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Contemporary understanding of the risk factors for chronic kidney disease in cold area

Xinrui Wei, Yongchen Wang*

Abstract

The management of chronic kidney disease (CKD) patients in cold areas is an important task in the daily practice of primary medical and health institutions. An important way to reduce the burden of CKD is to achieve early identification of and implement timely intervention on the relevant risk factors. Studies have shown that diet, alcohol, tobacco, air, sedentary and other factors in cold areas have negative impacts on human kidneys; yet, our current understanding of the effect of cold stimulation on CKD remains blurry. This paper introduces the research progress of risk factors related to CKD in cold areas and analytically summarizes the pathogenesis of CKD caused by cold stimulation, aiming to provide a reference work for the prevention, screening, evaluation, and management of CKD in cold areas.

Keywords

chronic kidney disease; cold areas; eating habits; lifestyle; cold stimulation

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The Second Affiliated Hospital of Harbin Medical University, Harbin 150086, China

**Corresponding author Yongchen Wang, E-mail: yongchenwang@163.com*

Chronic kidney disease (CKD), characterized by decreased glomerular filtration function (< 60 mL/min/1.73 m^2) and increased proteinuria excretion (≥ 30 mg/24h), has been increasing worldwide in recent years. From 1990 to 2017, the full-age prevalence rate of CKD increased by 29.3% and the case fatality rate increased by 41.5%, according to the Global Burden of Disease Chronic Kidney Disease Association in 2020[1]. The cost of renal replacement therapy (RRT) (that is, dialysis or kidney transplantation) for end-stage kidney disease (ESKD) is high, placing a great burden on patients, families, and countries[2]. The occurrence of CKD is related to many factors, including irreversible factors such as age and gene and reversible factors like eating habits, lifestyle, living environment and so on. Investigations show that cold environment is one of the independent risk factors that increase the morbidity and mortality of chronic diseases[3]. Similarly, cold areas have a profound impact on the epidemiology of CKD because of some unique human and environmental factors.

1 The general situation of CKD patients in China

CKD census data analyzed by Wang *et al.* demonstrated that the prevalence rate of CKD in China was about 11.6% as of 2010[4]. With the development of China Renal Network (CKNET), the studies on the characteristics and trends of CKD have been further extended and deepened in recent years. According to CK-NET data, 1.2 million people die of CKD each year globally, with China accounting for 170 000 deaths. In 2016, CKD patients accounted for 4.86% of all inpatients. The average hospitalization days of CKD patients was 20.33 days, which was higher than the median hospitalization days of 13 days for other non-communicable chronic diseases[5]. The average cost for hospitalization for CKD is about 15 405 Chinese yuan per patient, which is higher than that of other non-communicable chronic diseases. At present, China's medical insurance policy covers part of the cost of RRT treatment. It is estimated that after five years, the expenditure on CKD treatment will be 1.3 times of the government health expenditure in 2015[6]. It requires not only the unremitting efforts of the government and specialists, but also the joint participation of general practitioners and the general public to deal with this enormous challenge[7].

2 The relationship between cold areas and diseases

The 2019 Global burden of Disease report lists hypothermia as one of the top ten risk factors for death in old age[8]. The cold area of China is vast, and the regions are divided according to different standards such as temperature, building, hydrology and so on. The recent analysis on the global environmental

hypothermia and non-communicable disease burden points out that in addition to ischemic heart disease, which is the main concern of cold stress-induced health issues, we should pay more attention to CKD—the only disease whose changes in disability-adjusted life years and mortality caused by low temperature have not been effectively controlled between 1990 and 2019[9]. Interestingly, South Africa, as a typical tropical region, has a high incidence rate of CKD being ranked top 10 in this area[10], because South Africa has a high incidence rate of infectious diseases, of which up to 22 million people have HIV[11]. Studies have shown that infectious diseases such as HIV and schistosomiasis can eventually lead to CKD[12]. The incidence of CKD in Thailand as a typical tropical country is about the 20th[13]. Clearly, the relationship between low temperature and CKD is nonignorable. Take a look at China, whose cold area is vast, and the area is divided according to different standards such as temperature, building, hydrology and so on. On the basis of referring to international and domestic early standards, the Institute of Cold Regions of the Chinese Academy of Sciences has determined that the area of cold areas in China is about 417.4 × 10^4 km^2, accounting for 43.5% of China's land area, including most areas of Heilongjiang Province, Jilin Province, Liaoning Province and Inner Mongolia Autonomous region, as well as some mountainous areas of Gansu Province, Shanxi Province, Shaanxi Province, Xinjiang Province, Tibet Province and Yunnan Province[14]. According to the cross-sectional study of CKD epidemic in China, northeast and southwest regions (including most of the cold areas mentioned above) have the highest incidence of CKD[15].

Low temperature is also closely related to the aggravation and death of many common chronic non-communicable diseases, such as chronic obstructive pulmonary disease[16], coronary heart disease[17], diabetes[18], stroke and so on. Recently, a study conducted in Thailand connected the occurrence of joint and muscle pain related to with cold storage operations[19]. A few studies by Patten and other researchers revealed that the increase, the incidence of depression increases significantly with elevation of latitude[20]. In addition to low temperature, the risk factors caused by long-term cold can also lead to disease, due to the diversity of economy, culture, and medical treatment in different regions of China, the risk factor analysis presented in this article aimed at the representative cold areas in China (most of Heilongjiang Province, Jilin Province, Liaoning Province and Inner Mongolia Autonomous region).

3 Dietary habits and CKD in cold areas

China has a vast territory and a long history of civilization. Since as early as in the Spring and Autumn and Warring States period, there have been dietary differences between the south and the north. Unlike the south regions that have rich natural resources, warmer climate, and less harsh environmental impact, cold regions have short summers, long winters, and slow plant growth. In order to resist the severe cold, residents intake more oil, salt and protein. In order to cope with the shortage of fresh fruits and vegetables in winter, northern residents consume more pickled foods. Moreover, partly due less outdoor activities, the tobacco and alcohol cultures prevail[21]. Wang *et al.* used China Dietary balance Index-07, based on the dietary guidelines for Chinese residents, to analyze the dietary memories of more than 1 800 residents in cold areas for 3 consecutive days and summarize the characteristics of the traditional northern diet model. One the on hand, the traditional northern diet is characterized by overly higher intake of staple food, pickles, meat, and total fat and sodium than recommended. On the other hand, the intake of vegetables and fruits is inadequate[22]. The long history of such a stereotyped eating habits has blunted the northern residents' health cognition and awareness of diet patterns.

3.1 High-fat diet and CKD

It is well known that high-fat diet (HFD) can lead to hyperlipidemia, obesity, hypertension, insulin resistance (IR), kidney damage and other diseases. A cohort study showed that fat intake was positively correlated with the risk of obesity[23], and another study exhibited that obesity was associated with elevated triglycerides and cholesterol[24]. Saravanan *et al.* conducted an experimental study in C57BL/6J mice and confirmed the relationship between HFD and lipid metabolism disorders and IR[25]. A large-scale survey in northern China uncovered that the age-standardized prevalence rate of dyslipidemia among local residents was 31.2%, mostly characterized by elevated triglycerides (TG) and low high-density lipoprotein cholesterol (HDL-C)[26]. A report claimed that 1/3 of Russians suffer from hypertriglyceridemia[27]. Evidently, the health conditions caused by HFD in cold areas are an important issue in both fundamental research and clinical practice. A few well-accepted hypotheses on the mechanisms underlying the relationship between HFD and CKD are introduced below.

3.1.1 Lipid toxicity Theory

The theory of lipotoxicity, put forward by Moorhead *et al.* in 1982, holds that CKD is caused by abnormal lipid metabolism. Specifically, lipid accumulation damages glomerular basement membrane to increase the membrane permeability, rendering a loss of lipids and proteins through urine, thereby causing over synthesis of lipoproteins in the liver. Lipoproteins interact with lipuria and proteinuria and cause

mesangial cell proliferation and destruction and basement membrane thickening, leading to glomerulosclerosis[28]. A modified more comprehensive lipotoxicity theory suggests that HFD promotes oxidative stress, endoplasmic reticulum stress and inflammatory stress, eventually leading to renal atherosclerosis and chronic renal fibrosis[29].

3.1.2 Renin-Angiotensin System

Lipids produce almost all components of the renin-angiotensin system (RAS) (renin, angiotensinogen, angiotensin, angiotensin converting enzyme, *etc.*)[30]. Renal hypertension is the basis of CKD induced by HFD, which is partly due to visceral fat thickening and increased intra-abdominal pressure against the renal hilum and partly due to the activation of RAS. RAS activation participates in the reabsorption of NA^+, increases the extracellular fluid volume, promotes renal vasoconstriction, and increases renal artery pressure leading to glomerulosclerosis. In addition, angiotensin II (Ang-II), the most active component of RAS, participates in collagen and fibrin synthesis and promotes the fibrogenesis induced by transforming growth factor β (TGF- β)[31-32].

3.1.3 IR

Adipocytes can increase insulin secretion, and IR caused by inflammation or oxidative stress accelerates the progression from diabetes to diabetic nephropathy and promotes podocyte loss and proteinuria caused by impaired podocyte autophagy[33].

3.1.4 Others

A study demonstrated that following the calorie control in four patients with severe obesity, their albuminuria was significantly improved[34], suggesting that limiting HFD could effectively protect the kidney. According to the pathogenesis of HFD, application of RAS inhibitors, SGLT-2 inhibitors, or immunosuppressants could be beneficial to the control of CKD disease[35-37]. Recently, a cleavage activated protein (SCAP) degrader has been found to improve HFD-associated obesity, hyperlipidemia, and IR through the autophagy-independent lysosome pathway[38]. HFD is also associated with endocytosis mediated by a glycoprotein in the LDL receptor family. The mechanism for the detrimental actions of HFD involves hypertrophic and aging injury of proximal renal tubular endothelial cells with autophagy, injury of peri-tubular capillaries and glomerular degeneration, increases in fibrogenic and inflammatory mediators (PDGF-B and MCP-1)[39]. In contrast, inhibition of giant protein function can delay renal injury[39]. Transmembrane protein 126 (Tmem126b) is a type I assembly factor of mitochondria, which participates in HFD-induced renal injuries in terms of lipid accumulation, apoptosis and mitochondrial dysfunction[40]. Tmem126b inhibitors can activate the NRF-2 pathway and prevent the production of reactive oxygen species (ROS) to protect the kidney. These findings may provide new strategies for the prevention and control of HFD-related renal injury.

3.2 High-salt diet and CKD

According to the 2012 WTO guidelines, the daily salt intake of adults should be less than 5 g[41]; Salt intake in South African countries is generally in line with this standard[42]. However, in cold regions such as Norway and Finland, salt intake was as high as 10.2 ± 4 g/day for men and 7.4 ± 2.7 g/day for women[43]. A study on immigrants from Somalia to Norway showed that due to the influence of local dietary culture, daily salt intake by male immigrant increased to as much as 8.66 g[44]. Similarly, in the past 40 years, the daily salt intake of northern Chinese residents has reached 11.2 g[45].

Studies have shown that daytime cold exposure is significantly associated with higher salt intake[46]. Liedtke *et al.* found that people's appetite for sodium is related to the regulation of DARPP-32, dopamine receptors and STEP in the lateral hypothalamus, which is also involved in the expression of addiction genes (cocaine, opioids, *etc.*)[47]. There has been increasing awareness of the threat of excessive salt intake to health. An average of 4.3-years follow-up of 1 254 patients with stage CKD3-5 in Korea revealed that high salt led to the development of complex kidney disease in 38.7% of the patients enrolled in their study[48].

3.2.1 Renin-Angiotensin-Aldosterone System

Salt sensitivity, defined as salt-induced increase in mean arterial blood pressure (10mmHg)[49], is generally higher in CKD patients. The feedback inhibition of renin-angiotensin-aldosterone system (RAAS) in normal people after salt intake is different from that in salt-sensitive people. This phenomenon was first discovered by Parfrey[50]. Cao *et al.* found that blocking RAS can significantly reduce salt-induced renal macrophage infiltration and glomerular sclerosis index and improve tubulointerstitial fibrosis[51]. The novel findings of their study are that injection of AT1 inhibitors and central sympathetic blockers or blocking renal afferent nerves can reduce high salt-induced renal fibrosis, confirming that high salt promotes renal injury and activation of kidney-brain reflex, rather than the systematic renin angiotensin axis[51]. In addition, aldosterone also plays an important role in salt-sensitive hypertension and renal injury[52]. Therefore, RAAS activation is regarded as the basis of CKD induced by high salt.

3.2.2 Antidiuretic hormone

The increase of osmotic pressure of extracellular fluid induced by high salt promotes the production of antidiuretic hormone (ADH). ADH acts through V2 receptor, controlling renal collecting duct aquaporin 2 to activate the AMP/PKA pathway and participate in the establishment of osmotic gradient, thereby increasing water reabsorption, Na^+ retention, and extracellular fluid volume[53]. Increased volume can stimulate the dense macula, dilate the glomerular afferent arterioles, and activate RAS to cause contraction of the glomerular arterioles, leading to over-filtering of the glomeruli. Studies have shown that reducing salt intake can reduce ADH production[54], and ADH overproduction is directly associated with poor prognosis of CKD[55].

3.2.3 Oxidative stress and endothelial dysfunction

Kitiyakara *et al.* found that the high salt-induced increase in the expression of reduced coenzyme (NADPH) oxidase stimulated superoxide anion production and reduced superoxide dismutase, resulting in oxidative stress[56]. Oxidative stress not only weakens the vasodilating effect of NO and promotes renal vascular fibrosis, but also reduces the inhibitory effect of NO on PGF- β 1. High salt can promote PGF-β1 production in vascular endothelial cells, and the imbalance between them leads to endothelial dysfunction and accelerates the process of CKD[57].

3.2.4 Other

A large-scale experimental study in the Netherlands showed that when salt intake was lower than 6 g/d, CKD was decreased by 1.1% and albuminuria was improved[58]. However, other studies also showed that when salt intake is decreased to 3.8 g, renin, aldosterone, and triglyceride are significantly increased, even with increased mortality[59]. Therefore, excessively limiting salt intake does more harm than good. Future research on salt and CKD is needed to define the optimal range of salt intake and to set salt restriction guidelines for special kidney disease groups such as fatty nephropathy.

3.3 Diet with high protein and few fresh fruits and vegetables

3.3.1 High protein intake and CKD

WTO recommends that the protein intake of normal adults should be 0.83 g/kg/d[60] and more than 1.2 g/kg/d should be regarded as a high-protein diet (HPD). In a few cohort studies on the relationship between HPD and CKD, some researchers believe that HPD affects glomerular filtration rate (GFR) to aggravate CKD; however, controversies exist[61-63]. It appears that in the early stage of HPD, the increase of GFR might be a positive feedback mechanism for extruding excessive proteins in the kidney, which promotes the excretion of a large amount of waste beyond the nitrogen balance, in the cost of damaging the glomerular function. In contrast, after long-term HFD, the renal function reserve of CKD patients is mitigated, rendering a severe drop of GFR to the initial level or even lower. Of note, the source of protein has a greater impact on CKD than the amount of protein. One study reported by Chinese Singaporeans showed a strong dose-dependent relationship between red meat intake and the risk of ESKD[64] and another prospective study found that higher red meat intake was associated with an increased risk of CKD, even in people with normal kidney function[65].

3.3.2 Long-term high intake of red meat and CKD

The mechanisms of actions of long-term excessive red meat intake on CKD are not yet clear. Nonetheless, there have been several views on the issue. (1) Excessive red meat intake can result in obesity, hyperlipidemia, and renal enlargement, which are pathologically characterized by glomerular and tubular cell hyperplasia and hypertrophy. (2) Excessive red meat intake can also increase intestinal uremic toxins (TMAO, IAA, *etc.*)[66], and the increase of TMAO is related to the increase of CKD mortality[67], and uremic toxins can cause intestinal flora imbalance and promote inflammation and oxidative stress. (3) Moreover, excessive red meat intake can increase protein formylation, promoting ROS production, oxidative stress, endothelial dysfunction, *etc.*[68]. (4) Furthermore, excessive red meat intake can activate the inflammatory NF-κB pathway. (5) Additionally, excessive red meat intake can cause high acid load that can in turn damage renal function, which might be related to renal tubulointerstitial fibrosis caused by renin-angiotensin or complement replacement system activation by high ammonia concentration[69]. (6) Finally, excessive red meat intake can also increase phosphorus intake to enhance fibroblast growth factor 23 (FGF-23) which is regarded as a new risk factor for CKD and cardiovascular disease[70].

3.3.3 Plant protein, fruits and vegetables and CKD

Plant protein can reduce cholesterol, urine protein, and glomerular damage and delay the progress of CKD. CKD develops in rats fed with casein 160 days. The contents of endothelial NOS (eNOS) and caveolin-1 increase and NO decrease. Soy protein can relieve the inhibitory effect of caveolin on eNOS activity and promote the recovery of NO[71]. In addition, the antioxidant effect of estrogen in soybean and the direct

vasodilation effect of arginine are beneficial to CKD. Therefore, plant protein represented by soy protein is recommended as a substitute for some animal proteins.

As early as the 1950s, it was found that K^+ can reduce blood pressure and protect renal function[72]. A very low-protein diet rich in fruits and vegetables supplemented with amino acid analogues, can significantly reduce the renal acid load[73]. Goraya *et al.* found that for CKD patients with plasma total carbon dioxide > 22 mmol/L, the therapeutic effect of diet rich in fruit and vegetable and minimal net acid was as effective as oral alkaline drugs[74]. Surprisingly, a recent randomized controlled trial involving 9 229 participants with normal renal function in South Korea showed that eating low acid-producing vegetables also helped to prevent the occurrence of CKD in the general population[75].

3.3.4 Dietary recommendations and others

A healthy diet, which is rich in fruits, vegetables, fish, whole grains, fiber and polyunsaturated fatty acids with limited red meat and salt, benefits patients with CKD[76], and a very low-protein diet supplemented with amino acids and ketoacids is recommended as the intensive care diet for patients with CKD[77].

However, for elderly patients and dialysis patients, more protein may be needed due to insufficient energy synthesis or increased pathological energy consumption. For such patients, well-intentioned low-protein diet recommendations for CKD patients by physicians can cause muscular dystrophy, malnutrition, decreased resistance, and cachexia and can even increase mortality. Therefore, precautions should be taken when recommending dietary guidance for this group of patients. In addition, red meat is an important source of amino acids, iron, zinc, and other trace elements, whether CKD patients should abandon this protein source is still open to question. Future research may be orientated to the following directions: (1) the exact mechanism of the effect of high-protein diet on renal function; (2) to control the exact ratio of different nutrients to determine their relationship with CKD; and (3) to set the dietary guidance for special patient groups.

4 Cold stimulation and CKD

Temperature can affect the occurrence and development of CKD. Sasai *et al.* reported that extreme high temperature could cause electrolyte disturbance, acutely aggravate CKD induced by renal dehydration, and increase hospitalization and mortality[78]. However, the latest decade-long global analysis shows that extreme cold can also increase age-standardized mortality of CKD patients[79]. When the kidneys of the rats were exposed to cold (4°C) for 12 hours, they became enlarged and developed focal necrosis, and the renal tubular epithelial cells also became degenerated and necrotic[80]. The cold stimulation-related renal injury has been confirmed by the animal experiment. To date, there have been only few studies on cold stimulation and CKD. The following subsections provide a succinct summary of published studies on the association of cold stimulation with CKD.

4.1 SNS and RAS activation

As early as 1975, Lovallo found that immersing hands or feet in a cold bath activated the sympathetic nervous system (SNS) through skin pain receptors and thermoreceptors[81]. Activating SNS contract peripheral blood vessels, increase cardiac blood volume, reduce heat dissipation, and protect important organs. First, SNS can promote the activation of RAS and increase the blood pressure. In addition, the activation of SNS can also decrease circulating leptin and obesity, while salt-sensitive hypertension in obese people is related to the synergistic effect of SNS and RAS[82]. More importantly, when SNS is dominant, heart rate increases and heart rate variability (HRV) decreases[83]. Experiments have shown that people with elevated resting heart rate are prone to early renal injury[84], and low HRV is an important indication for patients with end-stage CKD[85].

4.2 Brown adipose tissue and FGF-21

Published studies documented that brown adipose tissue (BAT) markers increase significantly in Siberian adults after cold exposure[86], and BAT is associated with increased levels of fibroblast growth factor 21 (FGF21)[87]. During acute cold exposure, liver-derived FGF21 increases to maintain core body temperature, which serves as a key signal to stimulate BAT. BAT is not only the main source of non-trembling heat production in mammals but is also a secretory organ to secrete FGF21[88-90]. On the one hand, FGF21 promotes browning of white fat and participates in cold acclimation with or without the UCP1 pathway[91]. On the other hand, FGF21 increases the deterioration of renal function, which is related to the development of inflammation, complications, and mortality in patients with CKD[92]. As the causal relationship between FGF21 and CKD is not clear, its potential value as a biological indicator of CKD is still being explored[93].

4.3 Inflammatory cell proliferation and mitochondrial damage

The pathogens causing upper respiratory tract infection (such as streptococcus, respiratory syncytial virus, *etc.*) are stable at low temperature and readily spread in the form of aerosols[94-95].

Upper respiratory tract infection is considered to be the cause of glomerulonephritis[96] and a risk factor for the aggravation of CKD. In addition the inflammatory cells in bronchoalveolar lavage fluid and lung tissue of mice exposed to 4°C for 8 hours for 14 days were found to be increased by about twice as much, indicating that cold stimulation could induce inflammatory response and promote endothelial injury[97]. It is also believed that hypothermia suppresses immune function through the regulation of inflammatory cells, and the longer the hypothermia time is, the stronger the immunosuppression is[98]. In addition, the delayed production of proinflammatory cytokines after the recovery of acute cold stress can also cause body damage[99].

Hypothermia can inhibit Na^+-K^+-ATP enzyme, leading to an imbalance of intracellular Na^+ and K^+ and triggering Ca^+ gated channel[100]. Short-term increase of Ca^+ affects the production of free radicals in mitochondrial respiratory frequency, while long-term increase of Ca^+ leads to mitochondrial swelling, rupture and activation of the apoptotic pathway[101]. The recovery of temperature after cold stimulation can also lead to mitochondrial mutation and oxidative stress[102], which may be one of the mechanisms for kidney injury caused by indoor and outdoor temperature difference in cold areas.

4.4 Vitamin D deficiency and platelet activation

The body can obtain vitamin D (V_D) through both ultraviolet and food methods, and the V_D synthesized through the skin induced by ultraviolet light accounts for 80% of the total V_D in human body. Latitude, season, and temperature all affect the ultraviolet rays reaching the surface. As a result, in areas with long winters, most residents suffer from V_D deficiency[103]. V_D not only promotes the absorption of Ca^{2+}, but also protects the kidney. Clinical trials have shown that urinary protein is significantly decreased in patients receiving V_D replacement therapy[104]. V_D can also protect podocytes and inhibit renal NF-κB inflammatory pathway. Therefore, residents in cold areas should be vigilant against V_D deficiency[105-106].

Cold stimulation can also activate platelet hyperresponsiveness and promote the expression of inflammatory factors such as CRP, BL-1, TNF-β and the occurrence of thrombotic complications of CKD[107-108].

5 Others

A meta-analysis of 2 755 719 participants uncovered that lifestyle changes can affect the occurrence and development of CKD[109]. Table 1 lists some recent or representative studies on the impact of cold stress on CKD in the population residing in cold areas, which is of a great value for developing community health management strategies.

6 Discussion

To date, the studies on cold areas and CKD have been mostly limited to short-term cold exposure. Whether the time and intensity of cold exposure and the indoor and outdoor temperature difference caused by advanced heating facilities in cold areas will have other effects on the kidney remains to be further studied. Meanwhile, specific eating habits, lifestyle, and environment in cold areas are related to the occurrence and development of CKD, and the management of chronic diseases is gradually changing from crowd intervention to individualized and refined intervention. Therefore, in order to improve the prevention and management of CKD community, grass-roots medical and health institutions should strengthen the capability of screening CKD risk factors and formulate the intervention programs to provide comprehensive and personalized services for residents in cold areas in the first place. Secondly, through health education activities, residents should be encouraged to conduct self-examination and abandon bad diet and lifestyle. Finally, establishing

Table 1 Some new studies of variable lifestyle and outcome across large populations (>1 000 participants)

Study reference	Location	Type	*n*	Lifestyle	Duration	Conclusion
Lee S[110]	Korea	Observational cohort	1 951	Smoking	5 years	Smoking is potentially harmful to the progress of CKD
Young S J[111]	Korea	Observational cohort	1 883	Alcohol	5 years	Heavy alcohol consumption affects CKD
Yuan H C[112]	China	meta-analysis	514 148	Alcohol	>30 years	Alcohol consumption is protective against CKD
Zhang N H[113]	China	Observational cohort	4 604	Activity	13 years	Activity is associated with lower mortality in CKD
Lukasz K[114]	Korea	retrospective cross-sectional study	3 554	Air pollution	10 years	The effects of air pollution on renal function were
Chang T I[115]	Korea	Observational cohort	7 405 715	Lower income	7 years	lower income levels affect CKD
Tripathy S[116]	America	prospective cohort	3 139	Lower education	20 years	Lower levels of education are associated with higher risk for CKD

CKD, chronic kidney disease.

a surveillance platform for chronic diseases such as CKD in cold areas to provide data for innovative research and management of CKD in cold areas.

Author contribution

Wei X and Wang Y contributed to the conception of the article. Wei X contributed significantly to analysis and manuscript writing. Wang Y is responsible for supervising. All authors read and approved the final manuscript.

Conflicts of interests

Wang Y is an Editorial Board Member of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of this member and his research group.

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