'Although it is interesting and addresses an important and timely topic, I am sorry to say it was not accepted for publication. *Overall, we ranked the study's ability to provide confident conclusions lower than we usually aim.*' Presumably this was because the trial was open-labelled, done in close to real-world conditions, and in a diverse study population. But our trials told the world what would happen if the drug was used in the real world, rather than whether the drug worked better than a dummy version.

Attitudes are evolving. Reviewers, regulators, and guideline developers are becoming more appreciative of the power and value of pragmatic trials: the ante-diluvian view that the only worthwhile trial is a two-armed placebo-controlled, regulatory, efficacy trial is fading.

Epidemic and pandemic preparedness

A standing, adaptive trial infrastructure that is ready to test treatments within days or weeks of a new infection or strain emerging, rather than within the usual years to decade, should be an essential part of our pandemic preparedness and will bring evidence about antibiotics and new antiviral drugs to bear on clinical care far faster than if we set up a bespoke trial for each new drug. Using online eligibility check and remote randomisation, routine data for measuring outcomes, self-sampling of both blood and microbiology swabs, and an integrated approach where the clinical teams in clinics and general practices around the country build on their unique relationships with their patients to explore the possibility of trial participation, but linked also to a mechanism for enabling sick people to participate in research without having to leave home, brings together an exemplar approach of how primary care can deliver policy-relevant, clinically actionable findings at scale, and quickly enough to be meaningful within epidemics and pandemics.

A request for donations to the Bodleian library

After the worst of the pandemic had passed, the Bodleian Library asked us for donations that captured something of the people and their lived experiences of

contributing to the Oxford COVID-19 pandemic studies, including PRINCIPLE and PANORAMIC.

I'd heard of war artists and seen some of their work: their paintings and sketches are different from photographs of war scenes, in that they capture an individual's interpretation and experience of what surrounded them, rather than an attempt to accurately represent what they saw. My own father fought with the 6th South African Armoured Division during the Second World War in North Africa and in Italy, and I recently discovered some watercolours (literally) in an old leather suitcase under my bed that he had painted of bombed villages in Northern Italy during the winter of 1945. These pictures captured far more than the damaged, peopleless buildings, and the snow. They drew me into his mind space, the horror of war as he experienced it, his homesickness, the bleakness, his loneliness, the tragedy, and the cry for healing.

I'd also heard about 'writers in residence'. But nowhere had I ever heard of a clinical trial or trials unit having an 'Artist in Residence'. But what better medium than visual art could there be to answer the Bodleian's call to ... 'tell not only the story of the University's response to the pandemic, but also the story of a myriad of individual COVID-19 research studies, projects and trials that emerged across Divisions. We are interested in capturing the evolution of the research that took place; the successes, failures and challenges big and small along the way...?'

Tanya Poole; the world's first Trial and Trials Unit Artist in Residence?

I'd seen two series of Tanya Poole's ink images of people connected by a common purpose but who have different, complementary roles, contributions, and personalities. A series of palaeontologists hunting for fossils in the great Karoo included individuals of different colours, religions, social strata, and skill-sets, all linked together in a single, scientific endeavour of exciting discovery. A series of a participants in a karate class showed variation in shape, size, expertise, and colour among people who had come together to enhance their skills and discover through communal action.

Tanya's ability to simultaneously capture diversity and communality spoke to me. Her unique ink medium touches onto, but goes well beyond the photographic; she reveals the depth and complexity of each individual while connecting each image to the others in the series.

A vital aspect of PRINCIPLE and PANORAMIC was our aim to ensure external validity through maximizing diversity and inclusivity in the trial population. Thus the art needed to communicate this, on the one hand being representative, but on the other being able to get under skin, deep into the lived experience of the contributors that all gave so much, including the nurses, statisticians, methodologists, GPs, research professions in the networks, funders, officials, and of course the study participants from every corner of the UK.

We were therefore absolutely delighted when we were able to engage Tanya Poole to be our world-first, Trials and Trials Unit Artist-in-Residence, a wonderful opportunity for taking forward the public understanding of science and trials research. We spent time together in our Units and GP practices in Oxford and travelled to different parts of the country together, meeting the real heroes of these trials in person and online.

The way Tanya spoke to people and listened to their stories about the experience of COVID-19, the experience of doing clinical trials under the most difficult circumstances, of inclusivity, camaraderie, of them going the extra mile day after day, hearing their moving accounts of contributing, using novel research methods and implementation approaches, and immersed herself in their stories and experiences, left us all no doubt that this was the right artist for this unique commission.

Benefaction from the Five Star Group and Dream Capital, USA

We found generous and insightful patrons in the Five Star Group and Dream Capital. Anish and Ankit Govan, Managing Principals, immediately grasped the importance of these connections and understood the vision of what we were trying to achieve through this exhibition.

Tanya Poole

Artist



The greatest challenge in making *The Panoramic Principle* was to research and condense the intense, humanist and complex endeavour of so many people into an artistic body of work which could serve as an homage, a celebration and an archive for the PRINCIPLE and PANORAMIC trials of the Nuffield Department of Primary Care Health Sciences of the University of Oxford.

When Prof. Christopher Butler contacted me in regard to creating this archive, I knew so little about trials and how Chief Medical Investigators worked that I thought that I would come and visit a series of laboratories at the University of Oxford and be faced with reams of data, but instead I came to the UK and started a journey of meeting some of the most profoundly altruistic and diverse individuals that one could ever have the privilege to meet.

Prior to this project, I had been working with the idea of communities of people who existed and connected outside of the scope of more regular communities. Having been born in Canada and having grown up in the Middle East, the UK and South Africa,

I had often found myself either without a sense of community, or in communities that were constantly shifting (like expat communities) or rigidly formed and regulated (communities under Apartheid South Africa), and the idea of real and radical connection became one that I wanted to explore with intention. This started with my work with a group of adolescents who were in the process of transformation from being children to becoming adults, through some tricky and difficult psychological stages. After this body of work (*The Becoming Child*), my focus shifted to the dojo where I taught karate. Sport, surprisingly, was an area in which a speedier transformation and connection was taking place between people of different races in Post-Apartheid South Africa. The members of the dojo were of all ages, races, faiths and socio-economic backgrounds. The wearing of the white *gi* unified us and removed some of our external differences, and the hierarchy of the belts we wore often subverted ideas of value we attached to our 'outside the dojo' selves. Two series of portraits emerged from this wider idea: *The Audience* (which was part of a larger solo body of work

titled *Thozama and Rose* and which included 19 large-scale ink portraits of students and senseis of the dojo) which was exhibited at Galerie M in 2015 Germany and was selected by Tumelo Mosaka in 2017 for *Tomorrows/Today*, at The Cape Town Art Fair which featured 10 emerging artists from Africa and the Diaspora and focused on artists who explore notions of urban environment in distinct, thought-provoking ways, and *Who Are You?*, a series of 30 ink portraits of karateka, exhibited in Pretoria in 2015.

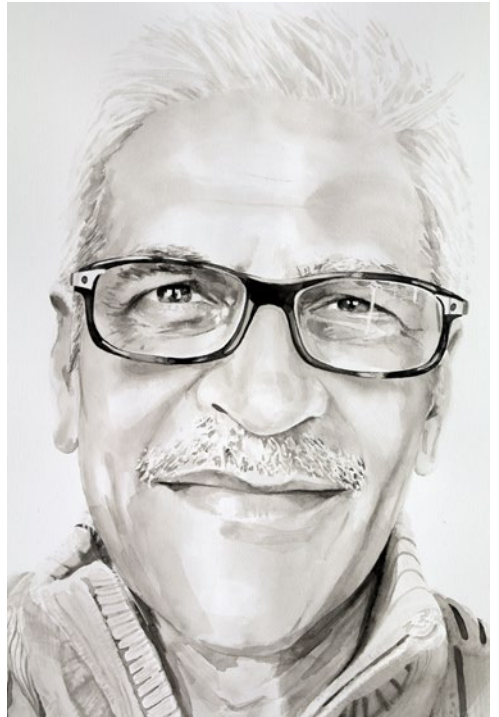
Later in my career, in 2016, having resigned as a Senior Lecturer in Art at Rhodes University in South Africa, I volunteered as an assistant to an all-female group of researchers and scientists at a palaeontology dig near Sutherland in the Cape, finding and researching plant and insect fossils from the Mid-Permian period. I learned how badly many of these women had been affected by embedded misogyny and racism in university and museum institutions. It was the time of the #MeToo movement, and our conversations centred around issues that had affected us in this area too. From this experience, and with a rereading of and homage to Rachel Carson's *The Silent Spring*, I created a group of 7 large-scale ink portraits, titled *The Researchers*, which were exhibited within my larger body of work, *The Whispering Spring* at Galerie M in Germany in 2018/2019.

In October 2023 I visited the UK from my studio in France and with the help of Prof. Chris Butler and Prof. Mahendra Patel, the Diversity and Inclusivity lead, I began meeting with people who were involved in the PRINCIPLE and PANORAMIC trials. I met people face-to-face and online. This was an information-gathering exercise and I realised quickly that I didn't need to know too much technically about the trials but that I did need to be alert and open to the people who were prepared to meet with me and the backstories that they shared when we met.

What started emerging was a sense of the scope and range of the trials through the people who were involved in creating and facilitating them, recruiting for them and participating in them. I began to gain an understanding of the sheer scale of human effort that it took to drive this project so far in such a compressed time-frame, I started to see the complexity of the whole, the networks of people and organisations who came together collaboratively, the intricate mechanisms of distribution that were overseen by tirelessly working organisers, the sacrifices that were made and the deep care that people took.



Professor Christopher Butler



Professor Mahendra Patel

Chris and I spoke about conceptually framing the archive as a series of portraits that could honour specific individuals but that could also serve as representatives for larger groups of people. There were hundreds of thousands of people who had participated in and contributed to the trials - we could never mention them all, let alone depict each one. Chris and Mahendra told me about their drive during the trials to reach deeply into all parts of UK communities - places where government messaging might not be reaching - to not only support people in this crisis time, but to also achieve access for the future of healthcare for all.

During this time of information-gathering, I met with a pharmacist from one of England's most economically deprived areas, with a young Paralympian who lives with Down Syndrome who, with his sister, campaigned for the trials. University students and the Provost from Bolton University who took on the recruitment campaign for their area shared their experiences, a cultural worker in Bradford who was a participant helped me understand the experience. I met doctors at their surgeries at the Windrush Clinic and in Cardiff, a group of medics came to meet me in a pub in Wales, doctors from England, Northern Ireland, Wales and Scotland gave up their time to speak to me. Individuals who created and supported the online technical support necessary explained the intense challenges, I heard about the many languages that information had been translated into, the nurses who had carried out their work in exceptionally difficult and high-risk circumstances, the spiritual leaders, the many people who worked on the trials who were there at the beginning, who burnt out, who were replaced by others who also burnt out. I met social media influencers who, on their platforms, helped in the recruitment drive. The different areas of expertise were multiple and the diversity of people in cross-section from Chief Medical Investigators to participants was incredible. I came away from this intense two weeks with a profound sense of the importance of connection, the value of community and the profundity of the truth that together we are much stronger than the sum of our parts.

At this point, having had a better understanding of the scope, scale and depth of the trials (which was so much more than I could have ever anticipated) I started what could only ever be an imperfect selection process, defined by the parameters of an exhibition and by time constraints. Reaching out to people I'd

met, I asked them to take photos of themselves for me to work from, I asked for eye-contact, warmth and a sense of connection, informality in their clothes and a quote from them on the trials that perhaps also could contain hints of their backstories. This methodology, which gave the 'sitters' agency over their representation mirrored the methodology of the trials, where participation was conducted online and telephonically, and only the drop-off of medication was done in person - meaning that the participant could literally contribute to the trials from their sickbed, without ever having to run the risk of spreading COVID-19 to others in places like clinics or surgeries. Many generously got back to me and as they did I started to paint a group of diverse people who were so important to the trials in their own right, but could also serve as stand-ins for larger groups within the PRINCIPLE and PANORAMIC trials.

Increasing the scale of the portraits meant that the 'sitters' can be seen as larger-than-life in a way that emphasises their symbolic nature: that they can be seen as significant beings in terms of their massive individual contributions and they can also hold representation for others (a doctor may represent her own contribution, she may also represent a community of other doctors and she could be seen as representing those who share her cultural heritage, for example).

Ink and paper, as materials, have the feel of Academia, of text and data and of archive, but they're equally able to describe the softness of skin and intelligence in the eyes. Pencilled text can conjure jotted thoughts and creative thinking and adds notes of each 'sitter': who they are and how their narratives intersected with the trials, their thoughts and experiences of the trials and their hopes for the future. These formal qualities of scale and medium and aesthetic integrate the individual portraits into a cohesive group, or a body of work. My hope is that this body of work will be able to open up for the viewer an intimation of the tremendous contribution, in a time of acute crisis and loss of life, of the individuals and communities who were involved in the PRINCIPLE and PANDEMIC trials. The progress that was made by these clinical trials is immeasurable in so many aspects and will have incalculable impacts on the future of research in healthcare. Every bit of this progress was made by individuals, who became a team, who became a community, who became communities and whose altruism makes them more than the sum of their parts.



The Panoramical Principle



Dr (Mrs) Oghenekome
Gbinigie-Thompson

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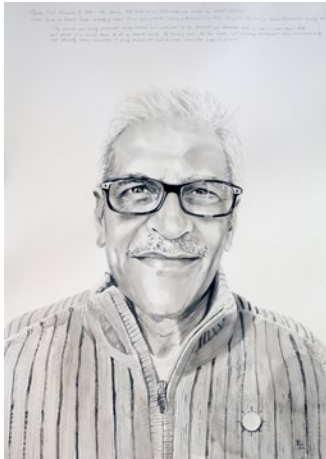
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*Dr. Oghenekome "Kemi" Abigail Gbinigie-Thompson, MA (Cantab), MB BChir, MRCP, DRCOG, DFRSH, PG Cert (Health Services),
DPhil (Oxon) Co-investigator in the MRCHEM and MRCHEM trials, University of Oxford.
8th of May 1986 - 28th of January 2024. In loving memory...*



Dr (Mrs) Oghenekome Gbinigie-Thompson

MA (Cantab) MB BChir MRCP DRCOG DFRSH PG Cert (Health Services) Dphil (Oxon)

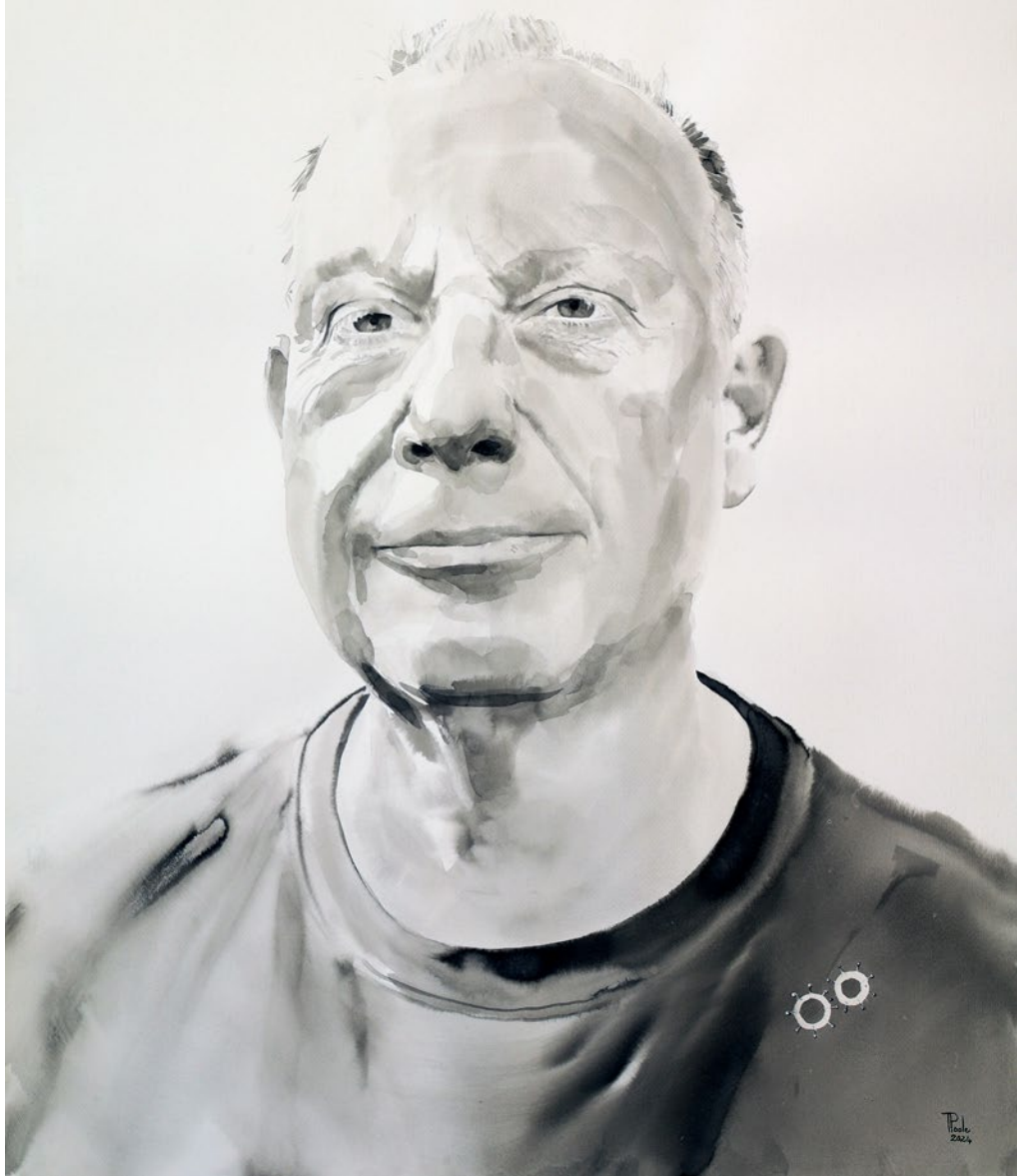
8th MAY 1986 – 28th JANUARY 2024

IN LOVING MEMORY



Dr. Mark Dolman, PhD MBA CChem MRSC, Deputy Chief Operating Officer, National Institute for Health and Care Research (Hames Valley and South Midlands).

"Working on this and other COVID-19 trials have been such rewarding work for the many Clinical Research Network staff involved being able to see the impact of the trial on the clinical decision-making within a short time of the conclusion of the study."



Dr Mark Dolman

PhD MBA CChem MRSC



'Working on this and other COVID trials have been such rewarding work for the many CRN staff involved being able to see the impact of the trial in the clinical decision-making within a short time of the conclusion of the study.'

Harkishan Mistry, participant.

"Bradford is a totally different community to what it was when I moved to England from Kenya in 1971 - it is now full of various and diverse communities. In Hinduism, *Seva* means selfless service, and being part in the PANORAMIC club was another way to help and contribute to the happiness and well-being of this diverse community we live in."



Harkishan Mistry

Participant



'Bradford is a totally different community to what it was when I moved to England from Kenya in 1971 – it is now full of various and diverse communities. In Hinduism, *Sewa* means selfless service, and taking part in the trial is another way to help and contribute to the happiness and well-being of this diverse community we live in.'

Dr. Nicholas P.B. Thomas BSc PhD MB ChB DCH DFSRH FRCGP . Clinical Director and Primary Care Specialty Lead - NIHR Thames Valley and South Midlands. Clinical Research Lead - Royal College of General Practitioners.

"The amazing thing about the trials is the way they changed clinical care across the world at a time when the world needed it - a simply incredible impact."



Dr Nicholas P B Thomas

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GP and Clinical Director and Primary Care Specialty Lead –
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'The amazing thing about the trials is the way they changed clinical care across the world, at a time when the world needed it – a simply incredible impact.'

Lady Anne Welch

Influencer and Sickle Disease advocate

"I was delighted to contribute to the success of The MIMEME and associated trials at Oxford University. This allowed for a diverse range of patient experiences and challenges to be addressed, emphasizing the importance of community-based engagement."



Lady Anne Welch

Influencer and Sickle Disease advocate



'I was delighted to contribute to the success of the PRINCIPLE and PANORAMIC trials at Oxford University. This allowed for a diverse range of patient experiences and challenges to be addressed, emphasising the importance of community-based engagement.'

Hazel Kirwin, participant

"I am so grateful to have participated in this trial personally, but also as a pharmacist working in the North East of England. I am hopeful that my contribution helped find more effective treatments for COVID-19, and helped widen access to treatment for my patients in one of the most deprived areas in the country."



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Rena Amin MPharm, MSc, IPresc, MFRPSII, FRPharms

"This trial (PRINCIPLE) enabled cultural inclusivity which was so vital for reaching out to hard-to-reach communities in evaluating existing treatments for the management of COVID-19. It establishes a need for community representation and demonstrates the importance of promoting equity in healthcare accessibility."



Rena Amin

MPharm, MSc IPresc MFRPSII FRPharms



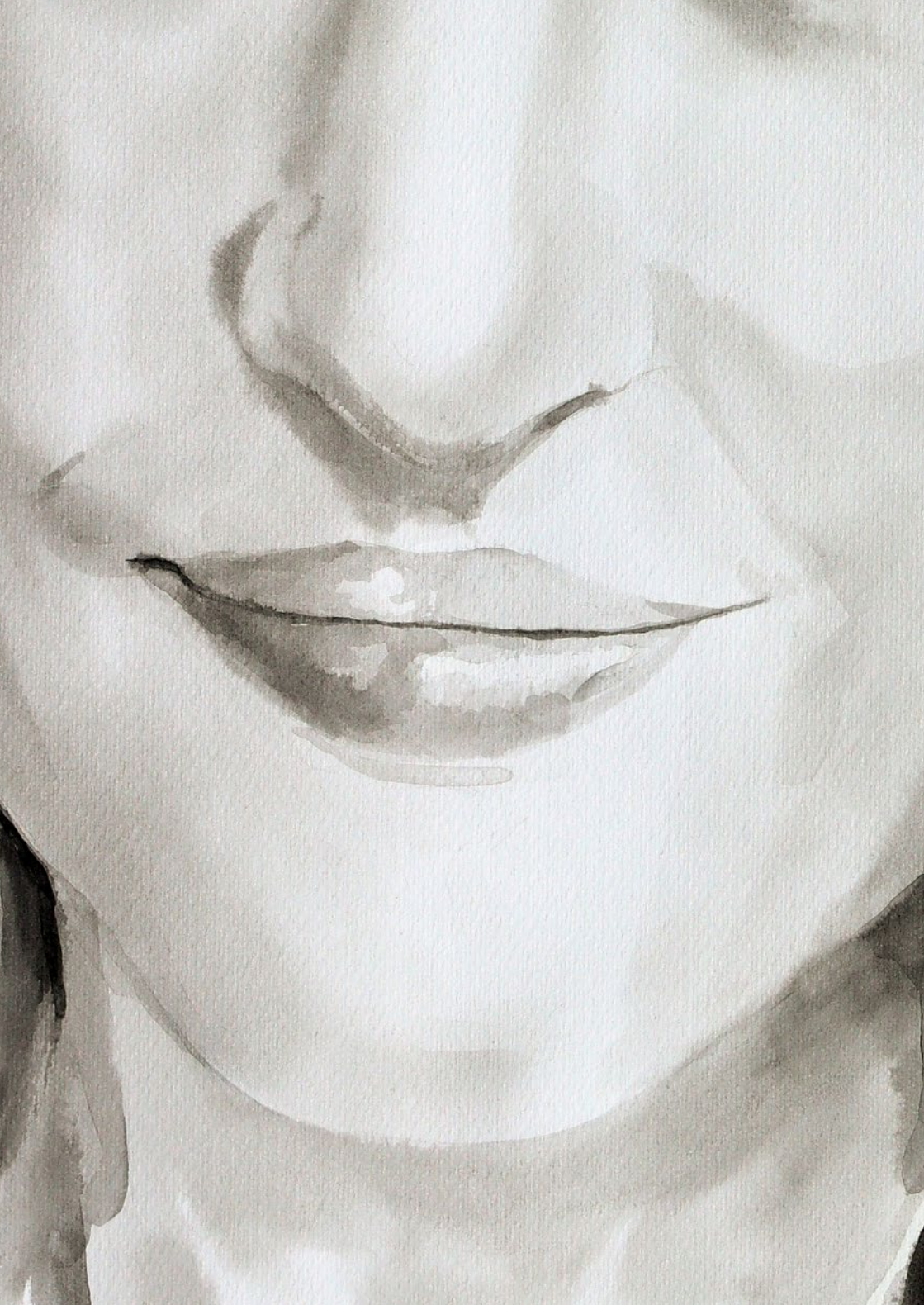
'This trial enabled cultural inclusivity which was so vital for reaching out to hard-to-reach communities in evaluating existing treatments for the management of COVID-19. It establishes a need for community representation and demonstrates the importance of promoting equity in healthcare accessibility.'

Lucy Cureton

Working on PANORAMIC is not like any other trial I've ever worked on. As with most COVID-19 trials, it is unpredictable and fast-paced, but the sheer size of PANORAMIC is what makes it so extraordinary. The trial has been designed to "take research to the patient." It is a complex and constant challenge.



Lucy Cureton



'My role as a Senior Trial Manager is to oversee the set-up and running of clinical trials within the Primary Care CTU. Working on PANORAMIC is not like any other trial I've ever worked on. As with most COVID-19 trials, it is unpredictable and fast-paced, but the sheer size of PANORAMIC is what makes it so extraordinary.



My role in PANORAMIC is more involved than it would be on a 'normal' study. The trial has been designed to 'take research to the patient', which means there are additional roles for the central trial team to cover. Once you add in the frequent meetings that are required to keep things running, the colossal task of dispensing study drugs from our CTU, and the additional complexities that come with running a COVID-19 study, it is a constant challenge. We have a fantastic trial team who all work tremendously hard to make PANORAMIC a success; I am consistently impressed with their creativity, dedication and resilience."

Dr. Harry Ahmed MB BCh MRCS MRCGP PGD (Epi) PhD

GP at Ramsey Primary Care Centre and Clinical Reader in Epidemiology at Cardiff University.

"HONORARIC had inclusivity embedded throughout, recruiting participants from across the UK, and crushing the concept of some research participants being hard to reach."



Dr. Harry Ahmed

MB BCh MRCS MRCGP PGD (Epi) PhD Cardiff



'PANORAMIC had inclusivity embedded throughout, recruiting participants from across the UK, and crushing the concept of some research participants being hard to reach.'

Bernadette Mundy RGN, DPSN Senior Clinical Research Nurse, Clinical Trials Unit, University of Oxford.

"There is so much to reflect on and so much to be proud of. It was an incredible time to have worked for the health service, to be a nurse and to be a key cog in the huge research wheel that was constantly turning like most healthcare workers, we had to change and adapt the way that we worked. The changes were sudden, unpredictable and unplanned. The effort and perseverance were immense. We worked in the most challenging of times; the world was in turmoil, people were frightened and it was very difficult. The workload was relentless and the pressures and responsibilities at times, felt enormous.

The early days on the days that really stand out in my memory. One of us knew what lay ahead so how long this would last, we only knew that there was an incredible urgency to get reliable treatments that would prove a way through the world to those every day, it often felt like we were working in the dark. We were a small team, coming on duty to the Clinical Trials Unit while most of the population were confined to their homes. There were no reliable medicines or vaccines that could be used to treat COVID-19 and the only ray of sunshine was research. I thought, we were being run around by mad doctors whilst they were still in our hospital premises. There was no compromise and the only ray of sunshine was research. It was important work on a global scale. The lessons we learned in research paved the way for AstraZeneca. The number of participants safely recruited to both trials will amaze me. But it is far more than that; anyone in the UK team played their part. Together we celebrated the highs and supported each other through the lows. It made us a stronger team. I am honoured and privileged to have been part of this journey with the multi-disciplinary team at the CTU - led so compassionately and expertly by Chris."



Bernadette Mundy

RGN DPSN

Senior Clinical Research Nurse, Clinical Trials Unit, Oxford University



'There is so much to reflect on and so much to be proud of. It was an incredible time to have worked for the health service, to be a nurse and to be a tiny cog in the huge research wheel that was constantly evolving. Like most healthcare workers, we had to change and adapt the way that we worked. The changes were sudden, unpredictable and unplanned. The effort and perseverance were immense. We worked in the most challenging of times, the world was in turmoil, people were frightened and it was very difficult. The workload was relentless and the pressures and responsibilities, at times, felt enormous.



‘The early days are the days that really stand out in my memory. None of us knew what lay ahead or how long this would last. We only knew that there was an incredible urgency to find reliable treatments that would pave a way through the woods. In those early days, it often felt like we were working in the dark. We were a small team, coming in daily to the unit while most of the population were confined to their homes. There were no reliable medicines or vaccines that could be used to treat COVID-19 and the only ray of sunshine was research. In PRINCIPLE, we were testing new aspects of trial delivery whilst they were still in our thought processes! There was no comparative trial to refer to, every aspect of PRINCIPLE was innovative. It was important work on a global scale!

‘The lessons we learnt in PRINCIPLE paved the way for PANORAMIC. The number of participants safely recruited to both trials still amazes me. But it is far more than that, everyone in the CTU team played their part. Together we celebrated the highs and supported each other through the lows. It made us a stronger team. I am honoured and privileged to have been part of this journey with the multi-disciplinary team at the CTU-led so compassionately and capably by Chris.’

Professor Nigel Hart, MD MMedSc FRCGP, Associate Director for General Practice and Primary Care, Centre for Medical Education, Queen's University, Belfast.
"Being involved in PIONEERIC taught us all about the great achievements that come from collaborative endeavour, team harmony. It was a privilege to be part of the team and sets the path for our future direction."



Professor Nigel Hart

MD MMedSc FRCGP

Associate Director for General Practice and Primary Care Centre for
Medical Education, Queen's University, Belfast



'Being involved in PANORAMIC taught us all about the great achievements that come from collaborative endeavour; teams transcend. It was a privilege to be part of the team and sets the path for our future direction.'

Jemima Browning and Will Browning - Social media campaigners and sharers of lived experiences to make the trials accessible for those with learning disabilities.

Jemima: "It was an honour to be part of these trials. It is very important to us to continue to create equal opportunities for those with disabilities and to make sure that reasonable adjustments are offered in healthcare to make it accessible and tailored to the needs of everyone."

Will: "I am proud to use my voice and I want to help other people like us get the same help as everyone else."



Jemima Browning and Will Browning

Social media campaigners and sharers of lived experiences to make the trial accessible for those with learning disabilities. Paralympian.



Jemima: 'It was an honour to be part of these trials. It is very important to me to continue to create equal opportunities for those with disabilities and to make sure that reasonable adjustments are offered in healthcare to make it accessible and tailored to the needs of everyone.'

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Paper: Ly, Mee Yu, DPhil, Professor of Clinical Trials and Biostatistics, Lead Statistician of AMOROUS

"Being part of this amazing and meaningful journey has been truly inspiring. The innovative methods we used in these trials during the pandemic have not only yielded success but have also become a guiding light for the future. Our collective efforts have reshaped the landscape of trials in primary care, demonstrating efficiency and agility in generating crucial evidence promptly. This milestone marks not just a moment in time but a testament to our commitment to advancing health care and setting a precedent for more efficient and impactful trials in the future."



Prof Ly-Mee Yu

DPhil

Professor of Clinical Trials and Biostatistics

Co-Director of Primary Care Clinical Trials Unit, University of Oxford.



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Professor (Dr) Mahendra G Patel OBE BPharm PhD FHEA Alumni FNICE FIPA India FIOPM Hon DHealth FRPharmS

Director, Centre for Research Equity, University of Oxford, Henry Hall of Health, University of Bradford, Visiting Professor, Birmingham City University, Adjunct Professor, Johns Hopkins, USA

"The inclusion and diversity recruitment strategy developed and implemented for the PRINCIPLES and BARRIERS trials has been a success beyond belief and serves as a crucial lesson to all on research equity. By reaching across the gaps, barriers and recruiting participants from socioeconomically and ethnically diverse communities it greatly informs how hard-to-reach communities simply do not exist."



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Director, Centre for Research Equity through pharmacy, communities and healthcare.
Nuffield Department of Primary Care Health Sciences University of Oxford



'The inclusion and diversity recruitment strategy developed and implemented for the PRINCIPLE and PANORAMIC trials has been a success beyond belief and serves as a crucial lesson to all in research equity.

By reaching across the four nations and recruiting participants from socioeconomically and ethnically diverse communities it firmly confirms how hard-to-reach communities simply do not exist.'

Christopher Butler, FMedSci, Clinical Director, Primary Care Clinical Trials Unit, University of Oxford:

"The PRINCIPLE and the ongoing PANDEMIC trials have innovated in: trial design (by using novel adaptive platform designs); trial delivery (by complementing traditional site-based recruitment ('the patient comes to the research'), with mechanisms to enable sick, or frail, people to participate without having to leave home ('taking research to the people'), and by addressing the 'inverse research participation law' which highlights disproportionate barriers faced by those who have the most to contribute, and benefit from research, and; - transforming the evidence base by evaluating new medicines to support guidelines and care decisions world-wide for COVID-19 and contribute to antimicrobial stewardship. PRINCIPLE and PANDEMIC represent models of innovation and inclusivity, and exemplify the potential of primary care to lead the way in addressing pressing global health challenges."



Christopher Butler

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Clinical Director, Primary Care Clinical Trials Unit, Oxford University.



'The PRINCIPLE and the ongoing PANORAMIC trials have innovated in: trial design (by using novel adaptive platform designs); trial delivery (by complementing traditional site-based recruitment ('the patient comes to the research') with mechanisms to enable sick, infectious people to participate without having to leave home ('taking research to the people'), and by addressing the 'inverse research participation law,' which highlights disproportionate barriers faced by those who have the most to contribute, and benefit from, research, and; in transforming the evidence base by evaluating nine medicines to support guidelines and care decisions world-wide for COVID-19 and contribute to antimicrobial stewardship. PRINCIPLE and PANORAMIC represent models of innovation and inclusivity, and exemplify the potential of primary care to lead the way in addressing pressing global health challenges.'

"The structure and processes have responded to unprecedented challenges in primary care research, setting and benchmarks in complexity, intensity and scale. The trials were for their subject matter design, which for the rapid evaluation of multiple treatments during a critical time in the pandemic, working in the first in primary care. The scale of these trials was staggering. Transitioning from research trials with the participants in a single and dense of a 2-3, to efforts involving hundreds of team members and engaging with up to 99,000 and across and across registration in a single day, required a monumental shift in how to develop evidence and evidence and process, working through night and weekend to bring our data to the front-line. The information required was massive, spanning across specialties and demanding significant external resources from various sources, especially during the most challenging times of the pandemic. Yet, it was these very challenges that showcased the resilience, dedication and selflessness of the staff and participants alike. They were essential and participants actively all they personally invested in the hope that they can make a positive difference and help others. The long-term impact of these trials in primary care research should be substantial. They demonstrated what is possible in terms of trial design, trial, recruitment, trial and trial public engagement. More than the benchmarks established, these trials can be viewed as a landmark in what can be achieved under the most demanding circumstances. They have inspired the expectation of what primary care can achieve and should that the public will step up in incredible numbers when given an opportunity to contribute and help. I am immensely proud to have been part of the research and I think it's fair to say that the work itself, I am proud to have collaborated with an incredibly selfless group of colleagues and participants. The collective efforts have not only advanced medical research, but also exemplified the profound impact of collective resilience and sacrifice in the face of adversity."

Micheál McKenna, Clinical Systems Manager, Clinical Trials Unit, Belfast Department of Primary Care, University of Belfast, and Research Lead



Micheál McKenna

BSc BEng
Clinical Systems Manager



‘The PRINCIPLE and PANORAMIC trials represented an unprecedented challenge in primary care research, setting new benchmarks in complexity, intensity, and scale. These trials, unique for their adaptive platform design, allowed for the rapid evaluation of multiple treatments during a critical time in the pandemic, marking a UK first in primary care.

The scale of these trails was staggering. Transitioning from managing trials with 500 participants in a year and teams of 5-6, to efforts involving hundreds of team members and engaging with up to 80,000 web visitors and 17,000 registrations in a single day, required a monumental shift. We had to develop entirely new systems and processes, often working long hours, through nights and weekends, to build and refine these systems in real-time.

The collaboration required was immense, spanning across specialties and demanding significant personal sacrifices from everyone involved, especially during the most challenging times of the pandemic. Yet, it was these very challenges that showcased the resilience, dedication, and selflessness of the staff and participants. When staff were exhausted and participants seriously ill they personally sacrificed in the hope they can make a positive difference and help others.

The long-term impact of these trials on primary care research cannot



be overstated. They demonstrated what is possible in terms of trial design, scale, recruitment speed, and direct public engagement. More than the treatments evaluated, these trials are a testament to what can be achieved under the most demanding circumstances. They have shifted the expectations of what primary health care can achieve and showed that the public will line up in incredible numbers when given an opportunity to contribute and help.

I am immensely proud to have been part of the PRINCIPLE and PANORAMIC trials. More than the work itself, I am proud to have collaborated with an incredibly selfless group of colleagues and participants. Our collective efforts have not only advanced medical research but also exemplified the profound impact of collective endeavor and sacrifice in the face of adversity.'

Richard Hobbs - Mercian Professor of Primary Care, Head, Nuffield Department of Primary Care, University of Oxford

"The PENSURE and PANCRASIC trials were an outstanding example of UK competitiveness in science - addressing globally important answers to key questions during a global pandemic and doing so quickly and efficiently. And an outstanding partnership between Oxford Primary Care, NHS GP practices, patients and the public, NHS data suppliers and the government funder."



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Acknowledgements for *The Panoramic Principle*

We are grateful to the funders, clinicians, research professionals, administrators, oversight committees, trial managers, data managers, IT professionals, statisticians, methodologists, regulators, government officials, Health Departments, and The NHS in all four UK nations that contributed to *The Panoramic Principle* through sharing their resources, knowledge, experience and stories. We thank the over 40,000 thousands of individuals who contributed to the PRINCIPLE and PANORAMIC trials through their generous participation - this exhibition is a tribute to and a celebration of every one of these participants. I am particularly grateful to the people listed below, most of whom have shared their time and recollections with me.

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Prof. Ly-Mee Yu

Nigel Mullins
Sophie Mullins-Poole

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‘Supporting this project of Clinical Trials Unit at the University of Oxford was essential for us, given the profound impact of COVID-19 globally. Partnering with Professor Mahendra Patel and other esteemed researchers reflects our commitment to advancing healthcare and promoting well-being, aligning with our ethos as a progressive hospitality company. We’re honoured to contribute to the remarkable efforts of the Clinical Trials Unit, the UK-wide PRINCIPLE and PANORAMIC collaboration, and the Centre for Research Equity, led by Professors Mahendra Patel and Chris Butler, and eagerly anticipate advancements in this vital research.’

Anish Govan – Managing Principal
Ankit Govan – Managing Principal
Five Star Group
Dream Capital

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