Maternity Research Theme Launch

19 September 2019

Warwick Clinical Trials Unit

Warwick Medical School

University of Warwick

Coventry, CV4 7AL

Maternity - http://warwick.ac.uk/maternityresearch

Maternity
http://warwick.ac.uk/maternityresearch

Programme for Launch of the Maternity Research Theme Warwick Clinical Trials Unit

Venue: Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick.

Date: 19 September 2019

Time	Event	Speaker
12.00 – 13.00	**Lunch & Networking**. Viewing the 'Holding Time' installation by Lisa Creagh / research posters	
13.00 – 13.10	Welcome and Introduction	Professor Debra Bick
13.10 - 13.25	Research at Warwick Medical School	Professor Sudhesh Kumar OBE
13.25 – 13.50	Parents facing 'difficult' babies: Long term consequences of crying, sleeping and feeding problems'	Professor Dieter Wolke
13.50 – 14.15	Why evidence is important to shape healthcare policy	Professor Jacqueline Dunkley-Bent OBE
14.15 – 14.30	Clinical trials in maternity care: past, present and future	Professor Debra Bick
14.30 – 14.45	Obstetric research at Warwick	Professor Siobhan Quenby
14.45 – 15.15	**Refreshments & Networking**	
15.15 - 15.25	Anticoagulants for Living FoEtuses in women with recurrent miscarriage and inherited thrombophilia (Alife)	Ms Sarah Lowe and Ms Jess Smith
15.25 - 15.35	Induction of labour for predicted macrosomia (The Big Baby trial)	Mrs Jackie Dewdney and Dr Sara Wood
15.35 –15.45	Chronic Endometritis and Recurrent Miscarriage (The CERM trial)	Mrs Amy Jackson and Dr Joshua Odendaal
15.45 - 15.55	Linking with City of Culture 2021 – Holding Time Coventry – City of Breastfeeding	Ms Lisa Creagh and Dr Joanne Fisher
15.55 – 16.05	Maternal Journal - creative journaling to support mental health and wellbeing	Ms Laura Godfrey-Isaacs
16.05 - 16.15	Using qualitative research in the clinical trials context	Dr Sophie Rees
16.15 – 16.25	The Tommy's Centre The Centre for Early Life Research	Professor Siobhan Quenby
16.25 – 16.35	Close	Professor Debra Bick

Speaker Biographies

Professor Jacqueline Dunkley-Bent OBE
Chief Midwifery Officer - NHS in England

Professor Jacqueline Dunkley-Bent has vast experience in healthcare provision. Jacqueline is the Chief Midwifery Officer for the NHS in England and is one of two National Maternity Safety Champions. She has previously been the Head of Maternity, Children and Young People at NHS England and is visiting Professor of Midwifery at Kings College London and London South Bank University.

She has worked as a midwife and a nurse and held senior positions in clinical practice, education, leadership and management including: Director of Midwifery and Nursing positions for Women's and Children's services at Imperial College Healthcare Trust & Guy's & St Thomas' NHS Foundation Trust.

Academic roles have included: Senior Lecturer, Curriculum Leader, LME and Professor of Midwifery. Her experience has seen her leading and influencing national maternity standards and guidance. She also influences healthcare, nationally and internationally through, education and publications and is frequently invited to speak at national and international conferences. She is a member of Tommy's Charity National Advisory Board as Midwifery advisor, and the Women of the Year management committee. Her voluntary work currently includes Midwifery Ambassador for the charity 'Saying Goodbye'.

In 2014 she received the HSJ, BME Pioneers award and in 2015 she was selected from over 100 nominations for inclusion on Nursing Times' Leaders 2015 list that celebrates nurses and midwives who are pioneers, entrepreneurs and inspirational role models in their profession.

Professor Sudhesh Kumar OBE
Dean of Warwick Medical School and Director of the Institute of Digital Healthcare – at the University of Warwick

Professor Sudhesh Kumar is Dean of the Warwick Medical School and Director of the Institute of Digital Healthcare at University of Warwick. He is also a Non-Executive Director on the University Hospital Coventry & Warwickshire NHS Trust Board and NHS Digital.

He is a clinical endocrinologist by background with 22 years' experience as a Consultant Physician in the NHS. His interests include developing novel approaches, including medical technology to managing obesity and diabetes that has helped to transform and improve patient care and treatment. His expertise includes adipocyte biology, whole body metabolism including indirect calorimetry, clinical trials and development and testing of novel technology based solutions. He has published over 240 papers and 6 books on these subjects.

Speaker Biographies

Professor Dieter Wolke
Professor of Developmental Psychology and Individual Differences – Department of Psychology at the University of Warwick

Dieter studied at the University of Kiel (Germany) and University of London and obtained his PhD from the University of London, Faculty of Science. He has worked at different colleges of the University of London (Institute of Education; King's College; Institute of Child Health) and the Universities of Munich, Hertfordshire and Bristol. Before his appointment at the University of Warwick, he worked in the research funding sector (Scientific Director of the Jacobs Foundation, Zurich, 2004-2006) while holding Visiting Professorships at the University of Bristol and University of Zurich.

Much of his research is interdisciplinary (psychology, social and medical sciences), longitudinal and in the field of Developmental Psychopathology. His major research topics are: 1. how preterm birth affects brain development and psychological development and quality of life; 2. early regulatory problems (crying, sleeping and feeding) in infancy and their long term consequences; and 3. Peer or sibling victimization (bullying): precursors, consequences and interventions. He is involved as PI/Co-PI in a range of follow-up studies in the UK and Germany including the ALSPAC cohort, EPICure Study and the Bavarian Longitudinal Study. He is joint manager of the Horizon 2020 RECAP project involving 12 countries trying to improve the lives of preterm children.

Dieter was the Chair of the Follow-up Care committee co-ordinating the Development of European Standards for Care of Newborn Health (EFCNI newborn-health-standards project). He received an honorary doctorate (Dr rer nat h.c.) from the Ruhr University Bochum, Germany, in 2014 for his contribution to Psychological Science. He has published over 300 original papers. He is listed in the 2018 Highly Cited Cross-Fields list honouring the most cited scientists in the world.

Speaker Biographies

Ms Lisa Creagh
Artist, London

Lisa Creagh is a multi-disciplinary artist who has collaborated with mothers to create a unique portrait of breastfeeding.

Holding Time, began with portraits of mothers breastfeeding which were then animated to show the high levels of intimacy and contact involved in the act. This was partnered with a Time Piece that 'grew' alongside the mothers, showing the added value of every second of that relationship. The idea was to address the cultural barriers to breastfeeding; the lack of positive imagery, the perception that breastfeeding is a 'waste' of time, the loss of status and value that women report feeling when breastfeeding. The work is enriched by an online programme: Creagh has interviewed mothers and health professionals about their experiences of breastfeeding and these have been popular on a dedicated YouTube channel.

Lisa Creagh is an artist and producer whose work spans the boundaries of art and activism. Educated at Goldsmiths College, she moved to New York after graduating where she experienced the early advent of digital media in the Dot Com industry. As a curator and producer she launched grass roots organisations such as the Brighton Photo Fringe in 2003. In 2006 she received critical acclaim for the participatory nature of Tidy Street, a site specific installation produced in collaboration with neighbourhood residents. In 2009 she received Arts Council support and commercial success with The Instant Garden, large decorative floral 'gardens' created from thousands of digital images. She has exhibited her work nationally and internationally and her work is held in many hospital and private collections.
lisacreagh@btconnect.com @lccreagh

Dr Sophie Rees
Research Fellow - Warwick Clinical Trials Unit, the University of Warwick

Sophie is a Research Fellow at the University of Warwick. She is a sociologist by training and has a doctorate in Health and Social Studies.

She has worked on several qualitative sub-studies at the Clinical Trials Unit and is currently working on developing research ideas and submitting grant applications.
s.rees.1@warwick.ac.uk

Speaker Biographies

Mrs Jackie Dewdney
Co-applicant on the Big Baby Trial - Erb's Palsy Group UK

I'm one of the trustees of the Erb's Palsy Group UK and more important mum to Samuel. I live in a small town called Shefford in Bedfordshire and love reading, too much sometimes according to my husband but I disagree reading much more important than housework.

I have been part of the Erb's Palsy group for about 11 years now and have seen a lot of changes. We have well over 2,000 families and professionals in the group, so the learning curve is permanent. We hold annual conferences for midwives or physios on a yearly basis, in addition to going out myself and talking through my own personal birth trauma with midwifery staff, students and anyone else who's interested.

I have been part of the big baby trial team since the beginning and am enjoying learning a whole new set of skills as to how trials are run and often ending up getting home after meetings and googling words I didn't quite understand.
jackie@erbspalsygroup.co.uk @erbspalsygroup

Mrs Amy Jackson
Co-founder of the Lily Mae Foundation, Coventry

Following the loss of her daughter Lily Mae in February 2010 Amy set out to help parents, their families and friends who were going to experience the same devastating and traumatic loss as herself. As a teacher of the hearing impaired, Amy decided to devote her life to setting up the Lily Mae Foundation to build many forms of support for bereaved parents to access.

Most recently Amy has undertaken training to become a Bereavement Support Worker. Amy now offers a unique one-to-one support service following the loss of a baby, through The Lily Mae Foundation. This Babyloss Support Service is highly regarded by clients and medical professionals.

Amy is a co-applicant on the CERM Trial and has thoroughly enjoyed being part of such a unique Research Trial from the beginning.
info@lilymaefoundation.org @TheLilyMaeFoundation

Speaker Biographies

Professor Debra Bick
Professor of Clinical Trials - Division of Clinical Trials at Warwick University of Warwick

Debra Bick is Professor of Clinical Trials in Maternal Health at the Warwick Clinical Trials Unit, University of Warwick and Editor in Chief of the journal 'Midwifery'. Her research, much of which has focused on interventions to improve women's physical and mental health following birth, has been funded by NIHR, DfID, The Health Foundation, Big Lottery and Burdett Trust for Nursing. She is currently leading research on women's and clinicians' views and experiences of postnatal care following hypertensive disorders of pregnancy, a multi-centre cohort study of postnatal morbidity, postnatal weight management for women who had higher BMIs at pregnancy commencement, pathways for women with medically complex pregnancies, and breastfeeding as an early intervention to prevent child obesity. In addition to leading research as a chief investigator, Debra is collaborating with colleagues on several large multi-centre trials and programme grants for applied research.

Debra is lead and/or co-author of systematic reviews for the Cochrane Library and Joanna Briggs Institute. She is Chair of the RCOG Intrapartum Clinical Studies Group, a steering group member of the NIHR 70@70 programme to support senior nurse and midwife research leadership, a member of the NIHR HS&DR programme Research Priorities Committee and independent panel member of the National Maternity and Perinatal Audit. She is currently supervising a number of PhD students funded by NIHR fellowships and midwives awarded NIHR pre-doctoral Clinical Academic Fellowships. Debra has contributed to several major policy reviews of maternity care in the UK and internationally and guidelines developed by NICE and the WHO. She is a visiting professor at King's College London, the University of Birmingham and at Bournemouth University. debra.bick@warwick.ac.uk @DebraBick

Dr Joshua Odendaal
Clinical Research Fellow / Obstetrician And Gynaecologist

Joshua attended medical school at Imperial College London. Whilst there he intercalated a BSc(Hons) in Medical Sciences with Surgery and Anaesthesia. He undertook a basic science project in women's health to gain a grounding in scientific technique. He went on to gain a national training number in obstetrics and gynaecology within the West Midlands and proceeded in training to registrar level.

He has recently completed the membership examinations of the Royal College of Obstetrics and Gynaecology. He has taken time out of training to further develop his academic career within the specialty and undertake a PhD. He is presently clinical research fellow for the CERM trial concurrently undertaking work on the clinical and basic science aspects of the trial.
joshua.odendaal@warwick.ac.uk

Speaker Biographies

Dr Sara Wood
Trial Coordinator - Division of Clinical Trials at Warwick
University of Warwick

Sara studied at the University of Reading where she obtained her first degree and her PhD in Bovine Reproductive Endocrinology. She has worked in the following clinical research organisations and pharmaceutical companies in Data Management departments for over 16 years: Quintiles (in Frankfurt-am-Main), MDS Pharma services, Quanticate, Astra and Astra Zeneca.

Sara has been a Trial Coordinator working on the Big Baby Trial at the Warwick Clinical Trials Unit, University of Warwick since January 2018. Her trial responsibilities include managing the receipt, tracking, entry and cleaning of the data; management and coding of Serious Adverse Events; organising meetings and liaising with sites from study set-up procedures to providing ongoing support.
sara.wood@warwick.ac.uk.

Ms Sarah Lowe
Trial Manager - Division of Clinical Trials at Warwick
University of Warwick

Sarah started working in clinical trials nine years ago when she joined Warwick Clinical Trials Unit (CTU) as a Data Entry Clerk. Since then Sarah has had various roles within the CTU and has worked on a wide range of trial portfolios including pain management, oncology and orthopaedic.

Sarah is now the Trial Manager for two of the reproductive health trials, ALIFE2 and CERM. Sarah's day to day tasks include answering queries from sites and providing support with recruitment, organising the content for Trial Management Group Meetings and visiting sites to ensure their suitability for a trial.

Within her role Sarah says that she most enjoys visiting hospitals and meeting the staff as this is the best way to build up a good relationship with those that you will be providing support to for potentially the next few years. Sarah said these visits are also a good way to hear about success stories that have come about due to a clinical trial, nothing is nicer than being told that due to research a woman has now become a mother, something which may never have seemed possible.
s.l.lowe@warwick.ac.uk

Speaker Biographies

Professor Siobhan Quenby
Professor of Obstetrics - Division of Reproductive Health, Warwick Medical School at the University of Warwick

Siobhan Quenby is the Director of the Biomedical Research Unit in Reproductive Health, Professor of Obstetrics at the University of Warwick, and Honorary Consultant at University Hospital Coventry and Warwickshire NHS trust. Siobhan has twenty years of experience in translational research into recurrent miscarriage and dysfunctional labour. She has published over 75 original articles and numerous book chapters on this subject.

She serves on several international and national committees; European Society for Human Reproduction and Endocrinology Early Pregnancy Special Interest Group, MHRA Expert Advisory Panel for women's health, Scientific Advisory Committee of the Royal College of Obstetricians and Gynaecologists (RCOG), RCOG Preterm Labour Clinical Study Group, RCOG Early Pregnancy Clinical Study Group. She is currently an Associate Editor for BMC Pregnancy and Childbirth and has served as an Associate Editor for Human Reproduction. Her work has received considerable media interest, including from national newspapers, BBC radio and TV, ITV and Channel 4 news. She is also a media spokesperson for the RCOG.

Ms Jessica Smith
Senior Project Manager - Division of Clinical Trials at Warwick University of Warwick

Jessica Smith is a Senior Project Manager (SPM) at Warwick Clinical Trials Unit and part of both the ALIFE2 and CERM trial teams. As an SPM Jessica is responsible for overseeing these trials which includes supporting the trial team with the successful delivery of these trials and being responsible for the trial budget ensuring resources are being spent and used appropriately.

Jessica has worked in clinical trials for ten years starting in 2009 as a NIHR Research Associate in Research Methodology at Warwick Clinical Trials Unit before undertaking an MSc in Clinical and Experimental Medicine at University College London (UCL). Jessica then returned to Warwick Clinical Trials Unit moving into trial coordination and trial management working on trials within both the emergency and critical care portfolio and the trauma and orthopaedics portfolio. In 2015 Jessica moved to UCL Cancer Trials Centre where she spent three years managing both a commercial Phase I and large Phase III trial of Investigational Medicinal Products (IMP) before returning to Warwick Clinical Trials Unit once more as a Senior Project Manager.
jessica.smith.1@warwick.ac.uk

Speaker Biographies

Laura Godfrey-Isaacs is an artist, midwife, creative producer and birth activist.

She aspires to bring her knowledge and experience in the arts to bring fresh interdisciplinary perspectives to inform midwifery education, practice, policy and research. She regularly presents at conferences, and creates interdisciplinary projects and campaigns, such as Maternal Journal www.maternaljournal.org which supports mental health and well-being through creative journaling.

She is currently Ambassador for Proceate Projects, Co-Chair of the Women's Equality Party's Health Committee, Board Advisor of The International Forum for Wellbeing in Pregnancy, and member of the Thought Leadership Group at the NMC reviewing midwifery education standards.

Blog: https://www.all4maternity.com/caring/blog/birth-art-culture @godfrey_isaacs
Website: www.lauragodfreyisaacs.com

Dr Joanne Fisher
Senior Research Fellow - Division of Clinical Trials at Warwick University of Warwick

Dr Joanne Fisher is a Senior Research Fellow in the Division of Clinical Trials. She completed a PhD in Psychology at the University of Warwick in 2001.

Joanne has undertaken research in doctor-patient communication, pre-hospital and emergency care, cancer rehabilitation and in reproductive health. Joanne is co-applicant on two large obstetric trials: Big Baby and the Chronic Endometritis in Recurrent Miscarriage (CERM) Trial. Joanne teaches on the MB ChB programme and on the taught CPD/in Warwick Medical School. She is involved in the development of new postgraduate courses in cardiovascular health and community care.

She is co-course leader for a new Patient and Public Involvement (PPI) training course. Joanne was the training and development lead in the Divisional of Health Sciences and now oversees the Division of Clinical Trials Training and Development Awards and Career Development Awards.
joanne.fisher@warwick.ac.uk

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WARWICK
THE UNIVERSITY OF WARWICK

Parents facing "difficult" babies: Long term consequences of crying, sleeping and feeding problems

Professor **Dieter Wolke** (Ph.D; Dr rer nat h.c.; C.Psychol; AFBPsS)

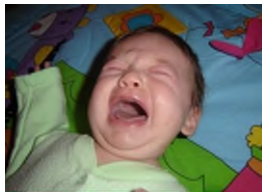
University of Warwick, Department of Psychology and Warwick Medical School

D.Wolke@warwick.ac.uk

www.dieterwolke.com

Early Developmental Tasks for Survival: Pre-programmed – Biologically Driven (First 3 Months)

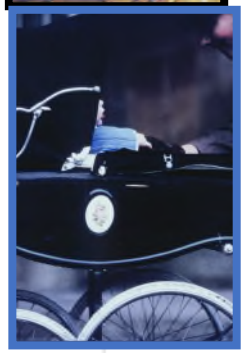
- Early Communication for survival: **Fussing/Crying**



- Staying alive and grow your brain: **Sleeping**

- Nutrition intake for survival: **Feeding**

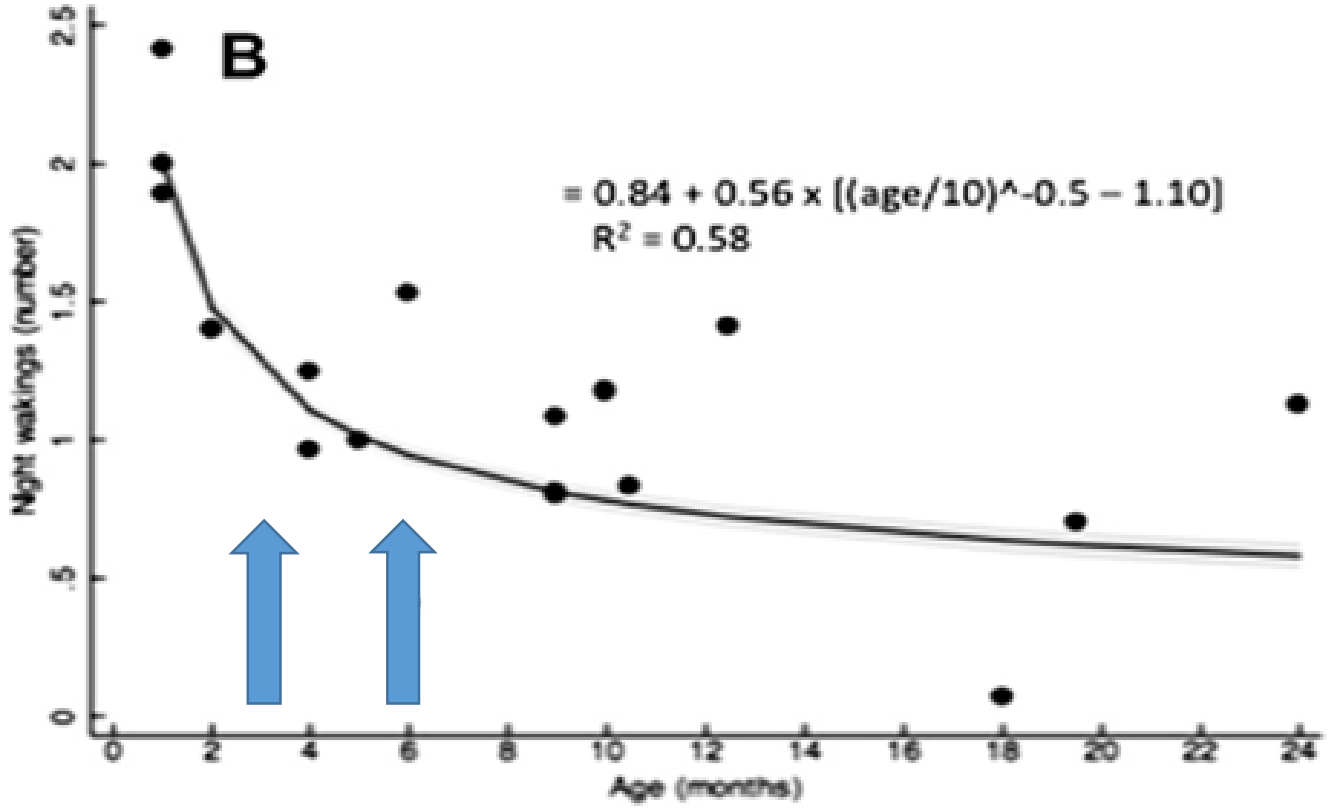
How Much Infants Fuss/Cry in the First 3 Months



Please note that this is an approximation of average to high fuss/cry amount percentiles based on the samples included in the meta-analysis. It should only be used as a rough guide to identify excessively crying infants according to age.

Wolke, D., Bilgin, A., & Samara, M. (2017). Systematic Review and Meta-Analysis: Fussing and Crying Durations and Prevalence of Colic in Infants. *The Journal of Pediatrics, 185, 55-61. doi:10.1016/j.jpeds.2017.02.020*

Average Number of Night Waking Over the First 24 Months of Age



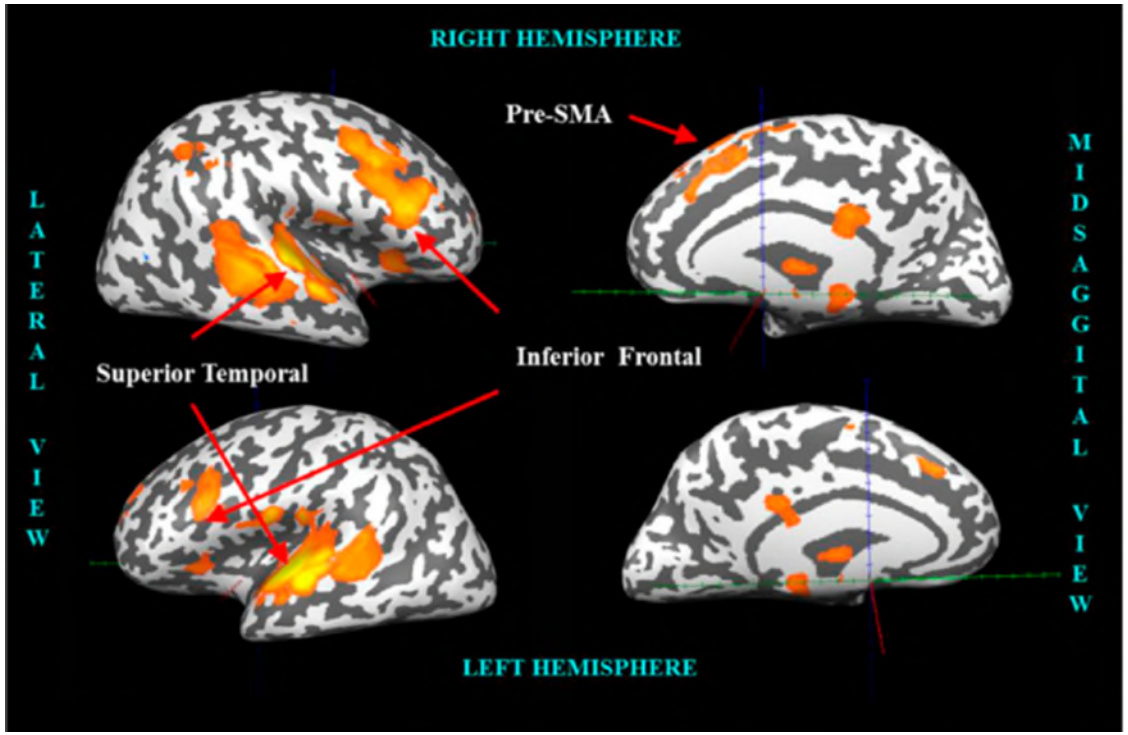
Galland, B. C., Taylor, B. J., Elder, D. E., & Herbison, P. (2012). Normal sleep patterns in infants and children: A systematic review of observational studies. *Sleep Medicine Reviews, 16(3), 213-222. doi:https://doi.org/10.1016/j.smrv.2011.06.001*

Normal Feeding Development

- Infants depend on their caregivers
- A third of their waking time is spent feeding
- A huge increase of infants' weight in first months of life

Intricate Relationship Between Crying, Sleeping and Feeding:

Fuss/cry leads to universal similar brain activation and preparation for action in mothers



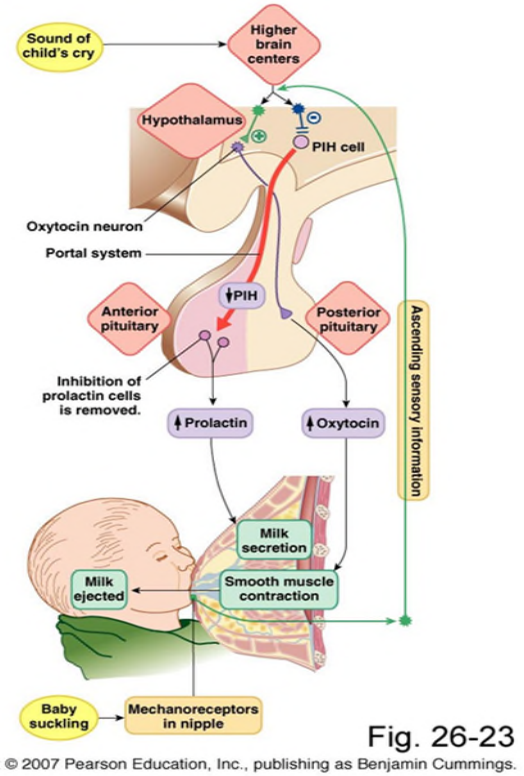


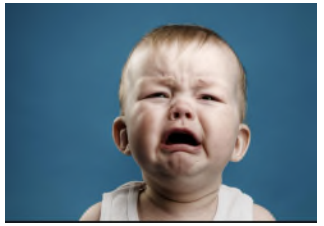
Fig. 26-23

Bornstein, M. H., Putnick, D. L., Rigo, P., Esposito, G., Swain, J. E., Suwalsky, J. T. D., . . . Venuti, P. (2017). Neurobiology of culturally common maternal responses to infant cry. *Proceedings of the National Academy of Sciences. doi:10.1073/pnas.1712022114*

Concept of Infant Regulatory Problems (RPs): Persistence of Inhibition Problems Beyond Period of Adaptation (3-6 months)

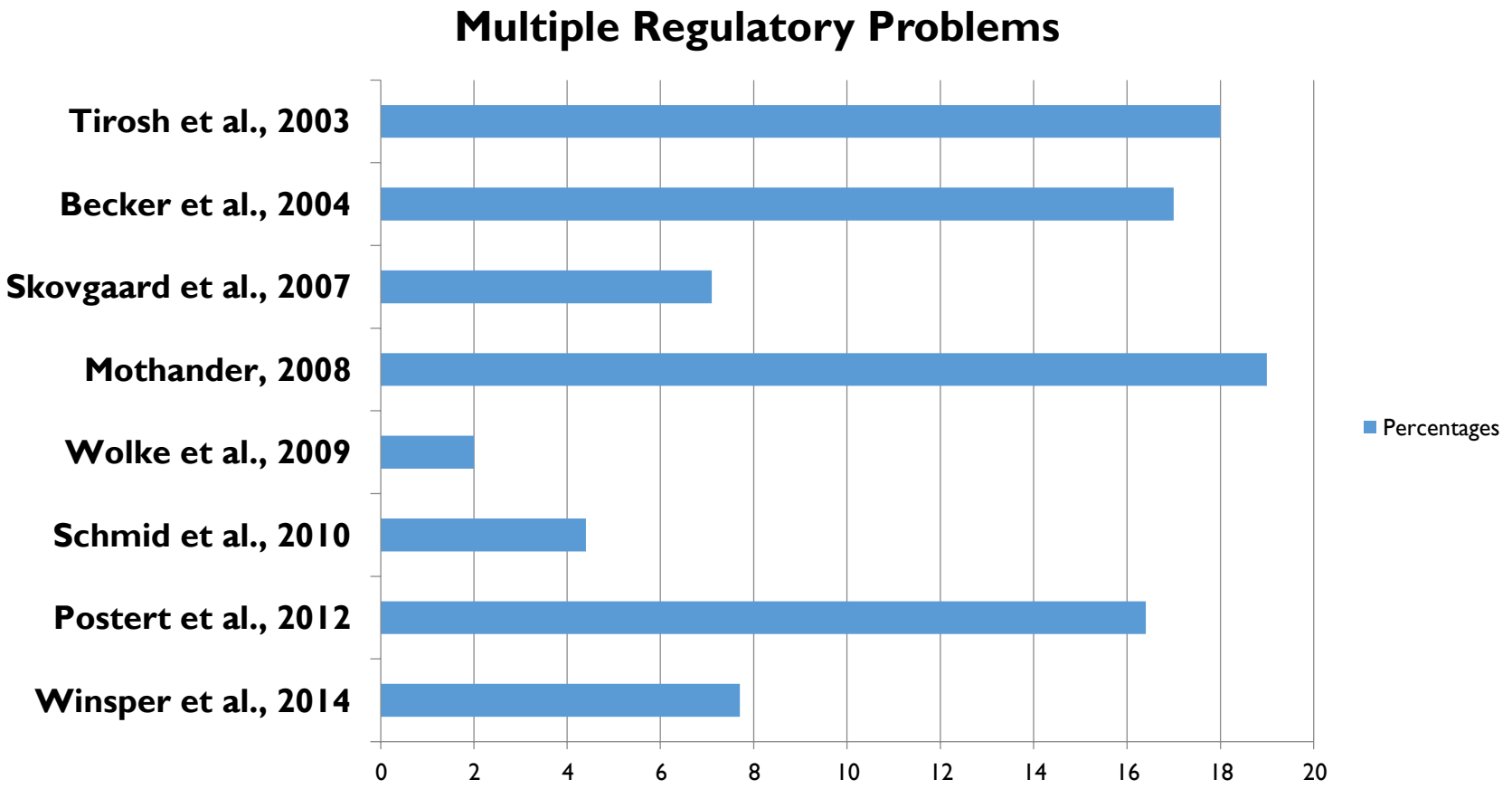
Infant regulation – inhibit a current response, return to a previous behavioural state

Regulation as inhibition of ongoing behaviour:



- **Crying**: The ability to stop crying: Excessive crying > 3 months
- **Feeding**: The ability to overcome neophobia: e.g. food acceptance
- **Sleeping**: The ability to settle back to a previous state: e.g. night settling

Prevalence


Multiple Regulatory Problems
Tirosh et al., 2003
Becker et al., 2004
Skovgaard et al., 2007
Mothander, 2008
Wolke et al., 2009
Schmid et al., 2010
Postert et al., 2012
Winsper et al., 2014
0
2
4
6
8
10
12
14
16
18
20
Percentages

Regulatory Problem: When Regulation is Not Accomplished After the 1st Bio-behavioural Shift

High Persistence of REG Problems

1st Bio-Behaviour Shift (3-6 months)

Crying curve –adaptation

Day-night sleep

Sucking to solid (salt preference)

Crying for attention

Sleep staging and self-soothing

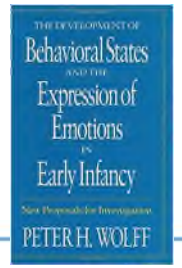
Feeding – transition to solids

2nd Bio-Behaviour Shift (9-12 months)

Attachment consolidation

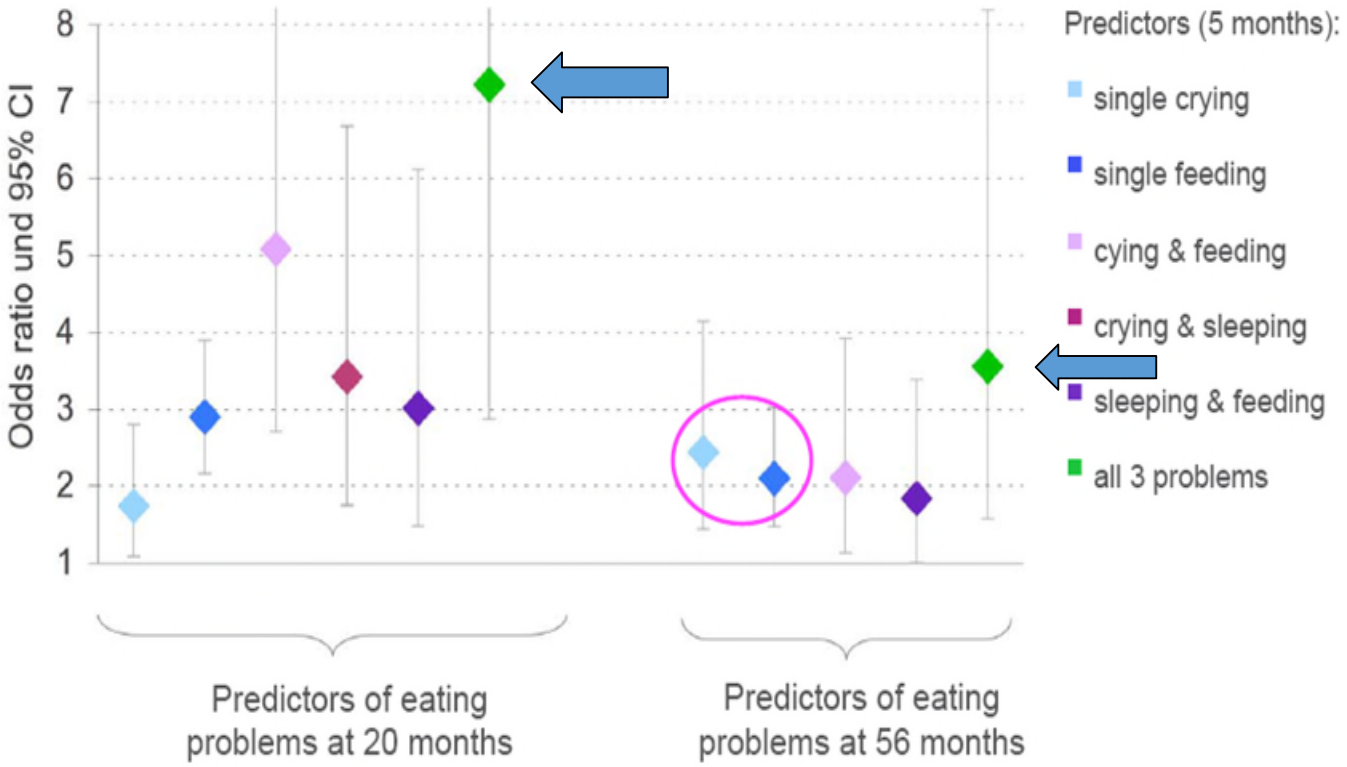
Social referencing

Crying, sleeping and feeding and attachment system



Results: Persistence of RP (II)

Outcome: Eating problems at 20 and 56 months



Problems of feeding, sleeping and excessive crying in infancy: a general population study

Anne Lise Olsen,[1] Janni Ammitzbøll,[2] Else Marie Olsen,[3,4] Anne Mette Skovgaard[2]

What this study adds?

- RPs between age 2 and 6 months are highly associated with RPs at age 8–11 months independently of maternal mental health problems and parent–child relationship problems.
- Community health nurses' assessment of RPs and parental and relational factors add to the knowledge on vulnerable infants and identify potential targets for intervention.
- Intervention towards RPs before age 6 months has potentials of reducing the progression of the child's symptoms and burden on the parents and the parent–child relationship.

Schmid, G., Schreier, A., Meyer, R., & Wolke, D. (2010). A prospective study on the persistence of infant crying, sleeping and feeding problems and preschool behaviour. *Acta Pædiatrica, 99(2), 286-290.*

Regulatory Problems: Poorer cognitive inhibition and disorganised attachment?

2nd Bio-Behaviour Shift (9-12 months)

1st Bio-Behaviour Shift (3-6 months)

Crying curve –adaptation

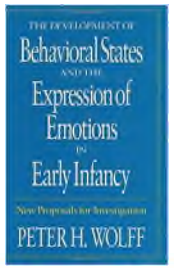
Day-night sleep

Sucking to solid (salt preference)

Crying for attention

Sleep staging and self-soothing

Feeding – transition to solids



Cognitive inhibition (1-2yrs)

Attachment


ATTACHMENT & HUMAN DEVELOPMENT
https://doi.org/10.1080/14616734.2019.1618882

Routledge
Taylor & Francis Group

Infant crying problems and symptoms of sleeping problems predict attachment disorganization at 18 months

Ayten Bilgin and Dieter Wolke

RESEARCH ARTICLE

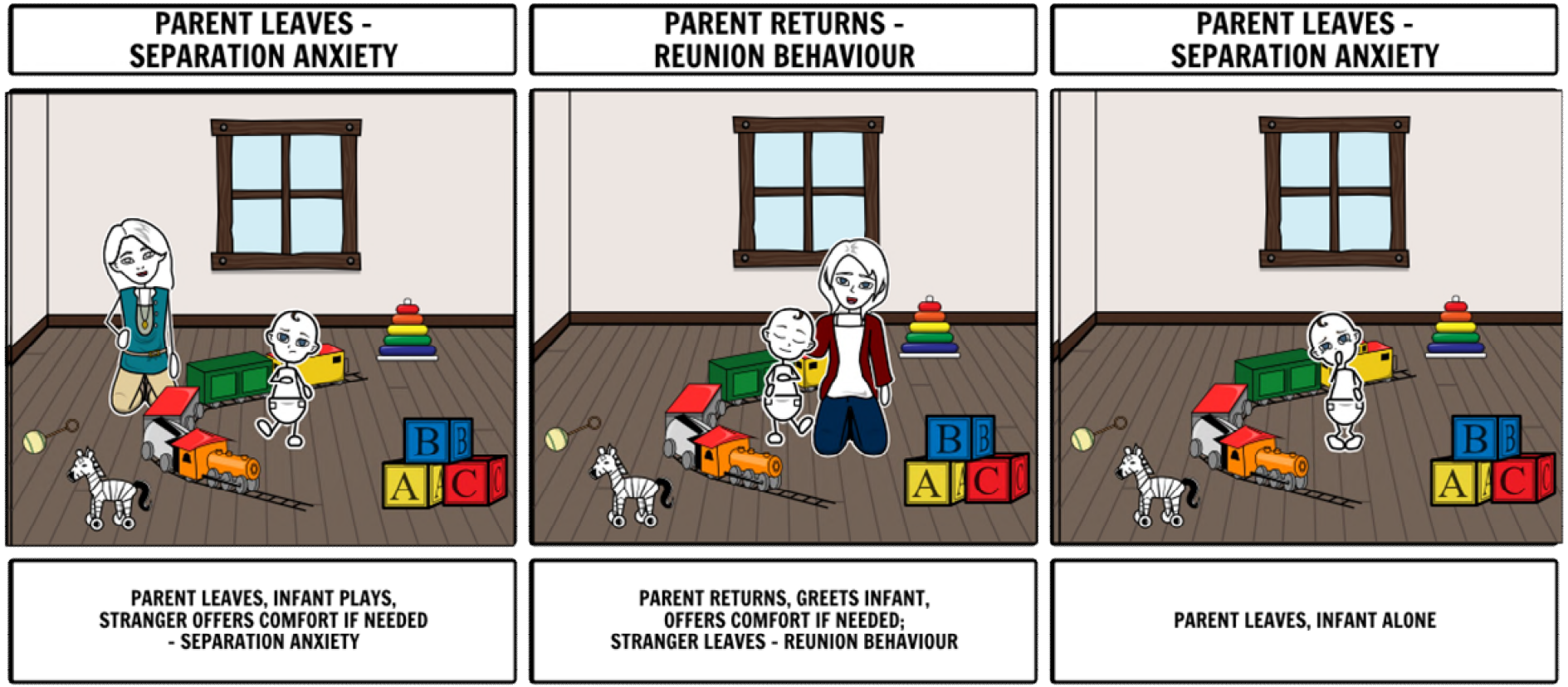
INFANCY

WILEY

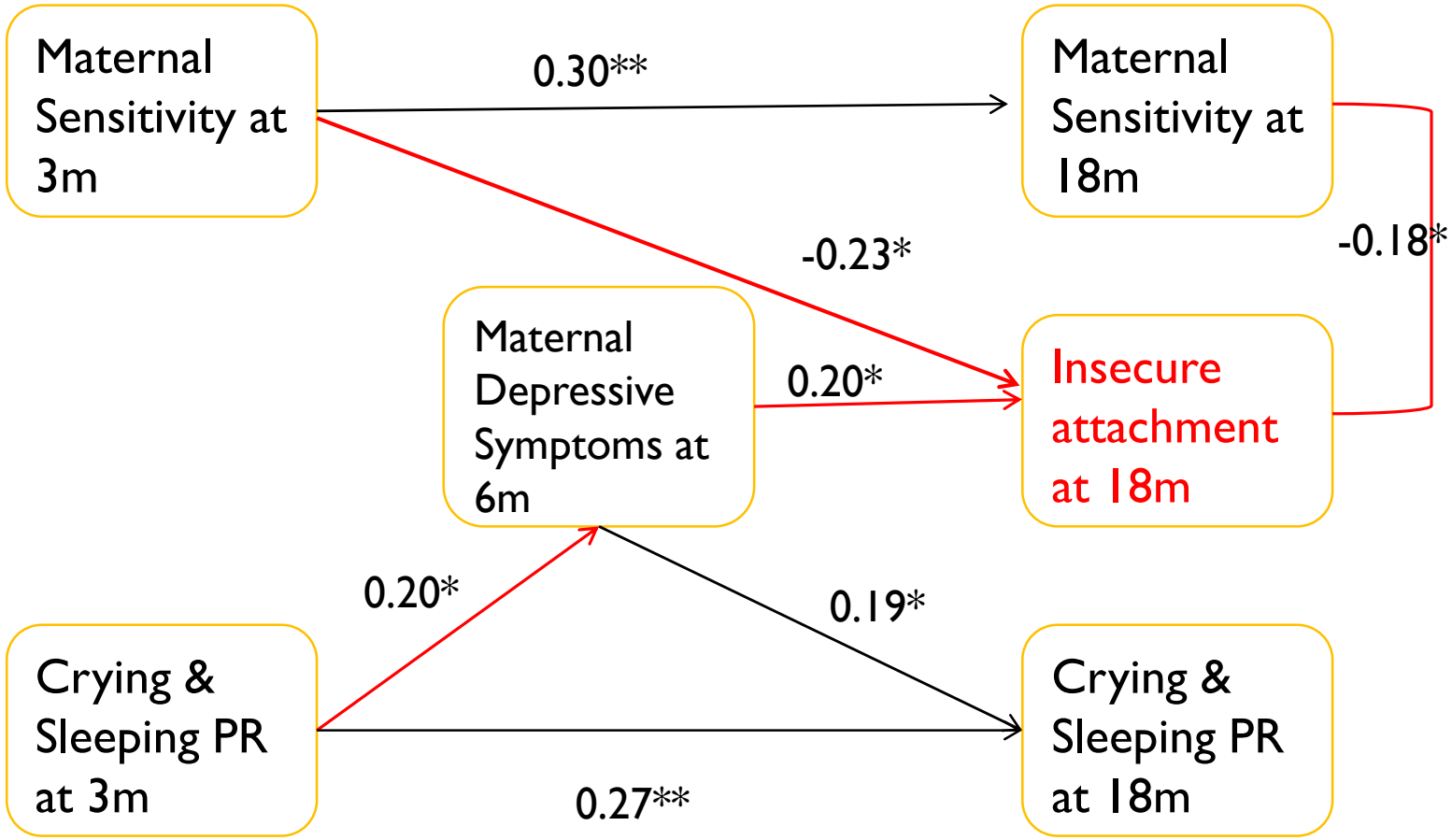
The association of infant crying, feeding, and sleeping problems and inhibitory control with attention regulation at school age

Nicole Baumann | Julia Jaekel | Linda Breeman | Peter Bartmann | Josef G. Bäuml | Mihai Avram | Christian Sorg | Dieter Wolke

Outcome: Ainsworth Strange Situation

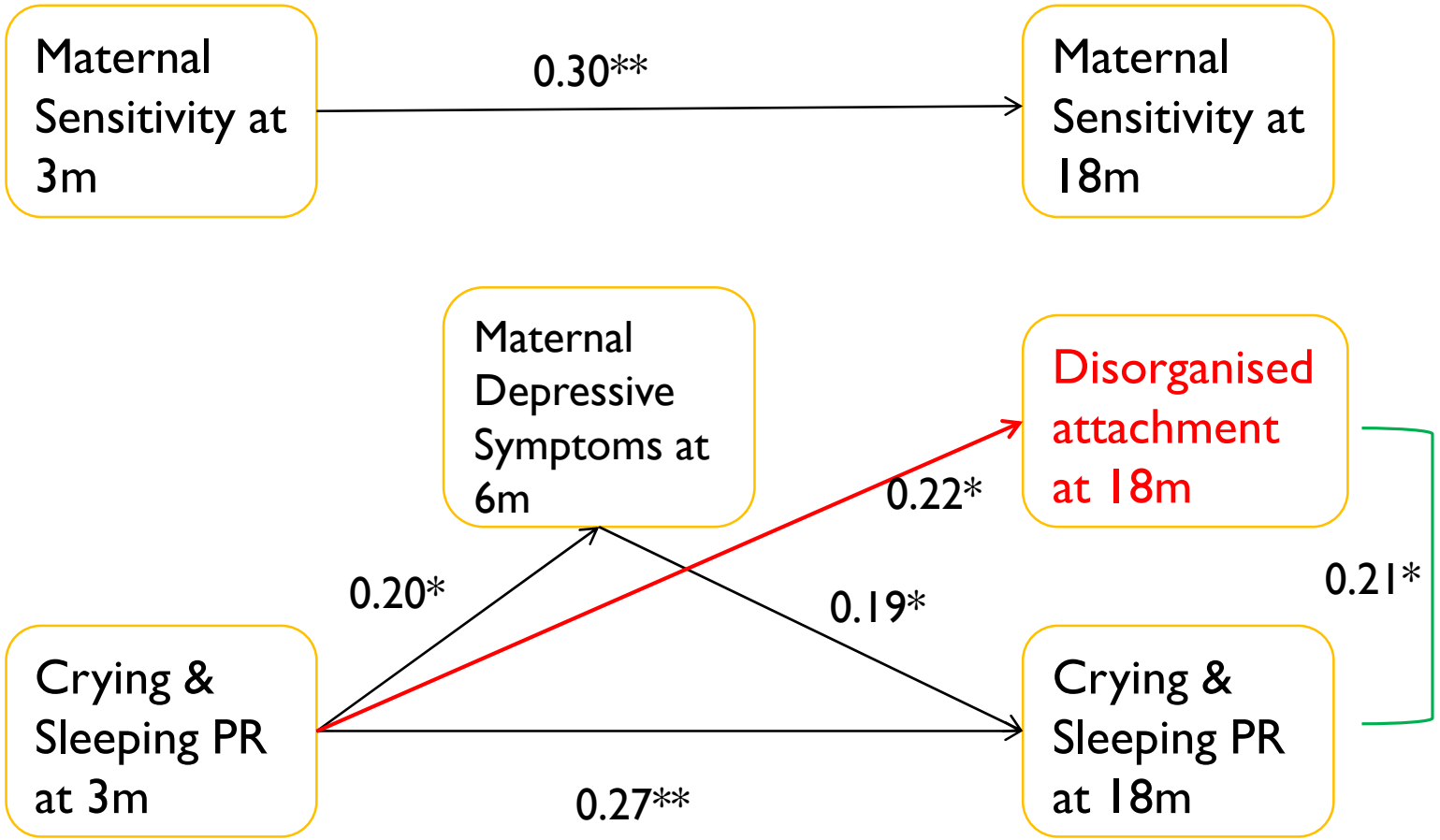


What is the association between early multiple regulatory problems and insecure attachment at 18 months?



Bilgin, A., & Wolke, D. (2019). Infant crying problems and symptoms of sleeping problems predict attachment disorganization at 18 months.
Attachment & Human Development, 1-25. doi:10.1080/14616734.2019.1618882

What is the association between early multiple regulatory problems and disorganised attachment at 18 months?



Note:
No association of Parenting and MRP

Bilgin, A., & Wolke, D. (2019). Infant crying problems and symptoms of sleeping problems predict attachment disorganization at 18 months. *Attachment & Human Development, 1-25. doi:10.1080/14616734.2019.1618882*

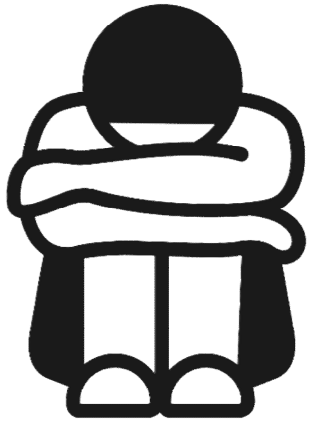
PARENTING - Misconceptions

- Erroneous conclusions from clinical studies
- Just because parenting interventions might work….*
- The Headache Problem

*Wolke, D., Gray, P., & Meyer, R. (1994). Excessive infant crying: a controlled study of mothers helping mothers. *Pediatrics, 94, 322-332.*

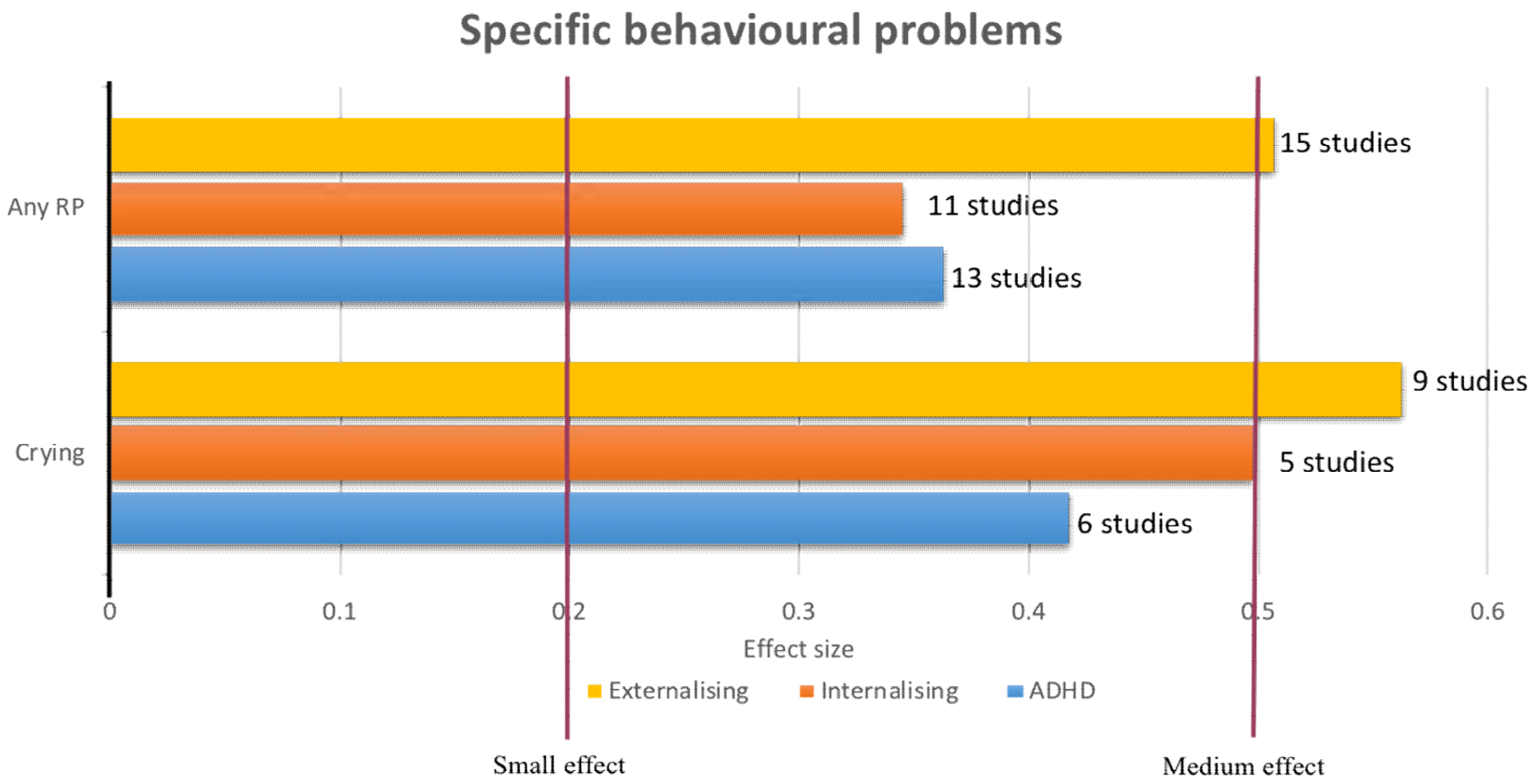
Early RPs and Later Development

? ?



Pictures from the Noun Project

Infant RPs and Long-term Outcomes
Meta-analysis (1987-2006)



Hemmi M, Wolke D, Schneider S. Associations between problems with crying, sleeping and/or feeding in infancy and long-term behavioural outcomes in childhood: a meta-analysis. Arch Dis Child. 2011;96(7):622-629.

Multiple or Persistent RPs: Effects up to Adulthood?

Multiple/Persistent RPs

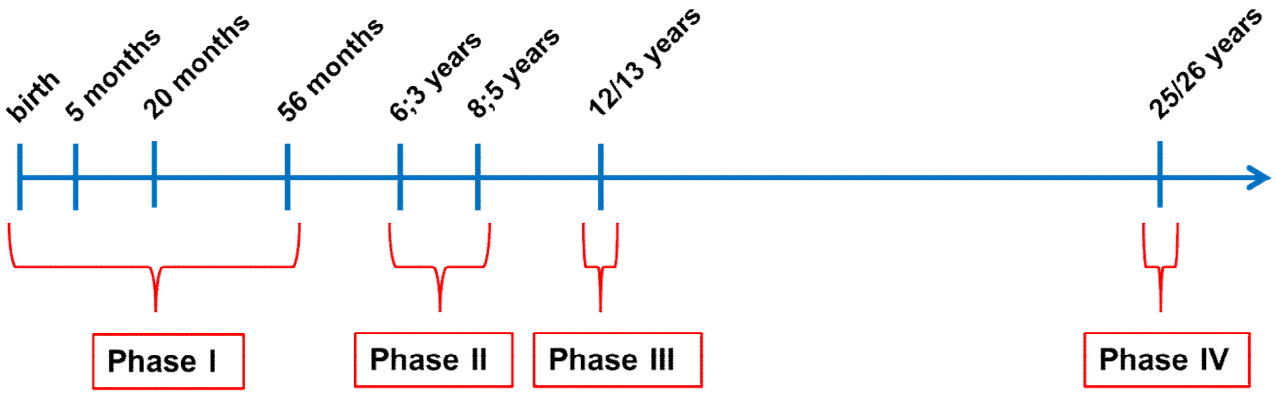
Adult Psychopathology

Bavarian Longitudinal Study

Design: Prospective longitudinal study

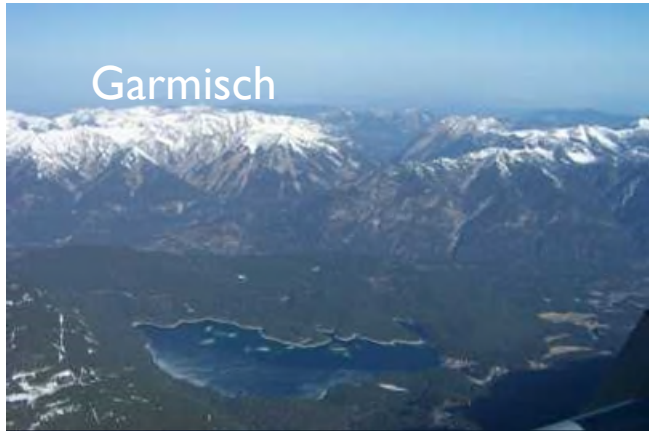
Population: Children born in South Bavaria (02/1985 - 03/1986)

Assessments: Crying, Sleeping and Feeding Problems assessed in Phase I*



*Schmid, G., Schreier, A., Meyer, R., & Wolke, D. (2010). A prospective study on the persistence of infant crying, sleeping and feeding problems and preschool behaviour. *Acta Pædiatrica, 99(2), 286-290.*

Schmid, G., & Wolke, D. (2014). Preschool regulatory problems and attention-deficit/hyperactivity and cognitive deficits at school age in children born at risk: Different phenotypes of dysregulation? *Early Human Development, 90(8), 399-405. doi:http://dx.doi.org/10.1016/j.earlhumdev.2014.05.001*



BLS

Population N=1495
(6 and 8 years data)

Excluded:
Single/non-persistent RPs or missing data (N=787)

Multiple/Persistent RPs N=138

Never RPs/Controls N=570

Eligible Sample for Prospective Case-Control Study N=708

Target Cases: N=80

Target Controls: N=240
(matched according to gestational age, sex, and socioeconomic status; cases:controls=1:3)

Assessment in Adulthood N=342

Multiple/Persistent RPs N=83

Never RPs/Controls N=259

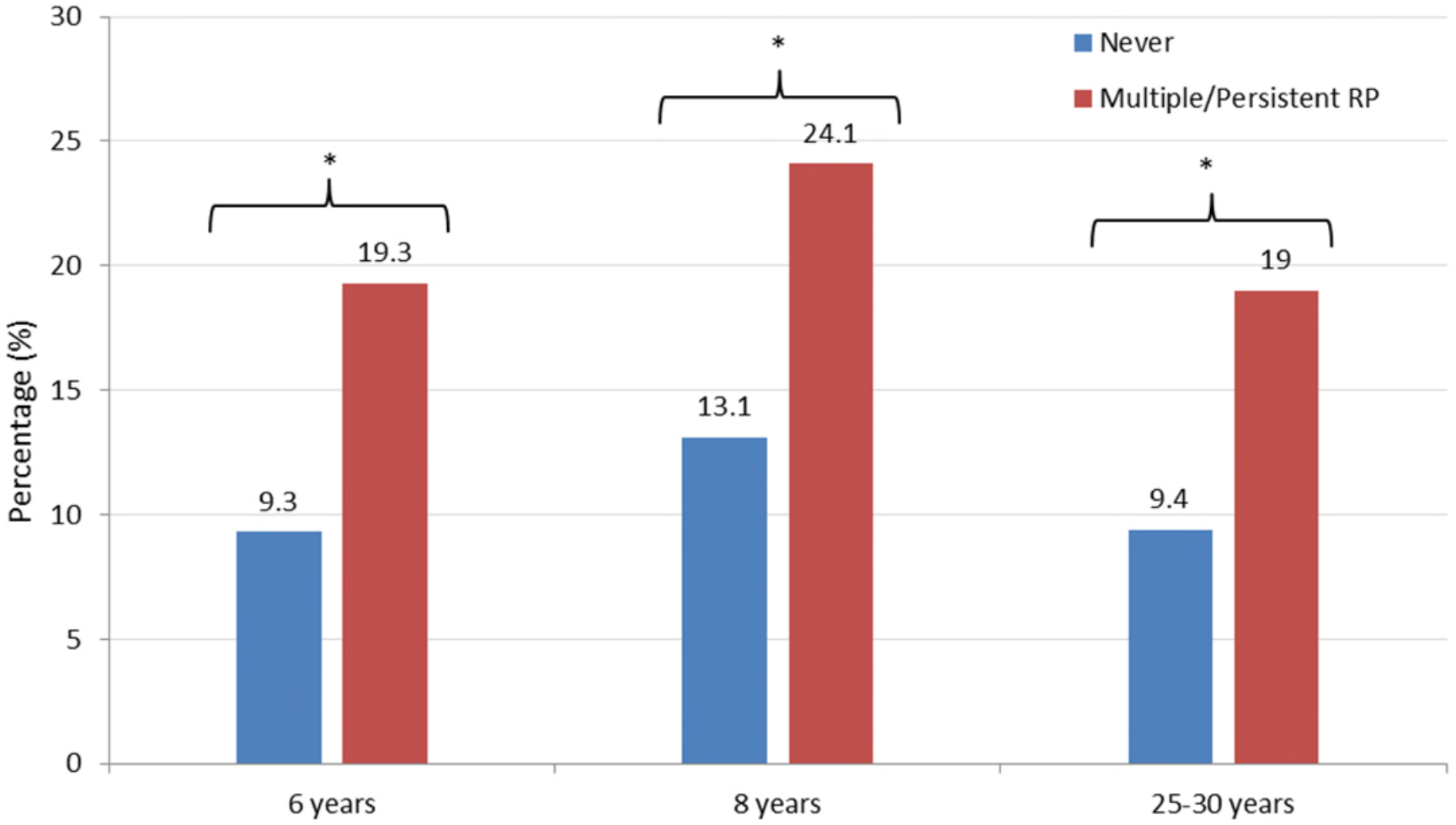
Available Data on Behaviour, ADHD and Cognitive Outcomes N=333

Multiple/Persistent RPs N=79

Never RPs/Controls N=254

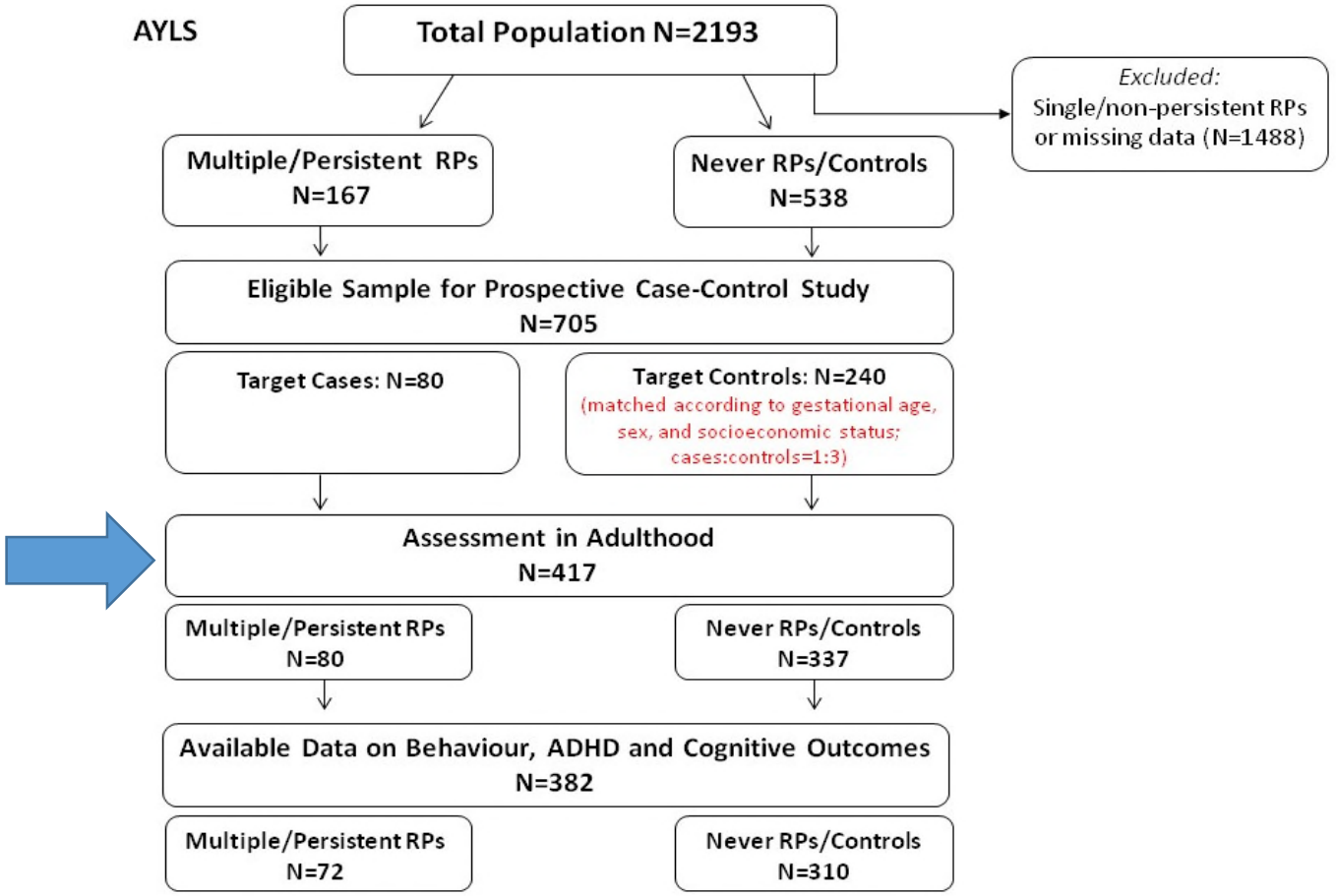
Birth cohort 1985/86

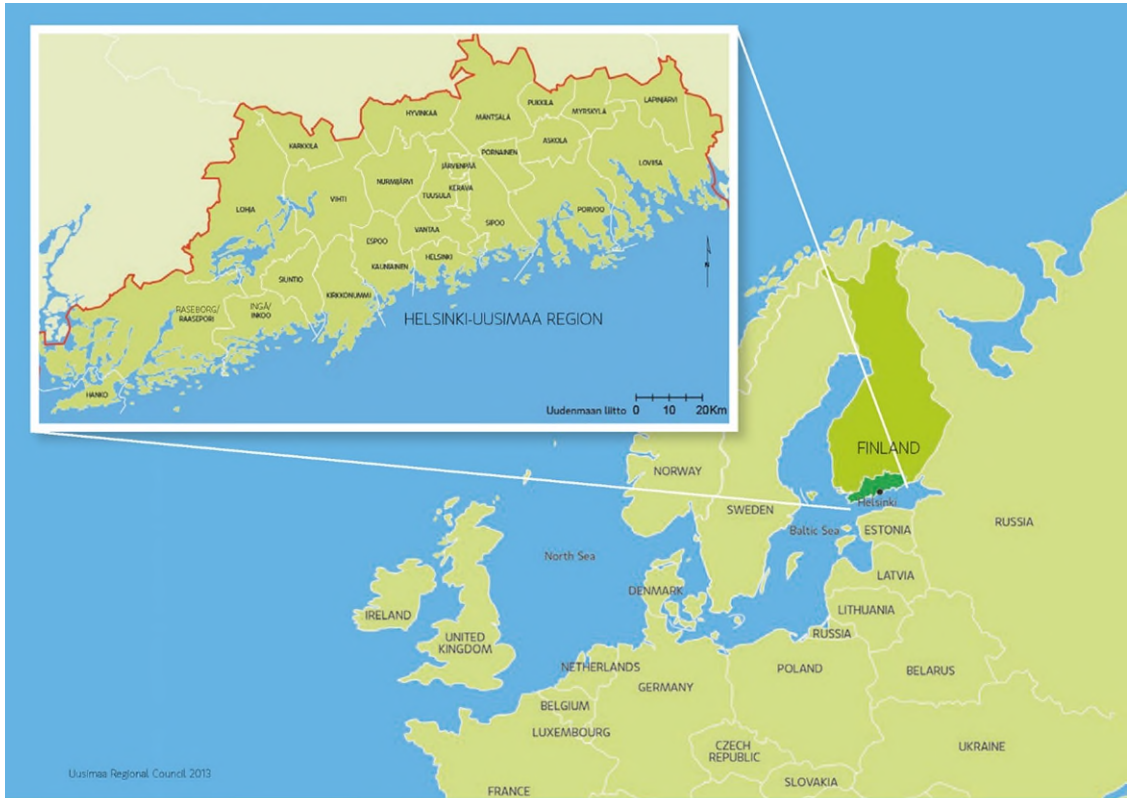
ADHD Over Time



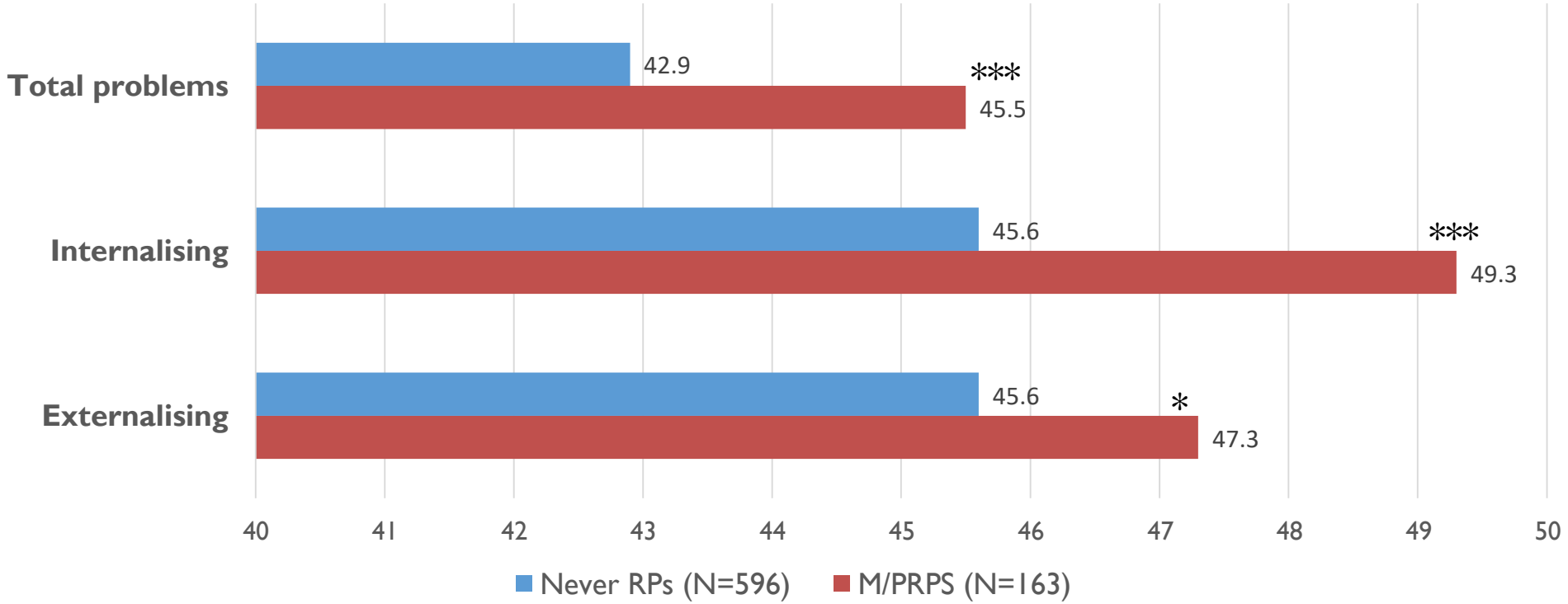
Bilgin, A., Baumann, N., Jaekel, J., Breeman, L. D., Bartmann, P., Bäuml, J. G., . . . Wolke, D. Early Crying, Sleeping, and Feeding Problems and Trajectories of Attention Problems From Childhood to Adulthood. *Child Development, 0(0). doi:doi:10.1111/cdev.13155*

Same Infant RPs measured - Follow –up into Adulthood AYLS





Combined Analysis BLS and AYLS at 26-30 Years (Outcome YASR T-Scores)



*P<0.05
***P<0.001

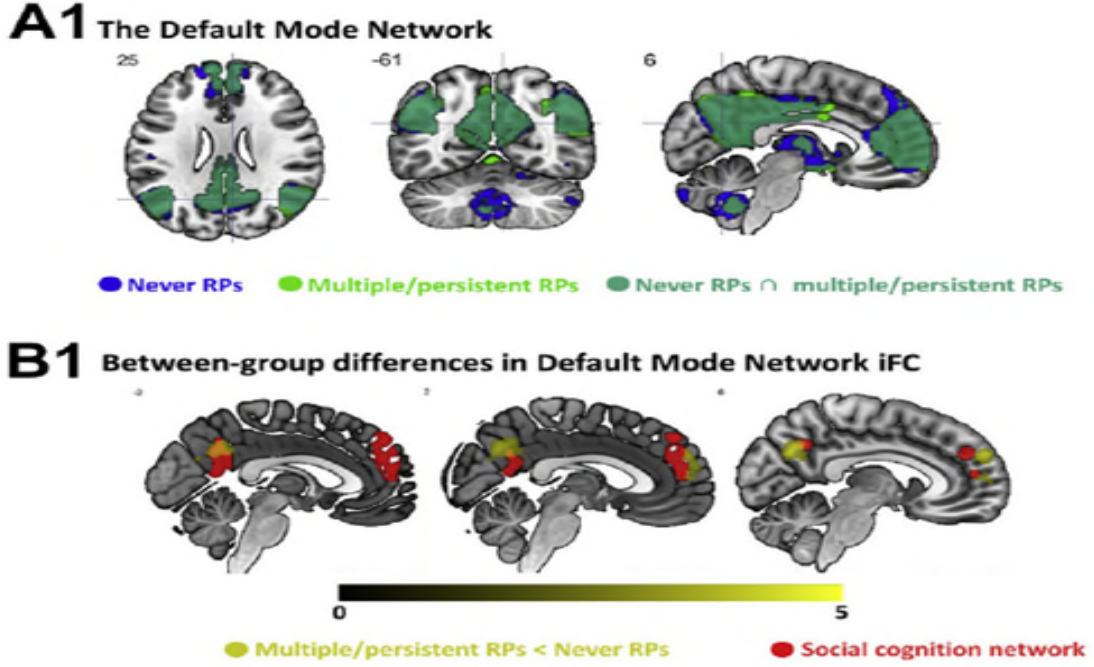
Regulatory Problems and the Brain

The Default Mode Network Mediates the Impact of Infant Regulatory Problems on Adult Avoidant Personality Traits

Josef G. Bäuml, Nicole Baumann, Mihai Avram, Satja Mulej Bratec, Linda Breeman, Maria Berndt, Ayten Bilgin, Julia Jaekel, Dieter Wolke, and Christian Sorg

Biological Psychiatry: CNNI

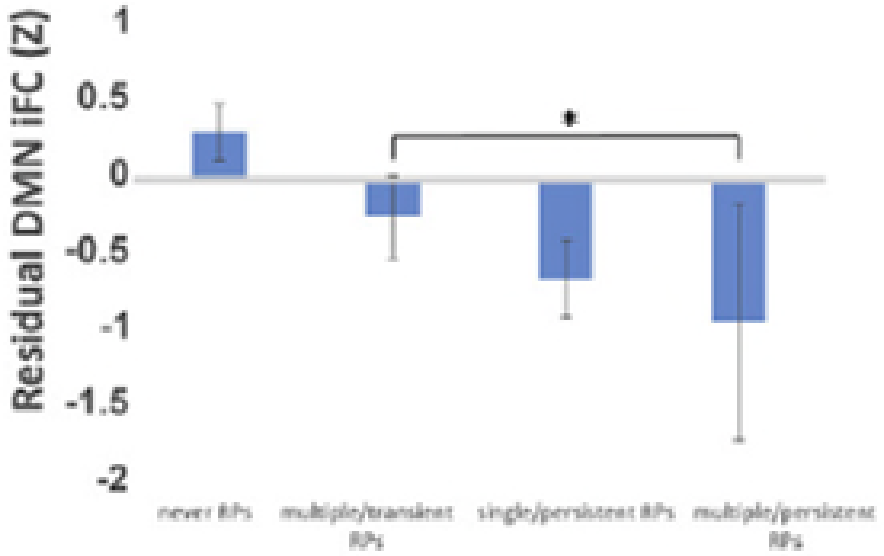
https://doi.org/10.1016/j.bpsc.2018.11.005



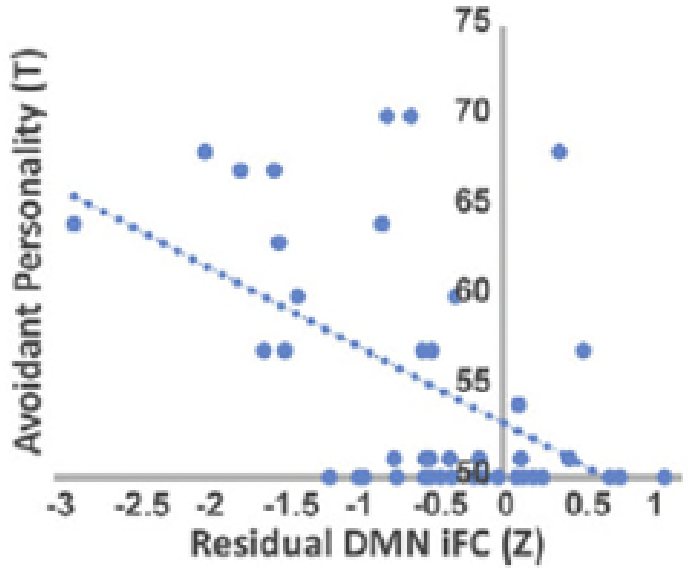
RP-associated iFC differences in the posterior DMN overlap with the social DMN and are associated with social-emotional problems.

DMN Activation:
How is it Related to Infant RPs and Avoidant Personality?

C1 Dose effect of infant RPs on DMN iFC

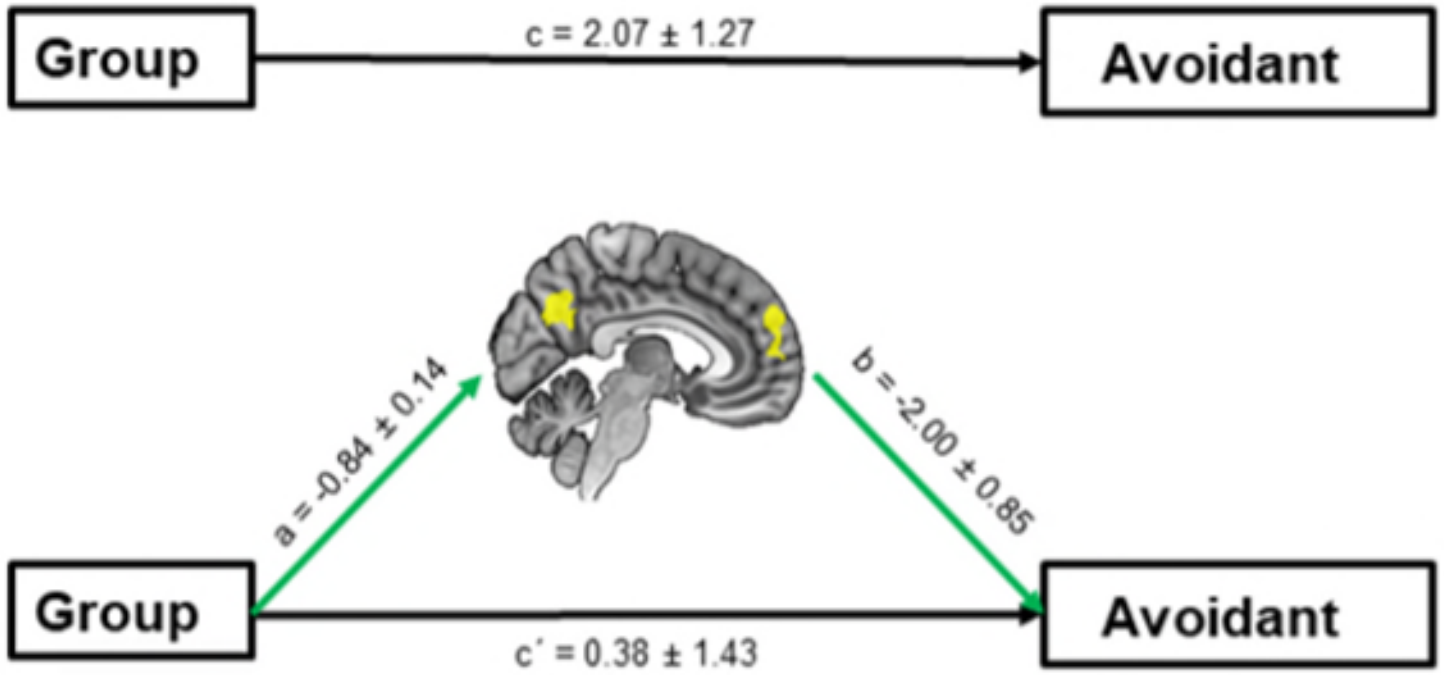


D1 DMN iFC correlates with avoidant personality



Bäuml, J. G., Baumann, N., Avram, M., Mulej Bratec, S., Breeman, L., Wolke, D., . . . Sorg, C. (2018). The Default Mode Network Mediates the Impact of Infant Regulatory Problems on Adult Avoidant Personality Traits. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. doi:https://doi.org/10.1016/j.bpsc.2018.11.005

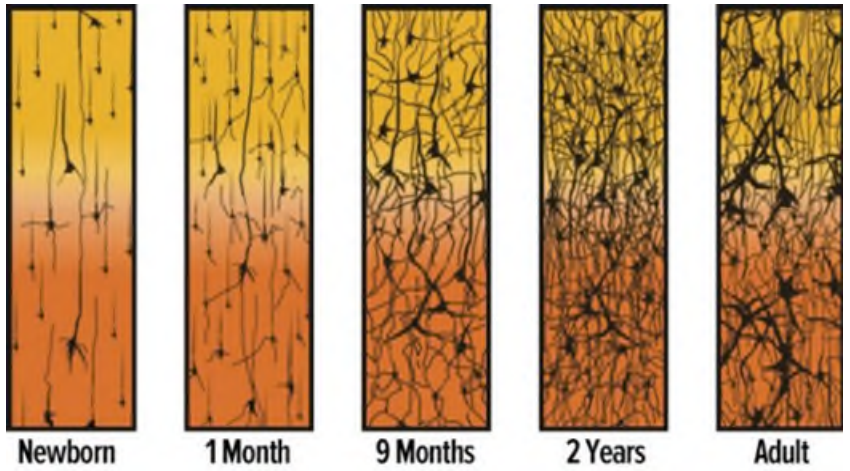
Decreased DMN iFC in the precuneus and medial prefrontal cortex mediates the association between RPs and adult social-emotional problems

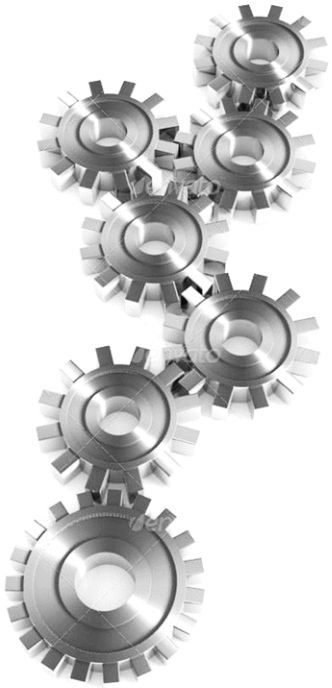


Bäuml, J. G., Baumann, N., Avram, M., Mulej Bratec, S., Breeman, L., Wolke, D. . . . Sorg, C. (2018). The Default Mode Network Mediates the Impact of Infant Regulatory Problems on Adult Avoidant Personality Traits. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. doi:https://doi.org/10.1016/j.bpsc.2018.11.005

To sum up

Early Regulatory Problems may initiate a cascade of dysregulation/poor inhibition: including poorer cognitive inhibition, dysregulated behavior and attachment and altered brain development and mental health





Winsper C, Bilgin A, Wolke D. Associations between infant and toddler regulatory problems, childhood co-developing internalising and externalising trajectories, and adolescent depression, psychotic and borderline personality disorder symptoms. *Journal of Child Psychology and Psychiatry;0(0) doi: 10.1111/jcpp.13125*

PUBLIC HEALTH PROBLEM: WHY IS THERE NO PREVENTION?

around 657.076 births in England and Wales in 2018

65.000-100.000 with Multiple Regulatory Problems per year

Editorial

Persistence of infant crying, sleeping and feeding problems: need for prevention

Dieter Wolke

do not master this transition in acquiring self-soothing and continue to fuss/cry at significantly higher levels (eg, >2 hours per 24 hours after 3 months) have been considered to have a RP.

Infants are born with sleeping near equally distributed across the first 24 hours but start to develop to sleep less during the day and more during the night within the first few weeks, aided by light alterations

Arch Dis Child: first published

Thanks to My Collaborators

Nicole Baumann

Dr Ayten Bilgin

Dr Catherine Winsper

Dr Mihai Avram

Dr Josef Bäuml

Dr Christian Sorg

Prof. Peter Bartmann

Dr Julia Jaekel

Dr Gabriele Schmid-Mühlbauer

Dr Linda Breeman

Prof Katri Raikkonen

Dr Kati Heinonen

Questions?

www.dieterwolke.com
D.Wolke@warwick.ac.uk

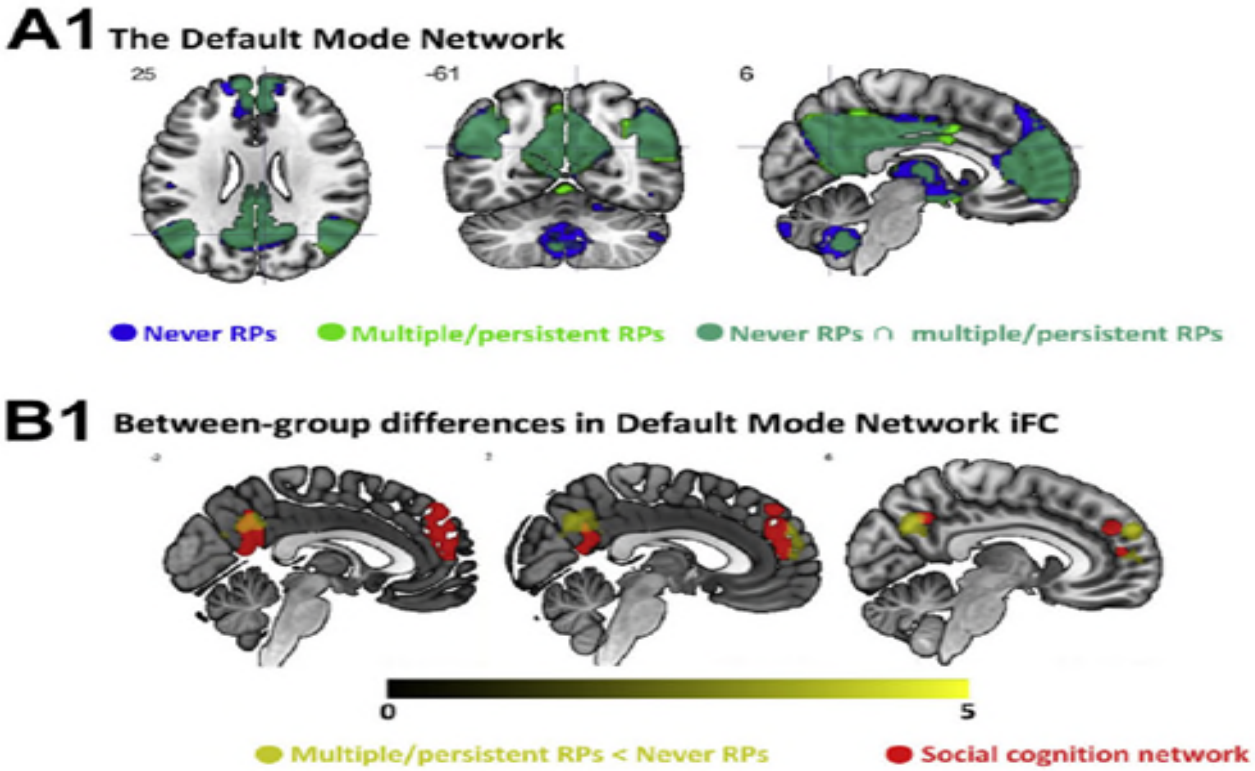
RPs and Later Mental Health:
The Cascade Model – Getting a Few Degrees Off Course?

Associations between infant and toddler regulatory problems, childhood co-developing internalising and externalising trajectories, and adolescent depression, psychotic and borderline personality disorder symptoms AQ1

Catherine Winsper[1]
Ayten Bilgin[2,3]
Dieter Wolke[1,2,✉]
Email D.Wolke@warwick.ac.uk

DOI: 10.1111/jcpp.13125

Social Deficits: Altered Social Brain?



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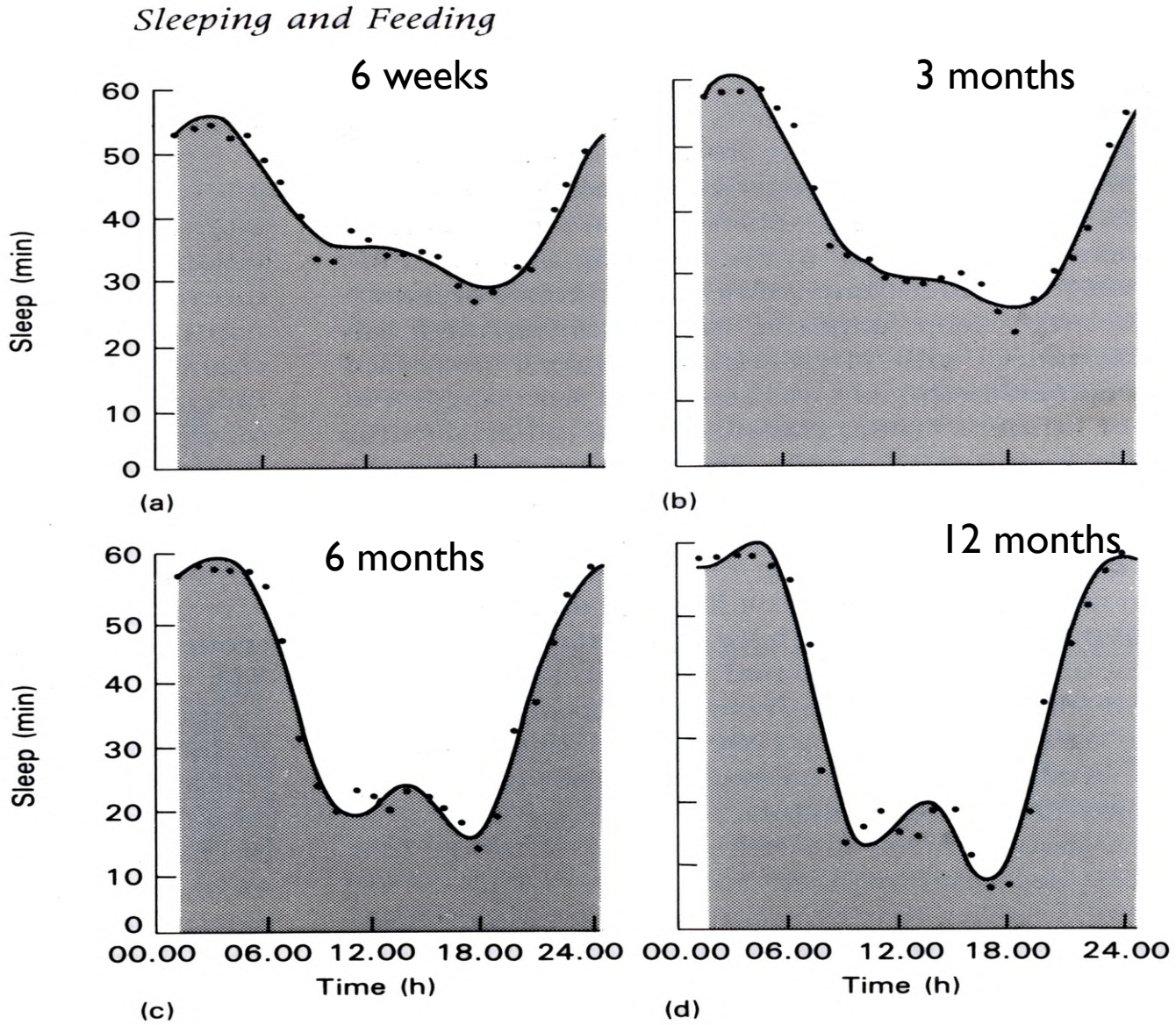


Bamford, F. N., Bannister, R. P., Benjamin, C. M., Hiller, V. F., Ward, B. S., & Moore, W. M. O. (1990). Sleep in the first year of life. *Developmental Medicine and Child Neurology, 32, 718-724.*

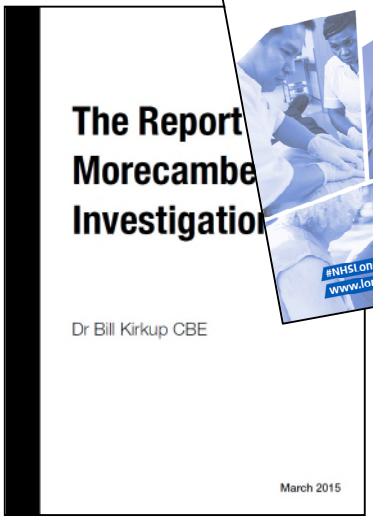
Why evidence is important to shape healthcare policy

Professor Jacqueline Dunkley-Bent OBE, Chief Midwifery Officer

Twitter @dunkleybent

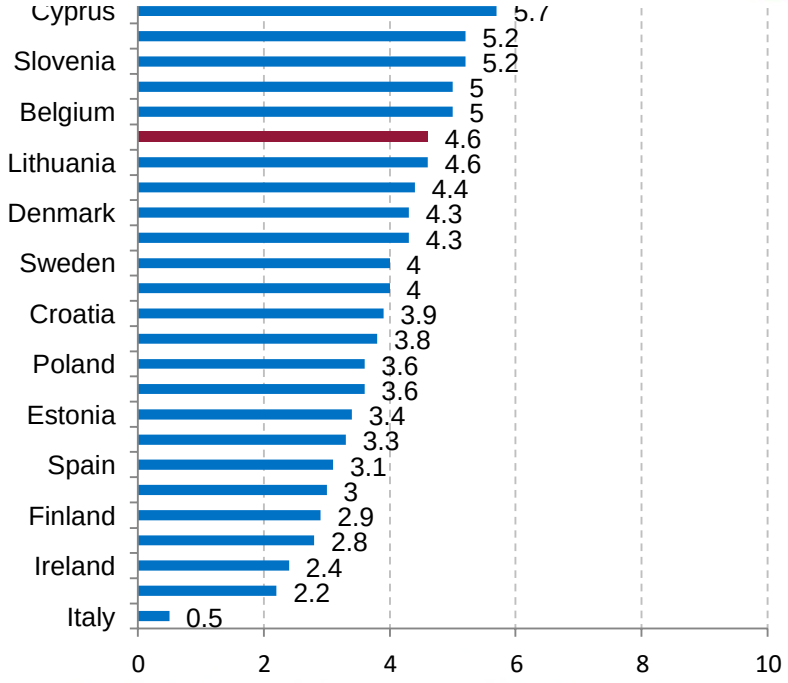
Inequalities in maternal mortality UK 2014-16

Women's experiences
Staff experiences
Quality of care-

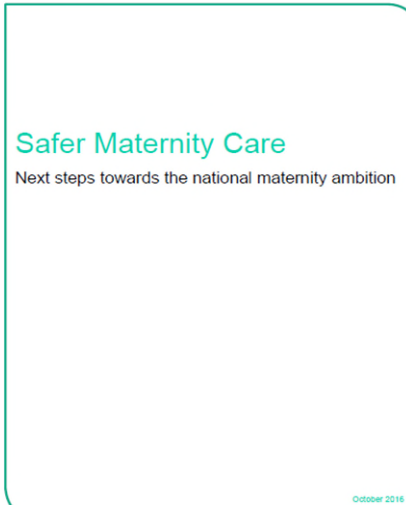


Black and Asian women have a higher risk of dying in pregnancy	
White women	8/100,000
Asian women	2x 15/100,000
Black women	5x 40/100,000
In deprived areas women are at greater risk of dying	
Least deprived	3/100,000
Most deprived	3x 11/100,000
Older women are at greater risk of dying	
Aged 20-24	7/100,000
Aged 35-39	2x 14/100,000
Aged 40 or over	3x 22/100,000
Women born outside the UK have the same risk of dying in pregnancy	
UK born	8/100,000
Non-UK born	1x 9/100,000

MBRRACE-UK

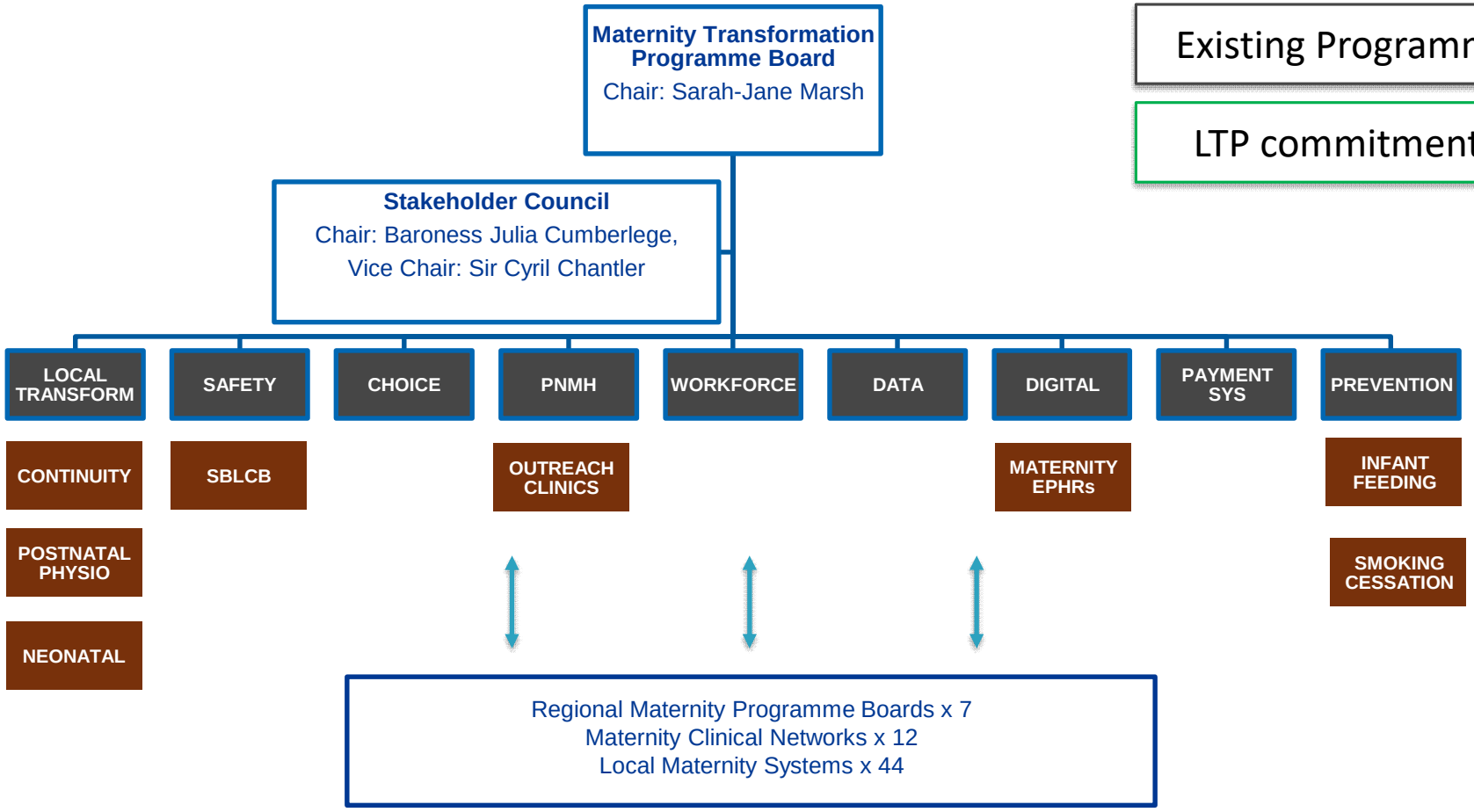


Department of Health



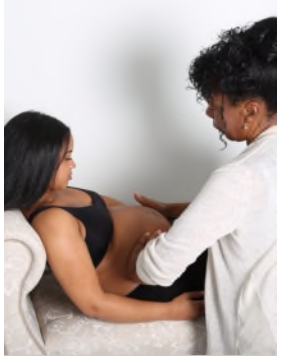
Source: Eurostat 2014

Embedding LTP into the Maternity Transformation Programme



CONTINUITY OF CARER

Targeted to women from communities that face the poorest health outcomes



What: Continuity of carer for most women by 2021 and targeted to those who will benefit most - 75% of women from certain Black/Black British and Asian/Asian British groups and those living in the most economically deprived areas by 2024

How: LTP funding for additional midwives / midwifery time and training to further support high quality, targeted care for those who face the poorest health outcomes.

Why: Mortality rates are reducing, stark health inequalities persist (MBRRACE-UK). Maternal mortality: Black women x5, Asian women x2, most deprived x3, Stillbirth rate increasing for Black babies - 121% ↑, Neonatal mortality: Black babies 50% ↑, Asian 66%↑, deprived areas x2

When: 2021 and beyond

POSTNATAL PHYSIOTHERAPY

Supporting women to recover from physical complications after birth

- **What:** Women have access to multidisciplinary pelvic health clinics and pathways across England via referral. Clinics provide training and support for other local clinicians working with women, such as GPs and midwives.
- **How:** LTP funding for additional midwives / midwifery time and physiotherapists to further support high quality care for women experiencing physical complications
- **Why:** Urinary incontinence 1/3 women (of these more than 2/3 still report it 12 years later), faecal incontinence 1/10, pelvic organ prolapse 1/12. Significant proportion of women with back pain and pain during intercourse. Cost to NHS £200m annually.
- **When:** Policy development, research and engagement in 2019/20, Pilots in 2020/21, Phased rollout 2021/22 , Full rollout 2023/24

MATERNITY "OUTREACH" CLINICS

Supporting women with mental health difficulties arising from,

or related to, the maternity experience

NHS England

What: Women who experience mental health difficulties will receive integrated maternity, reproductive health and psychological therapy.

How: LTP funding for funding for specialist mental health midwives and perinatal psychologists -maternity, reproductive

health and psychological therapy

Why: Mental health problems in pregnanc the first year after birth experienced by up 27% of women in the UK.

When: Rollout from 2021 onwards

INFANT FEEDING

Supporting women with evidence-based interventions

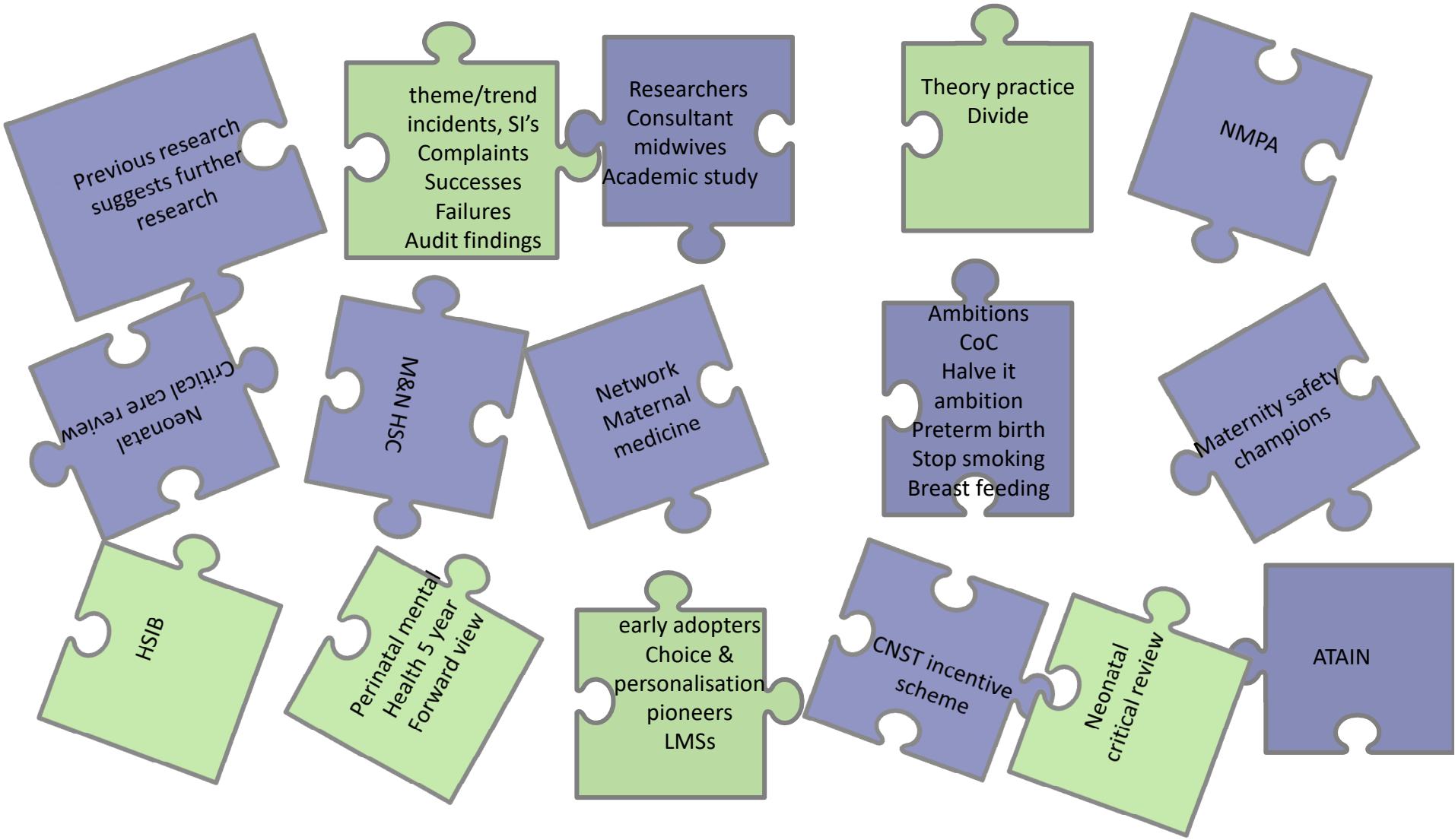
What: All maternity providers who do not already deliver an evidence based infant feeding programme will be supported to do so,

How: LTP funding to support providers to adopt and deliver an evidence based programme, such as the UNICEF Baby Friendly Initiative.

Why: UK breastfeeding rates at 6-8 weeks compare unfavourably with other countries in Europe and improvement efforts need to address significant regional variation. In London, 84% of children were breastfed at 6-8 weeks from October to December 2017. The average rate in the North East was 32% .
Variation within communities influenced by socioeconomic status and ethnicity.

When: Rollout to commence from 2019/20

Joined up thinking? Chaos? Or …



Personal story, what's yours?

- Demise of statutory supervision –lack of evidence?
- Continuity of carer -Sandall et al 2016. Cochrane review of 15 trials involving 17,674 women.
- Further research to explore findings of: fewer preterm births, fetal deaths less than 24 weeks, and all fetal loss/neonatal death associated with midwife-led continuity models of care
- Only Six out of the 13 trials were UK based

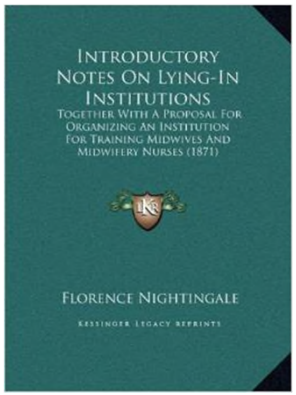
WARWICK

Clinical trials in maternity care. Past, present and future

Professor Debra Bick. Maternity Research Theme launch

Warwick Clinical Trials Unit Sept 19th 2019

Clinical trials in maternity care: past



Long-history of midwifery care in Northern Europe

Until early 20th century, majority of births took place in the home. More maternal deaths at hands of physicians and among women who attended lying in hospitals (Nightingale 1871)

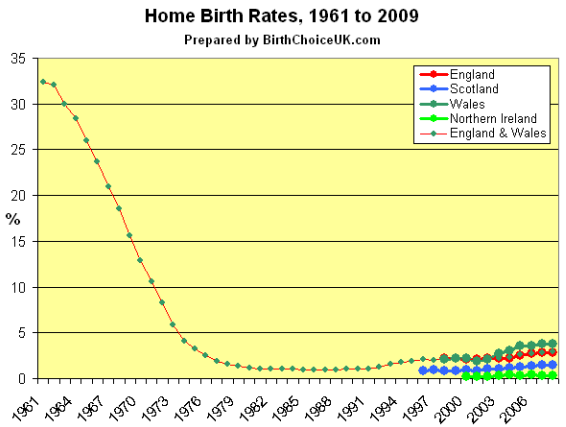
1902. First Midwives Act in England. By 1917 maternal deaths had halved and continued to decline during 20th century

Successive Midwives Acts in 1918, 1928, 1936

Launch of the NHS in 1948 entitled all women to routine antenatal, birth and postnatal care provided by a midwife and a GP

Clinical trials in maternity care: past

Gradual reduction in home birth. Hospital births deemed ‘safer’. Little evidence and no discussion with women



Move to hospital birth led to use of routine interventions, many on assumption of ‘benefit’ & the medicalisation of labour and birth – ‘seduction by authority’ (Grimes 2007)

Routine bowel preparation & perineal shaving at labour onset, x-ray pelvimetry, electronic fetal monitoring, induction & augmentation of labour, episiotomy, routine separation of women and their babies, timed breastfeeding – to name but a few

Archie Cochrane awarded the ‘wooden spoon’ to obstetrics in 1979 for ‘the worst use of randomised controlled trials’

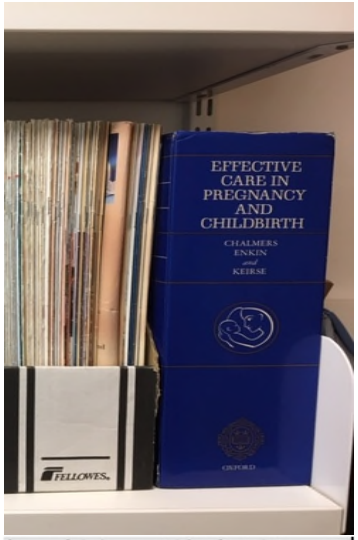
Clinical trials in maternity care: past

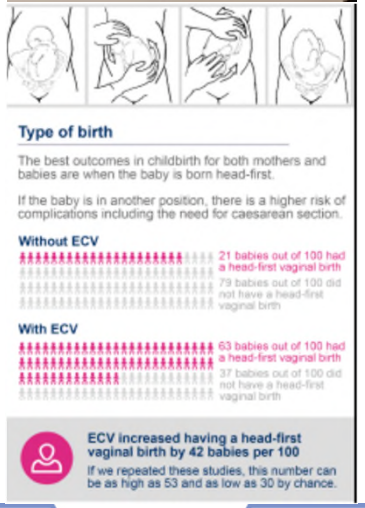
Women, midwives and obstetricians challenged practices. Recognised need for robust evidence of benefit. Described impacts of unnecessary intervention

Publication of '*Effective Care in Pregnancy and Childbirth*' and The Oxford Database of Perinatal Trials (1989). Paved the way for the Cochrane Collaboration. Pregnancy and Childbirth the first review group

Landmark Cochrane reviews include:

- Selective versus routine use of episiotomy for vaginal birth (Ziang et al 2017)
- Continuous CTG in labour (Alfirevic et al 2013)
- Magnesium sulphate for management of women with pre-eclampsia (Duley et al 2010)
- Midwife-led continuity of care models (Sandall et al 2016)
- Antenatal perineal massage for reducing perineal trauma (Beckmann and Stock 2013)
- External cephalic version for breech presentation at term (Hofmeyr et al 2015)





Clinical trials in maternity care: present

Recent trials have contributed to better maternity care

- Mobile compared with traditional epidural block for labour analgesia (COMET)
- Evidence-based assessment and repair of perineal trauma (PEARLS)
- Upright compared with supine positions for women giving birth with epidural analgesia (BUMPS. *BMJ research paper of the year 2018*)

Over 600 systematic reviews registered with Cochrane Pregnancy and Childbirth. Over 8,000 pregnancy trials registered on Clinical Trials & ISRCTN registries

Increased policy recognition that a healthy pregnancy leads to healthier life-course health for a woman and her infant

Clinical trials in maternity care: present

So trials have now informed all we need to know for optimal maternal care…….

Changing health profile of women who become pregnant; older age, higher BMIs, medical complications, physical and psychological co-morbidity increasing. Some adverse outcomes persist; still-birth and premature birth; indirect maternal deaths

Trials underway reflect current priorities for women and clinicians, before, during and after pregnancy

- Feasibility trial of commercial weight management groups for women with overweight or obese BMIs (SWAN)
- Pilot trial of midwifery training to encourage women to perform pelvic floor muscle exercises (APPEAL)
- Earlier birth of predicted larger birthweight babies (Big Baby)
- Prevention of recurrent miscarriage (CERM)

Clinical trials in maternity care: future

Need to reflect increasing maternal co-morbidity, social, cultural and environmental influences on life-course health of women and their families

Need trials which consider dissemination and implementation to reduce ‘research waste’. Hybrid & other novel trial designs (e.g. cohort multiple, stepped wedge, cluster randomized, registry trials)

Recognise importance of expertise of multi-disciplinary trial teams with expertise to develop, implement and evaluate complex interventions

Future work planned in postnatal triage, early labour management, perinatal mental health, breastfeeding following medically complex pregnancies

Important future for Maternity Research Theme as part of Warwick Clinical Trials Unit

Maternity Research, Warwick CTU

Thank you!

Email: debra.bick@warwick.ac.uk

Twitter: @debrabick

Website:
https://**warwick**.ac.uk/fac/sci/med/**research**/ctu/**maternity**

Alife 2

WARWICK
CLINICAL TRIALS UNIT

Presenters: Jessica Smith and Sarah Lowe

19 September 2019

FUNDED BY
NIHR | National Institute for Health Research

NHS
University Hospitals Coventry and Warwickshire
NHS Trust

Who is involved?

- Chief Investigator: Professor Siobhan Quenby
- Funder: Research for Patient Benefit Program
- Sponsor: University Hospitals Coventry and Warwickshire NHS Trust
- Trial Coordination: Warwick Clinical Trials Unit

Background

- 1-5% women experience ≥2 miscarriages
- >50% miscarriage remains unexplained
- Pregnancy failure is distressing for those who desire to have children
- One potential cause that isn't routinely investigated is Inherited thrombophilia

Background

- Inherited thrombophilia ("sticky blood") increases odds recurrent pregnancy loss

Inherited Thrombophilia	Odds ratio (95% confidence interval) recurrent loss <13 weeks[1]
Factor V Leiden	2.01 (1.3-3.58)
Activated protein C resistance	3.48 (1.58-7.69)
Prothrombin G20210A mutation	2.56 (1.04-6.29)
Protein S deficiency	14.72 (0.99-218.01)

- Partially explained by thrombosis in the placenta + inhibition of extravillous trophoblast differentiation

- Anticoagulants considered a possible treatment for women with recurrent miscarriage (RM) and inherited thrombophilia.

1. Rey, E. Kahn, SR. David, M. Shrier, I. (2003) Thrombophilic disorders and fetal loss: a meta-analysis. *Lancet* 15;361(9361):901-8.

Background

- Current Evidence:
  - 2 observational studies have shown a potential benefit of Low Molecular Weight Heparins (LMWH) in women with unexplained RM

ALIFE Study[1]

Randomised placebo controlled

Aspirin + LMWH vs aspirin vs placebo

Live birth rate 364 women with unexplained miscarriage

No difference in groups

SPIN study[2]

Randomised controlled trial

LMWH + aspirin vs standard care

Miscarriage rate in 294 women with ≥2 miscarriages

No difference between groups

Trial Evidence

No benefit for women with unexplained RM. Underpowered for patients with inherited thrombophilia

HepASA Trial[4]

Randomised controlled trial

LMWH + aspirin vs aspirin

Live birth rates in 88 women with recurrent miscarriage and autoantibodies or coagulation abnormality

No difference in groups

HABENOX[3]

Randomised placebo controlled

LMWH + placebo vs LMWH + aspirin vs aspirin

Live birth rate 207 women with ≥2 miscarriages

No difference in groups

1. Kaandorp SP, Goddijn M, van der Post JA et al. (2010) Aspirin plus heparin or aspirin alone in women with recurrent miscarriage. *N Engl J Med* 362:1586-1596.
2. Clark P, Walker ID, Langhorne P et al. (2010) SPIN (Scottish Pregnancy Intervention) study: a multicenter, randomized controlled trial of low-molecular-weight heparin and low- dose aspirin in women with recurrent miscarriage. *Blood* 115:4162-4167
3. Visser J, Ulander VM, Helmerhorst FM et al. (2011) Thromboprophylaxis for recurrent miscarriage in women with or without thrombophilia. HABENOX: a randomised multicentre trial. *Thromb Haemost* 105:295-301.
4. Laskin CA, Spitzer KA, Clark CA et al. (2009) Low molecular weight heparin and aspirin for recurrent pregnancy loss: results from the randomized, controlled HepASA Trial. *J Rheumatol* 36:279-287.

Background

- In acquired thrombophilia LMWH has a role in improving the live birth rate[1]
- Use of LMWH for women with RM and inherited thrombophilia is off label but established practice supported by local guidelines.
- Green-top Guideline 17 suggests “heparin therapy during pregnancy may improve the live birth rate of women with second-trimester miscarriage associated with inherited thrombophilias”[2]
- Polarised opinions amongst experts
- There is a need to establish whether anticoagulants are effective in reducing miscarriage in women with inherited thrombophilia experiencing RM.

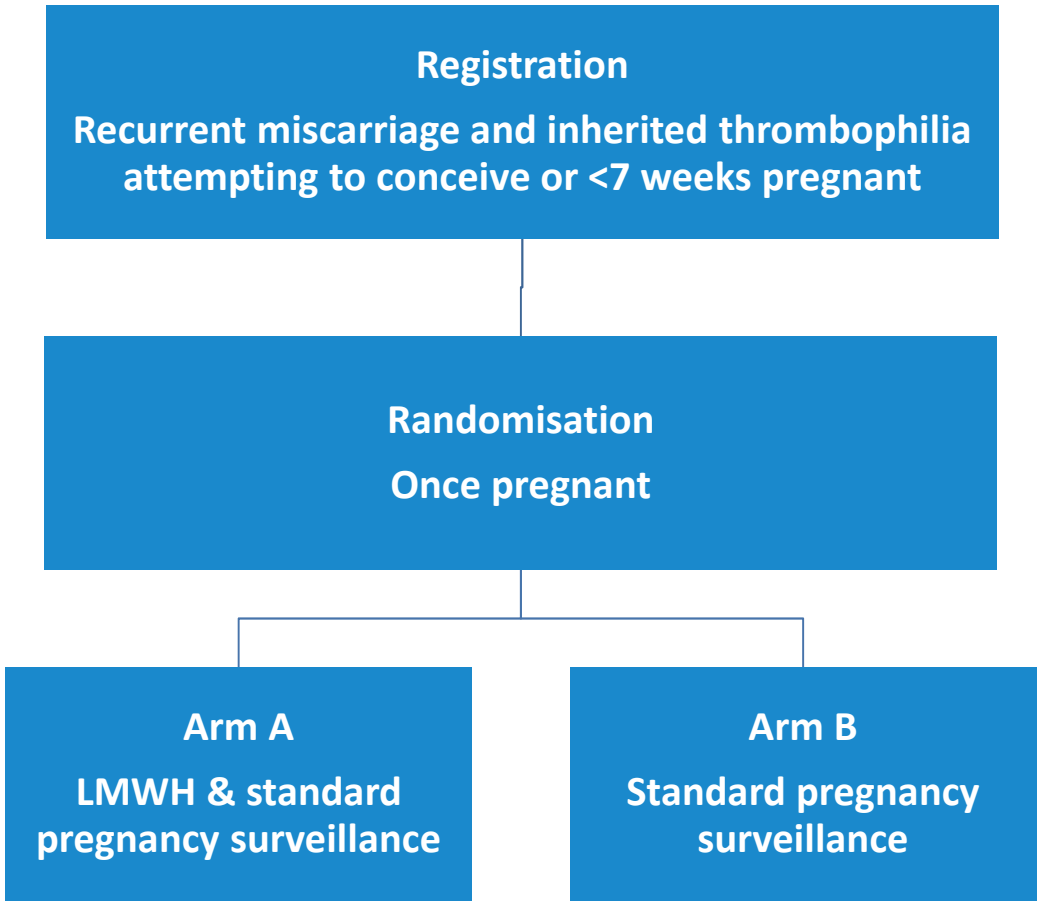
1. Rai, R. Cohen, H. Dave, S. Regan, L. (1997) Randomised controlled trial of aspirin and aspirin plus heparin in pregnant women with recurrent miscarriage associated with phospholipid antibodies (or antiphospholipid antibodies). BMJ 314:253-7.
2. RCOG (2011) The Investigation and Treatment of Couples with Recurrent First-trimester and Second-trimester Miscarriage. Green-top Guideline no. 17

ALIFE 2

Multi-centre randomised open-label, phase III clinical trial to compare LMWH with standard pregnancy surveillance in women with inherited thrombophilia and a history of recurrent miscarriage.

Change clinical practice across the world!

Trial Design



Trial Follow Up

12 weeks (+/- 2 weeks)

- Face to face
- Review dating scan
- Complete on treatment form
- If randomised to Arm A:
  - collect participant diaries
  - give out new participant diaries

24 weeks (+/- 2 weeks)

- Face to face or telephone
- Complete on treatment form
- If randomised to Arm A:
  - collect participant diaries
  - give out new participant diaries

36 weeks (+/- 2 weeks)

- Face to face or telephone
- Complete on treatment form
- If randomised to Arm A:
  - collect participant diaries
  - give out new participant diaries

End of trial

- 6-8 weeks post delivery or end of pregnancy
- Face to face or telephone
- Complete end of pregnancy form
- Collect:
  Patient diaries
  Unused IMP
  Sharps container

Alife 2

Trial Objectives

- **Primary Objective**
  - To evaluate the efficacy of LMWH in women with inherited thrombophilia and recurrent miscarriage and/or intrauterine fetal death (≥2)

- **Primary Outcome**
  - Live birth (defined as birth of a living child)
  - Clinically relevant bleeding (i.e. major bleeding and clinically relevant non-major bleeding)

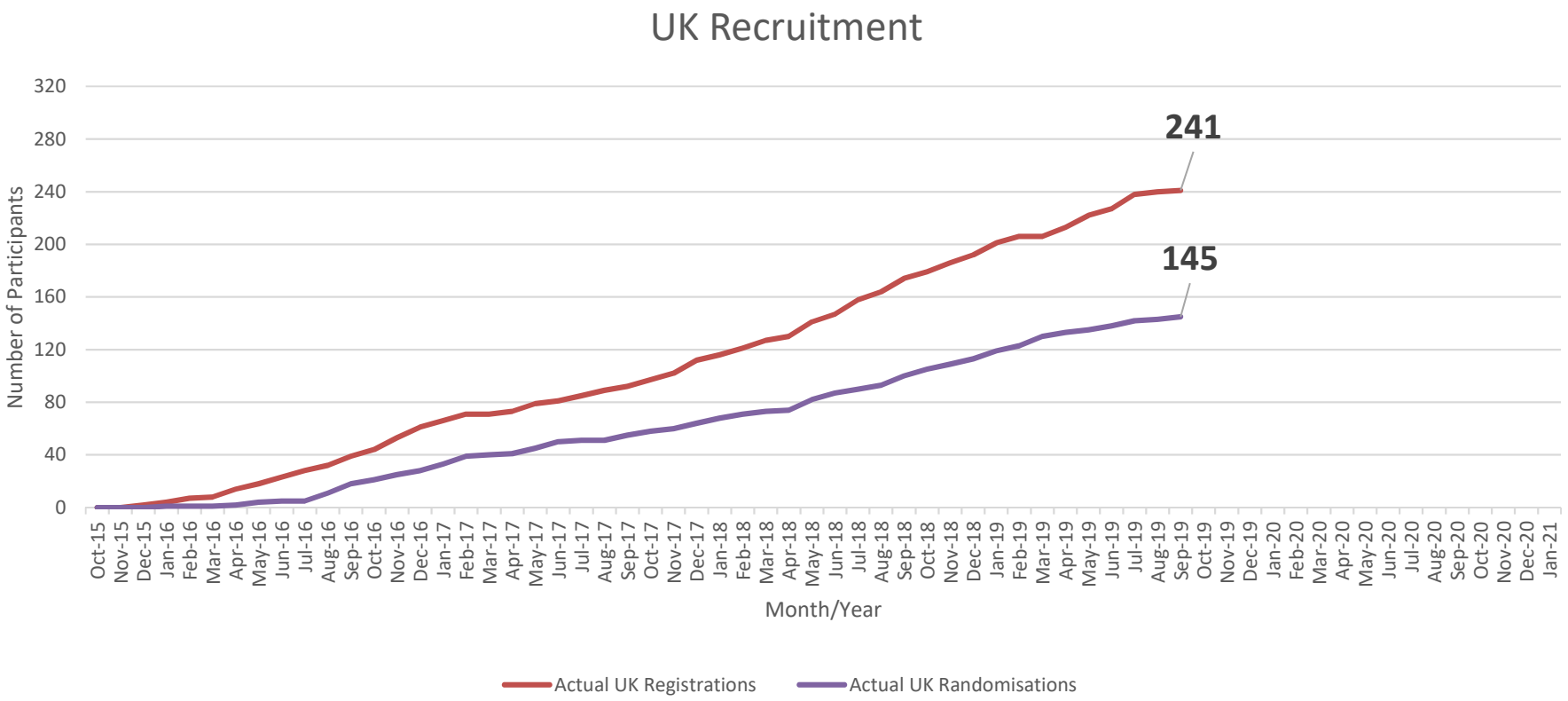
Sample size and timelines

- Register 400 women
  - 300 women in the UK
  - 100 women internationally (led by the Netherlands)
- Randomise 324 women
  - 243 women in the UK
  - 81 women internationally (led by the Netherlands)

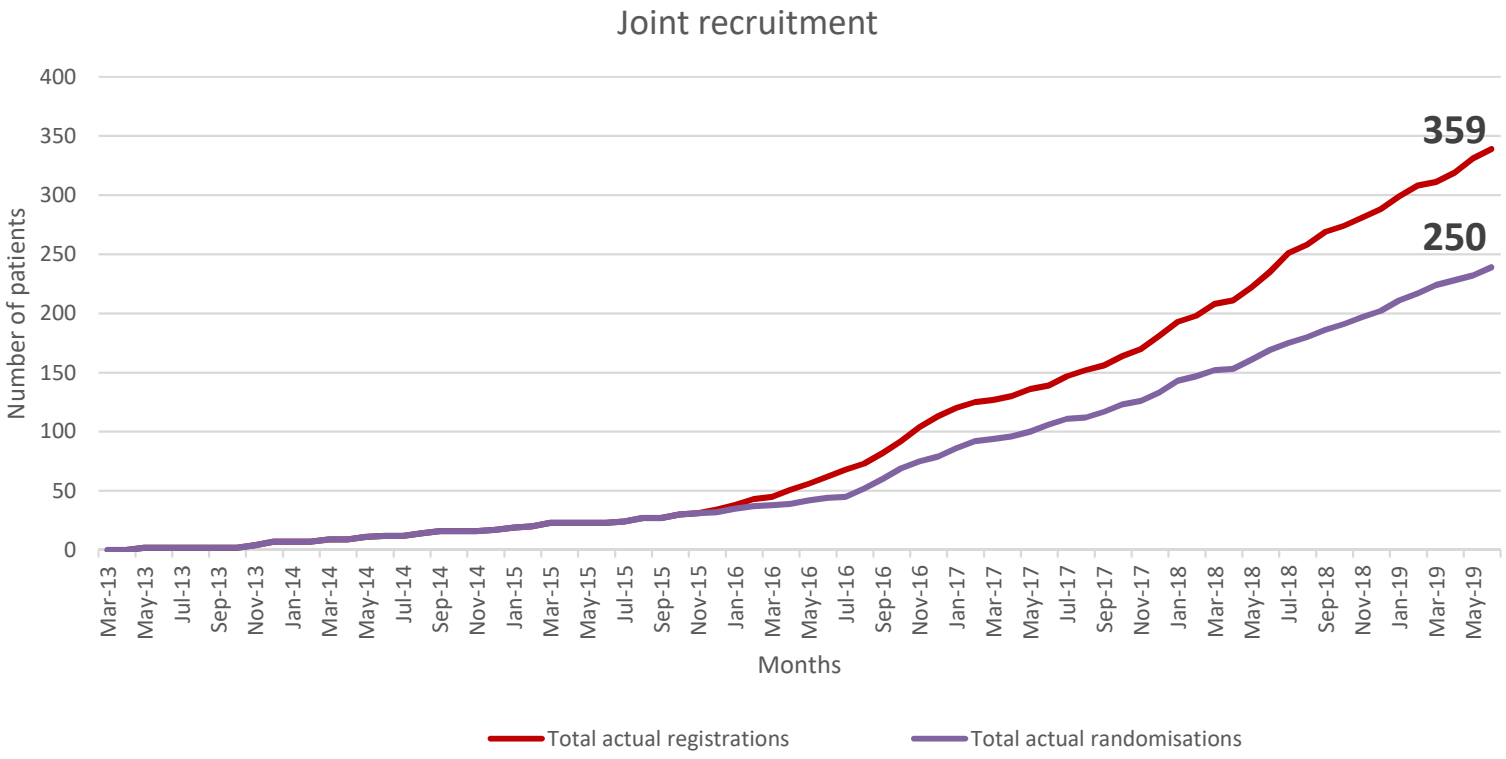
Trial Sites


Edinburgh
Glasgow
United Kingdom
Newcastle upon Tyne
NORTHERN IRELAND
Belfast
Isle of Man
Dublin
Liverpool
ENGLAND
WALES
Bristol
Cardiff
Southampton
Brighton
Plymouth
English Channel

Recruitment



Recruitment



Any questions?

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NHS
University Hospitals
Coventry and Warwickshire
NHS Trust

FUNDED BY
NIHR | National Institute for Health Research

This project was funded by the National Institute for Health Research, Research for Patient Benefit - RfPB (project number PB-PG-1013-32011)
The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the RfPB, NIHR, NHS or the Department of Health

The Big Baby Study

Presenters: Jackie Dewdney and Sara Wood

FUNDED BY NIHR | National Institute for Health Research

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perinatal institute for maternal and child health

epg Erb's Palsy Group

NHS The Shrewsbury and Telford Hospital NHS Trust

NHS University Hospitals Coventry and Warwickshire NHS Trust

Who is involved?

- Chief Investigators:
  - Prof. Siobhan Quenby
  - Prof. Jason Gardosi
- University Hospitals Coventry and Warwickshire
- The Erbs Palsy Group
- The Perinatal Institute
- Warwick Clinical Trials Unit
- Funded by the NIHR

Research Question

"Does induction of labour at $38^{+0} – 38^{+4}$ weeks gestation, in pregnancies with large for gestational age fetuses, reduce the incidence of shoulder dystocia?"

Background

- Complications from shoulder dystocia is one of the most common reasons for litigation

- Most cases occur in macrosomic fetuses
  - >90th centile on customised GROW
  - RCOG: >4.5kg

- Early delivery should reduce the babies weight at birth and hence mitigate the risk of shoulder dystocia

Anderson A. Ten years of maternity claims: an analysis of the NHS Litigation Authority data – key findings. Clinical Risk 2013;**19**(1):24-31.
Royal College of Obstetricians and Gynaecologists. Green–top Guideline No. 42. Shoulder Dystocia. 2 ed. London, 2012

Birth BACKGROUND

- 8 days overdue
- No complications during pregnancy
- Suffered Shoulder Dystocia
- Large baby 9lb 14 oz
- Bi lateral Erb's Palsy
- Left hospital with incorrect information and no extra support

How did /does it affect me?

Denial – nothing happened
Shock
Self blame – why me, why couldn't I give birth without hurting my child?
PTSD – nightmares, flashbacks
Mourning – loss of the 'perfect birth'
Depression – comes and goes still
Fear – social services
Re-occurring question of 'what did you do to your child ? !!!'
Cost – appointments, adjustments to Samuels clothing, adaptive equipment
Still find birthdays hard – too many memories

How does it affect Samuel?

Daily tasks – cutting food, washing, shoe laces, buttons, trousers, zips etc.

School – never had 100% attendance certificate due to appointments

Bullying – several times

Feels singled out due to laptop and TA to help in class

Unable to keep up with his peers, feels left behind

Frustration – broken 2 wardrobes and countless X-Box controllers

Surgery scary but fun to have time off school

PE at school , can't be involved in some lessons.

Unable to take his favourite subject Engineering in GCSE due to amount of extra help required

Easily distracted

Final thought

Treat each mum as an individual,

Listen and learn.

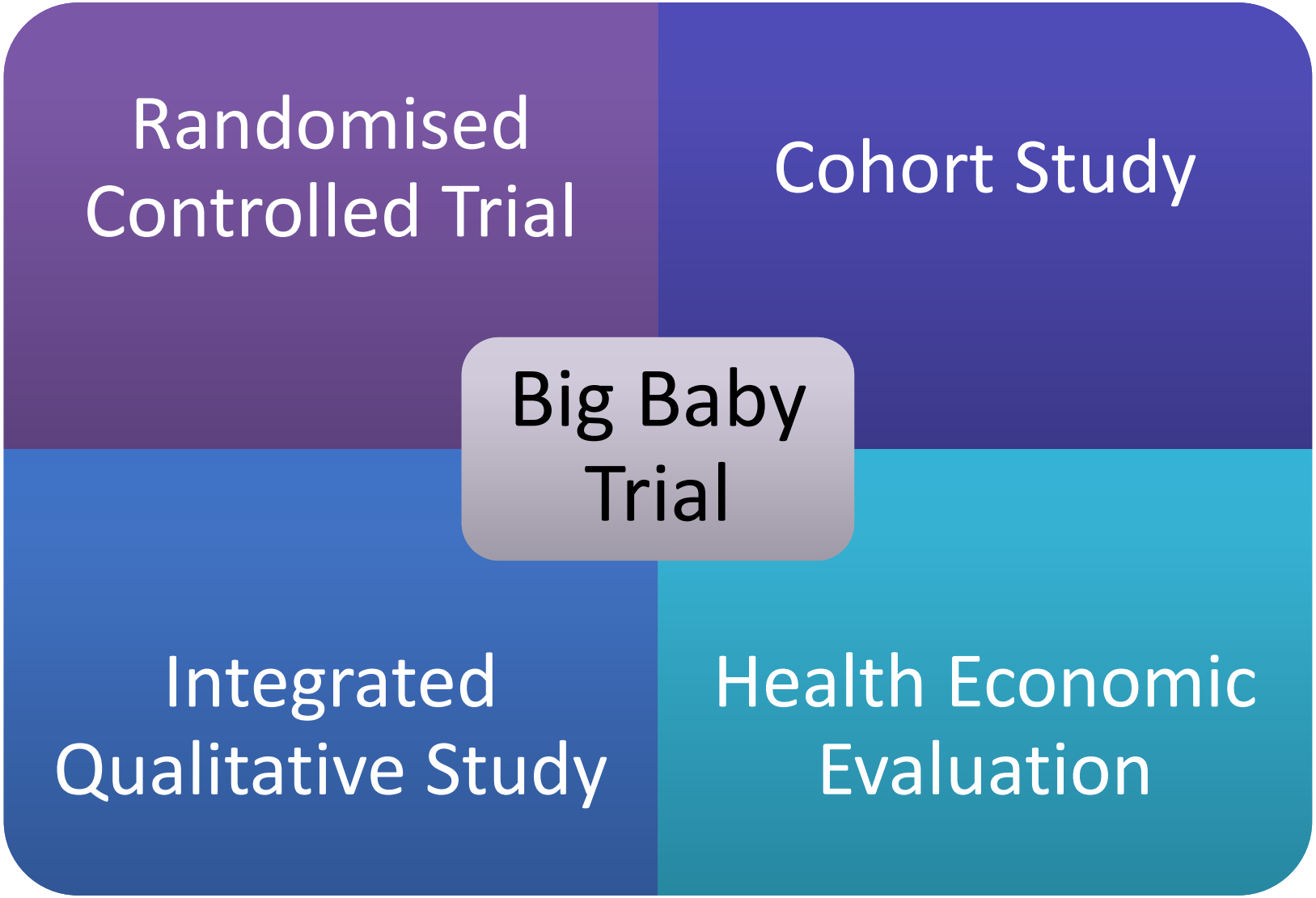
Objectives

Primary Objective

- To determine the effectiveness of induction at 38^{+0} – 38^{+4} weeks gestation in reducing the incidence of shoulder dystocia

Secondary Objectives

- To evaluate whether:
  - Expectant management increases the risk of neonatal birth injury
  - Induction increases the risk of infant complications related to prematurity
  - Induction increases the risk of birth injury to the mother



BigBaby CLINICAL TRIAL

Where are we now?

- The aim is to recruit 4000 women with LGA babies into the trial
- We are recruiting in over 60 sites in England, Scotland and Wales with more to still come on board
- After 15 months we have recruited
  - 971 RCT participants
  - 566 Cohort participants

Thank you for listening

Questions?

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Chronic Endometritis and Recurrent Miscarriage – CERM Trial

Amy Jackson – Patient Representative

Joshua Odendaal – Clinical Research Fellow

FUNDED BY NIHR | National Institute for Health Research

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The Lily Mae Foundation

Supporting Parents and Families after a Stillbirth or Neonatal Death

Imperial College London

UNIVERSITY OF BIRMINGHAM

NHS University Hospitals Coventry and Warwickshire NHS Trust

The CERM Trial

- Randomised placebo controlled trial

- Aim:
  - To determine if Doxycycline administered prior to conception improves pregnancy outcome in women with recurrent miscarriage associated with chronic endometritis and explore mechanisms by which it can prevent miscarriage

The CERM Trial

Trial Design	
Population	Recurrent miscarriage ≥ 2 CD138 screen positive – randomise and follow up CD138 screen negative – follow up 3,062 Patients to be screened 10 Sites across the United Kingdom
Intervention	Doxycyline 100mg BD for 14 days
Comparator	Identical placebo tablets
Co-primary outcomes	On-going pregnancy rate at 12 weeks Total live birth

Trial will provide definitive answers:

- Largest recurrent miscarriage trial in the world to date
- Chronic Endometritis and its link with recurrent miscarriage including how…
- Does Doxycycline improve clinical outcome?

Importance of taking part in trials

- Access new treatment
- Medical care and access
- Help others
- Support yourself

Importance of the CERM Trial

- Recurrent miscarriage patients experience
- Potential treatment for up to half of people with recurrent miscarriages
- Large population required
- Potential to decrease miscarriage rate significantly

Being a patient representative

- Offer a unique perspective based on experiential knowledge
- Helping with recruitment and dissemination of the trial results
- Support research
- Ensuring that information is presented in a patient friendly way

Acknowledgements

- The Lily Mae Foundation
- Prof Siobhan Quenby and Jan Brosens
- Prof Phil Bennett
- Prof Ari Coomarasamy
- Dr David McIntyre
- Dr Katherine Fishwick
- Warwick Clinical Trials Unit
- Trial Funders

Thank you – Questions?

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THE UNIVERSITY OF WARWICK

City of Breast Feeding 2021

WARWICK
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Lisa Creagh and Joanne Fisher

The importance

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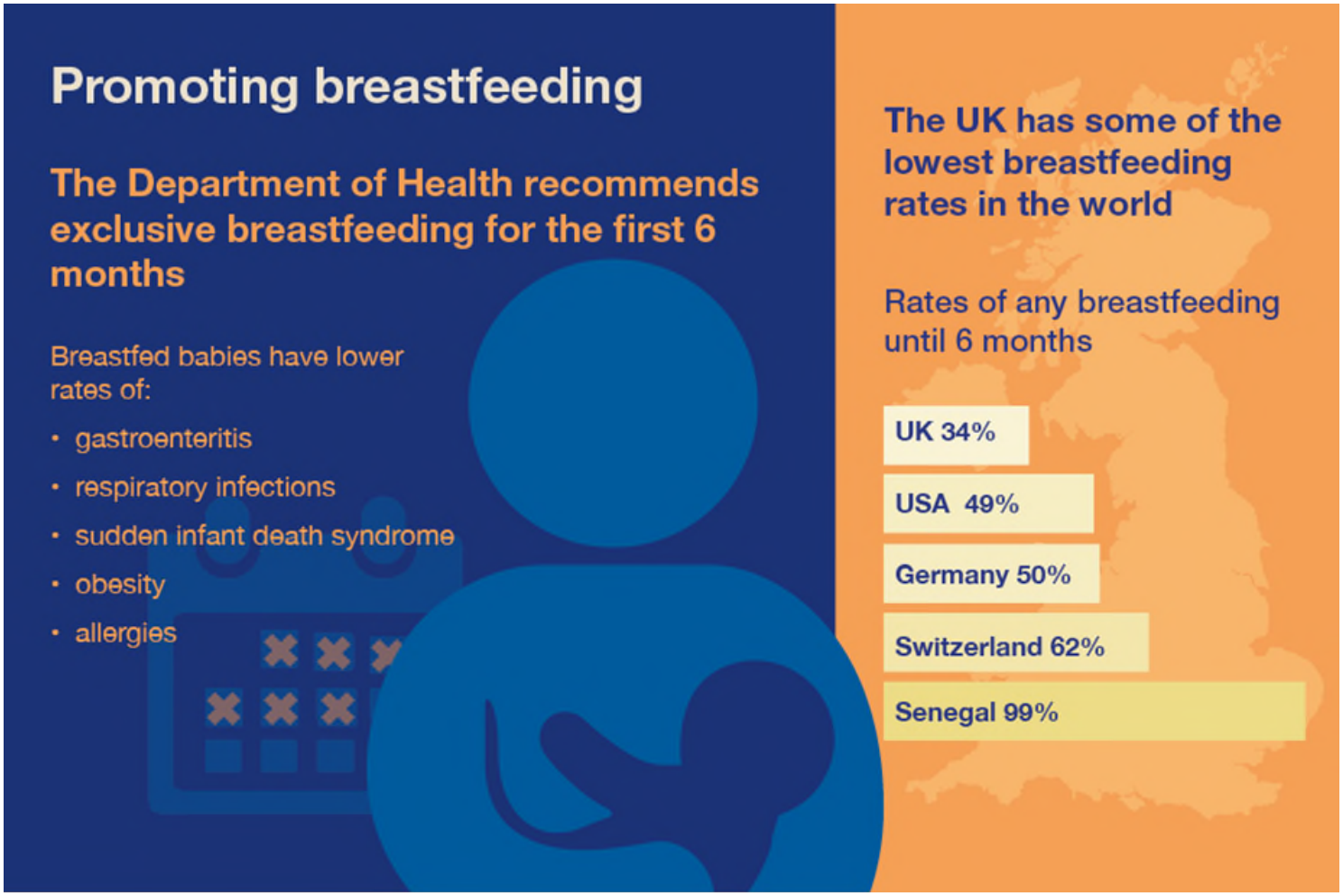

The figures

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Public Health England

THE BABY FRIENDLY INITIATIVE unicef

Breastfeeding in England

The UK government recommends exclusive breastfeeding for around 6 months and thereafter with other foods

74% of mothers start to breastfeed[2]

44% are breastfeeding at 6 weeks[3]

36% are breastfeeding at 6 months[4]

Only 1% of babies are exclusively breastfed until they are 6 months old[5]

Mothers who are young, white, from routine and manual professions and who left education early are least likely to breastfeed[6]

The Problem

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Whilst not every women wants to breastfeed, for those who do, it is important to try and overcome barriers, because not every women who stops BF wants to.

- Breastfeeding can be difficult and painful
- Increasing numbers of medically complex pregnancies
- Cuts to services - help not always available
- Embarrassment and negative public attitudes
- Fear their babies don't get enough milk / right nutrition
- Pressure to establish a feeding routine / sleep through
  Pressure to return to their 'pre-baby life-style'

The Project

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Holding Time Presentation

Any questions?

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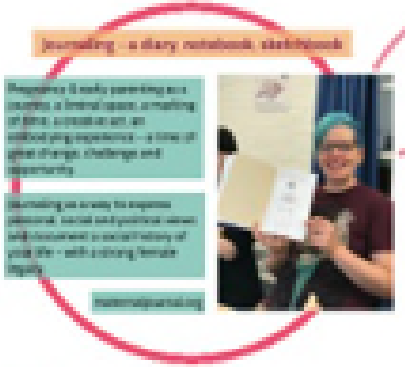
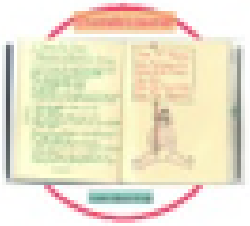
Joanne Fisher joanne.fisher@Warwick.ac.uk

MATERNAL JOURNAL





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Using qualitative research in the clinical trials context

Dr Sophie Rees

Maternity Theme Launch 19th September 2019
#MaternityResearchAtWarwick

@sophielour
S.Rees.1@warwick.ac.uk

What is qualitative research?

- Research which involves collecting non-numerical data about the social world and the behaviours and perspectives of people in it
- Understanding something from the perspective of those experiencing it
- Understanding what is happening in the real world
- Emphasises context

Common methods are:

- Interviews
- Focus groups
- Observations

@sophielour
✉ S.Rees.1@warwick.ac.uk

#MaternityResearchAtWarwick

Why do qualitative research in clinical trials?

Example questions:

- Is my intervention acceptable to patients? (Feasibility, intervention design)
- What are barriers and facilitators to entering the study? (Recruitment e.g. Big Baby)
- Why did my intervention work/not work? (Explaining trials results, transferability)

How to get started

- Talk to an experienced researcher!

@sophielour
✉ S.Rees.1@warwick.ac.uk

#MaternityResearchAtWarwick

Any questions?

@sophielour
S.Rees.1@warwick.ac.uk

The ALIFE-2 Trial

Researchers at Warwick Clinical Trials Unit, University of Amsterdam and University Hospitals Coventry and Warwickshire are undertaking a multi-centre randomised open-label phase III clinical trial, to see if Enoxaparin reduces miscarriage and improves the live birth rate in women with inherited thrombophilia (sticky blood).

Miscarriage is very distressing for couples and in over 50% of cases the cause is unexplained.

In women with inherited thrombophilia, thrombosis of the (microvasculature of the) placenta, and partially inhibition of extravillous trophoblast differentiation is suggested as a leading cause of miscarriage.

Women with inherited thrombophilia and recurrent miscarriage (RM) are often treated with Low Molecular Weight Heparins (LMWH).

The Royal College of Obstetricians and Gynecologists recommended low-dose aspirin plus heparin to prevent miscarriage and improve the live birth rate of women with second-trimester miscarriage associated with inherited thrombophilia's.

However, this is off-label use and there is a need to establish whether anticoagulants are effective in reducing miscarriage in women with inherited thrombophilia experiencing RM.

The trial is open and recruiting patients from 52 sites in United Kingdom, Netherlands, United States of America and Canada.

To date 8,401 women have been screened and 246 have been randomised.

ALIFE-2 is a collaboration between Professor Saskia Middledorp, Professor of Internal Medicine, at the University of Amsterdam and Professor Siobhan Quenby, Professor of Obstetrics, Warwick Medical School, at The University of Warwick and University Hospitals Coventry and Warwickshire.

Quotes from patients participating in Alife-2

"Joining the ALIFE2 trial was one of the best decisions we've ever made, I hope the results, when the trial is completed, help others in a similar situation."

"I just wanted to drop you a line to say a big thank you for all your help and support during my pregnancy. I would have been a nervous wreck without the support of you guys."

FUNDED BY NIHR | National Institute for Health Research

This trial is funded by a grant from the National Institute for Health Research (NIHR) under Research for Patient Benefit - RfPB (project number PB-PG-1013-32011).

This trial is Sponsored by University Hospitals Coventry and Warwickshire NHS Trust.

CERM trial website can be found at https://warwick.ac.uk/cerm

Maternity stream website can be found at https://warwick.ac.uk/fac/sci/med/research/ctu/trials/alife2

The Big Baby Trial

Researchers on the Big Baby Trial are trying to find out if starting labour earlier than usual, at 38 weeks, makes it less likely that shoulder dystocia will happen in women whose babies appear to be bigger than expected.

Shoulder dystocia is a complication that occurs in 1 in 150 vaginal deliveries. This is when after a baby's head has been born one of the baby's shoulders becomes stuck behind the woman's pubic bone, delaying the birth of the baby's body. Most babies born that have experienced shoulder dystocia will have no long term complications. But for some babies this can cause a stretching in the nerves of the neck, which may cause long-term weakness in the arm.

We know that shoulder dystocia occurs more often in bigger babies but there is uncertainty in how often this actually occurs. We estimate that shoulder dystocia could occur in 1 in 25 women with a big baby who have a vaginal delivery.

It has been suggested that if we can deliver bigger babies a few weeks early by inducing labour, this could reduce the chance of shoulder dystocia happening. Currently it is not clear whether it is better for women with big babies to have their labour induced or to wait for labour to begin naturally. To answer this question a clinical trial is needed.

We propose to study 4,000 pregnant women whose ultrasound scans suggests that their babies are bigger than expected. The randomised controlled trial will aim to recruit 4000 women identified as having large for gestational age babies between 35 and 38 weeks gestation.

The primary outcome is shoulder dystocia. This is defined as 'a vaginal cephalic delivery that requires additional obstetric manoeuvres to deliver the fetus after the head has delivered and gentle traction has failed'. The aim of this trial is to help women, obstetricians and midwives decide what the best way to deliver bigger babies is.

The collaborators working on this trial are from the following institutions:

"The Erb's Palsy Group are proud to be collaborating on this important study, having a labour complicated by shoulder dystocia can be a scary situation for both parents and clinicians. This study is a wonderful opportunity to look at whether or not induction of labour can be successful in reducing the incidence of this obstetric emergency from happening and possibly avoiding the need for further manoeuvres to ensure the safety of both Mum and Baby"

Karen Hillyer - Chairperson of the Erb's Palsy Group

FUNDED BY NIHR | National Institute for Health Research

This trial is funded by a grant from the National Institute for Health Research (NIHR) under the Programme Grants for Applied Research programme 16/77/02.

This trial is Sponsored by University Hospitals Coventry and Warwickshire NHS Trust.

Big Baby trial website can be found at https://warwick.ac.uk/bigbaby

Maternity stream website can be found at https://warwick.ac.uk/maternity

Blood Pressure in the Postnatal Period Study (BPiPP)

Women with hypertensive disorders of pregnancy are at risk of poorer health outcomes, but there is limited information on their postnatal health, if the care they received met their needs, or the extent to which it reflected evidence-based guidelines.

WARWICK CLINICAL TRIALS UNIT

BPiPP study - Blood Pressure in the Postnatal Period

The number of women with complex pregnancies is increasing. Better understanding the health impact of these disorders beyond pregnancy is a public health priority. Study findings will answer important questions and provide new information on the extent to which postnatal health differs amongst women with more complex pregnancies compared with lower risk women, if postnatal care is meeting women's needs and if it reflects national guidance. We will use findings to develop better pathways of care for all women giving birth.

BPiPP is a prospective cohort study currently underway in 12 NHS trusts across England. Women are identified and recruited on the postnatal ward of participating NHS trusts and invited to complete a short, 5 minute, baseline questionnaire. At three months postpartum recruited women are sent a follow-up questionnaire to complete. We are aiming to recruit over 1,000 women, split equally between those who did and did not experience hypertensive disorders in pregnancy.

Both questionnaires include questions on women's physical and mental health and the postnatal care they received. Questionnaires include the Edinburgh Postnatal Depression and EuroQol Group five validated questionnaires. Additionally, the baseline questionnaire captures information on women's health in pregnancy and some demographic information. The follow-up questionnaire captures more detailed information on participants' physical and psychological health and postnatal care received in addition to infant feeding, support and planning for future pregnancies.

With women's permission, their maternity records are being accessed to collate additional information on their medical/pregnancy history, demographics, delivery/birth, in-patient stay and health of women and their infants at hospital discharge.

This study is jointly led by Professor Debra Bick, University of Warwick and Professor Lucy Chappell, King's College London.

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KING'S College LONDON

Quote from Professor Debra Bick joint CI

"We need to know if women who have more medically complex pregnancies receive postnatal care appropriate to their needs compared to women who did not have complications, the extent to which their health needs may differ after pregnancy and identify gaps in postnatal care where we could potentially intervene to improve outcomes for women's health longer-term"

FUNDED BY NIHR | National Institute for Health Research

This study is funded by a grant from NIHR CLAHRC South London and the NIHR Research Professorship awarded to Professor Lucy Chappell

This trial is Sponsored by King's College London.

CERM trial website can be found at Bpipp-study@kcl.ac.uk

Maternity stream website can be found at https://warwick.ac.uk/fac/sci/med/research/ctu/trials/alife2

The CERM Trial

Researchers at Warwick Clinical Trials Unit and University Hospitals Coventry and Warwickshire are undertaking a prospective, multi-centre, randomised, double blind, adaptive designed, trial to determine if doxycycline given prior to conception reduces miscarriage and increases live births in women who have experienced two or more consecutive first trimester miscarriages with associated chronic endometritis.

Recurrent miscarriage (RM) causes considerable distress and psychological morbidity for women and their partners. The vast-majority of couples only receive supportive care, as few treatments have been shown to prevent miscarriage. There is evidence to suggest chronic endometritis (CE) is a cause of recurrent miscarriage.

CE is a chronic inflammation of the endometrium, diagnosed using CD138 immunohistochemistry. Studies have shown that antibiotics can improve CE. To find out if doxycycline given prior to conception improves the number of on-going pregnancies and total live births in women who have experienced two or more consecutive first trimester miscarriages, we are undertaking a prospective, multi-centre, randomised, double blind adaptive designed trial.

We will compare a pre-conception course of doxycycline (100mg twice daily for 14 days) to placebo in up to 1500 women with recurrent miscarriage associated with CE.

Primary outcomes will be on-going pregnancy at 12 weeks and total live births. A sub-group will additionally have endometrial and biopsies swabs taken both before and after intervention to assess the effect of doxycycline on, endometritis, decidualisation and the endometrial microbiome.

This trial is led by Professor Siobhan Quenby with collaborators from the following institutions:

Professor Siobhan Quenby said **"***this is an important trial, that may lead to a treatment, for women with recurrent miscarriage all over the world, who currently only receive supportive care***"**

FUNDED BY NIHR | National Institute for Health Research

This trial is funded by a grant from the National Institute for Health Research (NIHR) under the Programme Grants for Applied Research programme 17/60/22.

This trial is Sponsored by University Hospitals Coventry and Warwickshire NHS Trust.

CERM trial website can be found at https://warwick.ac.uk/cerm

Maternity stream website can be found at https://warwick.ac.uk/maternity

Postnatal care following hypertensive disorders of pregnancy: The PEONY Study

Researchers at Warwick Clinical Trials Unit and King's College London are looking at the planning and provision of care within the first 12 months of birth compliance with NICE on hypertensive disorders in pregnancy.

We explored views and experiences of care, health and lifestyle behaviours up to 12 months postnatally among women who had hypertensive disorders in pregnancy (HDP) and extent to which their support and care needs were met; and clinician's views and experiences of caring for women with HDP, including barriers to implementation of recommendations relevant to postnatal care.

HDP include gestational hypertension, chronic hypertension, pre-eclampsia-eclampsia and pre-eclampsia imposed on chronic hypertension. HDP are among the most severe maternal health problems experienced during, and in some cases, following pregnancy. HDP affect around 5%-10% of women globally, and a leading cause of maternal death. Rates are increasing due to more women commencing pregnancy at an older age, having an obese BMI or medical problem such as diabetes.

Given high and persistent levels of maternal morbidity following HDP, appropriate and timely clinician input to assess and promote postnatal health and well-being is imperative. Increased awareness of which women are at risk, together with advice offered to women on self-management of potentially modifiable risk factors such as weight management and tobacco smoking cessation, highlights the potential opportunity for postnatal care to benefit shorter and longer-term maternal health.

We interviewed 24 women who gave birth at four South London hospitals and experienced HDP. Interviews took place at four and 12 months postnatally.

Women's interviews showed some had poor understanding of HDP and its long-term complications. Having HDP impacted on infant feeding, affected their emotional well-being and information offered did not support their longer-term recovery. Clinicians' interviews showed that perceived barriers to implementation of National Institute for Health and Care (NICE) guidance included lack of appropriate care plans and pathways, poor continuity of care, poor advice on anti-hypertensive medication management, and uncertainty around responsibility for postnatal care. Failure to plan and tailor postnatal care to women's needs means there are missed opportunities to improve subsequent pregnancy and longer-term outcomes for those who have more medically complex pregnancies.

Professor Debra Bick said:
"Findings highlight the importance of planning for a woman's postnatal care. This could promote better communication between clinicians in different health settings, and ensure women are aware of the risks of HDP to their future health"

This study was led by Professor Debra Bick and colleagues from King's College London:

This study was funded by a grant from NIHR CLAHRC South London.

FUNDED BY NIHR | National Institute for Health Research

Maternity stream website can be found at https://warwick.ac.uk/maternity

Supporting women with postnatal weight management: The SWAN feasibility trial

WARWICK CLINICAL TRIALS UNIT

Researchers led by Professor Debra Bick undertook a feasibility study to consider if it was possible to conduct a future definitive trial of a postnatal weight management intervention to support women to manage their weight after giving birth.

We aimed to assess if offering information on positive health and 12 weekly commercial weight management sessions could support women with overweight and obese Body Mass Indexes at antenatal booking (BMIs ≥25kg/m^2) or women with normal BMIs (BMI 18-24.9kg/m^2) who gained more pregnancy weight than recommended, to better manage postnatal weight and health. We undertook a 'feasibility study' to provide information on whether this study could succeed, recruiting from one inner-city site in London.

We wanted to know if women would join a study to be randomly allocated to weight management sessions provided by Slimming World or usual care only (control); how long recruitment would take; if we could follow 130 women to 12 months postnatally; if the intervention supported lifestyle and postnatal weight change as assessed at 12 months postnatally; if study processes were acceptable.

We recruited 193 women, 98 were allocated to the intevention and 95 the control; 140 were followed to 12 months postnatally.

Intervention women had more weight change at 12 months postnatally than control women, with little differences in other health outcomes. Around half (47%) of the intervention group attended weight mangement sessions, with highest weight loss among 19 (41%) women who attended 10+ sessions.

We could recruit and follow women with higher BMIs, but other approaches are needed to recruit women with normal BMIs. The intervention was acceptable and relevant cost data could be collected.

Acceptability of the intervention was affected by a range of barriers that should be addressed in a future study to increase uptake. A definitive trial should now be undertaken.

Professor Debra Bick said. *'Women who commence pregnancy with higher BMIs are at greater risk of complications during and after giving birth. Interventions which could support women to better manage their health are urgently needed, and we are planning to conduct a definitive trial to see if interventions postnatally are effective'*

This trial was led by Professor Debra Bick with collaborators from the following institutions:

KING'S College LONDON

UNIVERSITY OF SURREY

nct 1ST 1,000 DAYS NEW PARENT SUPPORT

St George's University of London

The University of Nottingham

This trial was funded by a grant from The National Institute for Health Research Public Health Research Programme. Ref no: 14/67/14

FUNDED BY NIHR | National Institute for Health Research

This trial was sponsored by King's College London.

SWAN trial can be found at https://njl-admin.nihr.ac.uk/document/download/2007612

Maternity stream website can be found at https://warwick.ac.uk/maternity