Variation in human water turnover associated with environmental and lifestyle factors

PHYSIOLOGY

Variation in human water turnover associated with environmental and lifestyle factors

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Water is essential for survival, but one in three individuals worldwide (2.2 billion people) lacks access to safe drinking water. Water intake requirements largely reflect water turnover (WT), the water used by the body each day. We investigated the determinants of human WT in 5604 people from the ages of 8 days to 96 years from 23 countries using isotope-tracking (^{2}H) methods. Age, body size, and composition were significantly associated with WT, as were physical activity, athletic status, pregnancy, socioeconomic status, and environmental characteristics (latitude, altitude, air temperature, and humidity). People who lived in countries with a low human development index (HDI) had higher WT than people in high-HDI countries. On the basis of this extensive dataset, we provide equations to predict human WT in relation to anthropometric, economic, and environmental factors.

Water is essential for life (*1*), and daily water intake is necessary to prevent dehydration (i.e., net loss of body water) in most terrestrial animals, including humans (*2*). Total body water (TBW, measured in liters) is homeostatically controlled (*3*) and tightly regulated day to day by thirst and hunger drives that lead to the intake of fluids and food to offset water losses (*4*). Body water is lost as urine, insensible transcutaneous evaporation and sweat loss, respiratory water vapor, and water in feces (Fig. 1A). To maintain water balance, these losses must be matched by intake of water from liquids (drinking water and other beverages) and foods (*5*, *6*), water vapor in respiratory air intake, transcutaneous water uptake, and water formed during aerobic respiration and metabolism (Fig. 1A) (*2*, *7*). The total movement of water through the body, both intake and loss, is called water turnover (WT, measured in liters per day).

Despite adaptations to minimize dehydration, humans can survive for only ~3 days without consuming water (*1*). The risk of dehydration is greater under conditions requiring increased respiration, blood circulation, and sweating, such as during vigorous physical activity or in hot and humid environments (*3*). Insufficient water intake is a risk factor for heat stroke, urinary and kidney diseases, and cardiovascular failure (*8*, *9*). An understanding of WT and its determinants is critical for global public health decision-making regarding the provision of drinking water and water-enriched food (*10*).

Public health offficals need to be able to anticipate future daily water intake demands of their populations, especially during periods of impending crisis. Ideally, this would be based on scientific evidence regarding the levels of normal water intake. The current recommended intakes for water (*8*, *9*, *11*), however, rely on epidemiologic self-reported surveys or laboratory-based physiological studies with rather small sample sizes. Results obtained from self-reported intake surveys show large variations linked to imprecision in the assessment method. It is thus difficult to establish clear guidelines for worldwide public health actions from these sources of information. Most people who lack access to safely managed drinking water live in countries with a low human development index (HDI), but few studies have examined WT in those populations (*2*). To develop global guidelines for daily water intake, empirical measurements of WT under free-living conditions are required across a broad range of economic and environmental conditions.

We report WT and TBW for 5604 human subjects (3729 females and 1875 males) ranging in age from 8 days to 96 years from 23 countries around the globe and across a wide range of environments and living conditions (fig. S1 and table S1). We used the hydrogen isotope dilution and elimination technique, which provides an objective, accurate, reliable, and precise measurement of both TBW and WT under free-living conditions (Fig. 1B) (*7*). This method involves the subject drinking ~100 ml of water enriched with ~5% deuterated water. The deuterium floods into the body water pool, providing an estimate of TBW using the dilution principle (*12*). The excess deuterium isotope is then eliminated from the body by the elimination routes detailed in Fig. 1A. Because there is no enriched isotope tracer entering the system, the isotope enrichment declines exponentionally back to the baseline level. The rate constant of this exponential return to baseline multiplied by the body water pool is equal to the WT.

Data were obtained from the International Atomic Energy Agency Doubly Labelled Water (DLW) Database (*13*, *14*). The current study aimed to examine (i) the dependence of WT and TBW on age, body size, body composition, total energy expenditure (TEE, in megajoules per day), and physical activity level (PAL, which is the TEE/basal energy expenditure) through the human life course; (ii) the effects of climate, including latitude, altitude, outside air temperature, and humidity; and (iii) the potential influence of economic development as measured by the HDI.

WT was greatest in men 20 to 30 years of age and in women 25 to 60 years of age (Fig. 2A and table S2) and was lower in men >40 and women >65 years. TBW was also highest for adults 20 to 60 years of age (Fig. 2B). As a fraction of TBW, WT was highest in neonates (28.3 ± 7.2% per day) and decreased with age to 9.9 ± 3.0% per day in adults aged 18 to 40 years (Fig. 2C). TBW as a proportion of body weight also decreased with age, from 60.0 ± 6.4% of body weight from birth to 6 months to 50.4 ± 5.3% (males) and 42.0 ± 4.8% (females) at 60 years (Fig. 2D). Sex differences and the relationship with age and TBW in adults largely reflected variations in the percentage of body fat, which contains less water than muscle and other organs. The ratio of WT to TEE was 0.33 ± 0.09 liters/MJ (1.4 ± 0.4 ml/kcal) for adults, comparable to previous isotope-based measures (*15*) (Fig. 2, E and F).

Body size and composition, TEE, PAL, and climate variables were all correlated with

WT. After limiting our analysis to adults aged 18 to 60 years to avoid strong age effects (as shown in Fig. 2), bivariate analyses showed that WT was positively correlated with fat-free mass (FFM), TEE, and PAL and negatively correlated with percent body fat ($P < 0.001$) (Fig. 3, A to D). We found a significant curvelinear relationship between outdoor mean air temperature and WT and between latitude and WT ($P < 0.001$) (Fig. 3, E and F). Air temperature was positively correlated with WT when it was higher than 10°C ($P < 0.001$). Daily water intake was highest at ~0° effective latitude and lowest at –50° or +50° latitude. People living above the Arctic Circle had higher WT than those living at –50° or +50° latitude.

Linear regression analysis showed that age, FFM, PAL, air temperature, relative humidity, HDI, and altitude were significant predictors of WT in adults aged 18 years and older (table S3). We conducted multiple regression analysis (including first- and second-order polynomial terms) to examine potential nonlinear relationships between WT and the above variables in adults aged 18 years and older (table S4). The positive coefficient of the second-order term of air temperature indicated a curvilinear relationship between WT and air temperature. The negative coefficient of the second-order term of age also indicated a curvilinear relationship between WT and age. A nonlinear increase of WT with increase of air temperature is predicted from the standard Scholander curve (*16*) for the impact of ambient temperature on metabolic rate and evaporative water loss. In an additional test of these relationships, repeated-measures analysis for 72 people in spring and summer indicated higher WT in the summer (mean air temperature of 29°C) than in the spring (mean air temperature of 18°C) ($P < 0.001$), whereas TEE did not differ seasonally (Fig. 4, A and B).

WT of pregnant and lactating women is of interest because pregnant women have higher TBW and FFM than do nonpregnant women (*17*), and lactating women also lose water through milk production (*11*). Repeated-measures analysis of 63 women indicated that WT increases in the third trimester of pregnancy (+670 ml/d) and during lactation (+260 ml/d) compared with prepregnancy (Fig. 4C) (*17*). The increase of WT during pregnancy is consistent with the increase in TBW.

The highest WTs in our sample are consistent with the effects of temperature, climate, physical activity, and body size. Nine of the 1875 males had WT >10 liters/d; of these, four were athletes, four were adult Shuar forager-horticulturalists of Amazonian Ecuador (*18*), and one was a Caucasian with a normal BMI but was measured in the summer with a maximal air temperature of 31.7°C. Thirteen of 3729 females had WT >7 liters/d; of these, five were athletes, two were pregnant women who had extremely high BMI (>45 kg/m^2) and were measured in the summer; three had high BMI (>30 kg/m^2) and two were measured in the summer; and three were measured in the summer with a maximal air temperature of >30°C.

Lifestyle had clear effects on WT. Athletes had higher WT than nonathletes ($P < 0.001$; Fig. 5A and table S5). Hunter-gatherers, mixed farmers, and subsistence agriculturalists all had higher WT than those in industrialized economies ($P < 0.001$; Fig. 5B and table S6). People living in low-HDI countries had higher WT than those in middle- and high-HDI countries, even after adjustment for physiological and environmental variables ($P < 0.001$; Fig. 5C and table S7). The effects of body size, PAL, and air temperature were greater for people in low-HDI countries (Fig. 5, D to F). The smaller effects for these variables in high-HDI populations suggests that water needs are buffered against environmental influences through effective indoor climate control (e.g., air-conditioning). In high-HDI countries

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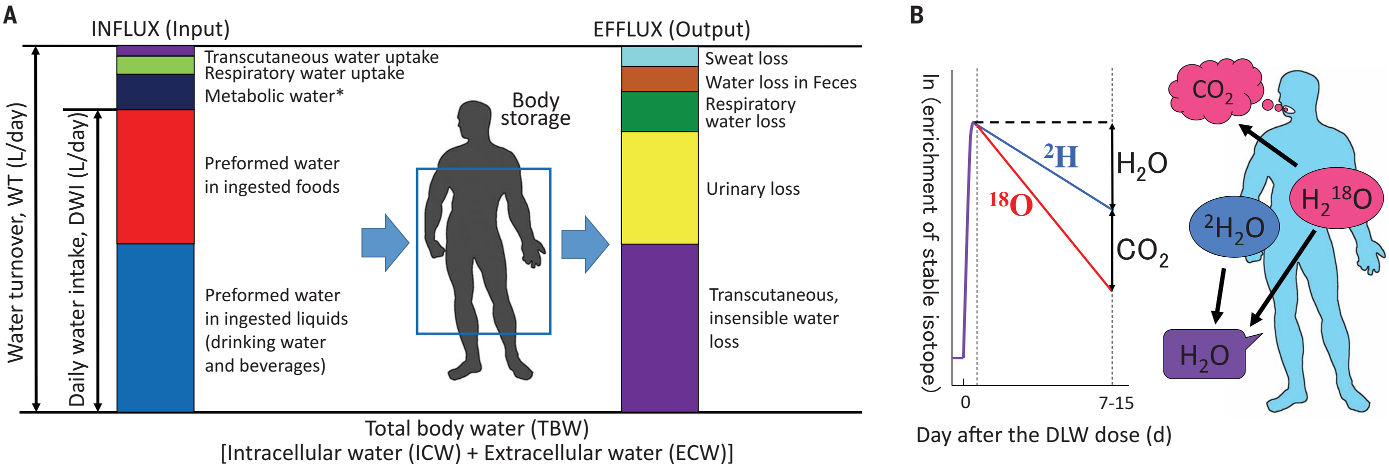

Fig. 1. Conceptual diagram of human WT and its measurement. (**A**) Conceptual diagram showing sources of water influx and efflux on human body. *Metabolic water produced inside a living organism as an end product of the oxidation of energy-containing substances in their food. (**B**) Hydrogen isotope dilution and elimination provides an objective measure of TBW and WT.

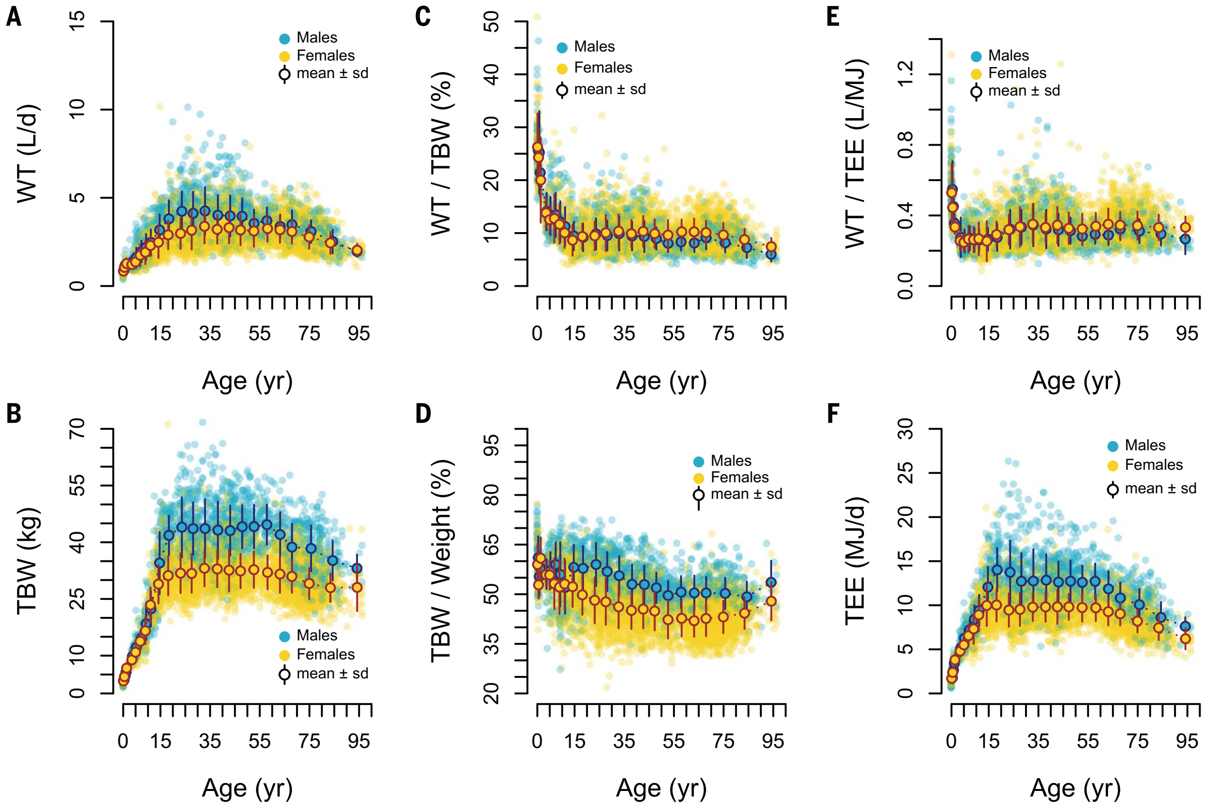

Fig. 2. Relationships between age and TBW or WT. Shown are relationships between age and TBW or WT in 3729 females (orange) and 1875 males (blue) aged 0 to 96 years with mean and SD. (**A**) WT (liters/d). (**B**) TBW (kg). (**C**) WT per TBW (%). (**D**) TBW per body weight (%). (**E**) WT per TEE (liters/MJ). (**F**) TEE (MJ/d). WT increases with age until ~30 years and is higher in men (4.3 liters/d) than in women (3.4 liters/d). WT significantly decreases after 40 years in men and 65 years in women, reaching an average WT of 3.1 and 2.8 liters/d in men and women >70 years of age, respectively. The average WT rate as a percentage of TBW is a maximum of ~25% in neonates, decreases with development, and is ~15% in 5-year-old children. At puberty, WT falls to ~10% and remains constant until age 40 in men and age 65 in women, after which it decreases. The average WT per TEE is about 0.33 liters/MJ (~1.4 ml/kcal) in adults. Note that the variation in WT is incredibly large: The low end for men and women is ~1 to 1.5 liters/day and the upper end is ~6 liters/day; outliers lie in the 10 liters/d range. On average, water accounts for 60% of the body weight in infants, 50% in older adults, and only 42% in women at 60 years of age, reflecting a larger percent body fat.

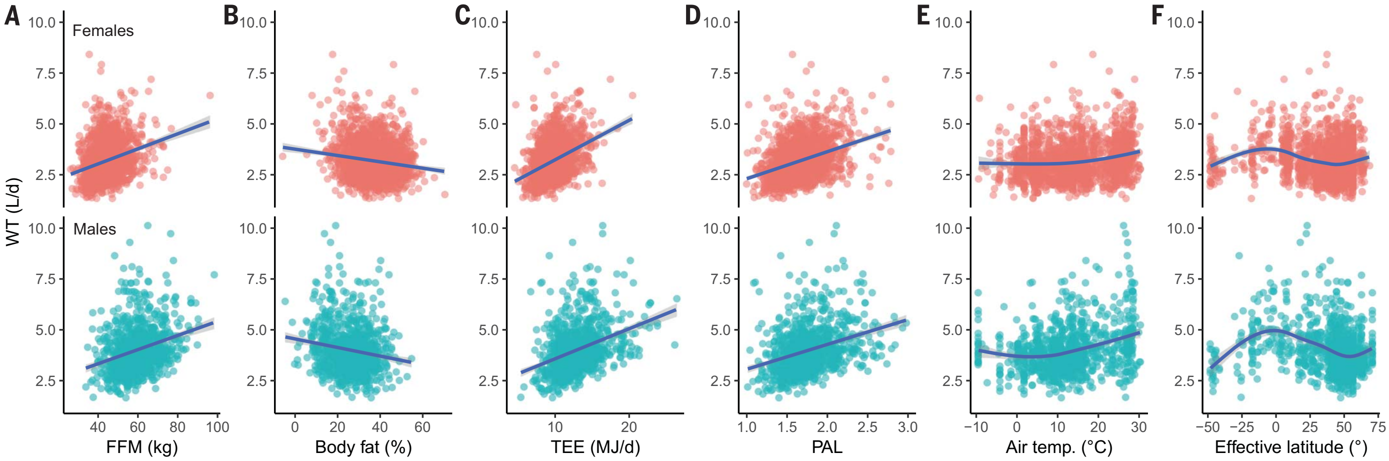

Fig. 3. Relationships between WT and body composition, TEE, physical activity, and environmental factors. Relationships between WT against FFM (**A**), percent body fat (**B**), TEE (**C**), PAL (**D**), air temperature (**E**), and effective latitude (**F**) in 1657 females (top panels; red) and 1013 males (bottom panels; blue) aged 20 to 60 years. The blue line represents generalized additive models with integrated smoothness. Pearson correlation analysis shows a positive correlations between WT and FFM (r = 0.442, P < 0.001), TEE (r = 0.488, P < 0.001), PAL (r = 0.388, P < 0.001), and altitude (r = 0.100, P < 0.001). WT was negatively correlated with percent body fat (–0.311, P < 0.001). Outdoor air temperature was only weakly correlated with WT in the whole sample (r = 0.160, P < 0.001). A significant curvilinear relationship between WT and the air temperature and between WT and effective latitude were observed (see text for details). Average WT reached the highest values at ~0° and the lowest values at ~–50° or +50° of effective latitude. People who lived near the Arctic Circle had higher average WT than those who lived around –50° or +50° of effective latitude.

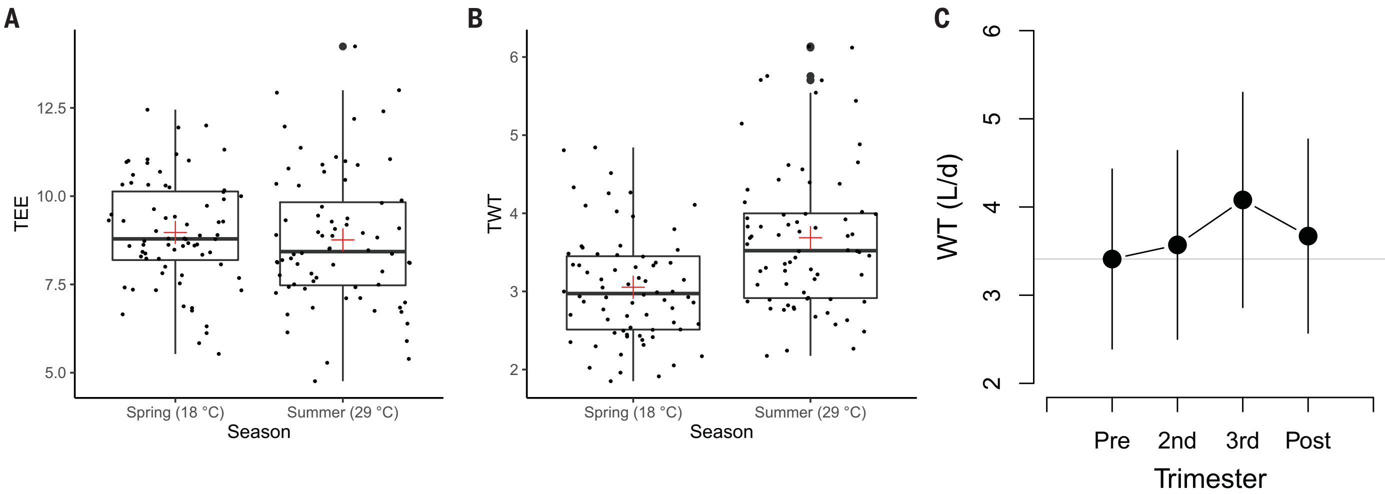

Fig. 4. Effect of season or pregnancy on WT. (**A**) Repeated-measures analysis of 72 people (31 females and 41 males) showing that WT was significantly higher in the summer (3.7 ± 1.0 liters/d), with an average temperature of 29°C, than in the spring (3.0 ± 0.7 liters/d), with an average temperature of 18°C (P < 0.001). (**B**) By contrast, TEE was not significantly different between summer and spring (P = 0.233). (**C**) Repeated-measures analysis of 63 pregnant women showing that the total WT was significantly higher during late pregnancy and lactation [data are from (*17*)]. Pre, pre-pregnancy; Post, 27 weeks postpartum.

with access to air-conditioning and heating, people are exposed primarily to a narrow range of indoor temperatures (18 to 25°C) (*19*). By comparison, people living in low-HDI countries are more likely to be exposed to ambient environmental temperatures without climate control. This view is consistent with the greater size-adjusted WT for hunter-gatherers and manual laborers compared with sedentary adults in industrialized countries (*2*). Similarly, a previous comparison of regional water use (*20*) noted that it is relatively high in Africa and relatively low in Europe, and results from our analysis may help to explain why.

We developed the following equation to predict WT (Fig. 6):

$$\text{WT (ml/d)} = [1076 \times \text{PAL}] + [14.34 \times \text{body weight (kg)}] + [374.9 \times \text{sex}] + [5.823 \times \text{humidity (\%)}] + [1070 \times \text{athlete status}] + [104.6 \times \text{HDI}] + [0.4726 \times \text{altitude (m)}] - [0.3529 \times \text{age (years)}^2] + [24.78 \times \text{age (years)}] + [1.865 \times \text{temperature (°C)}^2] - [19.66 \times \text{temperature (°C)}] - 713.1 \quad (1)$$

where sex is 0 for female and 1 for male; athlete status is 0 for nonathlete and 1 for athlete; and HDI is 0 for high-HDI countries, 1 for middle-HDI countries, and 2 for low-HDI countries. This equation explains 47.1% of the variation in WT: An increase in PAL of 1.0 induces an ~1000-ml increase in WT; a 50-kg increase in body weight induces an ~700-ml increase in WT; a 50% increase in relative humidity induces an ~300-ml increase in WT; and a 1000-m increase in altitude induces an ~500-ml increase in WT. Males exhibit ~400 ml more WT than do females of the same weight because males have greater FFM and a lower percent body fat. People who live in low-HDI countries exhibit ~200 ml more WT than people who live in high-HDI countries after

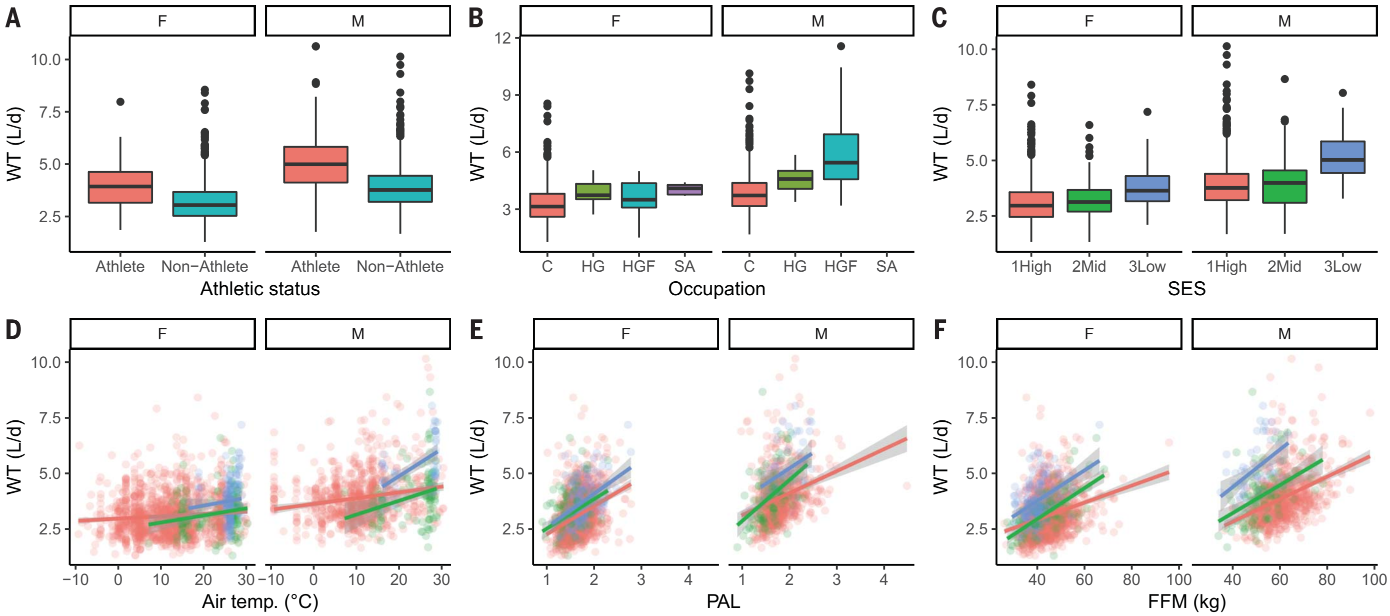

Fig. 5. Effect of lifestyle factors on WT. (**A**) Athletes had higher WT than nonathletes, even after adjusting for physiological and environmental variables ($P < 0.001$). (**B**) Hunter-gatherers (HG), mixed farmer and hunter-gatherers (HGF), and subsistence agriculturalists (SA) had higher WT than other people (C), even after adjusting for physiological and environmental variables ($P < 0.001$). Note that there are no males in the database who fell into the SA category. (**C**) People who lived in low-HDI countries had higher WT than people in high- or middle-HDI countries, even after adjusting for physiological and environmental variables ($P < 0.001$). (**D** to **F**) Relationship between WT and outdoor air temperature, PAL, and FFM. The countries were categorized as high-HDI (red), middle-HDI (green), and low-HDI (blue). (D) A significant interaction ($P < 0.001$) was observed between outdoor air temperature and HDI in WT. The association between outdoor air temperature and WT was weak in high-HDI countries ($r = 0.086$, $P < 0.001$) but strong in men in low-HDI countries ($r = 0.604$, $P < 0.001$). (E and F) A significant interaction ($P < 0.001$) was observed between HDI and PAL or FFM in WT. Correlation coefficients were significantly higher ($P < 0.001$) in low-HDI countries ($r = 0.484$ to 0.670, $P < 0.001$) than in high-HDI countries ($r = 0.367$ to 0.510, $P < 0.001$).

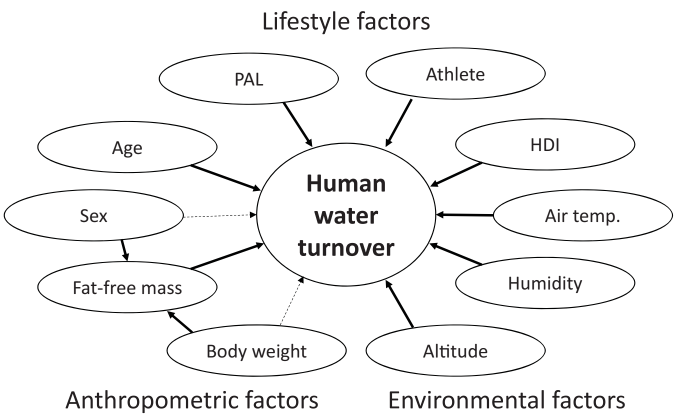

Fig. 6. Determinants of human WT. Objective measures of WT from a large global dataset indicate that WT is strongly related to anthropometric, lifestyle, and environmental factors.

controlling for the other measured variables. Athletes have ~1000 ml more WT than do nonathletes with everything else being equal. A U-shaped relationship between WT and air temperature shows ~1000 ml more WT at +30°C air temperature than the nadir between ±0 and +10°C air temperature, and also ~400 ml more WT at −10°C air temperature than that nadir. A curvilinear relationship between WT and age shows that the peak WT is between the 20s and 40s and decreases after the 50s; there is ~700 ml less WT at age 80 than at age 30.

A 20-year-old male weighing 70 kg who is not athletic, has a PAL of 1.75, and lives in a high-HDI country at 0-m altitude where the mean air temperature is 10°C and relative humidity is 50% has a predicted WT of 3.2 liters/d. A nonathletic 20-year-old female weighing 60 kg living at the same location will have a WT of 2.7 liters/d. By contrast, a 20-year-old male weighing 70 kg who is athletic, has a PAL of 2.5, and lives in a high-HDI country at 2000-m altitude where the mean air temperature is 30°C and relative humidity is 90% has a WT of 7.3 liters/d. An athletic 20-year-old female weighing 60 kg living at the same location will have a WT of 6.8 liters/d. In this equation, we used weight and sex as a proxy for FFM because body composition is not easily measured in the daily life. If body composition can be assessed, then the following equation can be used to predict WT (Fig. 6):

$$\text{WT (ml/d)} = [861.9 \times \text{PAL}] + [37.34 \times \text{fat-free mass (kg)}] + [4.288 \times \text{humidity (\%)}] + [699.7 \times \text{athlete status}] + [105.0 \times \text{HDI}] + [0.5140 \times \text{altitude (m)}] - [0.3625 \times \text{age (years)}^2] + [29.42 \times \text{age (years)}] + [1.937 \times \text{temperature (°C)}^2] - [23.15 \times \text{temperature (°C)}] - 984.8 \quad (2)$$

TEE was not included in the equations because sex, body weight, and PAL capture the variance explained by TEE. When FFM was included in the model, the effect of sex was not significant. The sex difference of WT can be explained by the sex difference of the FFM/body weight ratio.

Values of WT in this study represented average values under normal conditions. Many health conditions, including parasitic infections and diarrhea, affect water loss and intake (*21*). Additionally, the current study did not assess any indicators of hydration status and did not determine whether the participants were adequately hydrated. Older adults or vulnerable individuals have a higher risk of both acute and chronic dehydration (*22*, *23*) because they have a decreased thirst response. Medications, anorexia, or frailty and low TBW (storage) are associated with a lower skeletal muscle mass (i.e., sarcopenia). Skeletal muscle tissues contain a large volume of water, particularly in the intracellular space (*24*). Mean WT values presented here are not necessarily representative of all people or conditions (*21*) but do provide a comparative framework for investigating water intakes in populations with greater needs.

Objective measures of WT from a large global dataset indicate that it is strongly related to anthropometric, lifestyle, and environmental factors. We found significant correlations between WT and several known markers of health, wellness, and disease risks. WT is positively correlated with FFM, TEE, PAL, and athletic status and negatively correlated with percent body fat and age in adults. WT may therefore provide a useful integrative biomarker of metabolic health. Biomarkers that capture global metabolic health are generally lacking and of potentially enormous value for public health and medical management.

As shown in Fig. 1, we need to be aware that WT obtained by the hydrogen isotope dilution and elimination technique is not equal to daily water intake from liquids and foods. Metabolic water accounts for ~10% of WT, and respiratory water uptake and transcutaneous water uptake each account for 2 to 3% of WT. Therefore, daily water intake from liquids and foods is equivalent to ~85% of WT (*7*). An unsolved question is what percentage of water intake comes from food? Self-reported surveys around the world have suggested that 20 to 50% of daily water intake is from food (*5*, *6*, *11*). These estimates, however, are questionable because many studies using self-reported surveys underestimate energy, protein, and salt intake. Therefore, dietary survey methods probably also underestimate the water intake in food and overestimate that from drinking water and other beverages. Conversely, if people consume a higher-energy-density diet with lower water content (*25*, *26*), then they may need more water from drinks and beverages. Without measured water intakes from food, it was not possible to assess the relative contributions of food and drinking water or beverages to WT in this study, and indeed no studies to date have adequately addressed this issue. Nonetheless, the current study clearly indicates that one size does not fit all for drinking water guidelines, and the common suggestion that we should drink eight 8-ounce glasses of water per day (~2 liters) is not backed up by objective evidence.

We provide equations to predict human WT using environmental, lifestyle, and anthropometric factors guided by a large dataset. Improved guidelines are of increasing importance because of the explosive population growth and climate change the world currently faces, which will affect the availability of water for human consumption (*27*, *28*) and noningestive uses such as irrigation, cooling, and manufacturing (*29*). Presently, 2.2 billion people lack access to safe drinking water (*30*). The WT measures provided here can help to shape strategies for drinking water and water-enriched food management as the global population increases and the climate changes.

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SUPPLEMENTARY MATERIALS

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Science

Variation in human water turnover associated with environmental and lifestyle factors

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Human water requirements
Water requirements for human consumption may become more difficult to manage as changes occur in the Earth's climate and in human populations. Yamada *et al*. used an isotope-labeling technique to follow water intake and loss in individuals in a broad range of environments and living conditions. Total water input and output varied according to many factors, including body size, physical activity, air temperature, humidity, and altitude. The authors derived an equation to predict water usage according to such parameters. —LBR