Institution: University of Warwick

Unit of Assessment: A4 Psychology, Psychiatry and Neuroscience

Title of case study: Improving care by understanding the effects of preterm birth on child and adolescent development

1. Summary of the impact

Professor Dieter Wolke has led several research programmes that delineate the long-term health effects of prenatal exposure to stress and moderate/late preterm, very preterm, and extremely preterm birth. His research has had a direct impact on international medical guidelines and educational recommendations for babies born preterm. The research has also informed European political debate (via a White Paper for the European parliament) on healthcare policy related to after care for preterm or sick children; has influenced UK policy regarding the education of children born preterm; and has contributed to public and practitioner understanding through media items issued, for example, by the NHS and the Royal College of Obstetricians and Gynaecologists.

2. Underpinning research

Each year about 15 million babies are born prematurely worldwide. The numbers of babies being born extremely or very preterm (<32 weeks gestation), moderate/late preterm (32-36 weeks gestation) and near term (37-38 weeks gestation) are growing due to the increased risks of preterm birth in women who have children later in life, increased fertility treatment leading to increased multiple births (which are often preterm), and the increased use of elective caesarean sections (often carried out near term). These changes mean that more preterm and extremely preterm children survive: in England, around 60,000 babies are born very or moderate/late preterm each year.

Since his arrival at Warwick in 2006, Wolke's research has focused on the long-term cognitive, behavioural and life quality consequences of prematurity. Several large grants have supported his analysis of data from major longitudinal datasets [e.g. 8; 9] and involve national (e.g. Professor Neil Marlow, UCL) and international (e.g. Professor Peter Bartmann, Bonn) collaboration. Key findings from Wolke's research concern the effects of prematurity on survival, later health and psychological status and quality of life. These findings have been obtained by following children's development using a number of national and international longitudinal databases including the Millennium Cohort Study, the Avon Longitudinal Study of Parents and Children (ALSPAC), the Bavarian Longitudinal Study (BLS), and the EPICure Study. For example, the EPICure research investigates a national cohort of children (UK) born at less than 26 weeks gestational age in 1995, who have been followed up at 1 year, 2.5 years, 6 years, and 11 years of age. (A follow-up at 16 years and 19 years including full psychological, respiratory and MRI investigations is currently funded and underway.) The BLS in Germany is co-directed by Wolke and has now followed up very preterm children (<32 weeks gestation) and full term controls from birth to 26 years of age.

Wolke's research at Warwick has demonstrated that birth before term is related to a specific constellation of cognitive, learning, attention, emotional and social deficits later in life, combined with long-term health problems (a "preterm phenotype"). The deficits were observed across the gestation spectrum but were disproportionally highest in those born extremely or very preterm. These deficits include highly increased rates of attention deficit disorder, autism, and special educational needs. Overall, approximately 40% of babies born prior to 26 weeks of gestation and 25% of those born prior to 32 weeks of gestation show moderate to severe disabilities. Wolke's research has revealed not only the impact of preterm birth on various developmental outcomes but their potential mechanisms. For example, children born preterm show brain plasticity but this comes with trade-offs. While low workload tasks are solved at similar accuracy, difficulties occur with solving tasks of increasing workload that require recruitment of wider brain networks. Thus prematurity is particularly associated with specific mathematical problems at age 11 [3]. These cognitive, specific attention and social problems, as well as neuromotor impairments of preterm children contribute to poor academic performance [1]. To address the question of whether preterm children born in summer may benefit from delayed school entry, Wolke has and is examining admission policies for summer-born children on school performance and health using the UK Millennium Cohort Study [6] and BLS.

More broadly, Wolke has investigated how environmental factors such as prenatal exposures to alcohol or stress or early postnatal parenting affect emotional development and how cognitive stimulation and sensitive parenting may provide protection or lead to increased resilience in biologically "at risk" children. For example, several investigations into light drinking during pregnancy and the risk of socio-emotional problems and cognitive deficits up to age 7 years were reported (finding no adverse effects of light drinking [4, 7]). Other work has shown that parents of very preterm children are as, or even more, sensitive in their parenting as the parents of full-term children. Attachment problems occur more often in children born preterm despite sensitive parenting. Wolke has shown that highly sensitive parenting instills resilience against academic failure in very preterm children, with preterm children more susceptible to parenting styles than full term children (differential susceptibility), opening up potential new interventions for preterm children. Wolke has also examined the prevalence of eating problems and their association with neurological and behavioral disabilities and growth among extremely preterm children at age 6 years, finding that eating problems make an additional contribution to continued growth failure and may require early recognition and intervention [5]. Wolke's research is translational and he has validated a range of instruments utilising parents or teachers to conduct structured, inexpensive monitoring as a first step screening for expensive standard medical monitoring for outcomes associated with prematurity [2].

3. References to the research

Publications:

1. Marlow N., Hennessy, E. M., Bracewell, M. A., & **Wolke, D.** (2007). Motor and executive function at 6 years of age after extremely preterm birth. *Pediatrics, 120,* 793-804. DOI: 10.1542/peds.2007-0440
2. Johnson, S., **Wolke, D.,** & Marlow, N. (2008). Developmental assessment of preterm infants at 2 years: validity of parent reports. *Developmental Medicine & Child Neurology, 50,* 58-62. DOI: 10.1111/j.1469-8749.2007.02010.x
3. Johnson, S., Hennessy, E. M., Smith, R. M., Trikic, R., **Wolke, D.,** & Marlow, N. (2009). Academic attainment and special educational needs in extremely preterm children at 11 years of age: The EPICure Study. *Archives of Disease in Childhood – Fetal and Neonatal Edition, 94,* F283-F289. DOI: 10.1136/adc.2008.152793
4. Kelly, Y. J., Sacker, A., Gray, R., Kelly, J., **Wolke, D.,** Head, J., & Quigley, M. A. (2010). Light drinking during pregnancy: Still no increased risk for socioemotional difficulties or cognitive deficits at 5 years of age? *Journal of Epidemiology and Community Health, 66,* 41-48. DOI: 10.1136/jech.2009.103002
5. **Samara, M.,** Johnson, S., **Lamberts, K.,** Marlow, N., & **Wolke, D.** (2010). Eating problems at age 6 years in a whole population sample of extremely preterm children. *Developmental Medicine & Child Neurology, 52,* e16-e22. DOI: 10.1111/j.1469-8749.2009.03512.x
6. Quigley, M. A., Poulsen, G., Boyle, E., **Wolke, D.,** Field, D., Alfirevic, Z., & Kurinczuk, J. J. (2012). Early term and late preterm birth are associated with poorer school performance at age 5 years: a cohort study. *Archives of Disease in Childhood – Fetal and Neonatal Edition, 97,* F167-F173. DOI: 10.1136/archdischild-2011-300888
7. Kelly, Y., Iacovou, M., Quigley, M. A., Gray, D., **Wolke, D.,** Kelly, J., & Sacker, A. (2013). Light drinking versus abstinence in pregnancy – behavioural and cognitive outcomes in 7-year-old children: a longitudinal cohort study. *British Journal of Obstetrics and Gynaecology, 120,* 1340-1347. DOI: 10.1111/1471-0528.12246

Research grants:

8. PI: N. Marlow (UCL) 'EPICure: Population-based studies of survival and later health status of infants of 25 weeks gestation or less'; MRC: 2005-2012. This project was awarded in 2005 while Wolke was working for the Jacobs Foundation (Zurich), which, due to its charitable foundations, could not accept grant funding. When Wolke transferred to Warwick in 2006, Wolke continued as Collaborator with additional expenses being recovered separately. Wolke was then named as Co-I when the project was renewed in 2012: PI: Prof Neil Marlow, UCL; Co-I, D Wolke, Warwick 'EPICure @ 19 - the extremely preterm young adult'; MRC 01.07.2012-30.06.2016 £16,000
9. PI: P Bartmann, University of Bonn, Co-I: D Wolke, Warwick 'Bavarian Longitudinal Study – social adjustment and quality of life after very preterm birth: risk and resiliency from infancy to

adulthood'; Ministry of Science and Education (BMBF, Germany) 01.07.2009-30.06.2015 £634,757

10. PI: N Buck, Essex, Co-I: D Wolke, Warwick 'Understanding Society and the UK Household longitudinal study'; ESRC 2010-2015. £175,911
    Extended: "Understanding society and the UK Household longitudinal study". ESRC 01.04.2013-31.03.2018. PI: N Buck, Essex; Co-I: D Wolke, Warwick £257,269

4. Details of the impact

Political impact: Wolke's findings on the special education needs and eating problems of preterm births have informed political decision-makers. The chairwoman of EFCNI (European Foundation of Care for New-born Infants) notes of Wolke "it is because of his expertise that he was specifically invited to contribute to and be on the editorial board for the EFCNI White Paper of Maternal and Newborn Health and Aftercare Services 'Caring for Tomorrow' presented to the European Parliament in November 2011. The White Paper specifically references Professor Wolke's research [3] regarding special educational needs in extremely preterm children, the association between prematurity and eating problems at age 6 [5] and the use of parental reports as valid indices of child development [2]. It is important to recognise the significance of this White Paper and the role that Professor Wolke has played; this White Paper has been fundamental point which the EU has developed its policy and strategy for the delivery of healthcare to an ever increasing number of preterm babies being born. Hence Professor Wolke's research will have a far reach across Europe and its member states as well as being a focal point and reference across the world" [11].

The White Paper and the WHO report (see below) have led the European Parliamentary Policy Department Committee on Environment, Public Health and Food Safety (ENVI) to set up a workshop "Newborn Infants" (24 April 2013), in which the MEP (Health Working Group, ENVI Committee) stressed the need to identify the necessary policy changes at the EU level to improve maternal and newborn health, as well as to address inequalities across Member States in this area [12].

Furthermore, the report published by the World Health Organization (WHO) in 2012 entitled "Born too soon: the global action report on preterm birth" [13], refers to Wolke's work on neurodevelopmental and education outcomes [6]. The WHO report provides the first-ever national, regional and global estimates of preterm birth, shows the extent to which preterm birth is on the rise in most countries, and offers policy relevant recommendations to governments and NGOs. The report relates to WHO's leadership of an international campaign ("Millennium Development Goal 4") to reduce child deaths; hence Wolke's research has contributed to recommendations from WHO at an international level.

Impact on education: In the UK, the Department of Education's newly issued "Advice on the Admission of Summer born children – for local authorities and school admission authorities and parents" (July 2013) [14] cites Wolke's research at Warwick [6], the only research referenced. It is the first time that DoE has issued this guidance which details the framework that authorities must operate under. Preterm children are born before their expected date of delivery but their birth date is used to enrol them into school. Summer born preterm children enter school a year earlier than if they had been born at term. The CEO of BLISS [15] notes the significance of this report: "this long awaited guidance, that Bliss has been campaigning for many years, should significantly change the way by which Local Authorities in England manage the school admissions of very early gestation born children. This will positively impact many thousands of families every year" as it removes any statutory barriers to children being admitted outside their normal age group. The CEO of BLISS added [15] "Dieter's research has been crucial to Bliss's own policy work in each of the UK health economies, underpinning much of our advocacy for delivering the best possible care for babies and their families".

Clinical impact: Wolke's research has been included in guidelines regarding resuscitation of preterm children born at the limit of viability. His group's research on motor and executive function after extremely preterm birth [1] is cited in the 2011 Revision of the Swiss Recommendations published in the Swiss Medical Weekly [16].

The Swiss recommendations explicitly include for the first time that care of preterm infants prior

to 23 6/7 weeks should be limited to palliative care as a result of long-term developmental disorders associated with extreme preterm birth. These guidelines, endorsed by the Swiss Society of Neonatology, are used by physicians, midwives and nurses and other professionals involved in the perinatal care of preterm births in Switzerland.

Wolke's work [7] on light drinking versus abstinence in pregnancy published in 2013 was commented on by the Royal College of Obstetricians and Gynaecologists (April 2013) [17], produced considerable public interest, news reports and a comment from the Department for Health. Wolke's earlier research (which used data collected in the UK Millennium Cohort Study) on the absence of risk associated with light drinking during pregnancy [4] was used in a NHS online report 'Light drinking in pregnancy' [18].

Practitioners: The research from Wolke's group has also informed both the public and clinical practitioners through its wide dissemination. Wolke has given a large number of invited and keynote lectures (20 in 2012, 17 in 2011, 10 in 2010) including talks to paediatricians (e.g., European Academy of Paediatric Societies, 2010 and 2012), neonatologists (e.g., Gesellschaft fur Neuropadiatrie, 2010), and educational professionals (e.g., Institute of Education, 2013) [19]. This has led to specific material for teachers in information sheets issued by the Specialist Schools and Academics Trust ("Complex Learning Difficulties and Disabilities Research Project") [20], widespread media coverage and to numerous media appearances. The wide reach of his research has resulted in increased awareness of the need to develop different educational and intervention approaches for children born premature by teachers, clinical practitioners and among the general public.

5. Sources to corroborate the impact

11. Letter from Chairwoman of the Executive Board, EFCNI (European Foundation of Care for New-born Infants). European Foundation of Care for New-born Infants White Paper. http://www.efcni.org/index.php?id=1888
12. Workshop on Newborn Infants 24 April 2013 http://www.europarl.europa.eu/document/activities/cont/201307/20130719ATT70006/20130719ATT70006EN.pdf
13. Howson, C. P., Kinney, M. V., & Lawn, J. E. (2012). Born too soon: the global action report on preterm birth. Geneva: World Health Organization. http://www.who.int/pmnch/media/news/2012/preterm_birth_report/en/
14. Department of Education Document, p8. http://media.education.gov.uk/assets/files/pdf/a/advice_summer_born_children.pdf
15. Letter from Chief Executive, BLISS, UK charity working to provide the best possible care and support for all premature and sick babies and their families.
16. 2011 Revision of the Swiss Recommendations: Perinatal care at the limit of viability between 22 and 26 completed weeks of gestation in Switzerland. *Swiss Medical Weekly, 141,* w13280. (p7) http://www.neonet.ch/en/04_Recommendations/rec-ssn.php
17. Royal College of Obstetricians and Gynaecologists statement on BJOG study that suggests light drinking in pregnancy is not linked to developmental problems in childhood. http://www.rcog.org.uk/news/rcog-statement-bjog-study-suggests-light-drinking-pregnancy-not-linked-developmental-problems-c
18. NHS coverage on research relating to drinking by pregnant women. http://www.nhs.uk/news/2010/10October/Pages/light-drinking-in-pregnancy.aspx
19. Due to limitations on references and space, a few practitioner and public examples:
    a. 15th Annual Congress of the Perinatal Society of Australia and New Zealand
    b. SSAT's National Forum for Neuroscience in Special Education January 31 2013
    c. 4th Congress of the European Academy of Paediatric Society
    d. http://articles.washingtonpost.com/2008-09-02/news/36845369_1_parent-reports-behavior-problems-teacher-reports
    e. http://www.dnaindia.com/health/report-extremely-premature-kids-likely-to-face-learning-difficulties-by-age-11-1238441
20. Specialist Schools and Academies Trust: for special education teachers, designed to increase awareness of preterm consequences for development. http://complexld.ssatrust.org.uk/uploads/prembirth-info%20APRIL%202011.pdf