A practical solution to 'Continuing Care Site' issues in neonatal clinical trials

Session: Governance and Regulatory Issues

Clinical Trials Methodology Conference

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Overview

- What is a ‘Continuing Care Site’?

  ‘*Hospitals that are research active with a reduced level of involvement in a clinical trial. Occurs when an infant is recruited to a neonatal trial and is transferred to another hospital for continuation of their clinical care.’*
- NPEU CTU/Challenges faced when running Neonatal Clinical Trials
- I2S2 Trial example
- Other trials and future

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NPEU CTU

- NPEU Mission Statement:

  'To produce methodological rigorous research evidence to improve the care provided to women and their families during pregnancy, childbirth, the newborn period and early childhood as well as promoting the effective use of resources by perinatal health services.'

- Large portfolio of perinatal Trials in various stages
- Collaborative work with other Universities and NHS Trusts
- Part of the consortium leading the NIHR Medicines for Children Research Network (MCRN)

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Neonatal Trials

- 200+ Neonatal Units in UK
- Admit infants from >23 weeks gestation
- Stressful environment for parents
- Good will of clinicians and neonatal team – pragmatic trials with no direct payments

Background-I2S2 Trial

- Randomised controlled trial of Iodine Supplementation
- CTIMP involving daily dose of sodium iodide or sodium chloride (placebo)
- Sample size – 1,400 pre-term infants
- Recruiting in 19 sites in the UK

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The Challenge

- 50% of infants likely to be transferred from the recruiting centre
- Infants may be transferred multiple times and without warning and be required to continue treatment under trial protocol
- 200+ Neonatal Units
- 2 choices:
  - Restrict recruitment to infants that will not be transferred?
  - Infants withdrawn from trial once transferred?

The Challenge

- Gaining NHS permissions in receiving hospitals:
  - Contract with the Sponsor
  - Identified PI
  - Site files
  - Trial set up visit/ trial training

- All documents required for a clinical trial site involved in a CTIMP
- Site may potentially never receive I2S2 infant!

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The Solution

- Framework negotiated between:

  -NPEU CTU

  -R&D Forum

  -National Institute for Health Research Clinical Research Network Coordinating Centre-CSP Team

  -University of Oxford

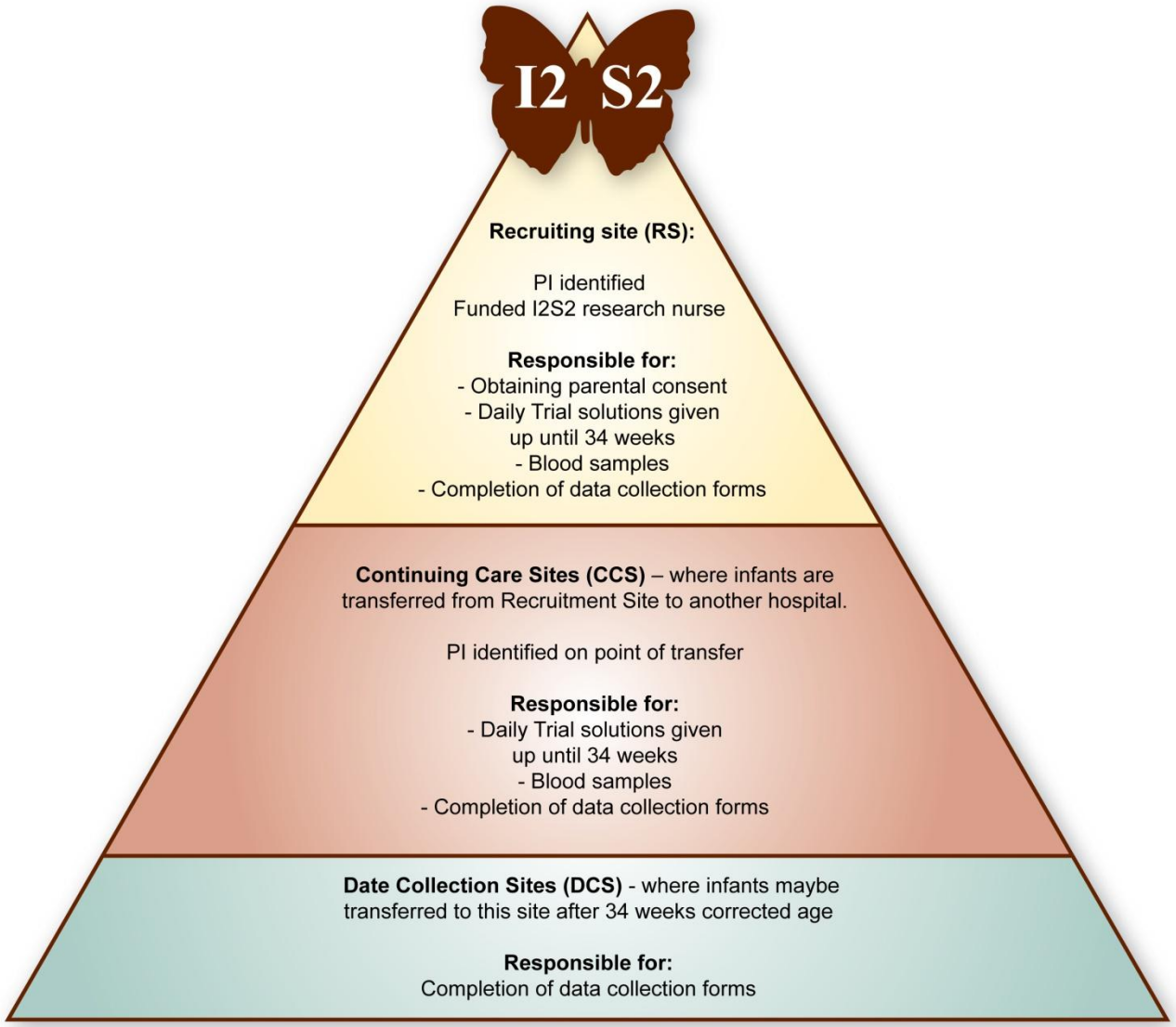
  -MHRA

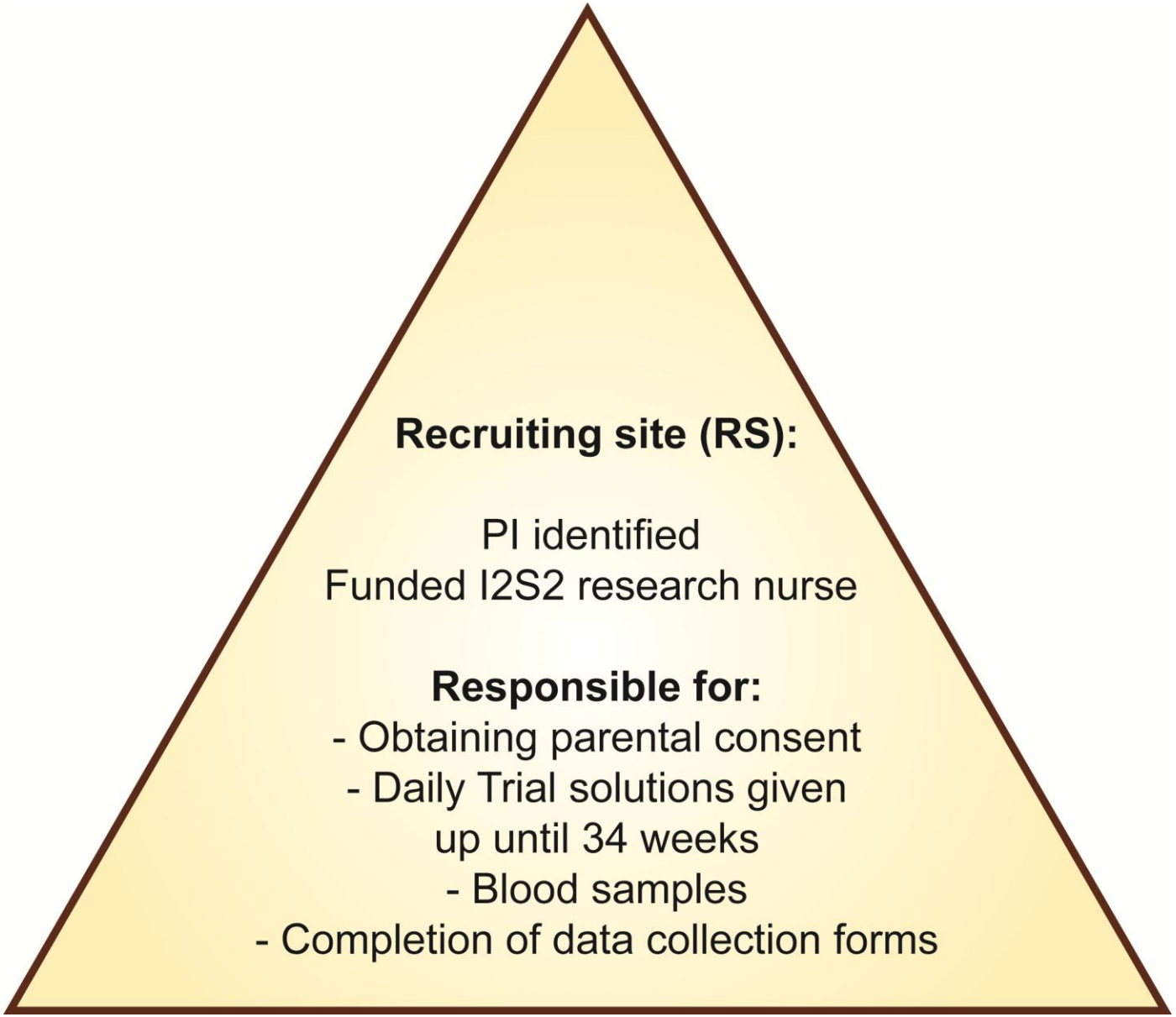
  -MRC

The Solution

Three-tiered approach with different levels of hospital involvement;

- Recruiting Sites (RS)
  - Nominated PI, funded I2S2 research nurse, contracts in place
- Continuing Care Site (CCS)
  - Level of involvement lower → level of RM&G review proportionate to risk
- Data Collection sites (DCS)


I2 S2
Recruiting site (RS):
PI identified
Funded I2S2 research nurse
Responsible for:
- Obtaining parental consent
- Daily Trial solutions given
up until 34 weeks
- Blood samples
- Completion of data collection forms
Continuing Care Sites (CCS) – where infants are transferred from Recruitment Site to another hospital.
PI identified on point of transfer
Responsible for:
- Daily Trial solutions given
up until 34 weeks
- Blood samples
- Completion of data collection forms
Date Collection Sites (DCS) - where infants maybe transferred to this site after 34 weeks corrected age
Responsible for:
Completion of data collection forms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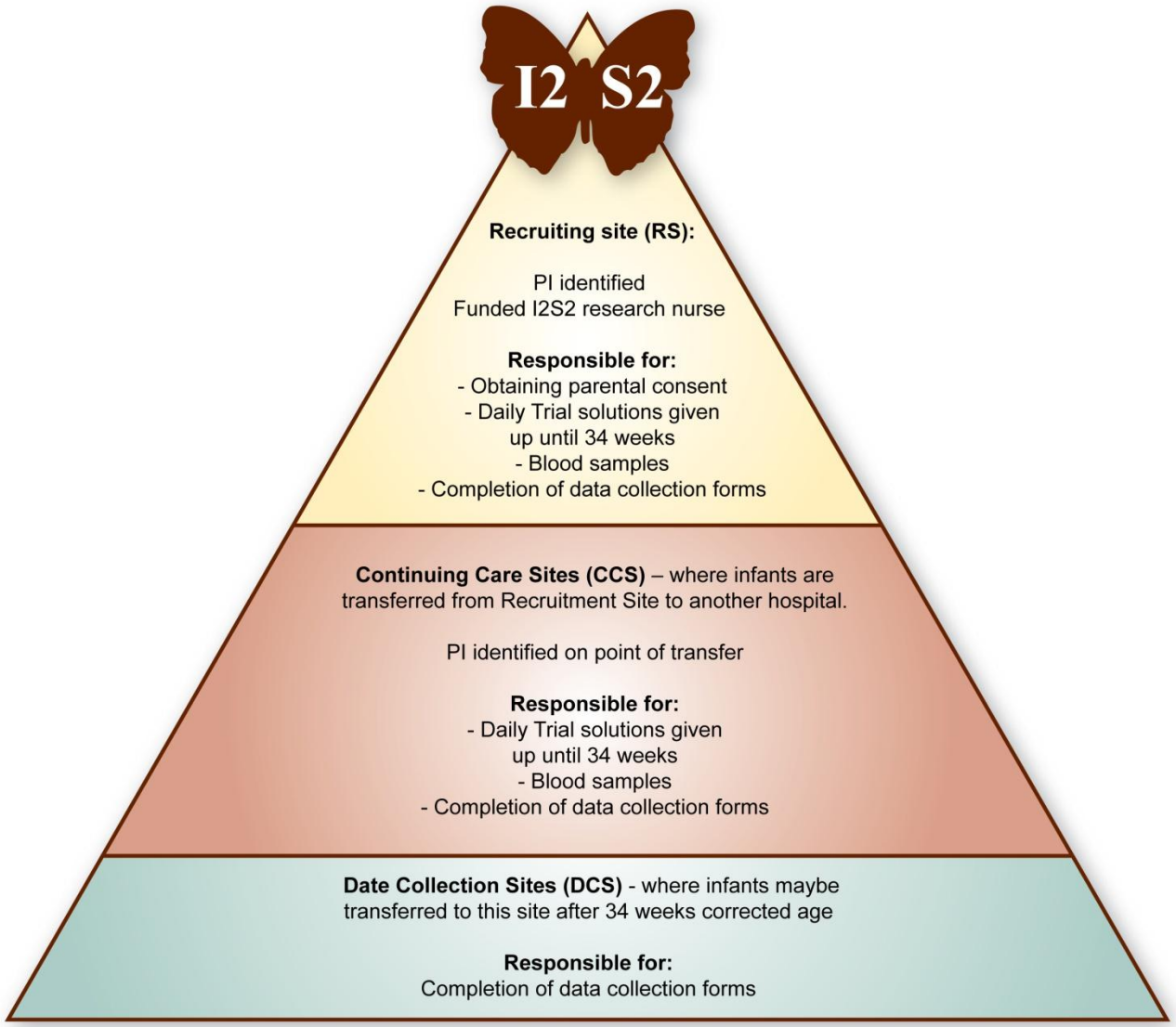
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The Solution

- Trusts instructed to carry governance checks and issue provisional approval-via CSP
- Transfers are notified to NPEU by the recruiting site
- Transfer pack accompanies the infant
- PI identified to accept care of the baby
- Reduced level of approval from CCS/DCS
- Periodic substantial amendments informing MHRA and REC of PI's

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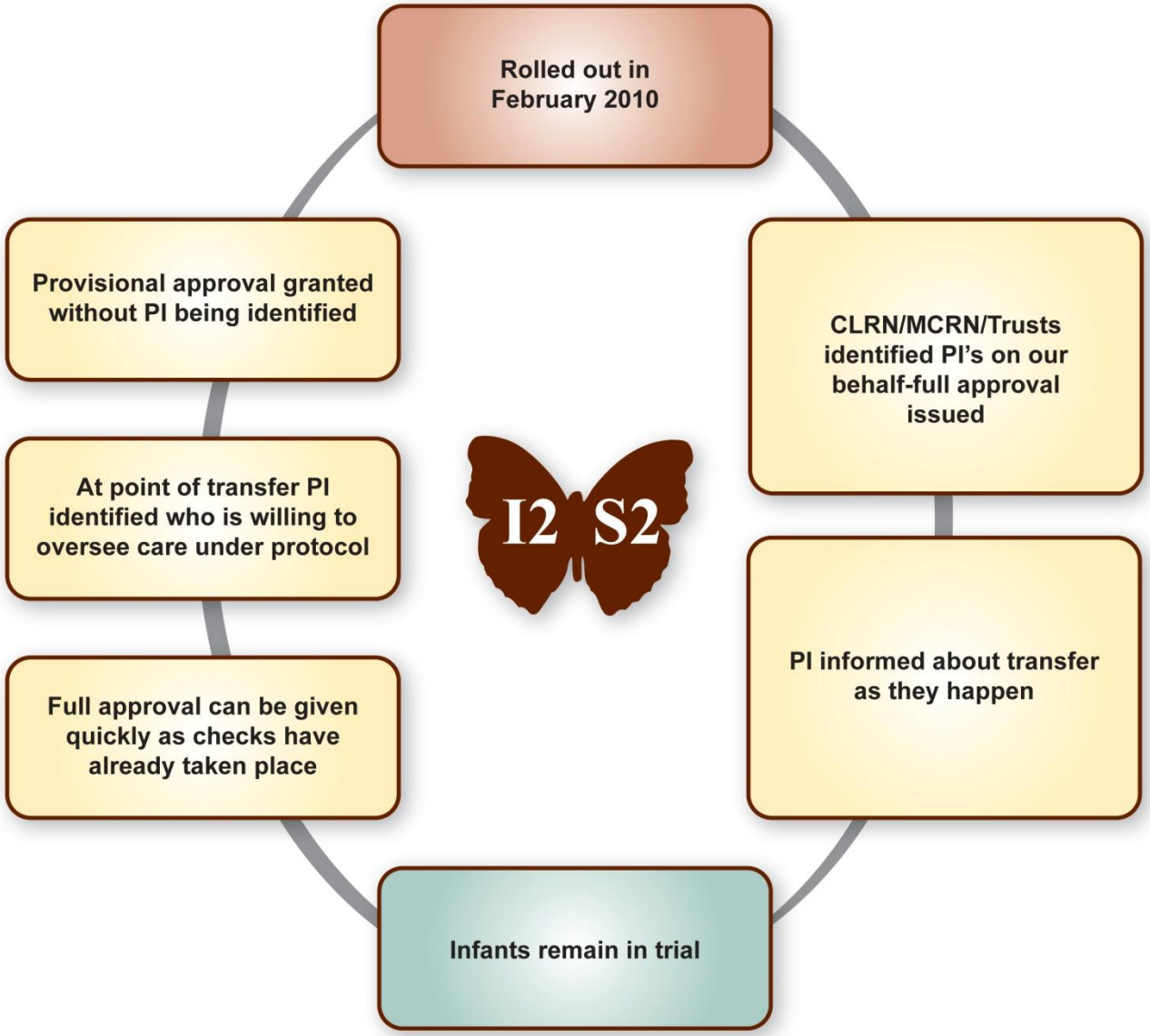
Logistics

- Statement of Responsibilities
  - Discussed and approved with R&D forum, BBC CLRN and NIHR CSP
  - Consistent with Research governance framework as clearly defines responsibilities of sites →no contract required
  - Addition of research governance section in protocol

Logistics

- CSP
  - IRAS application identifying all Recruiting Sites
  - List of 213 possible CCS uploaded onto CSP
  - Permission to use generic SSI
  - Proposed CSP local governance checks for CCS & DCS document

Implementation



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So has it worked?

- Variation across different CLRNS
- Contact with a clinician is required to discuss the trial
- Importance of clear paperwork and communication strategy agreed by Lead CLRN
- Training and experience-very dependent on the intervention

Experience

- New process – rolled out across other trials
  - NPEU CTU- PiPs-Probiotic study-in progress rolled out- June 11
  - Liverpool Women's NHS Foundation Trust- TINN Trial

    - 40 research sites for follow up (includes data collection, pharmacovigilance reporting and a stool sample).

    -New sites not required to be submitted to MHRA
  - MCRN- 'Good trial practice guide'
  - Other CLRN's adopted framework

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Acknowledgements

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  -The R&D Forum

  - National Institute for Health Research Clinical Research Network Coordinating Centre-CSP Team

  -Birmingham and Black Country CLRN

  -The University of Oxford.

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Thank you for listening

Any questions?

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