

12th & 13th October 2017

University of Liverpool

The Foresight Centre,

1 Brownlow Street, L69 3GL

**Longitudinal Developmental Science from
Birkenhead to Bangalore: sex differences and pathways
from pregnancy to child and adolescent mental health problems**



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From Birkenhead to Bangalore – investigating shared and distinctive perinatal risks and protective factors for child mental health in UK & India

MRC / ICMR funded
Oct 2015 – Dec 2018

Dr Helen Sharp

- UK** - H Sharp, A Rahman, J Hill , A Pickles
- NIMHANS** - P Chandra, , S. Srinath, G Desai, J Vijaysager, T Kishore
and K Thennarasu

FRIDAY, 5 SEPTEMBER

HEALTH | SCIENCE & TECHNOLOGY

University of Liverpool > News > Liverpool welcomes first Indian Fellows

PUBLISHED: AUGUST 27, 2014 | LEAVE A COMMENT | SHARE

Liverpool welcomes first Indian Fellows



The University of Liverpool has welcomed three Indian Fellows, as part of its Fellowship programme aimed at strengthening the international experience of research and teaching for early to mid-career researchers.

The first of 10 Fellows to arrive at the University over the next academic year, Professor Amit Chakraborty, from the

National Institute of Technology (NIT) Durapur; Professor Ashutosh Trivedi, from the Indian Institute of Technology (IIT) in Mumbai; and Professor Prabha Chandra from the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, will spend three to six months at Liverpool working with research teams to build long-lasting partnerships between the UK and India.

Ashutosh Trivedi is Assistant Professor in the Department of Computer Science and Engineering at IIT, where he focuses on developing theory, techniques, and tools for formal analysis, verification, and synthesis of hybrid systems. He is working with Dr Sven Schewe and Dominik Wojtczak at the University to use their mutual expertise to further the general understanding of stochastic control in cyber-physical systems.

Impact of mental health

Expert in women's mental health, Professor Prabha Chandra, is investigating the impact of mental health in pregnancy on fetal and infant outcomes. Working with Professor Atif Rahman, in the Institute of Psychology, Health and Society, she is interested in adapting interventions for perinatal depression in Indian women.

"Our Indian Fellows are the next generation of leaders in the field of science, health and technology."



- **Projects that were submitted during the fellowship and got funding**
- **ICMR- MRC joint initiative:** Psychosocial and nutritional predictors of child mental health: longitudinal study of shared and distinctive risk and protective factors in UK & India
- **Helen Sharp – UOL and Prabha Chandra – NIMHANS**
- **The Joint Global Research Programme: Women's and children's health –MRC- DBT- DFID**
- Multicomponent intervention to reduce home-exposure to second-hand smoke (SHS) during pregnancy and postnatal period: a randomised controlled trial
Atif Rahman- UOL; Prabha Chandra – NIMHANS and Rumana Huque – University of Dhaka



The whole team – June 2016





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at the Maudsley



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The Wirral Child Health and Development Study: pregnancy - 9 yrs

Social, emotional and biological processes in emergent
conduct problems

Dec 2006 – May 2018

Investigators

- Jonathan Hill
- Helen Sharp
- Andrew Pickles
- John Quinn
- Chris Murgatroyd



MRC

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Plus our team of 25 research staff and postgraduate students

Please go to website for links to study publications: <http://www.liv.ac.uk/psychology-health-and-society/research/first-steps/>

Wirral Aims – to identify the earliest origins of childhood conduct problems

- Evidence from studies of children and adolescents strongly suggests that different biological and psychological mechanisms underpin subtypes of aggressive and disruptive behaviour problems, implying distinctive pathways from infancy, which have yet to be elucidated.
- *Starting in pregnancy WCHADS aims to identify those pathways, representing distinct mechanisms and intervention targets*
- Study is also ideally set up to examine emotional problems and cognitive development

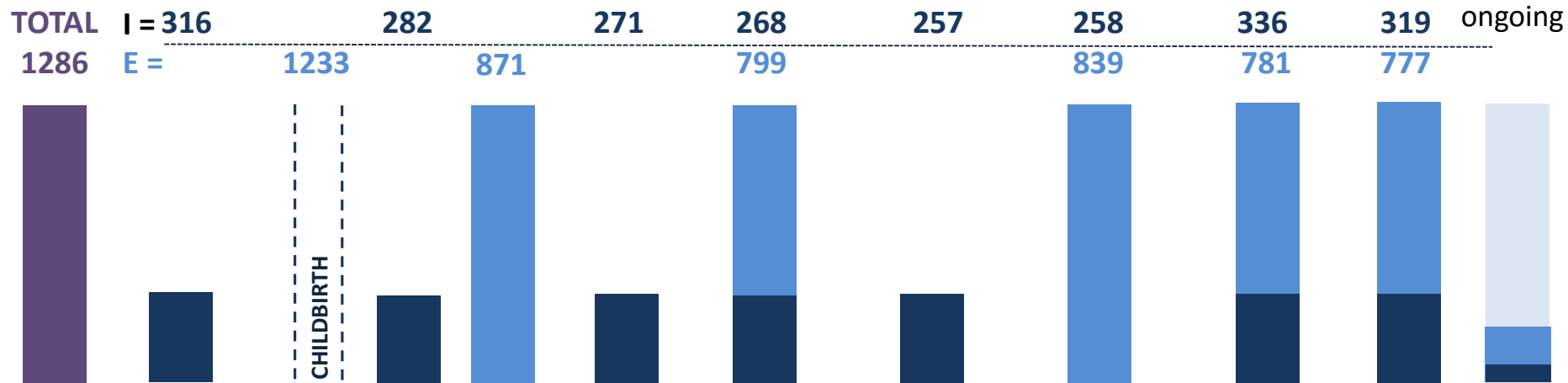




Design

- **Prospective longitudinal study**
 - starting at 20 wks of pregnancy with follow-up to 9 year old
- **Two stage epidemiological sampling strategy.**
 - Consecutive ‘extensive’ sample of first time mothers aged ≥ 18 years, English speaking and their partners.
 - Smaller ‘intensive’ sample stratified by relationship functioning assessed by screening at 20 weeks gestation
 - **Provides sample with elevated environmental and genetic risks for conduct disorders**
- Repeated measures design with both ‘Extensive’ and ‘Intensive’ sample follow-up.
- **Follow-up of whole sample allows general population estimates to be derived**
- Repeated measures – developmentally sensitive
- Multiple phases of assessment from pregnancy to age 9 years...
 - 20wks, 32 wks, birth, 4 weeks, 12 wks, 6 mo, 14mo, 2.5 yr, 3.5 yr, 4.5-5 yrs, 7 yrs and 9yrs.**

Wirral Child Health and Development Study – Stratified design and Measurement



PREGNANCY

20 wk PHASE 1
32 wk PHASE 2

CHILD BIRTH

PHASE 3

4-8 PHASE 4
9-12wks PHASE 5
7 mth PHASE 6
14 mth PHASE 7/8
2 ½ yrs PHASE 9
3 ½ yrs PHASE 10
4 ½ -5 yrs PHASE 11/12
7 yrs PHASE 13
9 yrs PHASE 14

= intensive sample (I)
 = extensive sample (E)
() = included intensive invitees

CHILD LAB ASSESSMENTS
 (mother-child interaction; cognitive, behavioural, social and emotional development; physiological reactivity; temperament and psychopathology; parenting quality; repeated DNA sampling)

PARENTAL MEASURES
 (Mental health, personality, life events, relationship quality, demographics, drug/alcohol/smoking)



4 weeks



6 months



14 months



2.5 years



3.5 years



4.5 years

Biological and environment processes - gene-environment interplay and foetal programming

Genes
Prenatal Stress
Life events
Deprivation
Maternal sensitivity
Early touch
Temperament
Physiology
Behaviors & emotions

Genes, Brain and Behavior
Official publication of the International Behavioural and Neural Genetics Society
Genes, Brain and Behavior (2013) doi: 10.1111/gbb.12033

Evidence for interplay between genes and maternal stress *in utero*: monoamine oxidase A polymorphism moderates effects of life events during pregnancy on infant negative emotionality at 5 weeks

J. Hill^{1*}, G. Breen¹, J. Quinn¹, F. Tibu¹, H. Sharp¹ and A. Pickles^{2*}

Received 7 January 2013, revised 22 February 2013, accepted for publication 25 February 2013



JOURNAL OF CHILD PSYCHOLOGY AND PSYCHIATRY
Journal of Child Psychology and Psychiatry 54:12 (2013), pp 1308–1317
doi:10.1111/jcpp.12

Evidence for interplay between genes and parenting on infant temperament in the first year of life: monoamine oxidase A polymorphism moderates effects of maternal sensitivity on infant anger proneness

Andrew Pickles,¹ Jonathan Hill,² Gerome Breen,¹ John Quinn,³ Kate Abbott,² Helen Jones,³ and Helen Sharp³

¹Institute of Psychiatry, King's College London, London, UK; ²University of Manchester, Manchester, UK; ³University of Liverpool, Liverpool, UK

OPEN ACCESS Freely available online
PLOS ONE

Frequency of Infant Stroking Reported by Mothers Moderates the Effect of Prenatal Depression on Infant Behavioural and Physiological Outcomes

Helen Sharp^{1*}, Andrew Pickles², Michael Meaney³, Kate Marshall⁴, Florin Tibu⁴, Jonathan Hill⁴

¹Institute of Psychology, Health and Society, University of Liverpool, Liverpool, United Kingdom, ²Department of Biostatistics, Institute of Psychiatry, King's College London, London, United Kingdom, ³Douglas Mental Health University Institute, McGill University, Montreal, Canada, ⁴Mental Health and Neurodegeneration Research Group, University of Manchester, Manchester, United Kingdom

Mothers' touch could change effects of prenatal stress
published on October 17 2012



Babies' heart rate response to stress was changed by how often a mother stroked the head, back, legs and arms

Psychological Medicine (2015), 45, 269–283. © Cambridge University Press 2014
doi:10.1017/S0033291714001342 ORIGINAL ART

Maternal antenatal anxiety, postnatal stroking and emotional problems in children: outcomes predicted from pre- and postnatal programming hypotheses

H. Sharp¹, J. Hill^{2*}, J. Hellier³ and A. Pickles³

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²Institute of Brain, Behaviour and Mental Health, University of Manchester, Manchester, UK
³Institute of Psychiatry, King's College London, London, UK

Study website: <http://www.liv.ac.uk/psychology-health-and-society/research/first-steps/>

Early psychosocial predictors of child mental health: longitudinal study of shared and distinctive risk and protective factors in UK & India (Jan 2016- Dec 2018)

UK - H Sharp, A Rahman, J Hill , A Pickles
NIMHANS - P Chandra, , S. Srinath, G Desai, J Vijaysager,
T Kishore K Thennarasu



- **AIMS**
- **To study early risk and protective factors for childhood mental health problems**
- **To identify prenatal and infancy risks that are common to Western and South Asian populations and those that are distinctive up to age 2 years.**
- **Findings will inform the development of effective early interventions to prevent future mental health problems in children and adolescents.**
- **We aim to work together to build capacity in India for longitudinal cohort studies.**

Objectives

- To follow children and families through infancy to early childhood, assessing developmental risks and behavioural outcomes in a South Indian sample of 650 women from PRAMM (Prospective Assessment of Maternal Mental Health) study.
- To use common measurement between the Wirral Child Health and Development Study (WCHADS) and Bangalore Child health and Development Study (BCHADS) to enable data analyses to be conducted of merged UK – Indian datasets.

Objectives continued...

- To measure factors related to maternal mental health and caregiving likely to be distinctively relevant to the South Asian setting, and examine them alongside factors identified in previous, predominantly Western, research.
 - Nutrition and prenatal stress
 - Gender discrimination
 - Postnatal caregiving environment
 - G x E interplay
- The current study will evaluate the relative contributions of these factors in early infant cognitive, emotional and behavioural development.

Advances in methodology - To develop culturally sensitive measurement of the caregiving environment, by combining the clinical and research knowledge of the Indian investigators with UK expertise in establishing new measures.

Example hypotheses



- Prenatal depression will predict behavioural and emotional problems in the child at 24 months of age, after controlling for postnatal maternal sensitivity, maternal depression and under nutrition in mother
- The extent of postnatal infant stroking will moderate the association between prenatal depression and child emotional and behavioural problems.

Mothers' touch could change effects of prenatal stress

published on October 17 2012



Babies' heart rate response to stress was changed by how often a mother stroked the head, back, legs and arms

Scientists at the Universities of Liverpool, Manchester, and King's College London, have found that mothers who stroke their baby's body in the first few weeks after birth may change the effects that stress during pregnancy can have on an infant's early-life development.

[Frequency of Infant Stroking Reported by Mothers Moderates the Effect of Prenatal Depression on Infant Behavioural and Physiological Outcomes](#)

Helen Sharp, Andrew Pickles, Michael Meaney, Kate Marshall, Florin Tibu, Jonathan Hill

Research Article | published 16 Oct 2012 | PLOS ONE

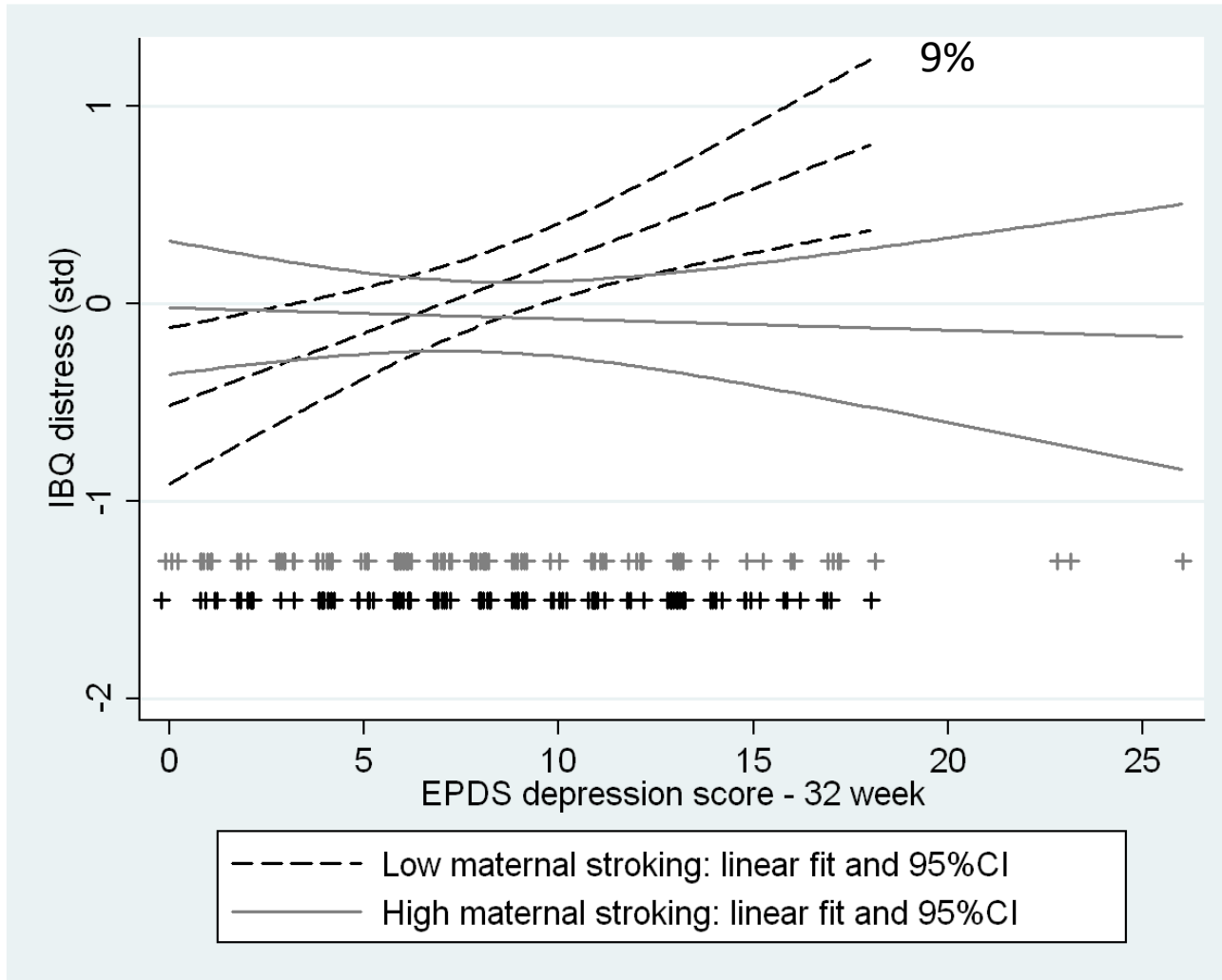
10.1371/journal.pone.0045446

- Studies in animals demonstrate sustained effects of prenatal stress on physiological stress reactivity and behaviour in the offspring (*fear and depression-like behaviours, altered HPA and cardiovascular regulation; Meaney et al 2007*).
- In animals, these effects are modifiable by early maternal behaviours, notably early licking and grooming behaviour. (*Vallee et al, 1999; Weinstock, 2008*)
- These effects are known to be mediated in animals via alterations in glucocorticoid receptor gene expression. (*Meaney et al 2007*)



- Consistent with the animal literature, human studies find that indices of prenatal stress such as maternal depression or anxiety in pregnancy also predict
 - altered HPA reactivity (*de Bruijn et al 2009*)
 - cardiovascular regulation (*Cottrell et al 2009*)
 - negative emotionality in infants (*Davis et al 2007*)
 - conduct disorders and emotional problems in children (*Glover, 2011; O'Connor et al, 2003; Seckl et al 2008*).
- Post-natal maternal behaviours may be expected to modify prenatal effects, but this has not previously been examined in humans.
- **We examined whether maternal stroking over the first weeks of life has similar physiological and behavioral sequelae in humans, to those of licking/grooming in rodents.**

Interaction between maternal stroking and prenatal depression on infant distress to limitations. Simple regression lines and 95% confidence envelopes showing the interaction between maternal reports of stroking (median split) and prenatal depression, with infant IBQ distress to limitations at 29 weeks ($p=0.007$ from multivariate regression).



IBQ 'distress to limitations' subscale = index of frustration proneness

Example hypotheses

- Adverse context of mothering (poor support and partner violence) will predict emotional and behavioural problems directly and be mediated via maternal depression and maternal sensitivity
- MAOA G by E predicting infant negative emotionality will be demonstrated in interaction with indices of overall sensitivity provided by caregivers in the Indian setting



Evidence for interplay between genes and parenting on infant temperament in the first year of life: monoamine oxidase A polymorphism moderates effects of maternal sensitivity on infant anger proneness

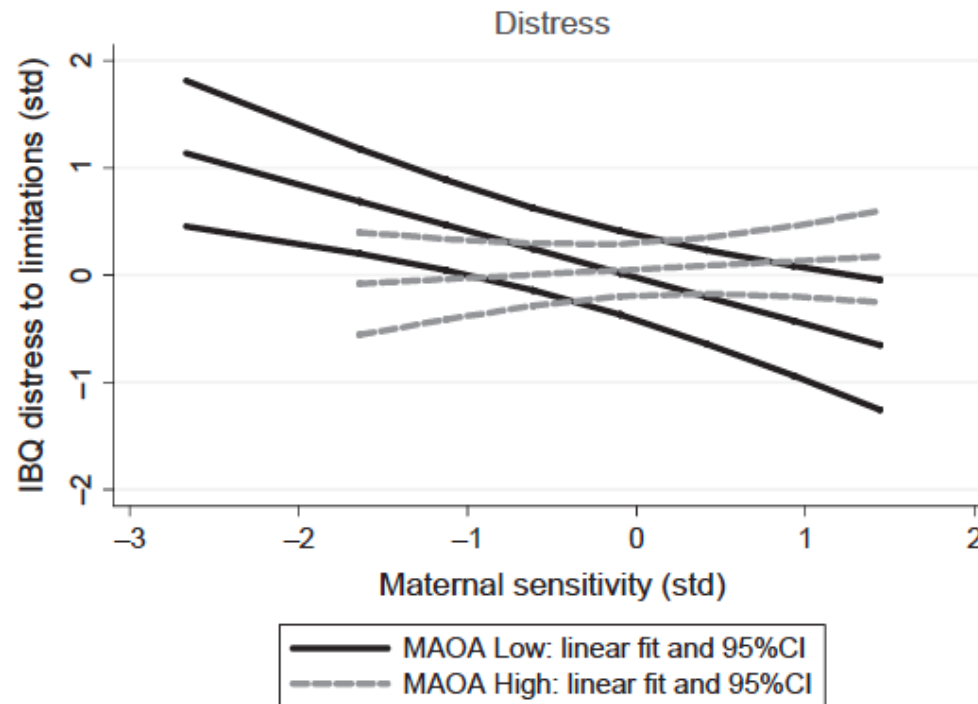


Figure 1 Population weighted infant distress to limitations (anger proneness) and maternal sensitivity by MAOA genotype. Regression lines are shown after covarying for confounder interactions and 29 weeks maternal report of infant distress to limitations. In females only homozygous individuals are included

Bangalore Sampling and Recruitment

- Longitudinal, prospective cohort study with repeated measures design
- Assessments: 1st trimester, 2nd trimester, 3rd trimester
8-10 weeks, 6 months, 12 months and 24 months
- Women identified in the antenatal clinic of two maternity units in geographical areas of Bangalore
- All pregnant women aged 18 years and above in the first trimester of pregnancy, were approached over a 20 month period. Exclude the most transient.
- Recruitment, data collection and retention are supported by close links with obstetricians, Anganwadi workers and management in the Bangalore Urban antenatal clinic centres.

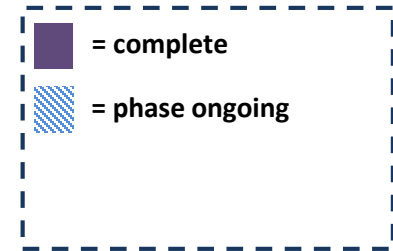
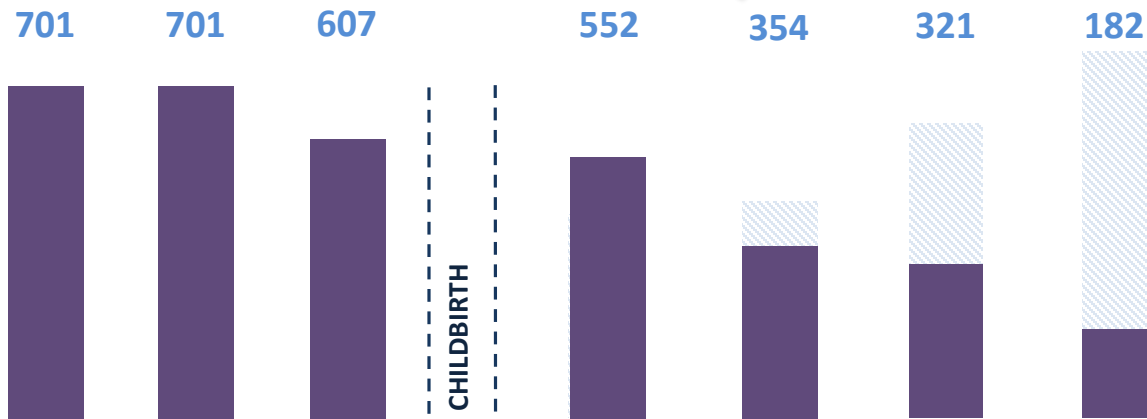
Bangalore Child Health and Development Study

– prospective longitudinal design and Measurement



ongoing

TOTAL 912



PREGNANCY

8-12 wk 1
20 wk 2
32 wk 3

9-12wks PHASE 5
7 mth PHASE 6
14 mth PHASE 7/8
2 yrs PHASE 9

CHILDBIRTH

PHASE 4

CHILD ASSESSMENTS

(mother-child interaction; cognitive, behavioural, social and emotional development; temperament and psychopathology; parenting quality; repeated DNA sampling)

PARENTAL MEASURES

(Pregnancy nutrition, Mental health, shared caregiving, gender discrimination, history of care and control in own childhood, life events, relationship quality, demographics)

Progress to date

- Antenatal recruitment of 901 pregnant women is now complete
- Slightly later than planned due to government changes mid-study to routine antenatal care.
- Last 200 had to be recruited in second trimester of pregnancy
- Postnatal follow-ups are well under way.
- 6 month assessments nearly complete
- Age 1 year and age 2 year – assessment phases ongoing.

Challenges and successes!

- Timing of receiving ICMR funding and therefore start date
 - knock on effects to 6 m phase
- Mobility of women living in urban slums
- Contacting women directly
- Filming in home setting & enabling attendance for research assessments in community venues
- Attention to cultural equivalence of measurement e.g., maternal mental health and caregiving
- Development opportunities for new measures e.g., gender discrimination, quantifying shared caregiving

Observing maternal sensitivity 6m

- Video removed

Observing maternal sensitivity 1 yr

- Video removed

Challenges and opportunities!

- Cross-cultural measurement – capturing meaningful variation (e.g, shared caregiving environment, maternal mental health, gender discrimination)
- **Enormous potential to inform focus for early interventions and have significant impact.**
- Overcoming barriers to research assessments in community venues
- Conducting home based assessments in urban slums
- Tracing families and locating homes
- Dealing with challenges from family members
- Communication with participants (husband holds phone / low literacy / no postal route)

Capacity building – takes many forms

- Weekly skype calls and team meetings
- Virtual knowledge network
- Statistics workshop and Research Methods
- Knowledge exchange: multiple domains - Genetics / Statistics / Psychology and Psychiatry



Assessment in the community





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Longitudinal Developmental Science from Birkenhead to Bangalore: sex differences and pathways from pregnancy to child and adolescent mental health problems

From Birkenhead to Bangalore – investigating shared and distinctive perinatal risks for child mental health

Dr Helen Sharp, University of Liverpool, Wirral & Bangalore Child Health and Development Studies

Cultural issues in assessing maternal mental health and mother infant interactions in the Bangalore Child Health and Development cohort study

Dr Geetha Desai, National Institute of Mental Health and Neuroscience, India, Bangalore Child Health and Development Study

Conceptualising cross cultural differences in early caregiving: comparative levels of instruction and mind-mindedness

Laura Bozicevic, University of Liverpool, Bangalore Child Health and Development Study

BREAK

Comparing and combining cohorts and the muddle of measurement

Professor Andrew Pickles, Director of Biostatistics, King's College London

Thank
You!