# Adequacy of Daily Fluid Intake Volume Can Be Identified From Urinary **Frequency and Perceived Thirst in Healthy Adults**

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#### ABSTRACT

**Objective:** Achieving and maintaining an optimal level of hydration has significant implications for both acute and chronic health, yet many hydration assessments are not feasible for the general public. Urinary frequency (UF) is a reliable method to self-assess hydration status in healthy individuals, and thirst can provide additional sensory information on adequacy of daily fluid intake volume (DFI). However, threshold values for these indices to detect optimal hydration have not been determined. In this study, we sought to determine threshold values for 24-hour UF and perceived thirst that could accurately distinguish between optimal and suboptimal hydration states.

Methods: Thirty-two healthy adults (age  $22 \pm 3$  years, body mass index  $24.9 \pm 4.1$  kg/m<sup>2</sup>) collected urine over 24 hours on four separate occasions, where UF was recorded as well as thirst at each void using a numbered perceptual scale. Using urine osmolality as the criterion standard, all samples were either classified as representing an optimal ( $\leq$ 500 mOsm kg<sup>-1</sup>) or suboptimal hydration status (>500 mOsm·kg<sup>-1</sup>).

Results: A 24-hour UF  $\leq$ 6 was able to detect suboptimal hydration with good accuracy (area under the curve [AUC] 0.815) and a 24-hour average perceived thirst rating > 3 ("a little thirsty") could detect it with reasonable accuracy (AUC 0.725). In addition, a UF  $\leq$ 4 had a considerably higher positive likelihood ratio to detect suboptimal hydration versus a UF  $\leq$ 6 (9.03 versus 2.18, respectively).

**Conclusions:** These analyses suggest that individuals with a 24-hour UF  $\leq 6$  or perceiving themselves to be, on average, "a little thirsty" throughout the day are likely to be suboptimally hydrated and thus underconsuming an adequate DFI.

Abbreviations: AIC: Akaike information criterion; AUC: area under the curve; AVP: arginine vasopressin; BMI: body mass index, CI = confidence interval; DFI: daily fluid intake volume; DOR: diagnostic odds ratio; LR-: negative likelihood ratio; LR+: positive likelihood ratio; NPV: negative predictive value; PPV: positive predictive value; ROC: receiver operating characteristic, SD = standard deviation; UF: urinary frequency; U<sub>osm</sub>: urine osmolality; U<sub>SG</sub>: urine specific gravity

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## Introduction

Mounting epidemiological and clinical data highlight the importance of consuming an adequate daily fluid intake volume (DFI), with multiple studies establishing an association between fluid intake and various health complications, including chronic kidney disease (1, 2), urolithiasis (3-5), and impaired glucose regulation in patients with type 2 diabetes (6). However, there are several critical barriers to individuals achieving an adequate DFI, including inter- and intra-individual variability in daily fluid needs and the ability to easily and accurately self-assess hydration status.

A number of factors influence individual variability in DFI needs including environmental conditions, physical activity levels, body morphology, and metabolism (7-9). For these reasons, blanket recommendations on a target DFI that individuals should strive to achieve come with a

number of caveats. In recent years, several studies have examined links between total DFI, markers of urinary concentration, and circulating levels of arginine vasopressin (AVP) (10, 11). These studies have raised the idea that while recommendations of a DFI based on principles of urinary water and solute excretion can certainly be of value (12), determining an objective method for individuals to selfassess hydration status and adequacy of their DFI could be of tremendous potential utility. An increase in urine output (and subsequently urinary frequency [UF]) is typically indicative of greater free-water clearance, suggesting suppression of circulating AVP and thus less renal conservation of body water. This has important implications given the apparent link between low-volume, highly-concentrated urine output and chronic disease risk (13, 14), as well as AVP contributing to the progression of chronic kidney disease and decline in glomerular filtration rate (15, 16).

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While anecdotally the notion of increased fluid intake correlating with increased urine output and UF (the number of times an individual urinates over 24 hours) has been understood for some time, our group recently demonstrated the validity and reliability of 24-hour UF as a method of hydration status assessment (17, 18). The use of UF as a tool to self-assess hydration status is appealing for a number of reasons, the most obvious being a lack of equipment and technical expertise needed to provide an individual with an estimate of whether or not their daily fluid intake needs are being met. However, despite these initial studies examining the use of UF as a hydration assessment tool, a threshold value for 24-hour UF that can detect a suboptimal hydration status has yet to be determined. That is, what 24-hour UF value indicates whether an individual is consuming a DFI that is able to compensate for all losses while also maintaining a urinary output which may reduce the risk of chronic disease (10).

Thirst perception acts as a powerful mechanism to maintain body fluid homeostasis, largely driven by increases in plasma osmolality beyond the narrow range in which renal adjustments to urine formation are dictated by changes in AVP (19, 20). Although the sensitivity of thirst can be influenced by a number of factors including age (21-23), diet (24), exercise (25, 26), and body temperature (27), it is still a relevant form of feedback for individuals to consume fluids in an effort to maintain optimal hydration on a daily basis. However, despite thirst being a key driver regulating daily fluid intake, its potential use as a marker to assess hydration status remains to be fully elucidated, particularly outside of athletic settings (28, 29). Thirst is often measured in a variety of settings in which hydration status varies (30, 31), but there is a lack of information regarding the level of thirst throughout a day that may provide a clinical cutoff to detect suboptimal hydration.

Therefore, the purpose of this study was to examine the diagnostic capability of UF and thirst to differentiate between optimal and suboptimal hydration states, both separately and when used in combination. Primarily, we sought to determine a threshold for these indices that could, with reasonable accuracy, provide a target value that could allow for a relatively straightforward means of determining whether DFI needs are being met and help to prevent suboptimal hydration. As a secondary aim, we tested the hypothesis that a combination of UF and thirst would be a more accurate estimate of hydration status versus either index alone.

# **Materials and methods**

# Study protocol

Thirty-two apparently healthy participants (n = 12 men, age  $22 \pm 3$  y, mass  $74.0 \pm 15.4$  kg, height  $172 \pm 9$  cm, body mass index [BMI]  $24.9 \pm 4.1$  kg/m<sup>2</sup>) were enrolled in this study where they completed four separate trials. In two trials, participants were free to consume fluids ad libitum over 24 hours (Ad libitum) and in the other two trials, participants were asked to restrict drinking fluids to a maximum

of 500 ml over 24 hours (Restricted). As part of an initial separate research question, within each set of trials (Ad libitum and Restricted), participants were asked to either void at a "first" urge throughout the day (i.e., a "2" on a previously described 0–4 perceptual scale) where 0 = no sensation, 1 = first sensation, 2 = first urge to void, 3 = strongurge, and 4 = uncomfortable urge (32) or void without consideration of their urge. Preliminary analyses indicated that UF and other urinary indices of hydration status were similar within each set of the Ad libitum and Restricted protocols. Thus, in order to focus on the research questions related to the relationships between UF and thirst with hydration status, data from each set of Ad libitum and Restricted trials were pooled for final analysis. Data from each trial still provided in the Results.

For 24 hours before and throughout each trial, participants abstained from alcohol and physical activity outside normal activities of daily living. Food and fluid intake over the 24-hour period was recorded on a food/fluid log and participants were instructed to replicate the same food intake for each trial. An average DFI from drinking fluids within trials in each trial condition was calculated from these records. Caffeine intake was not prohibited but was limited to a maximum of 500 mg/d. Participants who consumed caffeinated beverages during the testing periods were confirmed as non-caffeine-naïve via a 7-day caffeine intake recall questionnaire.

Participants were required to be healthy, free of any medications or supplements that may affect body fluid balance, and weight-stable throughout the duration of the study. Participants provided written informed consent that was approved by the University of Arkansas Institutional Review Board.

# Urine collection and analysis

For each trial, urine was collected over 24 hours with each trial separated by at least 24 hours. Participants were instructed to discard the first morning void sample upon waking and then collect all subsequent voids in a provided medical-grade collection container, with the following first morning void being collected as the final time point. Following urination, participants placed a demarcation on the collection container at the level of the urine after each individual void, while also indicating the urge to void at the time of urination, and perceived thirst. Thirst was recorded at each void on the collection container prior to urinating using a scale of 1 to 9 in 1-point increments where 1 = "not thirsty at all" through to 9 = "very, very thirsty" (33).

Twenty-four-hour urine samples were analyzed for specific gravity ( $U_{SG}$ ), osmolality ( $U_{osm}$ ), volume, and UF.  $U_{SG}$  was determined on each well-mixed 24-hour urine collection using a calibrated handheld refractometer (Master-SUR/NM, Atago, Japan).  $U_{osm}$  was measured in duplicate 250 µl samples using freezing point depression osmometry (Model 3250, Advanced Instruments Inc., Norwood, MA).

After  $U_{SG}$  and  $U_{osm}$  analyses, urine collection containers were emptied, and the number of void demarcations were

counted for UF. Water was then filled to each demarcation and weighed to the nearest 5 g (i.e., 5 ml; OHAUS Catapult 1000, Pine Brook, NJ) to determine individual void volumes throughout the 24 hours.

## Statistical procedures

Receiver operating characteristic (ROC) analyses were performed using MedCalc Statistical Software v. 18.6 (MedCalc Software byba, Ostend, Belgium) after classifying urine samples pooled from all trials according to 24-hour U<sub>osm</sub> as the criterion standard, where optimal hydration was defined as  $\leq$ 500 mOsm·kg<sup>-1</sup> and suboptimal as > 500 mOsm·kg<sup>-1</sup> (10). Although several U<sub>osm</sub> cutoffs have been proposed to determine adequate DFI (10-12), 500 mOsm·kg<sup>-1</sup> was chosen based on the evidence that this value may represent a sufficient target to reduce the risk of long-term health complications from inadequate fluid intake (10). During the Restricted trials, despite consuming > 500 ml (an additional  $662 \pm 612 \text{ ml}$ ), seven participants still presented with highly concentrated urine samples indicative of suboptimal hydration so these data were included in the analyses. The diagnostic capability to identify hydration status was tested using 24-hour UF and average thirst. Repeated measures of UF and thirst across the four trials were not accounted for in order to provide a more conservative area under the curve (AUC) analysis (34). Of the 32 participants enrolled in the study, all completed one of the two Ad libitum trials; however, one participant did not complete one of the Ad libitum trials, two participants did not complete either of the Restricted trials, and another participant did not complete one of the Restricted trials. Two participants did not record thirst ratings on one Ad libitum trial and one Restricted trial, respectively. Output from the ROC analyses provided an overall estimate of diagnostic accuracy (AUC) as well as a true positive rate (sensitivity) and true negative rate (specificity) of each of these markers to identify suboptimal hydration. The positive predictive value (PPV) and negative predictive value (NPV) of each variable was calculated as sensitivity/(specificity + false positive rate) and specificity/(specificity + false negative rate), respectively (35). Coordinates of the ROC curve were used to determine positive and negative likelihood ratios (LR + and LR -, respectively) and a threshold value that would be able to detect suboptimal hydration with the highest combination of sensitivity and specificity based on Youden's J index (36) (Note: given that the thirst perception scale changes in one-point increments, the nearest whole value was selected for simplicity of interpretation and utility.) Diagnostic odds ratios (DOR) were calculated as LR+/LR- (37).

A post hoc power estimate for the AUC analyses was performed (MedCalc Statistical Software) where the desired significance and power were set at 0.05 and 0.8, respectively. Given the ratio of suboptimal hydration positive to negative samples in our data set of  $\sim$  0.3, a minimum AUC of 0.7 that could be distinguished from a null hypothesis value of 0.5 required 85 total samples (65 cases positive for suboptimal hydration and 20 cases negative) to meet adequate power. Final analyses included  $\geq$ 120 total samples, of which  $\geq$ 84 were positive for suboptimal hydration and  $\geq$ 36 were negative.

Linear mixed effects modeling fit by restricted maximum likelihood was used to assess the combined contributions of thirst and UF in explaining variations in 24hour U<sub>osm</sub>. A multilevel model was utilized to account for the repeated observations within each participant (38). The linear mixed effects models were generated using the lmer function in the R package (39) lme4 (40) with thirst and UF as fixed effects and participant as a random effect (random intercept only). Final model selection (to obtain the best-fit model while maintaining model parsimony) was decided using Akaike information criterion (AIC) with a change greater than 3 indicating better model fit (41). Further, the significance of adding each new parameter to the model was compared using a likelihood-ratio test with the models fit using maximum likelihood and an alpha set at 0.05.

Paired *t* tests were used to compare values between trials within Ad libitum and Restricted protocols in 24-hour UF,  $U_{osm}$ ,  $U_{SG}$ , volume, DFI, average individual void volume, average perceived thirst rating, and average urge to urinate using SPSS v. 24 (IBM Corporation, Somers, NY). Data are reported as mean ± standard deviation (SD) or mean ± 95% confidence interval (CI) where noted. An alpha level of 0.05 defined significance for all tests.

# Results

## Total DFI

DFI from drinking fluids was higher overall in the Ad libitum versus Restricted trials (p < 0.001); however, DFI was not different between the two trials within either the Ad libitum ( $2554 \pm 1261$  vs.  $2252 \pm 1082$  ml, p = 0.085) or Restricted protocols ( $610 \pm 443$  vs.  $530 \pm 317$  ml, p = 0.273).

#### Urinary output and hydration markers

24-hour urinary variables for all trials are presented in Table 1. Within the Ad libitum protocol, there were no differences between trials in UF (p = 0.693), U<sub>osm</sub> (p = 0.386), U<sub>SG</sub> (p = 0.196), volume (p = 0.287), individual void volume (p = 0.098), or thirst (p = 0.780), but urge to void was higher (p = 0.004) when participants were able to urinate at an urgency of their choosing. Within the Restricted protocol, there were no differences between trials in UF (p = 0.163), U<sub>osm</sub> (p = 0.429), U<sub>SG</sub> (p = 0.092), volume (p = 0.323), individual void volume (p = 0.866), thirst (p = 0.437), or urge to void (p = 0.082).

When comparing values averaged across trials in each protocol, UF, volume, individual void volume, and urge to void were all significantly higher during Ad libitum versus Restricted (all p < 0.001) and U<sub>osm</sub>, U<sub>SG</sub>, and thirst were significantly lower (all p < 0.001).

Table 1. 24-Hour Urinary Varia	bles During the A	d Libitum and	Restricted Trials
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	Ad libitum				Restricted		
	Trial 1	Trial 2	Average	Trial 1	Trial 2	Average	
UF	7.1 ± 3.3	7.1 ± 3.0	$7.1 \pm 3.2^{\dagger}$	4.4 ± 1.5	4.1 ± 1.4	4.3 ± 1.4	
U <sub>osm</sub> (mOsm⋅kg <sup>-1</sup> )	$457 \pm 168$	$431 \pm 190$	$445 \pm 178^{++}$	878±133	$896 \pm 144$	887 ± 138	
U <sub>SG</sub>	$1.013 \pm 0.004$	$1.012 \pm 0.004$	$1.012 \pm 0.004^{\dagger}$	$1.023 \pm 0.003$	$1.024 \pm 0.003$	$1.024 \pm 0.003$	
Volume (ml)	$2097 \pm 1268$	$2333 \pm 1228$	$2213 \pm 1244^{\dagger}$	$895 \pm 393$	$864 \pm 470$	$880 \pm 428$	
Individual void volume (ml)	$298 \pm 112$	$335\pm138$	$317\pm126^{\dagger}$	210±77	$222\pm97$	$216\pm87$	
Thirst	$2.8 \pm 1.5$	$2.8 \pm 1.5$	$2.8 \pm 1.5^{++}$	$4.7 \pm 1.7$	4.7 ± 1.7	$4.7 \pm 1.7$	
Urge to void	$2.1\pm0.4$	$2.5\pm0.6^{\ast}$	$2.3\pm0.5^{\dagger}$	$1.9\pm0.4$	$2.1\pm0.5$	$2.0\pm0.5$	

Note. UF = urinary frequency;  $U_{osm}$  = urine osmolality;  $U_{SG}$  = urine specific gravity.

<sup>\*</sup>Significantly higher versus Trial 1 within Ad libitum protocol (p = 0.004);

<sup>†</sup>Significantly different versus average value in Restricted protocol (p < 0.001).

Table 2. Data Output From the ROC Analyses When a  $U_{\rm osm}>500\,$  mOsm  $kg^{-1}$  Is Used as the Criterion Value to Define Suboptimal Hydration

Index	AUC	Est. SE	95% CI	Sensitivity	Specificity	PPV	NPV	DOR
UF	0.815	0.041	0.735-0.895	0.884	0.595	0.857	0.712	10.90
Thirst	0.725	0.050	0.627-0.822	0.667	0.722	0.866	0.491	5.22

Note. UF = urinary frequency; AUC = area under the curve; SE = standard error CI = confidence interval; PPV = positive predicted value (proportion of results that are true positive results for suboptimal hydration); NPV, negative predicted value (proportion of results that are true negative results for suboptimal hydration); DOR, diagnostic odds ratio.

## **ROC** analyses

Data output for the ROC analyses are presented in Table 2. Both UF and thirst were able to accurately detect suboptimal hydration status (p < 0.001). Of the 123 pooled samples analyzed for UF, 86 (69.9%) were classified as suboptimal and 37 (30.1%) as optimal. Based on a Youden's J index of 0.478, a UF  $\leq 6$  (95% CI  $\leq 4$  to  $\leq 7$ ) was the associated threshold value. For perceived thirst, 120 pooled samples were analyzed (84 [70.0%] suboptimal, 36 [30.0%] optimal) and a Youden's J index of 0.333 yielded an associated threshold value of > 3 (95% CI > 2.4 to > 5.5). A visual summary of these analyses is illustrated in Figure 1, where the associated threshold values for UF and thirst and their ability to identify suboptimal hydration is shown. Positive and negative likelihood ratios for UF and thirst across various measured values are presented in Table 3. Although UF yielded a numerically greater overall diagnostic accuracy versus thirst, the difference between ROC curves was not statistically significant (p = 0.235).

#### Combining UF and thirst to estimate hydration status

Using multilevel regression, the addition of thirst appears to improve upon the predictive ability of UF alone to classify hydration status. Overall, it appears that the model improves with both the inclusion of UF ( $\Delta$ AIC = 50.08,  $\chi^2(1) =$  52.08, p < 0.001), and with thirst ( $\Delta$ AIC = 9.06,  $\chi^2(1) =$  11.06, p < 0.001). However, an additional interaction between thirst and UF did not further improve the model ( $\Delta$ AIC = 0.98,  $\chi^2(1) = 2.98$ , p = 0.08). The combined (thirst and UF) model information is presented in Table 4.

Utilizing the UF and thirst model, 24-hour  $U_{osm}$  can be estimated with fairly good precision. At any given value of UF, a 1-point increase in average thirst corresponds to approximately a 40-mOsm·kg<sup>-1</sup> increase in estimated

24-hour  $U_{osm}$ . Meanwhile, at any given value for average thirst, an increase in UF of 1 corresponds to approximately a 55-mOsm·kg<sup>-1</sup> decrease in estimated 24-hour  $U_{osm}$ .

#### Discussion

Growing evidence suggests the potential long-term health benefits of consuming an adequate DFI (1-5); however, the ability for individuals to accurately self-assess DFI and hydration status remains limited. In the present study, we sought to determine values for 24-hour UF and thirst that could accurately detect suboptimal hydration in young, apparently healthy individuals. Our analyses indicate relatively good diagnostic performance of 24-hour UF to differentiate between hydration conditions (AUC 0.815) with high sensitivity (88%). In addition, although a less sensitive indicator than UF, average thirst was also able to significantly differentiate between hydration conditions (AUC 0.725) with greater specificity. Interestingly, multilevel linear regression analysis revealed that a combination of UF and thirst may be a more accurate estimate of hydration status compared to either index measured alone. Taken together, these data suggest that a combination of monitoring daily UF and thirst may help to determine whether individual adequate fluid intake needs are being met.

A variety of factors contribute to variability in daily fluid intake requirements, both within and between individuals (7-9, 42). Further confounding this issue, there remains a lack of consensus on the most appropriate methods used to determine hydration status (43-49), particularly outside of controlled laboratory studies. While it is generally accepted that the best approach for determining hydration status is to assess a variety of indices (45, 49, 50), many of the most widely used markers in laboratory settings (e.g., blood/urine osmolality) are impractical for everyday use for the general public. Our group has previously demonstrated the utility of 24-hour UF as a valid and reliable indicator of hydration status (17, 18); however, the diagnostic capability of UF to detect hydration status is unknown. Data from the present study suggest that a UF  $\leq 6$  in young, healthy adults is likely to be representative of suboptimal hydration (Figure 1). Interestingly, a further reduction from this 24-hour UF value of only 2 led to a dramatic increase in the likelihood that an individual was suboptimally hydrated, as a UF <4



Table 3. Positive and Negative Likelihood Ratios for 24-hour UF and Thirst to Detect Subobtimal Hydration Derived from Coordinates of the ROC Curves

Index	Measured value	LR+	LR—
UF	≤3	9.47	0.76
	<u>≤</u> 4	9.03	0.54
	<u>≤</u> 5	2.35	0.43
	$\leq$ 6	2.18	0.20
	≤7	1.72	0.15
Thirst	>6	6.43	0.84
	>5	4.29	0.70
	>4	2.27	0.69
	>3	2.00	0.50
	>2	1.29	0.43

Note. LR+ = positive likelihood ratio; LR- = negative likelihood ratio; UF = urinary frequency.

Table 4. Multilevel Regression Using UF and Thirst to Estimate 24-Hour U<sub>osm</sub>.

	24-hour U <sub>osm</sub>				
Predictors	Estimates	95% CI	р	df	
Intercept	819.73	662.23 to 977.23	< 0.001	114	
Thirst	39.75	17.13 to 62.37	0.001	106	
UF	-54.70	-70.62 to -38.77	< 0.001	110	
Random effects					
$\sigma^2$	38001.24				
$\tau_{00}$ participant	9020.69				
ICC participant	0.19				
Observations	120				
Marginal R <sup>2</sup> /Conditional R <sup>2</sup>	0.463/0	.566			

Note. Note. CI = confidence interval; df = degrees of freedom; ICC = intraclass correlation; UF = urinary frequency.

**Figure 1.** Distribution of urinary frequency (UF) (A) and thirst (B) plotted against urine osmolality (U<sub>osm</sub>), grouped as either  $> 500 \ mOsm \cdot kg^{-1}$  (suboptimal hydration) or  $\leq 500 \ mOsm \cdot kg^{-1}$  (optimal hydration). Solid horizontal line represents the threshold values to detect suboptimal hydration and dashed lines their 95% confidence interval (Cl). Shaded areas represent the true negative (left) and true positive (right) classifications of suboptimal hydration using UF and thirst.

yielded a positive likelihood ratio of 9.03 (Table 3). In addition to UF, an average perceived thirst over 24 hours > 3(defined as "a little thirsty") was also able to detect suboptimal hydration, albeit with less accuracy than UF (Table 2). Similar to the trend observed with UF, a relatively high positive likelihood ratio of 4.29 was derived from an average thirst > 5 ("moderately thirsty"). As a secondary aim of the study, we were interested in testing the combined ability of UF and thirst to estimate hydration status. Although not necessarily predictive, it is interesting to note that combining UF and thirst significantly improved upon the ability of either index alone to estimate hydration status (defined using 24-hour U<sub>osm</sub>) such that at any given value of UF, a 1-point increase in average thirst corresponded to a  ${\sim}40$ mOsm·kg<sup>-1</sup> increase in estimated 24-hour U<sub>osm</sub>. Thus, from a practical standpoint, an individual could use the information gained from both indices to monitor shifts in 24-hour Uosm over several days (and subsequently daily fluid intake adequacy) that may be more accurate than using either index alone. Collectively, these analyses suggest that both UF and thirst may be viable methods for healthy individuals to self-assess hydration status and monitor the adequacy of their DFI.

In order to group urine samples in the present study by hydration status (optimal or suboptimal), U<sub>osm</sub> was used as the criterion variable. When a longer duration of urine collection is possible (i.e., 24 hours), U<sub>osm</sub> provides an attractive index of hydration status since it reflects the net change in body water balance, driven by both behavioral and neuroendocrine responses that influence renal concentration or dilution (11, 51). We used a  $U_{osm}$  value > 500 mOsm·kg<sup>-1</sup> as the criterion to define suboptimal hydration based on a previous investigation that suggested 24-hour values below this point were representative of optimal hydration, indicated by adequate fluid intake and subsequent urine formation and prevention of elevated plasma AVP (10). However, a variety of criterion values for U<sub>osm</sub> have been used in an effort to identify optimal values of DFI and/or 24-hour urine volume (10-13, 52). Interestingly, even using a more conservative classification of inadequate DFI of 800 mOsm·kg<sup>-1</sup> (11), additional ROC analyses of our samples yielded similar diagnostic accuracy (AUC 0.795 and 0.745 for UF and thirst, respectively) but different thresholds for the detection of suboptimal hydration ( $\leq 4$  and > 3.7). These findings present several key considerations. First, overall accuracy of 24hour values of UF and average perceived thirst appear to be similarly capable of detecting suboptimal hydration when using both liberal and more conservative classifications of hydration status based on U<sub>osm</sub>. However, while classifying samples based on a higher U<sub>osm</sub> provided similar sensitivity and specificity for thirst (73.3% and 70.7%, respectively), the UF threshold value of  $\leq$ 4 was accompanied by a substantially reduced sensitivity (64.6%) but greater specificity (81.8%). Collectively, these analyses suggest that across a range of U<sub>osm</sub> criterion values to define hydration status, the overall diagnostic ability of UF and thirst to detect suboptimal hydration remains intact, but at the expense of altered sensitivity and specificity.

# Methodological considerations

A number of factors related to age must be taken into consideration when examining the potentially complex interrelationships among UF, thirst, and hydration status. An increase in 24-hour UF typically accompanies increasing age (53) as well as a higher prevalence of abnormal voiding habits (54–56). Thus, it is unclear how the relationship between UF and hydration status may be augmented in older individuals that have abnormal voiding habits, possibly due to incontinence. Finally, secondary to changes in micturition behavior, a decline in the osmotic stimulation of thirst is common in older individuals (21, 23), ultimately resulting in a blunted thirst sensation (22). Together, these factors point to the need for further studies to investigate the utility of UF and thirst as methods of self-assessing DFI and hydration status in older individuals.

Gender disparities in urinary volume, concentration, and UF may also affect the interpretation of our findings, with previous work often observing a higher UF in women (53, 57) and sex-related differences in urinary volume and concentration (58, 59). Interestingly, a subanalysis of our data comparing the UF ROC curve coordinates between sexes revealed the same threshold value to detect suboptimal hydration ( $\leq 6$ ), with greater sensitivity in women versus men (96.2% versus 80.0%, respectively). However, given that our sample comprised young, healthy adults, only 12 of whom were men, future studies are warranted to further clarify how biological sex may affect the UF threshold to detect suboptimal hydration.

An important point to consider when determining the threshold values for UF and thirst is the sensitivity and specificity at the optimum value indicated from the ROC curve. In many cases, a threshold value that has both high sensitivity and high specificity would be ideal. For the present analyses, we used Youden's J index ([sensitivity + specificity] - 1) to select threshold values of UF and thirst at the point where the highest combination of sensitivity and specificity can be achieved (i.e., a combination of high true positive and high true negative rates, respectively) (36). However, the severity of the condition attempting to be diagnosed or detected must be taken into consideration, particularly the potential ramifications of achieving a false positive result (36). Indeed, despite the importance of maintaining adequate DFI and optimal hydration, if an individual were to be incorrectly classified as suboptimally hydrated based on either UF or thirst, the potential acute psychological and health consequences of this would likely be minimal. Assuming an individual were to make a behavioral change based on this false positive result, they may increase their DFI in order to achieve optimal hydration, the

outcome of which would likely be greater urine formation and subsequent urinary output.

A potential limitation of using thirst in the present study as a method of classifying hydration status from the ROC analysis is that we used an average value of the serial measures collected with each micturition over 24 hours. Thus, within a given day, thirst may fluctuate considerably depending on factors such as dietary intake and physical activity level (24-26), making it more difficult for an individual to identify whether they are thirsty due to inadequate DFI. In addition, previous work has demonstrated the potential for habitual daily fluid intake behavior to influence thirst perception, independent of the volume of fluid consumed (60). Across the four trials, intra-individual coefficients of variation were within a similar range  $(34\% \pm 20\%)$ ,  $45\% \pm 30\%$ ,  $29\% \pm 19\%$ , and  $32\% \pm 37\%$ ), and also similar to what others have reported for serial measures of other urinary hydration markers such as  $U_{osm}$  and color (45, 61). Given that our study design limited physical activity over the observation period and dietary intake remained consistent for each trial, further studies are needed to clarify the utility of perceived thirst as a method of identifying inadequate DFI and hydration status, particularly with consideration for individuals' habitual fluid intake.

# Conclusions

In summary, the ability to maintain an optimal hydration status through consuming an adequate DFI is hampered by a number of factors, including limitations for individuals to accurately self-assess hydration status. In this study, we demonstrated that suboptimal hydration is likely present in healthy, young adults when they urinate  $\leq 6$  times or when they perceive themselves to be, on average, "a little thirsty" over 24 hours, in the absence of strenuous physical activity. Given the associations between inadequate DFI and chronic health conditions, these findings have important clinical implications and can provide individuals with a target value of UF to achieve that is a straightforward, cost-efficient method to self-assess DFI and hydration status. Future studies are warranted to establish additional threshold values for UF and thirst that can detect suboptimal hydration in populations where UF and thirst may be augmented (e.g., older individuals and individuals with diabetes) and when athletic activity occurs during the day.

## Notes on contributors

MAT and MSG conceived and designed the experiments; ARC and MSG conducted research; MAT and MSG drafted the manuscript; all authors analyzed and interpreted data, read, and approved the final version of the manuscript.

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