



Impact of high, low, and non-optimum temperatures on chronic kidney disease in a changing climate, 1990–2019: A global analysis

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ABSTRACT

Background: Although a few studies have reported the relationship between high and low temperatures and chronic kidney disease (CKD), the global burden of CKD attributable to extreme heat and cold in recent decades remains unknown.

Methods: Based on the Global Burden of Disease Study (GBD) 2019, we obtained data on age-standardized mortality rates (ASMR) and age-standardized rates of disability-adjusted life years (ASDR) per 100 000 population of the CKD attributable to non-optimum temperatures from 1990 to 2019. The annual mean temperature of each country was used to divide each country into five climate zones (tropical, subtropical, warm-temperate, cool-temperate, and boreal). The locally weighted regression model was used to estimate the burden for different climate zones and Socio-demographic index (SDI) regions.

Results: In 1990, the ASMR and ASDR due to high temperature estimated -0.01 (95% UI, -0.74 to 0.44) and -0.32 (-21.66 to 12.66) per 100 000 population, respectively. In 2019, the ASMR and ASDR reached 0.10 (-0.28 to 0.38) and 2.71 (-8.07 to 10.46), respectively. The high-temperature burden increased most rapidly in tropical and low SDI regions. There were 0.99 (0.59 to 1.39) ASMR attributable to low-temperature in 1990, which increased to 1.05 (0.61 – 1.49) in 2019. While the ASDR due to low temperature declined from 22.03 (12.66 to 30.64) in 1990 to 20.43 (11.30 to 29.26) in 2019. Overall, the burden of CKD attributable to non-optimal temperatures has increased from 1990 to 2019. CKD due to hypertension and diabetes mellitus were the primary causes of CKD death attributable to non-optimum temperatures in 2019 with males and older adults being more susceptible to these temperatures.

Conclusions: The CKD burden due to high, low, and non-optimum temperatures varies considerably by regions and countries. The burden of CKD attributable to high temperature has been increasing since 1990.

1. Introduction

The Lancet Countdown to climate change mentioned that climate change would be the biggest health threat of the 21st century (Watts et al., 2021). Since 1981, the annual global temperature has been rising

steadily by a rate of 0.18 °C per decade, and the global land and ocean surface temperature was off the historical average by $+0.95$ °C in 2019, which was the second warmest year in the 140-year records (State of the Climate, 2021). These realities may indicate the unavoidable appearance of frequent heat waves in the future. The epidemiological evidence

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suggests that exposure to high temperature, defined as ambient temperature that are warmer than the optimum temperatures, is an important risk factor for many adverse health outcomes, including mortality and morbidity for specific causes (Guo et al., 2014; Arbuthnott et al., 2020; Qi et al., 2021). Even so, the effect of low temperature on specific diseases should not be ignored, because it is still the major cause of the global disease burden associated with non-optimum temperatures (Burkart et al., 2021). In recent years, as a result of changing climate, more and more extreme heat and cold waves occurred worldwide.

Chronic kidney disease (CKD) is an important cause of disease and economic burden due to the expensive renal replacement therapy for end-stage kidney disease (Liyanage et al., 2015). In 2017, 697 million people were diagnosed with CKD, and 1.2 million deaths were attributed to CKD worldwide, a 41.5% increase in mortality rate from 1990 (Bikbov et al., 2020). Among the risk factors for CKD, diabetes, hypertension, and glomerulonephritis are known to be the most common causes (Couser et al., 2011; Zhang et al., 2012; Hall et al., 2014). In recent years, high ambient temperatures were hypothesized to be the cause of CKD increase in regions like Central America, Sri Lanka, and India (O'Donnell et al., 2011; Orantes-Navarro et al., 2017; Johnson et al., 2019). Regional epidemiological studies have also revealed that heat and cold exposure are associated with exacerbating kidney disease. A multi-city study found that heat waves were significantly associated with an increased risk of hospitalization for chronic kidney failure for older adults in the United States (Bobb et al., 2014). A study in Queensland, Australia, found that both low and high temperatures were associated with hospitalization for acute kidney injury (AKI), and the association between high temperature and AKI hospitalization became stronger (Lu et al., 2021).

Previous studies have suggested that the potential mechanism of these causes of CKD due to hot temperature is related to the kidney injury caused by recurrent dehydration and heat stress (Johnson et al., 2019; Johnson et al., 2019; Glaser et al., 2016). In addition, a few studies have reported that exposure to extreme temperatures are associated with the emergency room visits population for CKD (Lin et al., 2021). The low temperature exposure can induce a decrease in the body's immune function and lead to the common cold, the infectious status of which may be related to kidney damage (LaVoy et al., 2011). Additionally, low temperature exposure can also induce hypovolemia, atrial dysrhythmias, and cold diuresis (Sun, 2010), which may intensify the kidney burden and cause kidney damage. Finally, diabetes and cardiovascular disease are the most common risk factors for CKD, which are greatly influenced by heat or cold (Li et al., 2014; Keatinge et al., 1997). Therefore, high and low temperatures may be related to CKD.

To date, previous researches on the impact of high and low temperature on CKD has been focused primarily on high temperature exposure in individual cities. No study has assessed the burden of CKD due to non-optimum temperatures, either hot or cold, at the global level in different climate zones and by age, sex, or socioeconomic status. An assessment of the global burden pattern of CKD due to non-optimum temperatures is of great importance because it adds a new knowledge that can help guide CKD prevention and control efforts under climate change. Thus, in this study, we assessed the CKD burden attributable to non-optimum temperatures in 204 countries from 1990 to 2019 and classified them into different climate and economic zones to understand their specific changing trends under climate change.

2. Methods

2.1. Data sources

The Global Burden of Disease Study (GBD) 2019 was a systematic survey that analyzed the impact of diseases, injuries, and risk factors on health by age, sex, and geography for the period between 1990 and 2019 (Murray et al., 2020). The online Global Health Data Exchange query tool (GHDx, <http://ghdx.healthdata.org/gbd-results-tool>) was used to

collect data on the burden of CKD attributable to high, low, and non-optimum temperatures database including global, regional, and 204 countries by gender and age from 1990 to 2019 (Vos et al., 2020). The burden indicators of CKD included mortality numbers, the age-standardized mortality rate (ASMR), and the age-standardized disability-adjusted life years rate (ASDR). The definition of CKD was based on the International Classification of Diseases, Tenth Revision (ICD-10) codes N18 (James et al., 2018), and CKD was classified into five categories in relation to its attributed cause: diabetes mellitus type 1, diabetes mellitus type 2, hypertension, glomerulonephritis, and other unspecified causes (Vos et al., 2020). The 204 countries were divided into five categories according to their socio-demographic index (SDI): including low, low-middle, middle, high-middle, and high. Additional detailed survey information has been reported in a previous study (Vos et al., 2020). The data annual average temperature for each country from the CRU CY v. 4.05 dataset provided by the Climatic Research Unit (<https://www.uea.ac.uk/web/groups-and-centres/climatic-research-unit>), and the detailed information of the dataset has been reported in the previous study (Harris et al., 2020).

2.2. Estimated CKD burden due to high, low, and non-optimum temperatures

A detailed description of the method for estimating the CKD burden attributable to non-optimum temperatures for GBD has been previously described (Burkart et al., 2021; Murray et al., 2020). Briefly, the non-optimum temperatures are defined as the temperature of the day at which the ambient temperature was above (i.e., high temperature) or below (i.e., low temperature) than that associated with the lowest risk of mortality. Given the different annual mean temperature zones and different exposure-response curves, as well as the spatially and temporally different cause composition, the theoretical minimum risk exposure level (TMREL) was defined as the daily temperature associated with temperature for the lowest mortality rate for all included cause-specific diseases for a specific location and year. Where high temperature is defined as a temperature above the TMREL and low temperature is defined as a temperature below the TMREL. The temperature estimates were obtained from the grid reanalysis dataset ERA5 generated by the European Centre for Medium-Range Weather Forecasts (ECMWF) with $0.25^\circ \times 0.25^\circ$ spatial and sub-daily temporal resolution was used (Hersbach et al., 2020). National population data and disease mortality data were derived from vital registration data sources collected in the WorldPop and GBD Cause of Death (CoD) databases, respectively (Johnson et al., 2021). With all these data, estimated CKD burden attributable to non-optimum temperature in six steps: (1) inclusion of risk and outcome pairs; (2) relative risk evaluation as a function of exposure; (3) estimation of burden indicators and non-optimum temperature exposures for CKD; (4) counterfactual level of risk factor exposure or TMREL; (5) relative risk (RR) of outcome reference TMREL; and (6) calculation of population attributable risk (PAF) scores and attributable burden. The effect of temperature may be deleterious or protective depending on whether the RR is greater or less than one (Murray et al., 2020).

2.3. Statistical analysis

Differences in population age structure across countries and regions may contribute to heterogeneity in quantifying the burden of CKD attributable to high, low, and non-optimum temperatures. To remove the effects of demographic differences, we used age-standardized mortality rates (ASMR) and age-standardized disability-adjusted life years rates (ASDR) to assess the burden of CKD attributable to non-optimum temperature and its changing trends from 1990 to 2019 in 204 countries and regions. The countries were divided into five climate zones based on average annual temperature, including tropical ($24\text{--}34^\circ\text{C}$), subtropical ($18\text{--}24^\circ\text{C}$), warm temperate ($10\text{--}18^\circ\text{C}$), cool temperate

(0–10 °C), and boreal (<0 °C) (Sayre et al., 2020). The ASDR and ASMR for CKD attributed to high, low, and non-optimum temperatures were based on locally weighted regression (LOESS) non-parametric regression models fitted to different SDI regions, continents, and climate zones. LOESS regression was used to fit a smooth curve to the country-specific pattern data through a weighted least squares method. Beta-coefficients (β) from linear regression models with their 95% uncertainty intervals (UI) were used to evaluate trends of CKD burden in a generalized linear model where p-values <0.05 was considered statistically significant. The β indicates the average change in the ASMR or ASDR rate per year due to high, low, and non-optimum temperatures. Data were analyzed using R software (version 4.0.2; <https://cran.r-project.org>).

3. Results

3.1. Global and different regions burden of CKD attributed to high, low, and non-optimum temperatures, 1990–2019

A significant increase was observed in global ASMR and ASDR attributable to high temperature from 1990 to 2019 (ASMR, $\beta = 0.004$, 95% UI: 0.003, 0.004 and ASDR, $\beta = 0.102$, 95% UI: 0.095, 0.110) (Fig. 1; Table S1). In 1990, the ASMR and ASDR associated with high temperature were -0.01 (95% UI: -0.74 , 0.44) per 100 000 population and -0.32 (95% UI: -21.66 , 12.66) per 100 000 population, respectively. In 2019, the ASMR and ASDR increased to 0.10 (95% UI: -0.28 , 0.38) per 100 000 population and 2.71 (95% UI: -8.07 , 10.46) per 100 000 population, respectively. The ASMR attributable to low temperature showed an increasing trend ($\beta = 0.003$, 95% UI: 0.001, 0.004), there were 0.99 (95% UI: 0.59 , 1.39) per 100 000 population ASMR attributable to low temperatures in 1990, which increased to 1.05 (95% UI: 0.61 , 1.49) per 100 000 population in 2019. On the other hand, the ASDR showed a decreasing trend ($\beta = -0.072$, 95% UI: -0.096 , -0.048), which declined from 22.03 (95% UI: 12.66 , 30.64) per 100 000

population in 1990 to 20.43 (95% UI: 11.30 , 29.26) per 100 000 population in 2019. In addition, there were significant differences in CKD death burden associated with high and low temperatures in different SDI regions (Fig. 1). The ASMR and ASDR attributable to high temperature fluctuated greatly between 1990 and 2019, especially the low, low middle, and middle SDI regions exhibited a rising trend. Nevertheless, the ASMR due to low temperature increased most significantly in the high SDI region ($\beta = 0.010$, 95% UI: 0.008 , 0.011), followed by a small increase in the middle SDI region (0.003 , 95% UI: 0.001 , 0.004), and decreased in the other SDI regions (Table S1).

There were significant differences in CKD burden attributed to high and low temperatures by climate zones (Fig. 2). Overall, compared with other areas, the ASMR and ASDR due to non-optimum temperatures in subtropical and warm temperate regions remained consistently higher during 1990–2019. From 1990 to 2019, the most rapid increase in CKD burden due to high temperature was observed in the tropical (ASMR, $\beta = 0.223$, 95% UI: 0.187 , 0.259), followed by a larger increase in the subtropical (ASMR, $\beta = 0.093$, 95% UI: 0.062 , 0.123). The CKD burden attributed to high temperature in other climate areas was much smaller. The CKD burden related to low temperature showed a slight decrease in the tropical and subtropical, but a slightly rising trend was observed in the warm, cold temperate, and boreal climate zones. At five world continents, we found that the greatest increase in high temperature burden was observed in Africa (ASMR, $\beta = 0.009$, 95% UI: 0.009 , 0.010), followed by Asia and Oceania. Notably, the global low temperature burden is decreasing in most regions, while it is increasing significantly in America (ASMR, $\beta = 0.021$, 95% UI: 0.017 , 0.024). Overall, the non-optimal temperatures burden in the America and Africa have shown an upward trend over the period 1990–2019 (Fig. S1).

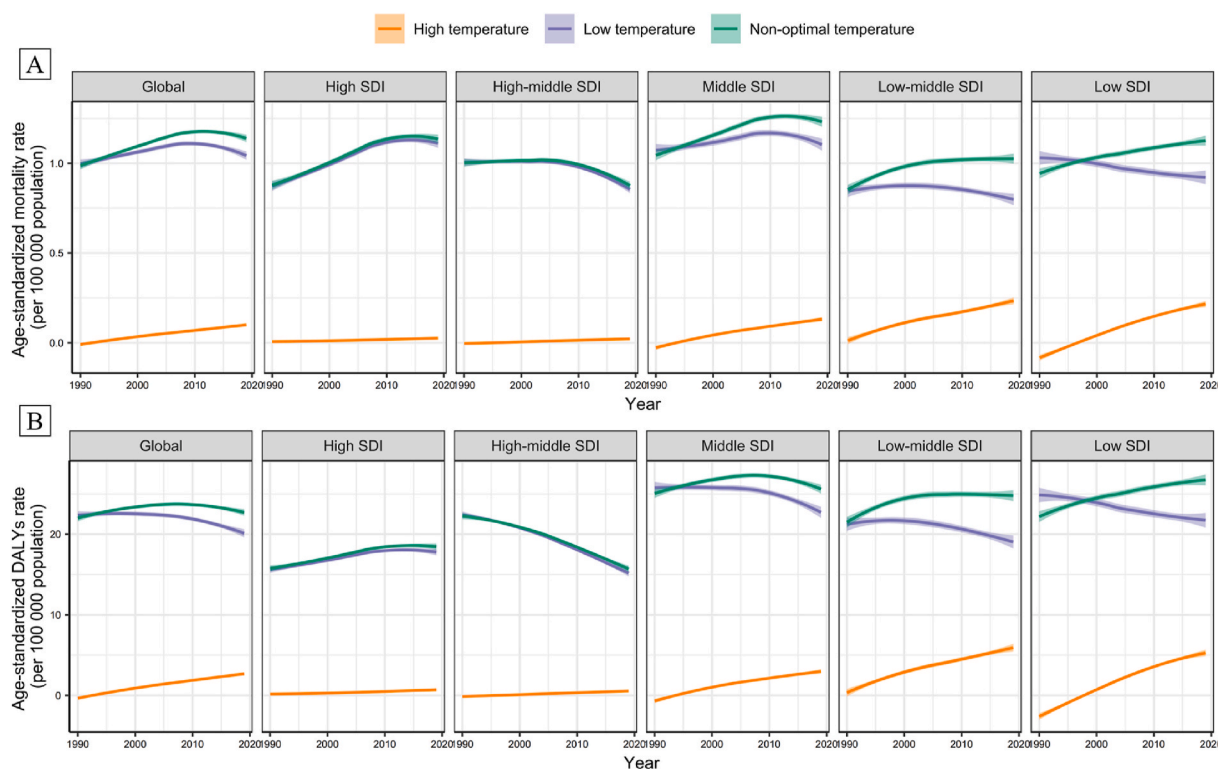


Fig. 1. Temporal trends in age-standardized mortality rate (per 100 000 Population) (A) and age-standardized DALYs rate (per 100 000 Population) (B) for chronic kidney disease associated with high, low, and non-optimum temperatures globally and SDI regions, 1990–2019. DALYs, disability-adjusted life years; SDI, socio-demographic index. Shaded areas represent 95% uncertainty intervals.

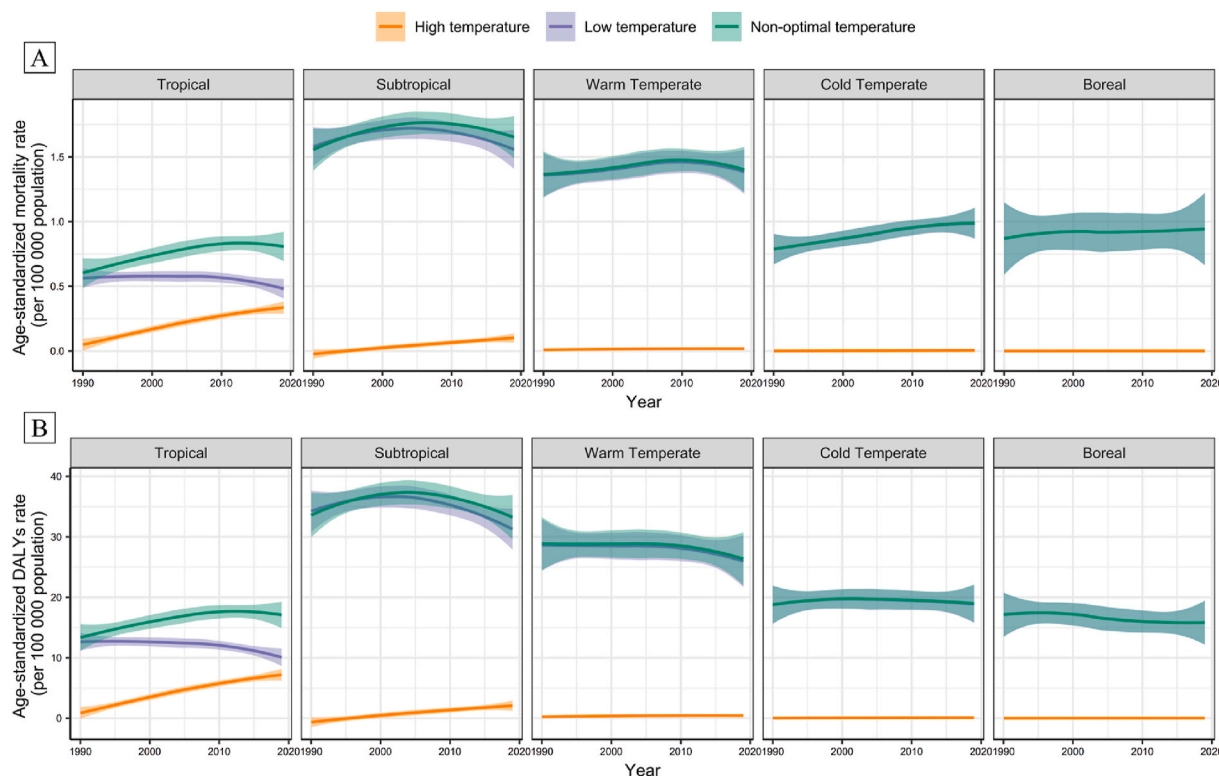


Fig. 2. Temporal trends in age-standardized mortality rate (per 100 000 Population) and age-standardized DALYs rate (per 100 000 Population) for chronic kidney disease due to high, low, and non-optimum temperatures in climate zones, 1990–2019. DALYs, disability-adjusted life years. Shaded areas represent 95% uncertainty intervals.

3.2. Deaths number and ASMR of CKD attributable to high, low, and non-optimum temperatures of different countries in 2019

In 2019, the countries with the biggest death number of CKD attributable to high temperature were India (3 622, 95% UI: 4 488, 11 080), Pakistan (1 014, 95% UI: –1 124, 3340) and Thailand (386, 95% UI: –1 428, 1255) (Fig. S2). The United Arab Emirates had the highest ASMR (2.02, 95% UI: 6.90, –5.90 per 100 000 population) attributable to high temperature, followed by Qatar (1.74, 95%UI: –1.54, 5.22 per 100 000 population), Mali (1.25, 95%UI: 4.69, 4.17 per 100 000 population) and Saudi Arabia (1.20, 95%UI: –1.86, 3.43 per 100 000 population) (Fig. 3). The number of CKD-related deaths attributable to low temperature in 2019 was the highest in China (16 204, 95% UI: 8 531, 24 320), followed by the United States (9 439, 95%UI: 6 107, 12 983), and India (6 751, 95%UI: –1 532, 13 605). Lesotho showed the highest ASMR attributable to low temperature, followed by Mexico and Afghanistan. In summary, Lesotho had the highest ASMR for CKD attributable to non-optimum temperature, while Nigeria had the lowest ASMR. From 1990 to 2019, the ASMR of CKD attributed to high temperature showed an increasing trend in most countries, particularly in countries at low latitudes (Fig. S3). The largest increases were found in the Philippines and the Federated States of Micronesia. For changing trends in CKD ASMR attributable to low temperature, the burden showed a decreasing trend in some countries but increased in others. The largest increases were found in Lesotho and Mexico, and the largest decreases were found in Mongolia, Cuba, and Syrian Arab Republic.

3.3. Classification of CKD due to different etiologies

Globally, CKD ASMR attributable to high and low temperatures increased significantly in both males and females from 1990 to 2019 (Fig. 4), and the increase in ASMR was greater for males than females. Among the different etiologies of CKD, the largest contribution of ASMR

attributable to high and low temperatures in both males and females were hypertensive CKD and type 2 diabetes CKD, followed by unspecified CKD. The percentages of ASMR attributable to high temperature due to hypertensive CKD, type 2 diabetes CKD, and other unspecified CKD in 2019 were 30%, 30%, and 20%, respectively. The corresponding percentages attributed to low temperature were 33%, 28%, and 23%, respectively. We found that CKD ASMR attributable to high and low temperatures increased in Central Latin America from 1990 to 2019. The CKD ASMR attributed to high and low temperatures in Central Latin America was larger than the global average value. In the etiology of CKD, the percentages of ASMR attributable to high temperature due to hypertensive CKD, type 2 diabetes CKD, and other unspecified CKD in 2019 were 28%, 28%, 22%. The proportion of ASMR attributable to high temperature caused by other unspecified increases in Central Latin America compared to the global in 2019. The CKD ASMR attributable to high and low temperature were much higher in males than females, particularly in Central Latin America countries such as El Salvador, Nicaragua, and Colombia (Figs. S4–S8).

3.4. In 2019, the global burden of CKD attributable to high, low, and non-optimum temperatures by age and gender

In 2019, we found that the global burden of CKD attributable to high and low temperatures was higher among males than females, and this sex difference gradually increased with age (Fig. 5). The CKD burden attributable to high and low temperatures increased with age. Similarly, the CKD burden attributable to low temperature also rose with age, but with a smaller increasing slope compared with high temperature initiating from the age group of 35–39 years, indicating a phenomenon of younger age burden of CKD associated with high temperature. In addition, the absolute number of deaths from CKD attributable to high and low temperatures increased with age, and the peak effect was found in the age groups of 70–74 years and 80–84 years, respectively. In the

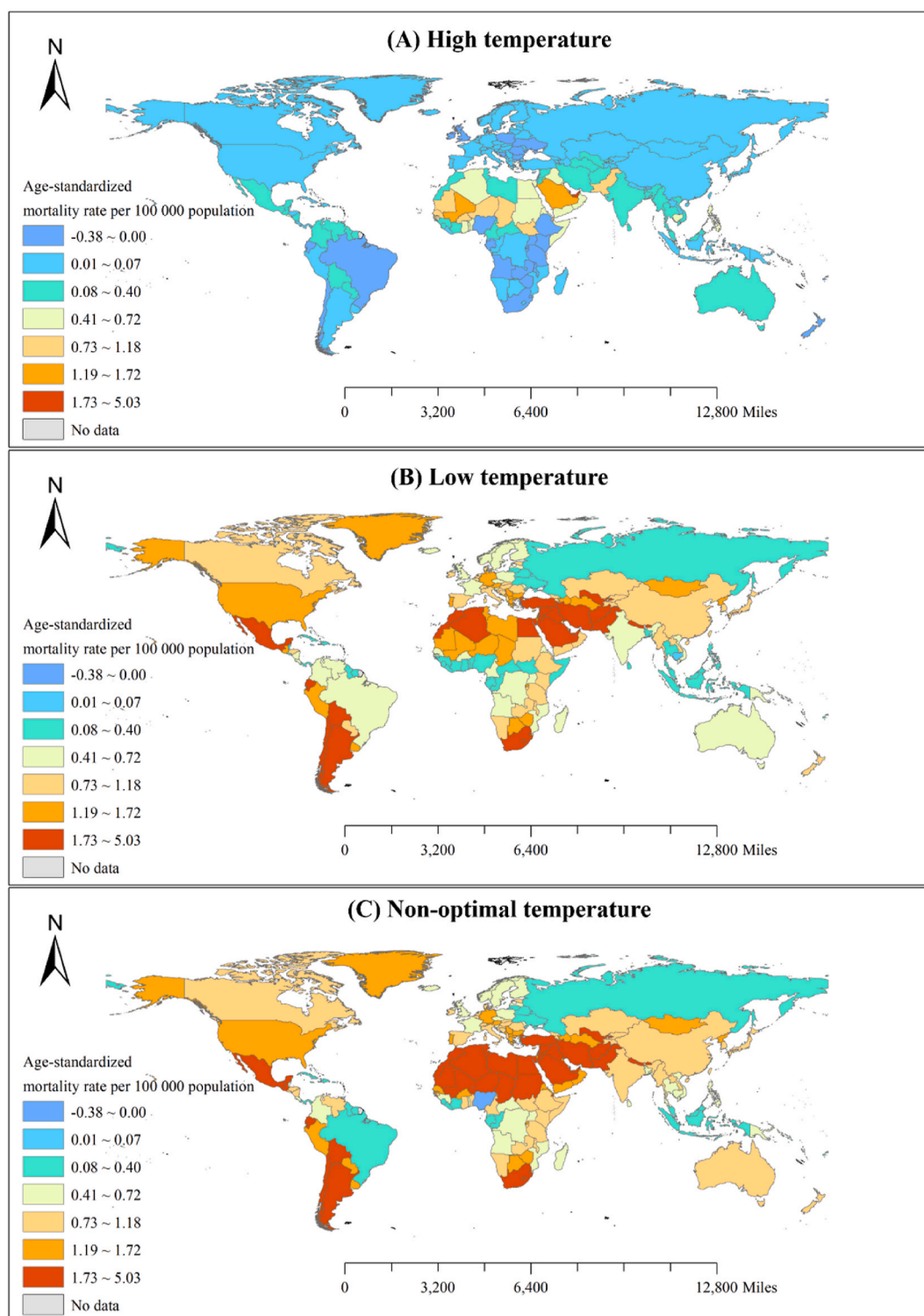


Fig. 3. Spatial distributions of age-standardized mortality rates (per 100 000 Population) for chronic kidney disease attributable to high (A), low (B), and non-optimum temperatures (C) in 2019.

younger age group (≤ 49 years), the CKD due to other and unspecified causes and glomerulonephritis were the major sources of CKD death burden attributed by high or low temperature in 2019 (Fig. S9), while they were hypertensive CKD and diabetes CKD in older age groups.

4. Discussion

This study assessed the current status and spatiotemporal trends of

the global CKD death burden associated with high, low, and non-optimum temperatures exposure during the period between 1990 and 2019. We found a heavy CKD death burden associated with high and low temperatures globally, particularly among men and older adults. Overall, the CKD death burden associated with low temperature was higher than the high temperature, but it increased significantly associated with high temperature in the past 30 years, particularly in tropical, sub-tropical regions and the regions with lower socio-economic level.

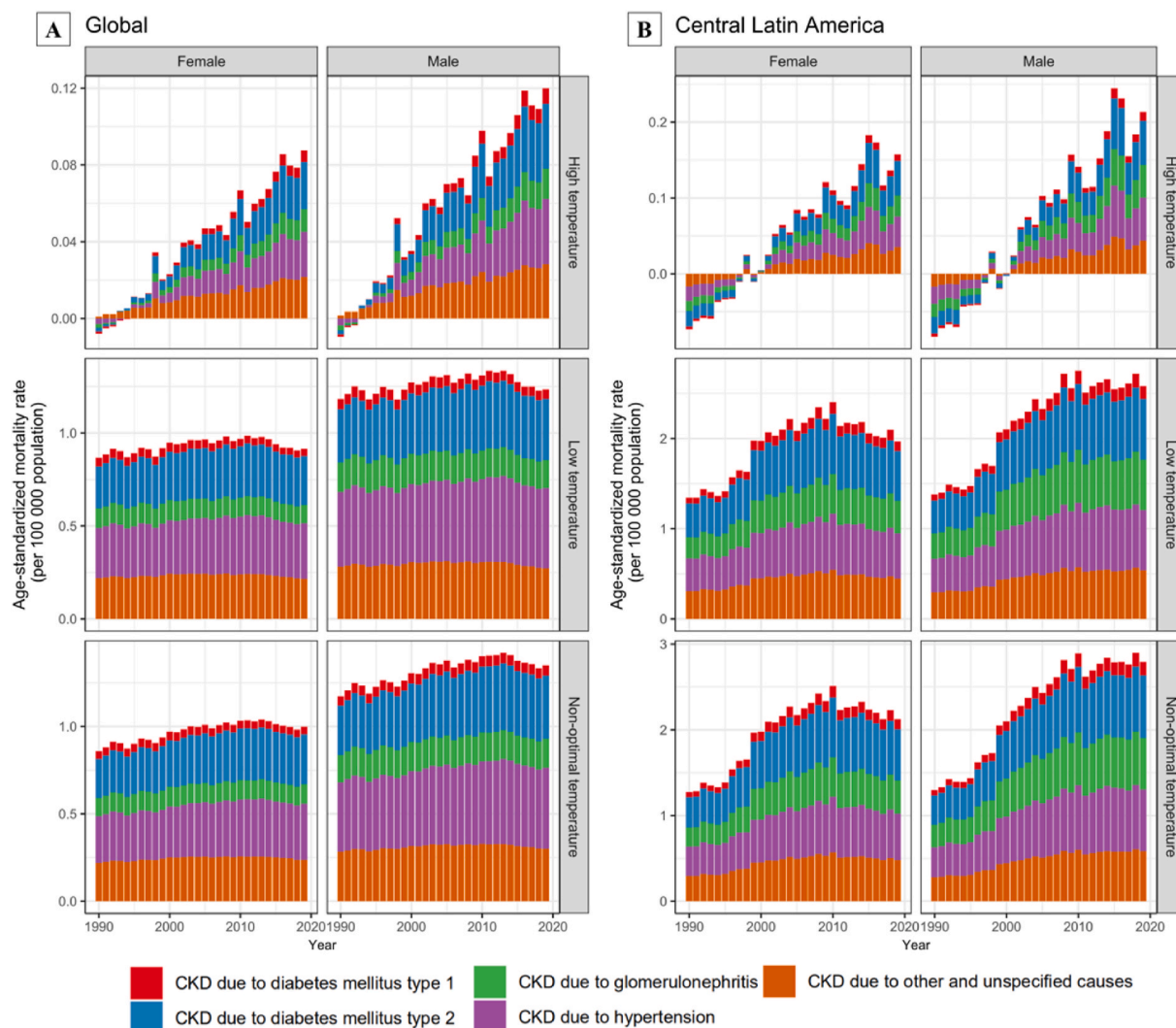


Fig. 4. Temporal trends in age-standardized mortality (per 100 000 Population) for CKD attributable to high, low, and non-optimum temperatures by etiology in Global (A) and Central Latin America (B), 1990–2019. CKD, chronic kidney disease.

Prior research had generally found a significantly higher burden of disease and death attributable to low temperature than high temperature. For instance, the GBD 2019 study of non-optimum temperatures exposure and the risk burden of all-cause mortality also showed that the average cold-cause mortality exceeded the heat-cause mortality in 2019 (Burkart et al., 2021). In addition, the Centers for Disease Control and Prevention (CDC) of the United States had reported increased cases of death from kidney failure due to hypothermia (CDC, 2005). Although the study found that high temperature led to an increase in CKD symptoms, this did not mean that high temperature caused CKD, and only suggested that high temperature could have an adversary impact on kidney function. Consistent with these results, we also found that the CKD death burden attributed to low temperature was higher than the burden attributed to high temperature. Usually, the duration of cold waves is greater than that of waves of high temperature (i.e., heat waves) (Guo et al., 2014). A national study reported that low temperature exposure was significantly higher than high temperature exposure (Ai et al., 2021). Although the global temperature has increased by about 0.7 °C over the 20th century and the global average surface temperature is currently increasing at a rate of 0.18 °C per decade (State of the Climate, 2021; Samset et al., 2020). The overall rise of ambient temperature is not particularly large. Since the CKD ASMR and ASDR due to high temperature is relatively low at beginning, and the average annual temperature increases slowly, the magnitude of change in CKD

burden due to high temperature is relatively small. Therefore, the CKD death burden associated with high temperature is still lower than low temperature.

However, the overall trend of global warming is likely to continue and become much worse in the recent climate forecasting report (Samset et al., 2020). So the current focus of people is more greatly placed on the health risks from high temperature (Cui et al., 2016). A study in Taiwan, China, found that higher temperature demonstrated a more severe effect on hospitalization for kidney disease (Lin et al., 2013). A study in New York also observed an association between high ambient summer temperature and acute kidney failure (Fletcher et al., 2012). Similar to the results found in the Australian for the CKD effects of heat waves (Hansen et al., 2008) and the CKD death of longer heat duration in Mediterranean cities (D'Ippoliti et al., 2010). Consistently, we also found a significant relationship between CKD death burden and high temperature, and there was a significant rise in CKD ASMR and ASDR attributable to high temperature from 1990 to 2019. We found an increase in ASMR but a decrease in ASDR due to low temperature from 1990 to 2019, indicating a shift to mortality due to CKD occurring at an older age. Possible reasons for this may be an aging population and that the elderly are more susceptible to cold stress due to lowered immunity and multiple chronic diseases (Liu et al., 2020; Flynn et al., 2005). Although the increase in renal replacement therapy with advances in healthcare will prolong CKD survival (Van Dijk et al., 2005; Heaf, 2017), previous studies have

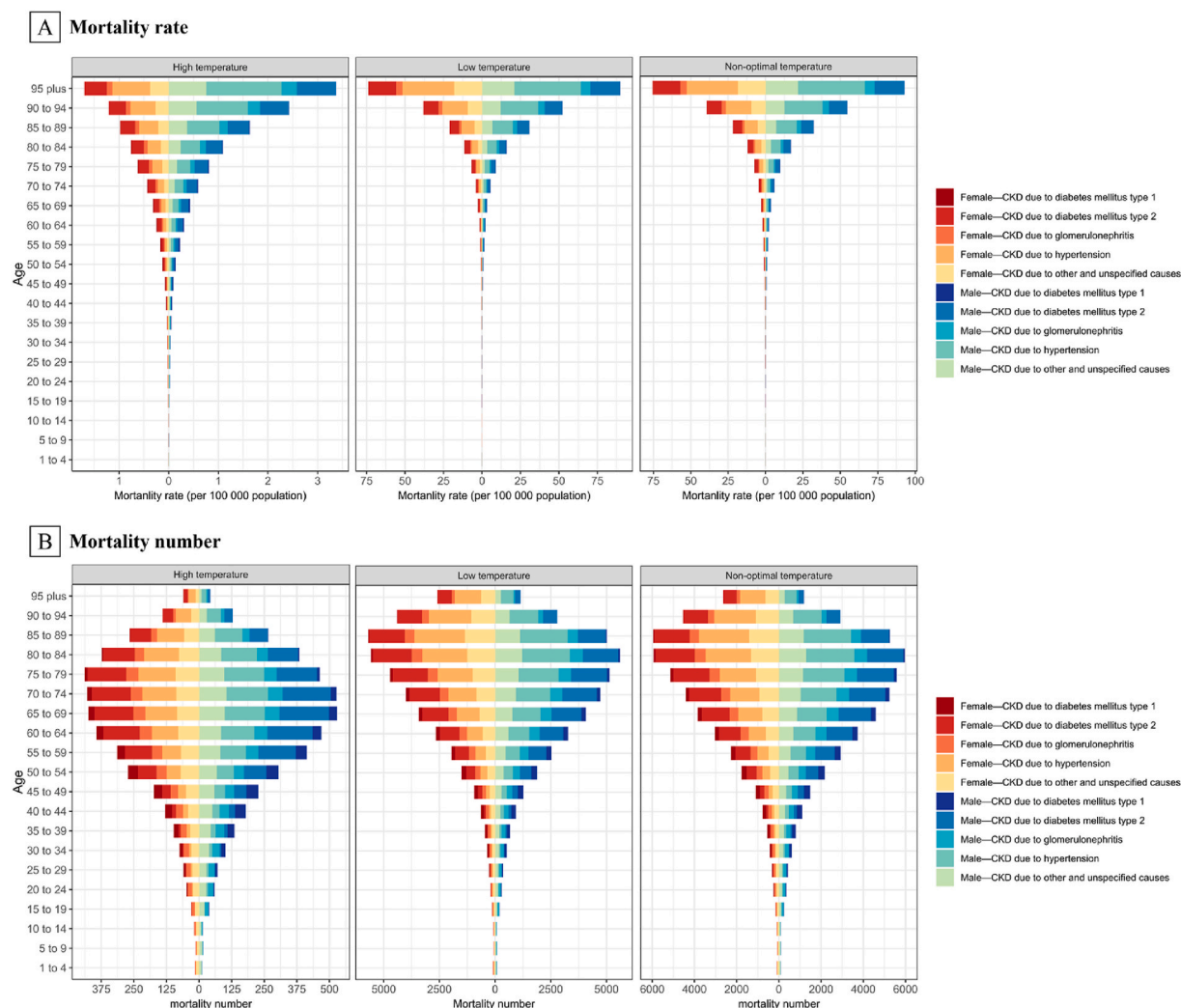


Fig. 5. Rate (A) and number (B) of global mortality for CKD due to high, low, and non-optimum temperatures by sex, age groups and etiology in 2019. CKD, chronic kidney disease.

shown significant disparities in access to renal replacement therapy in different parts of the world (Bello et al., 2017). Due to the high cost of renal replacement therapy, access to adequate CKD care and treatment remains inadequate for countries with lower levels of development resulting in higher mortality rates (Navaneethan et al., 2008). From 1990 to 2017, the global burden of CKD similarly found that the decline in CKD ASDR was not accompanied by a corresponding decline in CKD ASMR (Bikbov et al., 2020). Therefore, concerning the stable trend of CKD death attributed to low temperature during the past 30 years, more attention requires placed on the effect of high temperature under unavoidable global warming.

Previous studies have found strong geographical and inter-country variation in the relationship between temperature and diseases, as there are large differences in temperature in different longitude and latitude (Burkart et al., 2021). Based on this knowledge, we also found there was a significant rise trend of CKD death burden associated with high temperature since 1990 in the tropical and subtropical regions, while the CKD burden attributable to low temperature decreased slightly. Since the heat waves may occur more frequently and last longer in regions with a warmer climate and higher temperature (Stott, 2016), the future global climate warming may aggravate the adversary effect of high temperature on health. This may explain why the CKD burden attributable to high temperature has increased significantly in tropical and subtropical regions. In contrast, the rise in CKD burden attributed to

high temperature was not significant in temperate regions, probably because the rise in overall temperature has not yet been able to significantly increase hot weather in temperate regions (Samset et al., 2020; de Lorenzo and Liaño, 2017). Interestingly, the majority of the global tropical and subtropical regions are developing and underdeveloped countries (Li et al., 2015), namely in low and low-middle SDI regions, where we found raised CKD burden associated with high temperature. Therefore, the lower levels of economic development made a larger proportion of the population engaged in agriculture and outdoor work, who may be exposed to heat for longer periods and lead to severe CKD disease. Meanwhile, regions with a lower level of development may also own a lower level of infrastructure (air conditioning), health services, and health literacy of the population, which can make the people in these regions more vulnerable to high temperature (de Lorenzo and Liaño, 2017; Ormandy and Ezratty, 2015). Conversely, the ASMR attributable to low temperature decreased in low SDI region, because most countries with low SDI were in low latitude regions, which have lower levels of low temperature exposure. The frequent occurrence of extreme weather due to global climate change (Stott, 2016) might be a possible reason for the increased burden of low temperature in high SDI region.

Poor housing condition has long been linked to population exposure to indoor environmental hazards induced by climatic condition, such as high temperature. In France, vulnerable individuals living in a top-floor

apartment that is inadequately protected were found higher risk of heat-related mortality (Vandentorren et al., 2006). And in Chicago, living in buildings with fewer rooms and with flat roofs were found linked to heart-disease risk (Chan et al., 2001). As climate change exacerbates the heat exposure to the vulnerable population who live in a house without air condition compounded with poor insulation, that can consequently increase the temperature-related health risk, such as CKD.

In addition, we found there were apparent age and gender differences in CKD burden attributable to non-optimum temperatures, which was higher in men and older individuals regardless of heat or cold temperature. In Australia, elderly people were also found to be at high risk of kidney disease admissions during heat waves (Hansen et al., 2008). The Assessment and Prevention of Acute Health Effects of Weather Conditions in Europe (PHEWE) project also observed higher mortality associated with low temperature in the elderly of European countries (Analitis et al., 2008). This is because kidney function declines with age (Wang et al., 2014), and the older age is an important risk factor for CKD (Kazancioglu, 2013). In addition, the elderly are more susceptible to heat and cold stress due to lowered immunity and multiple chronic diseases (Flynn et al., 2005). Men are generally more engaged in outdoor activities and physical labor in high or low temperature environments, which may induce a more significant burden to the kidney by dehydration or glomerular enrichment and cause or aggravate clinical kidney disease. However, debates also exist among results like higher kidney risk of heat waves on women (Lu et al., 2021), and more particularly significant burden of CKD from heat in people aged 40–64 years (Lin et al., 2021). Since the GBD data are estimated and based on the cross-sectional design, the cause and effect of CKD due to non-optimum temperature in different age and gender may need more prospective studies to confirm.

In different CKD classifications, we found the highest proportion of CKD attributable to high and low temperatures were hypertensive and diabetes mellitus. It is well known that hypertension and diabetes are important risk factors for CKD (Kazancioglu, 2013), which are also sensitive diseases to high or low temperature exposures (Yang et al., 2016; Park et al., 2020). What's more, glomerulonephritis and unknown causes are also among the important subtypes of CKD caused by non-optimum temperatures. Particularly in Central America, the proportion of CKD ASMR attributable to high or low temperature CKD due to glomerulonephritis and unexplained nephritis is almost as high as that due to traditional factors such as diabetes and hypertension. Studies have found that this unknown kidney disease (also called “CKD of nontraditional origin” or “MesoAmerican nephropathy”) in Central America has been widely prevalent among agricultural workers, construction workers, and mine workers since the last century (Johnson et al., 2019; Wijkstrom et al., 2013; Wesseling et al., 2016), especially in adult males (Gonzalez-Quiroz and Silverwood, 2018). Meanwhile, similar unexplained kidney diseases have been found in several tropical regions, including India and Africa (Glaser et al., 2016). These areas are generally less developed, the agriculture and mine industries are their predominantly economic income sources, which may engage a large number of young laborers exposed to continuous heat exposure. These factors together may lead to the high CKD burden associated with high temperature (Johnson et al., 2019; Glaser et al., 2016), which may also explain the rapid increase over the past 30 years in hotter climate regions with lower SDI indices, particularly among the younger population under the condition of climate warming.

This study has some limitations. Firstly, the GBD 2019 estimated CKD burden indicator attributable to high, low, and non-optimum temperatures was only an estimate, and temperature effects were defined as short-term effects that occur on the day of exposure, so there may be limitations in underestimating the burden of associated with high, low and non-optimum temperatures (Burkart et al., 2021). Secondly, because the lack of relevant global aggregate data prevents us from explicitly interpreting infrastructure, behavior, or other population-specific characteristics, we may have underestimated the

CKD burden attributable to non-optimum temperatures. Third, there is misclassification in some countries due to the lack of detailed meteorological and CKD data. Fourth, we could not consider the effects of air conditioning and heating use on CKD mortality due to the lack of comprehensive national data, so the effects of high and low temperatures on CKD may be underestimated. Therefore, prospective studies in different regions of countries and animal experiments are necessary for further assessing the impact of non-optimum temperatures on CKD.

5. Conclusions

There are significant association of global CKD death and high, low, and non-optimum temperatures, but varies considerably by regions and countries. There is an robust increase trend of the global CKD death burden attributable to high temperature from 1990 to 2019, the global CKD death burden attributable to high temperature increased significantly, particularly in tropical and subtropical regions and in low and low-middle SDI regions. Our results call on more attentions and taking suitable adaptive strategies against the global climate particularly in these countries.

Authors' contributions

Li He & Baode Xue: Methodology, Visualization, Writing – original draft. **Bo Wang:** Conceptualization, Methodology, Data curation. **Ce Liu:** Conceptualization, Methodology, Data curation. **David Gimeno Ruiz de Porras:** Data curation, Supervision. **George L. Delclos:** Data curation, Supervision. **Ming Hu:** Data curation, Supervision. **Bin Luo:** Conceptualization, Supervision, Project administration, Writing – review & editing. **Kai Zhang:** Conceptualization, Supervision, Writing – review & editing.

Ethics approval and consent to participate

Not applicable.

Availability of data and materials

All data are available from open-access websites at <http://ghdx.healthdata.org/gbd-results-tool> and <https://www.uea.ac.uk/web/groups-and-centres/climatic-research-unit>.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2022.113172>.

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