

BMJ Open Quality Sustaining improved nutritional support for very low birthweight infants

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ABSTRACT

Background Postnatal growth failure (PGF) in very low birthweight (VLBW) infants is a result of factors such as prematurity, acute illness and suboptimal nutritional support. Before this project began, 84% of appropriately grown VLBW infants in our neonatal intensive care unit experienced PGF. The aims of this quality improvement project were to reduce the percentage of infants discharged with PGF to less than 50% within 2 years and to maintain a rate of PGF under 50%.

Methods All inborn VLBW infants were eligible for this study. Infants with congenital anomalies were excluded. We determined key drivers for optimal nutrition and identified potentially better practices (process measures) based on a review of the literature, which included more rapid initiation of starter total parenteral nutrition (TPN), aggressive use and advancement of regular TPN, and fortification of human milk when the volume of intake reached 80 mL/kg/day. Three Plan-Do-Study-Act (PDSA) cycles were tested.

Results Time to initiation of starter TPN was significantly reduced from 5.5 hours to under 3 hours. Regular TPN provided the goals for amino acids and lipids at increased frequency after the first two PDSA cycles. The proportion of infants whose milk was fortified at 80 mL/kg/day increased after the third PDSA cycle.

Conclusions We found a sustained decrease in the percentage of infants discharged with PGF from 84% at baseline to fewer than 50% beginning in 2010–2011 through 2016, with 23.1% of infants experiencing PGF in 2016. We have achieved improved nutritional support for VLBW infants using the model for improvement.

INTRODUCTION

Background and problem

Postnatal growth failure (PGF) in very low birthweight (VLBW) infants is very common and is the result of many factors including prematurity, acute illness and suboptimal nutritional support. As many as 97% of VLBW infants experience PGF (<10th percentile for weight at 36 weeks' postmenstrual age) in many neonatal intensive care unit (NICU) populations.¹ Recent data have shown that, although the incidence of PGF has decreased, 50% of VLBW infants were discharged at a weight less than the 10th percentile for postmenstrual age in 2013.² Poor growth in the NICU is predictive of suboptimal growth and neurodevelopmental outcomes following discharge,³ and nutritional practices in the

NICU are important determinants of growth velocity.⁴

Aggressive nutritional support for the VLBW infant appears to improve growth and development.^{5–6} Prior to birth, the placenta actively pumps nutrients into the fetus to support intrauterine growth and development. As much as 3.85 g/kg/day of amino acids cross the placenta into the fetus to provide the substrate for increasing muscle mass.⁷ After birth, the premature infant is disconnected from this nutrient source, and can quickly develop a nitrogen deficit contributing to suboptimal growth postnatally.

Current recommendations for parenteral nutrition in the VLBW infant are to begin a source of protein (amino acid solutions) as soon as intravenous access is obtained and to begin total parenteral nutrition (TPN) by the second day after birth.⁸ In addition, enteral feeds with either maternal expressed breast milk or donor human milk should begin by 2 days of age.^{9–12} When a certain volume of milk intake is tolerated, human milk should be fortified to provide increased protein, calories, calcium and phosphate necessary for lean body growth.^{13–15}

We reviewed the nutritional support and growth data for VLBW infants in our NICU in 2008 and found that 84% of appropriately grown VLBW infants at birth were being discharged home at weights that were <10th percentile, which we have defined as PGF. We began a multidisciplinary quality improvement project with the goal of reducing the percentage of infants, with birth weights that are appropriate for gestational age, discharged with PGF to less than 50% within 2 years. Our second aim was to sustain the incidence of PGF at less than 50%.

METHODS

Setting

The Penn State Health Children's Hospital NICU is a level IV regional quaternary NICU, with outborn infants accounting for 35% of annual admissions. The average number of admissions to the NICU over the time of this



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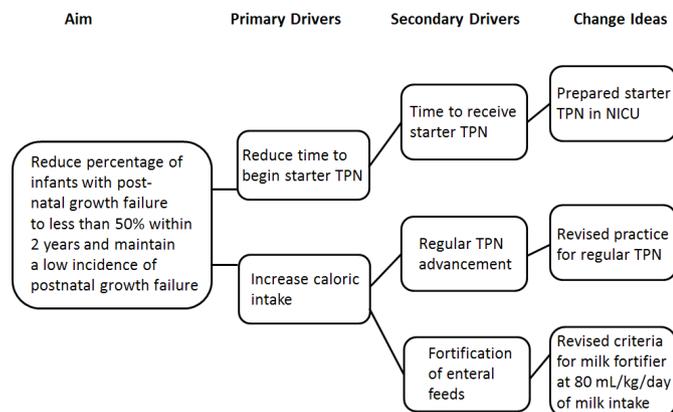


Figure 1 Key driver diagram showing the aim, and the primary and secondary drivers towards that aim, and the change ideas that were developed. NICU, neonatal intensive care unit; TPN, total parenteral nutrition.

project was 512 infants per year, of which there was an average of 83 annual VLBW admissions each year. All inborn infants with birth weights less than 1500 g were eligible for this study. Infants with known congenital anomalies were excluded. The mean birth weight of the infants included in this project was 1180 g, and the mean gestational age was 29 completed weeks.

The NICU staff includes a nutritionist, a pharmacist as well as other allied health professionals (respiratory therapists, and occupational and physical therapists). All TPN orders were entered by house staff, fellows or advanced practice clinicians (neonatal nurse practitioners, physician assistants) with input from both the nutritionist and the pharmacist using the electronic medical record, which includes a TPN calculator.

Process and outcome measures

After a thorough review of the literature, our multidisciplinary team, consisting of physicians (fellows, attending neonatologist), nurses and a NICU nutritionist, determined the key drivers for optimal nutrition and identified potentially better practices (process measures), as shown in figure 1. These included (1) more rapid initiation of starter TPN (a solution of 3% amino acids in either 5% or 10% dextrose); (2) aggressive use and advancement of regular TPN, which contains amino acids, dextrose, vitamins and minerals, trace elements, and intravenous lipids (Intralipid); and (3) fortification of human milk to 24 kcal/ounce when the infant's milk intake reached 80 mL/kg/day. Our practice has been to initiate enteral feedings within the first 2 days after birth once the infant was stabilised from a cardiovascular and respiratory standpoint. Starter TPN is continued for the first day after birth, and regular TPN is usually begun on the second day after birth.

We collected data on time to begin starter TPN, defined as the time from birth until the starter TPN was connected to intravenous access (either an umbilical venous catheter or peripheral intravenous catheter). We also collected data on the number of patients whose initial regular TPN

had 3 g/kg/day of amino acids and 2 g/kg/day of lipids, as recommended in the bundle of potentially better practices. We monitored the advancement of amino acids and lipids over the subsequent 4 days to determine the percentage of patients who were advanced by 0.5 g/kg/day for each macronutrient, as recommended in the bundle of potentially better practices. The intake of either mother's milk or donor human milk at which fortification was begun was recorded for each infant. In the most recent 3 years, we collected data on the percentage of infants who began fortification at 80 mL/kg/day (compliance with potentially better practices).

The outcome measure (PGF) was defined as the number of infants who were born with birth weights appropriate for gestational age who were discharged home at weights that were <10th percentile for their postmenstrual age.

Plan-Do-Study-Act cycles

1. First Plan-Do-Study-Act (PDSA) cycle bundle (January–March 2010):
 - a. Ready-made starter TPN available in the NICU: the previous system for providing early amino acid intake required that starter TPN be prepared in the pharmacy, delivered from the pharmacy to the NICU and then administered to the patient. The system improvement was to have ready-made bags of starter TPN in the NICU.
 - b. Education of staff on regular TPN (inservice conferences and staff meetings):
 - Start with 2 g/kg/day of lipid and 3 g/kg/day of amino acids.
 - Advance lipids by 0.5 g/kg/day to a maximum of 3 g/kg/day.
 - Advance amino acids by 0.5 g/kg/day to a maximum of 4 g/kg/day.
 - Advance glucose infusion rate from 5 mg/kg/min by 1–2 mg/kg/min each day to a maximum of 10–12 mg/kg/min.
 - c. Fortification of expressed breast milk when milk intake volume is 80 mL/kg/day.
2. Second PDSA cycle: place potentially better practices guideline in bedside reference manual (went online in 2012).
3. Third PDSA cycle: re-education of staff in the first quarter of 2015 (inservice conferences and staff meetings).

Data analysis

We collected data on time from birth to initiation and infusion of starter TPN at baseline and then each year after implementation of the new bundle. We also collected data on the compliance with initial regular TPN dosages (g/kg/day) of amino acids and lipids, as well as data on the compliance with advancement of these macronutrients on subsequent days of TPN infusion. The average volume of intake when milk fortification was begun was also collected. In the most recent calendar years, 2014–2016, we also examined the percentage of patients who began human milk fortification at 80 mL/kg/day.

We analysed the data using decision rules commonly applied to run charts, where a signal is considered significant when eight or more points are below (or above) the median for the data. We also used statistical process control methods to analyse control charts as appropriate, where eight or more points are below (or above) the mean for the data expressed in the control chart. Because the data for the time to begin starter TPN are continuous and the subgroups for each time point had multiple observations, we used X-bar and S-charts to analyse these data. To analyse the data for PGF, we used a P-chart since these data were discrete attributes classified as a proportion with PGF with unequal subgroup sizes. We used Minitab V.18 to analyse data and construct control charts.

RESULTS

Process measures

During the baseline period in 2009, the average time to initiate starter TPN was 5.5 hours (330 min). After implementation of the first bundle, we saw an immediate drop in the time to 3.5 hours (210 min). In the subsequent years through 2016, we have sustained this time to initiation of starter TPN to the goal of under 3 hours (180 min), except for the third quarter of 2013, as shown in the run chart (figure 2A). Control X-bar and S-charts show that this was a significant decrease in both the mean time to begin starter TPN as well as a significant decrease in the variability in the time to begin starter TPN (figure 2B).

We provided 3 g/kg/day of amino acids for 66% of VLBW infants on the first day of regular TPN during the baseline period in 2009. This has shown a steady improvement, so that 84% of VLBW infants received 3 g/kg/day of amino acids on the first day of regular TPN in 2016. During the baseline period in 2009, we only provided 2 g/kg/day of lipids for 18% of VLBW infants. This rapidly improved between 2010 and 2016, so that 2 g/kg/day of lipids were provided for 91% of VLBW infants in 2016.

There was an increase in the percentage of patients whose amino acids in regular TPN were advanced for subsequent days 3 through 6 as recommended (by 0.5 g/kg/day to a maximum of 4 g/kg/day), but the compliance with this recommendation was only between 20% and 67% between days 3 and 6 of regular TPN. In contrast, lipids were advanced as recommended (by 0.5 g/kg/day to a maximum of 3 g/kg/day) in 68%–90% of patients on day 3 between 2011 and 2016, in 64%–88% of patients on day 4 between 2010 and 2016, and in 68%–94% of patients on day 5 between 2010 and 2016. Since lipids were advanced to a maximum of 3 g/kg/day in the baseline period in 2009, by day 6 there was no change in the compliance with the recommendation to have reached the maximum infusion of lipids at 3 g/kg/day. In fact, we noted a decrease in the compliance with providing 3 g/kg/day of lipids on day 6 between 2014 and 2016, perhaps related to our enteral feeding practice of advancing milk feeds more consistently during these years so that lipids were no longer indicated for about 45% of VLBW infants

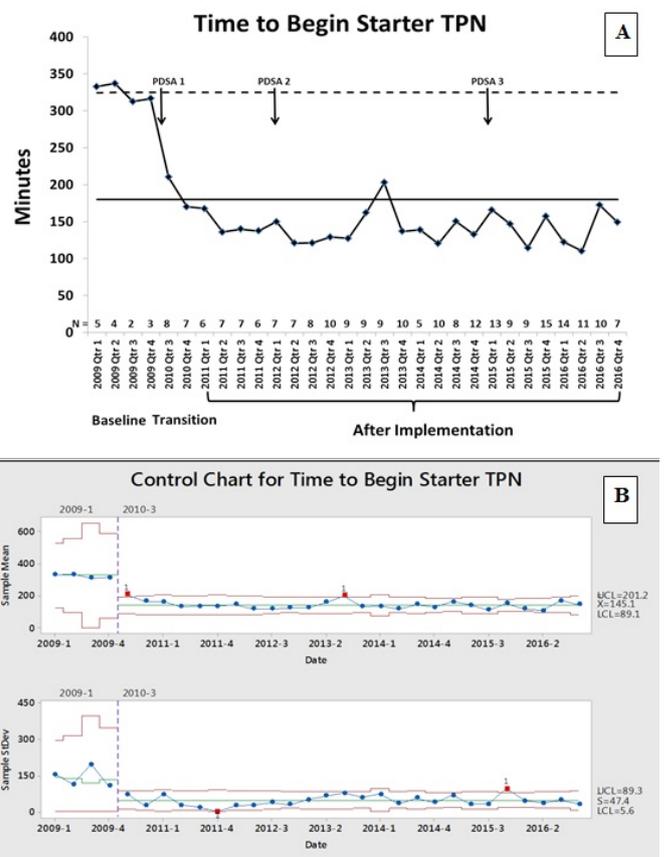


Figure 2 (A) Run chart showing the time to begin starter TPN. During PDSA cycle 1, we implemented the process whereby ready-for-use starter TPN was stored in the NICU rather than waiting for starter TPN to be made in the pharmacy. This significantly reduced the time to begin starter TPN within 1–2 years below the goal of 180 min (solid black line), which has been sustained through 2016. The dashed line represents the baseline median time to begin starter TPN, and there is a significant signal with 17 consecutive points below the median that began during the transition period in the third quarter of 2010 and continued through 2016. The numbers (N) of patients included in each quarter are shown just above the x-axis. (B) Control X-bar and S-charts of the time to begin starter TPN in minutes. Upper (UCL) and lower (LCL) control limits are shown for each chart, showing a significantly decreased mean time to begin starter TPN and a markedly decreased variability (SD). NICU, neonatal intensive care unit; PDSA, Plan-Do-Study-Act; TPN, total parenteral nutrition.

on day 6 in 2016 (our practice is to discontinue intravenous lipids when the volume of milk intake reaches 80–100 mL/kg/day).

During and after the implementation of the bundle of potentially better practices in the first PDSA cycle, we did not see a change in the mean volume of human milk intake at which fortification was begun. We re-educated the staff in 2014–2015 and examined the compliance with the recommendation to begin fortification at an intake of 80 mL/kg/day by recording the percentage of patients who did begin fortification at this volume of intake between 2014 and 2016. We saw an increase in the

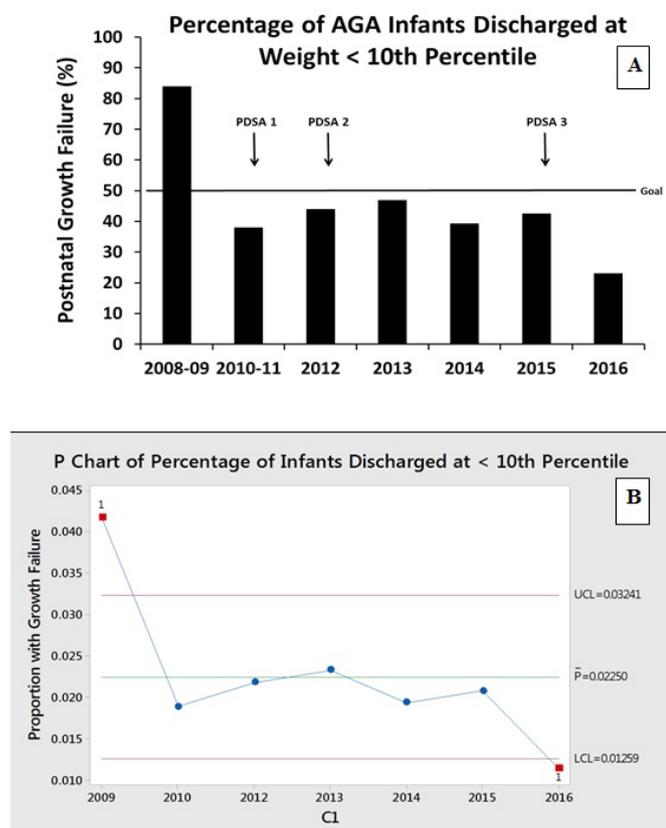


Figure 3 (A) Graph of the outcome measure showing that after implementation of PDSA cycle 1, reinforcing the guideline for human milk fortification by placing the bedside reference manual online (PDSA cycle 2) and re-education of staff (PDSA cycle 3), there was a sustained improvement in the percentage of infants born appropriately grown for gestational age who developed PGF (defined as discharge weight <10th percentile). The solid black line represents the goal of reducing the incidence of PGF to less than 50%. PDSA cycles are depicted by arrows. (B) Control P-chart shows a significant reduction in the proportion of very low birthweight infants with PGF beginning in 2010 (after PDSA cycle 1), which was sustained through 2016. There was a significant signal in 2016 showing a further reduction in PGF. LCL, lower control limit; PDSA, Plan-Do-Study-Act; PGF, postnatal growth failure; UCL, upper control limit.

percentage of patients who began fortification at 80 mL/kg/day from 31% in 2014 to 66% in 2016.

Outcome measure

We had a significant reduction in the percentage of VLBW Appropriate for gestational age (AGA) infants being discharged with PGF from the baseline of 84% in 2008–2009 to 38% in 2010–2011, as shown in [figure 3](#). We have sustained this percentage, meeting our goal of having fewer than 50% of AGA infants experiencing PGF through 2016. In 2016, only 23.1% of infants experienced PGF ([figure 3A](#)). The control P-chart shows that there was a significant decrease in the proportion of VLBW infants with PGF after implementation of the potentially better

practices, which was sustained and showed another significant signal (decrease in PGF) in 2016 ([figure 3B](#)).

LESSONS AND LIMITATIONS

We have achieved a sustained improvement in nutritional support for VLBW infants, as evidenced by a reduced incidence of PGF, by implementing systematic evidence-based changes in practice. When we began this project, the system for providing early amino acid intake required that starter TPN (a solution of 3% amino acids in either 5% or 10% dextrose) be prepared in the pharmacy, delivered from the pharmacy to the NICU and then administered to the patient. The system improvement of having ready-made bags of starter TPN in the NICU, which eliminated the delay encountered by waiting for this nutritional product to be mixed and then delivered, resulted in a decrease in the time to begin starter TPN from 5.4 to 2.2 hours. We speculate that this improvement most likely contributed to the decreased protein deficit that these infants experience in the first day after birth, which had the downstream effect on reducing PGF.

Prior to beginning this improvement project, subsequent regular TPN (including lipids, vitamins, minerals and elements, in addition to amino acids and dextrose) on day 2 would provide 2.8 g/kg/day of amino acids and 1 g/kg/day of lipids. In randomised controlled trials, initiation of higher dosages of intravenous lipid emulsions (2 g/kg/day) in VLBW infants was shown to be well tolerated without adverse effects.^{16 17} Higher intravenous lipid intake was associated with improved anabolism and improved nitrogen balance.¹⁷ Based on the evidence, we changed our practice of providing regular TPN so that we started with 3 g/kg/day of amino acids and 2 g/kg/day of intravenous lipids, and then advanced the amino acid dosage by 0.5 g/kg/day to a maximum of 4 g/kg/day and advanced the lipid dosage by 0.5 g/kg/day to a maximum of 3 g/kg/day. We saw a significant increase in the percentage of patients who received the goal of 2 g/kg/day of lipids on day 2 in the 2 years after implementation, which has been sustained through 7 years after implementation. Recently, a higher intravenous lipid dosage up to 3.8 g/kg/day was shown to improve postnatal head growth.¹⁸ This must be weighed against the risk of TPN-associated cholestasis when using intravenous lipids over a prolonged period of time.

We also demonstrated a modest increase in the percentage of patients who received the goal of 3 g/kg/day of amino acids on day 2 over the 7 years after implementation. Subsequent advancement of TPN from days 3 to 6 after birth also showed significant improvement in the percentage of patients in whom the goal for advancement of lipids from 2 to 3 g/kg/day was achieved over the 7 years after implementation. We also found a modest increase in the percentage of patients who received the goal of advancement of amino acids from 3 to 4 g/kg/day over the 7 years after implementation. The improvements in the provision of amino acids and lipids in regular TPN

most likely also contributed to the improved outcome of decreased PGF that we have shown. We speculate that the improved positive nitrogen balance achieved with higher amino acid intake and improved protein/energy intake ratios resulted in improved growth earlier than prior to implementation, which had the downstream effect on reducing PGF.

Recent evidence has shown that providing early concentrated amounts of parenteral amino acids to VLBW infants will improve postnatal growth and neurodevelopmental outcome.^{6 8 19 20} In addition, nitrogen balance can be improved with the use of early intravenous amino acid solutions.^{20 21} Starter TPN is designed to accomplish this. The initial nutritional support immediately after birth, provided by starter TPN, is followed by the intravenous administration of regular TPN which includes lipids, vitamins, minerals and elements, in addition to dextrose and amino acids. Studies have shown that advancing from 3 g/kg/day of amino acids in increments to a goal of 4 g/kg/day of amino acids improved growth, bone mineralisation and neurodevelopmental outcome in VLBW infants.^{6 22} The use of higher concentrations of amino acids and lipids, in a standardised, concentrated parenteral solution that included added macronutrients, was shown to improve postnatal head growth in preterm infants with birth weights <1200 g.¹⁸

Another potentially better practice we identified was to begin fortification of human milk feeds when the volume of intake reached 80 mL/kg/day. Early studies showed that providing enriched formula to preterm infants was associated with improved weight gain, nitrogen retention and neurodevelopment.^{14 23–25} Recent evidence has shown that feeding human milk to preterm infants is optimal in terms of feeding tolerance, promoting intestinal motility, reducing intestinal permeability, reducing late-onset sepsis and hospital costs, and reducing the incidence of necrotising enterocolitis.^{26–31} Fortification of human milk is necessary for providing increased protein, calcium, phosphate and caloric intake, which allows for improved growth prior to discharge.³² Recent studies suggest that initiation of fortification can occur at volumes of milk intake as low as 20–40 mL/kg/day.^{15 27 33} When we began this project in 2009, we developed and implemented a guideline that recommended fortification at a volume of milk intake of 80 mL/kg/day rather than waiting until intake was 120 mL/kg/day. In the current quality improvement report, measurement of the average intake of milk at which fortification was provided did not show improvement over the 7-year period. When data were analysed for the most recent 3-year epoch after a third PDSA cycle, which emphasised re-education of the potentially better practices, we did find a significant increase in the percentage of patients whose milk feeds were fortified according to this recommendation. We have recently changed this recommendation, based on our recent review of the literature, so that fortification now begins at a milk intake of 40 mL/kg/day. We are continuing to collect these process metric data. We speculate that the

improved earlier fortification of enteral feeds contributed to the improved outcome of reducing PGF.

A strength of this study is that this was a multidisciplinary effort including nurses, physicians and a dedicated neonatal nutritionist as part of the core quality improvement team. Having the neonatal nutritionist present on rounds in the NICU helped in the successful implementation of these practice changes. In addition, the unit-specific culture of quality improvement and patient safety helped in the implementation of the potentially better practices. These contextual aspects in our NICU were important for the success of the project. In the model for success in quality, context is theorised to be an important aspect in the implementation and spread of any improvement effort.^{34 35} The leadership of our academic medical centre is committed to supporting patient safety and quality improvement throughout the organisation, with departments of patient safety and quality improvement. The system change of having starter TPN ready-made and in the NICU, with the help and guidance of the pharmacy, resulted in a rapid and successful implementation of this practice. It is well documented that system changes have much more impact on implementation of process changes and outcomes than do educational efforts of staff.³⁶

There are, however, several limitations to this project that we recognise. First, other aspects of practice changes (such as development of a donor human milk programme, change in the type of fortifier from bovine milk-based to human milk-based fortifier) may have contributed to the improved outcome. However, the use of donor human milk and human milk-based fortifier did not occur until 2015 after we had already seen a significant improvement in the outcome. We also did not measure short-term growth parameters, such as days to regain birth weight and days to reach full enteral feeds.

The outcome measure of PGF has shown a significant and sustained improvement in the 7 years since implementation. We believe that improved nitrogen balance and amino acid and energy intake in the first few days after birth, along with earlier fortification of milk feedings in the first week after birth, significantly impacted the growth trajectory of the infants, leading to reduced PGF. This may have important implications for improving other neonatal outcomes, such as the incidence of bronchopulmonary dysplasia and necrotising enterocolitis, as well as better neurodevelopmental outcomes.

CONCLUSION

In summary, we have shown that a quality improvement project to improve nutrition in VLBW infants can be sustained by following the model for improvement, with changes in practice based on evidence-based medicine and improvements in the system.

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Contributors MK designed and planned the study, analysed the data, and wrote the manuscript. He is responsible for the overall content as guarantor. KM collected and helped analyse the data, and contributed to the writing of the manuscript. RJ collected and helped analyse the data. CG helped in the planning of the study, collected the data and contributed to the writing of the manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

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