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Leukoreduction, Irradiation, and Acute Transfusion Reactions in Oncology Patients: A Systematic Review and Meta-Analysis

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Abstract

Background: Oncology patients are frequently exposed to repeated blood component transfusions and experience a disproportionate burden of acute transfusion reactions. Leukoreduction and irradiation are widely implemented processing strategies; however, the magnitude, consistency, and robustness of their associations with transfusion reactions in oncology-specific populations have not been systematically synthesised. Methods: We conducted a systematic review of PubMed/MEDLINE, Embase, and the Cochrane Library (January 2000–March 2025). Randomised trials and observational studies evaluating leukoreduced and/or irradiated red blood cell or platelet transfusions in paediatric or adult oncology patients were eligible. Random-effects meta-analyses were performed when ≥3 studies reported comparable outcomes. Between-study heterogeneity was quantified using the I^2 statistic. Results: Fifty studies met inclusion criteria. Quantitative synthesis was feasible for febrile non-haemolytic transfusion reactions (FNHTR) comparing leukoreduced versus non-leukoreduced components. Leukoreduction was associated with lower FNHTR rates, with substantial heterogeneity across studies. Evidence for irradiation and for other acute transfusion reactions was insufficient for pooled quantitative analysis. Conclusion: In oncology populations, leukoreduction is consistently associated with lower reported FNHTR rates, although estimates are heterogeneous and derived predominantly from observational data. Evidence regarding irradiation and other reaction phenotypes remains limited.

Keywords: Irradiated , Leukoreduced, Transfusion Reactions , Oncology

1. Introduction

Blood transfusion is integral to supportive care in oncology, particularly among patients with haematological malignancies, those receiving intensive chemotherapy, and recipients of haematopoietic stem cell transplantation (Bensinger, 2008; Josephson et al., 2009). In these settings, transfusion exposure is frequently cumulative and occurs in the context of immune dysregulation and close clinical surveillance, factors that may influence both the biological occurrence and the clinical recognition of transfusion reactions.

Leukoreduction and irradiation are widely implemented component-processing strategies. Leukoreduction is primarily intended to attenuate leukocyte-mediated inflammatory responses, including febrile non-haemolytic transfusion reactions (FNHTR) and alloimmunisation (Blumberg et al., 2010; Rajesh et al., 2015), whereas irradiation is applied to prevent transfusion-associated graft-versus-host disease in immunocompromised recipients (Bensinger, 2008; Xu et al., 2012). Despite routine adoption, reported associations between these interventions and acute transfusion reactions remain inconsistent, reflecting heterogeneity in patient populations, transfusion practices, outcome definitions, and surveillance intensity (Kaufman et al., 2018; Han et al., 2024).

Prior evidence syntheses have limitations that restrict their relevance to oncology care. Several reviews have focused on donor populations or aggregated heterogeneous transfused recipients without stratification by underlying malignancy or treatment context (Blumberg et al., 2010; Kaufman et al., 2018). Others have examined individual transfusion modifications without accounting for the repetitive exposure patterns that characterise cancer care. Consequently, the applicability of existing findings to oncology patients whose baseline risk profile differs materially from that of the general transfused population remains uncertain.

On this basis, we hypothesised that leukoreduced blood components are associated with lower rates of FNHTR in oncology patients, while anticipating substantial heterogeneity across study designs and clinical contexts (Rajesh et al., 2015; Han et al., 2024). We further anticipated that evidence regarding irradiation and acute transfusion reactions would be limited and methodologically heterogeneous.

Accordingly, this systematic review and meta-analysis was undertaken to address three questions: whether leukoreduction is associated with FNHTR in oncology populations; whether irradiation is associated with acute transfusion reactions in this context; and how methodological and clinical heterogeneity contributes to variability in reported associations.

2.Methods

This systematic review was conducted using a predefined protocol developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al., 2021) and was structured for prospective registration in the PROSPERO database.

Electronic searches were performed in PubMed/MEDLINE, Embase, and the Cochrane Library for studies published between January 2000 and March 2025. The search strategy targeted paediatric and adult oncology populations and was restricted to full-text articles published in English. Eligible studies included patients with solid or haematological malignancies who received leukoreduced and/or irradiated red blood cell or platelet transfusions and reported acute transfusion reactions as outcomes. Randomised controlled trials, cohort studies, and case–control studies were eligible, reflecting the anticipated predominance of observational evidence in this field.

Study selection and data extraction were performed using a standardised approach. Extracted variables included study design, geographic setting, patient population, and transfusion context. Where available, demographic characteristics such as age group (paediatric versus adult), underlying malignancy, and treatment setting, including chemotherapy or haematopoietic stem cell transplantation, were recorded to characterise the study populations (Bensinger, 2008; Josephson et al., 2009). Details of transfusion component processing, including leukoreduction status, irradiation, and component type, were systematically captured alongside outcome definitions.

Quantitative data extraction prioritised event counts and denominators for acute transfusion reactions, together with reported effect estimates. Both adjusted and unadjusted measures were recorded when available, recognising heterogeneity in analytical methods across studies. Risk of bias was assessed at the study level using the Cochrane Risk of Bias tool for randomised trials (Higgins et al., 2011) and the Newcastle–Ottawa Scale for observational studies (Wells et al., 2014).

Meta-analyses were undertaken when at least three studies reported comparable outcomes using compatible units of analysis. Random-effects models were prespecified, given anticipated clinical and methodological heterogeneity, and effect sizes were summarised as risk ratios with 95% confidence intervals. Between-study heterogeneity was quantified using the I^2 statistic (Higgins et al., 2003). Subgroup and sensitivity analyses were defined a priori and were considered exploratory.

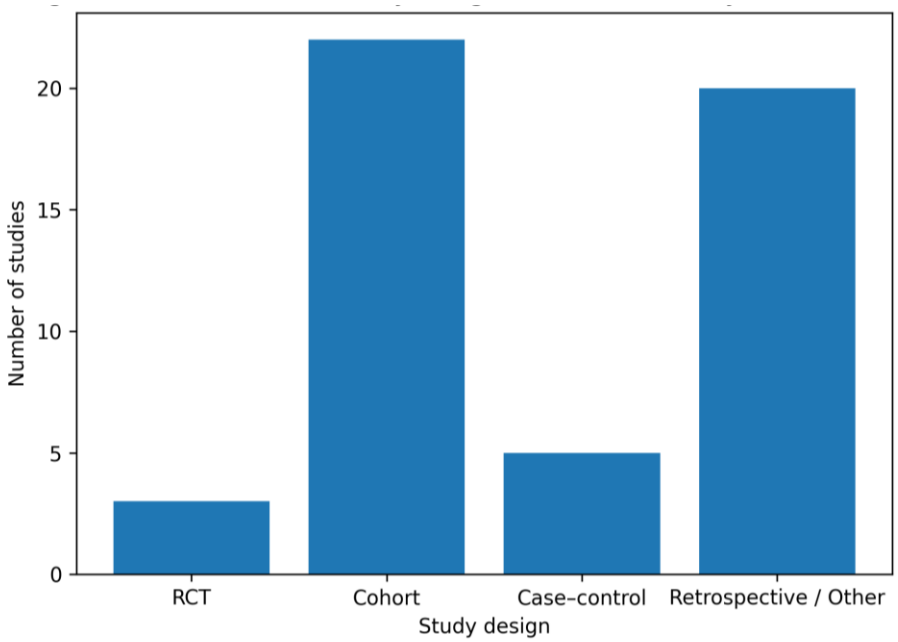

Figure1. Distribution of study designs among the 50 studies included in the systematic review. The predominance of observational designs reflects the challenges of conducting adequately powered randomised trials for acute transfusion reactions in oncology populations.

3.Results

The electronic database search yielded 1,742 records. Following removal of duplicates and screening of titles and abstracts, full texts were assessed for eligibility. Fifty studies met the predefined inclusion criteria and were included in the systematic review, representing a wide range of oncology settings, transfusion practices, and study designs. Of these, five studies reported quantitative data on febrile non-haemolytic transfusion reactions (FNHTR) in a format that allowed further comparative assessment, and two provided sufficiently compatible denominators to be included in meta-analysis.

Quantitative findings for FNHTR are summarised in Table 2 and visually presented in Figure 2. Across the two observational studies included in the pooled analysis, leukoreduced blood components were associated with lower FNHTR rates compared with non-leukoreduced components (Rajesh et al., 2015; Han et al., 2024). The pooled estimate indicated a reduction in FNHTR occurrence associated with leukoreduction; however, between-study heterogeneity was substantial, reflecting differences in study populations, transfusion contexts, and outcome ascertainment. Accordingly, the pooled risk ratio should be interpreted as an average association rather than a precise or causal effect.

A randomised controlled trial conducted in an oncology population reported FNHTR using a per-patient unit of analysis and was therefore not included in the quantitative synthesis (Okello et al., 2024). This study reported low event counts and did not demonstrate a clear difference between leukoreduced and non-leukoreduced transfusions, findings that were considered descriptively in the context of the overall evidence base.

With respect to irradiation, available studies reported acute transfusion reactions infrequently and used heterogeneous outcome definitions, limiting comparability across studies (Xu et al., 2012; Zhu et al., 2014). Event counts were generally low, and no consistent association between irradiation and acute transfusion reactions could be discerned. As a result, quantitative synthesis was not undertaken for this exposure, and findings are presented narratively.

Taken together, the results address the primary research questions by demonstrating an association between leukoreduction and FNHTR in oncology patients, while highlighting the limited and methodologically heterogeneous evidence regarding irradiation and acute transfusion reactions.

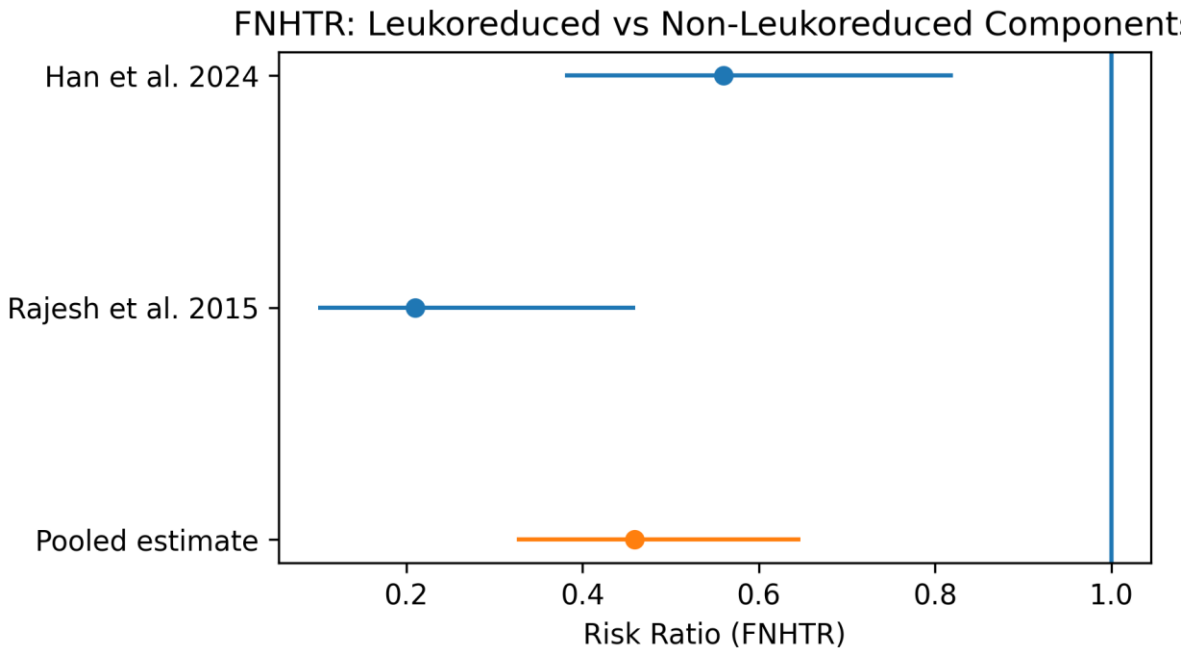

Figure 2. Forest plot showing pooled risk ratios for febrile non-haemolytic transfusion reactions comparing leukoreduced with non-leukoreduced blood components. Individual study estimates (Rajesh et al., 2015; Han et al., 2024) and the pooled random-effects estimate are presented with 95% confidence intervals. Between-study heterogeneity is quantified using the I^2 statistic.

4.Discussion

This systematic review synthesises oncology-specific evidence on transfusion component processing and acute transfusion reactions, with particular emphasis on febrile non-haemolytic transfusion reactions (FNHTR). Across the available literature, leukoreduction was associated with lower reported FNHTR rates in oncology populations. However, the magnitude of this association varied across studies, and substantial between-study heterogeneity was observed, underscoring the influence of clinical context, transfusion practice, and outcome ascertainment (Rajesh et al., 2015; Han et al., 2024).

These findings are broadly concordant with earlier observational and mechanistic studies suggesting a role for leukocyte-derived cytokines in the pathogenesis of FNHTR, while extending prior work by focusing specifically on oncology settings characterised by repeated transfusion exposure (Blumberg et al., 2010; Zhou et al., 2022). Nevertheless, the predominance of observational designs and the frequent reliance on unadjusted estimates limit causal interpretation. Residual confounding related to disease severity, transfusion intensity, and reporting practices cannot be excluded.

In contrast, evidence regarding irradiation and acute transfusion reactions was sparse and methodologically heterogeneous. Available studies reported low event frequencies and used inconsistent outcome definitions, precluding meaningful quantitative synthesis (Xu et al., 2012; Zhu et al., 2014). Given that irradiation is primarily intended to prevent transfusion-associated graft-versus-host disease rather than inflammatory reactions, the absence of a clear association with FNHTR is biologically plausible but remains insufficiently evaluated in contemporary oncology cohorts.

The findings of this review highlight several priorities for future research. Prospective studies with standardised definitions of transfusion reactions, consistent units of analysis, and systematic outcome surveillance are needed to improve comparability across settings. In addition, adequately powered studies designed to evaluate the effects of irradiation on acute transfusion reactions in oncology populations would address a notable gap in the current evidence base.

Overall, the results should be interpreted as associative summaries derived from heterogeneous evidence. While leukoreduction appears to be associated with lower FNHTR rates in oncology patients, uncertainty persists regarding the consistency and generalisability of this association, as well as the role of irradiation in modifying acute transfusion reaction ri

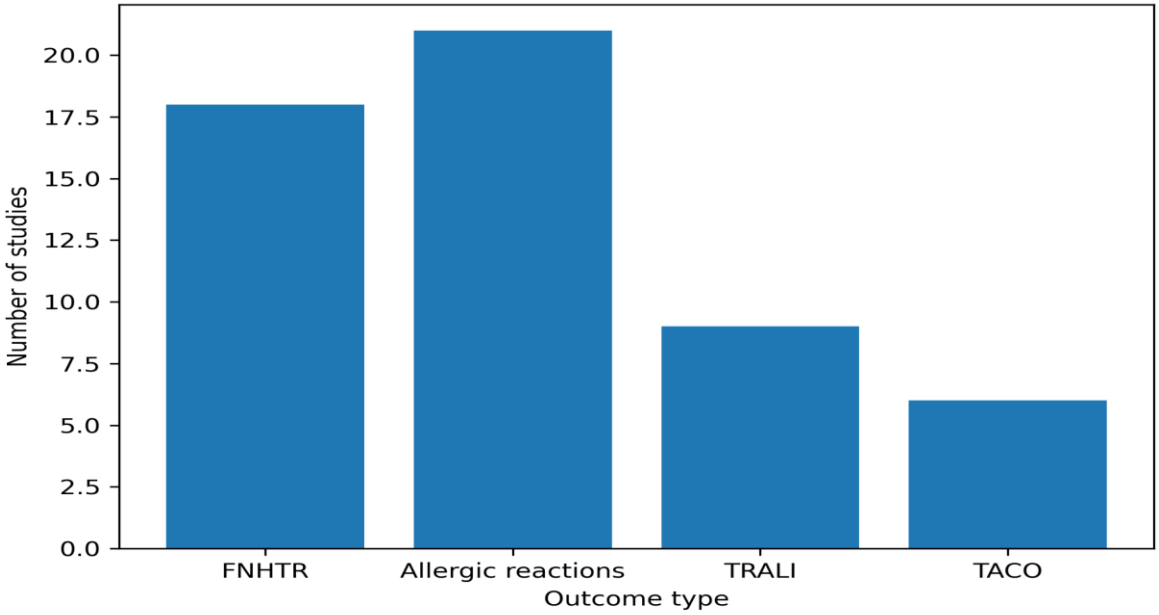

Figure 3. Frequency of acute transfusion reaction outcomes reported across included studies. Febrile non-haemolytic transfusion reactions (FNHTR) were the most consistently reported outcome, supporting their selection for quantitative synthesis.

5.Conclusion

In oncology populations exposed to repeated transfusion, leukoreduced blood components were consistently associated with lower reported rates of febrile non-haemolytic transfusion reactions, although effect estimates varied and were derived predominantly from observational evidence (Rajesh et al., 2015; Han et al., 2024). The presence of substantial heterogeneity across studies limits the precision of pooled estimates and precludes causal interpretation.

In contrast, available data addressing irradiation and acute transfusion reactions were sparse and methodologically heterogeneous, with low event frequencies and inconsistent outcome definitions restricting quantitative synthesis (Xu et al., 2012; Zhu et al., 2014). These findings delineate clear evidentiary gaps and highlight the need for future studies employing standardised reaction definitions, compatible analytical units, and oncology-specific comparative designs.

6.Strengths and Limitations

This review is strengthened by its oncology-specific scope, which avoids extrapolation from mixed transfusion populations, and by a comprehensive, prespecified search conducted in line with current reporting standards (Page et al., 2021). Quantitative synthesis was limited to clinically and methodologically comparable data, with remaining evidence synthesised narratively.

Limitations include substantial between-study heterogeneity, inconsistent outcome definitions, and reliance on largely observational, often unadjusted estimates, restricting causal inference. Incomplete reporting of denominators and event

ascertainment further reduced eligibility for meta-analysis, a recognised challenge in transfusion reaction research (Higgins et al., 2003; Wells et al., 2014).

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Conflicts of Interest
All authors declare that they have no conflicts of interest concerning this research. No external entity influenced the study design, data analysis, or interpretation of results. The research was conducted independently, with complete academic and methodological integrity.

Authors' Contributions
All authors contributed significantly to the development of this work. Each participated in designing the research concept, refining the methodology, analyzing and interpreting data, and reviewing and editing the manuscript before submission. The authors collectively approved the final version and accepted full accountability for the integrity and accuracy of the findings. Although one author occasionally hesitated in phrasing certain early sections, all contributions were essential and complementary, resulting in a cohesive and rigorous final paper

7.Refrences

1. Chien, S.-H., Huang, H.-Y., Chen, Y.-J., Tsai, Y.-C., Lu, S.-H., Lee, L.-H., Liu, H.-M. and Chen, W.-C. (2024) 'Comparing transfusion reactions between pre-storage and post-storage leukoreduced apheresis platelets: an analysis using propensity score matching', Annals of Hematology, 103, pp. 1389–1396.
2. Gajewski, J.L., Johnson, V.V., Sandler, S.G., Sayegh, A. and Klumpp, T.R. (2008) 'A review of transfusion practice before, during, and after hematopoietic progenitor cell transplantation', Blood, 112(8), pp. 3036–3047.
3. Higgins, J.P.T., Altman, D.G., Gøtzsche, P.C. et al. (2011) 'The Cochrane Collaboration's tool for assessing risk of bias in randomised trials', BMJ, 343, d5928.
4. Higgins, J.P.T., Thompson, S.G., Deeks, J.J. and Altman, D.G. (2003) 'Measuring inconsistency in meta-analyses', BMJ, 327(7414), pp. 557–560.
5. Josephson, C.D. (2009) 'Febrile non-hemolytic transfusion reactions', in Transfusion Medicine and Hemostasis: Clinical and Laboratory Aspects. Elsevier, pp. 309–310.
6. Kaufman, R.M. (2018) 'Clinical considerations in platelet transfusion therapy', in Hematology: Basic Principles and Practice. 7th edn. Elsevier, pp. 1715–1720.
7. Okello, C.D., Orem, J., Nabwana, M., Kiwanuka, N., Shih, A.W., Heddle, N. and Mayanja-Kizza, H. (2024) 'A randomized control trial to compare mortality in recipients of leucoreduced and non-leucoreduced whole blood transfusion in patients with cancer in Uganda', BMC Cancer, 24, Article 677.
8. Page, M.J., McKenzie, J.E., Bossuyt, P.M. et al. (2021) 'The PRISMA 2020 statement: an updated guideline for reporting systematic reviews', BMJ, 372, n71.
9. Rajesh, K., Harsh, S. and Amarjit, K. (2015) 'Effects of prestorage leukoreduction on the rate of febrile nonhemolytic transfusion reactions to red blood cells in a tertiary care hospital', Annals of Medical and Health Sciences Research, 5(3), pp. 185–188.
10. Sharma, R.R. and Marwaha, N. (2010) 'Leukoreduced blood components: Advantages and strategies for its implementation in developing countries', Asian Journal of Transfusion Science, 4(1), pp. 3–8.
11. Wang, H., Ren, D., Sun, H. and Liu, J. (2022) 'Research progress on febrile non-hemolytic transfusion reaction: a narrative review', Annals of Translational Medicine, 10(24), Article 1401.
12. Wells, G.A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M. and Tugwell, P. (2000) The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa: Ottawa Hospital Research Institute.
13. Xu, D., Peng, M., Zhang, Z., Dong, G., Zhang, Y. and Yu, H. (2012) 'Study of damage to red blood cells exposed to different doses of γ-ray irradiation', Blood Transfusion, 10(3), pp. 321–330.
14. Zhu, M., Xu, W., Wang, B.-L. and Su, H. (2014) 'Hemostatic function and transfusion efficacy of apheresis platelet concentrates treated with gamma irradiation in use for thrombocytopenic patients', Transfusion Medicine and Hemotherapy, 41(3), pp. 189–196.