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ORIGINAL ARTICLE

Age and Gender-Related Trajectories of Urine Osmolality in a Large-Scale Population Study: Physiological Mechanisms and Clinical Implications

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SUMMARY

Background: **To delineate the lifelong trajectories of urine osmolality (Uosm), a primary indicator of renal concentrating capacity, and to investigate the influence of age and gender in a large, non-Western population. This study aims to establish population-specific reference data and explore the underlying physiological mechanisms and clinical implications of observed trends.**

Methods: **This cross-sectional study analyzed retrospective data from 128,889 individuals (65,625 males, 63,264 females), aged 20 to 89 years, who underwent routine physical examinations at a single center in Shaoxing, China, between 2019 and 2022. First-morning urine osmolality was estimated using the electrical conductivity method on a Sysmex UF-5000 analyzer. Data were stratified by gender and 10-year age increments. Statistical analyses included independent *t*-tests and one-way ANOVA to compare mean Uosm values across groups.**

Results: **A profound and persistent sexual dimorphism was observed, with males exhibiting significantly higher mean Uosm than females across all age groups ($p < 0.001$). Overall mean Uosm was 657 mOsm/kg H_2O (95% CI: 655 - 659) for males and 598 mOsm/kg H_2O (95% CI: 596 - 600) for females. For both genders, Uosm peaked in the 20 - 30 year age group and demonstrated a progressive, inexorable decline with advancing age. This decline was gradual until age 70, after which it accelerated markedly. The absolute difference in Uosm between males and females was greatest in young adulthood and attenuated significantly in later life, with the narrowest gap observed in the > 70 - 80 year age group.**

Conclusions: **This large-scale study provides the first high-resolution demographic map of renal concentrating capacity in an East Asian population, revealing distinct age- and gender-specific trajectories. The findings confirm a universal pattern of age-related decline in renal function, likely driven by renal senescence and hormonal shifts, and a significant sexual dimorphism attributable to the influence of gender hormones on renal water and solute handling. The data highlight specific vulnerabilities - an endemic risk of suboptimal hydration predisposing to urolithiasis in men and a heightened risk of dehydration in the elderly - underscoring the need for age- and gender-stratified approaches in clinical nephrology, geriatric medicine, and public health.**

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INTRODUCTION

The centrality of renal concentrating capacity in health and disease - the physiological imperative of water homeostasis

Water is not merely a passive solvent but an essential and dynamic nutrient, indispensable for virtually all physiological functions that sustain life. It serves as the primary medium for biochemical reactions, a critical component of thermoregulation through heat dissipation and sweating, and the transport vehicle for delivering nutrients and removing metabolic waste products from cells [1]. The human body maintains a delicate fluid balance, with a daily turnover of 5 - 10% of total body water, necessitating precise and continuous regulation to preserve homeostasis [2].

The urinary system, and specifically the kidneys, function as the master regulator of this intricate balance. Its role transcends simple waste excretion, extending to the sophisticated control of blood volume and pressure, the maintenance of electrolyte concentrations, and the regulation of systemic acid-base status [3]. A cornerstone of this regulatory prowess is the kidney's remarkable ability to modulate urine concentration across a vast range, from a highly dilute state (~ 50 mOsm/kg H_2O) following excessive fluid intake to a highly concentrated state (> 1200 mOsm/kg H_2O) during periods of water restriction. This capacity is fundamentally dependent on the complex three-dimensional architecture of the renal medulla. The countercurrent arrangement of the loops of Henle and vasa recta, coupled with active solute transport in the thick ascending limb, establishes and maintains a powerful corticomedullary osmotic gradient. This gradient provides the driving force for water reabsorption from the collecting ducts, a process finely tuned by hormonal signals [4].

Urine osmolality: the gold-standard biomarker

Urine osmolality (Uosm) represents the definitive quantitative measure of renal concentrating capacity and overall hydration status. It reflects the total concentration of all osmotically active solutes dissolved in the urine, including electrolytes (sodium, potassium, chloride), urea, and glucose. Its measurement is considered the gold standard, offering superior accuracy and diagnostic insight compared to indirect proxies such as urine specific gravity, which can be confounded by the presence of large, non-osmotic particles [5].

The clinical utility of Uosm is extensive, providing a window into the integrated function of the hypothalamic-pituitary-renal axis. Abnormal Uosm values are pivotal in the differential diagnosis of a wide spectrum of pathologies. Elevated Uosm is a hallmark of dehydration, volume depletion, congestive heart failure, and the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Conversely, inappropriately low Uosm is characteristic of conditions such as excessive fluid intake (polydipsia), central or nephrogenic diabetes insipidus, and certain forms of acute tubular necrosis or severe pyelonephritis where the kidney's concentrating ability is impaired. Uosm is, therefore, a dynamic biomarker reflecting the body's moment-to-moment homeostatic response to circulating levels of arginine vasopressin (AVP), also known as antidiuretic hormone (ADH), the principal hormone governing renal water handling [6].

The unavoidable modulators: aging and gender

Two fundamental demographic variables, age and gender, exert a profound and inescapable influence on renal physiology. Aging is a universal process characterized by a progressive decline in the functional reserve of all organ systems, with the kidney being particularly susceptible [7]. This process, termed "renal senescence," involves a constellation of structural and functional alterations, including a gradual loss of nephrons, reduced renal blood flow, and a decline in glomerular filtration rate. While distinct from overt chronic kidney disease (CKD), these age-related changes diminish the kidney's capacity to adapt to physiological stressors, thereby increasing susceptibility to acute kidney injury (AKI) and the development of CKD [7,8].

Gender, as a fundamental biological variable, imparts a significant sexual dimorphism to renal structure, function, and disease susceptibility. Men and women exhibit well-documented differences in baseline renal hemodynamics and are known to have disparate risk profiles and progression rates for major renal pathologies, including CKD and urolithiasis (kidney stones) [9]. These differences strongly implicate the divergent roles of gender hormones - testosterone and estrogen - in modulating renal health and disease throughout the lifespan.

The Knowledge gap and study rationale

While the general influence of age and gender on renal function is well-established, much of the large-scale, population-level data defining these trends for Uosm originates from Western cohorts, particularly the U.S. National Health and Nutrition Examination Survey (NHANES). However, evidence of significant racial and ethnic variations in both renal biomarkers and the prevalence of kidney disease suggests that findings from one population cannot be uncritically extrapolated to others. For instance, studies have consistently shown that individuals of black ancestry have higher mean urine creatinine and osmolality compared to white individuals, even after accounting for factors like fluid intake and socioeconomic status [10].

This highlights a critical knowledge gap regarding the normative distribution of Uosm in other major global populations, such as those in East Asia. To address this gap, the present study leverages a uniquely large dataset (N = 128,889) from a real-world cohort of individuals undergoing routine physical examinations in Shaoxing, China. The primary objective is to construct the first high-resolution, lifelong trajectories of Uosm stratified by age and gender in this demographic. By doing so, this study aims to provide novel, population-specific re-

ference data, validate or challenge globally observed physiological trends in a major non-Western population, and explore the consequent clinical and public health implications for the region and beyond.

MATERIALS AND METHODS

Study design and population

This investigation was conducted as a large-scale, cross-sectional analysis of retrospective data. The study population consisted of individuals aged 20 to 89 years who participated in routine physical examinations at Shaoxing People's Hospital, a major regional medical center in Zhejiang Province, China, between July 2019 and March 2022. From the initial pool of examinees, a final cohort of 128,889 participants with complete urine osmolality data was included for analysis. This cohort comprised 65,625 males and 63,264 females. The study protocol received full approval from the Institutional Ethics Committee of Shaoxing People's Hospital. All procedures were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Data collection and laboratory analysis

Sample collection

All participants were instructed to provide a fresh, first-morning midstream urine sample of approximately 10 mL into a sterile, single-use plastic container. The collection of a first-morning void was specified to obtain a sample reflecting the kidney's maximal concentrating capacity after an overnight period of relative fluid restriction. Female participants were advised to schedule their examination to avoid sample collection during their menstrual period to prevent potential contamination. Samples were transported to the central laboratory for immediate analysis. In cases where immediate processing was not feasible, samples were stored under refrigeration at 2 - 8°C for a maximum duration of 7 days, a condition under which urine osmolality has been shown to remain stable.

Instrumentation and measurement principle

Urine osmolality was determined using a Sysmex UF-5000 Automated Urine Particle Analyzer (Sysmex Corporation, Kobe, Japan).This high-throughput instrument does not measure osmolality directly via colligative properties (freezing point depression) but rather estimates Uosm based on the measurement of urinary electrical conductivity [11]. The analyzer measures the ability of the urine sample to conduct an electrical current, which is primarily determined by the concentration of ionic solutes. This conductivity value is then converted into an osmolality value, expressed in mOsm/kg H_2O, using a proprietary, factory-calibrated algorithm. To ensure the accuracy and reliability of the measurements, the laboratory performed daily quality control checks using manufacturer-provided control materials (UF-CONTROL) and adhered to all calibration and maintenance protocols as specified by the instrument manufacturer and internal standard operating procedures.

Covariates and stratification

For the primary analysis, all participants were stratified by gender (male or female). To investigate the influence of age, both the male and female groups were further categorized into seven 10-year age strata: 20 - 30 years, > 30 - 40 years, > 40 - 50 years, > 50 - 60 years, > 60 - 70 years, > 70 - 80 years, and > 80 years. This stratification allowed for a detailed examination of Uosm trends across the entire adult lifespan.

Statistical analysis

All data processing and statistical analyses were conducted using R software (version 4.0.4; R Foundation for Statistical Computing, Vienna, Austria). The dplyr package was utilized for data manipulation and aggregation, while the ggplot2 package was employed for the creation of graphical visualizations. Continuous variables, specifically urine osmolality, were summarized and are presented as the mean with its corresponding 95% confidence interval (CI) to indicate the precision of the estimate.

Differences in mean Uosm between two independent groups (e.g., the overall comparison between males and females) were assessed using an independent two-sample *t*-test. For comparisons across more than two groups (e.g., the seven age strata within each gender), a one-way analysis of variance (ANOVA) was performed. For all statistical tests, a two-tailed p-value of less than 0.05 was considered the threshold for statistical significance.

This study was reviewed and approved by the Ethics Committee of Shaoxing People’s Hospital, and the ethical approval number is 2025-Scientific Research Project 112-Y-01.

RESULTS

Population-wide patterns of urine osmolality

Baseline characteristics and overall urine osmolality

The study cohort comprised 128,889 individuals who underwent physical examinations, providing a robust sample for analyzing demographic trends in renal function. The population was nearly evenly split by gender, with 65,625 (50.9%) males and 63,264 (49.1%) females. A highly significant difference in overall urine osmolality was observed between the genders. As detailed in Table 1, the mean Uosm for the entire male cohort was 657 mOsm/kg H_2O (95% CI: 655 - 659), which was substantially higher than the mean Uosm of 598 mOsm/kg H_2O (95% CI: 596 - 600) for the female cohort. This represents a mean difference of 59 mOsm/kg H_2O ($p < 0.001$), establishing a strong baseline sexual dimorphism in renal concentrating capacity within this population.

Table 1. Baseline characteristics and overall urine osmolality of the study population.

Characteristics	Overall	Male	Female	p-value
Number of Participants (N)	128,889	65,625	63,264	N/A
Age Range (years)	20 - 89	20 - 89	20 - 89	N/A
Mean Urine Osmolality (mOsm/kg H_2O), mean (95% CI)	N/A	657 (655, 659)	598 (596, 600)	< 0.001

p-value refers to the comparison between male and female groups using an independent *t*-test.

Table 2. Urine osmolality (mOsm/kg H_2O) by gender and age group.

Age group (years)	Male (N)	Male Uosm mean (95% CI)	Female (N)	Female Uosm mean (95% CI)
20 - 30	12,319	707.95 (703, 712)	14,254	634.26 (629, 638)
> 30 - 40	16,768	681.93 (678, 685)	20,101	609.40 (605, 613)
> 40 - 50	13,805	653.64 (649, 657)	14,494	583.73 (579, 588)
> 50 - 60	12,831	633.31 (629, 637)	8,112	573.40 (568, 578)
> 60 - 70	5,635	609.94 (604, 615)	3,913	558.94 (552, 565)
> 70 - 80	3,241	579.28 (572, 586)	1,795	542.46 (533, 551)
> 80	1,026	522.52 (511, 533)	595	469.47 (455, 483)

For male and female, the difference of mean Uosm between all age groups was statistically significant ($p < 0.001$).

Persistent sexual dimorphism in urine osmolality across the lifespan

To determine if the observed overall gender difference was consistent across different life stages, the cohort was stratified by 10-year age groups. The analysis revealed that the higher Uosm in males was not an artifact of population averaging but a persistent physiological trait evident across the entire adult lifespan. As shown in Table 2, within every corresponding age decade from 20 to over 80 years, males demonstrated significantly higher mean Uosm values than their female counterparts. The statistical significance for this inter-gender comparison was robust, with $p < 0.001$ in every age stratum.

The age-related decline in renal concentrating capacity

A clear and statistically significant inverse relationship between advancing age and Uosm was a primary finding for both genders. The data presented in Table 2 and visualized in Figure 1 illustrate a distinct lifelong trajectory. Renal concentrating capacity, as measured by first-morning Uosm, was highest in the youngest adult cohort (20 - 30 years), with mean values of 707.95 mOsm/kg H_2O for males and 634.26 mOsm/kg H_2O for females.

From this peak in young adulthood, Uosm exhibited a progressive and inexorable decline with each successive decade. The rate of this decline was relatively gradual and linear between the ages of 30 and 70. However, a notable inflection point occurred after the age of 70, where the slope of the decline steepened, indicating an accelerated loss of concentrating capacity in the elderly population for both men and women.

The Convergence in later life: age-dependent attenuation of the gender difference

While the sexual dimorphism in Uosm was persistent, the magnitude of this difference was not static across the lifespan. A key feature of the Uosm trajectory, clearly visualized in Figure 1, is the progressive narrowing of the gap between males and females with advancing age. The absolute difference in mean Uosm was at its largest in the youngest age groups, with a difference of approximately 74 mOsm/kg H_2O in the 20 - 30 year cohort. This gap gradually diminished through middle age and into the early elderly years, reaching its minimum point in the > 70 - 80 year age group, where the difference was less than half of that seen in young adults (36.82 mOsm/kg H_2O). This pattern of convergence suggests that while the fundamental gender difference remains, its physiological expression is significantly modulated by the aging process itself.

Figure 1 visually represents the data from Table 2, plotting the mean urine osmolality with 95% confidence intervals for each gender across the seven age groups. It

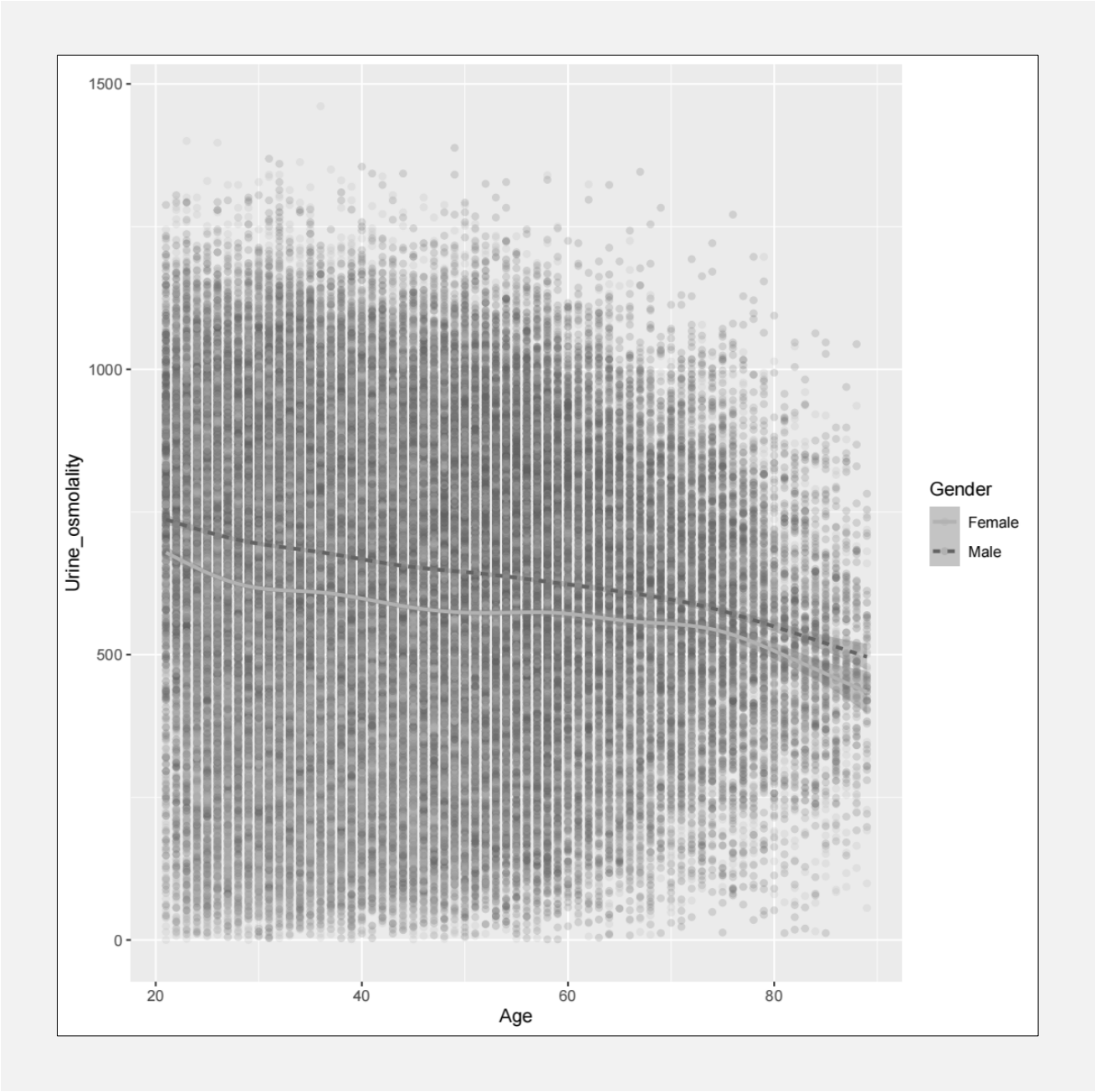

Figure 1. Age-related trajectories of mean urine osmolality in male and female participants.

illustrates the three primary findings: 1) males have consistently higher Uosm than females; 2) both genders show a decline with age, which accelerates after age 70; and 3) the gap between the genders narrows with advancing age.

DISCUSSION

A multi-layered interpretation of the findings

Synthesis of principal findings

This study, representing one of the largest investigations of urine osmolality to date and the first of its scale in a major East Asian population, provides a high-resolution demographic map of renal concentrating capacity across the adult lifespan. The analysis of over 128,000 individuals definitively confirms three cardinal patterns that characterize the interplay between age, gender, and

renal function. First, there is a profound and persistent sexual dimorphism, with males exhibiting significantly higher urine osmolality than females at every stage of adult life. Second, a clear, inexorable decline in Uosm occurs with advancing age in both genders, a trend that accelerates markedly after the seventh decade. Third, the magnitude of the gender-based difference is not static but attenuates significantly in later life, with male and female Uosm values converging in the elderly. These findings not only furnish crucial population-specific reference data for a non-Western demographic but also serve as a clinical and physiological springboard to explore the underlying mechanisms and public health consequences.

The physiological architecture of renal aging: Explaining the decline

The progressive, age-related decline in Uosm observed in this study is not an isolated laboratory finding but a robust clinical biomarker reflecting a deep, multi-system physiological decay characteristic of renal senescence. The trajectory plotted from our data provides a population-level confirmation of a well-established but complex biological process. The gradual decline until age 70, followed by a more precipitous drop, likely represents the point at which the cumulative insults of aging overwhelm the kidney's substantial functional reserve.

This decline begins with gross structural deterioration. The aging process is accompanied by well-documented changes in the kidney, including a reduction in renal mass, cortical thinning, and, most importantly, a progressive loss of functional nephrons due to global glomerulosclerosis and tubular atrophy [7]. This diminution in the number of filtering and concentrating units inherently limits the kidney's maximum functional capacity. This structural decay translates directly into functional impairment, evidenced by the known age-related decreases in glomerular filtration rate (GFR) and renal plasma flow [12]. Crucially, the kidney's maximal urine concentrating ability, the very function measured by Uosm, also diminishes progressively with age.

This functional decline is not merely a passive consequence of structural loss but is actively driven by a state of hormonal dysregulation. A key feature of the aging kidney is the development of AVP resistance, which manifests as a blunted response of the renal tubules to arginine vasopressin. Even when AVP is released appropriately in response to dehydration, the aging kidney cannot respond effectively to conserve water. This condition has been aptly characterized as an acquired form of partial nephrogenic diabetes insipidus, a state of impaired water handling that becomes more pronounced with age.

This hormonal resistance has a clear molecular basis. Studies in aging animal models have demonstrated a significant reduction in the expression of the AVP V2 receptor (V2R) and its critical downstream targets within the renal medulla [13]. These targets include the aquaporin-2 (AQP2) water channel, which is directly inserted into the apical membrane of collecting duct cells to permit water reabsorption, and key urea transporters (UTs) that are essential for generating the hypertonic medullary interstitium required for the concentrating mechanism to function [14]. The downregulation of this molecular machinery effectively cripples the kidney's ability to create a concentrated urine.

At the most fundamental level, these structural, functional, and hormonal changes are driven by the process of cellular senescence. The accumulation of senescent cells - cells that have entered a state of irreversible growth arrest - within the renal tubules and glomeruli is a hallmark of the aging kidney [7]. These cells are not inert; they adopt a senescence-associated secretory phenotype (SASP), releasing a cocktail of pro-inflammatory and pro-fibrotic factors that disrupt normal tissue architecture and function, impair regeneration, and contribute directly to the observed functional decline [15]. Therefore, the Uosm trajectory observed in our data is a powerful clinical signature of this multi-level aging cascade, from organ-level structural decay down to the cellular and molecular drivers of functional impairment.

Deconstructing the gender-based difference in renal function

The consistent and significant gap in Uosm between males and females, followed by its convergence in later life, is not an arbitrary finding. It is a direct physiological consequence of the distinct and often opposing actions of gender hormones - primarily testosterone and estrogen - on the fundamental renal mechanisms of sodium and water handling. The lifelong trajectory of this sexual dimorphism tells a hormonal story of androgenic influence and estrogenic withdrawal.

The androgenic influence: a mechanism for higher concentration in males

The consistently higher Uosm in males across the lifespan, a finding consistent with studies in other populations [9], points to a sustained physiological influence promoting greater urine concentration. Evidence strongly implicates testosterone in this process. Androgens are known to influence renal function and can increase blood pressure, in part by enhancing the tubular reabsorption of sodium and water [16]. A specific and compelling molecular mechanism has been elucidated: testosterone, acting via the androgen receptor present in renal tubular cells, directly upregulates the transcription and expression of the α-subunit of the epithelial sodium channel (αENaC). ENaC represents a critical, rate-limiting step for sodium reabsorption in the aldosterone-sensitive distal nephron [17]. By increasing the expression of ENaC, testosterone promotes greater sodium reclamation from the tubular fluid. This enhanced sodium reabsorption increases the interstitial osmotic gradient, which in turn drives the passive reabsorption of water through AQP channels, a process ultimately facilitated by AVP [6]. The net result is a more concentrated urine

and, consequently, a higher Uosm. This provides a direct, hormone-driven molecular explanation for the higher baseline renal concentrating capacity observed in males.

The estrogenic shield and menopausal shift

In contrast to testosterone, estrogens are generally considered to be renoprotective. In pre-menopausal women, estrogen modulates body fluid regulation in a distinct manner. It appears to lower the osmotic threshold for both AVP release and the sensation of thirst, promoting a physiological state that favors more diligent maintenance of hydration and avoids large fluctuations in plasma osmolality [18]. This establishes a different homeostatic set point for fluid balance in women compared to men, contributing to their relatively lower Uosm.

The most intriguing finding of our study - the narrowing of the Uosm gap after age 60, as the female Uosm trajectory begins to more closely parallel the male decline - strongly points to the profound physiological impact of menopause. The withdrawal of estrogen during the menopausal transition removes its unique modulatory and protective effects on renal function and fluid balance [19]. As this "estrogenic shield" is lost, the underlying, universal processes of renal senescence become more prominent and perhaps accelerate in women. Their renal function, no longer buffered by the effects of estrogen, begins to decline in a pattern that more closely resembles the male trajectory. This convergence is therefore not due to a change in male physiology but rather to a fundamental shift in female physiology, directly attributable to the loss of ovarian hormone production [20].

Clinical and public health implications

The descriptive demographic data generated by this study, when integrated with established clinical risk thresholds and fundamental physiological principles, transforms into powerful and actionable public health messages for specific, identifiable at-risk populations: men throughout their lives, and the elderly of both genders.

Urolithiasis risk stratification in men

A striking implication arises from the intersection of our findings with clinical research on urolithiasis. The mean Uosm for the entire male cohort in our study was 657 mOsm/kg H_2O. Independent, robust clinical studies have established specific Uosm thresholds that predict an elevated risk for the formation of calcium-oxalate kidney stones, the most common type of urolithiasis [21]. For men, this risk threshold has been identified as a 24-hour Uosm greater than 577 mOsm/kgH_2O [22].

The direct comparison of these two figures is alarming: the average male in our large, general population cohort exhibits a first-morning Uosm that is already substantially above the clinical risk threshold for developing kidney stones. While a first-morning sample reflects maximal concentration and 24-hour values would be lower, this finding strongly suggests that a state of chronic, suboptimal hydration may be endemic among men in this population. It provides a powerful, population-level physiological rationale for the known higher incidence of kidney stones in men [22]. This insight is not merely academic; it constitutes an evidence-based call to action for targeted public health campaigns promoting increased fluid intake, particularly for adult men, as a primary preventative strategy against a common and painful disease.

Geriatric hydration management: A perfect storm of vulnerability

For the elderly, our data reveals a different but equally critical vulnerability. The observed acceleration in the decline of Uosm after age 70 provides definitive, population-level confirmation of severely impaired renal concentrating capacity in this age group. This physiological deficit must be considered in the context of another well-known aspect of geriatric physiology: a progressive, age-related blunting of the thirst sensation. This combination creates a "perfect storm" for dehydration. The elderly have a diminished ability to conserve water due to their failing renal mechanisms, and this is compounded by a diminished physiological drive to consume water.

This dual deficit explains the high incidence of dehydration and its severe clinical sequelae - including delirium, falls, infections, medication toxicity, and acute kidney injury - in the geriatric population [23]. The critical clinical takeaway is that for older adults, thirst is an unreliable and dangerously late indicator of hydration need. This study's findings provide strong support for a paradigm shift in geriatric care, moving away from reactive, thirst-based drinking to proactive, scheduled hydration strategies. Such programs are a simple, low-cost, and highly effective intervention to prevent a cascade of serious, and often life-threatening, complications in this vulnerable population.

Establishing population-specific reference data

Finally, this study's primary contribution is the establishment of a crucial benchmark for Uosm in a major non-Western population. When compared to large-scale data from the U.S. NHANES, which reported a median Uosm of approximately 648 mOsm/kg H_2O in adults, our findings show broad similarities in the overall values and trends, suggesting the universality of the underlying physiological principles of aging and gender-based differences [24]. However, the specific mean values and age-related trajectories reported here are essential for the calibration of local laboratory reference ranges and the development of population-appropriate clinical guidelines in China and potentially other East Asian regions.

Strengths and methodological considerations

The foremost strength of this investigation lies in its immense statistical power, derived from a real-world sam-

ple of over 128,000 individuals spanning the full spectrum of adult life. This large-scale, non-selected cohort enhances the generalizability of the findings, providing a true snapshot of renal function in the broader community, which includes both healthy individuals and those with underlying comorbidities.

However, the study is not without important limitations that require careful consideration. The cross-sectional design reveals powerful associations between age, gender, and Uosm, but it cannot establish causality or track longitudinal changes within individuals over time. Furthermore, the analysis was limited by the lack of data on potentially significant confounders, such as diet (e.g., protein and salt intake), medication use (e.g., diuretics), and specific comorbidities (e.g., diabetes mellitus, chronic kidney disease), which are all known to influence Uosm. The exclusion of individuals younger than 20 years also leaves a gap in understanding the developmental trajectory of renal function from adolescence into young adulthood.

The most significant methodological consideration pertains to the technique used for measuring Uosm. The Sysmex UF-5000 analyzer estimates Uosm based on electrical conductivity, rather than measuring it directly via the gold-standard method of freezing point depression osmometry. This distinction is critical. Conductivity-based methods are highly sensitive to the concentration of charged ions (electrolytes) but are largely insensitive to major uncharged solutes, most notably urea and glucose [25]. External validation studies comparing the Sysmex UF-5000 to gold-standard osmometers have confirmed that while there is a general correlation, the methods can produce significantly different results, with wide limits of agreement [11].

This methodological characteristic introduces a potential systematic bias into our findings. In a mixed-health population like ours, the prevalence of conditions such as diabetes (which can lead to glycosuria) and variations in dietary protein intake (which affects urinary urea levels) is expected to be significant, particularly in older age groups. In participants with high levels of urinary glucose or urea, the conductivity-based method will systematically underestimate the true total urine osmolality. Consequently, the absolute Uosm values reported in this study are likely a conservative underestimation of the true population means. Moreover, because the prevalence of these confounding factors increases with age, this underestimation is likely more pronounced in the older cohorts. This implies that the true age-related decline in renal concentrating capacity may be even more severe than our data suggest. While this bias does not invalidate the observed trends of age-related decline and sexual dimorphism, it is a crucial interpretive lens through which the magnitude of these effects must be viewed.

CONCLUSION

Integrating demographics, physiology, and clinical practice

This large-scale investigation provides the first high-resolution characterization of urine osmolality across the adult lifespan in a major East Asian population, offering a unique and valuable demographic portrait of renal concentrating capacity. The definitive findings - a progressive, age-related decline in renal function that accelerates markedly after age 70, and a persistent sexual dimorphism that attenuates in later life - serve as a crucial population-specific benchmark.

These demographic patterns are not arbitrary but are the clinical expression of deep physiological drivers. The decline with age is a composite signature of renal senescence, reflecting the cumulative impact of structural decay, hormonal insensitivity to vasopressin, and the molecular downregulation of the kidney's water-conserving machinery. The profound difference between the genders is a direct consequence of the dynamic, lifelong influence of testosterone and estrogen on renal sodium and water handling.

The clinical relevance of these findings is both direct and actionable. The data unmask a potential endemic risk of suboptimal hydration among men, placing them at higher risk for urolithiasis, and reveal the "perfect storm" of vulnerability to dehydration in the elderly, who couple impaired concentrating ability with a blunted thirst drive. This evidence strongly advocates for the integration of age- and gender-stratified considerations into routine clinical nephrology, geriatric medicine, and preventative public health strategies. Future longitudinal research, ideally employing gold-standard freezing point depression osmometry, is warranted to validate these trajectories and further unravel the complex and clinically vital interplay between aging, gender, and renal health.

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Declaration of Interest:
All authors have no competing interests to declare.

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