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Trends in acute glomerulonephritis mortality among older adults from 1992 to 2021

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This study reports trends in acute glomerulonephritis (AGN) mortality in older adults (aged 65–94 years) and its association with age, period, and birth cohort across 204 countries and territories over the past 30 years, using data from the Global Burden of Disease (GBD) 2021 Study. An age-period-cohort model was used to estimate the overall annual percentage change in AGN mortality (net drift), annual percentage change for individuals aged 65–94 years (local drift), and longitudinal age-specific rates adjusted for period bias and period/cohort relative risks from 1992 to 2021. In 2021, there were 6213 AGN-related deaths globally (95% UI: 4460–7961). Between 1992 and 2021, the net drift for AGN mortality in high socio-demographic index (SDI) countries was 3.15% per year (95% CI 2.62–3.69), compared to − 1.18% per year in low SDI countries (95% CI − 2.01 to − 0.33). High-middle SDI countries had a decline of − 1.49% per year (95% CI − 1.80 to − 1.18), middle SDI countries − 1.52% per year (95% CI − 1.75 to − 1.28), and low-middle SDI countries − 1.78% per year (95% CI − 2.37 to − 1.20). Globally, high SDI countries showed an upward trend in AGN mortality, while others showed a downward trend. Despite the declining mortality in many regions, 15 high SDI countries, 5 high-middle SDI countries, 4 middle SDI countries, 5 low-middle SDI countries, and 3 low SDI countries showed poor or worsening outcomes in the most recent period and birth cohort. These findings suggest that AGN mortality trends are not related to a country's economic development, highlighting the need for high SDI countries to invest more in AGN-related healthcare.

Keywords Acute glomerulonephritis, Mortality, Age-period-cohort, Global burden of disease

AGN is mainly caused by nephritogenic strains of Group A streptococcal infection, and its typical clinical manifestations are acute nephritic syndrome, hematuria, proteinuria, hypertension, edema and renal dysfunction[1]. Most patients recover within a few days to a few weeks, and the overall prognosis is good[2]. AGN occurs primarily in children and the elderly with an increased relative risk, the prognosis of children is generally better than that of adults, and the prognosis of the elderly is often worse, so now primarily affects older adults (60 years and older) who have underlying and chronic conditions[3–5]. For example, with the increase in the incidence of myocarditis in the elderly, the incidence of AGN is also increasing, which is related to the drug treatment of the disease[6]. In addition, the elderly have more underlying diseases and complications, and the interaction of the type and amount of drugs taken by patients will also affect the metabolism and excretion of drugs, increasing the risk of death in the elderly[7]. The pathogens and pathways of AGN infection in the elderly are diverse[8,9]. Elderly patients have higher acute complications, renal impairment, nephritic proteinuria and mortality, they are the main death risk group of AGN[10]. Meanwhile AGN is also a leading cause of acute kidney injury and the main cause of death[11]. At present, AGN remains an important health problem in developing countries and some tropical regions of developed countries[12]. Therefore, in order to reduce the financial and medical burden, we should also pay more attention to elderly AGN patients[13].

Over the past three decades, advances in the diagnosis and treatment of kidney disease have dramatically reduced the overall mortality rate from kidney related diseases. To accurately assess trends in AGN mortality, an in-depth analysis of time trends in AGN mortality across all countries is necessary. For patients with AGN, the risk of death can be broken down into age, period, and birth cohort effects. At present, there is a lack of article on trends in AGN mortality or its relationship to age, change over time, or birth cohort. GBD is an international collaboration that uses harmonized methodologies and population data to generate a variety of indicators that provide data for analyzing disease trends on a global scale[14]. That includes 369 diseases and 87 risk factors in 204

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countries[15]. In this paper, we use GBD 2021 data and age cohort models to explore changes in AGN mortality of the elderly people aged 65–94 years in 204 countries and territories from 1992 to 2021.

Methods

Data sources

GBD 2021 provides updated estimates of descriptive epidemiological data for a total of 369 diseases in 204 countries and territories between 1992 and 2021. Using standardized tools within a Bayesian framework, the GBD network makes disease estimates using all available data across time, age and geography, as well as across health causes and domains, allowing information to be "borrowed" from existing data to be estimated for countries without a primary source of data, a process that allows the burden of AGN to be estimated for all regions of the globe[16]. All disease estimates for GBD include a 95% uncertainty interval (UI) based on the 25th and 975th ordered values of the posterior distribution. The analysis used each country's Socio-demographic Index (SDI), a measure that combines per capita income and average years of schooling, with higher numbers indicating higher socioeconomic levels[17]. Based on the 2021 SDI values, all countries are divided into five SDI quintiles. In GBD 2021, age-standardized mortality rates are calculated directly standardized from the global standard population. The net drift is an estimate derived from an age-period-cohort model that represents the overall annual percentage change in mortality.

Analysis of overall Temporal trends in AGN mortality

Population and age-standardized rates from 1992 to 2021 were used to assess overall trends in AGN mortality among older adults (65–94 years). Age-standardized mortality rates were calculated using global age-standardized population data from GBD 2021. We also break down the number of deaths by region and calculate the proportion of deaths in each region, and show the change in the distribution of deaths from the disease among older adults in different regions of the world.

Age-period-cohort modelling analysis of mortality data

This study used an age-period-cohort (APC) model framework to analyze trends in mortality by age, period, and birth cohort. The APC model aims to reveal the contribution of age-related factors to disease trends beyond traditional epidemiological analyses. Because the relationship between age, period, and cohort is linear (birth cohort = period - age), it is statistically impossible to estimate their individual influencing factors[18]. The APC model is done using the R tool. GBD 2021 AGN mortality estimates and population data for each country were used as data inputs for the APC model. In a typical APC model, the age and period intervals must be equal, i.e. the 5-year age group should be used in conjunction with the 5-year calendar period[19]. The fitted APC model estimates the overall time trend in mortality, expressed as the annual percentage change in mortality (i.e., the net drift in mortality, % per year)[20]. The net drift is determined by two parts: the trend part of the calendar time and the trend part of the continuous queue. The APC model also estimates the time trend in mortality within each age group, expressed as the annual percentage age change in age-specific mortality (i.e., the local drift in mortality, % per year), which reflects the trend in the birth cohort effect. The statistical test was bilateral, and $p < 0.05$ was significant. All analyses were done in R (version 4.3.1). We built the model using the APC-Web package in R and visualized it with the ggplot2 package[21].

Results

Global and regional trends in AGN mortality,1992–2021

Table 1; Fig. 1, Supplementary Fig. 1 show the number of deaths, all-age mortality and age-standardized mortality, and the net drift in mortality (estimated by the APC model). The number of AGN deaths increased from 4.128 million (3.121–5.391 million) to 6.213 million (4.460–7.961 million). In 2019, the global AGN mortality rate for all ages was 0.81 (0.58 to 1.04) per 100,000 people, and the AGN age-standardized mortality rate was 0.85(0.61–1.09) per 100,000 people, which was 0.91% (0.62–1.2) and 0.99 (0.70 to 1.28) lower than in 1990, respectively. It is important to note that the mortality rates for all ages in all SDI regions were generally consistent with age-standardized mortality rates. Globally, the APC model estimates a net drift in AGN mortality of − 0.66 (− 0.82 to − 0.50) per year, ranging from 3.15 (2.62 to 3.69) in high SDI regions to − 1.78 (− 2.37 to − 1.20) in low and medium SDI regions. Between 1992 and 2021, only regions with high SDI experienced an increase in global AGN mortality for old people.

Time trends in AGN mortality across different age groups

Figure 2A shows the annual percentage change in AGN mortality for each age group (i.e., local drift in mortality estimated from the APC model and capturing trends in birth cohort effects) from ages 65–94. Globally, the decline in AGN mortality rates in the 65–69 to 80–84 age groups is gradually decreasing, while the mortality rates in the 80–84 to 90–94 age groups are gradually increasing. The upward trend of the elderly gradually increases with age, and the change in the mortality rate of men is equal to that of women. Countries with high SDI experienced the greatest increases in mortality, and countries with low, low medium, medium and medium-high SDI decreased less. Local variations in mortality rates for each country are shown in the Supplementary Fig. S2–S6.

Figure 2B shows the time change in the distribution of age at death, which is an indirect marker of survival in the AGN population. Globally, there was a shift in the number of deaths from 65 to 94 years of age, and this trend was more pronounced in high and medium to high SDI countries, and elsewhere, the trend by age group remained largely unchanged over the study period. Among older people, in countries with high SDI, death rates

	Global(*N* = 204)		High SDI (*N* = 41)		High-middle SDI (*N* = 46)		Middle SDI (*N* = 41)		Low-middle SDI (*N* = 42)		Low SDI (*N* = 34)	
	1992	2021	1992	2021	1992	2021	1992	2021	1992	2021	1992	2021
Deaths: Number	4128 (3121 ~ 5391)	6213 (4460 ~ 7961)	235 (196 ~ 276)	984 (800 ~ 1151)	1211 (921 ~ 1613)	1392 (959 ~ 1901)	2239 (1651 ~ 2950)	3223 (2208 ~ 4185)	289 (155 ~ 503)	396 (226 ~ 586)	153 (47 ~ 371)	215 (73 ~ 459)
APC model estimates: Net drift of mortality	-0.66(-0.82~-0.50)		3.15(2.62 ~ 3.69)		-1.49(-1.80~-1.18)		-1.52(-1.75~-1.28)		-1.78(-2.37~-1.20)		-1.18(-2.01~-0.33)	
All-age mortality rate	1.20 (0.91 ~ 1.57)	0.81 (0.58 ~ 1.04)	0.22 (0.18 ~ 0.26)	0.49 (0.40 ~ 0.57)	1.37 (1.04 ~ 1.82)	0.76 (0.53 ~ 1.04)	2.70 (1.99 ~ 3.56)	1.41 (0.96 ~ 1.83)	0.62 (0.33 ~ 1.07)	0.35 (0.20 ~ 0.51)	0.90 (0.28 ~ 2.18)	0.58 (0.20 ~ 1.24)
EAPC	-0.91(-1.2~-0.62)		3.62(2.16 ~ 5.1)		-1.58(-1.79~-1.37)		-1.67(-1.94~-1.4)		-1.84(-1.92~-1.75)		-1.35(-1.5~-1.21)	
Age-standardized mortality rate	1.26 (0.95 ~ 1.65)	0.85 (0.61 ~ 1.09)	0.22 (0.18 ~ 0.26)	0.44 (0.36 ~ 0.52)	1.45 (1.10 ~ 1.93)	0.79 (0.55 ~ 1.08)	3.02 (2.21 ~ 3.98)	1.58 (1.08 ~ 2.04)	0.70 (0.37 ~ 1.22)	0.39 (0.22 ~ 0.58)	1.06 (0.32 ~ 2.60)	0.71 (0.24 ~ 1.52)
EAPC	-0.99(-1.28~-0.70)		3.14(1.66 ~ 4.64)		-1.79(-1.95~-1.63)		-1.74(-1.99~-1.48)		-1.87(-1.95~-1.78)		-1.26(-1.38~-1.15)	

Table 1. Trends in AGN mortality across Socio-demographic index quintiles, 1992 – 2021. All GBD bracketed data represent a 95% uncertainty interval; The parentheses for net drift indicate a 95% confidence interval. SDI = Sociodemographic index; APC = age-period-cohort.

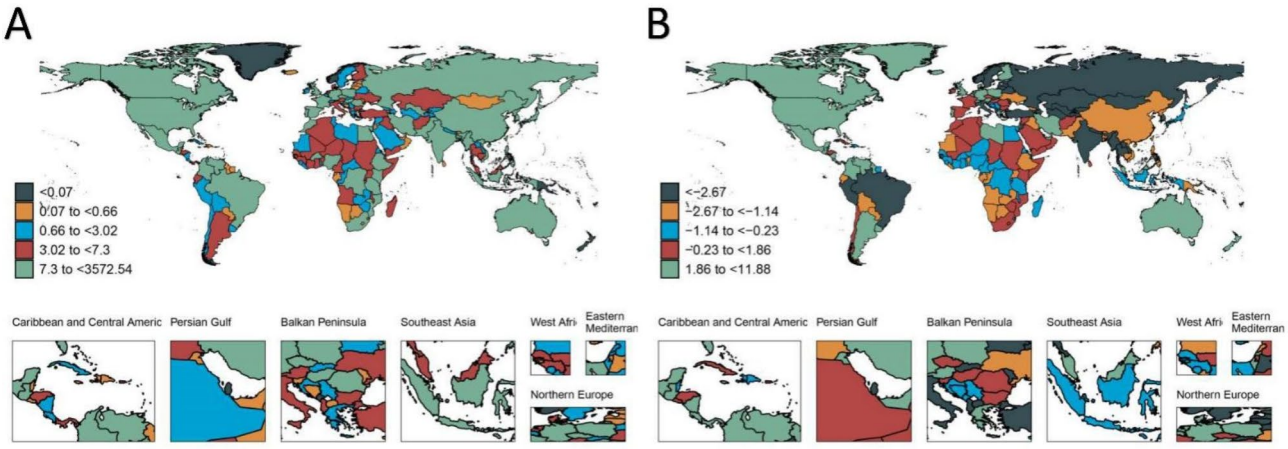

Fig. 1. The all-age mortality in 2021 (**A**) and net drift of mortality during 1992–2021 (**B**) for AGN in 204 countries and territories. (**A**) World map of all-age mortality for AGN. In 2021, the global all-age mortality rate was 0.81% [95% UI (0.58 ~ 1.04)] per 100,000 population. (**B**) World map of net drifts for AGN mortality, i.e., estimated annual percentage change of mortality from age-period-cohort model. Net drift captures components of the trends attributable to calendar time and successive birth cohorts. The global net drift of AGN mortality was − 0.66% [95% CI (− 0.82~-0.50)].

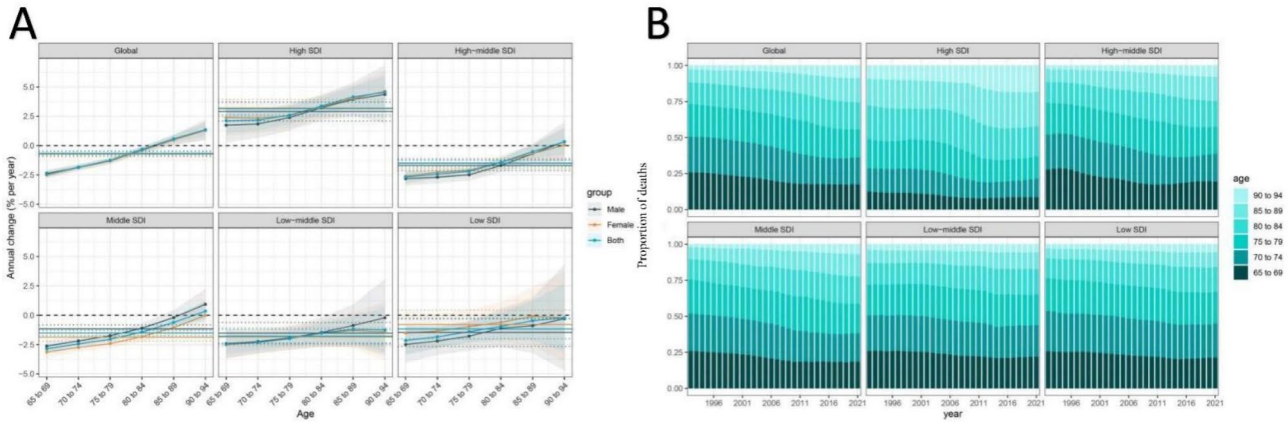

Fig. 2. Local drift and age distribution of AGN mortality by SDI quintile, 1992–2021. (**A**) Local drift of AGN mortality for six age groups (65–69 years to 90–94 years) due to age-period-cohort model estimation in 1992–2019. Dots and shaded areas indicate the annual percentage change in mortality and the corresponding 95% CI. (**B**) Time change in the relative proportion of AGN deaths by age group, 1992–2021.

in the 90–94 age group increased significantly, while those in other age groups remained largely unchanged. The age at death distribution for each country is shown in the Supplementary Figs. S7–S11.

Age, period, and cohort effects on AGN mortality

Figure 3 shows age-period-cohort effect estimates from the APC model via the SDI quintile (i.e., the age effect, expressed as a longitudinal age curve to represent the natural history of age-related AGN mortality; The period effect, expressed as the relative risk of mortality by period, is used to track progress over time; Cohort effects, expressed as relative risk of mortality by cohort, are used to track changes in mortality across birth cohorts). The age effect had a similar pattern across the different SDI quartiles, with the risk increasing with age, with the highest risk in people aged 90 to 94 years, indicating the lowest survival rate in this age group. Compared with other countries, Low -medium SDI countries have the lowest overall mortality rates for all age groups and Medium-SDI countries have the highest overall mortality rates. No significant gender differences were found in age effects. Over the study period, there was an overall downward trend in mortality risk across the different SDI quartiles. Over the past 30 years, the period effect has remained almost constant in all countries except those with high SDI, indicating little improvement in mortality. Countries with high SDI saw the most significant increase in risk over the period 2007–2021. As with the period effect, the cohort effect of decline in all countries except those with high SDI is a slow downward trend. The death rate for people born after the early 20th century

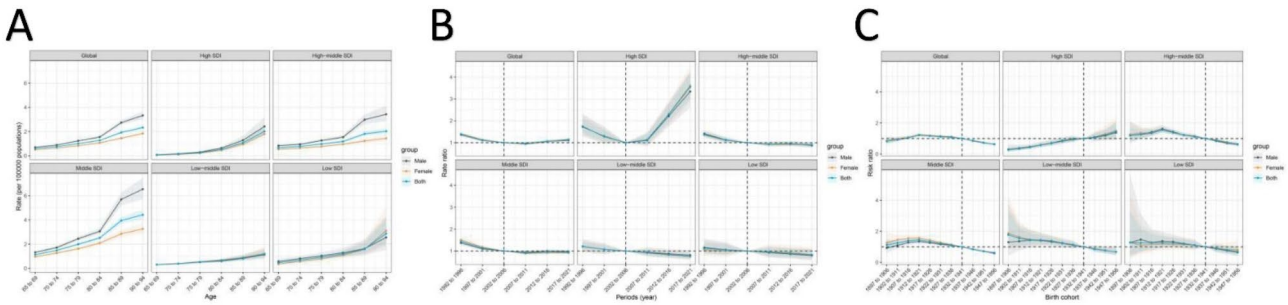

Fig. 3. Age, period, and cohort effect of SDI quartile on AGN mortality. (**A**) Age effects as expressed by a fitted longitudinal age curve of death rates adjusted for period bias. (**B**)The period effects are expressed as the mortality rate ratio and are calculated as the age-specific rate from 1992–1996 to 2015–2019. (**C**) The cohort effects are expressed by the relative risk of mortality and calculated as an age-specific ratio at birth for 1897–1906 cohort to 1947–1956 cohort, with the reference cohort set for 1932–1941. Dots and shaded areas indicate the mortality rate or mortality rate and the corresponding 95% CI.

in high-SDI countries has gradually begun to rise, while the risk in other countries has been slowly declining. The effects of age, period and cohort on AGN mortality by country are shown in Supplementary Figs. S12–S26.

Age-period-cohort effects in exemplary countries

We analyzed several typical countries in the SDI quintile to characterize major trends in AGN mortality around the world through age-period-cohort effects. Figure 4A shows countries with good age-period-cohort effects. Sweden has a favorable trend typical of countries with high SDI, with a decline in mortality among older adults aged 64–94 years in all age groups, as well as declining and low stable age, period and cohort risk. Italy stands out for its significant net drift, with the rate of decline in mortality among older people slowing as they get older in High-middle SDI countries. Thailand has shown a steady decline in deaths at all ages among medium-range SDI countries. Kyrgyzstan is the only country to see a significant drop in its mortality rate across all age groups in Low-middle SDI countries.

Figure 4B represents countries where the age-period-cohort effect on mortality is relatively unfavorable. Australia, like most other high SDI countries, is on an upward trend in the age distribution of death, with mortality rising slowly in the 65–84 years but rapidly among those > 84 years of age. Among the middle SDI countries, Mexico has the worst AGN mortality trends, showing persistently high levels in people aged 65–94 years, and worsening risk by age, period, and cohort in recent years. In low-middle SDI countries like Egypt and Nigeria, annual death rates barely changed.

The age distribution of deaths shows the relative proportion of deaths in each age group between 1992 and 2021. Local variations indicate annual percentage changes (% per year) in mortality rates for six age groups (from 65 to 69 to 90–94 years). The age effect is represented by a fitted longitudinal age curve of death rates (per 100,000 person-years) adjusted for period bias. The effect for each period is expressed as the relative risk of death (mortality ratio) and is calculated as the age-specific rate for each period and the rate for the period 2002–2006. The cohort effect is expressed in terms of the relative risk of death (mortality ratio) and calculated as the ratio for a particular age in each cohort with the ratio for the reference cohort 1932–1941. The shaded areas represent the corresponding 95% ci estimated for each point. SDI = sociodemographic index.

Discussion

Our study shows that overall global elderly AGN patients deaths appear to have been flat over the past three decades. Our analysis of GBD death estimates shows that AGN death rates have increased in many countries with high SDI, but have declined or remained flat in countries with moderate or poor economic conditions. We also found that the majority of AGN deaths occurred in the elderly (65–74), suggesting that health care systems should pay attention to AGNs in this age group. For the first time, we use the APC model to analyze time-of-death trends for AGNs on a global scale and compare them across different countries and regions, and use elderly mortality and age-standardized mortality to illustrate changes in AGN mortality. Our study makes full use of public health data to provide a detailed analysis of trends in the disease, and examination of period and cohort effects allows us to distinguish the sources of mortality trends and provide effective public health information for AGN. Our estimation of local drift values, on the other hand, allows us to understand time trends in mortality for each age group.

Globally, the estimated annual percentage change (EAPC) of elderly AGN patients in many countries with high SDI is on the rise except Sweden and Lithuania. Most countries have roughly the same proportion of deaths among all age groups. Kidney biopsy is a key option in the diagnosis of glomerular disease, it helps to determine the exact specific diagnosis, assess the level of disease activity and severity, and thus contribute to appropriate treatment and predict prognosis[22]. Every year, Sweden is investing more in disease registries, data analysis resources and information technology infrastructure, and spending on health care is increasing year by year, with a special focus on registrie-based research, on risk factors, on chronic diseases, and with a tradition of collecting epidemiological data dating back more than two centuries. The Public Health System has created one

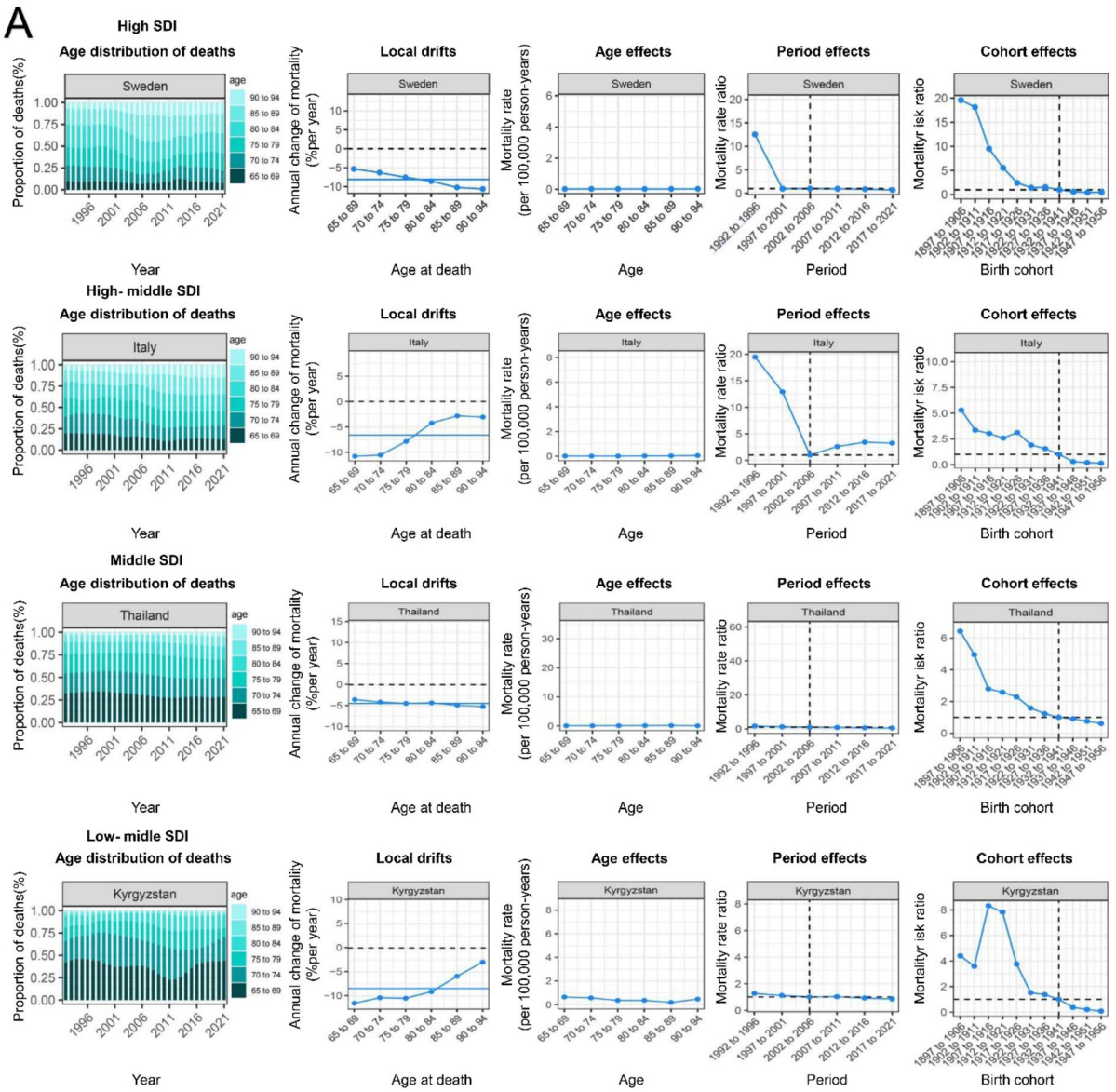

Fig. 4. Favourable (**A**) and unfavourable (**B**) age-period-cohort effects on exemplar countries across SDI quintiles.

of the most extensive health data system registries in the world[23]. And they have strict follow-up guidelines for kidney disease and screening for risk factors[24]. Changes in the incidence of kidney disease in Lithuanian national kidney biopsy data were analyzed, showing a certain degree of improvement in socio-economic conditions and improved diagnosis of the disease[25]. According to the Italian Kidney biopsy registry, glomerular kidney disease occurs more frequently in the elderly than in adults, and the incidence is higher in elderly patients with urinary tract abnormalities[26]. Italy is a southern European country with the highest proportion of senior citizens (aged 65 years or older) in Europe[27]. Italy has marked differences in health indicators, per capita expenditure, distribution of health professionals and quality of health services[28]. Data on kidney biopsies in national registries is a useful tool for nephrologists because it addresses some of the current challenges facing clinical research. These data can be used for epidemiological studies in health care and can address problems encountered in the prevention and treatment of kidney disease[29]. The annual rates of change in Thailand tend to flatten out, and they have kidney biopsies earlier, probably due to different ethnic and environmental changes, and Thailand differs from other countries in glomerular disease, which is the baseline data for later effective studies on appropriate and beneficial management[30].

Australians have one of the highest rates of chronic kidney disease (CKD) in the world[31]. AGN is also a major risk factor for the development of indigenous CKD[32]. Mandatory notification of the disease by clinicians began in 1991, and an AGN database was established to facilitate accurate disease surveillance and public health response in Australia[12]. The incidence of AGN is high among Indigenous Australians, often living in remote and rural communities, where living conditions are poor and sanitation facilities are often inadequate.

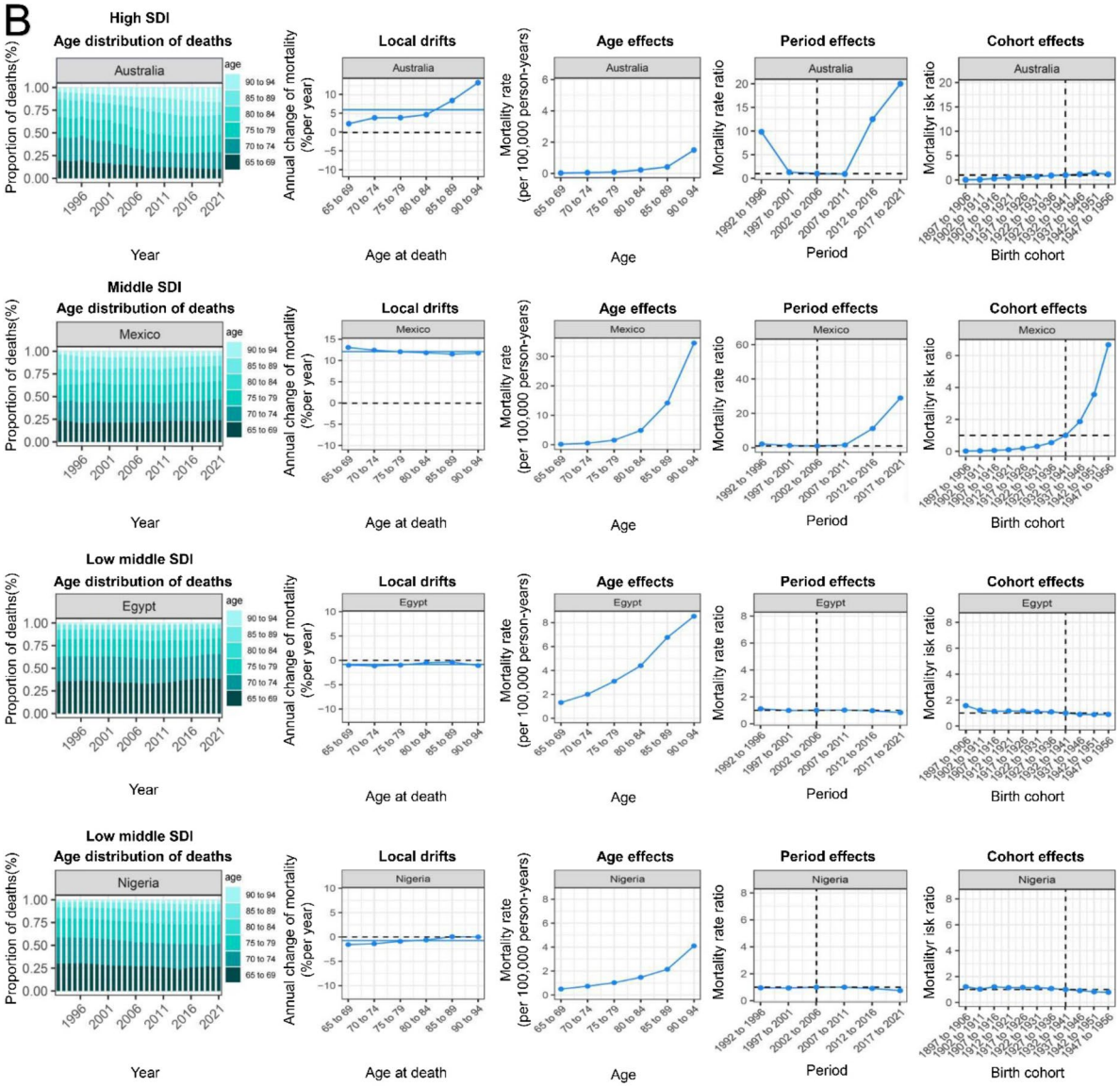

Figure 4. (continued)

Young people are mostly caused by streptococcal infections, while the elderly are mostly caused by autoimmune diseases and underlying diseases[33]. Indigenous children in Central Australia have the highest reported incidence of acute post-streptococcal glomerulonephritis worldwide. Urgent action is needed to improve housing and reduce overcrowding in towns and communities in central Australia to reduce the disease burden of related diseases[34]. With the aging of the population, the incidence of age-related diseases AGN is becoming more and more significant[35,36]. Mexico has one of the highest rates and prevalence of CKD, kidney disease is a public health problem[37]. According to the 2019 Global Burden of Disease (GBD) database, the incidence of CKD is 457 per 100,000 and the prevalence is 13 017 per 100,000. The states with the highest prevalence and incidence in 2019 were Mexico City, Veracruz, Morelos, and Tamaulipas. Diabetes and high blood pressure are common in Mexico, which has no centralized national registry for kidney disease[38]. Screening for disease in poor areas of Mexico often detects impaired kidney function, proteinuria, and cardiovascular risk factors. This suggests that targeted screening and intervention trials are feasible and necessary[39]. Currently, affected patients in developed countries tend to be the elderly, especially those with comorbidities such as diabetes and alcoholism[40]. Therefore, the problems related to senile nephropathy should be considered. Strategies to prevent and treat AGN that will reduce this burden are particularly important.

In summary, the increased mortality of AGN is likely due to the high prevalence of diabetes, hypertension, cardiovascular diseases, and other conditions in countries with high SDI. These comorbidities can complicate the clinical course of AGN, worsen kidney damage, make treatment more challenging, and hinder disease control, ultimately leading to a poorer prognosis and higher mortality rates. Older people may also have weaker immune systems or have less access to timely and appropriate treatment, leading to worse outcomes. Disparities in the quality and distribution of health care may persist in some countries, especially for minorities, rural populations

or people from lower socioeconomic backgrounds. These groups may face delayed diagnosis, suboptimal treatment, or fewer late-stage care options, leading to higher AGN mortality. How to solve these problems? First, governments and healthcare systems should invest in improving early screening for AGN, implementing regular blood and urine tests, and enhancing public health registries for kidney diseases. Second, primary care physicians treating high-risk populations, such as those with high blood pressure and diabetes, should focus on identifying kidney disease risk factors, enabling early detection and treatment of AGN. Third, special attention should be given to the elderly, with strengthened services for vulnerable groups and regular disease follow-up. Fourth, public health campaigns should be strengthened to raise awareness about AGN, emphasizing the importance of early treatment to improve prognosis. Finally, countries should invest in strategies for equitable resource allocation, ensuring the fair distribution of healthcare services, improving access to kidney care in rural areas, and providing timely diagnosis and treatment for vulnerable groups in remote locations.

The study has several limitations. First, there are limitations from the GBD model, which is due to the limited nature of collecting national data. Estimates of national GBD mortality are uncertain. This affects the uncertainty about age/period/cohort trends. Second, the GBD study used a single underlying cause of death. For older adults, AGN is unlikely to be a single cause of death. Therefore, the actual AGN mortality rate in the GBD study may have been misestimated. Third, the study looked at mortality data at the national level and did not look at differences within countries. Forth, The GBD database combines data from various sources, such as health surveys, hospital records, vital registries, and scientific studies. However, the quality and completeness of this data can vary. Finally, our study did not include direct country-level data on health systems. The inclusion of national and regional standards for the treatment and prevention of AGN in future GBD will help distinguish between the timely identification of AGN disease and the lack of timely treatment for the assessment of AGN deaths.

Given the large time span of over twenty years, there are likely to be significant imbalances in the SDI groupings among the included countries. While it may be tempting to exclude data from countries with uneven development to improve the reliability of the conclusions, this approach could reduce the generalizability of the findings. We grouped countries according to their SDI levels (low, lower middle, medium, upper middle, high) and analyzed trends within each SDI category separately. This would make it possible to compare countries with similar levels of development and minimize the impact of development-related differences. This approach helps ensure that the analysis is more even and fair, with less human intervention. The GBD data spans a long period of time, and socioeconomic factors, healthcare systems, and reporting practices may have changed during that time. We divided patient age and time periods every 5 years and birth age periods every 10 years, and analyzed trends over these time periods. This will help explain the temporal variation of SDI and its effect on mortality.

In the study, we conduct an in-depth analysis of AGN trends through GBD database. Applying the APC model to analyze AGN trends by age, period, and group also provides insight into the effectiveness of health system responses to disease, as opposed to traditional epidemiological surveys. Our age-period-cohort analysis of global AGN mortality found that a country's economic development was not associated with mortality from the disease. In many high-SDI countries, it is largely inadequate to manage AGN populations, whereas in some low-SDI countries better health could have been provided to this group. Therefore, regardless of the country, we should pay attention to the incidence and mortality of AGN in the elderly aged 65–94 years.

Data availability

Data availability statementData are available in a public, open access repository. All data used in this study can be freely accessed at the GBD 2021 portal We downloaded data from at the GBD 2021 portal (http://ghdx.healthdata.org/gbd-2021).

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Author contributions

H, T, and F, L contributed conception and design of the study; J,Y and H, Z collected the data; J,Y and H, Z performed the statistical analysis; H,T, and F, L wrote the first draft of the manuscript. All authors contributed to manuscript and approved the submitted version.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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