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Red Blood Cell Transfusion Strategies in Paediatric Leukaemia: Influences on Quality of Life and Survival Outcomes – A Scoping Review

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Abstract

Introduction: Haematological malignancies (*blood cancers*) include leukaemia, lymphomas, and myelomas. These cancers arise from genomic mutations affecting blood-forming tissues or immune system cells often leading to chronic anaemia resulting from the malignancy alone or its treatment regimens. Various treatment modalities can be imposed including, red blood cell (RBC) transfusions. Patient outcomes, which may be measured by survival rates, quality of life (QoL), and the risk of complications related to transfusions, can be influenced by transfusion strategies. Current guidelines emphasise tailored approaches that consider the patient's overall treatment plan, haemoglobin levels, and clinical condition.

Methods: Articles that included paediatric subjects from 0-18 years old and diagnosed with any subtype(s) of leukaemia and underwent any method of RBC transfusion strategies were included. The review adhered to the Joanna Briggs Institute methodology for conducting scoping reviews, and the PRISMA-ScR extension for systematic reviews and meta-analyses. Following a search strategy across multiple databases, 6 papers were identified and included in the review.

Results: From the six included articles, two articles focused on liberal RBC transfusion strategies and three articles on restrictive and liberal RBC combination transfusion strategies. Results from the included articles reported lesser mortality rates in paediatric administered with liberal transfusion strategies. Evidence relating to QoL outcomes was not substantially reported across the included articles.

Discussion: A liberal RBC transfusion was the commonest undertaken approach in paediatric subjects across the included articles. Nair Manjusha et al., 2018, Kerri Nottage et al., 2013, and Robitaille et al., 2012 concluded that a liberal RBC transfusion strategy was most effective in comparison to restrictive strategies. Most articles reported that a liberal RBC transfusion strategy resulted in less mortality. QoL was not substantially mentioned across the articles. Due to the limited number of articles, results are unclear regarding which strategy is most appropriate.

Conclusion: Results of this review present inconclusive findings regarding which strategy is most appropriate in the management of paediatric subjects diagnosed with haematological malignancies. Although a liberal transfusion strategy reported lesser mortality, increasing literature which rectify the limitations observed across the included articles is required.

Keywords: leukaemia; liberal; paediatric; QoL; RBC transfusion; restrictive; survival

Introduction

Leukaemia *(Leukemia)* refers to a group of malignancies of the blood and bone marrow [1]. Leukaemia occurs when a single, abnormal haematopoietic stem cell replicates and produces large numbers of identical or 'clonal' cells [2]. Haematopoietic stem cells (HSCs) are housed in bone marrow structures and employ a hierarchical function in producing blood cells and controlling inflammation. In subtypes like Acute Myeloid Leukaemia (AML) and Chronic Myeloid Leukaemia (CML), HSCs mutate and initiate a new generation of leukaemic stem cells, commencing the progression of the disease. These leukaemia stem cells self-renew, which may cause the disease to return even after treatment has been administered. The classification of leukaemia has been

divided into four major subtypes, which depend on whether the disease is acute or chronic in nature and also based on which white blood cell (myeloid or lymphoid) has been mutated [3]. These subdivisions target different types of blood cells within the bloodstream. Leukaemia is subcategorised based on 'morphology, immunophenotype, cytogenetic and molecular abnormalities' which are attributable to the respective subtype [4]. There are five main subtypes, which include: (i) Acute Lymphocytic Leukaemia (ALL), (ii) Acute Myelogenous Leukaemia (AML), (iii) Chronic Lymphocytic Leukaemia (CLL), (iv) Chronic Myelogenous Leukaemia (CML), and (v) Chronic Myelomonocytic Leukaemia (CMML) [5].

Leukaemia can frequently result in malignant cells occupying space within the bone marrow and adversely

impact normal blood cell production. As a result, RBC transfusions are administered to restore RBC and blood volume. RBC transfusions also aid in relieving anaemic symptoms in patients with leukaemia, such as, pale skin, fatigue, and shortness of breath. Due to these unique clinical manifestations and myelosuppressive chemotherapy treatment, maintaining a higher haemoglobin level in this patient population may be more effective than the standard strategy of maintaining a haemoglobin level of 70 g/L in improving QoL outcomes [6].

Leukaemia across the paediatric demographic accounts for approximately 33% of all new cancer cases for 0-14 year-olds and accounts for 31% of all reported paediatric deaths [7]. The incidence of childhood leukaemia can originate from genetic factors, environmental and chemical exposures, and altered patterns of infection during crucial stages of development [8]. paediatric leukaemias are typically diagnosed within the first year of life [9] and are rare entities, with fewer than 5,000 cases in the US each year [10]. Paediatric patients presenting with leukaemia are largely treated with chemotherapy and stem cell transplants of the bone marrow. Intravenous transfusions of stem cells from the blood and bone marrow from healthy donors are utilised alongside extensive radiotherapy and chemotherapy to eradicate abnormal cell production [11].

The life expectancy of paediatric patients with leukaemia is up to five years after diagnosis [12]. The five-year survival rate is accepted as a method by which cancer outcomes are measured in this population. Patients diagnosed with ALL have a 90% survival rate over five years, while paediatric patients with AML have lower survival outcomes between 60-70% [13]. For paediatric patients with leukaemia, QoL measures can be adversely impacted. Previous studies on ALL patients, both during treatment and in long-term survivorship, have shown that many experience reduced health-related quality of life (HRQoL), with some reporting persistent challenges years after treatment ends [14].

As RBC transfusion strategies are critical in managing bleeding and anaemia [15], these strategies are defined by the patient's clinical condition and the haemoglobin thresholds used to guide when a patient is transfused and mediate the level of blood and what blood components a patient receives [16]. Transfusions of healthy blood expose the patient to 'soluble and cell-mediated alloantigens, cytokines, and other cellular components' [17]. There are two main RBC transfusion strategies evaluated across the literature: (i) liberal strategies and (ii) restrictive strategies. A restrictive transfusion strategy seeks to maintain a lower haemoglobin level, usually between 7.0 g/dL and 9.0 g/dL, whereas a liberal transfusion strategy aims to maintain a higher haemoglobin level between 9.0g/dL and 10.0 g/dL [18].

Across the literature involving adult subjects, restrictive strategies are more commonly observed as more applicable across various care environments and can be favoured for improved patient outcomes in comparison with liberal strategies, although little is known about their applications among paediatric subjects [18, 19]. Several considerations need to be assessed when transfusing paediatric subjects, such as age, clinical stability, underlying health conditions, neurodevelopmental status, oxygen requirements, anaemia metrics, and other risks to undergoing transfusions [20].

RBC transfusion strategies may significantly affect QoL and survival outcomes in paediatric patients with leukaemia due to their role in managing treatment-related anaemia and improving oxygen delivery to tissues [21]. Optimal transfusion practices can help reduce fatigue, enhance physical functioning, and support overall well-being during intensive therapy [22]. Although overly liberal or restrictive transfusion thresholds may carry risks, such as increased exposure to transfusion-related complications or inadequate symptom management, respectively [23]. Tailoring transfusion strategies to individual paediatric patient needs may play a crucial role in both short- and long-term outcomes.

Therefore, a scoping review focusing on QoL and survival outcomes in paediatric patients is apt and is the crucial first step in assessing whether RBC transfusion strategies influence paediatric outcomes.

Objectives
1. Which RBC transfusion strategies are undertaken in paediatric patients (0-18 years old) diagnosed with any subtype of leukaemia?
2. Which RBC transfusion strategy is associated with increased survival rates in paediatric patients (0-18 years old) diagnosed with any subtype of leukaemia?
3. Which RBC transfusion strategy is associated with increased QoL in paediatric patients (0-18 years old) diagnosed with any subtype of leukaemia?

Materials and Methods
2.1. Protocol and Registration
This scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-ScR) [24] guidelines, as well as the Joanna Briggs Institute guidance for scoping reviews [25]. These items can be acquired through the supporting web addresses:
https://www.prisma-statement.org/extensions
https://jbi-global-wiki.refined.site/space/MANUAL/355862497/10.+Scoping+reviews
Additional registration for this scoping review was not required.

2.2. Eligibility Criteria
The PCC framework was applied to classify appropriate data sources for eligibility in this scoping review, before implementing a specified search strategy.

2.2.1. Inclusion Parameters

1. Population: paediatric patients diagnosed with any subtype(s) of leukaemia. For the scope of this review, paediatric subjects are characterised as human beings between the age of 0-18 years old. Data sources that report on both adult and paediatric populations will require the latter to be independently reported.
2. Concept: Articles which report on any method of RBC transfusion strategy(ies).
3. Context: Articles must report at least one of the following: (i) types of transfusion strategies within the target population; (ii) reports of liberal or restrictive RBC transfusions in paediatric patients diagnosed with leukaemia; (iii) QoL or survival rates of RBC transfusion strategies in the management of 'paediatric patients diagnosed with leukaemia.
4. Other: Articles published in the English language that were available for review between the 01.01.25 and 10.02.25.

2.2.2. Exclusion

(i) Articles which report on paediatric patients without leukaemia or paediatric patients with leukaemia not undergoing any RBC transfusion strategies (ii) Articles that refer to adult demographics (iii) Articles which primarily assess alternative treatment regimens in the management of this patient population. (iv) Articles which are published in any language apart from the English language. (v) Any article which fails to align with the objectives of this study.

2.3. Information Sources

The following databases were searched for relevant literature: PubMed, Cochrane Library, MDPI, Wiley, Elsevier, and Taylor & Francis.

2.4. Search

A preparatory search of Google Scholar was conducted to map the size and scope of the available primary, secondary, and grey literature on the subject prior to developing a search string. A series of keywords were applied in this process outlined in – '2.3.1. Keywords used in initial search of Google Scholar'. Once the search string was developed, it was trialled in both Google Scholar and PubMed and was amended as necessary. Once the search string, '2.3.2. Complete search string,' was developed, comprehensive searching was conducted across PubMed, Cochrane, MDPI, Wiley, Elsevier and Taylor & Francis and results were reviewed for inclusion.

Table 1. Keywords used in initial search of Google Scholar

Population Parameters	*Paediatrics with Leukaemia (<18)*
Timeline Parameters	*None*
Language Parameters	*Only articles published in English*
Keywords	*Red blood cell transfusions, paediatrics, leukaemia, quality of life, survival*

2.4. Complete Search String

("red blood cell transfusion" OR "RBC transfusion" OR "blood transfusion") AND ("paediatric leukaemia" OR "pediatric leukemia" OR "childhood leukaemia" OR "childhood leukemia" OR "acute lymphoblastic leukaemia" OR "ALL" OR "acute myeloid leukaemia" OR "AML") AND ("transfusion strategy" OR "transfusion threshold" OR "transfusion practice" OR "transfusion protocol") AND ("quality of life" OR "HRQoL" OR "health-related quality of life" OR "well-being" OR "functional status") AND ("survival" OR "mortality" OR "overall survival" OR "disease-free survival" OR "treatment outcome" OR "clinical outcome")

2.5. Selection of Sources of Evidence

Comprehensive database searching was conducted from 01.01.25 – 10.02.25. For all searching results, subsequent works cited and recommended articles were evaluated for relevant information for inclusion in this review. A phased process was adhered to and aided the selection of sources of evidence process.

Phase 1 - Identification: All databases were extensively searched, with all resulting articles alphabetically arranged in Microsoft Excel in order of author and year.

Phase 2 – Screening: From the database search, the titles and abstracts of all resulting articles were evaluated for eligibility in the review. Articles were directed to phase 3 of the sources of evidence selection process if an abstract wasn't obtainable.

Phase 3 – Eligibility: Selected articles that were likely eligible after title and abstract screening continued to be full text evaluated. A mentor at the URNCST Journal mentored paper initiative was consulted in cases of uncertainty in relation to article eligibility.

Phase 4 – Inclusion: Complete documentation of all articles that were deemed eligible were logged on Microsoft Excel and included in this review.

All four phases of the selection of sources of evidence process were conducted by a novice researcher studying the BSc Public Health Sciences, UCC.

2.6. Data Charting Process

All articles selected for inclusion were evaluated independently and information that is relevant to the objectives of the review was extracted during the data charting process. Pertinent information and data chosen for inclusion will be charted with the utilisation of extraction

tables. Extraction tables will organise all participating information clearly.

2.7. Data Items

Extraction tables were utilised to clearly collate all data obtained across each research article. A summary of information related to the population itself, and the design features of each research paper was presented in the first extraction table. A second extraction table will summarise all information regarding specified RBC transfusion strategies and categorised data across all studies. All included extraction tables related to each objective stated at the beginning of this scoping review.

2.8. Synthesis of Results

The summarisation and charting of included data sources and relevant information was executed precisely to ensure that results are clearly assembled. Collation and summarisation of available data reflected the most appropriate method of data synthesis, as every article recorded its results differently. The synthesis of results was organised according to the objectives of this review.

Results

3.1. Selection of Sources of Evidence

The completed searching strategy is depicted in Figure 1: PRISMA Flowchart below. Overall, a total of 66 resulting articles were identified during the search of PubMed, Cochrane, MDPI, Wiley, Elsevier, Taylor & Francis. All resulting articles were imported to Microsoft Excel where 5 duplicates were removed. 61 articles underwent title and abstract screening with 24 articles excluded at this point. 37 articles underwent full-text investigation, and 31 articles were subsequently excluded. Overall, 6 articles were included in this review.
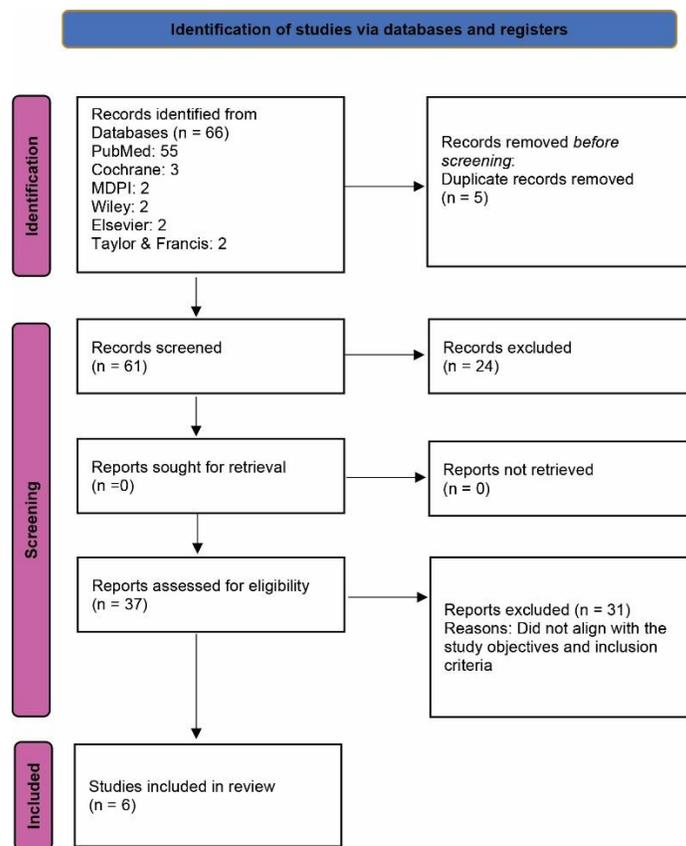

Figure 1. PRISMA Flowchart [24]

3.2. Characteristics of Sources of Evidence

The scoping review included 6 articles, including three research reports, one observational study, one clinical trial, one randomized pilot, and one respective study. The articles included were published between 2012-2024 and had a wide geographical range. Articles originated in India, USA, Canada, Poland, and Jordan. The majority of included articles recruited their subjects from universities and/or medical centres. Varying sample sizes were observed across the included articles, with the smallest sample size consisting of 6 subjects and the largest sample size consisting of 982 subjects. The age range across the included articles ranged from 0-18 years old. In-depth characteristics can be found in Table 1 below.

Table 2. Characteristics of Sources of Evidence

	Author and year	Geographical characteristics	Subject source	Time range of data collection	Study design	Number of subjects	Age of included subjects (Y = years)
1	Nair Manjusha et al., 2018 [26]	Trivandrum, Kerala. India	Departments of Pediatrics and Transfusion Medicine, Regional Cancer Centre	January-August 2016	Observational Study	66	1-14Y
2	Robitaille et al., 2012 [27]	Canada	Canadian Blood and Marrow Transplant Group	NR	Clinical Trial	6	1-18Y
3	Kerri Nottage et al., 2013 [28]	Tennessee, United States of America	St. Jude Children's Research Hospital (St. Jude)	1962-2004	Research Report	982	5-10Y
4	Malgorzata Sawicka-Zukowska et al., 2024a [29]	Bialystok, Poland	Department of Pediatric Oncology and Hematology, Medical University of Bialystok, Jerzego Waszyngtona 17, 15-274 Bialystok, Poland	January 2010-December 2019	Research Report	551	0-18Y
5	Malgorzata Sawicka-Zukowska et al., 2024b [30]	Bialystok, Poland	Department of Pediatric Oncology and Hematology, Medical University of Bialystok, Jerzego Waszyngtona 17, 15-274 Bialystok, Poland	January 2010-December 2020	Research Report	88	0-18Y
6	Khaldoun Alkayed et al., 2013 [11]	Al-Jubeiha, Amman, Jordan	Department of Pediatrics, King Hussein Cancer Center	2007-2009	Respective Study	120	<19Y

NR: Not reported

3.3. Results of Individual Sources of Evidence
Variation existed between the included articles regarding the transfusion criteria and exact transfusion protocols utilised across the sample populations. Transfusion criteria refer to specified haemoglobin levels which determine how many units of blood are transfused, while the transfusion protocol aims to optimise patients' QoL outcomes. Many articles reported on some type of quality of life or survival rates assessment.

3.4. Synthesis of Results
Leukaemia type
Six of the included articles stated which subtype(s) of leukaemia the subjects had. ALL and AML were reported in five of the six studies, MDS was reported in one of the six articles, and CML was subsequently reported in one of the six studies.

RBC Transfusion Strategy, Criteria and Protocol
Two of the included articles investigated liberal transfusion strategies exclusively, with three articles looking at both liberal and restrictive. Reports from Four included articles stated that the criteria for RBC transfusion strategy were when haemoglobin concentration levels fell below 8 g/dL [26, 28-29, 30]. Four articles reported that Total transfused volume (mL/kg) protocols were utilized across the study subjects [26, 27, 29, 30]. One article reported the dosage prescribed to the study subjects [27].

Quality of Life

Most articles reported on some form of QoL impacts or survival rates among the study subjects. Variation in survival rates were observed across the included articles whereby one article reported that 5 out of 6 subjects were still alive at a 2-year follow-up [27], one article reported improved survival rates with 10 or more transfusions resulting in increased survival surpassing ten years [28], and two articles reported no significant difference between low/high volume of transfused blood on survival [29-30]. The last study subsequently compared the number of living subjects (n=132) to that of the deceased (n=13) [11].

Table 3. Results corresponding both objectives across the included articles: (i) What RBC transfusion strategies are undertaken in paediatric patients with leukaemia (ii) Which RBC transfusion strategy is associated with improved survival rates and/or QoL in paediatric patients diagnosed with leukaemia?

Author & Year	Leukaemia Subtype	RBC Transfusion Strategy	Transfusion Criteria	Transfusion Protocol	Quality of Life (QoL)	Survival Rates
Nair Manjusha et al., 2018 [26]	Acute lymphoblastic leukaemia (ALL) Acute myeloid leukaemia (AML)	Liberal	Transfuse at 8-10 g/dL	Total transfused volume (mL/kg); Mean (SD) All leukaemia patients 47.82 (41.35). ALL patients 37.02 (27.58). AML patients 111.25 (53.03).	NR	NR
Robitaille et al., 2012 [27]	Acute myeloid leukaemia (AML) Myelodysplastic syndrome (MDS)	Liberal and restrictive	NR	RBC Dosage: 10 to 15 mL/kg unless otherwise dictated	NR	5/6 patients still alive at 2 years follow up. 1/6 patients died 6 months post transplantation.
Kerri Nottage et al., 2013 [28]	Acute myeloid leukaemia (AML) Acute lymphoblastic leukaemia (ALL) Chronic myeloid leukaemia (CML)	Liberal	Hemoglobin concentration falls below 8 g/dl, or if symptoms of anemia develop or worsen.	NR	NR	**10+ transfusions:** 5-10 years survival rate (116 subjects) =>10 years survival rate (280 subjects) **1-9 transfusions:** 5-10 years survival rate (82 subjects) >10 years survival rate (403 subjects)
Malgorzata Sawicka-Zukowska et al., 2024a [29]	Acute myeloid leukaemia (AML) Acute lymphoblastic leukaemia (ALL)	Liberal and restrictive	Hemoglobin concentration falls below 8 g/dl	(A) total amount of received blood in milliliters (during the whole treatment process), (B) total amount of received blood per kilogram of body weight, and (C) total number of received transfusion units—episodes of transfusion.	NR	No significant differences in survival between patients treated with low/high volume of transfused blood, especially in the group of patients with ALL. Subjects with AML and higher volumes of the blood transfused seemed to have higher chances of survival (HR = 2.62 [low versus high]; p = 0.1289)

Author & Year	Leukaemia Subtype	RBC Transfusion Strategy	Transfusion Criteria	Transfusion Protocol	Quality of Life (QoL)	Survival Rates
Malgorzata Sawicka-Zukowska et al., 2024b [30]	Acute myeloid leukaemia (AML) Acute lymphoblastic leukaemia (ALL)	Liberal and restrictive	In most patients, transfusion was performed in cases of lower than 8 g/dL.	Transfusion protocol 15–150 ng/mL	NR	Transfusion parameters and ferritin levels had no influence on the survival of the studied cancer patients.
Khaldoun Alkayed et al., 2013 [11]	Acute lymphoblastic leukaemia (ALL)	NR	The transfusion of packed red blood cells (PRBCs), single donor platelets collected by apheresis (SDPs), or fresh frozen plasma (FFP) of 10–15 mL/kg was considered as a transfusion event.	NR	NR	Alive: 132 subjects Dead: 13 subjects

NR: Not reported

Discussion

The purpose of this scoping review was to identify, map and chart all available literature regarding which RBC transfusion strategy is most effective in increasing QoL and/or survival rates in paediatric patients (0-18 years old) diagnosed with any subtype of leukaemia. The primary objectives of this review were as follows:

1. Which RBC transfusion strategies are undertaken in paediatric patients (0-18 years old) diagnosed with any subtype of leukaemia?
2. Which RBC transfusion strategy is associated with increased survival rates in paediatric patients (0-18 years old) diagnosed with any subtype of leukaemia?
3. Which RBC transfusion strategy is associated with increased QoL in paediatric patients (0-18 years old) diagnosed with any subtype of leukaemia?

After comprehensive searching for articles which correlated with the review objectives, an overall lack of resulting articles that had both liberal and restrictive comparator arms highlighted that this is a significantly under-research area and signalled a need for increasing research conducted in this area. As a result, conducting a scoping review on this research question was deemed the most appropriate method of assessing the size and scope of available literature on the subject.

Summary of Evidence
Types of RBC Transfusion Strategies

Across the included articles two of the six studies exclusively evaluated the liberal strategy, while Three subsequent studies out of the 6 evaluated both combination restrictive and liberal strategies. Due to the limited knowledge on paediatric patients, available information on the adult population was used as a comparator to map the size and scope of what is known about paediatric patients. Nair Manjusha et al., 2018 reported in their observational study that a liberal RBC transfusion strategy proved most effective in comparison to a restrictive strategy within this paediatric (1-14 years) population, where positive results were identifiable after all leukaemia patients were transfused with a total blood volume of 47.82mL/kg. Dissimilarly, the findings of a retrospective study conducted by Anna Waszczuk-Gaida et al., 2016 reported conflicting findings and stated that survival in adult patients with AML was significantly longer in those who were not dependent on RBC transfusions, however this could be due to these patients not being as anaemic [31]. Nair Manjusha et al., 2018 subsequently reported similar outcomes for ALL patients whose total transfused volume was 37.02mL/kg and in AML patients who were transfused with 111.25mL/kg of RBCs. This aligned with Kerri Nottage et al., 2013 whose research report stated favourability towards a liberal RBC transfusion strategy within the subject pool of paediatric (5-10 years) patients. Robitaille et al., 2012

clinical trial reported that five out of six patients who were transfused liberally were still alive at a two year follow up, while one out of six patients who received a restrictive transfusion died post transplantation within this paediatric (1-18 years) population. In comparison to an adult population, a review conducted by Erica Wood et al., 2020 reported that among the adult population diagnosed with MDS, showed that a restrictive transfusion threshold delivered the same QoL outcomes as a liberal threshold [32]. The restrictive RBC transfusion strategy was reported within three of the included articles, in conjunction with a liberal RBC transfusion strategy. Robitaille et al., 2012 clinical trial concluded that the restrictive RBC transfusion strategy resulted in higher mortality, with one out of six paediatric (1-18 years) population dying post transplantation. In contrast, a retrospective cohort study carried out by Martin David Berger et al., 2012 stated that restrictive RBC transfusion practices had similar or even better survival rates in ICU adult patients [33]. A research report by Sawicka-Zukowska et al., 2024 reported that both liberal and restrictive practices had no significant differences between paediatric (0-18 years) patients treated with low/high volume of transfused blood, especially in the group of patients with ALL.

QoL and/or Rates of Survival
(i) Liberal Transfusion Strategy
The articles selected for inclusion in this scoping review were extensively assessed for QoL and survival outcomes in relation to both liberal and restrictive transfusion practices within the paediatric patient population. The first observational study by Nair Manjusha et al., 2018 independently reported on the liberal transfusion practise and concluded that no subsequent QoL outcome was observed amid the process of the study in relation to the liberal transfusion strategy. Dissimilarly, Kerri Nottage et al., 2013 observed in their research report that 396 paediatric patients receiving a liberal RBC transfusion had a higher survival rate compared with the restrictive practices. Out of a paediatric (5-10 years) patient pool of 396, 116 subjects had an average survival rate between five and ten years, while 280 subjects receiving a liberal transfusion survived for more than ten years post-transplantation. This same research report stated how the restrictive practices saw 82 subjects survive between 5-10 years post restrictive transplantation, while 403 subjects subsequently died in less than ten years. In contrast, a study conducted by Arturo Pereira et al., 2010 concluded that a history of heavy RBC transfusions among adults had been identified as a predictor for shorter survival. The clinical trial conducted by Robitaille et al., 2012 supported this by reporting that in relation to patient survival five out of six patients were still alive at two years follow up after receiving a liberal transfusion, while one out of six patients died 6 months post transplantation due to a restrictive RBC transfusion strategy. It is important to note that the sample

size is small due to the fact that the study was stopped by the DSMB for safety concerns.

(ii) Restrictive Transfusion Strategy
In relation to QoL and/or survival outcomes for paediatric patients receiving a restrictive RBC transfusion, the clinical trial by Robitaille et al., 2012 concluded that a restrictive RBC transfusion strategy was higher in likelihood to result in mortality. Dissimilarly, a retrospective study conducted by Jansen AGJ et al., 2004 stated that adults with AML being treated with liberal and restrictive transfusions revealed no difference in mortality [34]. The next research report that reported on QoL outcomes in relation to restrictive transfusion practises was conducted by Sawicka-Zukowska et al., 2024 stated that there were no significant differences between both the liberal and restrictive RBC transfusion processes between paediatric (0-18 years) patients treated with low/high volume of transfused blood, especially in the group of patients with ALL. This research report further stated that subjects with AML and higher volumes of blood transfused seemed to have higher chances of survival which closely agrees with the observations drawn by Manjusha et al., 2018 and Kerri Nottage et al., 2013. On the contrary, a cross-sectional study conducted by Alexander Pine et al., 2017 reported that it is unclear whether the restrictive practice alters clinical outcomes in adults with AML [35]. A final respective study undertaken by Khaldoun Alkayed et al., 2013 further stated that out of 145 paediatric subjects included in the study, 13 had died post transplantation.

Limitations
It is important to view the results of this scoping review in light of several limitations. The inclusion criteria required articles to be written in English, which may have limited the scope of the literature reviewed. The small number of articles retrieved and subsequently included in the review (n=6) indicates an overall lack of available literature on the subject, which could affect the applicability of the results. Furthermore, an underpowered study was observed across the included articles, which could limit the generalizability of the results. Many included articles did not report on controlling confounding in their statistical analysis, which was another limitation observed. A lack of clinical trials were observed throughout this study. Majority of the included studies are retrospective which can limit the strength of evidence and the ability to establish causal relationships. Retrospective studies are prone to biases including, selection and information biases. This can be compared to well-designed prospective clinical trials. This limitation may impact the generalizability and reliability of the findings.

Conclusions
To conclude, this research article aimed to assess the size and scope of available literature regarding which

RBC transfusion strategies were undertaken in paediatric patients diagnosed with any subtype of leukaemia. This study identified that a liberal transfusion strategy was the most common throughout the included articles. Evidence from this article suggests that there is limited research on paediatric patients with leukaemia as none of the included articles reported substantially on QoL. In relation to paediatric survival rates, evidence from the included articles reported that a liberal transfusion strategy resulted in lesser mortality rates. The small number of articles retrieved and subsequently included in the review (n=6) indicates an overall lack of available literature on the subject, which could affect the applicability of the results. Increasing literature is urgently required to substantiate research findings as this patient demographic is under researched in relation to RBC transfusion practices. As a result, conducting a scoping review on this research question was deemed the most appropriate method of assessing the size and scope of available literature on the subject.

List of Abbreviations
ALL: acute lymphocytic leukaemia
AML: acute myeloid leukaemia
CLL: chronic lymphocytic leukaemia
CML: chronic myeloid leukaemia
CMML: chronic myelomonocytic leukaemia
HRQoL: health-related quality of life
HSC: haematopoietic stem cell
MDS: myelodysplastic syndrome
QoL: quality of life
RBC: red blood cell

Conflicts of Interest
The author declares that they have no conflict of interest.

Ethics Approval and/or Participant Consent
This scoping review examined previous studies and articles. Therefore, no approval or participant consent was required.

Authors' Contributions
Conceptualization, E F: investigation, E F: methodology, E F: project administration, E F: resources, E F: writing - original and final draft preparation, E F: The author has read and agreed to the published version of the manuscript.

References
[1] Juliusson G, Hough R. Leukemia. Prog Tumor Res. 2016;43:87–100. Available from: https://doi.org/10.1159/000447076
[2] Davis AS, Viera AJ, Mead MD. Leukemia: an overview for primary care. Am Fam Physician. 2014 May 1;89(9):731–8. Available from: https://pubmed.ncbi.nlm.nih.gov/24784336
[3] Chen J, Huang C, Zhu Y, Dong L, Cao W, Sun L, et al. Identification of similarities and differences between myeloid and lymphoid acute leukemias using a gene-gene interaction network. Pathol Res Pract. 2015 Oct;211(10):789–96. Available from: https://doi.org/10.1016/j.prp.2015.07.007
[4] Whiteley AE, Price TT, Cantelli G, Sipkins DA. Leukaemia: a model metastatic disease. Nat Rev Cancer. 2021 Jul;21(7):461–75. Available from: https://doi.org/10.1038/s41568-021-00355-z
[5] Penn Medicine. Types of leukemia [Internet]. Philadelphia (PA): Penn Medicine; 2022. Available from: https://www.pennmedicine.org/cancer/types-of-cancer/leukemia/types-of-leukemia
[6] Estcourt LJ, Malouf R, Trivella M, Fergusson DA, Hopewell S, Murphy MF. Restrictive versus liberal red blood cell transfusion strategies for people with haematological malignancies treated with intensive chemotherapy or radiotherapy, or both, with or without haematopoietic stem cell support. Cochrane Database Syst Rev. 2017 Jan 27;1(1):CD011305. https://doi.org/10.1002/14651858.CD011305.pub2
[7] Mohammadian-Hafshejani A, Farber IM, Kheiri S. Global incidence and mortality of childhood leukemia and its relationship with the Human Development Index. PLoS One. 2024 Jul 2;19(7):e0304354. Available from: https://doi.org/10.1371/journal.pone.0304354
[8] Metayer C, Dahl G, Wiemels J, Miller M. Childhood leukemia: a preventable disease. Pediatrics. 2016 Nov 1;138(Suppl):S45–S55. Available from: https://doi.org/10.1542/peds.2015-4268H
[9] Roberts I, Fordham NJ, Rao A, Bain BJ, et al. Neonatal leukaemia. Br J Haematol. 2018 Jul;182(2):170–184. Available from: http://doi.org/10.1111/bjh.15246
[10] Adams M. Childhood leukemia: 5 things parents should know [Internet]. Houston (TX): MD Anderson Cancer Center; 2021. Available from: https://www.mdanderson.org/cancerwise/5-things-parents-should-know-about-childhood-leukemia.h00-159463212.html
[11] Alkayed K, Al Hmood A, Madanat F. Prognostic effect of blood transfusion in children with acute lymphoblastic leukemia. Blood Res. 2013 Jun;48(2):133–8. Available from: https://doi.org/10.5045/br.2013.48.2.133

[12] ACCO. What is the expected lifespan of a child with leukemia? [Internet]. New York (NY): ACCO; 2018. Available from: https://www.acco.org/childhood-leukemia-life-expectancy/

[13] Doernbecher Children's Hospital. Understanding pediatric leukemia [Internet]. Portland (OR): Doernbecher Children's Hospital, OHSU; 2025. Available from: https://www.ohsu.edu/doernbecher/understanding-pediatric-leukemia

[14] Garas A, McLean LA, De Luca CR, Downie P, McCarthy MC. Health-related quality of life in paediatric patients up to five years post-treatment completion for acute lymphoblastic leukaemia: a systematic review. Support Care Cancer. 2019 Nov;27(11):4341–51. Available from: https://doi.org/10.1007/s00520-019-04747-8

[15] Franchini M, Marano G, Mengoli C, Pupella S, Vaglio S, Muñoz M, et al. Red blood cell transfusion policy: a critical literature review. Blood Transfus. 2017 Jul;15(4):307–17. Available from: https://doi.org/10.2450/2017.0059-17

[16] American Red Cross. Blood transfusion process [Internet]. Washington (DC): American Red Cross; 2019. Available from: https://www.redcrossblood.org/donate-blood/blood-donation-process/what-happens-to-donated-blood/blood-transfusions/types-of-blood-transfusions.html

[17] Remy KE, Hall MW, Cholette J, Juffermans NP, Nicol K, Doctor A, et al. Pediatric Critical Care Blood Research Network (Blood Net). Mechanisms of red blood cell transfusion-related immunomodulation. Transfusion. 2018 Mar;58(3):804–15. Available from: https://doi.org/10.1111/trf.14488

[18] Carson JL, Stanworth SJ, Dennis JA, Trivella M, Roubinian N, Fergusson DA, et al. Transfusion thresholds for guiding red blood cell transfusion. Cochrane Database Syst Rev. 2021 Dec 21;12(12):CD002042. Available from: https://doi.org/10.1002/14651858.CD002042.pub5

[19] Mirski MA, Frank SM, Kor DJ, Vincent JL, Holmes DR Jr. Restrictive and liberal red cell transfusion strategies in adult patients: reconciling clinical data with best practice. Crit Care. 2015 May 5;19(1):202. Available from: https://doi.org/10.1186/s13054-015-0912-y

[20] Lacroix J, Hébert PC, Hutchison JS, Hume HA, Tucci M, Ducruet T, et al. TRIPICU Investigators; Canadian Critical Care Trials Group; Pediatric Acute Lung Injury and Sepsis Investigators Network. Transfusion strategies for patients in pediatric intensive care units. N Engl J Med. 2007 Apr 19;356(16):1609–19. Available from: https://doi.org/10.1056/NEJMoa066240

[21] St Lezin E, Karafin MS, Bruhn R, Chowdhury D, Qu L, Bialkowski W, et al. NHLBI Recipient Epidemiology and Donor Evaluation Study (REDS)-III Program. Therapeutic impact of red blood cell transfusion on anemic outpatients: the RETRO study. Transfusion. 2019 Jun;59(6):1934-1943. https://doi.org/10.1111/trf.15249

[22] Prochaska MT, Zhang H, Babajide R, Meltzer DO. The effect of red blood cell transfusion on fatigability after hospital discharge. Blood Adv. 2020 Nov 19;4(22):5690-5697. https://doi.org/10.1182/bloodadvances.2020003364

[23] Schaap CM, Klanderman RB, Peters AL, Vlaar APJ, Müller MCA. Ultra-restrictive transfusion thresholds in critically ill adults: are we ready for the next step? Transfusion Med Rev. 2025 Apr;39(2):150893. https://doi.org/10.1016/j.tmrv.2025.150893

[24] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med. 2018 Oct 2;169(7):467–473. https://doi.org/10.7326/M18-0850

[25] Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil H. Scoping reviews. In: Aromataris E, Lockwood C, Porritt K, Pilla B, Jordan Z, editors. JBI Manual for Evidence Synthesis. JBI; 2024. Available from: https://doi.org/10.46658/JBIMES-24-09

[26] Nair M, Kuttath V, Nair AR, Rajeswari B, Chellappan G, Thankamony P, et al. Iron overload in children with leukemia receiving multiple blood transfusions. Indian Pediatr. 2018 Nov 15;55(11):962–965. Available from: https://www.indianpediatrics.net/nov2018/nov-962-965.htm

[27] Robitaille N, Lacroix J, Alexandrov L, Clayton L, Cortier M, Schultz KR, et al. Excess of veno-occlusive disease in a randomized clinical trial on a higher trigger for red blood cell transfusion after bone marrow transplantation: a Canadian Blood and Marrow Transplant Group trial. Biol Blood Marrow Transplant. 2013 Mar;19(3):468–473. https://doi.org/10.1016/j.bbmt.2012.12.002

[28] Nottage K, Gurney JG, Smeltzer MP, Castellanos M, Hudson MM, Hankins JS. Trends in transfusion burden among long-term survivors of childhood hematological malignancies. Leuk Lymphoma. 2013 Dec 22;54(8):1719-1723. https://doi.org/10.3109/10428194.2012.750724

[29] Sawicka-Żukowska M, Topczewska M, Krawczuk-Rybak M, Grubczak K, Beyer EC, et al. Iron overload in children with acute lymphoblastic and acute myeloblastic leukemia—experience of one center. Cancers. 2024 Jan 15;16(2):367. https://doi.org/10.3390/cancers16020367

[30] Sawicka-Żukowska M, Krętowska-Grunwald A, Topczewska M, Krawczuk-Rybak M, Grubczak K. Is serum ferritin a predictor of blood transfusions outcome and survival in childhood lymphomas and solid tumors? Cancers. 2024 Nov 6;16(22):3742. https://doi.org/10.3390/cancers16223742

[31] Waszczuk-Gajda A, Mądry K, Machowicz R, Drozd-Sokołowska J, Stella-Hołowiecka B, Mital A, et al. Red blood cell transfusion dependency and hyperferritinemia are associated with impaired survival in patients diagnosed with myelodysplastic syndromes: results from the first Polish MDS-PALG registry. Adv Clin Exp Med. 2016 Jul–Aug;25(4):633-641. https://doi.org/10.17219/acem/62397

[32] Wood EM, McQuilten ZK. Outpatient transfusions for myelodysplastic syndromes. Hematology. 2020;2020(1):167-74. https://doi.org/10.1182/hematology.2020000103

[33] Berger MD, Gerber B, Arn K, Senn O, Schanz U, Stussi G. Significant reduction of red blood cell transfusion requirements by changing from a double-unit to a single-unit transfusion policy in patients receiving intensive chemotherapy or stem cell transplantation. Haematologica. 2012 Jan;97(1):116–22. https://doi.org/10.3324/haematol.2011.047035

[34] Jansen AJG, Caljouw MAA, Hop WCJ, van Rhenen DJ, Schipperus MR. Feasibility of a restrictive red-cell transfusion policy for patients treated with intensive chemotherapy for acute myeloid leukaemia. Transfus Med. 2004 Feb;14(1):33–38. https://doi.org/10.1111/j.0958-7578.2004.00477.x

[35] Pine AB, Luger S, Stone RM, Erba HP, Garcia-Manero G, Lee AI, Podoltsev NA, et al. Wide variations in blood product transfusion practices among providers who care for patients with acute leukemia in the United States. Transfus Med. 2017 Feb;57(2):289–95. https://doi.org/10.1111/trf.13934

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