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Patterns and Trends in The Incidence of Leukemia in Children and Young Adults in Northern England by Age, Sex, Socioeconomic and Urban-Rural Status

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Abstract

Leukemia is the most common cancer among children and young adults, comprising 30% of case worldwide. While global studies identify geographic and demographic disparities in incidence, long-term trends in northern England remain underexplored. This study examines leukemia incidence among individuals aged 0–24 years in northern England from 1968 to 2021, focusing on age, gender, socioeconomic status, and urban/rural residence. Data were sourced from the Northern Region Young Persons Malignant Disease Registry. Incidence rates were calculated by age group (0–14, 15–24 years), sex, deprivation quintiles (Townsend Deprivation Score), and urban/rural status. Temporal trends were analyzed using Joinpoint regression to estimate annual percentage changes (APCs). Poisson regression was used to explore the effects of demographic and socioeconomic variables. Findings revealed that higher leukemia incidence was observed in the 0–14 age group, particularly among 0–4-year-olds. Males consistently showed higher rates than females. Incidence in 0–14-year-olds increased annually (APC 0.83%, 95% CI: 0.33%, 1.31%). In contrast, 15–24-year-olds exhibited an initial rise (1.02%, 95% CI: 0.64%, 5.09%) followed by a post-1995 decline (-1.05%, 95% CI: -4.65%, 0.31%). There was an increased incidence in rural areas in 2016–2021, whilst there was no significant association with deprivation. These results highlighted that leukemia incidence in northern England varied according to age, sex, and geography during 54 year time period.

Keywords: Leukemia, Epidemiology, Temporal Trends, Children and Young Adults, Northern England, Socioeconomic Disparities

Introduction

Leukemia is a type of cancer that arises from the uncontrolled proliferation of leukocytes in the blood and bone marrow (1). It is the most frequent type of cancer affecting children and young adults, accounting for 30% of all childhood and young adult cancers (2). Leukemia can be classified into various subtypes with acute lymphoid leukemia (ALL) being the most frequent among the age group of 0-24 years (2). According to the Global Cancer Observatory (GLOBOCAN), an estimated 88,786 newly diagnosed cases of leukemia were reported worldwide in 2022 among children and young adults aged 0-24 years, with the world Age-Standardised Incidence Rate (ASIR) reported to be 2.9 per 100,000 per year (3).

Numerous studies have demonstrated substantial geographic disparities in childhood leukemia incidence worldwide, influenced by factors such as age, gender, ethnicity, and socioeconomic status (4,5). Population-based data have shown that the incidence of childhood leukemia is highest amongst children aged 0-4 years with ALL being the most frequent subtype in this age group (6–8). The combined world ASIR for this group (0-4 age group) is 4.0 per 100,000 population (7). Notably, the incidence of ALL in the 0-4 years age group is fourfold greater in comparison to children aged 10 and older (9). Comparative studies from diverse populations worldwide reveal a higher incidence of leukemia in males compared to females (10–14).

There is also evidence that urban-rural dwelling status and socioeconomic status can impact childhood leukemia incidence. Studies consistently suggest that urban areas compared to rural areas (15–17) and more affluent compared to less affluent communities (18,19) exhibit higher rates. These findings highlight the complex interplay of environmental, social, and genetic factors in the development of childhood leukemia. therefore, this study investigates the patterns and trends in the incidence of leukemia in children and young adults aged 0-24 years in Northern England, examining differences by age, gender, socioeconomic status, and urban/rural status.

Materials and Methods

Data for this study were obtained from the Northern Region Young Persons Malignant Disease Registry (NRYPMDR) which is a population-based cancer registry established in 1968 and held within the Royal Victoria Infirmary Hospital, Newcastle upon Tyne, and hosted by Newcastle University (20). This registry records all malignant neoplasms diagnosed in children and young adults under 25 years who live in the northeast of England and north Cumbria or are treated in one of the region's hospitals (20). The morphology and primary site of each tumor are coded using the International Classification of Diseases for Oncology (ICDO-2). The cases are then categorized according to the International Classification of Childhood Cancers (ICCC) (14). Geocoding postcodes to derive precise geographic coordinates was crucial for linking each case to the specific residential area of the affected individual.

Population data and area-based deprivation measures, specifically the Townsend Deprivation Score (TDS), were obtained to assign deprivation quintiles (21). TDS is a measure of material deprivation used to quantify the level of deprivation in a specific area. It is derived from four key variables of census data: unemployment, non-car ownership, non-home ownership, and household overcrowding

(22). A higher TDS values indicates greater deprivation (23). Census data at Lower Super Output Area (LSOA) level were used to determine mid-year population estimates for 1971, 1981, 1991, 2001, and 2011 (21). Deprivation quintiles were assigned using time-varying census data, using the census closest to each diagnosis period: 1971 census for diagnoses in 1968–1975; 1981 census for 1976–1985; 1991 census for 1986–1995; 2001 census for 1996–2005; 2011 census for 2006–2015; and 2021 census for 2016–2021. This ensured that deprivation estimates reflected approximate socioeconomic conditions contemporaneous with each diagnostic period.

The Rural-Urban Classification (RUC) framework was used to classify LSOAs based on the area's level of rural and urbanisation characteristics to help analyse and understand the differences in socioeconomic conditions. RUC 2011, developed after the 2001 census, was consistently applied throughout the study (24). Urban rural status based on RUC 2011 was applied consistently across all study years due to the absence of a comparable historical classification. TDS-based deprivation quintiles and urban-rural status were assigned for each LSOA. To ensure geographic consistency over time, all socio-demographic measures were harmonised using 2021 LSOA boundaries (see supplementary material for further details).

Statistical Analysis

The study population comprised patients aged 0-24 years, diagnosed with leukemia in the northern region of England between 1968 to 2021. Initially, crude incidence rates were calculated by age group (0-14, 15-24 years), sex (M, F), population-weighted quintiles of deprivation (Q1 least deprived to Q5 most deprived), and urban-rural status (urban and rural areas are defined based on the RUC classification framework).

Joinpoint trend analysis software (25) was used to estimate the annual percentage change (APC) of trends in leukemia incidence over time by age, sex, urban-rural, and socioeconomic status. STATA software was used for data cleaning/ preparation and regression modelling. Analyses were conducted using STATA (26) software. The statistical significance was evaluated at a p-value of <0.05, and a 95% confidence interval (CI) was utilised to estimate the precision of the point estimates. All statistical tests were two-sided.

Results

A total of 1,662 leukemia cases were recorded during the study period, comprising 1,213 acute lymphoid leukemias (ALL) (72.9%), 332 acute myeloid leukemias (AML) (20.0%), 72 chronic myeloproliferative or myelodysplastic leukemias (CML/MDS/other) (4.3%), and 45 other/unspecified leukemias (2.7%). Separate analyses by subtype were not performed as further stratification of these subtypes by age, sex, deprivation, or urban rural status resulted in numbers too small for reliable Joinpoint or regression modelling. Therefore, all subsequent analyses focus on all leukemias combined. We note there is a category in the data called "010 Leukaemias, myeloproliferative diseases, and myelodysplastic diseases" which has 17 cases which is grouped here with "Unspecified/Other". It is likely most of these cases are ALL and some AML but without certainty, best placed under "Other".

Descriptive Analysis

Table 1 presents the number of leukemia cases and age-specific incidence rates (IR) per 100,000 people across different demographic and socioeconomic categories, spanning time periods from 1968 to 2021. Overall, individuals aged 0-14 years exhibited a consistently higher incidence rate compared to those aged 15-24, peaking between 2006-2015 with an IR of 4.91 (95% CI 4.29, 5.54). Males demonstrated higher incidence rates than females across all time periods, though rates fluctuated slightly. Deprivation quintiles showed variable trends, with Q1 (least deprived) initially having a higher incidence, but a rise in incidence rates is observed in more deprived quintiles (Q4 and Q5) in recent years. The timeframe for this observation is relatively shorter and should be interpreted with caution. Rural areas, which initially had lower incidence rates, displayed a notable increase over time, surpassing urban areas in recent years (2016-2021) with IRs of 4.14 and 2.94, respectively. This may reflect a shift in leukemia incidence patterns by geography and socioeconomic groups.

Trend Analysis

Figure 1 presents the Joinpoint trend analysis by A. Age group, B. Sex, C. Deprivation Quintile, and D. Urban-Rural Status. The incidence of leukemia in those aged 0-14 years has shown an increasing trend from 1968 to 2021 with an Annual Percent Change (APC) of 0.83% (95% CI: 0.33%, 1.31%) per year. Those in the age group 15-24 years have shown an upward trend from 1968 to 1995, and a decreasing trend is noted from 1995 onwards. The APC for those in the 15-24 years age group is initially at 1.02% (95% CI: 0.64%, 5.09%) which is then followed by a non-significant decline of -1.05% (95% CI: -4.65%, 0.31%) during 1995-2021. Examining incidence trends by sex, males consistently show higher leukemia incidence rates than females over the entire study period, as evidenced by the trend line for males being above that of females. Although the APC for females (0.58%, 95% CI: -0.17%, 1.32%) is slightly higher than that for males (0.42%, 95% CI: -0.12%, 1.32%), the overlap of confidence intervals (both CI's contain 0) indicates no significant difference in the rates of change in incidence over time, despite the overall higher incidence rates in males.

Initially, leukemia incidence was higher in urban areas than in rural areas. However, by 1993, the incidence rates converged, and thereafter, rural areas showed a statistically significant increase (APC 1.52%, 95% CI: 0.63, 2.38), surpassing and remaining higher than the incidence in urban areas, where no significant change was observed (APC 0.23%, 95% CI: -0.69, 1.15).

The least deprived Townsend quintile showed no change in incidence, with a non-significant Annual Percent Change (APC) of -0.68% (95% CI: -2.21, 0.77). In contrast, the highest, although not statistically significant, increase was observed in the most deprived quintile (APC 1.25; -0.03, 2.50). Quintiles 2 and 3 exhibited slight, non-significant decreases in incidence, with APCs of -0.42% and -0.12%, respectively, while quintile 4 showed a non-significant increasing trend (APC 1.07%, 95% CI: -0.21, 2.32). The trends across quintiles were not statistically significant, and the changes observed could be due to chance. The incidence trends for the most and least deprived quintiles were inversely related over the study period.

Discussion

The dataset spans 54 years from 1968 to 2021 facilitating analysis of long-term patterns and trends in the incidence of leukemia in the northern region of England. Leukemia incidence increased steadily from 1968 to 2015, with the data suggesting a downward trend in the final six years studied. Children aged 0-14 years experienced a higher overall incidence compared to the 15-24 age group, with the highest rates observed in children aged 0-4. This pattern aligns with studies conducted in the UK and internationally (8,10,27). Notably, the trend in children aged 0-14 years showed a statistically significant annual increase of 0.83%, whereas the 15-24 age group initially displayed an increase (1.02% per year) followed by a decrease (-1.05% per year) from 1995 onwards. The findings, particularly the observed childhood peak in leukemia incidence, align with Greaves' 'delayed infection' hypothesis, which proposes that early-life infections may act as a trigger for leukemia in genetically predisposed children by providing the necessary secondary event to initiate malignancy (28,29). Among the sub-types of leukemia, only ALL demonstrated a statistically significant increase incidence from 1968 to 1995. However, since 1995 this trend has plateaued until 2021. During this period there was no statistically significant change in the incidence rates which may indicate a lack of recent changes in environmental or infectious exposures affecting young children during this period. These findings are consistent with the results from Shah and Coleman's study in England and Wales (8). They found a 4% increase in trend per five years (0.8% per year) which is similar to that found in this region (northern England) with an increase of 0.83% per year. The authors also found that the overall 5-yearly increase in incidence was higher among those under 5 years (24% in children aged 1-4 years and 46% in those below 1 year) than those above 5 years of age (12-15%). These findings were consistent with the current study as those aged 0-4 years exhibited the highest incidence of leukemia. It is also important to acknowledge that improvements in diagnostic methods and specialist availability over time may have contributed to some of the increase observed in earlier decades, although these advances alone are unlikely to fully explain the trends.

Leukemia incidence rates were consistently higher in males than females across northern England, except during 2006-2015. While males had a higher overall incidence, the APC was slightly higher in females (0.58% per year) than in males (0.42% per year), though this difference was not statistically significant and may reflect a chance variation between males and females. Previous studies in the UK (14), Nordic countries (10), and Korea (13) also report higher leukemia incidence rates in males, potentially due to biological differences such as hormonal influences, genetic susceptibility, and varying environmental exposures. Further research is needed to better understand the underlying mechanisms contributing to these observed sex differences (30).

The incidence of leukemia in rural areas displayed a notable upward trend from 1968 to 2021, with an APC of 1.52% per year, compared to a smaller increase of 0.23% in urban areas. While urban areas initially exhibited higher incidence rates, rural rates surpassed them after 1993. These findings contrast with studies from the US and Spain, which report higher urban incidence rates (15–17). The initial urban predominance may relate to greater industrial exposure in these areas (15). The recent rural increase could possibly relate to increased herbicide and pesticide use (31). Although environmental exposures cannot be ruled out entirely, a more plausible explanation may involve societal changes such as increased population mixing, higher caesarean section rates, and early childhood social behaviors, that are becoming more common in rural and deprived areas, having previously been associated with urban populations. These shifting patterns may offer further support for the Greaves' hypothesis. However, the observed trends should be interpreted cautiously, as not all increases and decreases were statistically significant. Moreover, the reliance on a fixed RUC 2011 framework during all the time periods of the study (from 1968 to 2021) may not adequately reflect the changing urban-rural landscapes, potentially influencing the incidence of leukemia in certain areas. It is possible that areas that were classified as urban or rural in 2011 would be incorrectly classified at other times during the period of the study. Recognising that urban-rural classifications change over time is essential for accurately interpreting trends in leukemia incidence, as shifting population distributions may have influenced the patterns observed in this study.

The incidence rates of leukemia were higher in the least deprived quintile (Q1) of the Townsend Deprivation Score compared to the most deprived (Q5) in northern England; however, this difference was not statistically significant. Despite this, trends over time showed a decrease in incidence in the more affluent quintiles, while quintiles 4 and 5 presented upward trends of 1.07% and 1.25%, respectively. This gradual narrowing of the incidence gap between the least and most deprived groups aligns with findings from other studies in England and Wales (19,32,33), which suggest changing socioeconomic and environmental dynamics. Furthermore, the extensive timeframe of this study (1968 to 2021) necessitated the use of the Townsend Deprivation Score as a measure of socioeconomic status since the Index for Multiple Deprivation (IMD), established in 2000, could not be consistently applied throughout the entire study period. The IMD is widely used within the UK to classify relative deprivation for small areas, offering contemporary insights into socioeconomic disparities. This study assigned deprivation exposure, the Townsend Deprivation Score, based on the census year within 10 years of cancer registration. There may be some drift in accurately capturing socioeconomic disparities due to changes such as urban development, population migration, and economic shifts. TDS is based on four components: non-car ownership, unemployment, housing crowding, and non-home ownership. Socioeconomic changes, such as a shift towards renting homes rather than ownership, may lead to variations that TDS cannot adequately reflect in more recent years. This could result in either an overestimation or underestimation of the impact of socioeconomic factors on leukemia incidence. While the geography of deprivation generally remains consistent across different census periods (21), the temporal changes in socioeconomic dynamics should be considered when interpreting these findings, as these factors could have mitigated any real effects of deprivation.

Conclusion

This study identified a significant upward trend in leukemia incidence among children aged 0-14 years (APC: 0.83%), while a contrasting decrease was observed in the 15-24 age group from 1995 to 2021. Although males consistently exhibited higher incidence rates than females, there was no statistically significant evidence to support a consistent difference between the two groups. A notable finding was the statistically significant rise in leukemia incidence in rural areas compared to urban areas, suggesting a potential influence of environmental factors that warrant further investigation. Additionally, the study highlighted the potential impact of deprivation on leukemia incidence, though the use of Townsend deprivation might not fully reflect recent socioeconomic changes. Despite regional and temporal limitations, these findings underscore the need for continued monitoring and targeted research into the underlying risk factors contributing to these age, sex, and geographic disparities in leukemia incidence.

Study Limitations

This study was based on registry data spanning over five decades. While the long duration provides valuable insights into temporal trends, it is limited by changes in diagnostic criteria and classification over time, as well as improvements in diagnostic technology and the availability of specialists, which may have influenced incidence estimates. Although diagnostic information was available, subtype-specific analysis was not conducted, as the number of cases within each individual diagnostic category (other than ALL and AML) was too small to allow for meaningful or statistically robust trend analysis. Additionally, the study relied on area-level deprivation scores and a static urban-rural classification from fixed time points, which may not fully reflect population density, individual-level socioeconomic conditions or capture evolving patterns of settlement and deprivation across the study period. Finally, trends observed in the most recent years should be interpreted with caution due to shorter follow-up durations and possible underreporting in the registry, including potential delays related to the COVID-19 pandemic.

Ethical Approval

Newcastle University covers the data obtained from NRYPMDR for this study in accordance with the Data Security and Protection Toolkit (DSPT), which ensures that patient information is managed and treated securely. The General Data Protection Regulation (GDPR) exam was undertaken before the commencement of the research protocol development phase in order to access the data. To ensure strict compliance with GDPR, the access and analysis of patient information was strictly restricted to a university-authorised computer at Sir James Spence Institute, RVI. As no personally identifiable information of the patients was disclosed through the study, additional ethical approval was not required. Only anonymised data was used for the analyses of the study.

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Conflict of Interest

The authors declare no conflict of interest.

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Table 1 Number of cases (No.) and Age-Specific Incidence Rate with 95% Confidence Interval (IR (95% CI)) per 100,000 for Each Time Period by Age Group, Sex, Deprivation Quintile, and Urban-Rural Status

Variables	**1968-1975**		**1976-1985**		**1986-1995**		**1996-2005**		**2006-2015**		**2016-2021**	
	No.	IR (95% CI)	No.	IR	No.	IR	No.	IR	No.	IR	No.	IR
Age Group												
0-14	193	3.23 (2.78, 3.69)	226	3.70 (3.22, 4.19)	220	3.93 (3.41, 4.45)	229	4.39 (3.82, 4.96)	237	4.91 (4.29, 5.54)	129	4.45 (3.69, 5.22)
15-24	65	1.84 (1.39, 2.28)	92	1.94 (1.54, 2.34)	87	2.16 (1.71, 2.62)	72	2.04 (1.57, 2.51)	75	1.93 (1.49, 2.37)	37	1.19 (0.80, 1.57)
Sex												
F	111	2.38 (1.94, 2.82)	134	2.52 (2.09, 2.95)	123	2.60 (2.14, 3.06)	120	2.79 (2.29, 3.29)	154	3.62 (3.05, 4.19)	61	2.39 (1.79, 2.99)
M	147	3.03 (2.54, 3.52)	184	3.33 (2.85, 3.81)	184	3.77 (3.23, 4.31)	181	4.07 (3.48, 4.66)	158	3.55 (3.00, 4.10)	105	3.03 (2.45, 3.61)
Deprivation Quintile												
Q1	36	3.54 (2.27, 4.81)	54	3.42 (2.37, 4.47)	44	3.64 (2.63, 4.65)	49	3.59 (2.45, 4.73)	49	4.48 (3.36, 5.60)	22	3.97 (2.62, 5.32)
Q2	28	1.97 (1.00, 2.94)	29	3.06 (2.05, 4.07)	39	2.60 (1.62, 3.58)	32	2.52 (1.60, 3.44)	32	2.98 (2.02, 3.94)	20	4.83 (3.25, 6.41)
Q3	39	2.50 (1.59, 3.41)	49	2.49 (1.69, 3.29)	54	3.51 (2.56, 4.46)	48	3.09 (2.20, 3.98)	53	4.46 (3.46, 5.46)	34	3.47 (2.34, 4.60)
Q4	64	2.87 (2.17, 3.57)	54	2.28 (1.69, 2.87)	72	3.50 (2.73, 4.27)	81	4.13 (3.26, 5.00)	85	3.28 (2.55, 4.01)	50	3.05 (2.14, 3.96)
Q5	91	2.67 (2.19, 3.15)	132	3.28 (2.75, 3.81)	98	2.86 (2.30, 3.42)	91	3.43 (2.76, 4.10)	93	2.94 (2.19, 3.69)	40	1.49 (0.8, 2.18)
Urban-Rural Status												
Rural	51	2.76 (2.00, 3.52)	52	2.42 (1.76, 3.07)	58	3.05 (2.26, 3.83)	63	3.67 (2.76, 4.58)	79	4.67 (3.64, 5.70)	42	4.14 (2.89, 5.39)
Urban	207	2.70 (2.34, 3.07)	266	3.06 (2.69, 3.43)	249	3.23 (2.83, 3.63)	238	3.38 (2.95, 3.81)	233	3.32 (2.89, 3.75)	124	2.94 (2.43, 3.46)

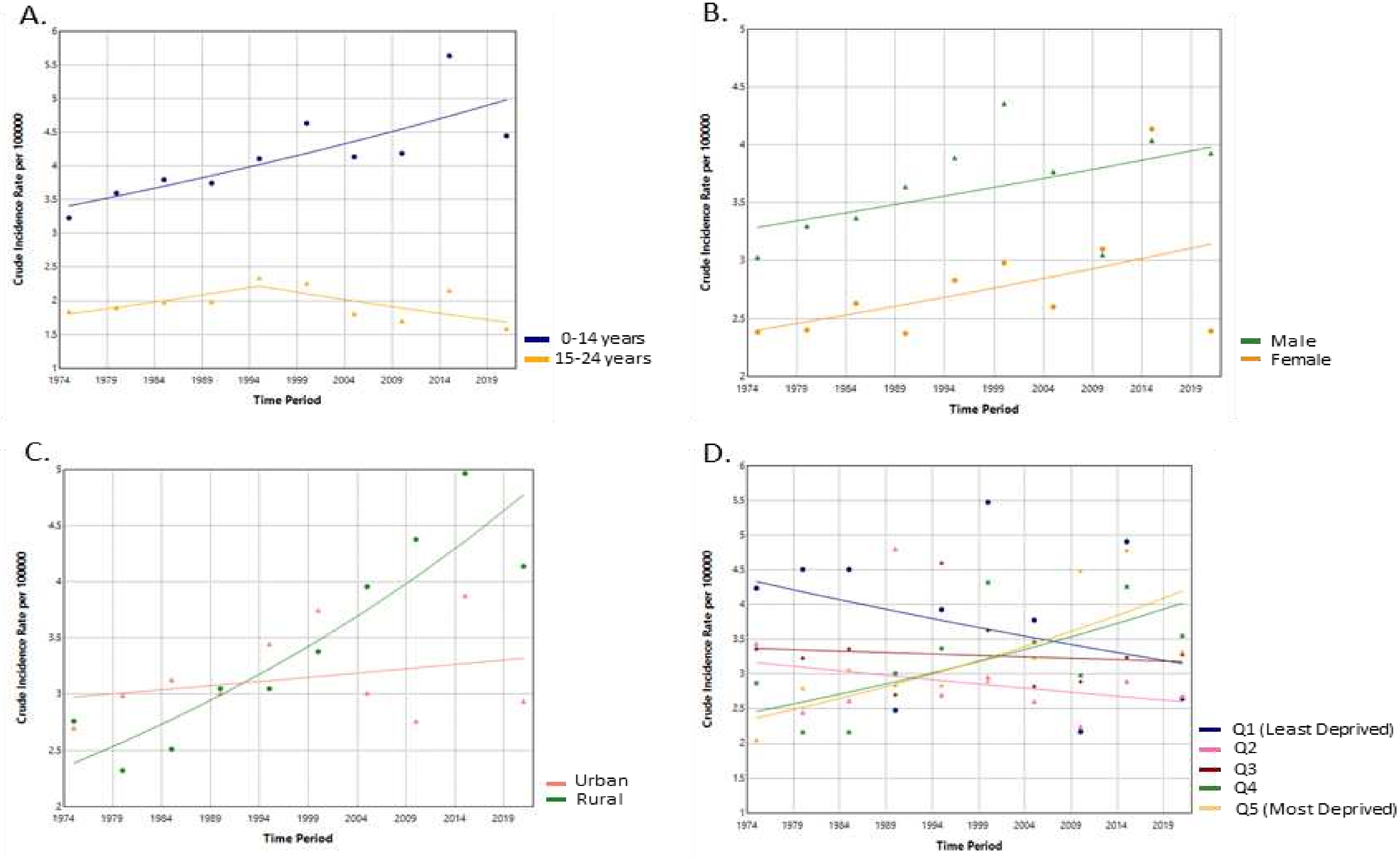

Figure 1 Joinpoint Trend Analysis by A. Age group, B. Sex, C. Urban-Rural Status, and D. Deprivation Quintile