Preterm neonates benefit from low prophylactic platelet transfusion threshold despite

varying risk of bleeding or death.

SUPPLEMENTARY MATERIALS

Susanna F. Fustolo-Gunnink¹⁻³, Karin Fijnvandraat^{2,4}, David van Klaveren⁵⁻⁶, Simon J. Stanworth⁷⁻⁹, Anna Curley¹⁰, Wes Onland¹¹, Ewout W. Steyerberg¹² Enrico Lopriore¹³ and Johanna G. van der Bom^{1,3} for the PlaNeT-2 MATISSE Collaborators

Table S1. Published prediction models assessing major bleeding or mortality in preterm neonates.

Author, year	Model description	Reference
Luque, 2014	A prediction model for severe intraventricular hemorrhage (IVH) was developed in 4747 very low birthweight infants in 6 South-American countries. Model variables were selected using stepwise selection procedures, and no external validation was performed. It is unclear to what extent the variables in the model are predictors or consequences of the bleeds, as no attempt was made to correct for timing of the exposure relative to the outcome. Significant predictors for major IVH were lower gestational age (GA), lower birth weight (BW), male, antenatal steroids, cesarean section, lower 1 min Apgar, mechanical ventilation, respiratory distress syndrome (RDS). Mechanical ventilation is not available in the PlaNet-2 database, and RDS is diagnosed later in life (not at baseline or moment of randomisation).	1
Vogtman, 2012	A prediction model for severe IVH was developed in 1782 neonates with GA <32 weeks or BW <1500 grams in Germany. Thirty predictors were tested using stepwise selection while only 149 events occurred during the study. Significant predictors for major IVH were lower GA, 1 min Apgar <6, early sepsis (<3 days), no pathological Doppler results, intrapartum tocolytics. Doppler results and presence or absence of intrapartum tocolytics are not available in the PlaNet-2 database.	2
Singh, 2013	A prediction model for severe IVH was developed in 2917 neonates with GA <34 weeks and who had not received indomethacin. Neonates with missing outcome records (n=253) were excluded. It is unclear how selection of predictors was performed. Significant predictors for major IVH were low GA, mode of delivery, low BW, gender, antenatal corticosteroids, caesarean section, outborn delivery and low 5 minute Apgar score.	3
Eustolo- Gunnink, 2019	A dynamic prediction model for severe bleeding was developed in 640 neonates with GA <34 weeks and at least one platelet count <50x10 ⁹ /L. In this model, though not a baseline model, postnatal age and mechanical ventilation were predictors with a time-constant effect. Intra-uterine growth retardation (IUGR) and platelet count were predictors with time-varying effect, their effect may not have been present at baseline. In a sensitivity analysis, the model also accurately predicted mortality risk.	4
NICHD, 2008	The NICHD outcomes model predicts a set of outcomes including mortality in infants with GA 22-25 weeks. This model contains GA, BW, sex, singleton birth and antenatal corticosteroids.	5
NICHD, 2008 References		5

- 1. Luque MJ, Tapia JL, Villarroel L, et al. A risk prediction model for severe intraventricular hemorrhage in very low birth weight infants and the effect of prophylactic indomethacin. *J. Perinatol.* 2014;34(1):43–8.
- 2. Vogtmann C, Koch R, Gmyrek D, Kaiser A, Friedrich A. Risk-adjusted intraventricular hemorrhage rates in very premature infants. *Dtsch. Arztebl. Int.* 2012;109(31–32):527–533.
- 3. Singh R, Gorstein S V, Bednarek F, et al. A predictive model for SIVH risk in preterm infants and targeted indomethacin therapy for prevention. *Sci. Rep.* 2013;3:2539.
- 4. Fustolo-gunnink SF, Fijnvandraat K, Putter H, et al. Dynamic prediction of bleeding risk in thrombocytopenic preterm neonates. 2019;
- 5. Tyson JE, Parikh NA, Langer J, Green C, Higgins RD. Intensive Care for Extreme Prematurity Moving beyond Gestational Age. *N. Engl. J. Med.* 2008;358(16):1672–1681.

We wish to acknowledge the contribution of the clinical sites involved in the trial: Timothy Watts, Helen Broomfield, Beatriz Lopez Santamaria, Evelina London Children's Hospital, Guy's & St Thomas' NHS Foundation Trust; Anna Curley, Vidheya Venkatesh, Rizwan Khan, Gusztav Belteki, Heather Smethurst, Rosie Maternity Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; Ajit Mahaveer, Nicola Booth, Karen Dockery, Imelda Mayor, Anna Hendrickson, Clare Clifford, St Mary's Hospital Manchester University NHS Foundation Trust, Manchester, UK; Porus Bustani, Pauline Bayliss, Sheffield Teaching Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; Paul Clarke, Priya Muthukumar, Karen Few, Katherine Lloyd, Norfolk and Norwich Hospital, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK; Zoltan Molnar, Sheula Barlow, Sharon Baugh, John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; Enrico Lopriore, Romy Berkhout, Division of Neonatology, Department of Pediatrics, Leiden University Medical Center, Leiden, the Netherlands; Helen McElroy, Helen Harizaj, Medway Maritime Hospital, Medway NHS Foundation Trust, UK; Manobi Borooah, Rachel Jackson, Heather Barrow, Elizabeth Department of Neonatology, Birmingham Women's and Children's NHS Simcox, Foundation Trust Birmingham, UK; Sunit Godambe, Sara Barnett, Imperial College Healthcare NHS Trust London, UK; Anton van Kaam, Wes Onland, Debbie Nuytemans, Department of Neonatology, Emma Children's Hospital, Academic Medical Centre, Amsterdam, the Netherlands; Simon Power, Claire Abbott, Patsy Graham, Royal Bolton Hospital, Bolton NHS Foundation Trust, Bolton, UK; Oliver Rackham, Joanne Mullen, Sharon Hughes, Lucy Lewis, Arrowe Park Hospital, Wirral University Teaching Hospital NHS Foundation Trust, Wirral, UK; Sundeep Harigopal, Linda Smith, Julie

Groombridge, Tracey Downes, Royal Victoria Infirmary, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK; Charlotte Huddy, Naomi Hayward, Vana Wardley, St George's Hospital, St George's Healthcare NHS Trust, London, UK; Shobha Cherian, Mallinath Chakraborty, University Hospital of Wales, Cardiff and Vale University Health Board, Cardiff, Wales; Sarah McCullough, Louise Woodhead, Joanne Reed, Chloe Rishton, Grainne O'Connor, The Royal Oldham Hospital, Pennine Acute Hospitals NHS Trust, Oldham, UK; Anna Curley, Rebekah Prabharan, National Maternity Hospital, Dublin, Ireland; Raju Narasimhan, Claire Lodge, Nikki Childs, Kylie Reid, Joanna Lees, Natalie Mattos-Harris, Royal Preston Hospital, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK; Mark van der Hoeven, Neonatal Intensive Care Unit, MUMC, Maastricht, the Netherlands; C Harikumar, Wendy Cheadle, Alex Ramshaw, Julie Colarossi, Sharon Clarke, University Hospital of North Tees, North Tees and Hartlepool NHS Foundation Trust, North Tees, UK; Anitha James, Royal Gwent Hospital, Aneurin Bevan University Health Board, Newport, Wales; Mithilesh Lal, Amanda Forster, Helena Smith, The James Cook University Hospital, South Tees Hospitals NHS Foundation Trust, South Tees, UK; Andre Kroon, Annelies Bos, Division of Neonatology and Elise Huijssen-Huisman, Department of Pediatric Hematology, Erasmus MC-Sophia Children's Hospital, Rotterdam, the Netherlands; Melanie Sutcliffe, Sharon Kempson, Nick Denyer, Lyndsay Bibb, New Cross Hospital, The Royal Wolverhampton NHS Trust, Wolverhampton, UK; Andy Cox, Heather Collier, Emily Andrews, Burnley General Hospital, East Lancashire Hospitals NHS Foundation Trust, Burnley, UK; Vimal Vasu, Shermi George, Claire Moloney, William Harvey Hospital, East Kent Hospitals University NHS Foundation Trust, Ashford, UK; Esther d'Haens, Liesbeth Groot Jebbink-Akkerman, Princess Amalia Department of Pediatrics, Department of Neonatology, Isala Clinics, Zwolle, the Netherlands; Paul Munyard, Barbara Bromage, Royal Cornwall Hospital, Royal Cornwall Hospitals NHS Trust, Cornwall, UK; Tim Scorrer, Tamsyn Wilson, Queen Alexandra Hospital, Portsmouth Hospitals NHS Trust, Portsmouth, UK; Ellen de Kort, Tinneke Jonckers, Marieke Vervoorn, Department of Pediatrics and Neonatology, Máxima Medical Center, Veldhoven, the Netherlands; Dr David Sweet, Patricia McCreesh, Sonia McKenna, Muriel Millar. Royal Jubilee Maternity Hospital, Belfast Health and Social Care Trust. Belfast, UK; David Grier, Mike Smith, Sara Gilpin, Judith Ratcliffe, Craigavon Area Hospital, Southern Health and Social Care Trust, Craigavon, UK; Damien Armstrong, Julie Brown. Altnagelvin Area Hospital, Western Health and Social Trust, Derry/Londonderry, UK; Dr Conor O'Neill. Antrim Area Hospital, Northern Health and Social Care Trust Antrim, UK; Willem de Boode, Wendy Jansen, Department of Neonatology, Radboud University Medical Center, Radboud Institute for Health Sciences, Amalia Children's Hospital, Nijmegen, the Netherlands; Christopher Knight, Nicki Thorne, Kirsty O Brien, Musgrove Park Hospital, Taunton & Somerset NHS Foundation Trust, Taunton, UK; Susan Chatfield, Rachel Wane, Elizabeth Ingram, Bradford Royal Infirmary, Bradford Teaching Hospitals NHS Foundation Trust, Bradford, UK; Christian Hulzebos, Annelies Olthuis, Department of Pediatrics, Beatrix Children Hospital, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands; Anthony Ryan, Siobhan Foley, Carol-Anne O'Shea, Cork University Maternity Hospital, Cork, Ireland; Karen Luyt, Joanne Innoles, St Michael's Hospital University Hospitals Bristol NHS Foundation Trust, Bristol, UK; Osama Hamud, Imran Ahmed, Natalie Talbot, Sunderland Royal Hospital, City Hospitals Sunderland NHS Foundation Trust, Sunderland, UK; Nicola Pritchard, Susan Hallett, Royal Berkshire Hospital, Royal Berkshire Hospital NHS Foundation Trust, Reading, UK; Poonam Belani, Claudia Chetcutiganado, Yvonne Miller, Luton & Dunstable Hospital, The Luton and Dunstable Hospital NHS Foundation Trust, Luton, UK; Sanjeev Deshpande, Sarah Kirk, Princess Royal Hospital, Shrewsbury & Telford NHS Trust, Shrewsbury, UK.