Timing of Stoma Closure in Neonates: the ToSCiN mixed-methods study

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Disclaimer: This report contains transcripts of interviews conducted in the course of the research, or similar, and contains language which may offend some readers.

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Scientific summary

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Scientific summary

Background

Neonates undergoing emergency abdominal surgery for problems such as necrotising enterocolitis (NEC), spontaneous intestinal perforation (SIP) or a congenital bowel obstruction frequently require a stoma. While stomas can be life-saving, they pose a number of challenges including fluid and electrolyte imbalance, local wound and skin problems, malnutrition and growth failure. Reversing (closing) these stomas with a second operation is therefore an essential part of an infant's recovery. The timing of stoma closure is known to vary between hospitals and, indeed, clinicians and the best time remains unclear, with conflicting evidence from published studies of low methodological quality.

Rationale

Determining the best time to close stomas in neonates is imperative, as it has significant implications for:

1. *infant health outcomes* (e.g. stoma complications and growth)
2. *families* (e.g. reduced neonatal unit stay, healthcare burden, time off work)
3. *healthcare providers* [e.g. neonatal unit bed-days, parenteral nutrition (PN) use, surgery, cost].

In addition, reducing unwarranted variability in surgical care is a key priority for the NHS. The most methodologically robust way to determine optimal timing of stoma closure would be through an adequately powered randomised controlled trial (RCT).

A trial of different stoma closure times in neonates is likely to be challenging, due to:

1. *the patient group* who have heterogenous underlying diseases and comorbidities
2. *clinician factors* such as willingness to recruit
3. *parent factors* such as trial acceptability.

This study aimed to explore these potential challenges and determine if a trial comparing 'early' and 'late' stoma closure is feasible.

Aims

The overarching aim of the Timing of Stoma Closure in Neonates (ToSCiN) study was to answer the question: is it feasible to conduct a RCT comparing 'early' versus 'late' stoma closure in neonates?

Objectives

The specific objectives of the ToSCiN study were:

- to establish current UK practice for stoma closure in neonates
- to determine whether there is equipoise among clinicians (neonatal surgeons and neonatologists) and allied health professionals (specialist nurses and dietitians) over when it is best to close stomas in neonates
- to define 'early' and 'late' stoma closure for a potential trial

- to define a population of neonates for inclusion in a trial (in whom there is significant uncertainty over timing) and determine how many infants are eligible for inclusion
- to establish the most appropriate design and outcome measures for a trial
- to determine the willingness of parents, neonatal surgeons and neonatologists to include neonates in a trial that would randomise to 'early' or 'late' stoma closure and identify potential barriers to recruitment
- to assess the suitability of using routinely collected data for gathering clinical information for a trial.

Methods

The ToSCiN study used a mixed-methods approach (qualitative and quantitative methodology) and comprised three parallel workstreams.

Workstream 1: Survey of clinician and allied health professional perspectives on neonatal stoma closure

An online survey was sent to clinicians and allied health professionals involved in the care of newborn infants with stomas at neonatal surgical units across the UK. The survey questions and a series of clinical scenarios to explore current practice/preferences, perspectives on 'early' versus 'late' stoma closure, which groups of infants should be included in a trial comparing these, preferred trial design including outcomes and barriers to achieving the optimal timing of closure.

Workstream 2: Parent and clinician perspectives regarding a clinical trial of neonatal stoma closure

This workstream took place in eight UK neonatal surgical centres and comprised three elements:

(2.1) An observational cohort study of neonates who had a stoma formed

Key clinical and demographic information was recorded prospectively. The data set comprised factors that could influence the timing of stoma closure and outcomes which are likely to be important in a future trial.

(2.2) Questionnaires for the principal clinicians (surgeon and neonatologist) caring for each infant recruited to the cohort study

These were completed at three time points and explored the acceptability of a hypothetical trial to clinicians for each infant. Time points: (1) approximately 1 week after stoma formation to explore randomising the infant to a trial, (2) 6 weeks after stoma formation to explore following an allocation to early closure intervention and (3) 12 weeks after stoma formation to explore following an allocation to late closure comparator.

(2.3) A qualitative study incorporating: (1) focus groups with clinicians and (2) interviews with parents of neonates who had a stoma

Multidisciplinary healthcare professional focus groups explored equipoise, current practice and views on early versus late closure, willingness to recruit to a trial, acceptability of a trial and prioritised outcome measures.

Parents of infants in the cohort study and additional parents recruited via social media were invited for a telephone or video interview. Their views were explored on: having a child with a stoma, acceptability of a trial, timing of recruitment, potential barriers to trial participation, trial participant information materials, approach to consent for a trial and prioritised outcome measures.

Workstream 3: Analysis of three existing national databases

Analyses were carried out on three existing national data sets [from the National Neonatal Research Database (NNRD), The British Association of Paediatric Surgeons Congenital Anomalies Surveillance

System (BAPS-CASS) and Hospital Episode Statistics – Admitted Patient Care (HES-APC)]. The analyses aimed to: (1) establish current UK practice, (2) define a population for trial inclusion and provide the number of eligible infants and (3) establish values for key outcome measures.

Consensus meeting

This was held using an online video platform at the end of the study period when data collection and preliminary analysis had been completed. Professionals and parents previously involved were invited and further parents were recruited via social media.

A summary of results from the three workstreams was presented to attendees. Facilitated small group discussions took place, followed by a summary of small group discussions presented by group facilitators to all attendees, and electronic voting was conducted about trial acceptability and design.

Results

Workstream 1 Results

One hundred and sixty-six professionals completed the survey with at least one respondent from each of the 27 UK centres. Six weeks was the most commonly stated target time for closure across all scenarios, although there was a high degree of variability, with intervals of 12 weeks or more frequently advocated. While 70–76% of respondents preferred closure prior to discharge in preterm infants and a term infant with jejunostomy, only 46% preferred this in term infants with ileostomy. A sizeable proportion (41%) use weight, rather than time, to determine when to close a stoma. Thematic analysis of free text identified nine key themes influencing decision-making, mostly related to nutrition, growth and stoma complications.

With regard to potential trial design, 86% of respondents indicated they would include preterm infants with NEC/SIP and 72% term infants with other conditions. Closure at 6 weeks was the most commonly cited timing of early intervention; the preferred later time point was 12 weeks. Growth was most commonly selected as the favoured primary outcome for a trial, followed by time to full feeds, length of stay and duration of PN.

Workstream 2 Results

Cohort study

Fifty-six infants were enrolled from eight UK units. Infants were mostly preterm (44/56), with median birthweight 961 g (range 415–3962 g). The cohort comprised 37 infants with NEC/SIP and 19 with other diagnoses. Most stomas were in the small bowel, formed at a median of 8 days (range 1–80 days).

At 1 week following stoma formation, 18/56 infants were mechanically ventilated, 8 were receiving inotropes and 13 had received blood products in the preceding 24 hours. At this point, surgeons stated they would be willing to randomise 31 infants (59%) into a hypothetical trial of 6- versus 12-week closure. The commonest reason for not being willing was the infant being 'too small or premature'.

At 6 weeks post stoma, median weight was 2024 g (range 795–4460 g) and nine remained ventilated. Eighty per cent (42/56) were reported to have gained weight in the past week. Median enteral feed volume was 127 ml/kg/day, stoma output was < 20 ml/kg/day in 86% and stoma-related complications were reported in one-third. Surgeons would be willing to follow theoretical trial allocation for 'early' closure in 17/56 (33%). In nine infants, the stoma had already been closed. The main reasons for not being willing to follow trial allocation were current clinical status and size. Among infants whom surgeons said they would not be willing to follow trial allocation, most (16/25) were < 28 weeks' gestation at birth and were lighter (median weight 1609 vs. 2090 g).

Twelve weeks after stoma formation, median weight was 2548 g and 10% (4/52) remained ventilated. Most (23/42; 55%) were still receiving PN (a higher proportion than at 6 weeks) and 12% (5/42) were not receiving any enteral feed. Stoma-related problems were present in one-third and one-quarter had stoma output > 20 ml/kg/day. Surgeons stated they would be unwilling to follow trial allocation of closure at 12 weeks in 24 infants: 12 of these had required earlier stoma closure and 9 (mainly premature infants) were considered unsuitable for stoma closure for a variety of mainly clinical reasons (rather than logistical or family factors). Again, most infants for whom the surgeon was unwilling to follow trial allocation were < 28 weeks' gestation at birth (13/24).

Overall stoma closure took place before the end of the data collection period in 82% (46/56 infants, 4 infants died with a stoma in situ and 6 infants still had a stoma). Median time to closure was 9.9 weeks (range 4.4–28.3 weeks), at median 88 days of age and weight of 2631 g.

Qualitative study

We interviewed 24 parents (17 mothers, 7 fathers) of babies who required a stoma in the last 3 years in the UK (July 2021–February 2022). Fifteen parents were recruited via hospital sites and nine via social media. Thirty-six staff (14 surgeons, 10 consultant neonatologists, 6 neonatal surgical nurses, 2 research nurses, 1 dietitian and 3 'other' roles) from five study sites took part in one of six focus groups (November–December 2021).

Most parents and staff considered the proposed ToSCiN trial to be acceptable and wanted the research question to be answered. Staff would be willing to randomise babies, except the most extremely preterm, to the trial and parents would hypothetically consent to their baby taking part if the 'emotive' 'early' (6 weeks) and 'late' (12 weeks) terminology was changed.

Some parents and staff, however, had clear trial arm preference and concerns about the alternative trial arm. They felt that decisions about when to close a stoma should be led by the overall health and well-being of the baby. Stoma-related factors, logistical and organisational factors and family factors also influenced views on acceptable timing of stoma closure. These findings highlight potential challenges for recruitment and retention and trial success.

Workstream 3 Results

While direct comparison was limited by differences in data set populations and coverage, there was a reasonably consistent number of potentially eligible infants with a stoma for NEC/SIP across data sets, with 163 in 1 year in the BAPS-CASS cohort and mean annual volumes of 193 (NNRD) and 192 (HES-APC). HES-APC was used to estimate non-NEC infant numbers, as it had the most comprehensive coverage, with a mean of 118 per year. The total UK population of potentially eligible infants would therefore be approximately 300 per annum.

Median stoma durations for babies with NEC/SIP were as follows: BAPS-CASS 63 days; NNRD 60 days and HES-APC 78 days. For infants with stomas for other reasons, closure was usually earlier: NNRD 45 days; HES-APC 74 days; and in the BAPS-CASS meconium ileus cohort, 51 days. HES-APC included babies who were discharged home with a stoma in situ, hence longer median stoma durations.

Consensus meeting

The consensus meeting was attended by 52 individuals from a range of health professional and non-professional backgrounds, including 7 parents. Voting on key aspects of trial design showed: (1) 83% favoured including all infants with a stoma, (2) 58% favoured comparing closure at 6 weeks after stoma formation with expectant management rather than comparison to a specific late timepoint, and (3) the favoured primary outcomes were weight gain/growth (38%) and length of hospital stay (32%).

Conclusions

We found that a randomised trial of early compared to late stoma closure in neonates is feasible and is important to families and health professionals. We identified the following components as being critical to a successful future trial:

- comparison of closure at 6 weeks versus expectant management
- comparison that accounts for completed gestational age, rather than solely duration of stoma.

We identified the potential population and outcomes for such a trial and established that a sufficient population exists in the UK. We also identified that a trial comparing 'early' and 'late' closure at rigidly defined time points (e.g. closure at 6 compared to 12 weeks) would not be feasible.

The principal challenge for trial conduct was found to be the 'baby-led' narrative that came through strongly from study participants. Parents and professionals appeared to lack equipoise in certain scenarios. However, this lack of personal equipoise is not exclusive to ToSCiN, and similar themes have been overcome in trials in the past (including complex surgical trials) by optimising communication. Our findings provide valuable insight into how best to do this in a future trial. Other challenges identified include: (1) concerns about inclusion of extremely preterm infants, (2) concerns about infants waiting too long for stoma closure if randomised to the 'late' comparator arm and (3) logistical arrangements for closing a stoma at the time dictated by trial allocation.

These challenges are eminently addressable, by designing the trial to: (1) incorporate a degree of flexibility (e.g. using 'expectant management' as the comparator), (2) make allowances for certain groups (e.g. having a higher corrected gestational age limit for extremely preterm infants) and (3) ensure parents and professionals are aware both trial arms are standard practice and valid treatment options.

Key research recommendations

We recommend the following population, intervention, comparator and outcome (PICO) as a starting point to inform the design of a future trial:

Population: neonates with stomas, excluding those with a stoma as part of a fixed treatment pathway, for example, anorectal malformations and Hirschsprung's disease.

Intervention: stoma closure at 6 weeks post stoma formation and where 32 weeks post-conceptual age has been reached.

Comparator: expectant management with stoma closure undertaken when the clinical team determines is best for the infant.

Outcomes: weight gain/growth or length of hospital stay should be the primary outcome measure.

In order to optimise a trial, we recommend the following practical steps:

- Involve higher volume neonatal surgical centres for efficient recruitment.
- Ensure trial staff at each centre are highly trained regarding current standard practice and equipoise.
- Approach parents 1–2 weeks after stoma formation.
- Provide resources to centres to permit stoma closure as per the trial protocol, for example, for ring-fenced operating theatre time and possibility of extended hospital stay.

Study registration

This study is registered as IRAS Project ID 278331, REC Reference 20/LO/1227.

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