Our year in review
2017-18

Prematurity

Is the leading cause of childhood mortality in the world today.

Leaves many babies with life-long disability.

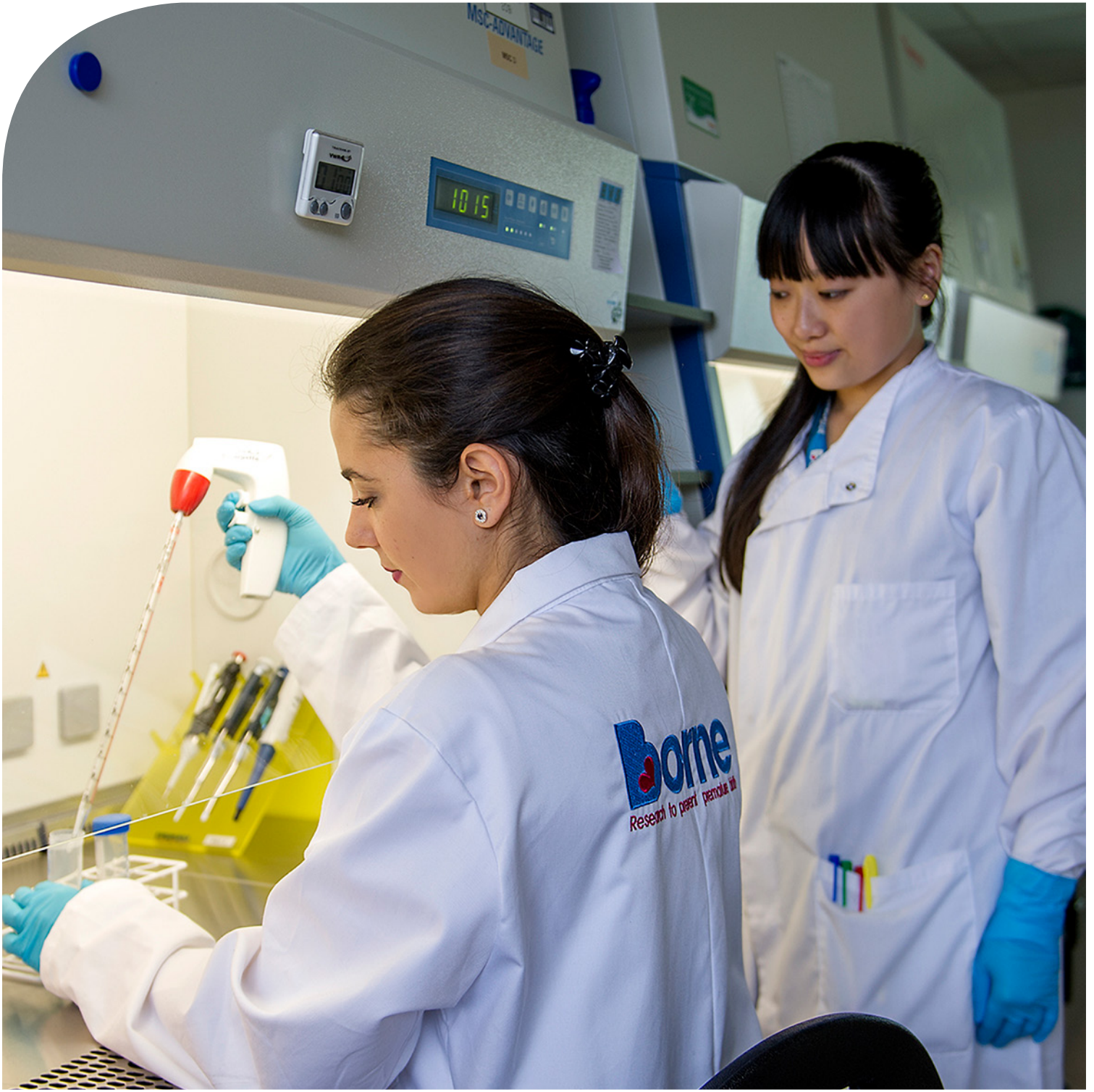
Destroys the joy of parenthood, replacing it with fear and anxiety for the future.

Is too often unexplained.

Cannot be stopped.

“The largest barrier to the development of diagnostic, treatment and prevention strategies for preterm birth and stillbirth is our inability to comprehend the biological processes of pregnancy and

World Health Organisation
2010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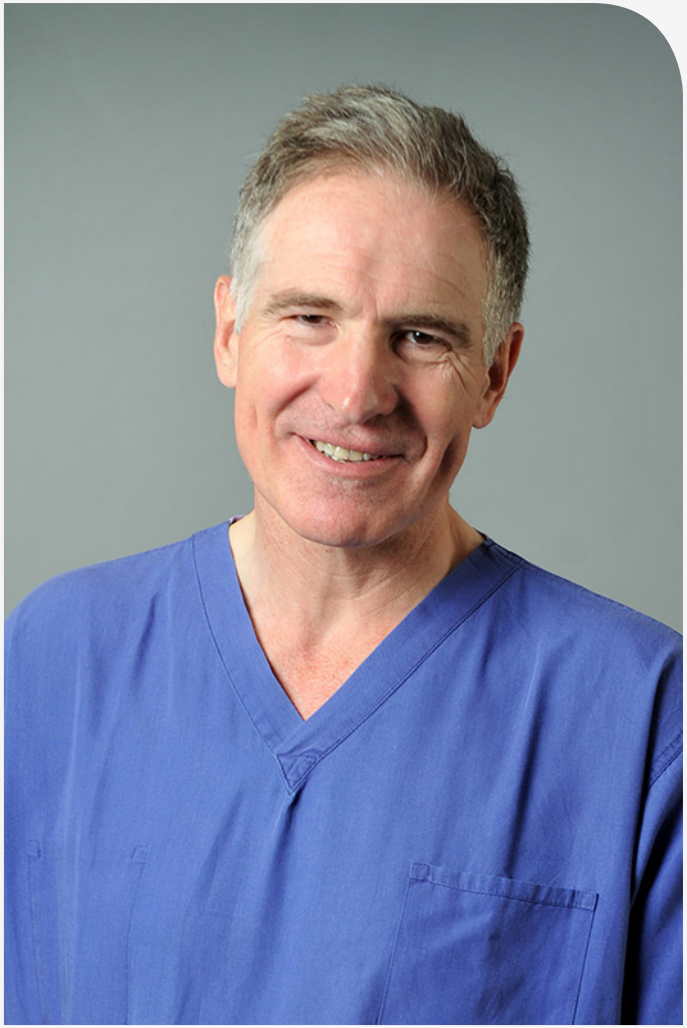
Borne
Research to prevent premature birth

Message from our Founder



Borne is here today because so many of you feel as passionately as I do that we need a deeper understanding of pregnancy and scientific breakthroughs to prevent preterm birth. With your financial support, we have been able to make ground-breaking, paradigm-changing discoveries which have transformed the way we think about pregnancy and labour. Today, with your continued support, we are trialling the first new treatment for the prevention of preterm labour in over 50 years.

Our next step is to look even deeper at the very beginning of pregnancy to answer these fundamental questions: how does a woman's body allow a pregnancy to thrive and grow; what are the very first signs that a pregnancy may not progress normally; and what can we do to improve the chances for that baby?

To answer these questions, we are studying 2,000 women at the beginning of pregnancy in great detail, storing their samples for later analysis once we know the outcome of the pregnancy. We will then tease out the subtle changes in the mother's responses to pregnancy, detecting the differences and uncovering the mechanisms that cause a particular pregnancy to end early.

None of this is possible without your generosity. We have a clear vision and the ambition to change the future for millions of unborn children in the generations to come. Please help us to realise our vision.

Professor Mark Johnson
Founder and Chief Scientific Officer, Borne

Our year in research

Delaying the onset of preterm labour

Labour, once established, cannot be reversed. But if we can delay the onset of premature labour and keep babies in the womb for longer, we would significantly improve the chances of these babies surviving and thriving without any long-term disability.

Preterm labour has many causes. Historically, studies on preterm labour have not distinguished between the different causes, meaning that the data have been confusing and often contradictory. Scientists have not been able to characterise the distinct pathways involved in the different forms of preterm labour.

Borne-funded Clinical Scientist, **Natasha Singh**, who was awarded her MD in 2017, collected more than 2,000 samples from women delivering at different stages of pregnancy so that we could begin the painstaking task of understanding the similarities and differences in the sub-types of preterm labour. Samples collected in established labour were differentiated from those in early labour. Natasha has shown that inflammation does not cause term labour but is a consequence of it. She found that inflammation plays a critical role in infection-induced preterm labour, but not in idiopathic preterm labour.

Our research investigating the processes and mechanisms that are responsible for the initiation of labour at the cellular level focused on understanding the role of cyclic adenosine monophosphate (cAMP). This is a key intracellular messenger that mediates smooth muscle relaxation in the airways, gastrointestinal tract, heart and uterus. Borne-funded Clinical Scientist, **Angela Yulia**, who was awarded her PhD in 2017, defined the critical changes in the cAMP pathway that determine the onset of term and preterm labour.

Her work is continued by **Alice Varley**, our youngest Borne-funded Clinical Scientist to date. She is working with Professor Manuela Zaccolo, a world leading cardiac scientist at Oxford University, studying the sub-cellular localisation of cAMP action in myometrial cells. She is joined by **Jonathan Li**, who is the recipient of the Robert McAlpine Studentship award. Jonathan is working to understand the changes in the cAMP-effector pathway that occur in early labour. He is working to understand how they change a relaxed uterus into a powerful contractile muscle.

Both students work under the supervision of post-doctoral scientist **Vignesh Jayarajan**, who joined us after completing his PhD in Berlin on cAMP action in the heart.

Post-doctoral scientist, **Pei-Fong Lai**, continues to study the effects of aminophylline in the laboratory, understanding how it regulates myometrial contractility.

ProgrAm: Testing a new treatment to delay preterm labour

Clinically, we see parallels between asthma and preterm labour. In asthma, airway inflammation leads to the contraction of bronchial smooth muscle, narrowing the airways and making breathing difficult. cAMP agonists, such as aminophylline, are the mainstay of the acute management of asthma, reversing the contraction of bronchial smooth muscle and making it easier to breathe.

Over the last two years, we have studied the effects of aminophylline in the laboratory to understand how it regulates myometrial contractions. Combined with progesterone, our hypothesis is that aminophylline can be an effective treatment to delay the onset of preterm labour.

The first set of feasibility trials involving women who present with high risk of preterm labour at Chelsea and Westminster Hospital began in November 2017.

This is very exciting as we are finding a new application for an existing, readily available drug and close to identifying a new therapeutic approach – the first new treatment in 50 years – that can help delay the onset of preterm labour. This work epitomises our approach of "bench to bedside".

Clinical Scientist **Natasha Singh** with baby Dana, the first baby borne out of ProgrAm.

Research Midwife **Maria Sogo** (left) and Clinical Scientist **Natasha Singh** (right) with **Nihad Abdelaziz** (centre), the first patient to take part in Borne's feasibility study.

Can Omega-3 fatty acids prolong pregnancy?

Our original data, published in 2016, showing that low levels of fish oils in the blood increased the risk of preterm delivery received further support from a paper based on data from Scandinavia.

They replicated our findings suggesting again that correcting a woman's fatty acid profile might prolong pregnancy.

AnnieBelle has studied how the maternal fatty acid profile influences the maternal immune system at birth. She has explored the transfer of maternal fatty acids to the fetus, understanding the roles of the key placental transporters.

Our next steps are to investigate:

- The best way to correct a fatty acid imbalance;
- The benefit of pre-conceptual compared with post conception correction; and
- The impact of changing the fatty acid profile on the maternal immune system.

Scientist: **AnnieBelle Sassine**, who is completing her PhD in 2018

Our year in research

Understanding the origins of pre-eclampsia

Katerina has been working on pre-eclampsia, one of the great obstetrical syndromes of our time. Pre-eclampsia occurs in around 5% of pregnancies; it is responsible for 10% of preterm births.

Katerina used a range of laboratory techniques to trace the origin of pre-eclampsia including working with samples taken from women with pre-eclampsia and fetal growth restriction. These studies provided critical insights into how changes in the function of the enzyme DDAH can cause pre-eclampsia. DDAH indirectly controls the levels of the key molecule, nitric oxide.

Nitric Oxide controls the tone of our vessels: high levels cause the relaxation of smooth muscle cells within blood vessels and lower blood pressure; low levels result in vasoconstriction and higher blood pressure.

During pre-eclampsia, DDAH activity is reduced resulting in the observed increase in the mother's blood pressure. Importantly, these studies provide the first evidence that altered placental function has an impact on maternal physiology, and mechanistic insights into the conversation between the placenta and the mother.

Pre-eclampsia is responsible for 10% of preterm births.

Scientist: **Katerina Georgopoulou**, who is completing her PhD in 2018

Our year in research

Understanding heart disease in pregnancy

Francois is in the first year of his work investigating the impact of heart disease on pregnancy outcomes. Heart disease is a leading cause of maternal death. Women with heart disease have around 1% chance of dying during pregnancy and childbirth. Around 20% of pregnancies complicated by heart disease deliver preterm, the majority because of maternal complications.

Conversely, pregnancy can accelerate disease progression in women with heart disease and increases the chance of heart attacks in older women.

Understanding the interaction between maternal heart disease and pregnancy will help us to explain the importance of the dramatic changes in the mother's cardiovascular system during pregnancy, specifically the link between heart disease and preterm birth.

Clinical Scientist: **Francois Dos Santos**, who started his PhD in 2017

Studying HIV in pregnancy to understand the maternal immune system

The incidence of preterm birth amongst HIV positive women is roughly double that of HIV negative women. Despite multiple studies, the reason for the discrepancy is not well understood.

Alex is studying the impact of HIV on the pregnancy-induced changes in the maternal immune system. He has highlighted areas of the immune system that may contribute to the onset of preterm birth.

In particular, he has identified a population of cells modulating immune responses, regulatory T cells (Tregs) that behave differently in the HIV positive group. He has also highlighted a deficiency of dendritic cells, which link the innate and adaptive immune systems, presenting foreign antigens to effector cells.

Significantly, these differences may drive a more active inflammatory response to foreign antigens in the mother and/or fetus that could trigger the onset of preterm labour. Further studies are planned to understand the impact of changes in Treg function and dendritic cell numbers.

Scientist: **Alex Cocker**, who is completing his PhD in 2019

Expanding the Borne Centre for Preterm Birth Research

The Borne Centre for Preterm Birth Research is situated on Imperial College facilities at the Chelsea and Westminster Hospital.

We have been investing in our laboratory facilities, and recently appointed new technicians and a full-time research manager. At the hospital, we have a team of research midwives focused on running Borne-funded clinics and recruiting women to our studies.

We have an established research team in place focused on investigating the processes and mechanisms at the cellular level responsible for the initiation of labour.

In particular, the scientists are focused on the cAMP pathways leading to spontaneous preterm labour.

The intent is to understand what mechanisms trigger the onset of labour, and to identify new therapies that can delay the onset of preterm labour.

We have started a new programme of research, targeting both biomarkers of preterm birth in low risk women and the role of the immune system in preterm birth.

We aim to recruit 2000 women, who are pregnant for the first time.

We will follow the development of their pregnancies from 12 weeks until birth, collecting and storing samples at every stage of pregnancy for further analysis.

We have started a new programme of research, targeting both biomarkers of preterm birth in low risk women and the role of the immune system in preterm birth.

2,000

low-risk women pregnant for the first time monitored at 12, 20, 28, 36 weeks.

300

women will present with threatened preterm labour, 160 will deliver preterm.

6

We will study women who deliver preterm 6 months after delivery or when their cycle has returned to normal.

This work will involve a multidisciplinary team working collaboratively to understand the processes that establish pregnancy. We will harness the power of discovery science to identify potential biomarkers in the low risk population that will allow us to screen all pregnancies detecting those at risk.

Multidisciplinary collaboration on a global scale

Our scientists and students are collaborating with experts from across the globe.

In the US, **Dr Roger Young** has studied the physiology of uterine cells, tissue, and the uterus as an intact organ throughout his 30-year career in academic medicine. We are working with him to develop a novel approach to further understand both normal and abnormal labour, and how to intervene when patients experience complications.

Professor Sam Mesiano is most recognised for his work on the mechanism by which progesterone maintains uterine quiescence during pregnancy. We are working together to understand how cAMP activity and effectors may interact with the progesterone receptor, altering its function to sustain pregnancy. This work supports our clinical trial of progesterone and aminophylline. We look forward to welcoming Sam to Borne as a Visiting Professor in 2019.

We are also working with **Dr Lou Muglia**, co-director of the Perinatal Institute at Cincinnati Children's Hospital Medical Center, who recently published his findings about the genetic associations with preterm birth in the New England Journal of Medicine. He has identified 3 mutations in the cAMP pathway associated with an increased risk of preterm labour. In this exciting collaboration, we are contributing our expertise on the cAMP pathway to design experiments to investigate how these mutations may affect uterine function and fetal growth.

In the UK we have important collaborations with key researchers including **Professor Manuela Zaccolo** at Oxford University who is the UK leader in the field of the subcellular localisation of cAMP activity. Together, we are studying how this changes in myometrial cells with the onset of labour.

Professor George Baillie is the Chair of Molecular Pharmacology at Glasgow University and the Dean for post-graduate research. He is an expert in the inhibition of cAMP metabolism, particularly the role of phosphodiesterases, the mechanism through which aminophylline increases myometrial cAMP levels. We are working together to identify novel cAMP agonists and to understand how cAMP works in the muscle of the womb.

Dr Nesrina Imami at Imperial College is an international expert on viral infection and the immune system. Rates of preterm birth are high in HIV, Ebola and other viral infections. The objective of our work is to understand how infection alters the maternal immune response to pregnancy and how that can lead to preterm labour.

The Natural Killer (NK) cell is a key component of the maternal immune system. Overactivity has been associated with pregnancy complications ranging from

miscarriage to preterm labour and fetal growth restriction. **Professor Hugh Brady** is an Imperial College Professor of Immunology. We are working with him to understand the interaction between the placenta and maternal immune system. The project also involves **Professor Anne Dell**, who is an FRS and Professor of Carbohydrate Biochemistry, to understand how the placenta may evade maternal immune detection by a process called glycosylation. This is where sugar molecules are attached to proteins to disguise them from the immune system.

Our work is investigating the role of placenta glycosylation in pre-eclampsia.

We are working with **Elaine Holmes**, Professor of Chemical Biology, to interpret the metabolome and microbiome analysis of the samples we are collecting. Elaine is the Head of the Division of Computational and Systems Medicine and a Professor of Chemical Biology in the Department of Surgery and Cancer at Imperial College. Her focus is on the discovery and development of metabolic biomarkers of disease in personalised healthcare and population studies with significant contributions to cardiovascular, neuroscience and infectious disease research.

We have also agreed to collaborate with **Beijing Genomics International**, the largest genomics company in the world, responsible for the sequencing more than 70% of the known genomes in the world.

Roger Smith is the Laureate Professor in the School of Medicine and Public Health in Newcastle University in Australia. He is the Co-Director of the University of Newcastle's Priority Research Centre for Reproductive Science, and the Director of the University's Mothers and Babies Research Centre and the Department of Endocrinology at John Hunter Hospital. He has spent his career working on the endocrinology of preterm birth, discovering the placental clock and working on novel drug delivery methods. Our units are linked, with Borne funding a post-doctoral scientist in Newcastle and exchanging researchers.

International development
We are exploring potential collaborationswith centres abroad in China, Africa and the Middle East. We are proposing a multi-geographical approach to understanding the interaction between population genetics and the environment on pregnancy outcome. These collaborations will give us a far broader understanding of what causes a baby to be born preterm and will identify population specific markers of preterm birth. In the longer term, once these centres are established, we will be able to conduct interventional studies to reduce the global burden of preterm birth.

Message from our Chairman

In the UK alone, 60,000 families are dealing with the devastating consequences of prematurity every year. The UK Government has committed to reduce preterm birth rates from 8% to 6% but this is an ambitious target given that the implementation of all recognized interventions would only reduce prematurity by 0.5%. There is much more that needs to be done to advance knowledge and develop effective interventions in this underfunded and overlooked area of women's and children's health.

Since becoming an independent medical research charity in 2016, we have been building our reserves to support the expansion of Borne's scientific team and the initiation of new programmes of research. We want to establish a strong reputation for investing in big science, supporting top quality research and attracting the best talent across multiple scientific and clinical disciplines to this area of research.

With your very generous support, we are committed to funding ambitious programmes of translational research that bring unprecedented expertise together through our main grant-holding institution, Imperial College. We will forge scientific collaborations to connect and establish a global network of research initiatives that embrace common objectives, and build capacity by attracting more up and coming talent through our grant-making partnership with Action Medical Research.

I am pleased with the progress that we have made in the last twelve months. Borne has established strong governance to ensure we uphold the highest levels of integrity and are spending your money efficiently and effectively. We have convened an illustrious Scientific Advisory Board that critically reviews the research that we fund to ensure we maintain scientific excellence and consult the right experts in our quest for new knowledge and solutions.

I am the father of five children who were all born premature. Two of my children are living with autism and cerebral palsy associated with being born too soon. Research lays the foundations for lasting change, and I am determined that we improve the outcomes for future generations of parents and children.

We are hugely grateful for your support and hope that more will join us on this vital voyage of scientific discovery.

Julian Mylchreest
Chairman of the
Board of Trustees

Our development as a charity

Borne received heartening support when it was launched as a research appeal with CW+, the Chelsea and Westminster Hospital charity. When we became an independent medical research charity in 2016, we were able to focus our fundraising efforts specifically on the research, and forge multidisciplinary collaborations with experts in related fields – from microbiology to immunology, systems medicine and pharmacology – to find answers to a problem that is the leading cause of childhood mortality and lifelong disability around the world.

In the last twelve months

- Borne has become an accredited member of the Association of Medical Research Charities (AMRC) which confirms we meet the high standards of practice set by respected funders of scientific research advancing medical discovery. It enables Imperial College to seek funding support from the Higher Education Funding Council for England and Wales (HEFCE) for its overheads, ensuring every penny of funds awarded to Imperial to benefit the research work.

- We have become a non-commercial Partner of the National Institute of Health Research's Clinical Research Network. This partnership enables our NHS partner, the Chelsea and Westminster Hospital NHS Trust, to receive funding support for our clinical research at the hospital.

- We have convened an independent Scientific Advisory Board of eminent experts that will evaluate the scientific team's strategy and work as critical friends of Borne.

- With the support of Borne Ambassadors, Dean and Sarah Mumm, we began fundraising in Australia to appoint a post-doctorate fellow at the Hunter Medial Research Institute. Through this collaboration, scientists in Australia will be working on projects that are aligned with Borne's research objectives and methodologies.

- We have successfully undergone equivalency determination and are certified to have 501(c)(3) federal income tax exempt non-profit status in the United States. Through CAF America's Friends Fund, we can accept tax-deductible contributions from US donors and grants from other 501(c)(3) organisations in the US.

Your Support

We want to thank everyone who has contributed so generously to our work.

Borne's work is only possible because of the support of a growing network of Friends, Champions and Foundation Donors who share Borne's vision and our hope that Borne's discoveries will have the potential to give thousands of babies a better start in life.

In the last twelve months

- We have broadened our base of financial support to include major donors from as far afield as San Francisco and the Middle East.
- Philanthropic trusts and foundations such as the Robert McAlpine Foundation are investing in our scientists.
- We welcomed new Foundation Donors who not only invest in the research but also in the growth of the charity.

Borne Patrons **Caro Greenwood** and **Will Greenwood MBE**,
Borne Patron Dame **Darcey Bussell** and Borne Ambassador **Jason Fox.**

We are grateful for the generous support of our very active and passionate Patrons and Ambassadors, who have helped bring new supporters to Borne and strengthen our connection with those who know us.

We supported a very successful fundraising gala for our inaugural school partnership with Eaton House Belgravia in May.

Borne's Golf Day at Sunningdale has become an annual fixture on our golfing supporters' calendar.

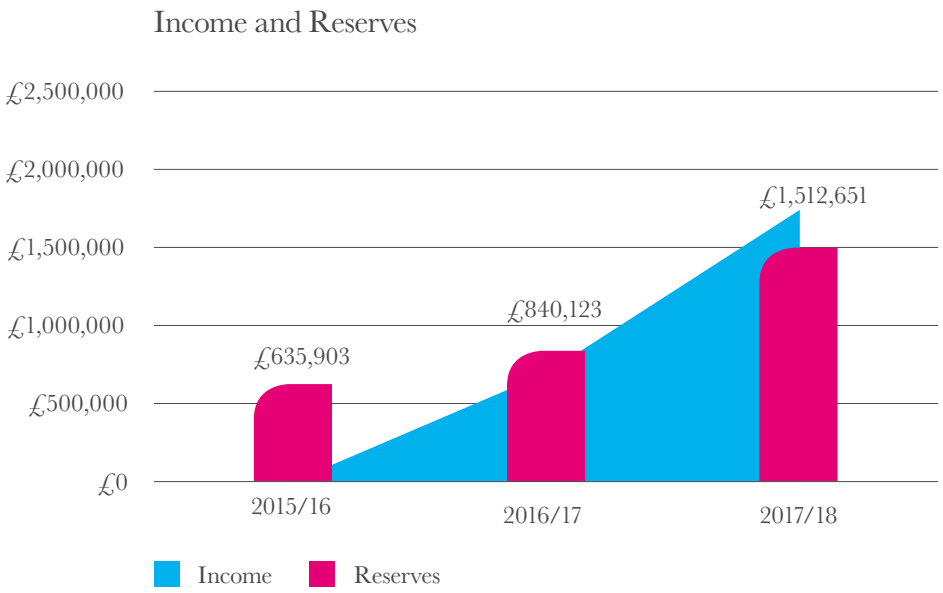
In November, we hosted our third biennial Wonderland Dinner themed 'The Secret Garden' on the eve of World Prematurity Day.

Towards the end of 2017, Borne began fundraising for the Arctic Challenge that took place in the second quarter of 2018, in the new fiscal year. The Challenge raised over £500,000 in support of the expansion of Borne's research.

Our financial performance

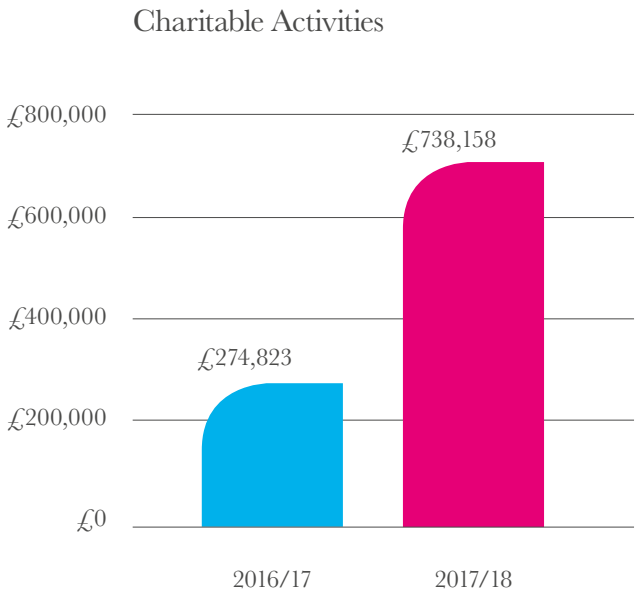
We have invested over £3 million into preterm birth research since we formed in 2013.

Since becoming an independent medical research charity, we have continued to diversify our sources of income and build our reserves to support the appointment of two additional principal investigators – research leads – with complementary expertise in reproductive immunology and the mechanism of human parturition. Along with the expansion of their respective scientific teams, this will close to double Borne's commitment in this field of research and break new ground in terms of the scale and direction of the work to find answers and treatments to prevent preterm birth.



We believe that by driving research through Borne-funded studies, we will attract funding from research councils and other grant-making bodies for further and larger studies, effectively leveraging the contribution of Borne's supporters several times over the initial investment.

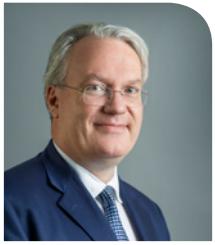
A significant portion of our expenditure on charitable activities is our core research grant to Imperial College London. In addition, we will continue to partner with Action Medical Research to jointly fund another £500,000 of new studies into the cause, prevention and treatment of preterm birth. Action's Scientific Advisory Panel will ensure an open, transparent, independent and impartial review of grant applications for funding.



How do we use your donations?

Your funds will be spent on the best quality science that addresses the questions that remain unanswered today when a child is born too soon. We will spend your money wisely and continue to look at ways to reduce costs and work more efficiently. Every £1 invested in fundraising raises £3.65 to spend on research and other charitable activities. We will always be open and respect your wishes about how and when we communicate with you.

Our Board of Trustees



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Mei Li Powell
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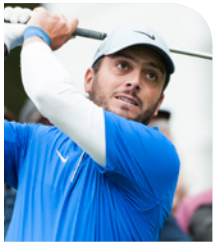

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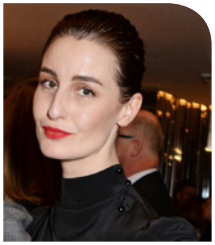

Erin O'Connor

Alistair Petrie

Photo credit: Daivd Reiss

Greg Rusedski

We believe every child should have the chance of a full and healthy life, unaffected by disability. A baby's first hours should not be its hardest, or its last.

Borne brings scientists and doctors together to advance our understanding of pregnancy, and to identify what causes premature birth so that we can improve outcomes.

We are assembling a world-class, multidisciplinary team with the vision and expertise to strive for the long-awaited breakthroughs that are needed.

We support capacity building by attracting more of the best scientific and medical minds to this area of research.

We want to invest in big science – the latest technology and bioinformatics expertise – and recruit significant cohorts of women to participate in our studies.

We will collaborate across institutions and geographical borders to create an inter-connected bio resource to accelerate scientific analysis and discovery.

We are Borne.

Borne

Research to prevent premature birth

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