Global assessment of leukemia care quality: insights from the quality of care index (QCI) from 1990 to 2021

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Summary

Background While advancements in leukemia care have been made, the global quality of care remains a concern. This study utilizes a modified quality of care index (QCI) to assess the global status of leukemia care.

Methods We analyzed data from the global burden of disease (GBD) study spanning 1990–2021. The QCI was constructed using principal component analysis, based on the weighted variances of key indicators. We compared the original QCI with our modified version, analyzed QCI trends across different age groups and leukemia subtypes, identified key influencing factors using linear mixed models (LMM), and used spatial autocorrelation analysis to verify the autocorrelation of the socio-demographic index (SDI) region. Then we employed the bayesian age-period-cohort (BAPC) model to predict future QCI trends.

Findings Between 1990 and 2021, both the age-standardized incidence rate (ASIR) and age-standardized death rate (ASDR) for leukemia exhibited a consistent decline. Our modified QCI method outperformed the original approach, particularly when the variance explained by the first principal component was below 80%, demonstrating higher correlation with the healthcare access and quality index (HAQI) (Pearson r = 0.91 vs. 0.89) and improved explanatory power (R^2 = 0.82 vs. 0.79). Over past three decades, QCI was highest in San Marino (97.72%) and lowest in Fiji (3.51%), with significant regional variations across SDI levels (F = 133.40, p < 2e-16). High-SDI regions had the highest QCI (78.50%; 95% confidence interval: 77.20%, 79.70%). QCI trends varied by age, peaking at 94.49% in the 15–19 age group in 2021 and declining to 0.44% in the 75–79 age group. LMM analysis identified sex, age, year, SDI region, and leukemia subtype as significant QCI determinants. Spatial autocorrelation analysis confirmed positive autocorrelation within SDI regions (Global *Moran's I* = 0.87, p < 2e-16). Projections suggest a generally fluctuating upward trend in QCI for leukemia, reaching 79.58% by 2046.

Interpretation The QCI serves as an effective metric for evaluating the quality of leukemia care. Our findings reveal a strong association between leukemia QCI and regional economic and educational development. Age is a critical factor, with an aging population contributing to a potential decline in QCI. These results underscore the urgent need for targeted interventions to enhance health services for older adults and to improve care quality in economically disadvantaged regions.

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Keywords: Leukemia; Quality of care; Global burden; Epidemiology; Linear mixed models

Introduction

Leukemias are a diverse group of hematopoietic cancers marked by the uncontrolled proliferation of abnormal white blood cells in the blood and bone marrow.[1] These malignancies encompass various biologically distinct subtypes and are classified based on morphology, immunophenotype, cytogenetics, molecular abnormalities, and clinical features.[2] Clinically, leukemia is categorized into five major types: acute myeloid leukemia (AML), acute lymphoid leukemia (ALL),

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Research in context

Evidence before this study

Leukemia remains a significant global health challenge, with a substantial global cancer burden despite advances in treatment over the past three decades. Prior research has been limited, particularly in assessing the quality of care received by leukemia patients. A systematic search conducted in October 2024 of PubMed and Google Scholar yielded 5010 relevant results, revealing notable regional and age-related disparities in leukemia care quality.

Added value of this study

This study is the first to estimate global leukemia care quality from 1990 to 2021 across SDI levels, regions, sex, and age, using a modified quality of care index (QCI). Employing linear mixed-effects and Bayesian Age-Period-Cohort (BAPC) models, it identifies key factors affecting care quality and predicts trends to 2046, underscoring the need for targeted interventions in low-SDI regions and for elderly populations.

Implications of all the available evidence

Refining the QCI and analyzing global care quality trends, this study provides predictive insights for the next 25 years, with significant implications for global resource allocation and reducing disparities in patient outcomes. This standardized framework for leukemia care assessment can guide policy interventions, particularly in under-resourced regions, to improve care and outcomes worldwide.

chronic lymphoid leukemia (CLL), chronic myeloid leukemia (CML), and other rarer forms.[3,4] Advances in therapies, including autologous hematopoietic cell transplantation, immunomodulatory drugs, and targeted monoclonal antibodies, have markedly improved the 5-year survival rate of leukemia, now approaching 50% across most age groups, with notable improvements except in patients over 70 years old.[5] Despite these advancements, leukemia continues to contribute substantially to the global cancer burden, with 643.58 thousand new cases and 334.59 thousand deaths reported in 2019.[6] The burden of physical symptoms in leukemia patients, including fatigue, musculoskeletal pain, and skin reactions, is among the highest across all hematological malignancies.[7,8] This underscores the need for continued focus on the quality of leukemia care.[9]

Quality of care, defined as the provision of appropriate and effective medical services that meet patient needs and improve health outcomes, is crucial in managing leukemia.[10] However, Variability in the quality of cancer care remains a significant challenge, as patients often experience a range of physical and quality-of-life issues during care.[11] Despite increasing focus, comprehensive data on leukemia care quality are scarce, and universal indicators for effectively measuring it are lacking.[12] In 2020, S.M. Campbell introduced a novel method for evaluating the quality of cancer careusing six major indicators.[13] Although effective, this method has faced criticism for its limited comprehensiveness and lack of detailed explanation.[14,15] Building on this foundation, the study employs a more comprehensive approach by modifying the quality of care index (QCI) to provide a robust and multidimensional evaluation of leukemia care quality. This approach aims to address the gaps identified in previous assessments and to better understand the factors influencing care quality, thereby informing future interventions and policy decisions.

Methods

Data sources

The global burden of disease (GBD) study provides comprehensive estimates of disease incidence and mortality for countries and regions worldwide by integrating multiple data sources, such as surveys, surveillance data, published literature, and hospital records.[16] Data was obtained from the Global Health Data Exchange GBD (http://ghdx.healthdata.org/gbd-results-tool). The GBD study employs the bayesian meta-regression tool DisMod-MR 2.1 to synthesize these datasets, generating consistent projections of incidence and mortality rates with a 95% uncertainty interval (95% UI).[17] In demographic analyses, standard world population percentages are derived from world health organization (WHO) statistical estimates,[18] while population for each age group is based on official United Nations estimates and projections, including census data from 1990 to 2023 and population projections from 2024 to 2046.[19]

Data collection

We utilized comprehensive epidemiological data on leukemia, including incidence and mortality rates, from 204 countries and territories spanning the period from 1990 to 2021. This dataset encompasses general demographic information such as age and gender. Specifically, we used GBD data on the incidence, mortality, prevalence, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs) for five major subtypes of leukemia: AML, ALL, CML, CLL, and other leukemia.[16] Due to the absence of data on deaths related to CLL in individuals under the age of 20, combined with the rarity of CLL occurrence in children and adolescents, data pertaining to individuals below 20 years of age were excluded from our analysis of CLL. The socio-demographic index (SDI) serves as a comprehensive predictive measure that reflects a country's overall level of development and its correlation with

human health outcomes.[20] The SDI ranges from 0 to 1, with lower values indicating lower educational attainment, lower income per capita, and higher fertility rates.[21] Countries and territories were categorized into five distinct regions—high, high-middle, middle, low-middle, and low SDI—according to the SDI framework developed by GBD researchers.[21] The healthcare access and quality index (HAQI) used in this study was developed by researchers from the GBD 2019 and serves as a key metric for evaluating the quality of healthcare across countries and regions.[22] For this research, leukemia cases were classified using specific International Classification of Diseases (ICD) codes (Supplementary Table S1).[23] The corresponding GBD codes for leukemia included B.1.28 for leukemia, B1.28.3 for AML, B1.28.1 for ALL, B1.28.2 for CLL, B1.28.4 for CML, and B1.28.5 for other leukemia.

ASR and EAPC

To quantify trends in leukemia incidence and mortality across different regions, we utilized the age-standardized rate (ASR) and the estimated annual percentage change (EAPC).[24] The ASR accounts for variations in age structures across populations by providing a weighted average rate based on age distribution.[25] It is calculated using the formula:

$$ASR = \frac{\sum_{k=1}^{n} \alpha_k \beta_k}{\sum_{k=1}^{n} \beta_k} \times 100,000$$

In this formula, α_k represents the age-specific rate for age group k, while β_k denotes the standard population for the same age group. The variable n indicates the total number of age groups. The ASR is expressed per 100,000 population, facilitating comparisons across different populations by adjusting for age structure differences. The age standardization was performed using the global standard population provided by the WHO to ensure consistency and comparability.

$$y = \alpha + \beta x + \varepsilon$$

$$EAPC = 100\% \times (e^{\beta} - 1)$$

In this model, y represents the log-transformed rate, such as incidence or mortality. The parameter α is the intercept of the regression line, while β represents the slope, indicating the annual rate of change. The variable x corresponds to the time variable, typically the year, and ε is the error term accounting for unexplained variability.[26]

Quality of care index

In this study, we derived four secondary indicators from six primary indicators to assess the parameters of care quality. These secondary indicators provide indirect measures of care quality, including the years of life lost to years lived with disability ratio (YLR), the disability-adjusted life years to prevalence ratio (DPR), the mortality to incidence ratio (MIR), and the prevalence to incidence ratio (PIR).[27] The YLR examines the balance between life years lost due to premature mortality and the reduction in quality of life resulting from disability. A higher YLR signifies that a disease predominantly leads to premature death, whereas a lower YLR indicates that the disease reduces quality of life but has a lower mortality rate.[28] The DPR evaluates the impact of a disease on population health relative to its prevalence. A higher DPR suggests that, despite lower prevalance, the disease has a substantial adverse effect on health, while a lower DPR indicates a more prevalent diseases with a milder health impacts.[29] Similarly, the MIR assesses the lethality of a disease by representing the proportion of diagnosed cases that result in death. The MIR reflects the quality and effectiveness of the care provided; therefore, lower MIR indicates more effective care.[30] Lastly, the PIR measures the relationship between the persistence of a disease over time and the incidence of new cases. A higher PIR implies that the disease tends to persist long-term in patients, characteristic of chronic conditions, whereas a lower PIR suggests that the disease may be acute, with patients typically recovering quickly or experiencing rapid progression.[29]

Principal component analysis (PCA) is a multivariate statistical technique that extracts linear combinations of different datasets as orthogonal components.[31] In this study, we used PCA to summarize these four indicators into separate components. We found that the original study used PCA to extract the first principal component (PC1) as a representative of QCI because PC1 usually explains the most variance, that is, it captures the largest amount of information in the data.[14,15] Given that the study aims to capture the overall trend summarizing the four indicators, using PC1 is appropriate, as it represents the linear combination with the greatest variance. However, in certain cases, such as the global AML QCI analysis, YLR, DPR, and MIR contribute similarly to PC1, while PIR predominantly influences the second principal component (PC2) and has limited impact on PC1. This suggests that valuable information in PC2 might be overlooked. To provide a more comprehensive and accurate QCI, we refined the traditional method by combining PC1 and PC2, weighted according to their explained variance. Subsequently, we applied a linear transformation to scale the QCI to a range of 0–100 to more clearly demonstrate differences, with higher scores indicating better quality of care.[32] The formulae are described below:

$$YLR = \frac{YLLs}{YLDs}$$

$$DPR = \frac{DALYs}{Prevalence}$$

$$MIR = \frac{Mortality}{Incidence}$$

$$PIR = \frac{Prevalence}{Incidence}$$

$$PC1 = \omega_1 \cdot YLR + \omega_2 \cdot DPR + \omega_3 \cdot MIR + \omega_4 \cdot PIR$$

$$PC2 = \omega_5 \cdot YLR + \omega_6 \cdot DPR + \omega_7 \cdot MIR + \omega_8 \cdot PIR$$

Here, ω_1, ω_2, ω_3, ..., ω_8 are the weights determined by the PCA process, reflecting each ratio's contribution to the component. PC1 represents the primary axis of variation in the data, and PC2 captures additional variability not explained by PC1.

$$PCA_{score}(x) = \left(\frac{Var(PC1)}{Var(PC1)+Var(PC2)}\right) \times PC1 + \left(\frac{Var(PC2)}{Var(PC1)+Var(PC2)}\right) \times PC2$$

In this equation, $Var(PC1)$ represents the variance explained by the first principal component, and $Var(PC2)$ represents the variance explained by the second principal component.

$$QCI(x) = \frac{PCA_{score}(x) - \min PCA_{score}(x)}{\max PCA_{score}(x) - \min PCA_{score}(x)} \times 100\%$$

In this formula, $QCI(x)$ represents the Quality Care Index for a given observation x. The $PCA_{score}(x)$ is adjusted by subtracting the minimum PCA score and dividing by the range of PCA scores, thus normalizing the index to the specified range. This normalization process ensures that the QCI reflects the relative quality of care, with higher scores indicating superior care quality.[33]

Linear mixed models

We employed linear mixed models (LMM) to examine the effects of various factors on the QCI in the presence of potential cross-confounding factors, such as age, sex, year, SDI region, and leukemia subtype. The LMM was chosen specifically to account for the hierarchical structure and potential correlations within the dataset. To address the non-independence of estimates due to repeated measurements within the same region, we incorporated location as a random effect. This approach controls for intra-regional correlations, yielding more robust and reliable parameter estimates.[34] The model is expressed as follows:

$$QCI_{ijkl} = \beta_0 + \beta_1 Age_i + \beta_2 Sex_j + \beta_3 Subtype_k + \beta_4 Year_t + b_l + \epsilon_{ijkl}$$

In this formula, $\beta_1 Age_i$ represents the fixed effect of age group on QCI, $\beta_2 Sex_j$ denotes the fixed effect of sex, $\beta_3 Subtype_k$ indicates the fixed effect of leukemia subtype, and $\beta_4 Year_t$ accounts for the fixed effect of the year. b_l represents the random effect for SDI region l, and ϵ_{ijkl} is the residual error term, capturing unexplained random variation.

Bayesian age-period-cohort model

The bayesian age-period-cohort (BAPC) model, rooted in bayesian principles, was originally developed to analyze demographic and epidemiological data.[35] Early research aimed to explore the distinct effects of age, period, and cohort on outcomes.[36] However, due to the inherent linear dependency among age, period, and cohort, analyzing these factors independently is challenging.[37] With advancements in modeling approaches, the BAPC model has gained recognition, particularly for its ability to address uncertainty. By incorporating prior distributions into the bayesian framework, the BAPC model can use historical data and expert knowledge to refine estimates, making it especially useful when data is limited or incomplete.[38] In this study, we used the estimated values and UIs (upper and lower limits) of six indicators, divided into 18 age groups, to predict QCI. We incorporated WHO-provided world standard population proportions, along with historical population data from 1990 to 2023 and projected data from 2024 to 2046. Our BAPC model structure is as follows:

$$Y_{ijk} \sim Poisson(\lambda_{ijk} \cdot N_{ijk})$$

where Y_{ijk} represents the observed leukemia case counts for the ith age group, jth time period, and kth birth cohort, N_{ijk} is the total population within the corresponding sex stratification, and λ_{ijk} is the predicted rate.

$$log(\lambda_{ijk}) = \alpha_i + \beta_j + \gamma_k$$

where α_i, β_j, *and* γ_k represent the age, period, and cohort effects, respectively. To ensure smooth trends, we applied a random walk prior and use bayesian inference to extrapolate future years from the posterior distributions of the period and cohort effects. We calculated and standardized the MIR, DPR, YLR, and PIR indicators from 1990 to 2046 to compute QCI and its UI. The uncertainty intervals of the original indicators, including their bounds, were integrated into the BAPC forecast to provide a conservative estimate for each year.

Statistics

In this study, we began with a descriptive examination of global leukemia incidence and mortality rates. Bootstrap testing was employed to compare estimates between 1990 and 2021. Then, we conducted a Kolmogorov–Smirnov test to assess the statistical significance of differences in QCI distributions between the original and proposed methods. We then introduced the HAQI as an external indicator, calculating pearson

correlation coefficients to evaluate associations between both QCI and HAQI. Linear regression models were constructed, and R-squared values were computed to measure the variance explained by the QCI. Additionally, we compared model complexity and fit using the akaike information criterion (AIC) and bayesian information criterion (BIC). Following this, we applied PCA to calculate the QCI for various countries and regions. We then performed a descriptive analysis of the QCI on a global scale, focusing on trends across different age groups. To assess the variation in QCI across regions with differing SDI levels, we conducted subgroup analyses using analysis of variance (ANOVA). To account for the potential complexity of the relationships between QCI and various factors, we employed LMM. Spatial autocorrelation analysis was then performed to confirm the spatial clustering of SDI levels. Additionally, we performed a 25-year projection analysis of QCI using the BAPC model. Key indicator values are presented with 95% UI. A two-sided *p*-value of less than 0.05 was considered indicative of statistical significance. All statistical analyses and visualizations were performed using R statistical software (version 4.4.1).

Ethics

The institutional review board granted an exemption for this study, as it utilized publicly accessible data that contained no confidential or personally identifiable patient information.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Global burden of leukemia

Globally, the incidence, mortality, and trend changes for leukemia from 1990 to 2021 are summarized in Table 1. In 2021, the incident cases for leukemia, AML, ALL, CLL, CML, and other leukemia reached 461.42 thousand, 144.65 thousand, 103.73 thousand, 117.99 thousand, 35.83 thousand and 59.23 thousand cases, respectively, with corresponding deaths increasing to 320.28 thousand, 130.19 thousand, 71.22 thousand, 45.57 thousand, 23.16 thousand and 50.14 thousand cases. Despite a several-fold increase in both incidence and mortality cases, the age-standardized death rate (ASDR) for leukemia has exhibited a rapid decline since 1990, while the age-standardized incidence rate (ASIR) has exhibited a slight downward trend. In 2021, AML reported the highest incidence rates among leukemia subtypes (Fig. 1A and B). The ASIR for leukemia, AML and ALL in 2021 were 5.63, 1.73 and 1.37 per 100,000 population, respectively, with the EAPC reflecting a slight decline (–1.17%, –0.03%, and –0.64%, respectively). The ASIR for CLL, CML, and other leukemia in 2021 were 1.39, 0.43, and 0.71 per 100,000 population, respectively, all demonstrating a downward trend in EAPC (–0.47%, –3.03%, and –0.42%, respectively). In 2021, AML reported the highest mortality rates among leukemia subtypes (Fig. 1C and D). In 2021, the ASDR for leukemia, AML, ALL, CLL, CML, and other leukemia were 3.89, 1.57, 0.90, 0.55, 0.28, and 0.60 per 100,000 population, respectively, all with declines in EAPC (–0.65%, –0.21%, –1.73%, –1.45%, –3.43%, and –0.73%, respectively). Overall, the ASIR and ASDR of leukemia showed a significant downward trend.

Comparison of QCI methods

During the QCI calculation process, we observed that when the variance explained by the PC1 exceeded 95%, there was no significant difference between the QCI values calculated by the two methods. However, when the variance explained by PC1 was less than 80%, our proposed method showed clear advantages over the original QCI values (Supplementary Table S2). For AML, we first applied the Kolmogorov–Smirnov test, which revealed a significant difference between the QCI values generated by the original method and our method ($D = 0.34$, $p < 2e\text{-}16$). Subsequently, we introduced an health metric, the HAQI, to calculate the pearson correlation coefficients between both QCI methods and the HAQI (original QCI correlation: 0.89, current QCI correlation: 0.91). Linear regression models were then constructed using both QCI values and the HAQI to assess the models' goodness of fit in explaining HAQI variations. The R^2 were higher for our current QCI (original QCI: 0.79, current QCI: 0.82), indicating a stronger explanatory power. To further validate the performance of the two methods, we analyzed the AIC and BIC values, which evaluate model complexity and fit quality. Our method yielded lower AIC (original QCI: 2728.04, current QCI: 2605.20) and BIC values (original QCI: 2740.06, current QCI: 2617.17), confirming its superiority. This improvement is particularly evident when the proportion of variance explained by the first principal component is lower, indicating that our proposed QCI method is more suitable under such conditions.

QCI trends in various countries around the world

We constructed specific QCI equations for different types of leukemia at various analytical scales. For leukemia, we began by assessing the correlations among four variables: YLR, DPR, MIR, and PIR. The analysis revealed strong correlations among YLR, DPR, and MIR, while PIR exhibited a weak correlation (Supplementary Fig. S1A). Utilizing PCA, we developed the equation model for leukemia. The first principal component explained 95.21% of the variance, with the corresponding equation: PC1 = –0.50 * YLR – 0.50 * DPR – 0.50 * MIR + 0.50 * PIR. The second principal

Measure	Metric	Leukemia			Acute myeloid leukemia			Acute lymphoid leukemia			Chronic lymphoid leukemia			Chronic myeloid leukemia			Other leukemia		
		1990 (95%UI)	2021 (95%UI)	Statistically Significant?	1990 (95%UI)	2021 (95%UI)	Statistically Significant?	1990 (95%UI)	2021 (95%UI)	Statistically Significant?	1990 (95%UI)	2021 (95%UI)	Statistically Significant?	1990 (95%UI)	2021 (95%UI)	Statistically Significant?	1990 (95%UI)	2021 (95%UI)	Statistically Significant?
DALYs	Number	11,761,683 (10,032,321–13,623,198)	10,982,836 (9,018,077–12,286,933)	No	3,342,913 (2,394,171–4,709,119)	4,135,056 (3,446,487–4,895,237)	No	5,455,115 (4,149,674–7,135,245)	3,719,777 (2,587,455–4,353,159)	Yes	715,876 (600,949–791,419)	1,002,495 (780,350–1,150,043)	Yes	1,070,234 (799,053–1,302,279)	686,351 (485,645–875,687)	Yes	1,177,544 (846,733–1,572,822)	1,439,157 (1,013,666–1,876,919)	No
	Rate	220.52 (188.10–255.42)	139.18 (114.28–155.70)	Yes	62.68 (44.89–88.29)	52.40 (43.67–62.03)	No	102.28 (77.80–133.78)	47.14 (32.79–55.16)	Yes	13.42 (11.27–14.84)	12.70 (9.89–14.57)	No	20.07 (14.98–24.42)	8.70 (6.15–11.10)	Yes	22.08 (15.88–29.49)	18.24 (12.85–23.78)	No
Deaths	Number	248,105 (217,786–277,354)	320,284 (274,969–349,050)	Yes	74,917 (58,730–94,714)	130,189 (113,625–149,385)	Yes	82,769 (64,015–105,554)	71,221 (49,169–83,167)	No	29,278 (25,730–31,837)	45,573 (37,693–51,085)	Yes	29,220 (23,525–34,251)	23,159 (17,503–28,477)	No	31,920 (24,158–41,197)	50,142 (36,918–62,836)	Yes
	Rate	4.65 (4.08–5.20)	4.06 (3.48–4.42)	No	1.40 (1.10–1.78)	1.65 (1.44–1.89)	No	1.55 (1.20–1.98)	0.90 (0.62–1.05)	Yes	0.55 (0.48–0.60)	0.58 (0.48–0.65)	No	0.55 (0.44–0.64)	0.29 (0.22–0.36)	Yes	0.60 (0.45–0.77)	0.64 (0.47–0.80)	No
Incidence	Number	311,648 (278,620–343,177)	461,423 (397,548–504,397)	Yes	79,372 (62,805–99,428)	144,645 (126,237–164,851)	Yes	98,149 (77,896–123,508)	103,727 (71,606–122,517)	No	57,961 (53,100–61,681)	117,987 (98,330–132,718)	Yes	39,482 (33,293–45,117)	35,831 (27,939–42,581)	No	36,683 (27,291–47,289)	59,232 (42,496–74,747)	Yes
	Rate	5.84 (5.22–6.43)	5.85 (5.04–6.39)	No	1.49 (1.18–1.86)	1.83 (1.60–2.09)	No	1.84 (1.46–2.32)	1.31 (0.91–1.55)	Yes	1.09 (1.00–1.16)	1.50 (1.25–1.68)	Yes	0.74 (0.62–0.85)	0.45 (0.35–0.54)	Yes	0.69 (0.51–0.89)	0.75 (0.54–0.95)	No
Prevalence	Number	913,608 (835,991–995,397)	1,715,911 (1,449,115–1,909,582)	Yes	122,732 (93,683–161,905)	204,429 (176,439–233,355)	Yes	237,056 (200,614–285,034)	386,812 (266,572–486,273)	Yes	306,132 (288,026–321,531)	721,066 (598,861–814,073)	Yes	57,606 (51,121–63,309)	63,728 (51,654–74,038)	No	190,082 (141,407–244,952)	339,873 (238,896–421,470)	Yes
	Rate	17.13 (15.67–18.66)	21.74 (18.36–24.20)	Yes	2.30 (1.76–3.04)	2.59 (2.24–2.96)	No	4.44 (3.76–5.34)	4.90 (3.38–6.16)	No	5.74 (5.40–6.03)	9.14 (7.59–10.32)	Yes	1.08 (0.96–1.19)	0.81 (0.65–0.94)	Yes	3.56 (2.65–4.59)	4.31 (3.03–5.34)	No
YLDs	Number	132,170 (95,540–173,960)	229,000 (161,685–301,171)	Yes	22,090 (15,114–31,376)	39,321 (27,930–51,618)	Yes	34,596 (23,419–48,846)	45,084 (27,788–63,715)	No	41,008 (29,804–52,376)	91,451 (65,134–120,596)	Yes	10,793 (7677–14,495)	10,432 (7064–14,514)	No	23,683 (15,511–33,562)	42,712 (28,705–59,963)	Yes
	Rate	2.48 (1.79–3.26)	2.90 (2.05–3.82)	No	0.41 (0.28–0.59)	0.50 (0.35–0.65)	No	0.65 (0.44–0.92)	0.57 (0.35–0.81)	No	0.77 (0.56–0.98)	1.16 (0.83–1.53)	Yes	0.20 (0.14–0.27)	0.13 (0.09–0.18)	No	0.44 (0.29–0.63)	0.54 (0.36–0.76)	No
YLLs	Number	11,629,513 (9,916,394–13,478,022)	10,753,836 (8,862,609–12,069,351)	No	3,320,823 (2,375,973–4,679,399)	4,095,734 (3,415,731–4,851,329)	No	5,420,518 (4,122,886–7,096,333)	3,674,693 (2,561,500–4,299,470)	Yes	674,868 (561,863–749,964)	911,044 (704,583–1,050,843)	Yes	1,059,442 (789,565–1,290,243)	675,920 (477,068–864,273)	Yes	1,153,861 (828,777–1,539,990)	1,396,445 (976,890–1,826,497)	No
	Rate	218.04 (185.92–252.70)	136.27 (112.31–152.94)	Yes	62.26 (44.55–87.73)	51.90 (43.28–61.48)	No	101.63 (77.30–133.05)	46.57 (32.46–54.48)	Yes	12.65 (10.53–14.06)	11.54 (8.93–13.32)	No	19.86 (14.80–24.19)	8.57 (6.05–10.95)	Yes	21.63 (15.54–28.87)	17.70 (12.38–23.15)	No
ASIR	Rate	6.89 (6.22–7.49)	5.63 (4.83–6.17)	Yes	1.77 (1.43–2.16)	1.73 (1.51–1.98)	No	1.79 (1.42–2.24)	1.37 (0.95–1.64)	Yes	1.55 (1.41–1.64)	1.39 (1.16–1.56)	No	0.94 (0.81–1.07)	0.43 (0.33–0.51)	Yes	0.84 (0.64–1.08)	0.71 (0.51–0.90)	No
ASDR	Rate	5.56 (4.97–6.13)	3.89 (3.34–4.25)	Yes	1.69 (1.36–2.08)	1.57 (1.37–1.80)	No	1.55 (1.21–1.96)	0.90 (0.62–1.05)	Yes	0.83 (0.74–0.90)	0.55 (0.46–0.62)	Yes	0.72 (0.59–0.84)	0.28 (0.21–0.34)	Yes	0.77 (0.60–0.98)	0.60 (0.44–0.75)	No

Abbreviations: ASIR, age-standardized incidence rate; ASDR, age-standardized death rate; DALYs, disability-adjusted life years; YLDs: years lived with disability; YLLs, years of life Lost; UI, uncertainty interval. Note: The units for Deaths, Incidence, and Prevalence are measured in cases, while DALYs, YLDs, and YLLs are measured in person-years. The rates for all indicators are expressed per 100,000 population.

Table 1: **Comparative analysis of leukemia subtypes in terms of DALYs, deaths, incidence, prevalence, YLDs, YLLs, ASIR, and ASDR between 1990 and 2021.**

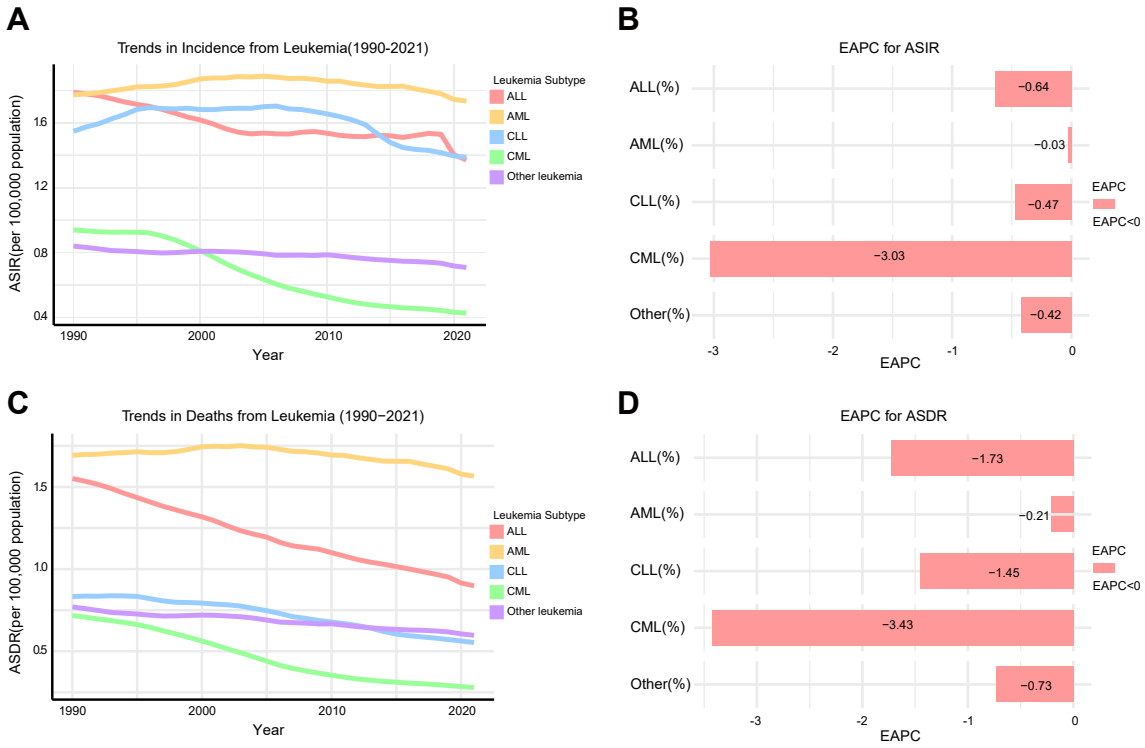

***Fig. 1:* Trends in incidence and deaths of leukemia subtypes from 1990 to 2021.** (A) Age-standardized incidence rate (ASIR) of leukemia subtypes from 1990 to 2021. The graph shows the trends in ASIR for ALL, AML, CLL, CML, and other leukemia. (B) Estimated annual percentage change (EAPC) for ASIR of different leukemia subtypes. (C) Age-standardized death rate (ASDR) of leukemia subtypes from 1990 to 2021. The graph illustrates the trends in ASDR for the same leukemia categories, demonstrating a general decline over time. (D) EAPC for ASDR of different leukemia subtypes.

component accounted for 3.54% of the variance, with the equation: PC2 = –0.46 * YLR – 0.53 * DPR + 0.57 * MIR – 0.42 * PIR (Supplementary Fig. S1B). However, for AML, PC1 explained 67.50% of the variance, and PC2 explained 27.06% of the variance (Supplementary Fig. S1C and D). Similarly, we performed correlation and principal component analyses for ALL, CLL, CML, and other leukemia (Supplementary Table S3). Following this, we calculated the overall QCI by averaging the overall changes including DALYs, mortality, incidence, prevalence, YLDs, and YLLs in each country from 1990 to 2021. The results indicated that Andorra, Switzerland, and San Marino demonstrated exceptionally high QCI levels in leukemia care (88.46%, 89.54%, and 97.72%, respectively), on the contrary, Fiji, Kiribati, and Papua New Guinea reached bottom QCI levels in leukemia care (3.51%, 5.35%, and 7.47%, respectively) (Fig. 2A). However, it is concerning that several African countries, including Guinea and Mozambique (4.78% in ALL and 22.52% in AML, respectively), as well as island nations such as Kiribati (17.96% in other leukemia), ranked at the bottom of the global QCI levels (Fig. 2B–F and Table 2). The combination of low medical infrastructure and environmental constraints hampers the ability of healthcare institutions in these countries to provide high-quality care to leukemia patients. To further investigate regional disparities, we conducted an univariate analysis based on global national SDI classifications. The Welch's ANOVA was applied for data meeting normality but not homogeneity of variance. Dunn's test was consistently used for post hoc analyses. The results indicated that the QCI for leukemia varies significantly across different SDI levels. The QCI was highest in regions with high SDI at 78.50% (95% confidence interval [CI]: 77.20%, 79.70%), followed by high-middle SDI at 63.70% (95% CI: 59.30%, 68.00%), middle SDI at 39.10% (95% CI: 34.90%, 43.40%), low-middle SDI at 23.40% (95% CI: 22.00%, 24.80%), and lowest in low SDI regions at 21.60% (95% CI: 20.60%, 22.60%). No significant differences were observed between the low-middle and low SDI regions in leukemia, however, significant differences were detected among the other SDI groups ($F = 133.40$, $p < 2e\text{-}16$) (Fig. 3A). When stratifying by leukemia subtypes (AML, ALL, CLL, CML, and other leukemia), significant differences were found across the five SDI groups. The QCI in the high SDI group was notably higher than in all other SDI categories (Fig. 3B–F). These findings suggest that the SDI level of a region significantly impacts the QCI for leukemia.

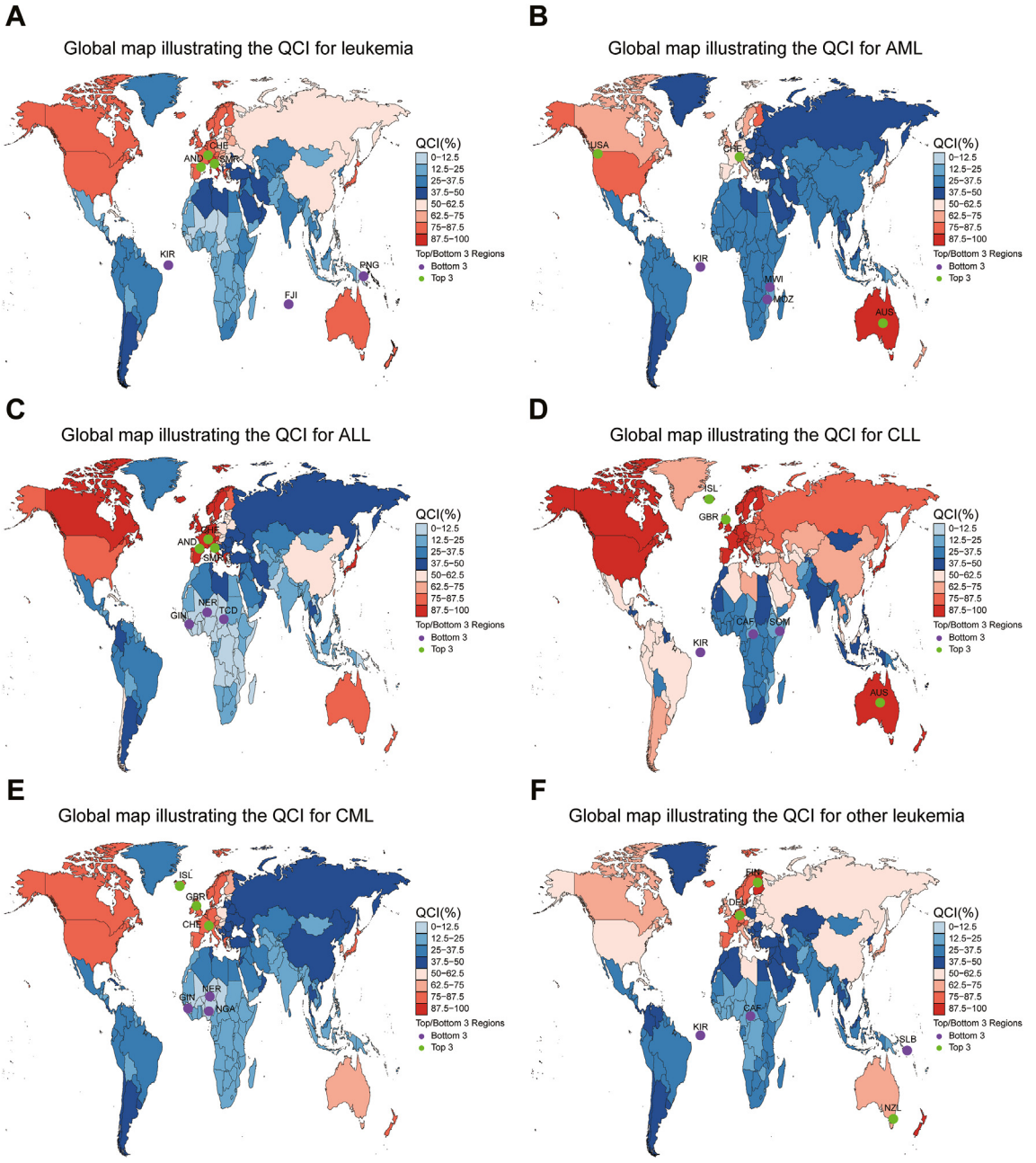

***Fig. 2:* Global distribution of overall QCI for leukemia.** (A) Global map illustrating the QCI for leukemia. Regions are color-coded, with lighter shades of blue indicating lower QCI levels and darker shades of red indicating higher QCI levels. Purple markers highlight the three countries with the lowest QCI rankings, while green markers highlight the three countries with the highest QCI rankings. Countries are identified using iso3 codes. (B) Global map illustrating the QCI for AML with similar color-coding as in panel A. (C) Global map showing the QCI for ALL with similar color-coding as in panel A. (D) Global map depicting the QCI for CLL with similar color-coding as in panel A. (E) Global map representing the QCI for CML with similar color-coding as in panel A. (F) Global map displaying the QCI for Other leukemias with similar color-coding as in panel A.

QCI situation of each age group and sex group

The results for leukemia in 1990 showed that the 15–19 age group had the lowest QCI among youth, with a value of 21.42%. Among the elderly, QCI began to decline rapidly after age 75, reaching its lowest point at age 85+ (8.68%) (Supplementary Fig. S2A). By 2021, the QCI was highest for the 15–19 age group (94.49%) among youth, then gradually declined with age, reaching its lowest at 75–79 years old (0.44%) (Supplementary Fig. S2B). For AML, both 1990 and 2021 exhibited a

Order	Leukemia		Acute myeloid leukemia		Acute lymphoid leukemia		Chronic lymphoid leukemia		Chronic myeloid leukemia		Other leukemia	
	Location	QCI (%)	Location	QCI (%)	Location	QCI (%)	Location	QCI (%)	Location	QCI (%)	Location	QCI (%)
Top 20 regions												
1	San Marino	97.72	Switzerland	95.86	Switzerland	96.77	Australia	96.45	Switzerland	87.10	New Zealand	97.01
2	Switzerland	89.54	Australia	90.63	San Marino	95.80	Iceland	95.76	United Kingdom	86.63	Finland	92.48
3	Andorra	88.46	United States of America	75.86	Andorra	95.37	United Kingdom	95.67	Iceland	86.37	Germany	86.18
4	Italy	87.94	Finland	75.55	Monaco	95.10	Canada	95.65	Sweden	85.87	Iceland	83.87
5	Germany	87.46	Canada	70.09	Sweden	94.46	Switzerland	95.30	San Marino	85.68	Switzerland	83.37
6	Spain	87.39	Iceland	66.58	Italy	94.01	Japan	95.14	Monaco	84.89	Sweden	81.26
7	Monaco	87.29	New Zealand	64.87	Iceland	93.04	New Zealand	94.98	Andorra	84.73	San Marino	80.95
8	Sweden	87.20	Japan	64.34	Spain	92.69	San Marino	94.90	New Zealand	84.29	Netherlands	80.78
9	Canada	86.69	San Marino	64.18	United Kingdom	92.20	Italy	93.98	United States of America	84.25	Monaco	80.14
10	Iceland	86.07	Sweden	64.05	Greece	92.15	Netherlands	93.91	Italy	83.31	Spain	79.61
11	United Kingdom	84.28	Netherlands	63.18	Netherlands	91.89	Andorra	93.80	Netherlands	83.08	Austria	79.39
12	Austria	82.88	Italy	62.96	Canada	91.78	Sweden	93.56	Canada	82.26	Andorra	78.84
13	Netherlands	82.73	United Kingdom	62.93	Austria	91.52	Monaco	93.14	Norway	81.98	Belgium	77.02
14	New Zealand	82.13	Monaco	61.83	Belgium	90.25	Norway	92.87	Spain	81.85	Ireland	76.69
15	Ireland	81.93	Spain	61.81	Japan	90.04	Spain	92.79	Austria	80.30	Norway	76.68
16	Greece	81.45	Andorra	61.39	Germany	89.34	United States of America	92.71	Greece	79.30	France	76.60
17	Slovenia	81.41	Ireland	60.73	Norway	89.24	Austria	91.80	Japan	78.96	Luxembourg	75.50
18	Australia	80.82	Austria	60.14	Luxembourg	89.08	Germany	91.65	Ireland	78.90	Greece	74.91
19	France	80.01	Greece	59.97	France	88.47	Slovenia	91.50	Germany	78.68	United Kingdom	73.90
20	Norway	79.81	Slovenia	59.76	Ireland	88.25	Denmark	90.87	Denmark	78.29	Malta	73.51
Bottom 20 regions												
1	Fiji	3.51	Mozambique	22.52	Chad	4.75	Central African Republic	17.95	Nigeria	8.10	Kiribati	17.96
2	Kiribati	5.35	Kiribati	22.82	Guinea	4.78	Kiribati	20.21	Guinea	8.40	Central African Republic	19.52
3	Papua New Guinea	7.47	Malawi	23.58	Niger	4.99	Somalia	20.31	Niger	8.63	Solomon Islands	19.81
4	Guinea	8.32	Papua New Guinea	23.65	Nigeria	5.33	Haiti	22.29	Mali	9.69	Nauru	19.84
5	Central African Republic	10.31	Guinea	24.62	Kiribati	5.84	Ethiopia	22.73	Sierra Leone	10.90	Vanuatu	20.49
6	Nauru	10.71	Saint Kitts and Nevis	24.92	Guinea-Bissau	6.20	Afghanistan	23.12	Burkina Faso	12.06	Marshall Islands	20.51
7	Niger	10.78	United Republic of Tanzania	25.58	Sierra Leone	6.25	Guinea-Bissau	23.33	Chad	12.24	Guinea-Bissau	20.71
8	Mali	11.46	Sierra Leone	25.59	Haiti	6.55	Mozambique	23.83	Benin	12.28	Micronesia (Federated States of)	21.35
9	Marshall Islands	11.69	Burundi	25.77	Benin	7.27	Burundi	23.88	Guinea-Bissau	13.13	Fiji	21.54
10	Chad	11.85	Rwanda	25.79	Burkina Faso	7.61	Eritrea	24.06	Angola	14.41	Somalia	21.65
11	Tuvalu	11.86	Djibouti	25.99	Mozambique	7.65	Chad	24.49	Central African Republic	14.52	Haiti	21.82
12	Lao People's Democratic Republic	11.89	Nigeria	26.07	Mali	7.69	Angola	25.73	Liberia	14.83	Chad	21.86
13	Philippines	11.92	Haiti	26.07	Malawi	7.96	Rwanda	26.20	Senegal	15.14	Papua New Guinea	22.11
14	Micronesia (Federated States of)	12.20	Zambia	26.14	Burundi	8.23	Lesotho	26.20	Haiti	15.15	Niger	22.47
15	Sierra Leone	12.22	Solomon Islands	26.17	Liberia	8.32	Democratic Republic of the Congo	26.27	Afghanistan	15.21	Guinea	22.61

(Table 2 continues on next page)

Order	Leukemia		Acute myeloid leukemia		Acute lymphoid leukemia		Chronic lymphoid leukemia		Chronic myeloid leukemia		Other leukemia	
	Location	QCI (%)	Location	QCI (%)	Location	QCI (%)	Location	QCI (%)	Location	QCI (%)	Location	QCI (%)
(Continued from previous page)												
16	Angola	12.54	Nauru	26.24	Cameroon	8.33	Niger	26.43	The Republic of Côte d'Ivoire	15.66	Lesotho	22.77
17	Solomon Islands	12.66	Uganda	26.26	The Republic of Côte d'Ivoire	8.39	Solomon Islands	26.77	Cameroon	15.77	Tuvalu	22.90
18	Myanmar	12.73	Madagascar	26.33	Papua New Guinea	8.49	Zambia	26.88	Burundi	15.96	Ethiopia	23.31
19	Afghanistan	12.89	Eritrea	26.45	Togo	8.99	Lao People's Democratic Republic	26.95	Malawi	16.13	Eswatini	23.53
20	Vanuatu	12.93	Benin	26.47	Zambia	9.10	Guinea	27.10	Gambia	16.25	Sierra Leone	23.55

Table 2: **The top 20 and bottom 20 regions in the global overall QCI ranking.**

similar trend of increasing QCI with age. The <5 years age group had the lowest QCI (0.10% in 1990 and 1.28% in 2021, respectively), while the 85+ age group had the highest QCI (97.20% in 1990 and 96.84% in 2021, respectively) (Supplementary Fig. S2C and D). In the case of ALL, the trend in 1990 initially decreased and then gradually increased with age, with the lowest QCI in the 5–9 years age group (1.41%) and the highest in the 85+ age group (96.61%) (Supplementary Fig. S2E). In 2021, however, the QCI showed a gradual decline with age, with the <5 years age group having the highest QCI (98.52%) and the 85+ age group the lowest (1.84%) (Supplementary Fig. S2F). For CLL, both in 1990 and 2021, there was a rapid decrease in QCI after the 75–79 years age group, reaching the lowest point in the 85+ age group (9.58% in 1990 and 4.29% in 2021, respectively) (Supplementary Fig. S2G and H). CML in both years displayed a gradual increase in QCI with age, with the <5 years age group showing the lowest QCI (7.08% in 1990 and 8.90% in 2021, respectively) and the 85+ age group showing the highest QCI (73.51% in 1990 and 79.57% in 2021, respectively) (Supplementary Fig. S2I and J). For other leukemia, the QCI in 1990 first decreased and then increased with age, with the lowest in the 15–19 years age group (0.73%) and the highest in the 85+ age group (98.25%) (Supplementary Fig. S2K). In 2021, the QCI exhibited a fluctuating downward trend with age, with the <5 years age group having the highest QCI (99.97%) and the 85+ age group the lowest (0.97%) (Supplementary Fig. S2L). Overall, significant differences in QCI were observed across different years and age groups. Although the trends were consistent between genders, slight differences in QCI levels suggest that age, year, and gender may interact in complex ways, necessitating further analysis and validation.

The impact of each variable on QCI

Through a detailed analysis of each variable, we identified, age, sex, year, SDI region, and leukemia subtype as potential factors influencing the QCI. To address potential multicollinearity, we confined our analysis to data from five distinct leukemia subtypes. We computed the corresponding correlation coefficients and principal component equations to derive the QCI, accounting for all variables. The first principal component accounted for 67.90% of the variance, while the second explained 22.60% of the variance. We subsequently employed a LMM to construct a analysis model. Prior to modeling, the QCI data were standardized using Z-scores. As CLL lacked data for six key indicators, such as DALYs and deaths in the 0–19 age group, the analysis for each leukemia subtype was restricted to the 20–85+ age range. The fixed effects included in the model were sex, age, year, and leukemia subtype, while the SDI region variable was treated as a random effect to account for regional differences. We calculated the effect size estimates and standard errors for each fixed effect, assessing the significance of these estimates (Table 3). The results indicate that the sex variable had a significant negative impact on QCI ($beta = -0.06$, $p < 2e\text{-}16$) (Supplementary Fig. S3A), suggesting that, after controlling for other variables, men had significantly lower QCI scores compared to women. Age exhibited a nonlinear influence on QCI, with significant variability across different age groups. The younger age group (25–29 years) had the largest negative effect ($beta = -0.77$, $p < 2e\text{-}16$), while the middle-aged group (45–49 years) displayed a positive association with QCI ($beta = 0.07$, $p = 2.43e\text{-}14$). In the older age group (80–84 years), the effect size reverted to a negative coefficient ($beta = -0.03$, $p = 0.38e\text{-}2$), indicating a complex, multifaceted relationship between age and QCI (Supplementary Fig. S3B). Regarding the year variable, there was a significant positive trend from 1990 to 2021, with the estimated values increasing over time, indicating a steady improvement in QCI as medical resources advanced (year 1994: $beta = 0.06$, $p = 0.54e\text{-}2$; year 2021: $beta = 0.43$, $p < 2e\text{-}16$) (Supplementary Fig. S3C). Across different leukemia subtypes, the

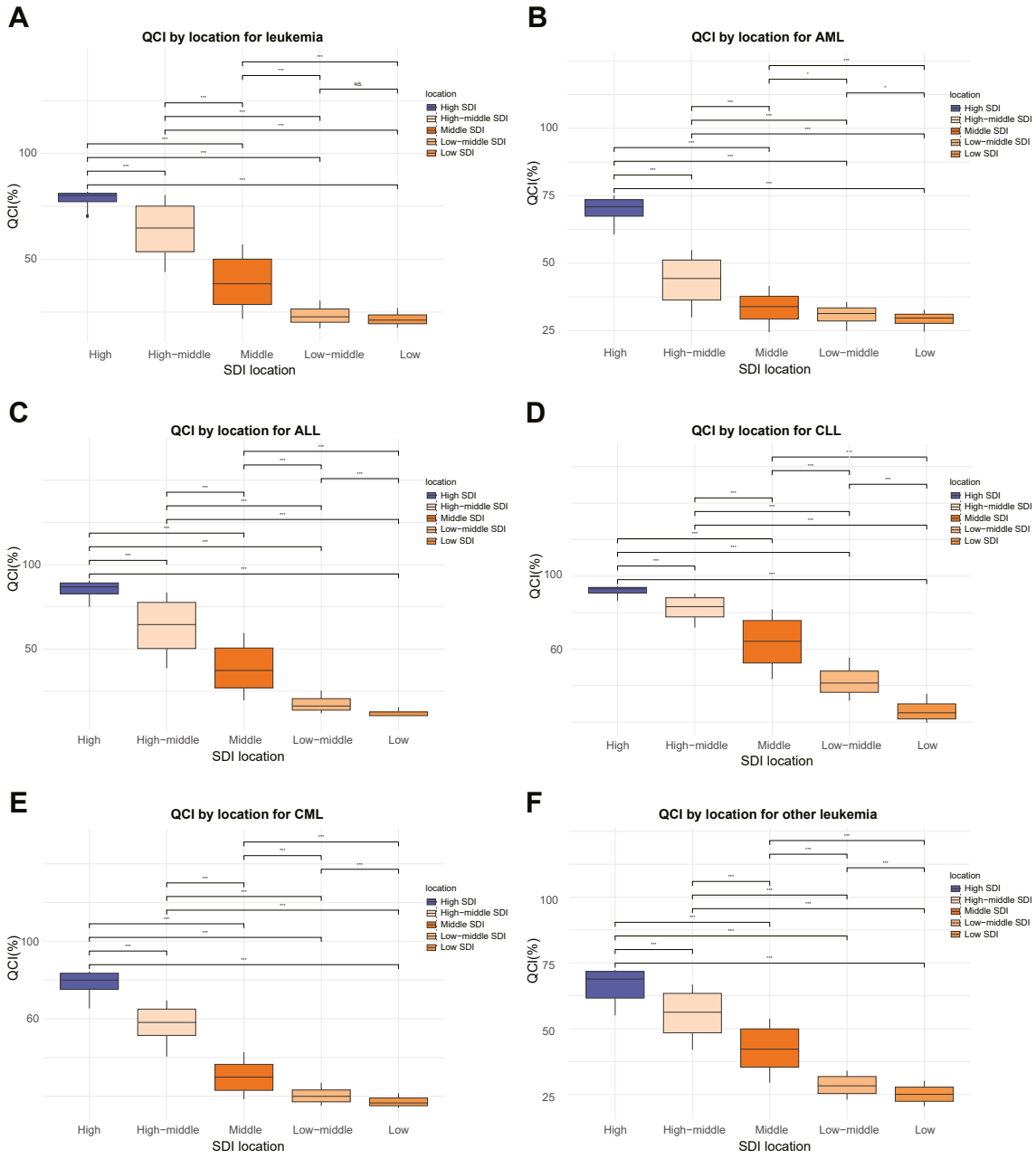

***Fig. 3*: Univariate analysis of QCI by SDI group for different leukemia subtypes.** (A) Boxplot of QCI by SDI group for leukemia: The boxplot represents the distribution of QCI for leukemia across different SDI locations (High, High-middle, Middle, Low-middle, and Low SDI). Each boxplot shows the median (line inside the box), interquartile range (box edges), and the range of data (whiskers). Asterisks above the plots denote the level of statistical significance for pairwise comparisons between SDI groups (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$). (B) Boxplot of QCI by SDI group for AML: Similar to panel A, this panel shows the QCI distribution for AML, stratified by SDI groups, with the same conventions for boxplots and significance levels. (C) Boxplot of QCI by SDI group for ALL: This panel shows the QCI distribution for ALL, stratified by SDI groups, with the same conventions for boxplots and significance levels. (D) Boxplot of QCI by SDI group for CLL: This panel shows the QCI distribution for CLL, stratified by SDI groups, with the same conventions for boxplots and significance levels. (E) Boxplot of QCI by SDI group for CML: This panel shows the QCI distribution for CML, stratified by SDI groups, with the same conventions for boxplots and significance levels. (F) Boxplot of QCI by SDI group for other leukemia: This panel shows the QCI distribution for other leukemia, stratified by SDI groups, with the same conventions for boxplots and significance levels.

Effects	Beta	Std.error	t value	p value
Fixed effects (Intercept)	−8.47e-01	2.40e-01	−3.53	0.02*
Sex				
Male	−5.78e-02	5.20e-03	−11.11	<2e-16 ***
Age				
25–29	−7.69e-01	9.73e-03	−79.01	<2e-16 ***
30–34	−7.99e-01	9.73e-03	−82.10	<2e-16 ***
35–39	2.13e-02	9.73e-03	2.18	0.03 *
40–44	−1.98e-01	9.73e-03	−20.29	<2e-16 ***
45–49	7.43e-02	9.73e-03	7.63	2.43e-14 ***
50–54	−7.86e-02	9.73e-03	−8.08	6.98e-16 ***
55–59	5.49e-02	9.73e-03	5.64	1.75e-08***
60–64	4.07e-02	9.73e-03	4.18	2.92e-05 ***
65–69	5.60e-02	9.73e-03	5.76	8.62e-09 ***
70–74	−7.07e-02	9.73e-03	−7.26	4.00e-13 ***
75–79	6.70e-02	9.73e-03	6.88	6.20e-12 ***
80–84	−2.81e-02	9.73e-03	−2.89	3.86e-3**
85+	−7.12e-03	9.73e-03	−0.73	0.46
Year				
1991	1.32e-02	2.08e-02	0.64	0.53
1992	2.73e-02	2.08e-02	1.31	0.19
1993	4.14e-02	2.08e-02	1.99	0.05*
1994	5.79e-02	2.08e-02	2.78	0.01**
1995	7.71e-02	2.08e-02	3.71	2.11e-4***
1996	9.59e-02	2.08e-02	4.61	4.08e-06***
1997	1.11e-01	2.08e-02	5.35	8.87e-08***
1998	1.25e-01	2.08e-02	5.98	2.25e-09***
1999	1.35e-01	2.08e-02	6.51	7.75e-11***
2000	1.48e-01	2.08e-02	7.11	1.17e-12***
2001	1.61e-01	2.08e-02	7.71	1.29e-14***
2002	1.74e-01	2.08e-02	8.34	<2e-16***
2003	1.88e-01	2.08e-02	9.02	<2e-16***
2004	2.06e-01	2.08e-02	9.88	<2e-16***
2005	2.28e-01	2.08e-02	10.94	<2e-16***
2006	2.50e-01	2.08e-02	11.98	<2e-16***
2007	2.69e-01	2.08e-02	12.90	<2e-16***
2008	2.85e-01	2.08e-02	13.70	<2e-16***
2009	3.00e-01	2.08e-02	14.43	<2e-16***
2010	3.16e-01	2.08e-02	15.19	<2e-16***
2011	3.29e-01	2.08e-02	15.83	<2e-16***
2012	3.41e-01	2.08e-02	16.39	<2e-16***
2013	3.52e-01	2.08e-02	16.91	<2e-16***
2014	3.63e-01	2.08e-02	17.45	<2e-16***
2015	3.72e-01	2.08e-02	17.89	<2e-16***
2016	3.81e-01	2.08e-02	18.29	<2e-16***
2017	3.92e-01	2.08e-02	18.82	<2e-16***
2018	4.04e-01	2.08e-02	19.39	<2e-16***
2019	4.14e-01	2.08e-02	19.91	<2e-16***
2020	4.23e-01	2.08e-02	20.31	<2e-16***
2021	4.30e-01	2.08e-02	20.68	<2e-16***
Cause				
Acute myeloid leukemia	−1.41e-02	8.23e-03	−1.71	0.09
Chronic lymphoid leukemia	1.68e+00	8.23e-03	204.18	<2e-16***

(Table 3 continues on next page)

effects varied in significance compared to the baseline condition of ALL. CLL had the largest positive effect on QCI (*beta* = 1.68, $p < 2e\text{-}16$), demonstrating significantly better care quality compared to the baseline. Conversely, AML showed a smaller effect (*beta* = −0.01, $p = 0.087$), though it approached borderline significance (Supplementary Fig. S3D). We also tested the significance of the random effects, and the results revealed that different SDI levels had a significant impact on QCI. The random effect estimate for the high SDI region (0.77) was notably higher than those of the other four SDI categories, aligning with the results of our univariate analysis. Upon completing the modeling, we performed a variance inflation factor (VIF) test, which returned a VIF value of 1 for all variables, indicating the absence of multicollinearity among the independent variables. An analysis of variance on the fixed effects revealed that sex, age, year, and leukemia subtype all had highly significant effects on QCI ($F = 123.4$, $p < 2e\text{-}16$). Among these, leukemia subtype had the strongest explanatory power, as evidenced by the largest variance value (*Sum Sq* = 11358.8), highlighting substantial differences in care quality across leukemia types. Lastly, a Kolmogorov–Smirnov normality test on the model residuals indicated that they did not strictly follow a normal distribution ($D = 0.02$, $p = 6.75e\text{-}08$). However, the Q–Q plot suggested that the residuals approximately conformed to normality (Supplementary Fig. S3E), and the kernel density curve of the histogram closely matched the normal distribution curve (Supplementary Fig. S3F), leading us to conclude that the model's residuals were sufficiently close to normal, ensuring model robustness. Given that the SDI region is an important factor influencing QCI, we conducted a spatial autocorrelation analysis to examine the clustering pattern of global SDI levels. The results revealed a significant positive spatial autocorrelation in SDI levels (Global *Moran's I* = 0.87, $p < 2e\text{-}16$). However, from a local perspective, areas with significant spatial autocorrelation were concentrated in Africa, where the Local Moran's I was higher than in other regions (Local *Moran's I* > 1, $p < 0.05$) (Supplementary Fig. S4A and B). In contrast, spatial autocorrelation in North America and Asia was not significant. These findings indicated that SDI levels in African countries are similar and exhibit spatial clustering.

QCI forecast trends from 2022 to 2046

The results of the LMM identified sex, age, year, leukemia subtype, and SDI region as the primary factors influencing QCI. To analyze global trends and project future QCI values across different leukemia subtypes, we employed the BAPC model, with detailed results presented in Supplementary Table S4. From 1990 to 2019, there was a consistent year-on-year increase in the QCI for leukemia, with the overall QCI reaching 81.47%

(95% UI: 71.68%, 88.68%) in 2019. However, in the subsequent two years, QCI experienced a slight decline, reaching 79.00% in 2021 (95% UI: 70.81%, 86.83%). The projections indicated that over the next 25 years, QCI would exhibit a generally fluctuating upward trend, potentially reaching 79.58% (95% UI: 77.14%, 100.00%) by 2046. The predicted QCI for women remained slightly higher than for men across all years (Fig. 4A). For acute leukemias, AML demonstrated a steady upward trajectory from 1990 to 2021, with its QCI increasing from 11.51% (95% UI: 0.00%, 18.92%) in 1990 to 72.88% (95% UI: 70.18%, 75.57%) in 2021. The forecast suggested that this upward trend will continue, with QCI expected to reach 98.99% (95% UI: 97.99%, 100.00%) by 2046 (Fig. 4B). In contrast, the trend for ALL diverged markedly from that of AML. ALL's global QCI rose sharply between 1990 and 2019, peaking at 94.05% (95% UI: 88.10%, 100.00%) in 2019, but subsequently declined, reaching 83.26% (95% UI: 75.29%, 91.24%) in 2021. The projection suggested that this downward trend will persist, with the QCI for ALL expected to decline to 59.92% (95% UI: 25.90%, 93.95%) by 2046 (Fig. 4C). Among chronic leukemias, CLL exhibited a year-on-year increase in global QCI from 1990 to 2013, reaching 80.08% (95% UI: 75.67%, 84.49%). After a brief decline from 2013 to 2021, QCI rose again, reaching 81.59% (95% UI: 77.67%, 85.51%) in 2021. It was predicted that QCI would continue to rise gradually over the next 25 years, reaching 88.31% (95% UI: 76.62%, 100.00%) by 2046 (Fig. 4D). CML followed a similar pattern to CLL, with global QCI fluctuating but increasing overall between 1990 and 2021, reaching 62.33% (95% UI: 56.93%, 71.94%) in 2021. The forecast suggested that CML's QCI would rise to 92.07% (95% UI: 84.14%, 100.00%) by 2046 (Fig. 4E). For other leukemia, the global QCI showed a consistent upward trend from 1990 to 2021, with QCI reaching 61.51% (95% UI: 56.51%, 64.27%) in 2021. The projection indicated that this upward trend would continue, with QCI expected to rise to 92.45% (95% UI: 90.02%, 100.00%) by 2046 (Fig. 4F).

Effects	Beta	Std.error	t value	p value
(Continued from previous page)				
Chronic myeloid leukemia	2.41e-01	8.23e-03	29.30	<2e-16***
Other leukemia	1.32e+00	8.23e-03	160.11	<2e-16***
	Low SDI	**Low-middle SDI**	**High-middle SDI**	**High SDI**
Random effects (Intercept)	−0.54	−0.39	0.30	0.77

Statistical significance: *:$p < 0.05$, **:$p < 0.01$, ***:$p < 0.001$.

Table 3: **Regression coefficients, standard errors and statistical inference values of each variable in the linear mixed model.**

Discussion

This study represents the first attempt to comprehensively quantify the quality of individual health care using a modified QCI metric. Previous studies on QCI have often overlooked the rigorous examination of variable correlation coefficients and variance explanation rates, mistakenly assuming that the PC1 accounts for most of the variance.[39,40] This assumption is particularly problematic when PC1 explains only 60%–80% of the variance, as this implies that critical information from other variables, such as YLR, DPR, MIR, and PIR, which may be more closely related to the PC2, could be neglected. Our results confirm this hypothesis. When the variance explained by PC1 exceeds 95%, there is no significant difference between the original and modified QCI values. However, when the variance explained by PC1 falls between 90% and 95%, although significant differences exist between the two QCI methods, their correlations with HAQI and model R^2 values remain similar, suggesting minimal divergence in performance under these conditions. Notably, when the variance explained by PC1 drops below 80%, the modified QCI exhibits a higher correlation with HAQI, higher R^2 values, and lower AIC and BIC scores, indicating a better model fit. This suggests that when the proportion of variance explained by PC1 is low, the modified QCI provides a stronger association with healthcare quality, lending strong support to our research hypothesis.[41–43] Additionally, our analysis reveals that PC1 and PC2 capture distinct quality dimensions, with variance-weighted QCI providing a more comprehensive care quality measure. By adopting this refined QCI, our study offers a detailed global analysis of leukemia care quality trends, disparities, and projections across regions, age groups, and leukemia subtypes.

Over the past three decades, the global burden of leukemia has exhibited a complex pattern in morbidity and mortality.[44] Our findings indicate a significant increase in the absolute number of leukemia cases and related deaths from 1990 to 2021, largely driven by population growth and aging.[45] AML has emerged as the subtype with the highest incidence and deaths, with an ASIR of 1.73 per 100,000 population and an ASDR of 1.57 per 100,000 population in 2021. The persistent high burden of AML underscores its aggressive nature and the challenges in its care. Although slight downward trends in ASIR (–0.03%) and ASDR (–0.21%) suggest progress, they also highlight the ongoing need for research and improvement in care strategies.[46] Our QCI analysis revealed significant disparities in the quality of leukemia care across countries, with higher QCI observed in nations with higher SDI levels, such as Iceland and Switzerland. These results reflect the substantial advancements in leukemia care achieved by developed countries. In contrast, many African nations, including Guinea and Mozambique, as well as Pacific island countries like Kiribati and Papua New Guinea, exhibited notably lower QCI, a trend consistent with findings from previous research.[15] The regional analysis

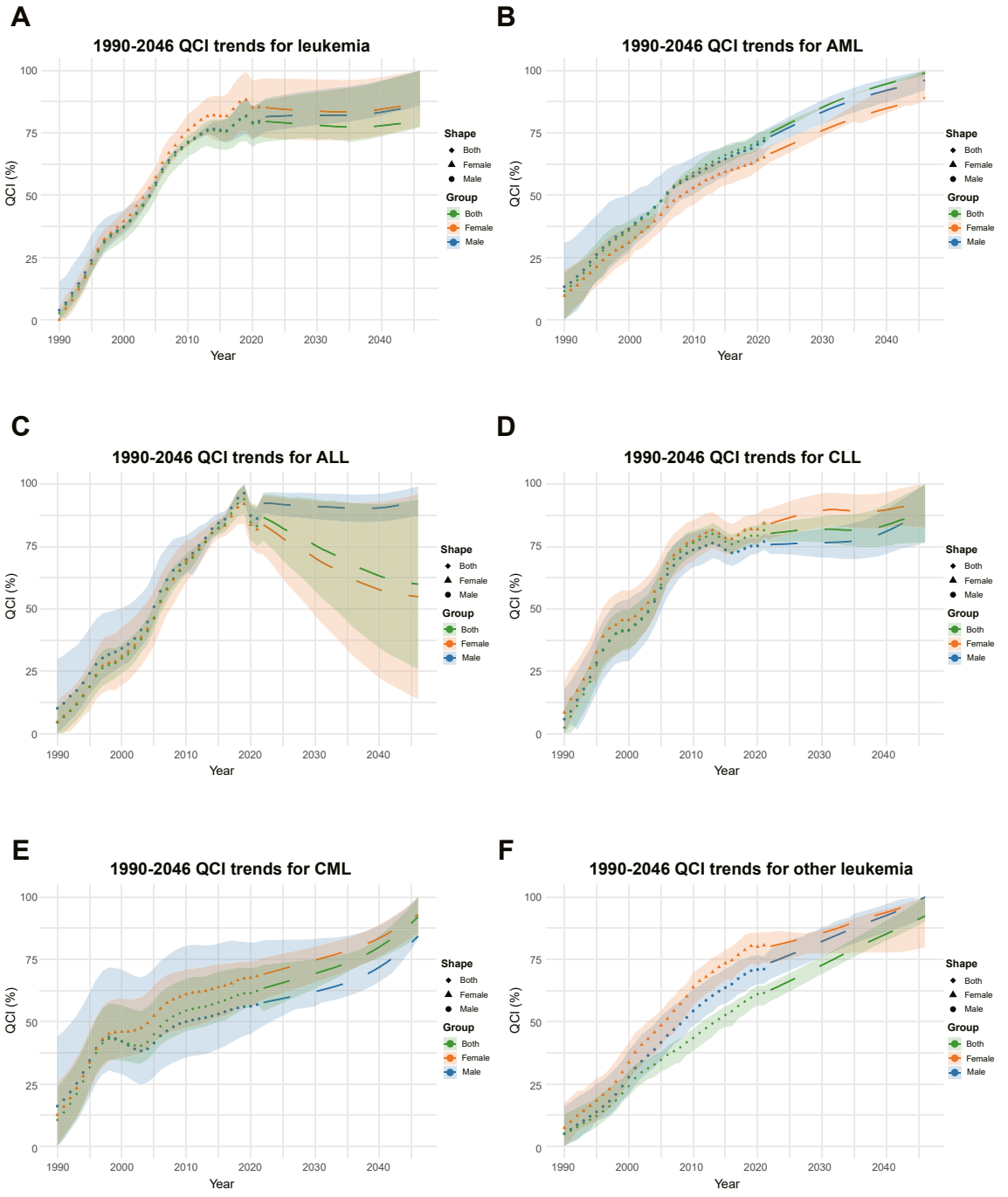

Fig. 4: **Projected trends in QCI for different leukemia subtypes by sex from 1990 to 2046.** (A) 1990–2046 QCI trends for leukemia: This panel displays the projected trends in QCI for leukemia, stratified by sex. Solid lines represent the predicted QCI for each group: blue for males, orange for females, and green for both sexes combined. The shaded areas around each line represent the uncertainty intervals. Triangles, circles, and squares indicate specific years where data points for females, males, and both sexes are marked, respectively. (B) 1990–2046 QCI trends for AML: The plot shows the projected QCI trends for AML, stratified by sex (both, male, female). Line and shape patterns are consistent with panel A. (C) 1990–2046 QCI trends for ALL: The projected QCI trends for ALL are displayed, with colors and shapes corresponding to each group (both, male, female) following the same format as previous panels. (D) 1990–2046 QCI trends for CLL: The panel shows projected QCI trends for CLL, with colors and shapes corresponding to each group (both, male, female) following the same format as previous panels. (E) 1990–2046 QCI trends for CML: The panel shows projected QCI trends for CML, with colors and shapes corresponding to each group (both, male, female) following the same format as previous panels. (F) 1990–2046 QCI trends for other leukemia types: The panel shows projected QCI trends for other leukemia, with colors and shapes corresponding to each group (both, male, female) following the same format as previous panels.

based on SDI classification demonstrated a clear gradient in QCI, with high-SDI regions achieving the highest scores, while low-SDI regions had the lowest. The significant differences between SDI groups at each level underscore the critical role of socioeconomic factors as key determinants of leukemia care quality.[47] These findings emphasize the urgent need for targeted interventions to improve leukemia care in low-SDI regions by strengthening health infrastructure and increasing access to advanced treatments. Furthermore, they underscore the importance of integrating socioeconomic factors into healthcare planning and resource allocation to achieve more equitable outcomes globally.[48]

The QCI analysis reveals distinct age-related trends in leukemia care quality. From 1990 to 2021, QCI scores consistently declined with age, particularly among individuals over 75, with the lowest scores observed in those over 85. While younger age groups, such as 15–19 years in 2021, showed significant improvements, the persistent decline in QCI for elderly patients remains a concern.[49,50] Subtype-specific trends varied: AML care quality improved with age, particularly for those over 85, while ALL showed the highest QCI in children under 5 years in 2021, reflecting advancements in pediatric care.[51] CLL demonstrated a sharp decline in QCI after 75 years, indicating challenges in elderly management,[52] while CML care quality improved steadily with age. Other subtypes exhibited inconsistent patterns, with notable disparities between the youngest (<5 years) and oldest (85+) groups. These findings highlight significant age-related inequities in leukemia care, with older patients consistently receiving lower QCI scores across subtypes. While trends were similar across sexes, slight differences suggest the need for further investigation. Targeted interventions are essential to address the unique challenges faced by older leukemia patients and to promote equitable care across all age groups.[53]

We conducted an in-depth analysis using LMM to assess the effects of age, year, sex, SDI region, and leukemia subtype on QCI. The model results indicated that the QCI for men was significantly lower than that for women (*beta* = –0.06, $p < 2e\text{-}16$), aligning with previous studies suggesting men may face more healthcare barriers, possibly due to health behaviors and lower service utilization.[54–56] Age had a non-linear effect: younger (25–29 years) and older adults (80–84 years) showed negative impacts on QCI, while middle-aged adults (45–49 years) showed a positive effect, potentially reflecting differences in comorbidities and healthcare access across age groups.[55,57] Leukemia subtype also significantly influenced QCI, with CLL showing the highest and AML the lowest scores. Chronic leukemias had higher QCI than acute leukemias, likely due to their slower progression and more manageable treatment.[58] Acute leukemias, such as AML and ALL, require rapid, intensive interventions due to aggressive disease progression and complications like infections and anemia, making their care more complex.[59,60] In contrast, chronic leukemias, such as CML and CLL, often allow for disease control with oral medications, such as tyrosine kinase inhibitors (TKIs) for CML and Bruton tyrosine kinase inhibitors for CLL, leading to milder side effects and better care quality.[61–63] SDI region analysis revealed that high-SDI regions had significantly higher QCI, indicating a clear gradient in care quality. This aligns with our univariate analysis and highlights the critical role of healthcare resources. Although the Kolmogorov–Smirnov test showed sensitivity, the Q–Q plot and kernel density histogram confirmed the approximate normality of residuals, demonstrating the robustness of our model despite potential biases.[64] These findings underscore the need for tailored support for acute leukemia patients and targeted improvements in low-SDI regions to enhance care quality globally.

The study analyzed the QCI for leukemia from 1990 to 2021 and projected its development over the next 25 years using the BAPC model. Our findings indicate a significant increase in the QCI for leukemia from 1990 to 2019, reaching 81.47% in 2019. This improvement is primarily attributed to advances in treatment options and substantial enhancements in supportive care.[65] Key breakthroughs in leukemia treatment include the clinical application and trials of innovative therapies such as CAR-T cell therapy, bispecific T cell engagers (BiTES), and BCR-ABL1 TKIs.[66] These therapies have provided new hope for patients with relapsed and refractory leukemia, significantly improving both complete remission rates and overall survival.[67] CAR-T cell therapy has been particularly revolutionary in treating lymphoid leukemia, especially B-ALL.[68] By reprogramming a patient's T cells to target specific cancer antigens, CAR-T therapy has dramatically increased remission rates for young patients with relapsed or refractory ALL since its approval in 2017.[69,70] BiTES, such as Blincyto (blinatumomab), have also demonstrated remarkable efficacy by directing T cells to bind and kill cancer cells, particularly in relapsed B-cell leukemias like ALL.[71] The development of TKIs, beginning with imatinib, has revolutionized CML treatment, enabling most patients to achieve long-term remission and near-normal life expectancy.[72] The approval of third-generation TKIs has further improved treatment outcomes, solidifying CML as a manageable chronic condition.[73] In addition to these treatment advances, supportive care has played a critical role in improving outcomes for leukemia patients by mitigating treatment-related complications.[74] Leukemia patients often experience severe complications from intensive treatments, such as chemotherapy and radiotherapy, including anemia, infection, and malnutrition.[75] The use of blood products, such as transfusions and platelet preparations, has effectively addressed anemia and thrombocytopenia, reducing the risk of severe complications.[76] Advances in antibiotics

and antifungal medications, particularly newer agents like voriconazole and posaconazole, have significantly lowered infection rates in immunocompromised patients, enhancing survival outcomes.[77] Nutritional support, through personalized interventions, has helped leukemia patients maintain adequate energy intake, preventing malnutrition and preserving immune function.[78] Additionally, the integration of mental health services has alleviated the psychological burden of prolonged treatment, improving patient compliance, emotional well-being, and overall quality of life.[79] Collectively, these supportive measures, coupled with advancements in medical technology and global health policies, have been integral to the rising QCI in leukemia management.

The QCI experienced a slight decline from 2019 to 2021, likely due to the healthcare strain from COVID-19, which diverted resources and impacted care quality for immunocompromised leukemia patients. Despite this dip, projections suggest a general upward trend in QCI, though regional and subtype-specific disparities will persist. This underscores the need for global coordination in health policy, particularly in low- and middle-income areas, to optimize resource allocation and reduce care quality gaps. The BAPC model predicts a rise in global QCI over the next 25 years, with significant subtype variation: while CLL and AML QCI are expected to improve, ALL QCI is anticipated to decline. This highlights the importance of tailored healthcare policies for each leukemia subtype. For ALL, which predominantly affects children and young adults, strategies should address both acute treatment and comprehensive recovery support, including mental health services and long-term monitoring to improve post-recovery quality of life. The projected ALL decline also suggests potential disparities, particularly in low-SDI regions, emphasizing the need for equitable resource distribution. To sustain improvements in CLL and AML care, continuous optimization of care models, driven by technological and pharmaceutical advancements, is essential. Future policies must balance targeted support for ALL with ongoing quality enhancements for other leukemia subtypes to achieve more equitable and effective leukemia care globally.

Our study has several strengths and limitations. First, while PC1 and PC2 reflect distinct aspects of care quality, the use of endogenous weights rather than empirically derived weights in the allocation process may introduce endogeneity issues.[80] Future validation and analysis using larger datasets are necessary to ensure optimal adjustment. Additionally, the GBD dataset lacks specific information on racial and ethnic differences in leukemia care, which limits our study's scope. Future research should incorporate these factors to provide a more comprehensive understanding of disparities in leukemia care.

LMM has strengths and limitations. It effectively handles hierarchical, multi-level data, reducing bias from data structure dependence. However, limitations include assumptions of independence among internal form of variables. While SDI regions show some clustering, spatial autocorrelation analysis reveals it is only significant in low-SDI and low-middle SDI regions, minimizing concern. Autocorrelation may also arise within yearly data, but the growth trend shown by the year difference is stable. The GBD model, despite reliance on extensive primary and secondary data, faces uncertainties that may affect result reliability, especially in low-SDI and low-middle SDI regions where data scarcity increases estimation uncertainty. Consequently, our QCI estimates, especially in low-SDI regions, should be interpreted with caution. Further research and data are needed to improve the accuracy and reliability of estimates in these regions. Despite these limitations, LMM offers a robust framework for understanding global leukemia care quality trends.

We employed the BAPC model for prediction, a method widely used in GBD research.[81–83] The BAPC model is particularly valuable for analyzing historical data, especially when data are limited or uncertain, as it integrates findings from previous studies to generate more reliable predictions. However, the model has limitations, as it generally assumes that age, period, and cohort effects evolve smoothly over time, maintaining a degree of consistency throughout the study period. In reality, advancements in medical treatments and changes in social environments may disrupt this stability. For example, new treatment breakthroughs or global infectious disease outbreaks can quickly alter the incidence and survival rates of certain leukemia subtypes, which the BAPC model may not fully capture. The model's predictive accuracy also depends largely on the quality of input data. If the underlying data are inaccurate, incomplete, or contain systematic biases, the model's results may be compromised. This issue is particularly pronounced in low-income areas, where data availability and quality are often limited, potentially leading to inaccurate predictions. Thus, the reliability of our predictive results requires further validation. Nonetheless, our predictions offer valuable insights and guidance for the future development of public health initiatives in leukemia.

In summary, the study demonstrates significant improvements in leukemia care quality from 1990 to 2021, yet substantial disparities persist between countries and regions with differing SDI levels. Low-SDI regions, especially in parts of Africa, continue to suffer from severe healthcare underinvestment, highlighting an urgent need for more equitable resource distribution to achieve global healthcare equity. For healthcare providers, our findings emphasize the importance of improving care for older leukemia

patients, particularly older men, who consistently show lower QCI scores. This group requires targeted, age-sensitive care that addresses comorbidities and is tailored to their specific needs. Furthermore, a priority should be placed on acute leukemia patients, especially those with ALL, who face a more aggressive disease course and worse prognosis than those with chronic leukemias. Timely, intensive interventions and ongoing support are crucial for these high-risk patients. This study underscores the need for targeted interventions and policy changes to improve care quality for leukemia patients globally, especially in underserved regions. By focusing on the most disadvantaged groups, we can strive for a future where high-quality leukemia care is accessible to all, regardless of geographic or socioeconomic factors.

Contributors

YP and FZ contributed to the study conception and design. YP and SP collected and verified the accuracy of the underlying data. YP performed the analyses. The first draft of the manuscript was written by YP. NZ and XL contributed to data interpretation. YP, FZ, QL, and NZ contributed to the evaluation of the methods and revision of the manuscript. All authors have read and approved the final manuscript for submission.

Data sharing statement

The data utilized in this study are publicly accessible from the following sources: the Global Burden of Disease Results Tool of the Global Health Data Exchange (https://vizhub.healthdata.org/gbd-results/), United Nations population estimates and projections (https://population.un.org/wpp/Download/Standard/CSV/), and the World Standard Population (https://seer.cancer.gov/stdpopulations/world.who.html). The code used for this research is available upon request from the corresponding author.

Editor note

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Declaration of interests

All authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102996.

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