The Value of Research

One of the key objectives of ICOMBO is to: "Promote and conduct projects and research regarding multiple birth development, care, and education." Research is a key focus for us this year and is the subject of this year's International Awareness Week. We recently conducted a survey to help us understand more about the needs of parents and multiples themselves when it comes to participation in research. The result will be a set of criteria that clearly explains what families and multiples want from the experience. It should hopefully help to move us on from families and twins being subjects of research to being supported by the research itself. Research with multiples can potentially have huge benefits for families with multiples and also the wider community through the understanding of wider aspects of human health and behaviour. So, let's look at various aspects of research about and with multiples.

Understanding More About Multiples

Hopefully, through scientific study, we can increase our understanding about multiples from conception through to development into adults. In addition to greater understanding of multiples this type of research will also provide information to guide decisions as we parent our multiples. Here are a few things happening in this space at the moment:

- Scientists are learning more about the different types of twins, beyond just fraternal and identical, but there is still more to uncover. For example, the theory is that identical twins occur when one egg is fertilised by one sperm, and then divides and splits within two weeks of conception. The later the split, the more likely identical twins are to share structures such as the placenta (two thirds of identical twins) and the inner sac (1% of identical twins, also known as 'MoMo', the only twins who can touch each other in the womb). However, no one has ever seen identical twins being formed under a microscope, so we don't know for sure what really happens or when. Indeed, there is an alternative hypothesis that all identical twins split very early (at the two-cell stage) with a proportion then fusing back together within a few days. For more interesting facts see the full article written by Associate Professor Jeff Craig, Deputy Director of Twins Research Australia. Or you can read full research paper – published in the American Journal of Obstetrics and Gynaecology written by Jeff Craig, Helen McNamara, Stefan Kane and Mark Umstad. Read the full free-access paper with comprehensive diagrams of the many different types of twinning here.

- Some interesting research happening in New Zealand to look at differences in DNA between identical twins that may be useful for forensics. Rebecca is investigating DNA methylation, a

modification of the DNA molecule that can change how genes are expressed but not their underlying DNA sequence. For further information.

- The issue of twins together or separate at school has been debated for a long time and some schools do enforce separation. A recent study from Goldsmiths, University of London, finds no strong evidence that putting twins into different classes at school is better for them academically. This is the case for both identical and non-identical twins. It says there should be no strict rules on separating twins, and it should be left to the youngsters, their parents and teachers to decide what is best. Further information on the study can be found here. It is also important to remember that academic achievement is not necessarily the main factor considered for separation. We need to understand more about the psychosocial outcomes for children with separating vs being in the same class, the dynamics of their relationships, emotional wellbeing and achievement. Ultimately it is an individual choice and based on what will benefit the children the most.

Studies to Improve Multiple Pregnancy Outcomes

Multiple pregnancies are higher risk than a singleton pregnancy and it is critical that research is conducted to improve pregnancy outcomes. Data from the UK shows multiple pregnancies make up only 3 per cent of all pregnancies but contribute to 6.5 percent of stillbirths and 13.7 percent of neonatal deaths. The data in other countries does vary, in part due to different criteria for the gestation at which a stillbirth is recorded, but for the most part it is very similar. Almost half of multiple births are premature and this is a main contributing factor to the high death rate. Surviving preterm babies often face neurological damage and disabilities (for example, twins are 6x more likely to have cerebral palsy than singletons). There are a number of areas where research has been lacking and these include twin growth charts, reducing premature birth and looking at the most effective treatments for TTTS in the short or longer term. Hence Tamba has been running a number of research projects including the most recent 'The Big Research Appeal' which is raising money for the largest research programme of its kind in the world.

About five years ago Tamba launched the Beanstalk Appeal to raise money for research to produce the world's first accurate twin pregnancy growth charts. These took a little longer than they expected to get onto hospital systems but in July 2017 the first twins were born who had been measured using the new charts – a significant landmark in medical history! These charts have become widespread in the UK and are slowly spreading to other parts of the world.

The second step was the creation of a UK Twin to Twin Transfusion Syndrome (TTTS) Registry to record all cases of TTTS in order to gather key data to improve clinical practice, measure short and long term outcomes and improve treatment options. A comprehensive set of data is being collected to help build a true picture of TTTS cases in the UK, the survival rates and outcomes. Crucially, a national UK Registry will provide a tool to assist the improvement of clinical skills and practice and therefore help to provide better patient care at a local, regional and national level. It will also establish a platform to allow long term follow up of TTTS survivors at a national level showing the longer term neurodevelopment

outcomes. The data will also be invaluable for future ongoing research into TTTS, for example, the longer term consequences of individual treatments. Eventually they hope to replicate this model internationally.

The third step is the Big Research Appeal and so far, Tamba, together with the British Maternal & Fetal Medicine Society (BMFMS), have commissioned five crucial clinical studies:

1. Single intrauterine fetal death in monochorionic twin pregnancies
2. Neurodevelopment outcomes in twin pregnancies with complications, including twin to twin transfusion syndrome (TTTS), single intrauterine death, selective intrauterine growth restriction, twin reversed arterial perfusion sequence (TRAPS) and twin anaemia polycythemia sequence (TAPS)
3. Prevalence of monochorionic monoamniotic (MCMA) twin and triplet pregnancies and to compare birth outcomes and clinical management of these pregnancies
4. Emergency Cerclage in Twin Pregnancies at Imminent Risk of Preterm Birth
5. Examination of the Myometrial Transcriptome in Twin Pregnancies

Tamba is now currently seeking funding to support two further studies.

In addition to this, Tamba's research programme has led to a twenty-fold increase in the number of fetal medicine centres publishing research papers on the complexities of treating multiple pregnancies. This demonstrates that the multiple birth community can make a difference and achieve great things.

Studies Using Twins

In addition to research to specifically benefitting families with multiples ICOMBO has an interest in wider research projects that involve multiples as study 'subjects'. It is important that we ensure that we protect the interests of multiples and ensure researchers understand all the implications of such studies. With their similar genetic makeup, twins represent an ideal opportunity to study health and behaviour issues. Differences between identical and fraternal twins (who on average share 50% of their DNA) reveal interesting insights and provide the optimal way to tease genetic effects from the environmental effects. Studies can also provide scientific insights into genetics conditions such as diabetes, heart disease, and obesity, as well as the effects of alcohol and tobacco use. By identifying the genetic components of these health problems and others through twins research, it is possible to develop early interventions and treatments.

Some of the interesting findings from recent research include:

- Twins were the subjects in a recent study of substance abuse in teens: "Parents spend a lot of time worrying about the influence of peers on teen substance use. A new study examines if there is a genetic component that drives teens' desire for risk taking and novelty. A key finding revealed genetic influences that are unique to the growth in substance use. With each passing year, genetic

differences between individuals become more and more important in explaining why substance use increases in some adolescents but not in others." Read more

- The OATS aims to find out what influences memory and thinking as we age. It investigates environmental influences such as lifetime physical and mental activity, socioeconomic environment, and nutrition. It also investigates how biological factors such as hypertension and antioxidant levels interact with genes to influence brain ageing. Since, over time, the expression of genes varies depending on different influences in the environment, by studying twins, OATS aims to determine which influences on the ageing process are genetic, which are environmental, and how the two interact. Read more

- Surveying identical twins is allowing researchers to identify the separate genetic and environmental factors that may contribute to acne severity. This twin study further supports that there may be a genetic phenotypic link, though social and environmental factors may also have an influence in the disease process. Read more

- A test to diagnose cerebral palsy at birth, which could allow infants access to critical early interventions, is one step closer thanks to research with twins. It is also especially relevant for the multiples community as cerebral palsy is more common in twins and triplets (and possibly higher order multiples but there is insufficient data to know the rates) than singletons. There are at reasons for this: Multiple pregnancies are more likely to result in premature delivery. Premature birth often results in low birth weight newborns. Both are risk factors for Cerebral Palsy. Read more

- Many interesting insights are being provided from study of identical twins where one went into space for a year while the other remained on Earth. There have been many reports of this study, although some of them have been rather misleading including that Scott Kelly's DNA itself had changed. However, what researchers observed was changes in gene expression, which is how your body reacts to your environment. These changes were probably within the range for humans under stress, such as mountain climbing or scuba diving. It is not surprising that spaceflight affects how much expressing certain genes do, particularly those involved in immune function, DNA repair pathways, and bone growth. Read more

- Following on from the space study two experienced mountaineers are in the middle of a month-long expedition to Mount Everest, while their twins stay at sea level. The primary goal is to search for possible changes in gene expression as a result of the stressful environment at high altitude. Read more

The world of research on multiples is fascinating and we never seem to stop uncovering new insights!