



CHYLD

CHILDREN WITH HYPOGLYCAEMIA AND THEIR LATER DEVELOPMENT



CHYLD Study Update:

Issue 2, December 2012

Thank You to all Friends of the CHYLD Study



**CHYLD Study
Principal Investigator
Jane Harding,**

*Professor of Neonatology,
Deputy Vice-Chancellor
(Research),
University of Auckland*

*"Thank
you...for your
generous
support in
helping us
get to this
point"*

The CHYLD study team are pleased to share with you this update on our activities over the last exciting and very busy year (see page 2).

There has been lots of hard work, and lots of milestones to celebrate. In May, we celebrated having an assessment venue of our very own for the first time with the opening of Kahikatea Research House in Hamilton (see page 2).

Our first meeting with our International Advisory Group in August (see page 6) provided a wonderful opportunity for the whole team to come together for reflection about where we are going and how we will get there.

We are also delighted to report that earlier this month we achieved a major milestone, completing the assessments of our two-year-olds (see page 3). A total of 403 two-year-old

children have been assessed, representing an outstanding 75% follow-up rate; higher than we dared to hope and a tribute to the professionalism, persistence and commitment of the whole assessment team.

The assessors will be having a well-earned break over the next couple of months, before continuing with assessments of 4.5-year-olds, while the data team is hard at work entering, checking and re-checking the thousands of data points collected so far. We hope to be ready for the complex and all-important task of initial data analysis in early 2013.

As we draw breath before this next crucial phase of the study, we would like to thank all of you, our Friends of the CHYLD Study, for your generous support in helping us to get to this point. We would not be here without your many

contributions, your enthusiasm and your belief in this important project.

Thank you for sharing our vision of improving the future care, health and development of babies at risk of neonatal hypoglycaemia and their families.

I know that I speak for the entire team when I say that your contributions do make a difference for us, for the outcomes of the study, and for children in New Zealand and worldwide.

Many thanks and best wishes for 2013,

Jane Harding

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CHYLD Study Update:

What is the CHYLD Study?

“A low blood sugar level (hypoglycaemia) is a common problem in newborn babies, and sometimes causes brain damage”

A low blood sugar level (hypoglycaemia) is a common problem in newborn babies, and sometimes causes brain damage. However it is not known which babies will suffer brain damage or at what blood sugar levels; the duration, severity and frequency of the hypoglycaemia may all be important.

In order to learn more about which of these aspects of hypoglycaemia are important for brain damage, the CHYLD study is

assessing a group of almost 600 children, all born at Waikato Hospital in Hamilton and all at risk of hypoglycaemia, who had very careful monitoring of their sugar levels in the first few days after birth.

We are assessing their growth, neurological function, vision, cognitive and language development, memory, executive function, general health and family environment, at two and at four-and-a-half years of age. We will

then determine the relationship between these outcomes and the periods of hypoglycaemia that many of them experienced as newborns.

This information will help provide critical information about how newborn babies should be monitored and treated in order to prevent brain damage with its long-term consequences while minimising unnecessary interventions in newborn babies.



**Coila Bevan,
Senior Research
Nurse and
Assessment
Coordinator**

2 Year Old Follow Up: A Very Successful 2012!

The CHYLD study started follow-up assessments of 2 year olds in June 2010, and has been very busy since then. During 2012 we have been assessing an average of fifteen 2 year olds and five 4.5 year olds each month.

Most importantly, and thanks to the support and dedication of the families of the children in our cohort, we have now completed our assessments of 2 year olds!

The last assessments of 2 year olds took place in November 2012, capping a very successful two-and-a-half years of locating, contacting, and assessing children for the study.

Coila Bevan, a Senior Research Nurse and the 2-year study Assessment Coordinator, has held responsibility for locating, contacting, and booking the families, as well as booking the assessors and facilities for each child's assessment.

She has had excellent support from Jenny Rogers, Maori Re-

search Nurse, who has traced numerous families and also performed developmental assessments on more than 50 children for the study.

Jenny has also worked closely with Dr Trecia Wouldes and Judith Ansell to train assessors and to ensure that developmental assessments are standardised between assessors and over time.

Our assessment team has travelled all over the Waikato, and all over New Zealand when needed, to reach children and complete assessments of their physical, cognitive, visual, and behavioural development.

We are very pleased to report that these efforts allowed us to see a total of 403 children, earning a very high follow-up rate of 75%. Our minimum required rate was 60%, or 300 children, so we are very pleased with the success of our assessment team!

Four post-graduate students

(Judith, Sandy, Nabin, and Anna) have been performing research towards their PhDs or Honours theses as part of the follow-up of 2 year olds [see pages 5-6].

These students have made enormous contributions to the study, and in the process have had the opportunity to validate testing techniques and to present some of their work at international conferences.

Now that data collection is complete for the 2-year-old follow-up study, the data management team [see page 5] are busy collating and cleaning data for our PhD students to analyse with the help of our statisticians.

During 2013, we hope to see the results of these analyses published in scientific journals and presented at scientific conferences, and also to alert community groups and health professionals of the important health outcomes.



**Jenny Rogers,
Maori Research
Nurse and
Developmental
Assessor**



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4.5 Year Follow-Up Update

The 4.5 year follow up is progressing well, and we expect numbers of assessments to pick up in June 2013, when more of the children will be turning four-and-a-half each month. Many of these children still require tracing as they have moved address since their assessment at two years of age, or they were not assessed at two.

The developmental assessments for 4.5 year olds are different from those for two-year-olds, which has meant further training for our assessors to ensure they are familiar with the new tests. These include the Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery VMI), and the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV).

In 2012, the Sheridan Gardiner test for visual acuity was added to the suite of vision tests used in the four-and-a-half year as-

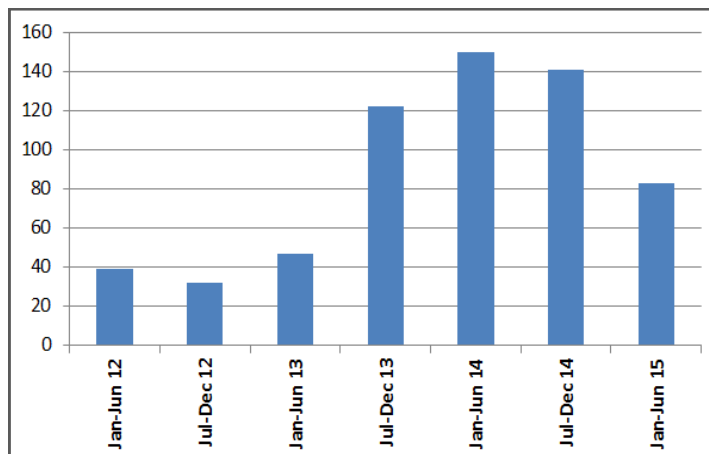


Chart: Number of children turning four-and-a-half years old, and becoming eligible for assessment, per six month period from 2012 to 2015.

essment. This short test is designed especially for people below reading age, and complements the current tests carried out on the pre-schoolers in the CHYLD study.

Each test helps to build a complete picture of the children's progress, eventually contributing to our understanding of how hypoglycaemia in the newborn

period may affect their development later in life.

By mid-November, we had assessed 56 four-and-a-half-year-olds, giving us an 94% follow up rate so far. This is a good indication of a very successful year of recruitment. We are hoping that this very high follow-up rate can be maintained into 2013.

B4 School Check

All children in New Zealand are eligible for a free health check-up before they start school, called the "B4 School Check".

In collaboration with the Ministry of Health, we agreed that with parents' permission, data for children who have had the B4 School check will be made available to the CHYLD study team. This data sharing will be important for two reasons:

First, the results of the vision assessment used in the B4 School check, the Sheridan Gardiner test, will be able to be compared with the results of this and other vision assessments done for the CHYLD study.

This will provide important validation of the testing techniques used in both the CHYLD study and the B4 School check.

Second, the B4 School check includes a number of other assessments, including of hearing and dental health, which are not part of the CHYLD study assessment.

This additional data will provide us with a more comprehensive picture than we might otherwise have of the development and health of these children before they start school.

"This collaboration with the Ministry of Health will be invaluable in analysing health outcomes for babies with hypoglycaemia"

Professor Jane Harding



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CHYLD Study Update:

Kahikatea Research House, Hamilton

Until recently, the majority of assessments for children in the CHYLD study were being performed at Braemar Hospital in Hamilton, where we were fortunate enough to be provided with a space to host families.

We have however experienced an increasing number of children being eligible for assessment at 2 years of age, along with the addition of many children from the potential 616 child cohort becoming old enough to be assessed at four and a half years. The space required to perform assessments and host families, as well as the time we required this area for were becoming more than Braemar was able to offer.

After exploring prospective venue options, we have secured the exclusive use of a private house in Hamilton. Kahikatea Research House is privately owned by Braemar Hospital, and is being rented by the CHYLD study.

With three assessment rooms, a spacious living area and a kitchen and bathroom, the house provides us with a more comfortable and workable space for multiple assessments per week, storage facilities, flexibility and full time, 7 day access.

The house was blessed on the 2nd of May in a ceremony including Chaplains and Kaitiaki from Maori Health Services in the

Waikato.

The team from Te Puna Oranga have been generous in their offer to help us support the families involved in our research, and together we have been able to articulate our philosophy about how Kahikatea House fits in with the goals of the CHYLD study. The verse on the left will be translated into Maori and displayed in both Maori and English in the family room of Kahikatea Research House.

The first assessment at was held at the house on May 23rd, and since then we have seen many families attending assessments there each week.

***“The native
Kahikatea tree
represents our
hopes for the
children of
Aotearoa New
Zealand; to grow
tall, straight and
strong, in a
supportive
environment
reflecting Aroha
and
Manaakitanga”***



Members of the CHYLD study team outside Kahikatea Research House in Hamilton, 2012



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New CHYLD Study Coordinator: Jessica Charlton

Jessica joined the CHYLD study in June 2012, to take on coordination of both the 2 year follow-up and the 4.5 year follow-up.

Jessica's role is essential for communication between the project investigators and each of our multi-disciplinary teams. Her role also includes manage-

ment of both human and material resources, and policies, processes and documentation.

In 2013, Jessica will be working closely with the data management team [see below] to finalise the 2-year-old follow-up data and analysis, and facilitating distribution of the study results to key groups of people

in the healthcare sector and community.

Jessica will also continue to support the assessment team by monitoring timelines and recruiting staff as numbers of children being assessed for the 4.5-year-old follow-up study increase.



Jessica Charlton,
CHYLD Study
Coordinator

CHYLD Data Management Team

Dr Janine Paynter, **Data Manager/Statistician**

Janine oversees data entry, clerking and quality control for all of our assessment results, and databases.

She contributes to statistical analyses for the researchers in the group, and will soon be heavily involved in the analysis of the 2 year follow-up data, due to begin early next year.

Dr Greg Gamble, **Biostatistician**

Greg has been the senior statistical advisor for the CHYLD study since its outset and has provided invaluable input into the design of both 2 and 4.5 year old follow-ups, as well as interim analyses of data.

This year, he has been focusing on developing the data analysis plan for the 2 year follow-up study.

Karen Frost, **Database Manager**

Karen joined us in late 2011 and is currently building a secure database where researchers and the data team can enter, store and access a reliable, accurate and real-time version of all study information.

The database will improve appointment scheduling and keeping track of communication with study participants.



Dr Janine Paynter,
Data Manager/
Statistician

Anna Gsell, **Data Manager**

Anna joined us in October 2012, to help with the increasingly demanding workload for the data management team as they finalise the 2 year study datasets.

Anna is managing specific datasets, ensuring that all our data systems are rigorous, providing quality control, and will be involved in data analysis.
[Photo page 8]

Rebecca Young, **Data Research Assistant**

Rebecca joined the team at the start of 2012 and has completed data entry for the many items of information about mothers and babies that form the baseline data for the study.

She is currently cleaning these datasets to find discrepancies and missing data, and to ensure that the results are ready for analysis. [Photo page 8]

Grace McKnight, **Data Research Assistant**

Grace joined us in December 2011 and holds responsibility for receiving and logging all of the assessment information once they arrive in Auckland.

Grace makes digital back up files of all results, checks data integrity and enters all of the data collected by assessors into the CHYLD study databases.
[Photo page 8]



Karen Frost,
Database
Manager



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CHYLD Study Update:



**Sandy Yu,
Optometrist and
PhD candidate**

Sandy Yu, Optometrist and PhD candidate

Sandy is an optometrist based in Auckland. Her PhD project involves the development of a novel method of assessing vision in young children using psychophysics.

Sandy has developed a method of measuring how the brain assesses movement ("motion processing") using an assessment that determines motion coherence thresholds. This vision test is important, as children with

developmental delays often have a deficit in global motion processing, when compared to children of normal development.

The area of the brain that is important for vision, and particularly motion processing, is also thought to be at risk of damage by hypoglycaemia in the newborn period.

As well as the motion coherence threshold, Sandy's team are using

a range of techniques to assess vision in the 2 year olds of the CHYLD study.

"We hope that the outcomes of this research will not only enable us to build a more accurate picture of the visual capabilities of infants who have experienced neonatal hypoglycaemia, but also of normal two year olds, a population on which vision research has been scarce." - Sandy Yu



**Judith Ansell,
Psychologist and
PhD candidate**

Judith Ansell, Psychologist and PhD candidate

Judith, an Educational Psychologist, began working with Liggins in 2007 as an assessor for two earlier follow-up studies in pre-term babies.

In 2009 she took up the opportunity of undertaking a PhD with Professor Jane Harding on development of the two-year-old children involved in the CHYLD study. She began the first two year old assessments in July 2010 and since then has had contact with many families and personally assessed 100 children.

Most of these assessments have been within the wider Waikato Region, although others have involved travel to Whangarei, Wellington and many places in

between.

Judith says that the very generous way in which families have given their time to be part of the study has been memorable, with families showing a real interest in both the results and in being part of further assessment.

An area of particular interest for Judith is the young children's emerging executive function, or their ability to control their thinking and behaviour through processes such as attention, working memory and problem solving.

Some of the techniques used to assess these cognitive processes in young children were devel-

oped for this study. Judith says that continuing to develop these processes offers the possibility of early assessment and intervention with at risk children which may decrease their risk of developing learning problems at school age.

We hope that the developmental data being collected can be used in conjunction with information about the babies' blood glucose concentration in their first week of life, to understand more about how blood glucose concentrations affect child development. This information will contribute to the understanding of a safe blood glucose concentration for newborn babies.



**Arijit
Chakraborty,
Optometrist and
PhD candidate**

Arijit Chakraborty, Optometrist and PhD Candidate

Arijit began his PhD project with the CHYLD study in February 2012, after moving to New Zealand from India.

He is studying within the Department of Vision Science and Op-

tometry under the supervision of Ben Thompson, Nicola Anstice and Rob Jacobs.

Arijit is looking at the effect of neonatal hypoglycaemia on visual development up to 4.5 years of

age. He has been performing the vision assessments on our 4.5 year-olds since shortly after his arrival, and will see many more as the number of 4.5 year-olds being assessed increases in June 2013.



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Matt Signal, Bioengineer and PhD candidate

Matt is a PhD candidate in Bioengineering at the University of Canterbury.

After receiving his bachelors degree in mechanical engineering (first class honours), he embarked on his postgraduate research topic titled "Continuous Glucose Monitoring and Tight Glycaemic Control in Critical Care Patients".

As part of his PhD, he has been

analysing the data obtained from the continuous glucose monitors that were used to monitor sugar levels in a study of babies at risk of hypoglycaemia in the first few days after birth.

Babies who were recruited into that study are now being followed up by the CHYLD study, so their continuous glucose monitoring data form an essential part of the CHYLD data.

Matt had a very successful year in 2012, publishing two papers in scientific journals (*Diabetes Technology and Therapeutics* and *Bio-Medical Engineering Online*).

Matt also gave three presentations at two international conferences (*IFAC Symposium on Biological and Medical Systems, Budapest, Hungary* and *Annual Diabetes Technology Meeting, San Francisco, CA*) [see page 8].



Matt Signal,
Bioengineer and
PhD candidate

Nabin Paudel, Optometry PhD Candidate

Nabin began his PhD project with the CHYLD study in March 2012, after moving to New Zealand from Nepal.

Nabin is studying in the Department of Vision Science and Optometry alongside Arijit, also under the supervision of Ben Thompson, Nicola Anstice and

Rob Jacobs.

Nabin is looking at visual development in our cohort at two years of age, and comparing this with their visual function at 4.5 years of age.

Since shortly after joining the study, Nabin has been very busy

performing the vision assessments on our two-year-olds. To accomplish this, he has been based in Hamilton for several months.

With the recent successful completion of our 2-year-old assessments, Nabin is currently relocating back to Auckland.



Nabin Paudel,
Optometry PhD
candidate

Anna Timmings, Medical and BSc(Hons) Student

Anna is a medical student who has joined the CHYLD study to complete her honours project in between her 5th and 6th years of medical school.

Anna's contributions to the CHYLD study include numerous assessments of paediatric growth and health measures throughout 2012. She has been looking at a variety of influences on health outcomes for two-year-olds in our cohort, and submitted her Honours thesis on this research late this year.

Anna collected information on primary and hospital care, immunisations and growth for almost 150 two year olds seen in the CHYLD study this year.

She found that two thirds of these children had at least one hospital visit before turning 2 years old. She also compared health outcomes for preterm babies against those for term babies.

Preterm infants had twice as many inpatient stays at hospital as term infants, and also ap-

peared to suffer more from respiratory problems, requiring both more primary care and more hospital care.

Interestingly, preterm infants were also more likely to have missed opportunities to be immunised when they visited the doctor.

Anna's contributions to the CHYLD study are much appreciated, and we wish her all the best for her intern year at Tauranga Hospital in 2013.



Anna Timmings,
Medical and
Honours student



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CHYLD Study Update:

Publications and Presentations in 2012

Published journal articles:

Harris, D. L., Weston, P. J., & Harding, J. E. (2012). Incidence of neonatal hypoglycemia in babies identified as at risk. *Journal of Pediatrics*, 161 (5), 787-791.

Signal, M., Le Compte, A., Chase, J. G., Harris, D. L., Harding, J. E., Harris, D. L., & Weston, P. J. (2012). Impact of retrospective calibration algorithms on hypoglycemia detection in newborn infants using continuous glucose monitoring. *Diabetes Technology and Therapeutics*, 14 (10), 883-890.

Signal, M., Le Compte, A., Harris, D. L., Weston, P. J., Harding, J. E., Chase, J. G., on behalf of the CHYLD Study Group (2012). Using Stochastic modelling to identify unusual continuous glucose monitor measurements and behaviour, in newborn infants. *BioMedical Engineering Online*, 11: 45, 2012.

Conference presentations:

Ansell, J., Wouldes, T., Paynter, J., Gamble, G., Harding, J.E., for the CHYLD Study Team. "Developmental outcome at 2 years is similar in later preterm and term infants at risk of hypoglycaemia". *Journal of Paediatrics and Child Health*, 48(Suppl. 1), 18-19, A036, 2012. (Presented at the Perinatal Society of Australia and New Zealand 16th Annual Congress, Sydney).

Signal, M, LeCompte, AJ, Harris, DL, Weston, PJ, Harding, JE and Chase, JG (2012). "Impact of Calibration Algorithms on Hypoglycaemia Detection in Newborn Infants Using Continuous Glucose Monitors," Proceedings of the 8th IFAC Symposium on Biological and Medical Systems (BMS12), Budapest, Hungary.

Signal, M, LeCompte, AJ, Harris, DL, Weston, PJ, Harding, JE and Chase, JG (2012). "Using a Stochastic Model to Detect Unusual Continuous Glucose Monitor Behaviour in Newborn Infants," Proc 8th IFAC Symposium on Biological and Medical Systems (BMS12), Budapest, Hungary.

Signal, M, LeCompte, AJ, Harris, D, Weston, P, Harding, J and Chase, JG (2011). "Sensitivity of Recalibrated Continuous Glucose Monitor Data," Proceedings of the 11th Annual Diabetes Technology Meeting (DTM2011), San Francisco, CA.

Yu, TY, Thompson, B, Anstice, N, Jacobs, R, on behalf of the CHYLD Study group (2012). "Global motion psychophysics in two-year-old children for early detection of dorsal visual stream deficits". (Presented at the New Zealand Applied Neurosciences Conference, Auckland).

Yu, Tzu-Ying (Sandy), on behalf of the CHYLD Study team (2012). "The effects of neonatal hypoglycaemia on vision and visual development at the age of two-years". (Presented at the Waikato Clinical School Biannual Research Seminar, Hamilton).

Yu, Tzu-Ying (Sandy), on behalf of the CHYLD Study team (2012). "Assessing visual function and motion processing in two-year-old children who were at risk of developing neonatal hypoglycaemia". (Presented at the New Zealand National Eye Centre Seminar Series, Auckland).

Yu, Tzu-Ying (Sandy), on behalf of the CHYLD Study team (2012). "Assessing visual function and motion processing in two-year-old children". (Presented at the World Council of Optometry Southern Regional Congress, Melbourne).



Anna Gsell,
Data Manager



Grace McKnight,
Data Entry
Assistant



Rebecca Young,
Data Entry
Assistant



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International Advisory Group



Members of the CHYLD study team and International Advisory Group, 2012

On August 9th and 10th, the CHYLD study team came together for a whole team meeting at the Liggins Institute, University of Auckland. This was an excellent opportunity to review progress and future goals.

We were joined by members of our international advisory group. Discussions revolved around the methodology being used to assess children and record results, such as consideration of test – re-test reliability and how assessments might be further developed.

It was reassuring to see that all assessments are being performed consistently, and that the results we are getting so far are following expected patterns for a population of two year olds. We discussed ways in which we can

improve our methodology going forward, including adding new vision tests to the protocol which will allow us to assess vision more comprehensively and obtain a more detailed dataset.

The input of our international advisors was particularly valuable in contributing towards an analysis plan. Now that we have finished the assessments for the two year olds, we hope to begin modelling some of the data in 2013.

The overall aim will be to develop a predictive algorithm including perinatal variables that will allow us to understand the relationship between neonatal hypoglycaemia and later developmental outcomes.

Having the whole team together, from data staff to assessment and clinical staff and visitors, facilitated productive discussions and sharing of knowledge, and was enjoyed by all who attended.

More recently, from December 10th to 13th, we also enjoyed a visit from Professor Robert Hess. Prof Hess has been particularly involved in the vision assessment aspects of the study, but was only able to join the August meeting by videoconference.

It was extremely valuable to talk in person with all of our international advisors. We are looking forward to their ongoing input to the CHYLD study during the next phase of this exciting project.

Visiting members of our international advisory group in August 2012:

- Professor Bill Hay, MD (Neonatology) from University of Colorado School of Medicine;
- Professor Darrell Wilson, MD (Paediatric Endocrinology) from Stanford School of Medicine.

Also attending via videoconference:

- Professor Robert Hess, PhD, DSc (Ophthalmology) from McGill University-Montreal
- Dr Tonse Raju, our NIH programme director

Visiting members of our international advisory group in December 2012:

- Professor Robert Hess, PhD, DSc (Ophthalmology) from McGill University-Montreal