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An ABC of embedded trials

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UK Neonatal Collaborative

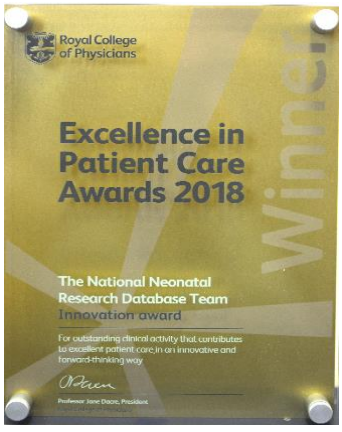
Embedded clinical trials are set in routine health care, and use routinely recorded electronic data

A Accurate data

B Benefit and buy-in

C Confidence and trust

Beyond embedded trials
A proven model of real-world health data to improve patient care: the UK National Neonatal Research Database



UK National Neonatal Research Database

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Established 2007; to-date contains data on over 1 million infants; 100000 new patients added annually

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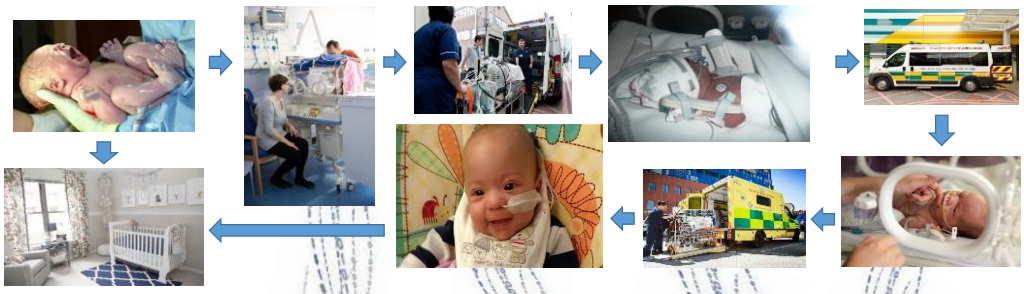
Slide courtesy of Dr Chris Gale



Commercial Electronic Patient Record
200 Neonatal Units

National Neonatal Research Database
Neonatal Data Analysis Unit
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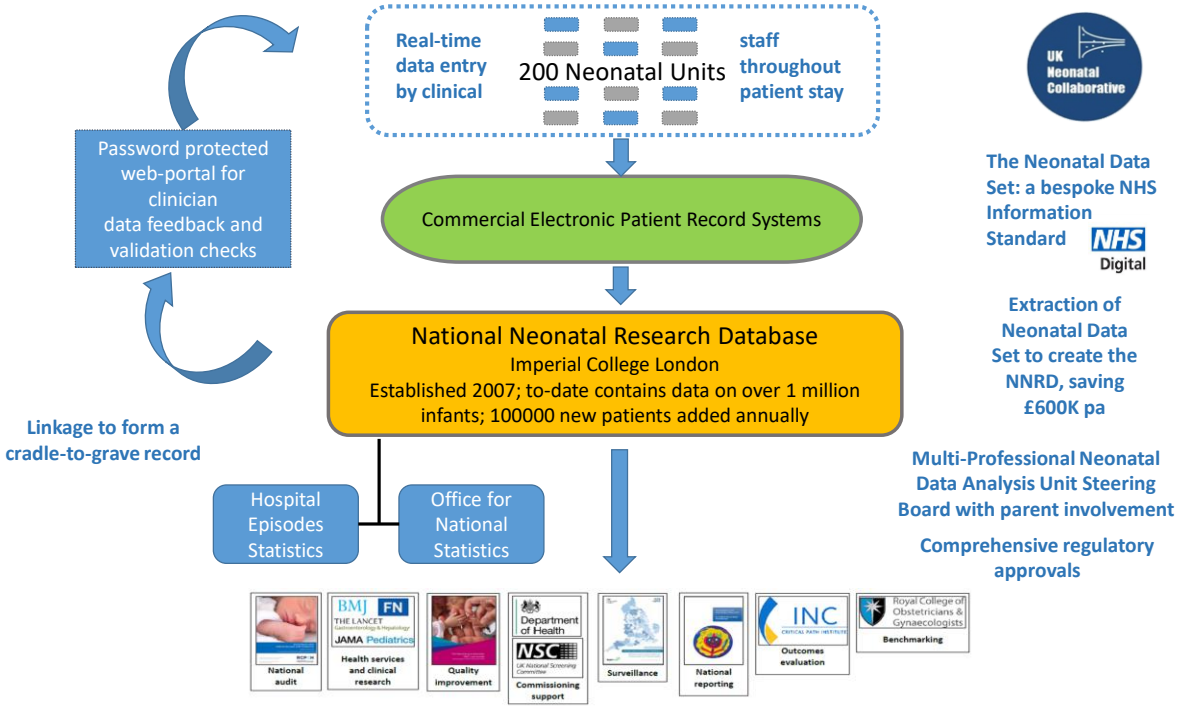
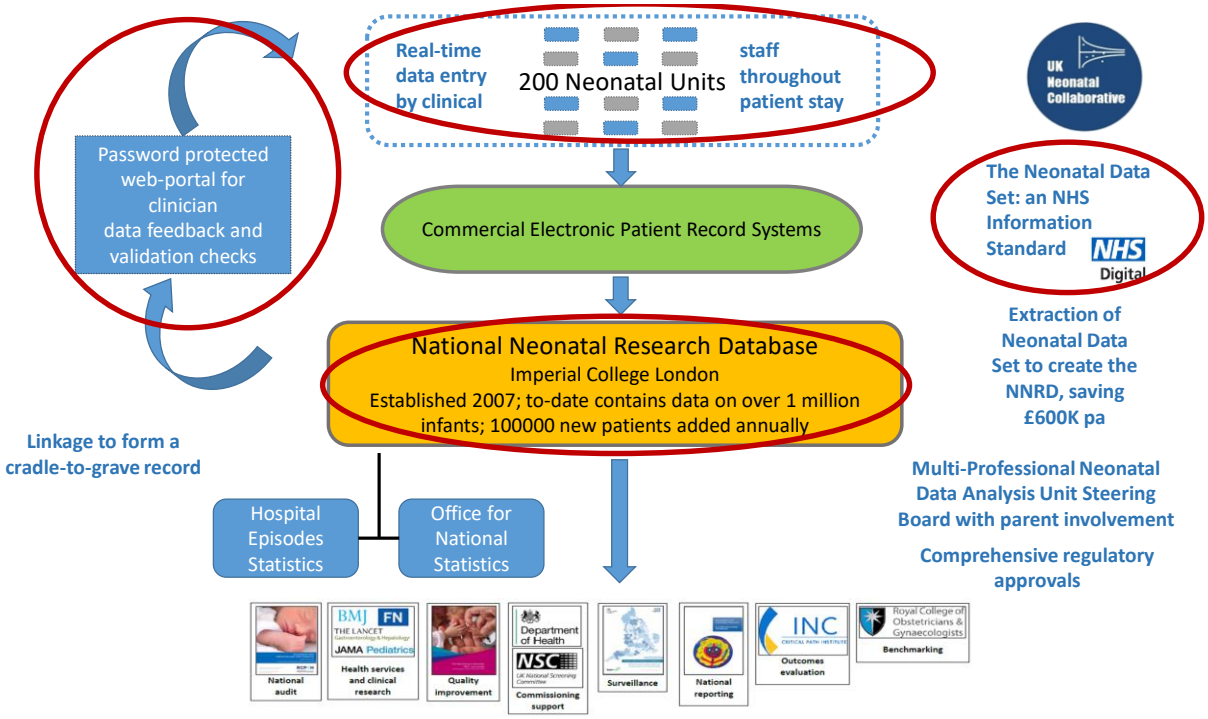


Accurate data

What quality assurance processes are in place?

- Patient identification
- Randomisation
- Monitoring
- Ancillary data
- Outcomes



Benefit and buy-in

Who are your stakeholders?	Clinicians, researchers, academics, industry sponsors, patients, parents, health service deliverers, policy makers?
What benefits do stakeholders want?	Every stakeholder group will have their own priorities
Why should healthcare staff record data and why should patients participate?	Preliminary exploration of motivators is essential

Experimental versus comparative effectiveness research

Evaluating a new experimental treatment

- Comparison is made against accepted best practice or placebo
- Parents are asked if they consent for their child to be randomised
- If they decline, the child receives the "accepted best practice"

Evaluating treatments in wide use, but where the evidence-base is uncertain

- Comparison of treatments in accepted use
- Parents are asked if they consent for their child to be randomised If they decline, the child receives ..... what the doctor decides ...
- Even though the doctor does not know which is best

A positive approach to research:
Randomisation as a standard of care for comparative effectiveness evaluations

- "Treatment A and treatment B are used by doctors everyday; we want to give your baby, and every other baby the best treatment, but we do not know which this is"
- As we do not know which is best, we will give every baby an equal chance of getting the best treatment (this is called randomisation); we will then be able to find out which is better
- If we don't do this we will never find out which treatment is better and many babies will continue to receive the wrong treatment
- You are free to opt-out if you wish

Is this ethically valid?

- **Justice:** the patient is treated fairly
- **Beneficence:** the doctor fulfils his/her obligation to act in the patient's best interests
- **Non-maleficence:** the doctor fulfils his/her obligation to do no harm
- **Autonomy:** the parent can opt-out, freely and without coercion

Research ethics committee decision-making in relation to an efficient neonatal trial

C Gale, M J Hyde, N Modi, on behalf of the WHEAT trial development group

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CG and MJH contributed equally.

- With the support of the UK Health Research Authority we submitted the same comparative effectiveness research protocol to 12 UK National Research Ethics Committees (REC)
- We tested 4 principles for application in comparative effectiveness trials:
  - Trial data from routine electronic patient records
  - Simple, short information sheet
  - Opt-out consent
  - Explicit mention of possible inclusion benefit

What this study adds?

- The UK Research Ethics Committees find the use of electronic patient records, short participant information sheets and mention of inclusion benefit to be acceptable in neonatal comparative effectiveness research.
- There is inconsistency between the UK Research Ethics Committees in relation to the validity of opt-out consent processes for neonatal comparative effectiveness research.
- The wider application of these methods may facilitate larger, more efficient randomised controlled trials.

- Electronic patient record use acceptable to all REC
- One REC raised concerns about the short parent information sheet, 9 about opt-out consent and 10 about inclusion benefit
- Nine REC granted a favourable final opinion
- The UK Health Research Authority now accepts all principles including opt-out and has issued guidance to all REC

Confidence and trust

How will stakeholder confidence and trust be secured and maintained?

- Data are secure
- Stakeholders will be consulted and involved
- All stakeholders have opportunity to use data
- Outcomes are reliable
- Data will not be "sold"

- Multi-stakeholder steering board
- Newsletters
- Annual stakeholder conference
- Acknowledgement and authorship
- Clear data access process
- Multiple types of use and outputs

- No data use without informing neonatal units (service evaluations) or explicit agreement (opt-out and opt-in approaches)
- Dissemination of protocols
- Publication of outputs
- Requirement by industry to commit to publish
- Parent involvement
- Consultation with ex-patients

- Accurate, quality-assured, timely data
- Benefit wide and stakeholder buy-in secured
- Confidence and trust
- Ethical issues acknowledged and addressed
- Funding mechanism
- Multiple uses demonstrated
- Regulatory approvals

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