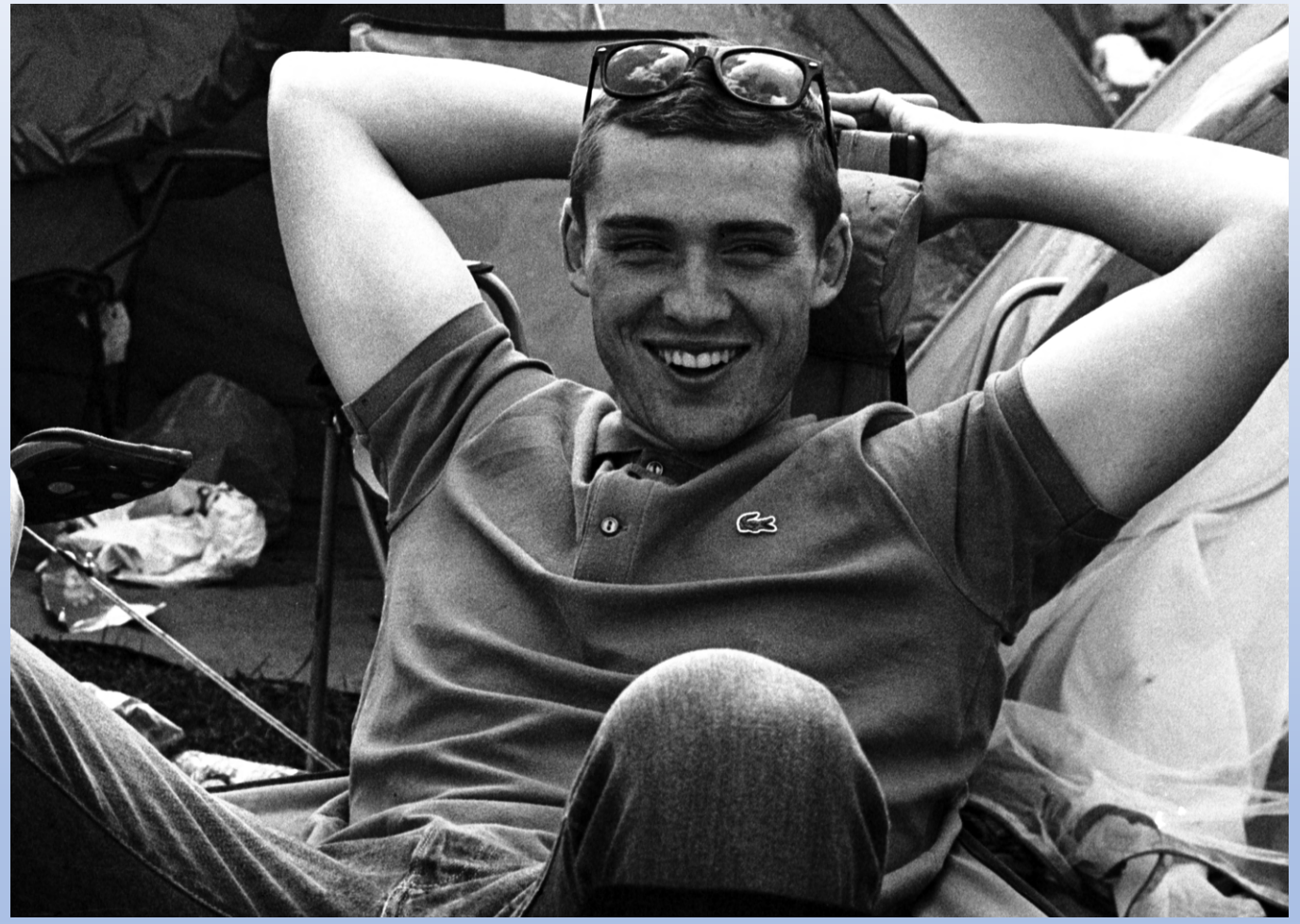
Alexander Jansons Myocarditis UK

Research Strategy 2020 – 2025

Finding Tomorrows Cures Today



Alexander Jansons Myocarditis UK was founded in July 2013. The charity, originally known as the Alexander Jansons Fund, was set up after the death of Alexander Jansons at age 18.

At the time, there was little to no information available on this inflammatory heart condition and the Jansons family vowed to rectify this situation.

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Forward

When the charity was founded in 2013, the Jansons family could not have predicted the success that they would achieve in both raising the funds needed to fund research, but also the esteem that the charity would gain in cardiovascular circles

Despite the successes achieved in research till now, Myocarditis remains a mostly undiagnosed cause of acute heart failure, sudden death and chronic dilated cardiomyopathy

Myocarditis is an inflammatory condition affecting the heart. It is usually due to a virus but increasingly is recognized to have a genetic basis. It causes heart failure, sudden death and major rhythm disturbances. It appears to do this through an effect on the body's immune system. Much is still not understood about the condition including how common it is and why viruses are the cause of the condition. One thing we do know about myocarditis is that it can be acute, subacute, or chronic, and there may be either focal or diffuse involvement of the myocardium. In symptomatic patients, the cardiac presentation is frequently one of acute heart failure, although a syndrome mimicking acute myocardial infarction or a tachyarrhythmia, including sudden death or high – grade heart block may occur.

Our research strategy reaffirms Alexander Jansons Myocarditis UK commitment to excellence and places a great emphasis on funding the most talented scientists at all stages of their career. We will continue to fund research that ranges from expanding our current research and taking new steps in identifying genetic markers and clinical research on patients. We will expand our current strengths, such as conducting our research on a national scale as well as being able to offer the continued patient support framework that we have become known for.

New funding streams will be devised to support continued international collaboration between Dr Sanjay Prasad, Royal Brompton and Harefields Hospital and Professor Langor, MIT. We hope that our efforts, together with Professor Langor who is regarded as one of the worlds leading Bioengineers, will start to yield notable progress in nanoparticle drug delivery to further improve the treatment of patients with Myocarditis. Further funding will also enable us to provide a monitored and regulated support network for those diagnosed with myocarditis

AJMUK and the funding we provide to research is totally reliant on the generosity of people who donate their time and money to our cause. We are a 100% profit free organization and all our funds go directly to researching the causes, treatments and cures for myocarditis.

I hope you agree that our track record thus far and our vision for the future make a compelling case for continuing to support Alexander Jansons Myocarditis UK.

Andy Jansons

Chair of Alexander Jansons Myocarditis

OUR RESEARCH STRATEGY 2020-2025

EXECUTIVE SUMMARY

In the coming years we will strive to maintain our minimum amount pledge by continuing to fundraise as a charity to as well as to make forays into additional revenue streams to increase the resources available for continued medical research

We remain committed to supporting the best researchers funding research into all forms of myocarditis, and funding only research that is judged to be excellent through independent review. We have also identified new initiatives and areas in which we could support myocarditis research to accelerate progress. Four approaches outline how we will achieve our objectives:

OUR OBJECTIVES FOR OUR RESEARCH STRATEGY ARE

- Continue to close the current gaps in our knowledge. Considerable progress has been made at research level in our understanding of the molecular pathophysiology of myocarditis but, at the clinical level, myocarditis has been resistant to successful scientific inquiry.
- Further understand and explore the potential genetic basis to include a clearer understanding of genetic and biomarker determinants of ventricular Remodeling and the effects this has on survival in myocarditis.
- Increase the support, understanding and awareness of myocarditis to further improve patient care.

Forging Partnerships:
We will support research collaborations across borders and disciplines and where feasible, join forces with other funders to support a more comprehensive and in-depth research programs

Targeting unmet needs:
We will support research by informaticians, nurses and allied health professionals to not only increase research capacity but to share knowledge with linked cardiovascular services.

Fighting all forms of Myocarditis:
We will continue to support research into myocarditis in all its forms, whether common or rare.

From petri dish to patient:
We will continue to fund research including clinical studies, population studies looking specifically at facilitating the translation of research into patient care.

AJMUK RESEARCH

A STRATEGIC FOCUS

In 2013 we first outlined the need for an in-depth study and deeper understanding of myocarditis. At the time, there were no targeted treatment therapies for patients showing deterioration specific to inflammation. The challenges in treating patients with this condition on limited knowledge allowed us to begin to identify the basis for funding research. It was these markers that allowed us to begin to define and reaffirm the central role of the research by committing to:

- Identifying the challenges in treating patients with myocarditis.
- Improve our understanding.

The need for research

Whilst virus infections are common, and the vast majority of patients will recover spontaneously, what remains unclear is why some patients should develop inflammation of the heart – often with devastating consequences. The predisposition of some patients, either because of risk factors or a genetic marker to develop myocarditis, and the drugs used to treat and improve the outcome, remains crucial.

Research is central to our mission to spread the awareness and create a widely shared knowledge base so that we can ultimately save more lives.

What, and how, we fund

- Alexander Jansons Myocarditis UK is a 100% nonprofit charity with the sole aim of creating awareness and funding research. We have been working, since 2013, closely in partnership with The Royal Brompton and Harefields Hospital, to establish a research program that will allow us to both further improve our understanding of myocarditis and to formulate the best strategy to achieve our aims.

- We have raised and provided funds that have seen the creation of a national registry to identify how common myocarditis is and to be able to follow patients from diagnosis through to recovery. In an initial cohort of six key hospitals, within London, to undertake cardiac MRI and the collection of blood samples for biomarker analysis to determine which are most predictive of disease severity and clinical outcomes at an early stage. Funded research has allowed us to provide pilot data so that we can establish if there is a genetic predisposition or aetiology causing myocarditis.

- We are a response –mode funder, believing that the most effective way of fully understanding myocarditis and providing viable treatment and support to patients, is to allow the research community to identify the gaps in knowledge and generate the research ideas and approaches to best fill those gaps.

Outlining the need for Research

According to the World Health Organization/International Society and Federation of Cardiology (WHO and ISFC) definition and classification system, myocarditis is an inflammatory disease of cardiac muscle, usually diagnosed on endomyocardial biopsy (EMB) by established histological, immunological and immunohistochemical criteria.

Myocarditis can be acute, subacute or chronic, and there may be either focal or diffuse involvement of the myocardium. In symptomatic patients, the cardiac presentation is frequently one of acute heart failure (HF), although a syndrome mimicking sudden acute myocardial infarction or a tachyarrythmia, including sudden death, or high – grade heart block may occur.

Myocarditis refers to the clinical histological manifestations of a broad range of pathological immune processes in the heart. Alterations in the number and function of lymphocyte subsets and macrophages and antibody-mediated injury are typically found in patients with acute and chronic myocarditis. The immune reaction in the heart causes structural and functional abnormalities in cardiomyocytes, which in turn leads to regional or global contractile impairment , chamber stiffening, or conduction system disease. It is an underdiagnosed cause of acute heart failure, sudden death and chronic dilated cardiomyopathy.

Myocarditis is a challenging diagnosis to make due to the heterogeneity of clinical presentations.

The Impact Of Our Research

Our first step towards forming our new research strategy was to conduct an in-depth review and complete update of our current research achievement so that we may evaluate how far we have come and where best to prioritize our research moving forward.

The short-term prognosis of acute myocarditis is usually good but varies widely according to the underlying artiology (Caforio et al,2013) Those patients who initially might recover develop recurrent dilated cardiomyopathy and heart failure, sometimes years later. Because myocarditis presents with non-specific symptoms including chest pain, dispnoea and palpitations, it often mimics more common disorders such as coronary artery disease. In some patients, cardiac MRI and endomycardial biopsy can help identify myocarditis, predict risk of cardiovascular events and guide treatments. Outcome and prognosis of myocarditis depends on aetiology, clinical presentation and disease stage. Acute myocarditis resolves in about 50% of cases in the first 2-4 weeks, but about 25% will develop persistent cardiac dysfunction and 12-25% may acutely deteriorate and either die or progress to end stage DCM with a need for heart transplantation. Biventricular dysfunction at presentation has been reported as the main predictor of death.

Our increased knowledge and understanding of myocarditis in all its forms has enabled us to confidently raise awareness about this condition. We have helped by numerous people either by offering support as they come to terms with their diagnosis or that of a loved one, offering comfort by providing information that they were unable to have access to and in saving lives as medical staff are better informed and equipped to make improved diagnosis.

A Strategic Review

- The research that we have funded has allowed us to gain valuable insight into the incidence and prevalence of myocarditis in the UK as well as to understand and further improve how myocarditis is presently diagnosed, assessed and treated within the UK.

- Our biobank of patients with myocarditis has enabled us to make advances in the determining of risk markers (including genetic) and to begin to understand if certain candidate genes eg titin, predispose to greater adverse remodeling after disease onset.

- Since beginning in 2013, understanding the scale of myocarditis and correctly assessing the current UK practice with regards to diagnosis, treatment and management has been a key element in our research. We established strong links and direct contact with cardiology units, as well as with A and E units, to gauge the scale and to collect data. Working closely with patients and researchers, we have been able to better address patient concerns.
- Thus far, our research has been historical and anecdotal with little accurate insights into how common myocarditis is in the UK and virtually no data on the geographical and gender or age spread within the UK.
- Genetic and biomarker determinants of Ventricular remodeling and survival in Myocarditis is of vital importance as we are recognizing that dilated cardiomyopathy – one of the most important consequences of myocarditis is NOT just a random occurrence but underpinned by a gene abnormality.

OUR RESEARCH STRATEGY 2020 -2025

OBJECTIVES

The objectives of our research strategy are to:

- Discover the reasons why patients get myocarditis and how many develop this condition each year.
- To decipher what is happening at cell level to cause patients with myocarditis to develop heart failure and major rhythm disturbances
- Explore and support the psychological impact of myocarditis on patients and the need for increased awareness.

FORGING PARTNERSHIPS

The Alexander Jansons Myocarditis UK charity strongly supports the ethos of investing in the careers of promising young scientists through to established senior staff with a wealth of experience to offer.

By conducting an in-depth research strategy we were able to contact and make use of skills and information within the NHS to help us achieve our mission of further awareness and increased information and understanding on myocarditis.

In the UK, one young person dies suddenly each week due to undiagnosed myocarditis and heart transplantation is required in 1%- 8% of patients. Myocarditis can affect the heart’s ability to pump and the heart's electrical system, causing abnormal heart rhythms. It is thought to be due to an overreaction of the body’s immune system and currently we do not have specific treatments. Many patients with myocarditis get better but in a third of patients the heart becomes weaker and enlarges (dilated cardiomyopathy). This represents an important indication for cardiac transplantation and therefore early detection and treatment are key priorities.

Following valuable discussions with our patients and the Jansons Trust, we have devised a study to focus on patients with advanced heart failure following myocarditis to understand why some individuals may be more susceptible to rapid progression to dilated cardiomyopathy. This will be addressed by identifying the proteins present within the heart and blood of affected patients to know if there is a protein signature that could provide insights into disease progression and recovery. This knowledge could lead to better ways of predicting which patients are at higher risk of deteriorating or dying after an initial episode of myocarditis as well as to new potential treatments. This ambitious project would not be possible without the support and inspiration offered by the Jansons Trust.

Dr. Alma Iacob BMBCh, MA (Oxon), MRCP

Clinical Research Fellow

Imperial College London and The Royal Brompton and Harefield NHS Foundation Trust.

“There are currently no targeted therapies for myocarditis. I am interested to develop novel therapies and medicines for myocarditis research. The Jansons foundation were integral to support me in developing this hypothesis and understand the mechanisms of how this devastating disease effects the heart . Using cellular models we were able to now for the first time we have developed and identified drugs that we see are able to have an effect in reversing many of these processes. Such an ambitious project in the space of a few years would not have been possible without the bold plans and agility of the Jansons trust . ”

-Dr Rameen Shakur MD PhD(Cantab)

Massachusetts Institute of Technology

Boston

USA

We value the contribution of every staff member to patient care and will continue to forge ongoing and sustainable partnerships within the NHS.

Over the next 5 years we will:

Unite National Collaboration

Alexander Jansons Myocarditis UK has been asked by the British Heart Foundation to lead a national program of research into myocarditis and this will allow us to take forward findings from all our research endeavors into a UK based national study. This will include 7 key themes to address which patients get myocarditis, why do they get it and what to do about it. A clinical trial is planned to look at new treatment into myocarditis. This will involve a collaboration of around 15 large UK centers.

Support Healthcare Researchers

Our research is delivered by a diverse and multi-skilled set of team members and we will continue to allow for opportunities for aspiring researchers to join us in understanding myocarditis. We understand that there are many diverse fields in treating myocarditis from diagnosis, to research through to the mental health impact on patients and all of these will be made available to healthcare professionals in these fields to lead research in their specialist areas and improve the quality of care for patients with myocarditis.

Support Our Researchers and Build Relationships

Dr Alma Iacob will continue the work of Dr Amrit Lota with a focus on studying patients with severe myocarditis requiring a transplant or artificial heart pump. Alongside this, she will be looking at understanding why the heart has been so badly affected by myocarditis. We will continue to utilize the data gathered from MIT in our search for a myocarditis cure.

FIGHTING ALL FORMS OF MYOCARDITIS

Alexander Jansons Myocarditis UK funded research has enabled progress to be made in a much misunderstood and under-funded area of cardiovascular research.

Our new strategy aims to reinforce our commitment to funding high-quality research into all forms of myocarditis so that we can understand how many UK patients are affected each year, how many patients develop myocarditis and what is happening at cell level to cause myocarditis to develop into heart failure and result in major rhythm disturbances.

Who has and who will develop myocarditis?

Thus far, our data has been historical and anecdotal with little accurate insights into how common myocarditis is in the UK and there has been virtually no data on the geographical and gender spread within the UK

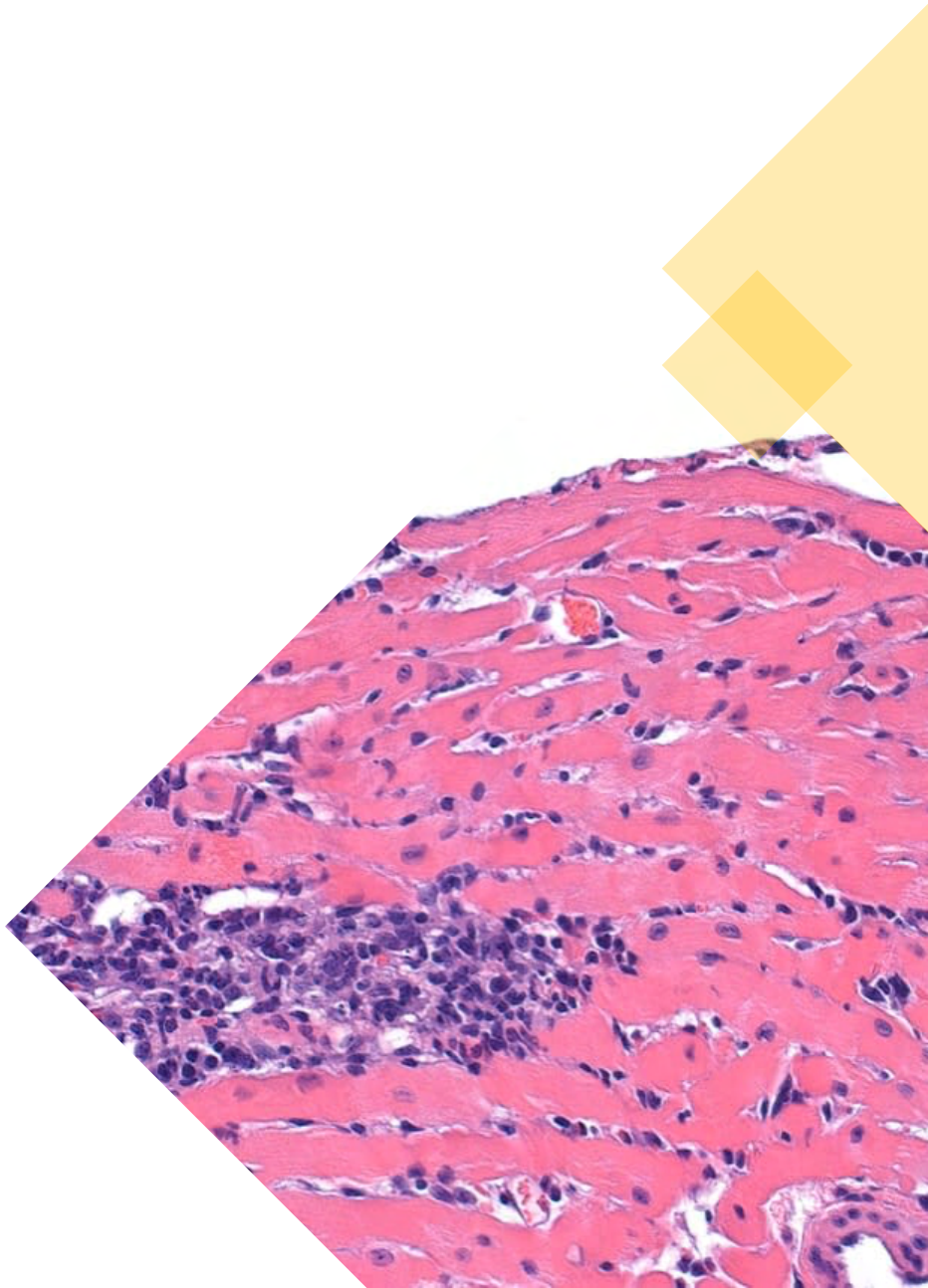
We have tackled this issue by working with NHS Digital to obtain 20 years of anonymized medical records for patients hospitalized with myocarditis and where this word was used in their discharge code. This, for the first time, allows us to see the geographical spread of myocarditis across the UK, the gender differences, how long patients were hospitalized for as well as mortality figures. We also have been able to obtain from this data on seasonal trends and what tests were performed. For the first time, we show accurate data for the number of patients hospitalized with myocarditis in the UK and how there is a significant gender imbalance – more commonly affecting men with certain months seeing large surges. After 2 years, we now have data on days in hospital and mortality rates.

Over the next 5 years we will interrogate this data further using support from data scientists to understand why there are more affected patients in SE England than anywhere else - are these detection rates, availability of tests such as MRI scanners or is it a genuine reflection of the status – it informs education on medical teams, resource planning, awareness campaigns and areas where policy and research should focus.

Why do patients get myocarditis

- Increasingly, we are recognizing that dilated cardiomyopathy – one of the most important consequences of myocarditis - is not just a random occurrence but underpinned by a gene abnormality. Knowing if a patient is at risk of myocarditis could allow much earlier identification of the risk to the patient, better risk stratification and potentially (although far away at this time) a cure.
- We have studied a large cohort of patients with myocarditis and used next generation gene sequencing to understand with high accuracy if patients have a gene defect that we now know predisposes to different types of heart disease.

The next 5 years will be crucial to our understanding that in a subset there is a gene abnormality that disproportionately associates with myocarditis compared to healthy normal control populations. We will continue to verify this in an unrelated and independent cohort of patients from the Netherlands to see if these findings are replicated.



Myocarditis at Cell Level

Understanding cellular changes in the heart due to myocarditis will help understand which pathways are mainly affected and in turn therefore, which treatments may help to reverse these changes. It is also crucial to understand how get these treatments to the right place and at the right dose.

Rameen Shakur has been working in Professor Robert Langers lab at MIT, Boston. Rameen has been looking at cell models to understand signals within the cell using human “engineered” cells where he has constructed a scaffold system to bring the many different types of cells seen in the heart in an artificial organ.

The research conducted by Rameen Shakur and MIT has resulted in myocarditis being studied extensively by one of the best scientists in the world. Once the data has been analyzed we would aim to include a clinical trial one of the potential treatments identified.

TARGETING UNMET NEEDS

The importance of early and better recognition of individual patient risk would allow much better monitoring, more aggressive medical therapy whilst simultaneously offering increased reassurance to those patients likely to do well and recover.

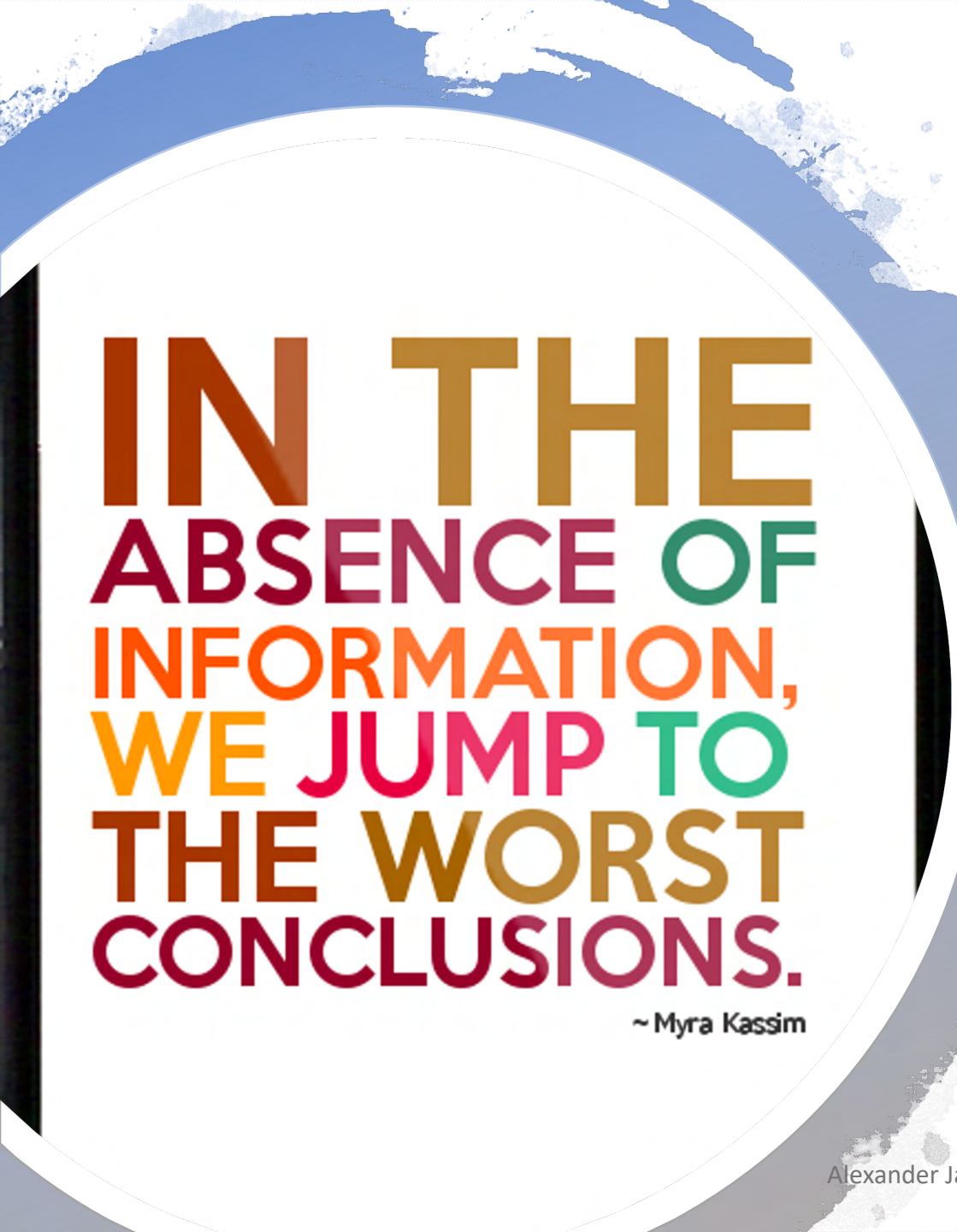
Our research undertakings until now have enabled us to build a multidisciplinary team looking at protein, metabolite and imaging markers to identify and build a “signature” of recovery. This has been made possible by establishing a large biobank of patients with confirmed diagnosis of myocarditis over the last 5 years. These patients have then been followed up over time to to see which model best predicts recovery and deterioration. The model will combine all the data available on the patient including from all routine tests as well as the above markers to allow precision characterization of patients.

The next phase of the research is to begin accurate and detailed analysis of both the protein and metabolite markers and to combine this with further research using the data from our work on genetics to allow us to identify and research the treatments towards the abnormalities identified.

COVID19 has had a huge global impact with the numbers of patients affected. The overall burden of myocarditis in this cohort is approximately 7%.

The majority are mild however the need for further investigation using a community-based study to understand how the larger cohort of mildly ill rather than hospitalized or severely ill patients have been affected and whether it causes any long-term effects.

Over the next 5 years we plan to look at the impact of COVID19 on the number of NHS admissions across the UK and to separately continue to update data on the number of national admissions across the UK due to myocarditis.



FROM PETRI DISH TO PATIENT

The Psychological Impact of Myocarditis

Alexander Jansons Myocarditis UK has always prided itself on their ability to understand both the need for research and awareness. Initial feedback from patients showed very high levels of stress and anxiety following the diagnosis. This level of anxiety increased exponentially in cases where patients were previously fit young individuals.

Working with clinical psychologists, we have measured the stress and anxiety levels in our cohort of patients using objective measures and these have shown levels in direct comparison with the stress levels seen in PTSD individuals.

In the next 5 years we will:

- Continue to grow the membership of our Facebook support group for Myocarditis patients and improve the service we offer our members. With increased funding we hope to add local psychology services so that we may provide a competent forum to support patients nationally.
- An intensive Awareness strategy is in place to make both the public and members of the medical fraternity more aware of myocarditis symptoms and to make information easily available to all.
- To create a comprehensive basic guide to myocarditis, the terminology used in diagnosis and treatment and understand what comes next. This will be circulated throughout the NHS and be available to download and print by all.

“The frightening thing was being discharged after 5 days of monitoring with no improvement in my symptoms so being at home with heart rate going up and down was scary! I also agree with other members of this group, that the lack of knowledge and treatment plan does NOT leave you feeling confident.”

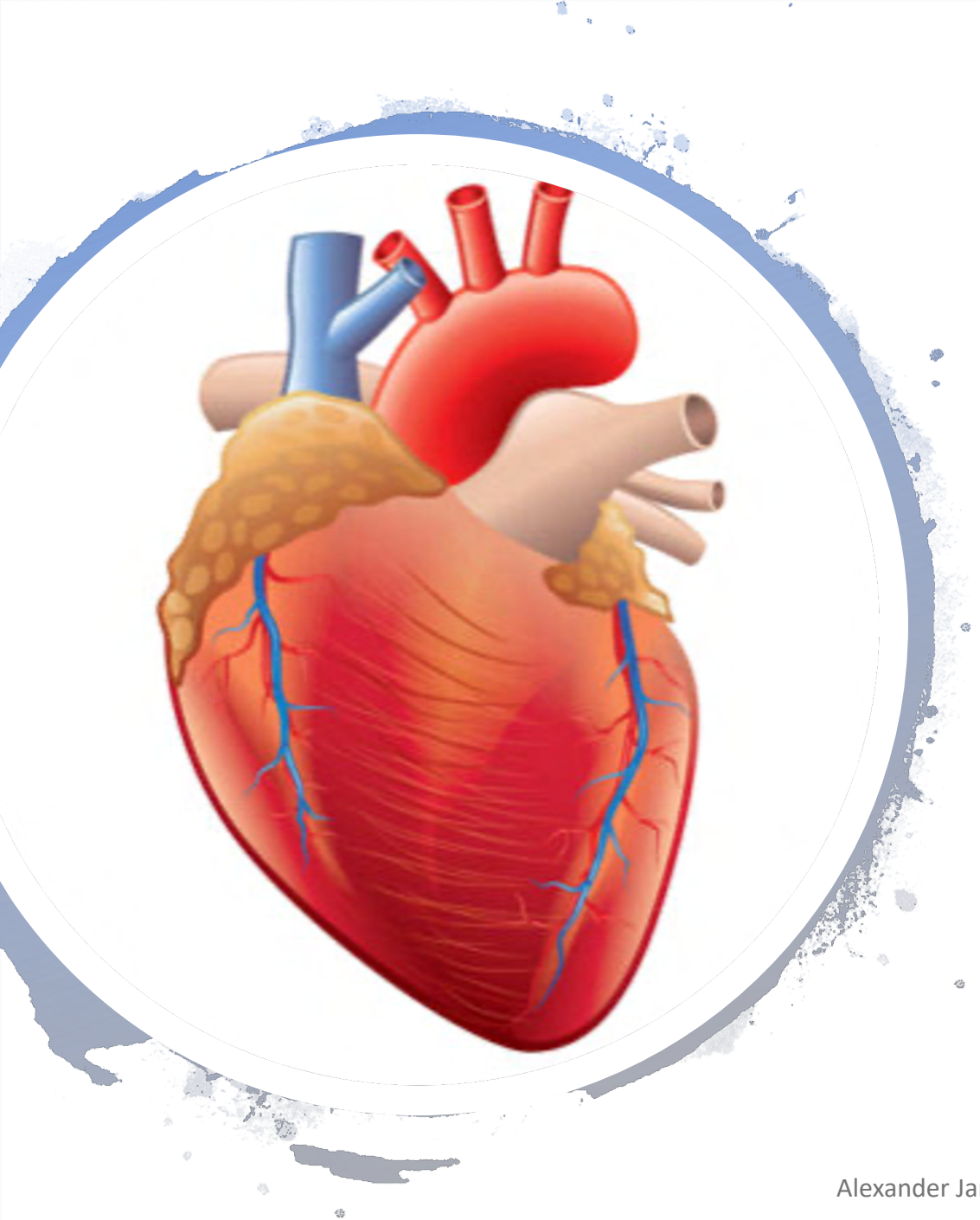
-Emma Bradley -

“It’s the not knowing that leaves you feeling even worse! I had no idea what caused it and my Occupational Nurse had never heard of it. I was left to find my own information via google and a Facebook group”

-Lisa Auty -

“ The realization that a virus can affect your heart to such a degree was terrifying. I never knew what caused mine and that added to the anxiety. No one seemed to have any information and I was told to google it and wash my hands often. As well as medication for my heart I am now taking anxiety medication.

- Janice Simmonett -



Working To Maintain And Improve The Research Environment

- We believe in talent and dedication and as such fund researchers at every stage of their career. We will continue to work to identify new ways to attract more of the world's best Bioengineers in the world and include the best research laboratories to ensure our research remains active.
- Alexander Jansons Myocarditis will continue to report individual stories of discovery and life-saving advances through social media, our website and elsewhere.
- We will continue to monitor the quality of scientific publications from the research we fund and to evaluate the outcomes and impact of our research. Most importantly, we will continue to measure our success by the impact of our funded research on those people with myocarditis thorough out the UK.

MEASURING PROGRESS

Alexander Jansons are committed to achieving the greatest impact from every donation. We ensure that all research funded by us is published in research papers and made available to all our supporters and the general public.

We will continue to report individual stories from anyone affected by myocarditis as well as all progress we make via our website, social media, the news and anywhere else.

Our pledge to increase awareness will be successfully measured against providing useful and cohesive information regarding myocarditis in all its forms and having this available throughout the NHS for any registered practitioner to access and distribute to patients.

These measures will benchmark our ongoing progress against the objectives of the research strategy.

ACKNOWLEDGEMENTS

We developed this strategy by consulting with Dr Sanjay Prasad and several members across the research and care community. We would like to thank everyone who contributed.

Particular thanks go to the Trustees of our charity, those patients and carers that gave their time and offered valuable comments and suggestions. We are immensely grateful to every person who has donated to the charity and supported our events. Their support has and always be, invaluable.

MYOCARDITIS UK

Alexander Jansons Myocarditis UK

For 7 years we have driven the campaign for increased research into myocarditis in all its forms. Our work has been central into raising awareness for this little-known condition and has helped save lives. For those lives we were unable to save, we have offered a haven for the loved ones left behind and will continue our mission to Fund Tomorrows Cures Today.

- Email: sarah@myocarditisuk.com
- www.myocarditisuk.com