

Background to MothersBabies First Project

To assist the committee in its consideration of this proposal I have outlined below some background and the purpose of MothersBabies.

MothersBabies first project: Mothers and Babies Microbiome Study

OVERVIEW

There is not much that is more important than giving a baby the best chance of healthy life.

The health of mother and child is a foundation for our future. Presently far too many mothers and babies are suffering needlessly and in many cases for the whole of their lives from illnesses and diseases that may be preventable with appropriate intervention during the precious months before conception, through pregnancy and during the early months of life.

Our goal is to demonstrate that the biology of a mother's gut bugs (microbiota) either pre-pregnancy or during pregnancy - or both, contains critical preconditions for both the mother and her baby's health and if this microbiota is perturbed this leads to illnesses associated with pregnancy and therefore subsequent illness in the child, as well as some common life-long, chronic and debilitating physical and mental illnesses in mothers, babies and children.

MothersBabies will fund ground breaking evidence based research in microbiome science into the clinical domain that should drive change in pre-pregnancy and pregnancy health and will help millions of mothers, their babies and their families and bring pervasive economic and social benefits for our community.

Some simple statistics demonstrate the magnitude of the problem:

- Prematurity is on the increase – in 2016 it was 8.6%, up from an average of 7%, (average gestational aged 33+3)
- Food allergies 1:20 in children
- Asthma affects 1:9 Australians, totaling 2.5million
- ADHD – 7.8% diagnosed in 2003, 9.5% in 2007, 11% in 2011
- Autism (Spectrum Disorders) – 2.46% of children aged 10-14 (getting better stats on this)
- Obesity – 1:4 children and 2:3 adults and increasing
- Mental Health - Anxiety 1: 4 Depression 1:7 adults

Details on the source of these statistics are attached (1)

Every baby in Australia deserves to have the best possible start in life. This should be a normal expectation for every mother and father. New and mounting evidence is showing it is feasible and timely to introduce innovative evidence based management and treatments to support conception, pregnancy and perinatal physical and mental health. It is critical to lifelong health and happiness for every child.

BACKGROUND

Over 2000 years ago Hippocrates, the father of modern medicine said “All disease begins in the gut.” He also said “let food be your medicine and medicine be your food.” For thousands of years mothers have been preparing for birth, caring for and feeding their babies and listening to their own mother’s, their doctors, their midwives, their friends and current medical science about what is best for baby. Most mothers tend to be very motivated to do what is best for their baby, even if they are not motivated to do what is best for themselves. They will generally rely on what they consider the safest source of information in order to do so. For some mothers, handed down wisdom works and is enough. Others require the rigour of evidence based medicine or the advice of a GP, obstetrician, paediatrician or other medical professional. These professionals certainly require evidence based proof of a particular approach before offering it as a strategy to improve health or cure disease or advise on how to best prepare for pregnancy or care for a baby.

The modern science of medicine has sought answers to curing diseases and saving human lives in ever progressing ways and through evidence based analysis in studies of: disease specific treatments, the sources of diseases in human DNA, disease treatment through genetic engineering and immunotherapy and other

sophisticated approaches, and the study of epigenetics - to name a few. Medical science has now developed a very sophisticated knowledge of how human biology works at a cellular level. This includes the signaling and communications systems that integrate and regulate our immune system and neurology and importantly the relationships of our biology with the trillions of microbial networks that we play host to in our gastrointestinal tract. More recently this level of detailed knowledge has increasingly led the science of medicine, along with its rigour in evidence based analysis, back to the gut. The new language of the gut is the microbiome, the microbiota, the gut-brain axis, the brain-immuno-gut connection, nutrition, probiotics, prebiotics, and the role of microbes, including beneficial and pathogenic bacteria and viruses, in our health. We now have emerging evidence based medical data to show, that some common diseases and illnesses like asthma, autism, diabetes, obesity, allergies, cardiac, and autoimmune conditions are associated with the health of microbes in our gut. There are many scientists around the world currently studying this in great detail and with specific focus on many different diseases and stages of human life.

The Study MothersBabies wishes to support

An outline of the study MothersBabies wishes to raise money for is attached. It is a study of the microbiome of mothers pre-pregnancy, during pregnancy and after birth and includes the microbiome of their babies. So why is MothersBabies seeking funding for this study? Answer: This aligns directly with the mission of MothersBabies.

The Mission of MothersBabies is:

To optimize the future health of humanity by empowering mothers-to-be to transform their health pre-pregnancy, during pregnancy and at birth so that their health and the health of their babies is optimized for life. In so doing promote the prevention and the control of disease in human beings.

The Vision of MothersBabies is:

For women to have the resources and evidence based knowledge to enable them to give birth to babies whose health is optimized for life. In so doing prevent or control diseases that their babies could otherwise experience throughout their lives.

An outline of the study states “the links and significance of the microbiome in pregnancy are starting to become apparent but are far from definitive and detailed scientific and clinical work needs to be performed to deepen our understanding. More importantly it is highly desirable, and feasible, to manipulate the microbiota safely towards a more favourable composition that would prevent unhealthy outcomes and protect the mother and her baby.”

It goes on to say “The overarching aim is disease prevention. This would change the face of antenatal care, screening options and treatment for those common conditions the world over. These longitudinal prospective studies are currently unparalleled anywhere in the world and would provide the evidence base to transform global health.”

We know that the basic biological platform for a baby is laid down in the first few days of pregnancy. We hope that the study will show what biological conditions in the gut allow diseases to occur in babies and children and how an intervention will help to alleviate and cure them. Its significance for disease prevention and control will be, we believe, profound.

Thank you in advance for considering this proposal.

Kind regards

Catherine Oates Smith

Attachment 1 - Statistics

PREMATURITY:

Ref: The Australian Institute of Health and Welfare’s Australia’s Mothers and Babies report 8.6% of all mothers had a preterm birth with the average age of 33+3 weeks gestation up from a previous average of 7%.

Pre-term babies are more likely to be admitted to a special care nursery (72%) compared to term (10%) and post term (13%)

Australian Institute of Health and Welfare 2016. Australia’s mothers and babies 2014—in brief. Perinatal statistics series no. 32. Cat no. PER 87. Canberra: AIHW.

ALLERGIES:

Food allergies: 1:20 children versus 2:100 in Australian adults

4.1 million Australians (19.6%) have at least one allergy If current trends continue there will be a 70% increase in the number of Australians with allergies from 4.1 million now to 7.7 million by 2050 (19.6% to 26.1%) Individuals with allergies and their families bear 49% of the cost of allergic disease.

2007 calculated cost of allergies is \$7.8 billion dollars (broken down into: to lower productivity (“presenteeism” \$4.2 billion), direct medical costs (\$1.2 billion) lower employment rates (\$1.1 billion), absenteeism and lost household productivity (\$0.2 billion) and premature death (\$83 million))

Rates of hospitalisation for anaphylaxis increased by 50% from 2005 to 2012 (Mullins et al 2015) **Ref:** <https://allergy.org.au/about-ascia/info-updates/613-july-15-2015-anaphylaxis-now-more-prevalent-in-older-children-and-adolescents>

Not only does Australia have one of the highest prevalences of allergic disorders in the developed world, but recent studies have demonstrated a doubling in some conditions such as allergic rhinitis (hay fever), eczema but more recently, potentially dangerous anaphylaxis (mainly due to food) as well. Asthma, hay fever, chronic sinusitis and “other allergy” comprise 4 of the top 10 most common long-term self-reported illnesses in youth aged 12-24 years in Australia.

The estimated cost to Australians who suffer from allergy due to reduced quality of life (the “burden of disease”) is estimated at \$21.5 billion, approximately

double the estimated figures for arthritis (\$11.7 billion) and hearing loss (\$11.7 billion).

Ref: Economic Impact of Allergies November 2007 – published by ASCIA (Australasian Society of Clinical Immunology and Allergy)

ASTHMA:

1 in 9 Australians have Asthma.

Rate of asthma amongst indigenous Australians is twice as high as that of no-indigenous Australians. More common in people living in socioeconomically disadvantaged areas

Cost: 0.9% of all direct health spend on disease \$655 million in 2008-2009

Ref: The burden of chronic respiratory conditions in Australia: a detailed analysis of the Australian Burden of Disease Study 2100 – published July 2017.

ADHD:

Autism spectrum disorder (ASD) / ADHD / LD – language learning disability

This is a lovely table

Age	% in pop	Number	ASD 1%	ADHD 6.8%	LD 10%
0-4	6.5	1,456,485	14,565	99,041	145,650
5-9	6.35	1,422,874	14,229	96,755	142,290
10-14	6.7	1,501,300	15,013	102,088	150,130
15-19	7	1,568,523	15,685	106, 666	156,850

The statistics are all drawn from independent sources 1% of population diagnosed with ASD (Autism Spectrum, including Aspergers) Bob Buckley Computational Genomics Laboratory, John Curtin School of Medical Research, The Australian National University Canberra ACT 0200 Australia 5%-10% of population diagnosed with ADHD (Australian Guidelines on Attention Deficit Hyperactivity Disorder (ADHD) June 2009)

Childhood community prevalence of 6.8% is found in Australia (7- Graetz B, Sawyer M, Hazell P, Arney F, Baghurst P. Validity of DSM-IV ADHD subtypes in a nationally representative sample of Australian children

and adolescents. *J Am Acad Child Adolesc Psychiatry* 2001; 40:1410-1417.)

10% of population diagnosed with a Language Learning Disability (Andrew Dean Fildes Foundation)
The population of Australia is 22,407, 468. (Australian Bureau of Statistics)

Total 0-19 yrs with one of the above disabilities

With ASD 59,492

With LD 594,920

With ADHD 404,649

Total 951,871 children and young people

OVERWEIGHT AND OBESE:

Over the past 25 years, the prevalence of overweight and obese first time mothers increased from 17.5% to 23.7%. Were overweight and obese women to have moved down one BMI category during 2010-2014, the following could have been averted: 19% of pre-eclampsia, 15.9% of macrosomia, 14.2% of gestational diabetes, 8.5% of caesarean deliveries, 7.1% of low for gestational age birthweight, 6.8% of post partum haemorrhage, 6.5% of admissions to special care nursery, 5.8% of prematurity, and 3.8% of fetal abnormality. (Source of citation: Cheney et al, *Med J Aust.* 2018 Feb 19;208(3):119-125).

In 2014–15, about 1 in 4 (26%) Australian children and adolescents aged 2–17 were overweight or obese.

That's around 1.2 million children and adolescents (ABS 2015). In 2014–15, almost two-thirds (63%) of Australians aged 18 and over were overweight or obese. Put another way, approximately 11.2 million adults were overweight or obese (ABS 2015).

ABS = Australian Bureau of Statistics”

Children:

In 2014–15, about 1 in 4 (26%) Australian children and adolescents aged 2–17 were overweight or obese. That's around 1.2 million children and adolescents (ABS 2015). About 1 in 6 (18%) children and adolescents aged 2–17 were overweight but not obese, while about 1 in 13 (8%) were obese.

One in 5 (20%) boys aged 2–17 were overweight but not obese, while 7% were obese. Among girls of the same age, around 1 in 6 (16%) were overweight but not obese and 9% were obese.

MENTAL HEALTH:

Fourteen per cent of Australian children and adolescents aged 4-17 have mental health or behavioural problems.

This rate of mental health problems is found in all age and gender groups. Boys were slightly more likely to experience mental health problems than girls.

There is a higher prevalence of child and adolescent mental health problems among those living in low-income, step/blended and sole-parent families.

Mental health problems were experienced by 21.1% of males and 22.1% of females with weekly household incomes of less than \$580, compared to 8.9% of males and 9.1% of females living in households with a weekly income of more than \$1,030.

For youth living in step / blended families (25% of males, 19.7% of females) and sole parent families (22.2% of males, 26.7% of females) reported experiencing mental health problems, compared to youth (11.3% of males, 10.7% of females) living with their original parents together.

Only one out of every four young persons with mental health problems had received professional health care. Family doctors, school-based counsellors and paediatricians provide the services that are most frequently used by young people with mental health problems. Younger children (4-12) were more likely to visit paediatricians and family doctors, while older children were more likely to visit school-based counselling services.

Even among young people with the most severe mental health problems, only 50% receive professional help. Parents reported that help was too expensive or they didn't know where to get it, and that they thought they could manage on their own.

[1] Australian Bureau of Statistics. (2007). National Survey of Mental Health and Well-being: Summary of results. Catalogue No. 4326.0. Canberra, ACT: Australian Bureau of Statistics. [To download PDF click here]

[2] Ibid.

[3] Sawyer, M. G., Arney, F. M., Baghurst, P. A., Clark, J. J., Graetz, B. W., Kosky, R. J., Nurcombe, B., Patton, G. C., Prior, M. R., Raphael, B., Rey, J., Whaites, L. C., & Zubrick, S. R. (2000). Child and adolescent component of the National survey of Mental Health and Well-being. Canberra, ACT: Mental Health and Special Programs Branch of the Commonwealth Department of Health and Aged Care.

[4] Australian Bureau of Statistics. (2007). Op. Cit.

Attachment 2 Outline of the Study

A healthy pregnancy producing a healthy baby is a fundamental tenet of a strong and thriving community. Many factors impact on the outcomes of pregnancy including genetic, dietary and life style choices.

Over the past decade, it has become clear that the large collection of microorganisms that live within and on our bodies (the microbiome) plays a major role in maintaining our health. A fine balance of the microbiome ensures a healthy host, while a disturbed balance (dysbiosis) caused by a myriad of factors such as poor diet, lack of exercise and inappropriate use of antibiotics, have been implicated in many human diseases, including poor outcomes of pregnancy such as obesity, diabetes, pre-eclampsia, preterm labour and hypertension. Studying the changes in the microbiome that occur during pregnancy and correcting any dysbiosis before pregnancy may offer a unique opportunity to prevent negative outcomes and ensure a healthy generation of babies.

We have designed the definitive study to investigate the relationship between changes in the microbiome during pregnancy and clinical outcome. Phase 1 will involve recruitment of women who are planning pregnancy (i.e. preconception). We aim to recruit 2000 women and will analyse their microbiomes prior to pregnancy, at each trimester of pregnancy, at time of delivery and for at least 1 year following birth. Women will provide self-collected vaginal and oral swabs and a small stool sample at these time points. Stool and oral samples would also be requested from prospective partners, and from the babies during the first year of life. This part of the study will provide unique knowledge about each pregnancy and how the microbiome status impacts on the various outcomes. We will identify unique microbiome signatures (fingerprints) that can predict each outcome, e.g. normal, preeclampsia, diabetes, etc. These signatures could be used prospectively to advise women planning pregnancy.

The second part of Phase 1 will run concurrently with the study described above and is a smaller interventional trial in 100 non-pregnant child bearing age women. Women will be randomised to receiving pro/pre-biotic combination(s) or placebo for 3 months. Microbiome samples will be analysed before starting the intervention, monthly during the 3-month treatment and for 3 months afterwards. This study aims to define

the optimal method of manipulating the microbiome towards a healthy balance and will form the basis of the intervention in the Phase 2.

Phase 2 is a large clinical trial which will recruit at least 1000 women planning pregnancy and then randomising them to receiving the chosen safe intervention or placebo and monitoring their individual microbiomes prior to pregnancy, during pregnancy and for a year following birth to see if the intervention had an impact on outcomes of pregnancy. We will also analyse the microbiome of the babies to establish whether the maternal intervention had a positive impact on the health and development of the infants. This cohort of babies could be followed up for several years to establish longer term outcomes, e.g. rates of allergy, eczema, asthma, autism and childhood developmental milestones.

Katie and Estelle's stories with photos



Kate's Story

My life revolves around food. After completing my Bachelor of Fine Arts degree I decided to further my studies by attending Le Cordon Bleu. Two years later, after very intensive study, I became the first Australian and also the first woman to fully complete the Le Cordon Bleu Cuisine and Patisserie course in the Australian arm of Le Cordon Bleu. Several years later I launched my boutique catering business, Something from Kate.

Running a successful catering business would seemingly be enough for anyone but 7 weeks ago I had my third child. After experiencing dietary issues with my first two children, and even my own experiences as a child, I just knew that she would follow the same pattern.

As a little girl I had a whole battery of tests to work out why I was suffering so badly with eczema, asthma and gut related issues. The results came back showing I had a severe intolerance to cow's milk protein. This issue has been passed on to all three of my kids.

MothersBabies

My first child Molly had the cow's milk protein intolerance which meant she just didn't gain the weight she was supposed to, it literally went in one end and out the other. I was dismissed by health professionals who told me that Molly had failed to thrive and to put her on formula. I knew deep in my soul this wasn't the solution. I also knew I had bucket loads of milk so it wasn't a supply issue. If I had followed that particular paediatrician's advice it would have been a disaster. Once diagnosed with the intolerance, dairy was cut out of my diet and Molly went from strength to strength.

My second child, Sebastian, was a whole lot worse. He had numerous protein intolerances that caused him severe pain and caused his mother to despair that anyone in the medical profession would take my instincts seriously and not discount what was happening, labelling me as an over anxious mother. I finally changed GPs and it was Dr Jeremy who actually looked at my son, I mean REALLY looked at my son and not at me and my sleep deprived explanations. He cradled my small boy in his hands and spent maybe 5 minutes just observing him and not saying a word. He finally turned to me and said " he is one unhappy little boy, let's get to the bottom of this". It was a hallelujah moment for me and perhaps even stopped me tipping over that precipice into severe depression. Having a baby that screams all day and night is harder than I can say.

After seeing a paediatric specialist it was discovered he had a whole list of protein intolerances that were causing him to bleed in his bowel and give him severe cramping...constantly. How terrible to start life in constant pain! I changed my diet dramatically, under supervision, and it was found Seb had intolerances to gluten, dairy, soy, nuts and eggs. Well, that pretty much left me eating meat and salad but to physically see Seb change personality and become the happiest and most laid back of children was a miracle. For me, well I became a mother who could again enjoy my baby instead of just trying to survive. Unfortunately, after going off gluten with my son it set off an intolerance in me, making me throw up if wheat was ingested but Seb at age 5 is completely fine with no food related issues at all.

I went into my third pregnancy with all this knowledge behind me. So this time from the moment Claudi was born I ate no gluten and no dairy. This was with the backing of the paediatrician. A couple of weeks down the track we had to remove soy from my diet due to explosive liquid poo but this has seemingly solved the problem and I have a very chilled happy baby.

It is such a wonder to me that this time I can truly enjoy my beautiful little baby and Claudi is content and happy, just as she should be.





Estelle's Story

My husband and I have always known we wanted to start a family one day. The majority of my life I had taken conceiving and having children for granted. It wasn't until I learnt of my sister's struggle with conception and her diagnosis of Polycystic Ovary Syndrome that I started to consider that I may also have some difficulty. More red flags appeared when, after stopping oral contraception, I did not have the return of my menstrual cycle or ovulation.

It was found that I too have PCO and, whilst they couldn't determine if it was the syndrome or not, there was little possibility of conceiving naturally, especially as it appeared I would need help to ovulate.

It wasn't until I was having a conversation regarding gut health, and how it affects your whole body, with Catherine (Oates-Smith) that I came to think that there was perhaps another avenue I could explore. I was particularly drawn to the advice that I see to any problem before I conceive to ensure I don't pass any "intolerances or allergies" on to my baby through poor gut microbiome.

My relationship with food has always been a bad one, if something didn't make me throw up it would send me running to the bathroom or huddled over



in pain. I spent many months discussing this and other problems with my GP before, with the help of a gastroenterologist and tests, it was determined that I have acute Irritable bowel syndrome.

I immediately started the FODMAP diet to ensure I could maintain and treat my symptoms and repair my gut flora before trying to have a baby. Little did I know that within months of starting and vigilantly following the FODMAP diet, not only was my health the best it had ever been, but my cycle and ovulation returned of its own accord. When my husband and I decided to start trying for our family we fell pregnant with a healthy baby girl within the first cycle.

After having seen the scans of my ovaries from prior to starting the FODMAP diet, and knowing my success with conception, I can only attribute this to following the diet and maintaining a healthy and balanced stomach/digestive system. Throughout my pregnancy and nursing I continued to follow my diet whilst finding within its limitations things that I could eat to properly nourish my growing baby and still ensure the microbiome that I passed on to her would be as healthy as possible. I do not wish my daughter to struggle as I have with both food and her cycle and hope that through my awareness and actions she will benefit.

