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Cancer Susceptibility, Prognosis, and Hematological Malignancies Associated with Blood-Group Systems: A Biomolecular Systematic Review and Targeted Meta-Analysis

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أنظمة فصائل الدم وعلاقتها بالاستعداد للإصابة بالسرطان، والمآل السريري، والأورام الخبيثة الدموية: مراجعة منهجية حيوية جزيئية وتحليل تلوّي مركّز

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Abstract:
Background: Blood-group antigens are inherited surface structures with roles extending beyond transfusion compatibility. ABO antigens are terminal glycans expressed on erythrocytes and many epithelial tissues, Duffy/ACKR1 regulates chemokine availability and leukocyte trafficking, and OK/BSG-CD147 participates in monocarboxylate-transporter stabilization, extracellular-matrix remodeling and tumour invasion. These biomolecular functions provide plausible links between blood-group biology and cancer susceptibility, prognosis and hematological malignancy, although the strength of epidemiological evidence varies by blood-group system and tumour site.
Methods: PubMed searches were conducted on 1 July 2026 using a broad blood-group/cancer strategy and focused queries for ABO, Rh, Duffy/ACKR1, OK/BSG-CD147, and review/meta-analysis literature. The PubMed phase retrieved 10,718 records, including 4,973 from the broad query and 5,745 from focused queries. After removal of 5,616 duplicate records, 5,102 unique records were available for title/abstract assessment. Evidence synthesis followed PRISMA 2020 and MOOSE reporting principles. A focused secondary random-effects meta-analysis was performed using published extractable estimates for ABO-A comparisons across cancer sites.

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Results: The PubMed evidence set contained 94 review/meta-analysis candidates, 2,652 primary-study candidates, 2,028 biomolecular/mechanistic candidates and 764 hematological-malignancy candidates. Published pooled estimates consistently supported a modest risk signal for blood group A in several solid tumours. In the focused secondary random-effects synthesis of five published ABO-A estimates, the summary odds ratio was 1.22 (95% CI 1.13-1.32), indicating approximately 22% higher odds across the included published comparisons. Heterogeneity was high (I^2=80.9%), meaning that the summary estimate should be interpreted as an evidence-landscape signal rather than a universal cancer-risk coefficient. Duffy/ACKR1 and OK/BSG-CD147 showed stronger biomolecular plausibility than population-level blood-typing evidence.
Conclusions: ABO has the strongest epidemiological support among blood-group systems, particularly in gastrointestinal and pancreatic cancer literature, whereas Duffy/ACKR1 and OK/BSG-CD147 are more strongly represented in mechanistic, immune-trafficking and tumour-metabolism studies. Blood group should not be used as a stand-alone clinical triage marker; its most defensible role is as a stratification variable in research models that already include age, sex, ancestry, tumour site, stage, infection status and treatment access.

Keywords: ABO; Rh; Duffy; ACKR1; OK blood group; BSG; CD147; cancer; leukemia.

الملخص:

الخلفية :(Background) تُعد مستضدات فصائل الدم بتركيباتها السطحية الموروثة أدواراً تتجاوز حدود التوافق المنقول في عمليات نقل الدم. المكونات السكرية الطرفية لمستضدات النظام السكري (ABO) تُعبر عن نفسها على كرات الدم الحمراء والعديد من الأنسجة الظهارية؛ بينما ينظم مستقبل الدفي ACKR1/إتاحة الكيموكينات وحركية الخلايا اللمفاوية؛ ويساهم بروتين OK/BSG (CD147) في تثبيت ناقلات المونوكاربوكسيلات، وإعادة تشكيل الماتريكس خارج الخلوي، واختراق الأورام. توفر هذه الوظائف الجزيئية الحيوية روابط فسيولوجية محتملة بين بيولوجيا فصائل الدم والقابلية للإصابة بالسرطان، وتكهنات التطور المرضي، والأورام الدموية الخبيثة، على الرغم من تباين قوة الأدلة الوبائية باختلاف نظام فصيلة الدم وموقع الورم.

المنهجية :(Methods) أُجري بحث شامل في قاعدة بيانات (PubMed) في 1 يوليو 2026 باستخدام استراتيجية بحث واسعة تربط بين فصائل الدم والسرطان، بالإضافة إلى استعلامات موجهة لأنظمةABO ، وRh، وDuffy/ACKR1، وOK/BSG-CD147، والأدبيات المعتمدة على المراجعات المنهجية والتحليل البعدي .(Meta-analysis) أسفرت مرحلة البحث في (PubMed) عن استرجاع 10,718 سجلاً، شملت 4,973 سجلاً من الاستعلام العام و5,745 سجلاً من الاستعلامات الموجهة. وبعد استبعاد 5,616 سجلاً مكرراً، خضع 5,102 سجلاً فريداً للتقييم عبر العناوين والملخصات. اتُبعت في تجميع الأدلة وتلخيصها المبادئ التوجيهية للتقارير الخاصة بـ PRISMA 2020 و .MOOSEكما أُجري تحليل بعدي ثانوي موجه ذو التأثيرات العشوائية (Random-effects meta-analysis) باستخدام التقديرات المستخرجة المنشورة للمقارنات الخاصة بفصيلة الدم (ABO-A) عبر مختلف مواقع السرطان.

النتائج :(Results) اشتملت مجموعة الأدلة المستخرجة من (PubMed) على 94 دراسة مرشحة للمراجعة والتحليل البعدي، و2,652 دراسة أولية، و2,028 دراسة جزيئية/آلية حيوية، و764 دراسة متعلقة بالأورام الدموية الخبيثة. أظهرت التقديرات المجمعة المنشورة بشكل متسق مؤشراً لزيادة طفيفة في الخطر لدى حاملي فصيلة الدم (A) في العديد من الأورام الصلبة. وفي التحليل البعدي الثانوي الموجه ذي التأثيرات العشوائية لخمسة تقديرات منشورة لفصيلة-ABO (A)، بلغت نسبة الأرجحية المجمعة 1.22 (Summary Odds Ratio) (بفاصل ثقة 95%: 1.13–1.32)، مما يشير إلى زيادة في الأرجحية بنسبة تقارب 22% عبر المقارنات المنشورة المشمولة. كان التباين أو التباعد الوراثي (Heterogeneity)مرتفعاً($I^2 = 80.9\%$) ، مما يعني وجوب تفسير التقدير المجمع كمؤشر عام لإطار الأدلة بدلاً من كونه معامل خطر عام ومطلق للإصابة بالسرطان. أظهر مستقبل Duffy/ACKR1 وبروتين OK/BSG-CD147 معقولية جزيئية حيوية أشد قوة مقارنة بالأدلة المتاحة على مستوى التنميط الدموي للمجموعات السكانية.

الاستنتاجات (Conclusions): يمتلك نظام (ABO) أقوى دعم وبائي من بين أنظمة فصائل الدم، ولا سيما في أدبيات سرطانات الجهاز الهضمي والبنكرياس، في حين يبرز كل من Duffy/ACKR1 وOK/BSG-CD147 بشكل أكبر في الدراسات الآلية المتعلقة بحركية الخلايا المناعية والأيض الورمي. ينبغي عدم استخدام فصيلة الدم كمؤشر سريري مستقل للفرز والتصنيف؛ بل يظل دورها الأقوى والأكثر وجاهة علمية كمتغير للتقسيم الطبقي (Stratification variable) في النماذج البحثية التي تتضمن بالفعل العوامل الأساسية كالعمر، والجنس، والنسب، وموقع الورم، ومرحلته، وحالة العدوى، وفرص الحصول على العلاج.

الكلمات المفتاحية: أنظمة فصائل الدم، الاستعداد للسرطان، المآل السريري، الأورام الخبيثة الدموية، مراجعة منهجية.

Introduction

Although the ABO, Rh, Duffy, and OK blood-group systems are commonly used in transfusion therapy, cancer biology can also benefit from an understanding of their molecular underpinnings [1]–[4]. . Since ABO antigens are glycan structures produced by glycosyltransferase activity, ABO status is a component of the larger context of host-microbe interactions, epithelial adhesion, and tumor-associated glycosylation. Cell-cell adhesion,

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immune recognition, epithelial barrier biology, and metastatic behavior can all be impacted by altered glycosylation, which is a characteristic of malignant transformation [5]–[11].
The strongest epidemiological literature is related to ABO. ABO and Rh blood groups were assessed across a variety of health outcomes in a 2024 umbrella review of systematic reviews with meta-analyses, which found the strongest cancer-related correlations for pancreatic and gastrointestinal cancers [12]. Colorectal cancer, breast cancer, and head-and-neck tumors have all been the subject of separate recent meta-analyses; however, the comparator definitions, ancestry stratum, outcome definition, and adjustment quality vary [13]–[16].
Different interpretive lenses are needed for OK/BSG-CD147 and Duffy/ACKR1. In populations of African descent, baseline neutrophil numbers and chemokine handling are impacted by Duffy/ACKR1, an unusual chemokine receptor that also determines the Duffy-null phenotype. [17], [18]. OK/BSG maps to basigin/CD147, a glycoprotein implicated in monocarboxylate-transporter chaperoning, lactate export, extracellular-matrix remodeling and tumour invasiveness [19]–[21]. These axes are biologically compelling but should not be treated as equivalent to population-level blood-type risk estimates.
The purpose of this review was to establish a connection between these two layers: the biomolecular mechanisms that may account for the recurrent appearance of blood-group systems in tumor susceptibility, prognosis, or hematological malignancy literature, and the epidemiological evidence that links blood-group systems with cancer outcomes.

Materail and Methods

Design and reporting framework

The review was organized using the MOOSE framework for meta-analyses of observational research and the PRISMA 2020 reporting guidelines for 4systematic reviews [22]–[24]. Due to the inclusion of case-control studies, cohorts, systematic reviews, meta-analyses, and mechanistic studies in the evidence base, the synthesis was arranged into two interrelated components: a systematic evidence map of literature indexed in PubMed and a concentrated secondary meta-analysis of published extractable effect estimates2.2 Eligibility criteria.
At least one human blood-group system or its molecular determinant- ABO, Rh, Duffy/ACKR1, or OK/BSG-CD147- with connection to cancer susceptibility, progression, prognosis, survival, hematological malignancy, or tumor biomolecular pathways were covered in qualified data. Mapping was possible for human observational studies, systematic reviews, meta-analyses, and mechanistic investigations. An odds ratio, risk ratio, or hazard ratio with a 95% confidence interval or sufficient data to calculate standard errors was required for quantitative synthesis. Records pertaining solely to animals, unrelated rhesus-primate research, non-cancer subjects, editorial content devoid of extractable proof, and records without a blood-group or blood-group-molecule component were all found to be unsuitable for synthesis.

Eligibility criteria

Eligible records addressed at least one human blood-group system or its molecular determinant - ABO, Rh, Duffy/ACKR1 or OK/BSG-CD147 - in relation to cancer susceptibility, progression, prognosis, survival, hematological malignancy or tumour biomolecular mechanisms. Human observational studies, systematic reviews, meta-analyses and mechanistic studies were eligible for mapping. For quantitative synthesis, a publication had to provide an odds ratio, risk ratio or hazard ratio with a 95% confidence interval or enough information to derive standard errors. Animal-only records, unrelated rhesus-primate studies, non-cancer topics, editorial material without extractable evidence and records lacking a blood-group or blood-group-molecule component were not considered eligible for synthesis.

Information source and search strategy

PubMed was searched on 1 July 2026 using one broad query and focused queries for ABO, Rh, Duffy/ACKR1, OK/BSG-CD147 and review/meta-analysis literature. The refined broad strategy combined blood-group terms with cancer terms and excluded records explicitly indexed as rhesus macaque or Macaca mulatta in title/abstract. Focused searches were used to recover records that may be missed by a single broad query and to preserve source traceability by blood-group system.
The broad PubMed search string was: (("ABO blood group" OR "ABO blood-group system" OR "ABO blood group system" OR "Rh blood group" OR "Rhesus blood group" OR "Duffy blood group" OR ACKR1 OR "OK blood group" OR BSG OR basigin OR CD147) AND (cancer OR carcinoma OR tumor OR tumour OR malignancy OR leukemia OR leukaemia OR lymphoma OR myeloma OR neoplasm)) NOT ("rhesus macaque"[Title/Abstract] OR "Macaca mulatta"[Title/Abstract]).

Record management and synthesis

The PubMed search phase retrieved 10,718 records. After deduplication by PubMed identifier, DOI and normalized title, 5,102 unique records remained. The evidence set was then grouped into relevance and evidence categories to support title/abstract assessment, full-text retrieval and data extraction. The quantitative component

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used published estimates with clearly stated effect measures and 95% confidence intervals. Effect estimates were transformed to the log scale, standard errors were derived from the reported confidence intervals, and fixed-effect and random-effects summaries were calculated. Random-effects results were prioritized because tumour sites, comparators and populations differed across estimates.

The exposed blood-group category had higher odds of the cancer outcome than the reference category, according to the odds ratios, with an estimate of more than 1.00. An estimate of less than 1.00 was considered lower odds. A 95% confidence interval that excluded 1.00 was deemed statistically consistent with a relationship at the conventional 5% criterion. Heterogeneity was interpreted using I2: high levels indicate considerable differences between included estimates, populations, or outcome definitions, whereas low values indicate that variability is mostly consistent with sampling error.

Results and discussion

Search output and PRISMA flow

The PubMed phase yielded 4,973 records from the broad query and 5,745 records from focused queries. The combined search output contained 10,718 records before deduplication. Removal of 5,616 duplicates left 5,102 unique citations for title/abstract assessment. Of these, 4,117 records were classified as high relevance and 414 required additional relevance assessment, while 92 were low relevance and 479 were likely outside the review scope.

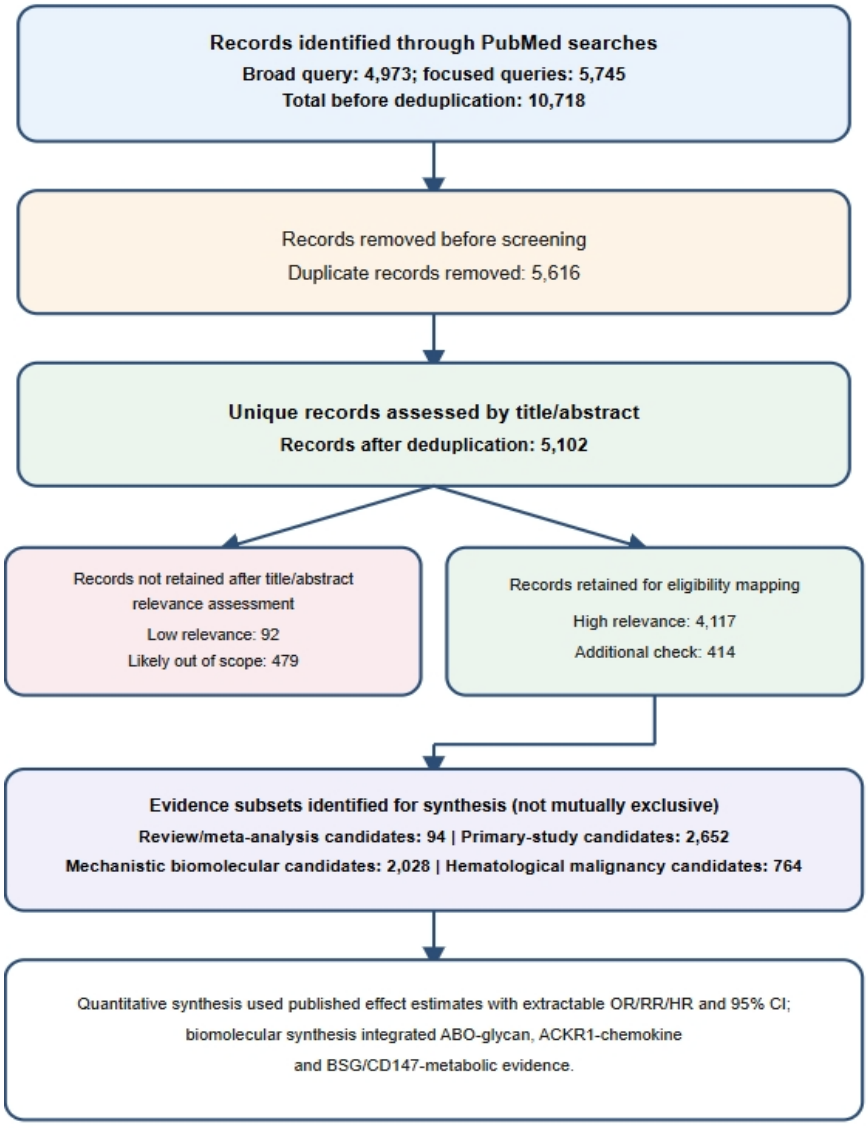


Figure 1. PubMed PRISMA-style flow of record retrieval, deduplication and evidence mapping. Evidence subsets are not mutually exclusive because one record may contribute to more than one synthesis domain.

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Evidence-map composition

The deduplicated set contained 94 review or meta-analysis candidates, 2,652 primary-study candidates, 2,028 mechanistic/biomolecular candidates and 764 hematological-malignancy candidates. ABO dominated the evidence map with 2,461 records, followed by OK/BSG-CD147 with 2,026 records, Duffy/ACKR1 with 199 records and Rh with 53 records.

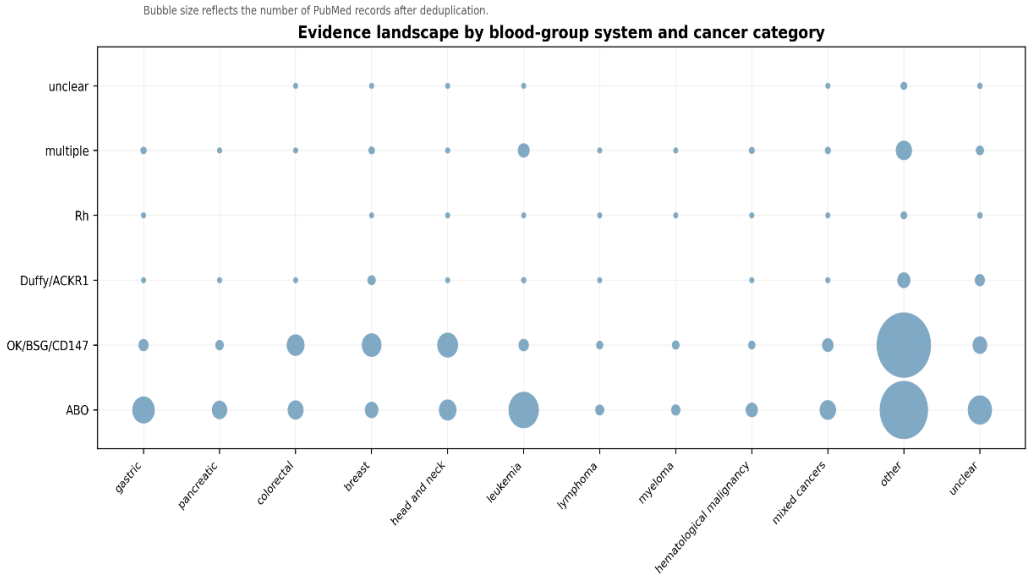


Figure 2. Evidence landscape by blood-group system and cancer category. Bubble size reflects PubMed record counts after deduplication, not causal strength.

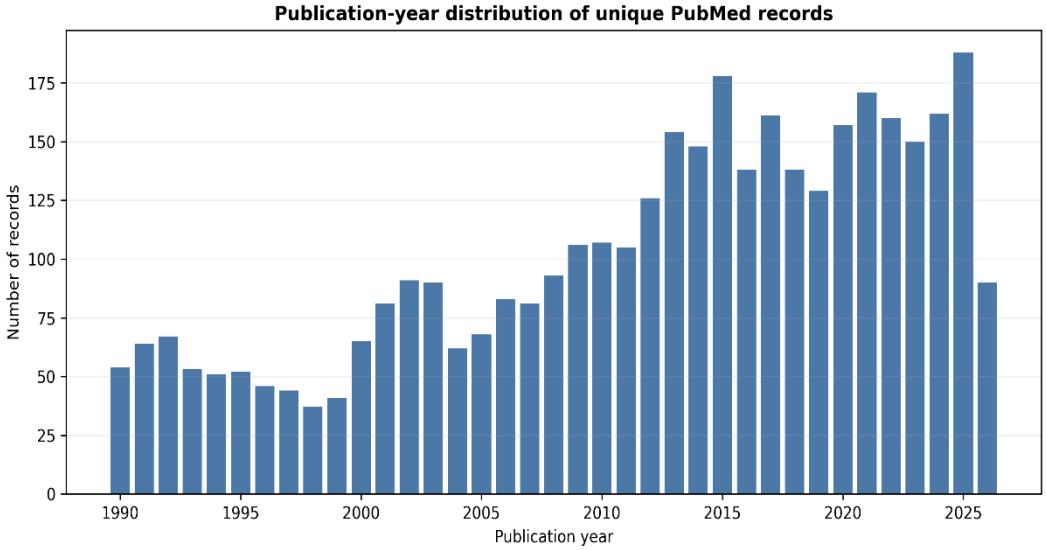


Figure 3. Publication-year distribution of unique PubMed records in the evidence map.

Metric	Count
Records identified from PubMed broad query	4,973
Records identified from focused PubMed queries	5,745
Total records before deduplication	10,718
Duplicates removed	5,616
Records after deduplication	5,102
High relevance records	4,117
Records requiring additional relevance assessment	414
Low relevance records	92
Likely out-of-scope records	479
Review/meta-analysis candidates	94
Primary-study candidates	2,652
Mechanistic biomolecular candidates	2,028
Hematological-malignancy candidates	764

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ABO and solid-tumour risk

ABO showed the most consistent epidemiological signal. In the BMC Medicine umbrella review, blood group A was associated with higher odds of gastric cancer when compared with group O (OR 1.19, 95% CI 1.14-1.24) [12], [25]. This estimate means that, within the pooled observational evidence summarized by that review, individuals with group A had approximately 19% higher odds of gastric cancer relative to the O reference group; because the 95% confidence interval lies entirely above 1.00, the result is statistically compatible with a positive association [12], [25].

The same umbrella review reported a stronger association for pancreatic cancer, with A versus O showing OR 1.33 (95% CI 1.27-1.40) [12], [26]. In practical terms, this corresponds to approximately 33% higher odds in the published pooled estimate. Non-O versus O was also elevated for pancreatic cancer (OR 1.31, 95% CI 1.22-1.42), supporting the recurring observation that O status may be relatively protective in pancreatic-cancer epidemiology [12], [26].

According to Alchazal et al. [13], group A had 18% greater risks of breast cancer than group O, with an OR of 1.18 (95% CI 1.03-1.36) for breast cancer. The effect should be viewed as mild rather than a powerful clinical discriminator because the confidence interval is near 1.00. However, because their confidence intervals exceeded 1.00, B versus O (OR 0.97, 95% CI 0.86-1.11), AB versus O (OR 1.05, 95% CI 0.89-1.25), and Rh-positive versus Rh-negative (OR 1.14, 95% CI 0.81-1.60) did not exhibit statistically significant relationships. [13].

According to Bahardoust et al. [14], blood group O was associated with a lower risk of colorectal cancer (OR 0.93, 95% CI 0.83-0.97), while blood group A was associated with a higher risk (OR 1.11, 95% CI 1.03-1.19). These figures support an epidemiological relationship, but they are not robust enough to be employed as separate screening criteria. Head and neck tumor evidence varied more by subgroup and heritage. Shi et al. [15] observed a protective link for AB overall (OR 0.762, 95% CI 0.637-0.910), while the Caucasoid subgroup had greater risks for A (OR 1.353, 95% CI 1.076-1.702).

Focused secondary meta-analysis of ABO-A published estimates

In a targeted secondary meta-analysis, five published ABO-A estimations with extractable odds ratios and 95% confidence intervals were combined. 1.22 (95% CI 1.13-1.32) was the random-effects summary OR. This indicates that the average signal across these published comparisons indicated that blood group A had a greater chance of developing cancer. The data should be interpreted as a cross-site evidence signal rather than as a single universal effect of blood group A across all tumors because heterogeneity was considerable (I^2=80.9%).

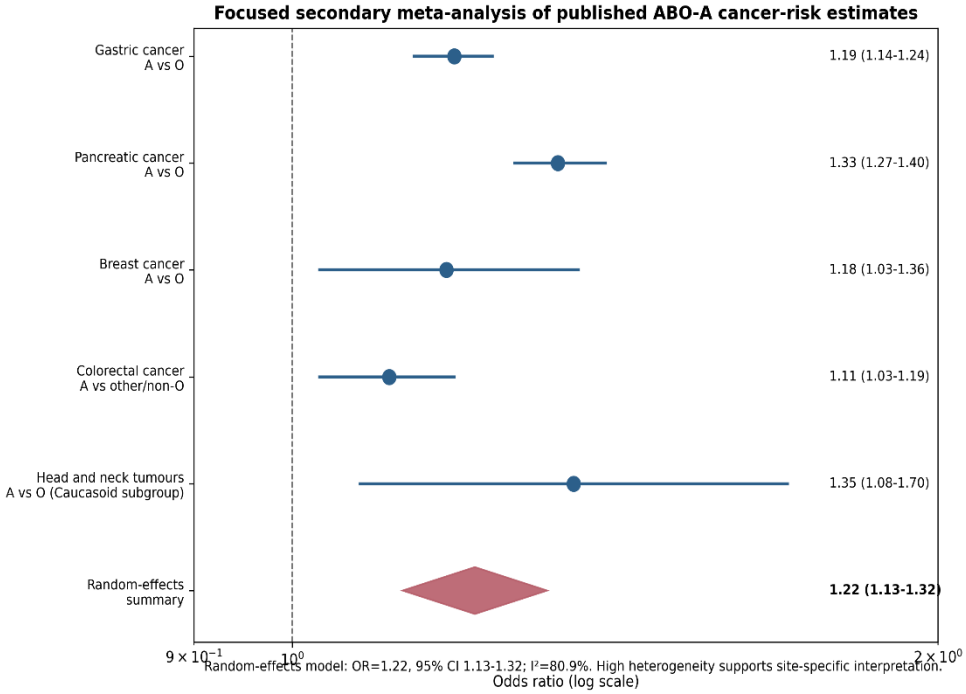


Figure 4. Focused secondary meta-analysis of published ABO-A cancer-risk estimates. The summary estimate is shown for evidence integration, but site-specific interpretation is necessary because heterogeneity is high.

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Cancer outcome	Comparator	Effect estimate	95% CI	Interpretation	Source
Gastric cancer	A vs O	OR 1.19	1.14-1.24	Higher odds; CI excludes 1.00	Liu et al., 2024
Pancreatic cancer	A vs O	OR 1.33	1.27-1.40	Higher odds; CI excludes 1.00	Liu et al., 2024
Breast cancer	A vs O	OR 1.18	1.03-1.36	Higher odds; CI excludes 1.00	Alchazal et al., 2025
Colorectal cancer	A vs other/non-O	OR 1.11	1.03-1.19	Higher odds; CI excludes 1.00	Bahardoust et al., 2023
Head and neck tumours	A vs O (Caucasoid subgroup)	OR 1.35	1.08-1.70	Higher odds; CI excludes 1.00	Shi et al., 2024

Rh, Duffy/ACKR1 and OK/BSG-CD147 evidence

"Rh evidence was comparatively sparse in the PubMed map and did not show the same repeated population-level cancer-risk pattern as ABO. In breast cancer, Rh-positive versus Rh-negative was not statistically conclusive in the recent meta-analysis because the confidence interval crossed 1.00 [13]. As detailed in fundamental blood-group genetics [27], Rh antigens are complex transmembrane proteins without glycan termini, which may explain why Rh does not share the same epithelial glycosylation-driven cancer pathways seen in ABO."

Duffy/ACKR1 evidence is biologically important but epidemiologically less mature as a blood-typing cancer-risk system. ACKR1 binds and presents chemokines and influences leukocyte trafficking; the Duffy-null phenotype is also relevant to baseline neutrophil counts, especially in individuals with African ancestry [17], [18]. This matters clinically because neutrophil thresholds can affect chemotherapy decisions, but it does not imply that Duffy status alone predicts cancer onset or mortality [17], [18].

OK/BSG-CD147 was heavily represented in mechanistic literature. Basigin/CD147 supports MCT1/MCT4 membrane localization, lactate transport, extracellular-matrix remodeling and invasion-associated signaling [28]-[31]. This creates a plausible biomolecular bridge between the OK blood-group system and tumour metabolism. Nevertheless, CD147 mechanistic expression should not be equated with routine OK blood typing; they represent related but distinct levels of biological evidence [19]-[21].

Hematological malignancies and leukemia

Hematological malignancy records formed a substantial component of the evidence map. Recent myeloid-neoplasm literature suggests that ABO distribution may differ in adults and adolescents with myeloid neoplasms, with Zhou et al. [32] reporting a higher prevalence of blood type A in several myeloid-neoplasm categories and a lower prevalence of AB. This is a population-distribution signal and does not by itself establish biological causality.

Leukemia also presents a separate laboratory issue: malignant hematopoiesis can alter or weaken ABO antigen expression and cause blood-group discrepancies. Therefore, in leukemia and plasma-cell dyscrasia, ABO may be relevant both as an inherited population variable and as an acquired serologic finding. The latter is diagnostically important but should not be confused with inherited cancer susceptibility [33].

Biomolecular interpretation

Figure 5. Biomolecular model linking blood-group systems with cancer-relevant pathways. The model separates ABO glycan biology, Duffy/ACKR1 chemokine buffering and OK/BSG-CD147 metabolic-invasion biology.

The most coherent biological explanation for the ABO-cancer association is not that erythrocytes themselves drive cancer. Rather, ABO glycosyltransferases determine terminal glycan structures that are expressed in epithelial tissues and secretions, influencing general disease susceptibility and host-pathogen dynamics [5]–[8].These structures can affect microbial adhesion, mucosal inflammation, coagulation biology through von Willebrand factor and factor VIII levels, and cell-adhesion phenotypes [34], [35]. These pathways are most plausible in gastric, pancreatic and colorectal cancer, where mucosal biology, inflammation and epithelial glycosylation are central to disease development [36]–[43].

Duffy/ACKR1 adds an immune-trafficking layer. By binding chemokines and shaping leukocyte gradients, ACKR1 may influence tumour immune microenvironments [44]. The clinical relevance is currently strongest for interpreting neutrophil counts and treatment thresholds rather than assigning cancer-risk categories.

OK/BSG-CD147 adds a tumour-metabolism layer. CD147 stabilizes monocarboxylate transporters, particularly MCT1 and MCT4, enabling lactate export [45] and supporting the acidic metabolic microenvironment that promotes invasion, immune escape and treatment resistance [46]–[49]. This makes BSG/CD147 a strong

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mechanistic cancer node, but population-level OK blood-group cancer epidemiology remains much less developed than ABO epidemiology.

Clinical interpretation

The practical interpretation is conservative. Blood group is not a screening test, staging criterion or treatment-priority tool. Age, tumour stage, symptoms, performance status, histology, molecular tumour profile, infection status, comorbidity and treatment access remain much stronger determinants of clinical management. Blood-group information may be useful in research stratification, subgroup analysis, transfusion planning and interpretation of hematologic parameters, particularly for Duffy-null associated neutrophil ranges.

For clinicians, the strongest current message is that ABO status may contribute modestly to risk modelling in selected cancer sites, especially gastrointestinal and pancreatic cancer literature, but it should never replace established guidelines. For researchers, the strongest message is that blood-group systems should be integrated with biomolecular covariates rather than treated as isolated categorical variables.

Discussion

This PubMed-based review confirms that blood-group cancer evidence is uneven across systems. Ever since the landmark discovery by Aird et al. [16] linking group A to gastric malignancy. ABO is supported by multiple systematic reviews and meta-analyses, with recurring modest associations in gastric, pancreatic, breast, colorectal and head-and-neck cancer literature. The biological plausibility of these signals is reinforced by the role of ABO in glycosylation, epithelial biology, host-microbe interactions, coagulation, and cancer-related inflammatory pathways [50], [51]. However, effect sizes are generally modest and highly context-dependent

The high heterogeneity in the focused secondary meta-analysis is not unexpected. The included published estimates differ by tumour site, comparator, ancestry group, case definition and adjustment strategy. The summary OR therefore should be viewed as an integrated signal that group A repeatedly trends above the null in several solid-tumour settings, not as a single risk multiplier applicable to individual patients.

The review of biomolecular cancer biology is expanded from traditional blood type via Duffy/ACKR1 and OK/BSG-CD147. ACKR1 links chemokine dynamics, neutrophil interpretation, and blood-group biology. The OK system is linked to MMP activation, invasion, lactate export, and tumor metabolism through BSG/CD147. Although the present epidemiological evidence is not as mature as ABO, these systems are crucial for mechanistic reasoning.

Limitations

First, PubMed was the bibliographic source used for the current structured evidence map. Although the search was broad and supplemented by focused queries, additional databases such as Scopus, Web of Science and Embase may recover records not indexed in PubMed. Second, the quantitative synthesis used published pooled estimates and extractable published comparisons, rather than reconstructing every primary study dataset. This design is appropriate for evidence integration but should be distinguished from a primary-study individual effect extraction meta-analysis. Third, Duffy/ACKR1 and OK/BSG-CD147 evidence is largely mechanistic or biomarker-based, making it less suitable for pooled population-risk estimation. Fourth, ancestry, geography, infection exposure, secretor status, tumour site and adjustment quality are major confounders in blood-group epidemiology.

Conclusion

Cancer susceptibility is most consistent with the ABO blood group system which has the strongest epidemiological evidence for cancer associations, particularly in gastric and pancreatic cancer and with more subtle signals in breast, colorectal and head-and-neck cancer. Through the routes of immunological trafficking and tumor metabolism, respectively, Duffy/ACKR1 and OK/BSG-CD147 offer significant biomolecular background. The evidence supports blood group as a mechanistic insight and research stratification variable, rather than as a stand-alone clinical decision rule.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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Appendix A. Search log summary

Search	PubMed reported count	Records downloaded	Search date
Main broad query	4,974	4,973	2026-07-01
Focused query 1, ABO	2,744	2,743	2026-07-01
Focused query 2, Rh	131	131	2026-07-01
Focused query 3, Duffy/ACKR1	206	206	2026-07-01
Focused query 4, OK/BSG/CD147	2,086	2,086	2026-07-01
Focused query 5, systematic reviews and meta-analyses	580	579	2026-07-01

Appendix B. Extraction fields for study-level updating

Recommended extraction fields for the human-reviewed evidence table include: first author, year, country, design, population, cancer type, blood-group system, comparator, cases, controls, effect measure, effect value, 95% CI, adjustment variables, outcome definition, follow-up duration, risk-of-bias domains and notes on biological interpretation. The review workbook accompanying this manuscript contains structured sheets for these fields.

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