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Ensuring neonatal human milk provision: A framework for estimating potential demand for donor human milk

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ABSTRACT

Using donor human milk (DHM) for preterm infants, where the mother's milk is unavailable, protects infants against potentially fatal necrotising enterocolitis. When used optimally, DHM can support mothers to establish breastfeeding. Understanding the relationship between clinical choices for DHM provision and the resulting demand is important. For policymakers, it informs decision-making around the provision of DHM based on cost-benefit analyses. For milk banks, it helps plan for required capacity, donor recruitment and supply-side collections. This study presents a framework for estimating DHM potential demand for infants born preterm, which allows for various sources of secondary population data, different feeding protocols and policy options for DHM provision. A Monte Carlo Simulation (MCS) is developed which follows the framework, simulating annual births (based on historical data) and incorporating uncertainty related to infant and maternal populations. A case study on human milk banking serves as the basis for the application of the framework and the modelling approach. Our model estimates the overall demand for DHM in England and Wales, the local level demand for NHS Trusts in England and provides an indication of the associated uncertainties. Our study provides a useful tool to enrich the strategic and operational level decision-making environment, benefitting both policymakers and milk bankers by providing a better understanding of the impact of policy decisions on the future development of the milk bank infrastructure.

1. Introduction

There is rising recognition of the significance of an exclusive human milk diet for neonates (Forbes et al., 2018; Miliku et al., 2021; Pärnänen et al., 2022; Victora et al., 2016). However, for some infants, mother's own milk (MOM) might not be available for a range of reasons, including delayed lactogenesis, maternal separation, insufficient glandular tissue, or contraindicated medications. The recently published recommendations by the World Health Organization (WHO) regarding the care of small and sick infants emphasise the essential provision of donor human milk (DHM) in situations where there is a lack or insufficiency of MOM supply (WHO, 2022). This recommendation is a crucial component of a comprehensive lactation support package, aiming to safeguard preterm infants from life-threatening complications (*ibid.*). Notably, scholarly societies such as the *European Society for Paediatric Gastroenterology Hepatology and Nutrition*, the *American Academy of Pediatrics (AAP)*, and the *Japan Pediatric Society* also recommend DHM as the first-line supplement to any shortfall of MOM for low birth weight (LBW) premature infants (Arslanoglu et al., 2013; Eidelman & Schanler, 2012; Mizuno et al., 2020).

The dominant rationale for DHM provision, as per recent Cochrane review (Quigley, Embleton & McGuire, 2019), has been the reduction of the risk of developing the life-threatening condition necrotising enterocolitis (NEC). Beyond the immediate clinical benefits of protecting infants from complications, the use of DHM in the context of optimal lactation support could also play a role in protecting, promoting, and supporting breastfeeding (WHO & UNICEF, 2018). This is based on data which shows that availability of DHM in hospital settings can motivate and support mothers to subsequently provide their infants with MOM (Kair & Flaherman, 2017; Mondkar et al., 2021; Ponnapakkam et al., 2021; Zipitis, Ward & Bajaj, 2015). In the UK, DHM would typically be provided in hospital settings for a limited time between birth and when MOM becomes fully available, the so-called *Bridging* period. Limited supplies have meant DHM is usually reserved for very low birth weight

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(VLBW) (birth weight [BW] <1.5 kg), and premature (born ≤32 weeks of gestational age [GA]) infants (WHO 2022).

Despite several global and regional recommendations being developed on providing human milk for VLBW infants when MOM is unavailable, the nominal cost of DHM is perceived to be high. Per litre of DHM, it was previously calculated to be in the region of $150 (Spatz, Robinson & Froh, 2018) in a US study; while a study of a German hospital yielded a total marginal cost of €82.88 per litre of pasteurised DHM, as compared to €10.28 of formula (Fengler et al., 2020). Another study from Italy calculated that even though in 2019 the average cost per litre amounted to €231, through working at maximum capacity the milk bank price could have been reduced to €209 per litre (Salvatori et al., 2022). Cost is considered a major barrier to the use of DHM in hospitals and neonatal intensive care units (NICUs). In a UK survey, 64.6 % of NICUs cited cost as the main reason for not using DHM (Zipitis et al., 2015). However, a recent systematic review highlighted the cost-effectiveness of DHM versus standard feeding in infants (Zanganeh, Jordan & Mistry, 2021).

Human milk banks (HMBs) are organisations that provide a service that ensures appropriate and safe handling of perishable human milk. Globally, at least 750 HMBs exist, with a rising trend (Human Milk Bank Global Map, n.d.; Shenker et al., 2021). HMBs provide the infrastructure for the collection, testing, processing and delivery of DHM. They recruit and screen mothers who can offer a surplus to their own infant's needs. The collected milk is typically pasteurised, screened microbiologically, and stored in controlled conditions before being dispatched to hospitals. Yet another source of demand is from the community, where HMBs can provide surplus milk for infants to families facing feeding challenges (Griffin et al., 2022). However, DHM demand from neonatal units is prioritised. While recruitment criteria for donors vary based on the country where an HMB is located, the number of donors recruited is likely to depend on the demand for DHM and the capacity of the individual HMB. Importantly, demand for DHM has been reported to be rising (Schultz, 2022), with some HMBs facing significant strain in 2021 across the UK (Shenker et al., 2023). Therefore, an estimate of the needs of the hospitals would enable service planning, as well as strategies to optimise donor recruitment and collections, to better meet the rising clinical demand for DHM.

The provision of DHM needs to primarily allow access to those who would most benefit from its entitlement. These are mainly premature newborns (born at less than 32–34 weeks GA), VLBW and other vulnerable infants. Such a DHM feeding policy should arguably consider, as a minimum, the following three factors: (a) cut-off points for DHM entitlement for babies, which are determined from infant birth metrics (IBM) such as gestational age and/or birth weight, (b) the duration of provision, and (c) budgetary implications owing to the relatively high upfront costs of DHM. Evaluation of the multiple options would allow for informed decision-making within regulatory bodies and hospitals.

Despite worldwide recognition by the leading health organisations of the importance of a human milk diet, that also includes DHM provision, there is so far little understanding about the possible scale of DHM demand. Our work addresses the important but largely unaddressed area of DHM demand estimation. Our focus is on assessing the **potential** demand based on population characteristics to capture all potential DHM users, thereby aiming to estimate the "ceiling" of demand. This understanding of the maximum potential demand, an ideal scenario without supply or financial constraints, draws a somewhat aspirational picture of where the system could aim to get to. This is intended as a tool for next-step policy development, as it would allow for the exploration of various dimensions such as existing infrastructure, financial capacities, and supply considerations, and finally the feasibility assessment for a proposed provision policy.

With this in mind, we developed a framework for calculating the **potential** demand for DHM as a function of different feeding protocols used in hospitals. The framework is implemented through a probabilistic Monte Carlo Simulation model to estimate the overall potential demand for DHM using the study setting of infants born in hospitals in England and Wales. The model serves two purposes: (a) at a local level, it allows for the estimation of DHM for individual NHS Trusts and investigation of several "*what if*" scenarios that explore the sensitivity of volumes to choices around feeding protocols; (b) at a strategic level, the model considers the regional demand from hospitals that procure DHM for infants and enables exploration of the impact of potential changes in feeding protocols in terms of the expected demand at a regional scale. A better understanding of potential demand for DHM is likely to be instrumental as it should allow more informed decision-making for various stakeholders. From HMBs' perspective, knowledge of potential demand within their catchment should facilitate more informed planning on operational aspects such as donor recruitment, infrastructure needs and financial planning. For hospitals this informed insight could enable them to devise resilient strategies that efficiently navigate the fluctuating supply, considering the donation-based system. Finally, given the changing landscape and greater focus on extending provision of human milk globally, our framework and model developed are likely to empower the policy makers to consider feasibility when formulating policy for DHM provision policy or guidance.

The subsequent sections of this paper are organised as follows. Section 2 introduces the related research that provides an exploration of the relevant literature, while Section 3 introduces our research setting-human milk banking in England and Wales. In Section 4 we present the general framework for estimating the potential demand for DHM, which is followed in Section 5 by application of our framework to a case study by means of a Monte Carlo model. In Section 6 beyond presenting the results of selected experiments at national and regional levels, we also highlight the assumptions and limitations. Additionally, we present a Qualitative System Dynamics model that captures interactions and feedback loops which are likely to be of influence when moving from potential to realised demand for DHM in NICUs. Finally, Section 7 contains a discussion of our findings, their managerial implications, and conclusions.

2. Related work

Our literature review has identified only four papers that have used OR approaches in the context of HMBs. The study of network expansion by Cao et al. (2016) uses a case study of milk banking in South Africa. By incorporating equity-based objectives, it utilises heuristics to solve a mathematical model. The computational experimentation provided insights into the dynamics in the relationship between efficiency and equity when examining different levels of supply and demand and the possible mismatch arising from those (Cao et al., 2016). Sun et al. (2022) investigated internal HMB day-to-day operations that ensure product safety. Their work is based on a case study of a milk bank in Texas, USA. Through mathematical models, the authors optimise decisions in the production of DHM that maximise the production utility while minimising associated labour efforts. Chan et al. (2023) through combining a predictive machine learning model and optimisation, centres around the decision of which batches of donations to pool (combine) together with the aim of achieving a target macronutrient level content. The most recent publication by Staff et al. (2023) explores the application of Conceptual Modelling (CM) within the context of human milk banking operations utilising the Hearts Milk Bank, England, as a case study. It introduces a detailed narrative on developing a conceptual model for managing perishable inventories to address the complexities of inventory management and the perishable nature of human milk within the milk banking supply chain.

While the literature on OR and HMB is limited, the supply chain of donor blood is a related field that has received considerable attention. Blood supply chain (BSC) management covers multiple areas, such as optimisations of inventory policies (Baesler et al., 2014; van Sambeeck et al., 2022; Simonetti et al., 2014), collection and production

(Ghandforoush & Sen, 2010; Osorio, Brailsford & Smith, 2018), location-allocation (Chaiwuttisak et al., 2016; Sharma et al., 2019), allocation of stock to multiple hospitals (Katsaliaki, Mustafee & Kumar, 2014), distributed execution of BSC (Mustafee et al., 2009), applications of technologies to optimise operations (Hemmelmayr et al., 2010), and more.

Both HMBs and Blood Banks demonstrate several similarities. They rely on voluntary donations of human bodily fluid; the products need careful processing, and their perishable nature translates into limited shelf-life; hence, overproduction and storage over a long time horizon is not a possibility. Thus, careful consideration and planning is essential to match supply and demand effectively, for both milk and blood products.

On the other hand, there are also notable differences between the DHM supply chain and BSC. Alternatives to DHM exist, namely the manufactured human milk substitute of infant formula. Thus, unlike donor blood, which has no substitute, the use of DHM in hospital settings is not universal; and the actual demand for DHM is highly uncertain. Yet another difference is the shelf-life of DHM. As DHM can be frozen, its shelf-life is significantly longer (measured in months) than that of blood products (measured in days). Owing to these differences, inventory planning for DHM is likely to differ from that of blood.

The BSC constitutes a mature field of study, with well recognised demand uncertainty studied and modelled. Even though, according to Osorio et al. (2018), "the use of deterministic demand forecasts is rarely adequate and a robust decision must consider uncertainty and variability in demand", Luo and Chen (2021) consider blood demand to be of heterogenous nature; a first arm of scheduled surgeries representing a deterministic demand, and a second of emergency care representing a highly variable stochastic demand. In a 2019 review of models and methods for BSC management (Pirabán, Guerrero & Labadie, 2019), demand is grouped into stochastic, forecasting and deterministic categories, with stochastic being the most prevalent (>60 % of reviewed studies included demand modelling), and forecasting the least. The forecasting and deterministic demand models are mostly based on historical data, in some cases augmented with population-level demographics for forecasting purposes (Volken et al., 2018). On the other hand, due to the non-universal use of DHM (provision choice) and the unavailability of empirical data on DHM demand there is a dearth of quantitative investigations and modelling studies in this area.

No previous studies on DHM potential demand estimation have been identified. However, several related studies in other healthcare fields have described models that estimate potential demand based on epidemiological data on disease prevalence within a target population. The examples of this approach to estimating demand in the prior literature are associated with schedules for disease treatments (Farrugia, Bansal & Marjanovic, 2022) or dosage for preventative intervention through vaccination programmes (Amarasinghe & Mahoney, 2011). Other studies also aim to assess the population size in need of specific services, for instance, bariatric surgery in Australia (Sharman et al., 2018), care services for the frail and elderly in a city of Wales (Palmer et al., 2021) and palliative care in Germany (Scholten et al., 2016). Beyond assessing potential demand, a study might also consider the known level of availability of the services. This helps us to assess the proportion of the population that might be affected due to a shortage of current provisions (Sharman et al., 2018). For a hypothetical influenza pandemic, the study by Meltzer et al. (2015) investigated the potential demand for masks and respirators during hospitalisation in the United States. The study by Carias et al. (2015) used a similar context and focussed on respirators. By assuming different pandemic scenarios for the severity of symptoms, the models calculated the number of deaths that could be averted based on the different provision levels of supplies.

What is apparent from the set of identified studies is the heavy reliance on deterministic methods for demand estimation, including implementation using spreadsheet models (Carias et al., 2015; Harper et al., 2004; Meltzer et al., 2015). Despite being a user-friendly tool for planning and management (Cooper, Brailsford & Davies, 2007), spreadsheets may not be the optimal choice for building complex models; maintaining large models can also be challenging. Models developed using spreadsheets often rely on deterministic inputs, which will likely result in an inability to capture inherent uncertainty and variability in real-life scenarios. Monte Carlo Simulation (MCS) techniques by incorporating random sampling and probability distributions, provide a more realistic outlook that enables the assessment of risk and uncertainty, and assessment of a wide range of potential outcomes. Such models create a more realistic decision-making environment. Despite these advantages, only a few publications reported using MCS as a standalone technique for demand estimation. The study by Ji et al. (2014) utilised MCS to evaluate electric bicycle sharing. In this study, the model estimated the number of bicycles and batteries that would be required, given different scenarios concerning trip lengths, trip duration, and battery recharge rates. Haque et al. (2014) employed the technique to generate estimates of future water demand for a region in Australia. By incorporating factors related to future uncertainties, such as projected population size, climatic conditions and water restriction levels, the model allowed the analysis of the distribution of future water demand.

In MCS, the generation of outputs from the models for exploratory research is constrained by boundaries of parameters used in the estimate calculation, typically either utilising standardised scenarios, such as used in the influenza pandemic study (Meltzer et al., 2015) or by making use of previously published models, for example, Scholten et al. (2016). For our study, while there are commonalities with prior work in terms of population-based demand estimation, there is a lack of published models for the needs of infants for DHM provision. Instead, exploratory parameter ranges were used, which are considered plausible based on inputs collected from stakeholders, including a senior neonatal feeding expert (please refer to the acknowledgement section).

3. Case study

The case study relates to the provision of DHM by HMBs in England and Wales (E&W). While no national policy for DHM provision exists for E&W, a recently published report: "The Use of Donor Human Milk in Neonates / A BAPM Framework for Practice" by the British Association of Perinatal Medicine (BAPM) recommends that, in the absence of MOM, DHM ***may*** be considered for babies born below 32 weeks gestation and/or weighing less than 1500 g (BAPM, 2023) (this forms the basis for a subset of exploratory parameters in the Framework implementation section). Local HMBs operate in accordance with the *National Institute for Health and Care Excellence (NICE)* Clinical Guideline on the Operation of a Human Milk Bank (NICE, 2010a), which specifies guidance around the donations and handling of DHM. The demand for DHM for VLBW and vulnerable infants comes primarily from the individual NHS Trusts operating in E&W, making up the regional demand. In this case study, we establish the expected regional demand for DHM under various feeding policies.

There are 15 active milk banks in the UK, with 13 based in England, a single national service in Scotland, and one milk bank in Northern Ireland; the latter also supplies DHM to the Republic of Ireland (UKAMB, n.d.). As no separate milk bank is operating in Wales, a recently established hub of Hearts Milk Bank ensures DHM provision in South Wales (Swansea Bay University Health Board, 2022).

The operations of typical UK-based HMBs are complex and can be classified into the following four stages (Fig. 1):

- **Stage 1** - **Recruitment of potential donors:** This involves either an interview or a questionnaire-based assessment to check health-related status and lifestyle factors that might impact the quality and safety of donor milk. A blood test is also performed to check for infections such as HIV and hepatitis B and C. Upon successful completion of the assessment, a sub-set of the potential donors join the HMB's donor pool.

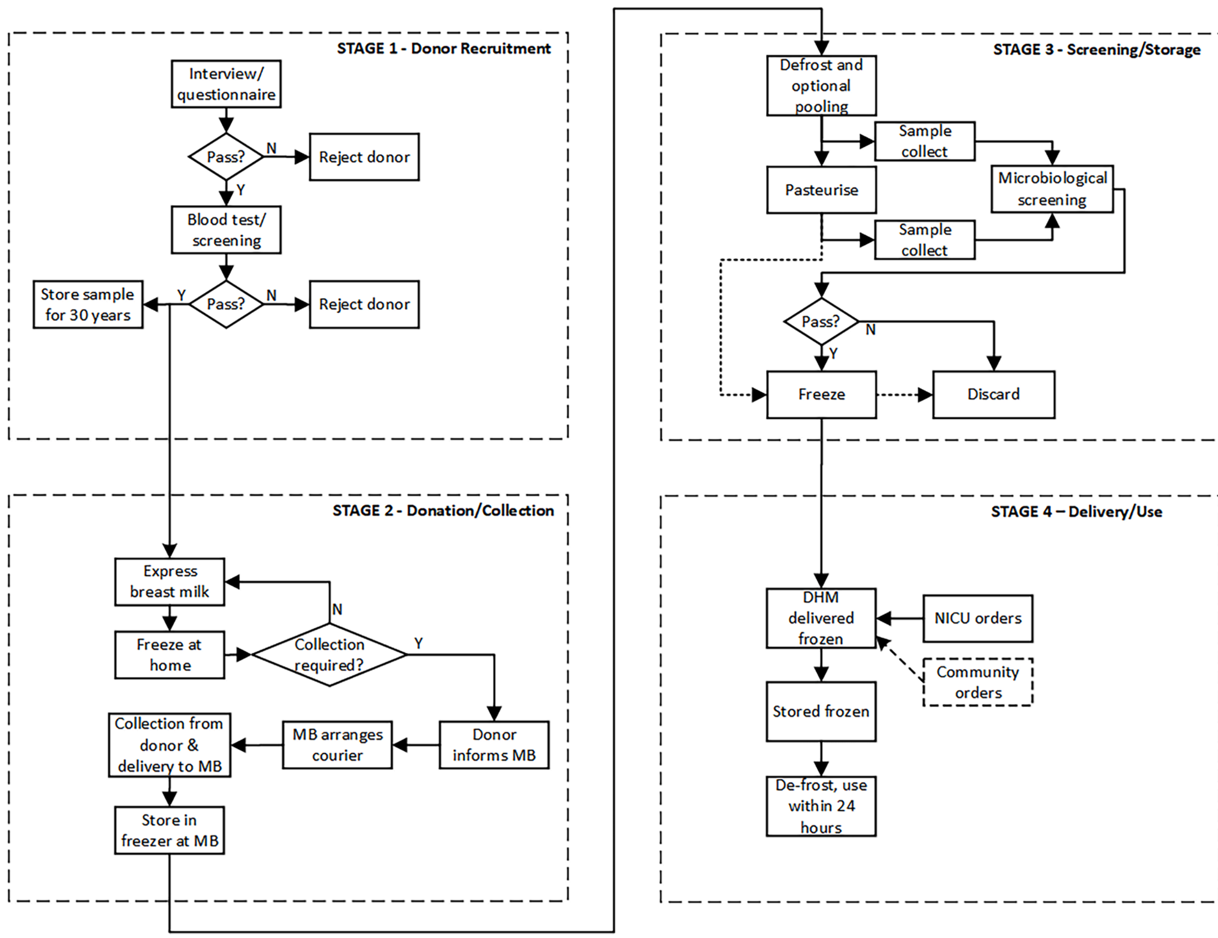

Fig. 1. Operations of a typical UK milk bank.

- **Stage 2 - Milk donation and collection**: Typically, two types of donations exist. The first type comprises donors who express milk and store it in a home freezer; when sufficient volume has accumulated, HMBs are informed to arrange for collection. The second type constitutes donors who expressed and stored milk during their infant's hospital stay, and milk is only donated to HMBs after the infant has been discharged.[1] Since the maximum storage duration of frozen breast milk (before pasteurisation) is three months (NICE, 2010b), it is vital to note the date of expression. The milk is typically collected frozen.
- **Stage 3 - Processing and storage stage:** The milk is defrosted at the HMB for pasteurisation. Microbiological screening (bacterial count) is performed before and after pasteurisation. If the screenings pass the NICE criteria, the DHM is re-frozen and stored. These processes related to pasteurisation, screening and storage generally involve high costs, including time-intensive staffing costs. This results in a relatively high price of DHM compared to infant formula.
- **Stage 4 - Orders from hospitals and the community and delivery from HMBs:** Hospital orders for DHM will usually originate from NICUs that provide care for VLBW babies. Orders are placed according to the stock control procedures at the hospitals. Some demand may originate from the community, although in E&W, few HMBs support non-hospitalised infants (Bramer et al., 2021). DHM is delivered frozen for storage in either hospital or home freezers. At this point, the maximum storage duration is six months from the date of expression (NICE, 2010b). Prior to use, the DHM is defrosted and must be used within 24 h.

Note that the maximum combined storage time for Stages 2, 3 and 4 is six months. Understanding the demand for DHM from the customer NHS Trusts is important to allow better planning of the supply chain, and for managing many aspects of HMB operations. These include whether to adjust donor recruitment efforts (**stage 1**), for example, to assess whether additional recruitment drives are required to meet forecasted demand. For the associated donor screening, contracts may be placed with third-party laboratories and HMBs will need to ensure sufficient capacity is available at the quoted costs. HMBs will also need to ensure adequate storage capacity is available for the projected demand (**stages 2 and 3**), and usage beyond NICU provision at times when higher volumes of DHM are available. Understanding DHM demand further allows HMBs to plan and assess whether equipment and staff levels may need to be adapted to meet forecasted demand (**stage 3**). The demand also has implications for transportation from donors (**stage 2**), delivery to hospitals (**stage 4**) and other logistical considerations, such as centralised versus localised DHM storage.

Understanding changes in DHM requirements and availability enables hospitals to plan logistics (such as available freezer storage capacity; **stage 4**) and costs of DHM. At the national level, this model allows policymakers to assess DHM volumes associated with possible national policy initiatives for DHM use and its likely impact on NHS budgets.

[1] For these cases recruitment and screening (Stage 1) may take place for milk that has been previously collected.

4. Framework for the estimation of potential demand of DHM

This section presents a general framework for estimating the potential demand for DHM. Unlike most studies, the case study has been presented first. It highlights the primary motivation of the work - the need to estimate the demand for DHM from the perspective of both the healthcare providers and the HMBs.

The three fundamental elements that form the basis of the framework are (a) the use of underlying literature to determine infant birth metrics (IBM), specifically birth weight, gestational age and other metrics related to newborns, (b) the use of secondary demographic data on birth rates, and (c) the development of a logic flow that enables the implementation of the framework using a demand model (this could be a deterministic model or be programmed, as presented in Section 5 for our case study using a probabilistic model). The framework facilitates adjusting for local assumptions and the nature of local birth statistics data and, following the steps in the logic flow, allows for the development of a model specific to the setting under investigation. Visual representation of logic flow and data requirements are presented in Fig. 2.

As per the framework, each infant born is considered while estimating the potential demand per given population. The overall volume required per infant would vary, depending on IBM, namely BW and GA at delivery, and subsequent weight gain characteristics, and hospital use protocols.

Referring to Fig. 2, the framework's logic flow implementation could be aided by approaching the framework as a two-phase framework. The first phase (Phase I) necessitates gathering local data and making local adjustments. It comprises of steps A-E. The second phase (Phase II), comprising of steps 1–6, estimates the potential DHM demand.

4.1. *Phase I – gather externally-defined inputs*

First, the elements that relate to the population settings being investigated will need to be identified (A to E, Fig. 2). These are the birth statistics of the population (A), birth weight statistics (B), policy for DHM provision (C), growth curves (D) and feeding regimes (E).

A- Numbers of births in the population: Population-level data collection presents an opportunity to capture important demographic snapshots, changes and trends at a certain granularity of time. While numbers of births are commonly available in high-income countries, records from low- and middle-income countries of the statistics vary and therefore might not be easily accessible (Phillips et al., 2018).

B- Birth statistics: The records describing characteristics of infants in a population at question, such as GA and BW at birth.

C- Hospital policy: For DHM this specifies the subset of infants who would be eligible to receive DHM. There may not be a consistent regional policy. Thus, in one organisation, the answer to the question "*who is entitled to get DHM?*" might be decided on a purely individual *ad hoc* basis and practitioner judgment; in other settings, all infants might have access to DHM if they meet certain characteristics for a defined duration of time (e.g., all newborns born before 32 weeks GA for a maximum duration of 3 days). Our framework allows for the latter option. Also, concerning policy, the framework might be applied for purely exploratory purposes, by following "*what if*" scenarios, rather than representing an actual policy, thereby allowing potential demand to be assessed for different policy options.

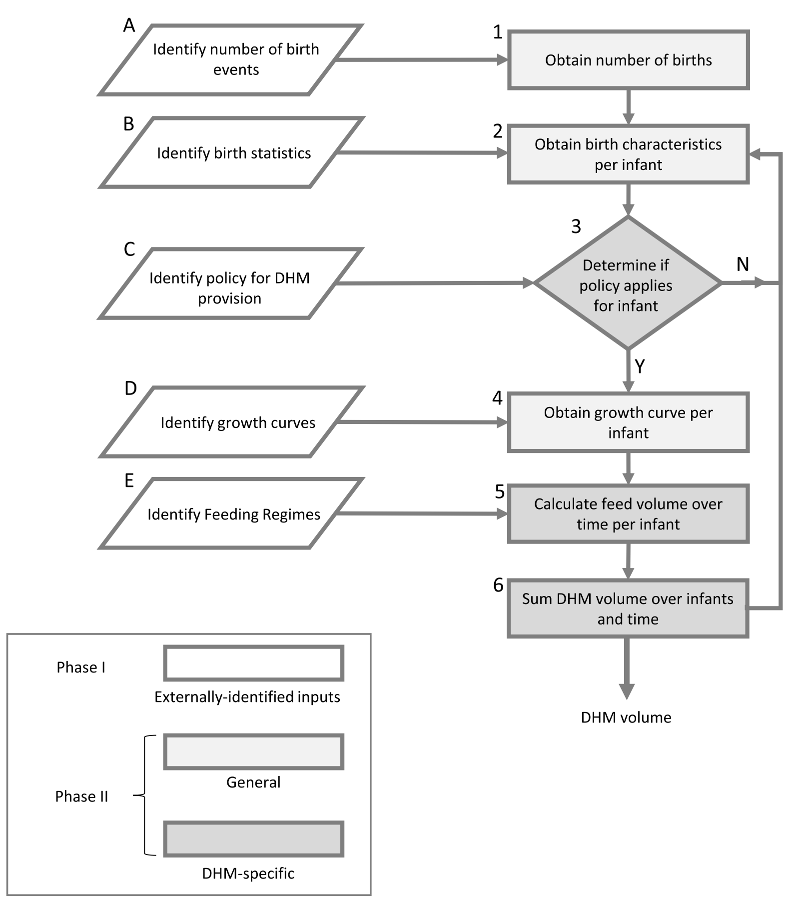

Fig. 2. Logic flow of DHM estimation framework.

D- Growth curves: Given the historical weights at birth, the centiles followed by postnatal longitudinal weight gains are commonly calculated, published and used by medical professionals. BW is strongly associated with mortality risk during the first year (Wilcox, 2001), and subsequent weight gains in general allow growth monitoring as part of the paediatric management of the infants.

E- Feeding Regimes (FRs): In hospital settings FRs are used to determine the standardised volumes and pace of feeding an infant, irrespective of the nature of the feed (infant formula or human milk). They are typically determined based on BW and/or GA. As there is heterogeneity in terms of GA and BW, FRs are likely to be defined separately for subpopulations of infants depending on IBM. An example of a FR might read: recommendation for infants born weighing less than 1 kg is: *feed is introduced at 20 ml/kg/day with a daily increase of an additional 10 ml/kg/day, until reaching final feed volume of 180 ml/kg/day.*

4.2. Phase II – calculations for estimation of the potential DHM demand

The Phase II of the framework can be implemented using either a deterministic or probabilistic strategy. In the former one, the calculations, using averages as a basis, would produce final results that reflect the average potential demand. For sufficiently large populations under investigation, the deterministic model implemented in a user-friendly spreadsheet may not have significant uncertainty and thus can serve as a useful tool to improve decision-making processes. On the other hand, in investigations that involve smaller populations, a probabilistic strategy is likely to provide insights on uncertainty to enhance decision-making. Irrespective of that choice, steps 1–6, as outlined in Fig. 2, are to be followed to calculate the DHM potential demand. Briefly, for a population in question, after establishing the number of births (step 1) and obtaining the birth characteristics per birth (step 2), it is assessed whether the policies in place qualify an individual infant for DHM provision (step 3). The identified growth curves then define the infant's weight gain trajectory over time, which are assumed to follow the assigned centiles at birth (step 4). Given the specified FR, the DHM feed volume is calculated per infant (step 5). Finally, step 6 sums DHM assigned to the qualified sub-population to arrive at the final volume of DHM.

The outlined framework guided our study design, data sources identification, and analysis, informing the development of a probabilistic Monte Carlo model (and a deterministic spreadsheet model for cross-verification purposes- see Appendix A for description and cross-verification results). The developed MCS was used to calculate potential DHM demand specific to the case study presented in this paper.

5. Framework implementation

5.1. Gathering externally defined inputs (Phase I)

Following the logic flow of the DHM estimation framework (Fig. 2), the identification of five externally defined inputs, namely birth numbers (A); birth statistics of the population (B); policy for DHM provision (C); BW statistics and growth curves (D); and FRs (E) were undertaken.

(A, B) Number of Births and Birth statistics of the population: Depending on the granularity of the analysis to be performed, an "ideal" data set for building the model would give the distribution of births per desired IBM as defined by FRs, i.e., BW per week (and day) of GA, at either the regional level or at the hospital level. As this was not available at the time the analysis was performed, in any publicly available reports, a yearly Trust-level publication of NHS Maternity Statistics published by NHS Digital was used instead (NHS Digital, 2019), which provides data on the number of deliveries per three-weekly GA clusters per NHS Trust in England. As well as the Trust-level data for England, Office for National Statistics (ONS) weekly data for the national level for England, and England plus Wales, has also been included in the model (ONS, 2019).

(C) Policy for DHM provision: As previously mentioned, with the exception of the recently published national guidelines that define the population for possible provision to infants born below 32 weeks GA (and/or weight <1500 g) (BAPM, 2023), the UK lacks an overarching policy that states "*who should be entitled*" to access DHM. Consequently, only a subset of hospitals/Trusts have integrated DHM use into their standard practice. Through background reading and multiple discussions with experts in the field, including the neonatal team members and the co-authors from Hearts Milk Bank, two broad policies to account for both infants' characteristics, as well as maternal lactational status, were developed. Those policies were deemed plausible scenarios to apply within the model for exploration purposes to calculate potential regional demand.

Policy 1 The *Bridging* policy is targeted at the provision of DHM for a relatively short period in the initial days Postpartum (PP), until MOM becomes fully available and replaces DHM provision. The parameters assume all the infants born at or below parameter Y (GA weeks) would receive 100 % of the required feed in the form of DHM for X number of days (Fig. 3A).

Policy 2 The *Beyond Bridging* policy is intended for infants whose mothers cannot provide MOM to satisfy the full dietary need of their infants. The policy consists of two populations of mothers: (a) those who are unable to provide any MOM (e.g., previous double mastectomy, undergoing chemotherapy, or certain medication requirements) and whose infants would require the provision of full feeds, (b) mothers with a shortfall of MOM and whose infants require supplemental feed, often referred to as "top-ups". Policy 2 is limited by an upper boundary of GA (postmenstrual age, that is, weeks corresponding to GA at birth plus elapsed time since birth) defined as a parameter Z (number of weeks) (Fig. 3B). As also shown in the figure, in most circumstances *Beyond Bridging* would follow Policy 1 directly; however, the parameters could be defined in a way such that if $Z > Y + X$, some infants would only have DHM provision as a result of Policy 2.

(D) Birth weight statistics and subsequent growth curves: Information about individual births with reported birth weights per week of GA (BW at GA) was not publicly available in the case study setting. Therefore, the statistical model, as defined by Norris et al. (2017), was used to establish the BW centiles at each GA for singleton babies born between 24 and 40 weeks. The data was further adjusted for multiples using NHS statistics (NHS Digital, 2010, worksheet-"Table-30″). Also, as the PP growth curves for premature babies were not identified we followed the well-recognised assumption that "optimum growth of preterm infants is considered to be equivalent to intrauterine rates" (Fenton & Kim, 2013). Therefore, the current model assumes that singleton infants follow the PP growth curve as defined by Norris et al. (2017), whereas multiples follow the PP growth curve as defined by Buckler and Green (1994).

(E) Feeding Regimes (FRs): In E&W, feed volumes for premature babies in NICUs are not standardised. Further, we were not able to identify empirical data related to actual volumes of feeds. Thus, an online survey of NHS hospitals with specified recommended feeding volumes based on infants' metrics was conducted based on publicly available information. As those were heterogeneous in nature, our findings of the survey are summarised in Table B1 (Appendix B). Based on the survey finding, we defined representative FRs (A, B and C) for three groups/populations of infants (Table 1). **Group A** consist of the most vulnerable infants delivered prematurely- between 22 and 28 weeks GA (in comparison, a full-term delivery is 38–42 weeks GA). 22 weeks is generally considered the lower limit for survival outside of mother's womb. For some other infants, despite being born beyond the 28 weeks GA, if their BW is <1000 g, they would

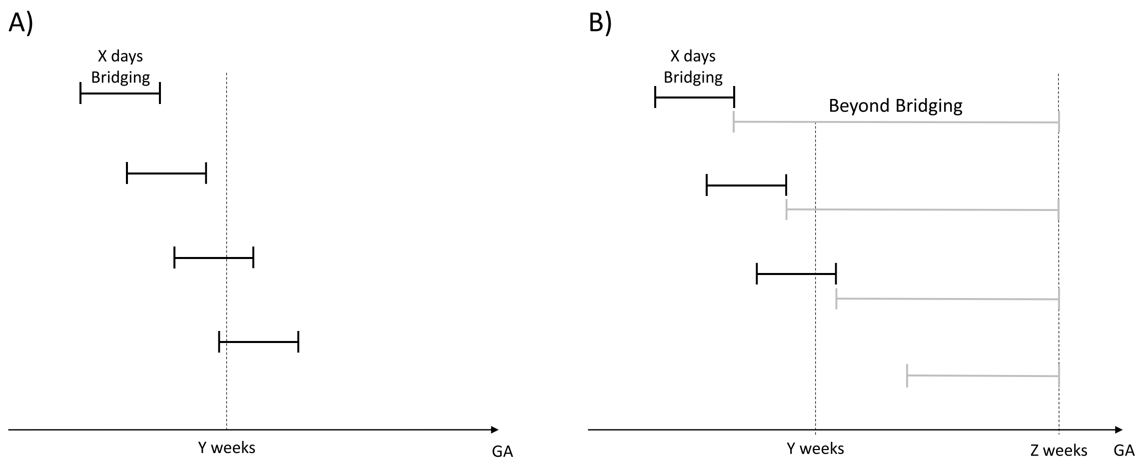

Fig. 3. Outline of model parameters relating to policies. (A) *Bridging* policy starts at any GA that is less or equal to *Y* weeks and continues for a duration of *X* number of days, irrespective of where it has started. (B) *Beyond Bridging* policy could be a continuation of *Bridging* policy for the infants born at or below *Y* weeks GA, or if above *Y* as standalone policies for those infants. The length of DHM supply is defined by the *Z* week boundary.

Table 1
Feeding regimes assumed in the case study.

	Group A	Group B	Group C
GA (weeks)	<28 weeks	<32	>= 32
BW	or <1000 g	–	–
Initial (mL/kg/day)	20	26	45
Increment (mL/kg/day)	20	30	30
Target (mL/kg/day)	180	180	180

still fall in the Group A of FR. **Group B** consist of newborns delivered between 28 and 32 weeks GA. **Group C** comprises of infants delivered beyond 32 weeks GA. For both Groups B and C, infants with birth weights of less than 1000 g are excluded since they are treated as Group A.

5.2. Estimation of the potential DHM demand (Phase II)

The model for the case study was developed based on the framework and used the Monte Carlo simulation (MCS) method. It was implemented in Python, version 3.9 and is publicly available at [https://github.com/m-staff/MCS_DonorHumanMilk_2024]. To estimate the total DHM volume, the step-by-step procedure of the simulation is illustrated in the numbered boxes shown in Fig. 4; the boxes correspond to **steps 1–6** of the framework. While steps 1, 3, 5 and 6 are straightforward calculations, particular attention was required for steps 2 and 4 due to the nature of the externally identified inputs.

Step 2a/2b: At the NHS Trust-level, deliveries are reported over two channels (Hospital Episode Statistics (HES) and Maternity Safety Data Sheet (MSDS)), on 3-weekly GA intervals. The reporting channel was first selected per NHS Trust by selecting the more populated reporting channel. “Expansion” from 3-weekly to daily reporting was then performed probabilistically, following the proportions reported in the weekly statistics for singletons and multiples in NHS Maternity Statistics (NHS Digital, 2010).

As the identified data for numbers of births represents the number of deliveries, that is mothers giving birth rather than the number of babies being born, and therefore not taking into consideration multiple births, the data set needed “expanding” by probabilistically adding the expected number of babies from multiple births. The statistics from NHS Maternity Statistics (NHS Digital, 2010), reporting the number of singletons and multiple births separately per GA was used to allocate the numbers of singletons and multiple births over the reported number of deliveries. Also, as the great majority of multiples’ births are twins (approx. 98 % (ONS, 2019)), to limit the complexity of the model, only one additional infant per multiple birth event was added. Finally, in this step the sex is randomly assigned for each infant, assuming an equal split between males and females.

Step 2c/4: For each infant, the BW centile gets probabilistically assigned; this then defines the birthweight and the growth curve which the infant is assumed to subsequently follow. Please note that, unlike in the framework where steps follow ascending order, our simulation code step 4 precedes step 3 for technical convenience.

A summary of statistical distributions and parameters is provided in Appendix C.

6. Results

By following the steps outlined in our framework, we were able to estimate the potential demand of DHM for our case study. The publicly available birth statistics allowed us to conduct the analysis at two levels. At the macro-level for England and Wales, and the micro-level only for the individual NHS Trusts in England, as no data for Wales was available.

6.1. Findings at the national level for England and Wales

Using the ONS dataset for 2018 for live births in England and Wales (ONS, 2019), for the data source corresponding to step A/B in Fig. 2, we proceeded to compute the DHM potential demand. The calculation involved several combinations of policy parameters for the given population, using 1000 MCS iterations. The set of FRs are fixed (Section 5.1). Two sets of calculations that consider all babies born at or below defined cut-offs (weeks GA) are presented below. The first covers Policy 1 and considers the DHM provision for different lengths of *Bridging* duration (*X*). The second expands the provision of Policy 1 to include the extended provision of DHM, subsequent to *Bridging*, under Policy 2.

6.1.1. Provision estimations for policy on bridging

In the case of *Bridging* alone, we explored how demand would change if all the live births were capped at a specified GA in E&W and were under a single overarching policy for the different combinations of the model parameters. Policy 1 evaluates the provision of DHM for all babies born at or below 30, 32 or 34 weeks GA under four different scenarios pertaining to the *Bridging* length of 3, 4, 5, or 6 days (Fig. 5).

Fig. 5 compares scenarios and how setting parameters at different values influences the estimated volumes required to serve the population. By maintaining cut-off at a constant level (e.g., 30 weeks GA; Fig. 5, blue bars) while extending duration of provision from 3, 4, 5, or 6 days, the mean annual volumes amount to 988, 1683, 2571 and 3660 litres,

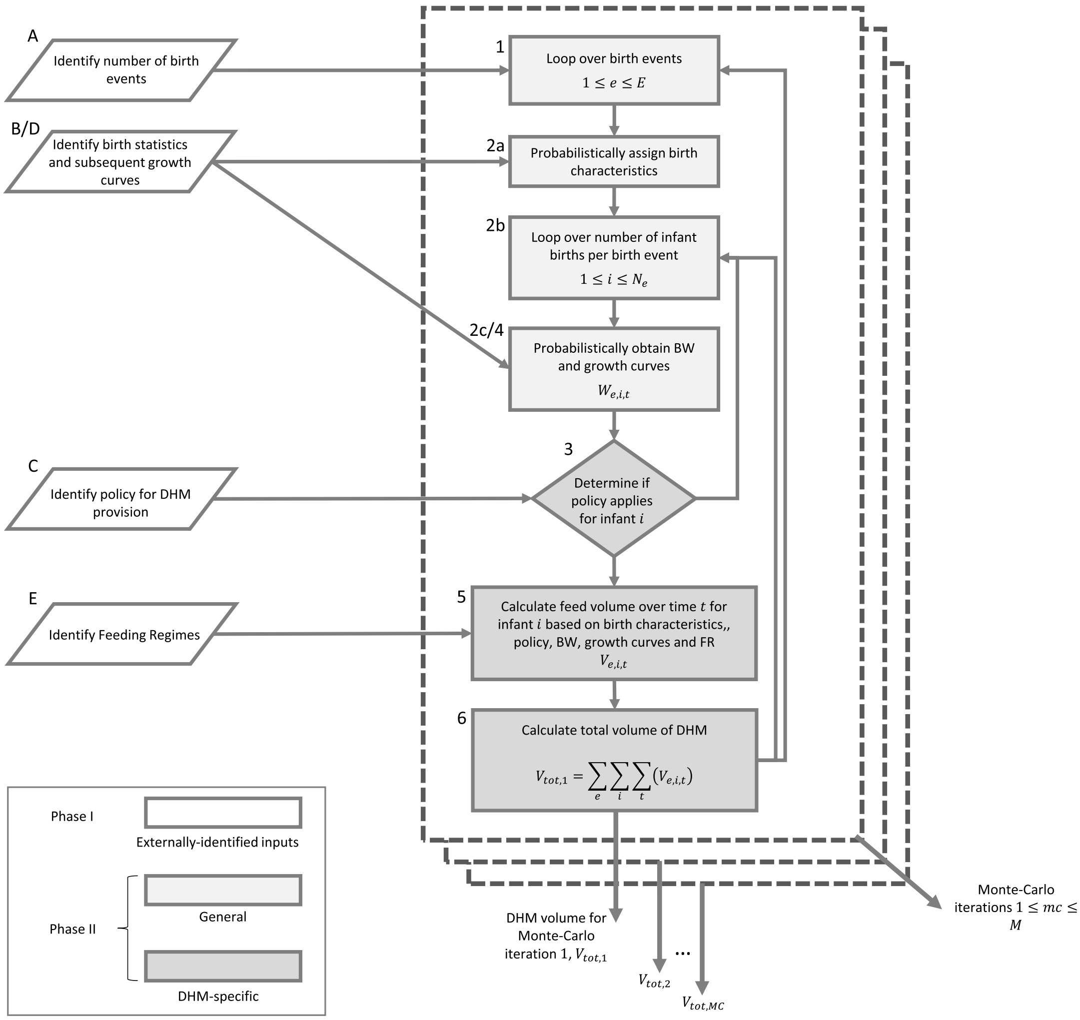

Fig. 4. Monte Carlo simulation outline and flow as implemented in Python.

respectively. Moreover, by keeping the length of provision at a constant level (e.g., 6 days; Fig. 5, rightmost cluster of bars) the model allows examination of the influence of selecting different populations for DHM provision on the volumes of provision. Capping infants included in the Policy 1 at 30 weeks GA (blue bar), 32 weeks GA (orange bar) and 34 weeks GA (grey bar) translates to an estimated annual DHM volume of 3660, 9364 and 26,774 litres, respectively.

6.1.2. Provision estimation when policies on bridging and beyond bridging are considered together

Our model can accommodate Policy 2 as a standalone policy. However, since our current investigation primarily focuses on VLBW and premature infants, who would receive the initial feeding through *Bridging* provision, we present the outputs considering both policies as a stacked histogram (Fig. 6). The mean volumes due to Policy 1 (the same as shown in Fig. 5) and Policy 2 are represented in the histogram as dark-coloured and light-coloured sections, respectively. Fig. 6 captures the same set of scenarios due to Policy 1 as described above. The final mean volume calculated also includes an additional population of infants whose mothers' lactation is either absent or insufficient (achieved by applying *Beyond Bridging* to that subpopulation capped at constant GA≤34). As no reliable statistics explaining the lactational status of the maternal population was identified, after conversations with experts in the field the following parameters were assumed to be within realistic range. 1 % of mothers were assumed to be unable to supply any MOM to their infants (hence, all those infants we allocated 100 % of their dietary needs until 34 weeks postmenstrual age, followed by alternative feeding means), and a further 20 % of mothers were assumed to have undersupply at the constant level of 50 % (hence, infants who qualified for that would result in combinational feeding consisting of 50 % DHM). The mothers were selected randomly through the stochastic Monte Carlo model.

Considering the "most generous" provision scenario calculated in this section (*Bridging* up to 34 weeks GA (*Y*) for six days PP, enriched with *Beyond Bridging* for up to 34 weeks of postmenstrual age (*Z*)), the estimation of the total volume of DHM reached 38,490 litres annually for E&W. This can be contrasted with 988 litres per annum for a scenario with the most "limiting" parameters, which only covers the 3-day provisions for *Bridging* (0 % for Policy 2) for all births at or below 30 weeks GA.

Concerning the highest DHM volumes calculated (annual volume of 38,490 litres), given that there are 13 milk banks in England, if all contributed at equal levels, the volume per milk bank would equate to just below 3000 litres per annum. The average donor donates 8 litres over the donating period (according to authors' experience in the field) which equates to 370 donors per milk bank on average. For the most "limited" policy, requiring 988 litres annually, each milk bank would need to produce under 80 litres annually to provide cover to the most-needy cases within E&W, corresponding to fewer than ten donors per HMB (again with the assumption of 8 litres average donation).

The estimated DHM volume is highly sensitive to assumed policy parameters, particularly those related to GA (blue versus orange versus

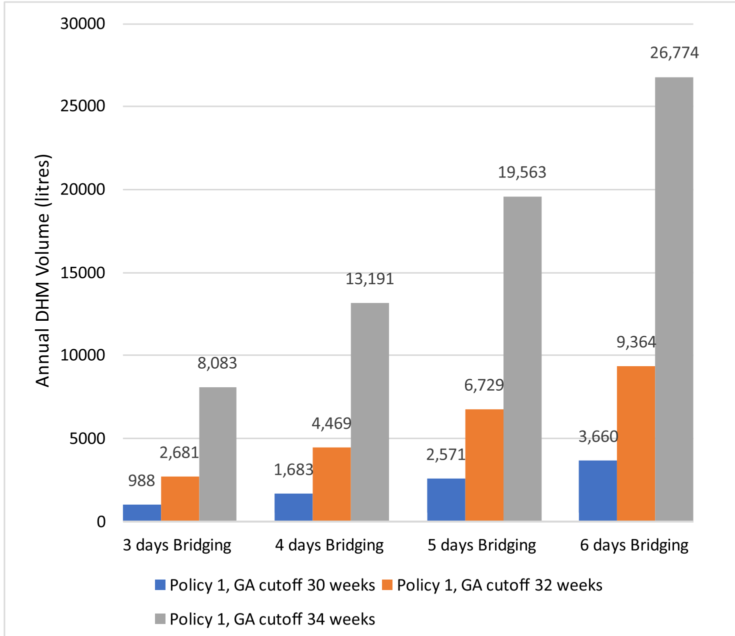

Fig. 5. DHM mean volume estimates for E&W for *Bridging* alone (Policy 1), obtained from 1000 MCS iterations. The data is arranged in clusters of lengths of provision of DHM PP in number of days. The coloured columns represent the estimated demand for subpopulations of babies born at or below 30 weeks GA (blue), 32 weeks GA (orange) and 34 weeks GA (grey). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

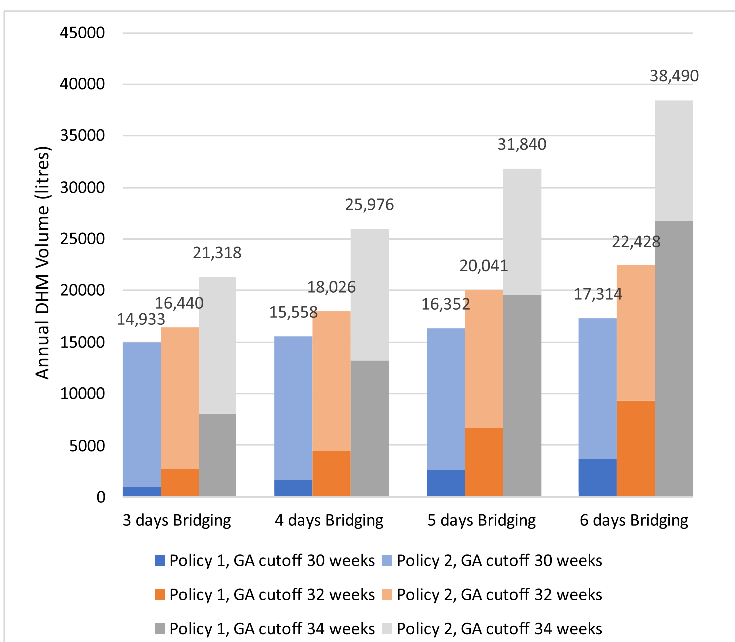

Fig. 6. The volume estimates of DHM for E&W expressed as a sum of both policies. The results are obtained from 1000 MCS iterations. For the outputs, the *Bridging* parameters were set at the same level as in Fig. 5 (dark-coloured section of each bar) enriched with an additional allowance for *Beyond Bridging* (light-coloured section of each bar), with relevant cut-off points for provision stated in a figure legend.

grey within the clusters, especially for the Bridging component shown in Fig. 5). This is because the frequency of births increases rapidly as GA increases (an approximate 15-fold increase between GAs of 24 and 34 weeks), as well as the BW increasing (an approximate 3-fold increase, for the same weeks). The model, therefore, shows that careful consideration is required to make policy choices which could be translated into financial metrics via a cost-benefit analysis, and also to consider operational feasibility (HMB processing and storage capacity, etc.).

Additionally, it is noteworthy that our results suggest a low level of uncertainty at the national level, although this may not hold for smaller regional populations (see Section 6.2). The limited variability persists even when considering the 5th to 95th percentile range. For instance, in the results presented, even for the scenario which incorporates the smallest population of infants ($\leq$ 30 weeks GA) with the shortest provision through Policy 1 (3 days), the error bars would only extend between 981 and 994 (mean 988). As the population size increases, moving closer to full-term pregnancy, the 90 % percentile range yields even smaller error bars relative to the mean. Therefore, after careful consideration, the decision was reached not to include error bars, as they would become practically indistinguishable when visually plotted.

6.2. Findings at NHS trust level in England

Our more granular, Trust-level calculations are limited to England only. This is because The NHS Digital data set (2019) only provides Trust-level data for England (but not Wales).

There is considerable variation in the number of premature births between different Trusts and regions in England (for a map visualising the premature births see Appendix D). We examined the relationship between the number of premature births and the calculated potential demand for DHM. To do so, we selected four Trusts, namely *Barts Health NHS Trust* (Trust A), *Royal United Hospitals, Bath NHS Foundation Trust* (Trust B), *Harrogate and District NHS Foundation Trust* (Trust C) and *Torbay and South Devon NHS Foundation Trust* (Trust D), that displayed different characteristics of the population of premature births. Table 2 captures the summary of results for the estimated annual DHM volume. As the population sizes are significantly smaller than the national level, the number of MCS iterations was increased from 1000 to 10,000. Policy 1 was set to explore three scenarios, i.e., to provide milk for the entire population of infants born at ≤ 30, 32 and 34 weeks; additionally, the same parameters, as described in Section 6.1, were set for Policy 2.

With reference to the 2018 dataset, Trust A is the largest of the four Trusts with 465 live births of ≤34 weeks GA; Harrogate (C) and Torbay Trusts (D) both recorded a total of 25 live births at ≤34 weeks GA. Although Trusts C and D had the same number of births (at ≤34 weeks GA), it is interesting to note that for the scenario where GA cut-off for Policy 1 is set at ≤ 30 and duration for Bridging is six days, the total estimated volumes of DHM amount to very different levels, calculated as means of 8.4 and 21.8 litres, respectively. The differences result from different distributions of GAs at birth, exemplified when comparing the numbers of births at different stages of pregnancy. A closer examination of birth statistics reveals that in Trust C all 25 live births happened between 32 and 34 weeks GA, while in Trust D the birth are skewed towards lower GA with the number for the same 32–34 gestational window only amounting to 15, with a further 10 infants being born with greater prematurity- between 29 and 31 weeks GA. Trusts A and B have an even higher proportion of births at the lower GAs.

In Fig. 7, on the left-hand side we present the results for the case of Policy 1 alone, with 32 weeks GA cut-off *Y*, with the beyond bridging component added on the right-hand side (such that the right-hand side results correspond to the results in the middle section of Table 2). We decided to focus on this population of infants as a likely target, given the BAPM recommendations mentioned previously. While the mean values are higher with the addition of the beyond bridging component (as expected), the uncertainty is also higher (for both the box and whisker range). This is because, for bridging alone, it is assumed that the entire population of eligible infants are allocated DHM. In contrast, in the case of beyond bridging, a random population of infants is assumed to be allocated DHM, due to the assumed randomness of the lactational status. While the mean and median are closely aligned, the varying degree of uncertainty estimated from the MCS shows the importance of conducting such a probabilistic exploration of the potential demand when considering strategic planning.

Another aspect to bear in mind is that as infants born at lower GAs are assigned lower BW based on empirical growth curves, and the individual baby's feeding volume is proportional to weight, the volume required for Policy 1 (*Bridging*) is lower for babies born at lower GAs. Conversely, babies born at lower GA which fall into Policy 2 (*Beyond*

Table 2
Example outputs at Trust level, obtained from 10,000 MCS iterations.

		NHS Trust A *(Barts Health NHS Trust)*	NHS Trust B *(Royal United Hospitals, Bath NHS Foundation Trust)*	NHS Trust C *(Harrogate and District NHS Foundation Trust)*	NHS Trust D *(Torbay and S. Devon NHS Foundation Trust)*
Number of live births GA ≤ 34		465	100	25	25
		Annual volume of DHM (litres) mean, median (interquartile range)			
GA cut-off ≤ 30 weeks (*Y*), 34 weeks (*Z*)					
Bridging duration (*X*)	3 days	390.5, 389.3 (358.1–421.7)	83.6, 82.6 (69.6–96.9)	8.4, 8.3 (5.0–11.3)	18.2, 17.3 (12.0–23.4)
	4 days	405.6, 404.8 (373.9–436.5)	88.0, 86.9 (74.1–100.7)	8.5, 7.8 (5.1–11.2)	19.0, 18.1 (12.8–24.2)
	5 days	426.2, 424.4 (394.4–456.7)	93.7, 92.5 (79.3–106.8)	8.4, 7.8 (5.3–11.1)	20.5, 19.6 (14.1–25.8)
	6 days	452.3, 451.3 (420.5–482.3)	100.4, 99.3 (86.8–113.0)	8.4, 7.9 (5.0–11.2)	21.8, 20.9 (15.6–27.1)
GA cut-off ≤ 32 weeks (*Y*), 34 weeks (*Z*)					
Bridging duration (*X*)	3 days	424.4, 423.5 (391.5–455.3)	92.8, 92.0 (79.0–105.8)	10.6, 10.0 (7.2–13.5)	20.8, 19.9 (14.4–26.2)
	4 days	462.6, 461.2 (430.1–493.7)	103.0, 102.1 (88.8–115.8)	12.0, 11.5 (8.4–15.0)	23.3, 22.5 (17.0–28.7)
	5 days	511.9, 510.5 (479.4–543.0)	115.9, 114.7 (101.7–128.6)	13.6, 13.1 (9.9–16.8)	26.6, 25.8 (20.2–32.1)
	6 days	570.4, 569.0 (539.3–600.9)	131.1, 130.3 (117.3–143.9)	15.3, 14.9 (11.3–18.8)	30.6, 29.8 (24.5–35.9)
GA cut-off ≤ 34 weeks (*Y*), 34 weeks (*Z*)					
Bridging duration (*X*)	3 days	535.8, 534.8 (503.4–566.7)	114.7, 113.6 (101.0–127.3)	20.6, 20.1 (17.4–23.2)	26.8, 25.8 (20.7–31.9)
	4 days	644.9, 643.1 (614.0–674.8)	138.6, 137.6 (125.0–151.2)	28.3, 27.8 (25.5–30.7)	33.0, 32.1 (26.8–38.1)
	5 days	782.2,780.9 (751.3–811.8)	168.8, 167.8 (155.0–181.2)	37.8, 37.3 (34.8–40.2)	41.1, 40.1 (35.1–46.2)
	6 days	938.5, 937.1 (907.1–968.4)	203.2, 202.1 (190.1–215.2)	48.4, 48.0 (45.4–50.8)	50.2, 49.3 (44.5–55.0)

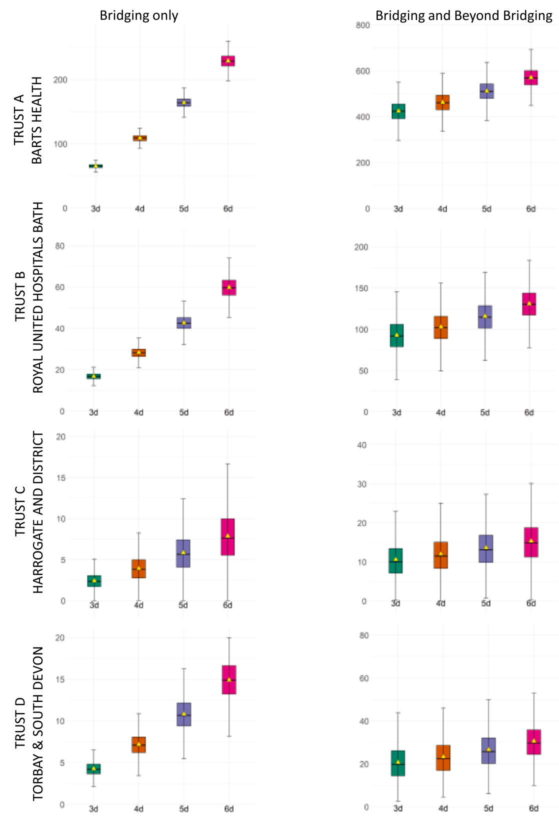

Fig. 7. Box and whisker plots of potential demand calculated for selected Trusts over 10,000 iterations of MCS, for GA cut-off $Y = 32$ weeks and $Z = 34$ weeks. The figure shows the mean (triangle), median (horizontal line), upper and lower quantiles (the box), and the largest and smallest observation within the range of 1.5 times the IQR above the upper quantile and below the lower quantile, respectively (whiskers). Please note that the y-axis scales are not aligned between the individual plots.

Bridging) would remain on this policy for longer, until time Z (see Fig. 3), therefore requiring a cumulatively higher mean volume of DHM when compared to babies born later. Therefore, the ratio of DHM mean volume due to Policy 1 and Policy 2 varies between Trusts; Trusts with proportionally more premature births have a lower fraction due to Policy 1. This indicates the importance of taking into consideration the birth characteristics of the setting when estimating potential DHM demand for planning purposes.

6.3. *Assumptions, limitations, verification and validation of the model*

The model was built based on the following assumptions:

- The number of days that DHM is provided for in the hospital setting is assumed to be the same over all hospitals. As mentioned above there are no nationally agreed guidelines for use, with different policies across the UK.
- The GA upper boundary for provision, i.e., the age at which provision stops which could be set to differ between different policies. While as recently published by BAPM (2023)the target population to be offered DHM is specified as infants born $\leq$ 32 weeks GA, this is a recommendation, rather than a strict guideline. As such, it is expected to be interpreted and adopted at varying levels within different contexts.
- Assumptions related to the demand/required milk volumes as a function of GA and birth weight at delivery, and subsequent weight gain.

For micro-level (NHS Trust) analysis, a limitation is the assumption that infants remain in the same hospital as they were born. However, in some critical cases, neonates may be moved to more specialist units in different NHS Trusts for specialist care. Additionally, wastage is not considered. If containers of DHM are not shared among infants, wastage may occur, which may lead to an increase in demand from certain Trusts. Ideally, long use-by-dates would be provided by HMBs to further reduce potential wastage, but this is not considered in the model. The needs for feeding of infants on the postnatal units or in the community were not taken into account in this model, but will be considered in future work.

In terms of data quality, the national-level ONS data used can be considered highly reliable. The main limitation is that postnatal deaths are not factored into the analysis. However, the prevalence of postnatal deaths is low; around 0.3 % (ONS, 2019)). As such, the resulting impact on the DHM estimates is also likely to be low. NHS Digital data for the Trusts had some missing data for reported GA (based on our analysis of the combined HES and MSDS dataset, it is around 7 %) and will lead to a moderate under-estimation of demand. The <1 % rate of combined stillbirths and postnatal deaths (ONS, 2019) are also unaccounted for, which would lead to a minor overestimation of demand.

Currently, insufficient secondary data is available to validate our model. Thus, we had to rely on face validity with domain experts. Our approach is supported in the simulation literature. For example, a literature review on hybrid simulation by Brailsford et al. (2019) found that 10 % of the 109 papers which included either framework and application (similar to our paper) or only an application, conducted face validity with domain experts. Additionally, in terms of model verification, a deterministic spreadsheet model was developed for cross-verification purposes which allowed the mean predicted DHM volumes to be compared for some simplified scenarios.

Based on reviewer comments (reviewers have been acknowledged), we complemented our MCS model with a Qualitative System Dynamics (QSD) model. The use of QSD is likely to enhance our communication with the stakeholders including policymakers who are amongst the key target audience for the present study. However, while within the realm of systems thinking, Richmond recommended applying the bifocal approach of keeping an eye on both “the forest” (big picture) and “the trees” (the details), we decided to focus on the logical “vantage (..) relative to the fray” (Richmond, 1994), and as such to limit the model to the NICU setting. This is in line with Forrester’s concept of “powerful small model(s) (…) [with] the insights sharply focused” (Forrester, 2007, p 362). The scope of the MCS model provided us a preliminary reference to define the scope of the QSD model using a causal loop diagram (CLD). As described in the section on MCS (Section 5), the calculation of potential demand, which represents a “ceiling” volume estimate, depends on the population of infants, mothers (including lactational status), and provision policy, hence in CLD we captured variables that relate to similar factors which feed into the central variable of *Total NICU DHM use* (Fig. 8). We also decided that as the potential demand estimations, beyond potentially influencing policymaking, are also intended to enable service planning at the lower echelon of the supply chain (the milk banks), the supply provided by HMBs to the hospital is also important to be included in our CLD (Fig. 8). In the diagram, the solid blue arrows and the dotted red arrows, are used to represent positive and negative correlations between pairs of variables, respectively, illustrating the interactions and influences within the system.

Balancing loop B1 (Fig. 8) illustrates that higher efforts invested in lactational support, whether arising organically from perceived benefits

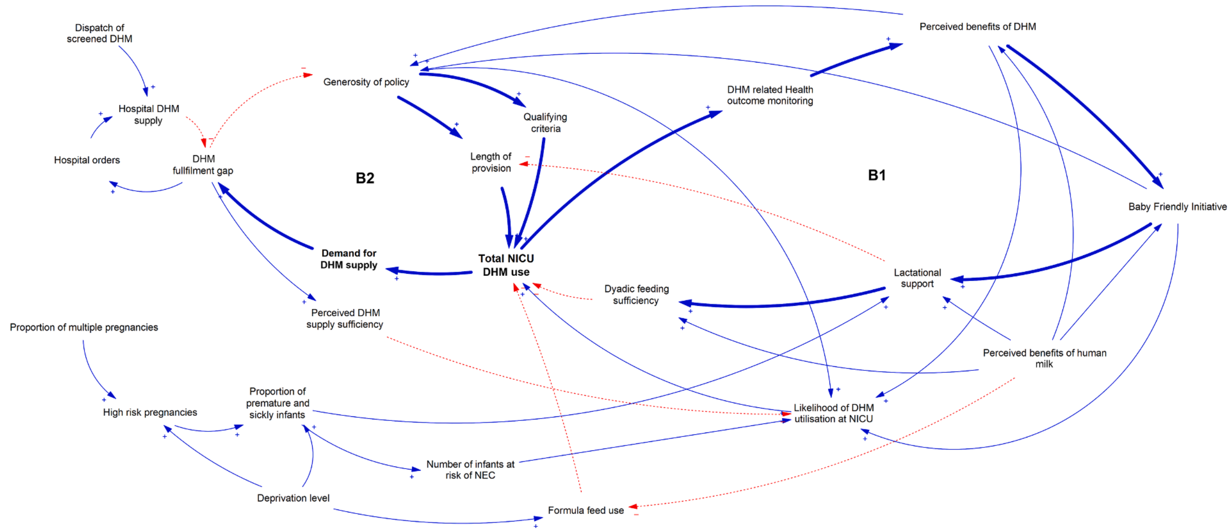

Fig. 8. Qualitative System Dynamics Causal Loop Diagram for DHM demand estimation in hospital NICU units using Vensim software. Dotted red arrows correspond to negative correlations whereas solid blue indicate positive correlations. Please note that bold lines are purely used to facilitate visual access to the described loops B1 and B2 in the main text. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

of human milk, or through formal undertakings by the hospitals such as engaging in the Baby-Friendly Initiative (BFI)[2] (which itself is likely positively correlated with perceived benefits of human milk), increase the perceived benefits of DHM over time.

Moving to the *Generosity of policy* surrounding the provision of DHM, this also hinges on its perceived benefits (again, either directly or through the influence of the BFI). A more generous policy would typically allow for longer provision per infant, and/or broader qualifying criteria of provision (this positive relationship is illustrated, within B2 loop (Fig. 8), using blue arrows from *Generosity of policy* to *Length of provision* and *Qualifying criteria*, respectively). This, in turn, is likely to lead to higher *Total NICU DHM use*, thereby leading to greater *Demand for DHM supply*. This increased demand is likely to highlight a *Perceived DHM fulfilment gap*, which, when closing the loop, could negatively impact and decrease the *Generosity of policy*. This cycle continues until a new cycle, where supply sufficiency of DHM amongst practitioners is perceived as plentiful due to decreased DHM use, hence reducing the DHM fulfilment gap. This reduction is likely to translate to a more generous policy for provision. This again, represents a balancing loop B2, which is likely to represent a "goal seeking" behaviour of the system over time.

7. Discussion and conclusions

Building on identified gaps in knowledge and with an understanding of the scale of demand for donor human milk, this study presents a generic framework for DHM volume estimation. Our framework guides the identification of the components that we understand to be important in DHM demand estimation. By following a stepwise process, the framework can be applied to investigate the potential demand of feed volumes required by different populations of infants. Given the WHO recommendations for VLBW infants to be fed with DHM (in cases where there is a shortfall of mother's milk), we developed a model that focussed on estimating the potential demand for DHM for infants born and cared for in hospitals and neonatal care settings. However, the framework can also be applied in other contexts.

The national results presented in Section 6.1 for England and Wales show a high sensitivity of DHM volume to policy for DHM provision, which means that careful consideration would be needed for any policy defined at the national level, as slight adjustments can have significant implications on the cost to the NHS, and the capacity required in the DHM supply chain. In particular, a steep non-linear increase in demand occurs in the case that policy for provision is extended to higher GAs as a result of the combination of a higher number of births and babies with higher birth weights requiring greater volumes of feed. The modelling at the local level provides a means for HMBs and hospitals to assess their own required DHM volumes as a function of policy, and hospital/catchment size, which varies considerably across NHS Trusts in England as shown in Section 6.2. The importance of using local birth characteristics when estimating potential DHM demand is demonstrated; particularly noteworthy is the impact of GA distribution on the considered policies. Additionally, as indicated previously, while our deterministic spreadsheet model based on average calculations might provide an option for rapidly obtaining estimates and capitalising on the familiarity and ease of use, e.g. using Excel and addressing the challenge of successful real-world implementation of OR models (Melão & Pidd, 2003) in healthcare, it is only likely to be useful with large enough populations, such as for the national analysis presented herein. On the other hand, utilisation of Monte Carlo probabilistic techniques on smaller, local level populations provides far superior insights. By incorporating randomness inherent to real life systems at multiple levels, our MCS model allows the uncertainty of the obtained demand estimates to be assessed.

While the present study focussed on England and Wales, the generalised methodology applies to other settings. As our case study calculations used different data at the local and national levels, it aptly reflects the adaptability of our model to different data sets. Also, by applying different parameterised policy settings for obtaining DHM demand estimates, we show the adaptability of our probabilistic Monte Carlo model that can be used for policy experimentation to support strategic planning.

The Human Milk Foundation are using the model to help develop a strategic approach to prioritising the neonatal provision of DHM alongside their community-based DHM and lactation support programme. This will form a future basis for validation, extending the

[2] The Baby-Friendly Initiative is a global program aimed at promoting and supporting breastfeeding practices in healthcare facilities to ensure optimal infant health and development. It includes guidelines and protocols for the safe and ethical use of donor human milk, emphasising its importance in providing essential nutrition and support to infants when breastfeeding is not possible. https://www.unicef.org/documents/baby-friendly-hospital-initiative#:~:text=UNICEF%20and%20WHO%20launched%20the,new%20mothers%20and%20their%20infants.

current face validation with empirical data.

Our MCS results indicates the need for careful consideration of the relationship between policy choices for DHM provision and the resulting demand. This is further supported as presented in our QSD model, which beyond hard, better quantifiable aspects incorporated in the MCS calculations, highlights also softer aspects relating to the perceptions of stakeholders. QSD provides a complementary tool for gaining a deeper understanding and directionalities of the system behaviour, showing influencing factors and feedback loops which would influence actual realised demand. Once experimented with and considered more broadly, the methodology for demand estimation introduced is likely to have significant implications to multiple stakeholders involved in the human milk supply chain, at operational and strategic levels of planning. Understanding demand is essential for HMBs and would enables strategic planning for future service provision. HMBs may, for example, adapt recruitment processes, adjust screening service contracts, consider equipment levels and staffing for donor support, DHM storage and processing. They would also likely need to manage stored milk reserves to meet demand whilst minimising wastage due to the limited shelf-life of the DHM. Also, a deeper understanding of the potential demand bound to the population served is likely to bring operational benefits, such as more informed decisions of the ability to fulfil emergency or external orders. Also, both HMBs and the hospital/ clinical teams are likely to become more empowered when deciding on inventory strategies, that would facilitate effective management of fluctuations in supply. Moreover, as the results generated by implementing the framework are likely to shed light on the potential scale of DHM requirements of the population in question to policymakers, it is likely to be instrumental when designing geographically-bounded provision policies/ guidelines. Furthermore, the implications and feasibility, when considering the expansion of geographical catchment by individual milk banks should be more readily realised when the decision-making environment is enriched by the use of our proposed methodology.

When developing our framework, we took extra care to make sure the generalisability for application to other settings could be achieved. On the other hand, when implanting frameworks at the case study level through MCS we paid special attention to identify specific local data sources, for instance in the case of feeding regimes which had to be extrapolated from local feeding guidelines rather than directly from empirical data. This points to future opportunities of data collection and dissemination, however as this relates to clinical and large-scale data collection, it is likely that it falls outside the scope of our study. However, future local collaborative undertaking of more diligent data collection of DHM usage at hospital sites to validate our model is a promising and necessary direction for future research. Leveraging the QSD methodology, we are currently exploring avenues for wider stakeholder engagement in the human milk supply chain, in order to deepen our understanding of a wider array of variables, that are likely to allow more nuanced understanding of supply-demand dynamics for DHM. For the future study, we are also planning to collect quantitative data that would aid us in the development of a System Dynamics model.

In summary, there is no known literature on DHM demand estimation. Thus, the paper is a novel contribution to the literature on milk banking and associated management and policy aspects. The work also has the potential for impact as it has implications for public health as it argues for a broader provision for DHM. Our contribution to practice relates to improved planning and evaluation of different policy options, with the indirect benefit of helping advance breastfeeding rates. Additionally, existing literature on demand estimation relies mostly on deterministic formulations. Therefore, our work also addresses an identified research gap in using Monte Carlo simulation for demand estimation in healthcare. This well-established and understood method will provide valuable insights and establish a reliable base for future resource planning, such as inventory planning, workforce management, and policy development, contributing to more resilient decision-making.

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Declarations of competing interest

The authors declare that they have no competing interests to declare, except NS and GW work as consultants in the field of human milk banking.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejor.2024.05.023. The MCS code is avaliable at https://github.com/m-staff/MCS_DonorHumanMilk_2024.

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