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Low-intake dehydration prevalence in non-hospitalised older adults: systematic review and meta-analysis

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<u>Abstract</u>

Background and Aims

Low-intake dehydration amongst older people, caused by insufficient fluid intake, is associated with mortality, multiple long-term health conditions and hospitalisation. The prevalence of low-intake dehydration in older adults, and which groups are most at-risk, is unclear. We conducted a high-quality systematic review and meta-analysis, implementing an innovative methodology, to establish the prevalence of low-intake dehydration in older people (PROSPERO registration: CRD42021241252).

Methods

We systematically searched Medline (Ovid), Cochrane CENTRAL, Embase (Ovid), CINAHL and Proquest from inception until April 2023 and Nutrition and Food Sciences until March 2021. We included studies that assessed hydration status for non-hospitalised participants aged ≥65 years, by directly-measured serum/plasma osmolality, calculated serum/plasma osmolarity and/or 24-hour oral fluid intake. Inclusion, data extraction and risk of bias assessment was carried out independently in duplicate.

Results

From 11,077 titles and abstracts, we included 61 (22,398 participants), including 44 in quality-effects meta-analysis.

Meta-analysis suggested that 24% (95% CI: 0.07, 0.46) of older people were dehydrated (assessed using directly-measured osmolality >300mOsm/kg, the most reliable measure). Subgroup analyses indicated that both long-term care residents (34%, 95% CI: 0.09, 0.61) and community-dwelling older adults (19%, 95% CI: 0.00,

0.48) were highly likely to be dehydrated. Those with more pre-existing illnesses (37%, 95% CI: 0.14, 0.62) had higher low-intake dehydration prevalence than others (15%, 95% CI: 0.00, 0.43), and there was a non-significant suggestion that those with renal impairment (42%, 95% CI: 0.23, 0.61) were more likely to be dehydrated than others (23%, 95% CI: 0.03, 0.47), but there were no clear differences in prevalence by age, sex, functional, cognitive or diabetic status. GRADE quality of evidence was low as to the exact prevalence due to high levels of heterogeneity between studies.

Conclusion

Quality-effects meta-analysis estimated that a quarter of non-hospitalised older people were dehydrated. Widely varying prevalence rates in individual studies, from both long-term care and community groups, highlight that dehydration is preventable amongst older people.

Implications

One in every 4 older adults has low-intake dehydration. As dehydration is serious and prevalent, research is needed to better understand drinking behaviour and assess effectiveness of drinking interventions for older people.

Keywords

Systematic review; Dehydration; Dementia; Aged; Geriatrics, Prevalence

1. Introduction

Studies report that many older adults have low-intake dehydration, caused by insufficient fluid intake (1-3), though robust prevalence data are lacking. It is unclear how consistent dehydration prevalence is across different older populations and reports often use unreliable measures of hydration status. Low-intake dehydration negatively impacts the health of older adults and is associated with urinary tract infection, hospitalisation, multiple long-term health conditions and mortality (1-4). While low-intake dehydration appears to contribute substantially to economic costs and pressures on health and social care systems (5-7), economic burden analyses of low-intake dehydration are difficult to conduct without robust prevalence data.

Older adults are at higher risk of low-intake dehydration than younger adults due to an interplay of physiological, physical, cognitive, psychological and communication factors. Ageing results in kidneys becoming less effective at concentrating urine, so older adults are less able to conserve fluid (8) while loss of the thirst sensation (the usual stimulus to drink) (8) reduces fluid intake. Diuretic medication stimulates fluid loss (9, 10), while reduced strength, grip and mobility (11) can impede access to drinks. Impaired cognition may lead to forgetting to drink, whilst fewer social opportunities to drink (12) and fear of urinary incontinence often leads to reduced fluid intake. While the UK National Health Service (NHS) recommends that adults consume 6-8 cups of drink daily (1.5-2 litres) (13), the European Society of Clinical Nutrition and Metabolism (ESPEN) recommends that women should consume 1.6L of drinks daily and men 2L in addition to 20% fluid from food (14). However, these guidelines might not be known by older people (15). Communication difficulties, cultural differences and language barriers may also result in reduced fluid intake

where older adults depend on others to provide drinks (16). Despite many risk factors having been evidenced, it remains unclear whether risk of dehydration continues to increase with increasing age or whether certain groups of older adults are at higher risk, associated with other factors, such as frailty and impaired physical and cognitive abilities. Where dehydration risk factors are modifiable there is potential to decrease this risk with appropriate interventions, thus contributing to healthy ageing.

The reference standard for assessing low-intake dehydration in older adults is directly-measured serum or plasma osmolality (>300mOsm/kg) (14, 17-19), which assesses the osmotic concentration of blood serum or plasma. With low-intake dehydration, plasma and serum become more concentrated, so osmolality rises (20). Calculated serum or plasma osmolarity using the Khajuria and Krahn equation can be used to accurately estimate osmolality, though other equations are less useful (20). While salivary osmolality demonstrates moderate diagnostic utility in older adults (21, 22) it is not commonly used as the technology is underdeveloped and susceptible to common confounding factors (including medications, recent food, and fluid intake), (22). These confounding factors are more easily accounted for in research settings. BUN/Creatinine ratio is accessible, thus routinely used, but lacks specificity to low-intake dehydration in older adults due to its reliance on healthy kidney function which decreases in ageing kidneys (1). Commonly used clinical signs and symptoms of dehydration, such as skin turgor or urine colour, are not diagnostically accurate among older adults (17, 23). Oral fluid intake may be recorded for clinical and research purposes but is infrequently reported over a complete 24 hours in community and long-term care settings (16, 24). Records are

frequently inaccurate as drinks intake is commonly estimated and not measured. Robust measurement of fluid intake involves measuring the contents of drinking vessels, making exact records of drinks consumed and accounting for fluids not consumed. The UK Fluid Intake Study in our Elders (FISE) study reported substantial differences between researcher-observed 24-hour drinks consumed by care home residents and care home drinks records (25).

Although a recent systematic review of 19 studies reported that 0.8% to 38.5% of nursing home residents were dehydrated (26), there are some eligible studies which were not included within the original review, as well as newer papers meeting inclusion, since the review was published. The authors of the 2018 systematic review also included some datasets twice, included some less robust measures of dehydration and did not investigate dehydration amongst community-dwelling adults (26). Accurate prevalence data and identification of groups most at risk of low-intake dehydration would enable targeted development and implementation of evidence-based interventions to prevent dehydration and its associated poor outcomes. In this systematic review, we aimed to establish the global prevalence of low-intake dehydration among adults aged ≥65 years in non-hospital settings, using robust measures of dehydration and investigated differences in dehydration prevalence between care settings, by age, multiple long-term health conditions and dependency level through robust systematic review methodology for prevalence studies (27, 28).

2. Methods

This systematic review and meta-analysis was pre-registered on PROSPERO (CRD42021241252) (29), followed Cochrane and Joanna Briggs Institute guidance for prevalence reviews (27, 28) and is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (30). We did not require or seek ethical approval, as this was secondary research.

2.1 Searches

We developed a complex search strategy (peer-reviewed using the Peer Review of Electronic Search Strategies (PRESS) 2015 guidelines), following the format: *[aged] and [prevalence or incidence] and [dehydration or fluid] and [human]*. The full text of the Medline search strategy, including Boolean operators, truncation, text and indexing terms, is available in the PROSPERO register. We searched Medline (Ovid), Cochrane CENTRAL, Embase (Ovid), CINAHL Complete/Ultimate, Proquest Dissertations Theses A&I/Global from inception until 20th April 2023 and Nutrition and Food Sciences from inception until 18th March 2021 (we were unable to update this search). There were no restrictions on publication status or language. We applied Cochrane's sensitive search filter to search for "humans", within Medline (Ovid) and Embase (Ovid) (28). We also examined the reference lists of dehydration-related systematic reviews, reviews and included studies.

2.2 Eligibility criteria

We assessed titles and abstracts, then full text papers, using Covidence software (31), independently in duplicate, against the inclusion criteria:

Participants: Adults aged \geq 65 years living in community or long-term care settings, in any part of the world, receiving fluids orally (sample mean age \geq 65 years, or \geq 80% of the sample was aged \geq 65 years, or where separate data was available for

participants aged \geq 65 years from a larger sample).

Exposure: Hydration status assessed by directly-measured serum or plasma osmolality, calculated serum or plasma osmolarity, salivary osmolality and/or 24-hour oral fluid intake (where fluids had been accurately measured for \geq 24 hours). *Study type*: Case studies, cross-sectional, cohort, or case-control studies, controlled clinical trials or before-after studies, each with at least five participants aged \geq 65 years.

We resolved any conflicts on study inclusion by discussion or by involving a third reviewer to arbitrate and make an overall decision. Members of the review team (DB and LH), who had relevant literature in the field, did not screen or data-extract their own papers.

We initially included studies that reported low-intake dehydration for participants from any setting within this review. Given the large number of included studies we then split the systematic review into two, with hospital setting studies being separated and considered in a separate review (32). This paper reports on studies from community and long-term care settings. We originally included the BUN:Creatinine ratio as an outcome measure. However this was later excluded as it does not accurately distinguish between impaired renal function and dehydration amongst older adults (1).

2.3 Data Extraction

The review team were trained in assessing inclusion, data extraction, risk of bias assessment and Covidence software (31). The whole review team piloted our data extraction template in Covidence using five papers, and the forms were edited for clarity (wording amendments and an additional question on delirium). We completed data extraction of the remaining papers independently in duplicate, resolving

disagreements, when there were discrepancies in data extracted, by discussion. Multiple reports (conference abstracts, publications and/or reports) from the same study were merged in Covidence to create one study. Wherever possible, we sought further information from linked papers, study websites and corresponding authors. In the case of 105 studies which referred to large cohorts, we sought the original datasets via study websites and authors. We excluded studies where key inclusion data were missing. Data extraction and risk of bias assessment were carried out independently in duplicate within Covidence. We extracted detailed data on bibliographic details, study and participant characteristics and outcome measures. Reviewers had fluent proficiency in spoken and written English, Dutch and German, and a good level of proficiency in spoken and written French and Spanish, to translate articles. We used the Microsoft Word translation tool and Google Translate to translate two articles from Korean and Japanese, for which we did not have language skills in, and used both tools to corroborate and validate each tool's translations.

2.4 Risk of Bias Assessment

We assessed risk of bias using an adapted version of the Joanna Briggs Institute 'Checklist for prevalence studies' (33). See Appendix 1 (Supplementary material) for our adaptations and Appendix 2 (Supplementary material) for how study-wide risk of bias was calculated and how it was used within quality-effects meta-analysis. We assessed studies as low risk of bias if they scored at least 2 out of 3 on questions 1-4, which related to the reliability of how fluid intake/dehydration was measured, how appropriately participants were recruited and how well described the participants and setting were described.

2.5 Data Analysis

Where study authors had provided data on the number of people dehydrated within their sample, in line with our recognised cut-offs (>300mOsm or <1.5L)¹, we used these numbers alongside the sample size. When these data were not provided, we used mean osmolality, osmolarity or oral fluid intake² and the measure of variance to estimate the number of people dehydrated based on a normal distribution. If no relevant data were provided, studies were ineligible for meta-analysis and narratively synthesised using Synthesis Without Meta-Analysis in Systematic-Reviews (SWiM) (34) guidance and treated as missing data within the meta-analysis. Some large datasets were downloaded from study websites, or requested from authors (NU-AGE (20, 35), NHANES 2017-March 2020 (36) and National Irish Survey (37)) and the datasets used to calculate numbers with low-intake dehydration, within relevant subgroups directly.

We used Meta-XL version 5.3 to conduct meta-analysis to determine the prevalence of low-intake dehydration within this systematic review (38, 39). We had planned to use random-effects meta-analysis, however this over-dispersed prevalence data, where there was gross heterogeneity, resulting in an unweighted average (38, 39). Instead, on the advice of the Meta-XL developer (Suhail Doi, (38, 39)), we used a quality-effects model, weighted by quality score using double arcsine transformation which the developers argue is superior in handling the heterogeneity in prevalence data (See Appendix 3). We assessed heterogeneity using I² and used forest plots

¹ The NHS recommends 1.5I-2.0L (6-8cups) of oral fluid intake, which varies to other global guidelines, so we decided to use 1.5L as a minimum, for our oral fluid intake cut-off.

² Oral fluid intake sometimes included fluids from foods – specific details of this are included within Appendix 6 'characteristics of included studies table'.

and tables to present the meta-analyses, sensitivity, and subgroup analyses. For studies that assessed more than one measure of hydration status we used the highest quality measure in meta-analysis for preference, the first of: directlymeasured serum or plasma osmolality, calculated serum or plasma osmolarity and 24-hour oral fluid intake. Meta-XL does not allow formal assessment of heterogeneity between subgroups, so we assumed that subgroups were distinct from each other when the mean assessment of heterogeneity was different by more than 0.2.

Our first meta-analysis was subgrouped by the measure of dehydration used. We planned to combine all outcome measures for further analyses if results from these subgroups were homogeneous; but if found to be heterogeneous, focus on the data from the most reliable measures of dehydration, serum or plasma osmolality, as our main analysis.

We planned sensitivity analyses removing studies at high risk of bias, as well as limiting to the most robust measures of low-intake dehydration: directly-measured serum or plasma osmolality and calculated serum or plasma osmolarity using the Khajuria and Krahn equation (40).

We used subgroup analyses to explore the following pre-specified sources of heterogeneity (detailed in the PROSPERO register):

- Care setting: long-term care setting, community setting
- Age: mean age 65-74, 75-84, 85+
- Health conditions (Diabetes, cognitive impairment and renal impairment were found to be associated with low-intake dehydration in the UK DRIE study, and so we explored this further in subgrouping): <2 conditions, ≥2 conditions
 (Diabetes, cognitive impairment and renal impairment) (Appendix 4)

- Renal impairment: No renal impairment (<20% within sample), renal impairment (sample has some renal impairment prevalence ≥20%)
- Cognitive impairment: No impairment, low impairment (>0-29% of sample has cognitive impairment/ dementia) Middle impairment (30-59% of sample has cognitive impairment/ dementia), High impairment (60-100% of sample has cognitive impairment/ dementia)
- Diabetes: No diabetes (<20% within sample), diabetes (sample has some diabetes prevalence ≥20%)
- Dependency on others: fully independent, mixed dependency (a mixed sample of participants with varying dependency levels, for assistance with drinking) (Appendix 4)
- Sex: Male, Female (not pre-specified, carried out post-hoc in response to peer-reviewer comments).

We used individual participant information from study datasets (where available) to conduct subgroup analyses. Where this was not possible, we included the whole study in the most appropriate subgroup.

3. Results

3.1 Search results

Searches identified 11,077 titles and abstracts, deduplicated in Covidence to 9,193 titles and abstracts. Screening independently in duplicate identified that 7,052 titles and abstracts were irrelevant and 2,234 were assessed as full texts. Of these, 61 were found to be eligible and included in the review. Full text studies were excluded for reasons such as wrong age group, wrong method of assessing hydration status, hospital setting (Appendix 5). Forty-four studies had sufficient data to be included within the meta-analysis (Figure 1).

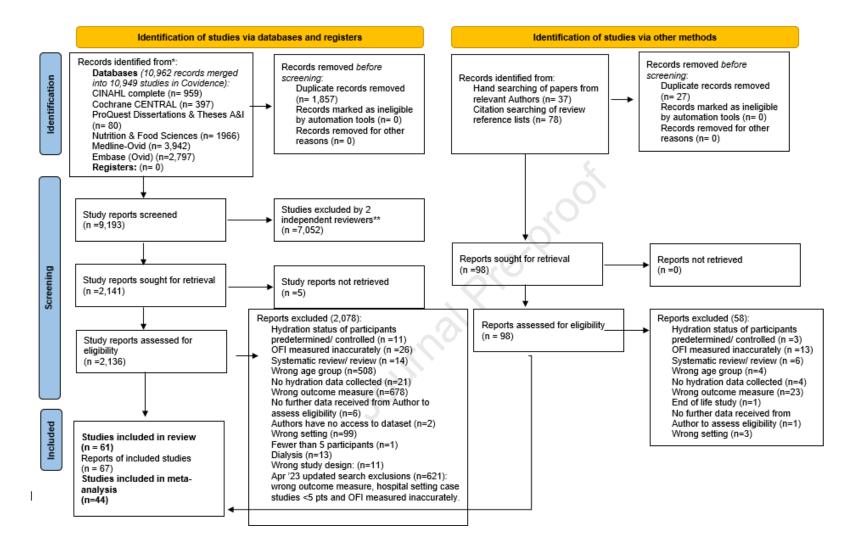


Figure 1: PRISMA flow diagram

3.2 Characteristics of the studies included

The characteristics of all included studies are detailed in the supplementary file (See Appendix 6). Of the included studies, 29 reported directly-measured serum or plasma osmolality (2,955 participants; 60.3% females (1, 17, 35, 41-67)) (of which 21 could be included in meta-analysis) (Table 1), six calculated serum or plasma osmolarity (3,891 participants, all 6 included in meta-analysis), 25 reported oral fluid intake (15,232 participants) (17 included in meta-analysis), and one salivary osmolality (53 participants) (not included in meta-analysis).

One osmolality study (included within meta-analysis) (49) was translated from Japanese into English, and one oral fluid intake study (not included within meta-analysis) was translated from Korean into English, using translation tools.

Author	Setting	Country	Sample	Study Design	Mean Age	Health Conditions	Mean Osmolality
			size				
*Albert et al.	Commu	United	18	Non-randomised	Control gp: 65 (SD 2)	Cognitive impairment	Experimental gp: 313 mOsmol/kg
(1989) (41)	nity	States		experimental	years	50%	(SEM 4)
				study	Experimental gp: 68		Control gp: 300 mOsmol/kg (SEM
					(SD 3) years.		3)
*Bossingham	Commu	United	21	3-arm crossover	Men: 72 years (SD 4)	None	Men: 291 mOsm/kg (SD 12)
et al. (2005 <i>)</i>	nity	States		non-randomised	Women: 75 years (SD		Women: 291 mOsm/kg (SD 4)
(42)				intervention study	4)		
Crowe et al.	Commu	United	6	Cross-sectional	72 years	None	285 mOsm/kg
(1987) (43)	nity	Kingdom					
Engelheart	Commu	Sweden	56	Cohort study	Home health care	Cognitive impairment	299 mOsmol/kg
et al. (2021)	nity				sample (n=69): 82		
(44)					years		

Author	Setting	Country	Sample	Study Design	Mean Age	Health Conditions	Mean Osmolality
			size				
Farrell et al.	Commu	Australia	12	Non-randomised	68 years (SD 3)	NR	283.5 mOsm/kg
(2008) (45)	nity			experimental			
				study			
Fraser et al.	Commu	United	27	Cross-sectional	NR (Age range: 70-83)	Cognitive impairment	289 U/L
(1989) (46)	nity	Kingdom				0%	
Kakeshita et	Commu	Japan	211	Cohort study	NR (Median age of	Renal impairment	NR
al. (2022)	nity				CKD group (n=121):	57.3%	
(47)					71 years, Non-CKD	Diabetes 23.2%	
					group (n=90): 65		
					years)		
*NUAGE and	Commu	United	1088	Cross-sectional	71 years (SD 4)	Cognitive impairment	303 mOsm/kg (SD 12.1)
Hooper et al.	nity	Kingdom				1%	
(2015) (20)		, Italy,				Renal impairment 16%	
		Netherla				Diabetes 4%	
		nds,					

Author	Setting	Country	Sample	Study Design	Mean Age	Health Conditions	Mean Osmolality
			size				
		France,					
		Poland					
*Hooper et	LTC	United	188	Cohort study	86 years (SD 8)	Cognitive impairment	293.4 mOsm/kg (SD 8.1)
al. (2016) (1)		Kingdom				54%	
						Renal impairment 42%	
						Diabetes 19%	
*Johnson et	LTC	Sweden	55	Cohort study	84 years	Renal impairment 22%	307.5 mOsmol/kg (SD 8.9)
al. (2018)							
(48)							
*Kajii et al.	Commu	Japan	71	NR	77 years (SD 7)	NR	287.1 (SD 5. 3) mOsm/L
(2005) (49)	nity						

Author	Setting	Country	Sample	Study Design	Mean Age	Health Conditions	Mean Osmolality
			size				
*Mack et al.	Commu	United	8	Non-randomised	69 years (SE 2)	NR	287 (SD 1) mOsmol/kg/H ₂ 0
(1994) (50)	nity	States		experimental			
				study			
*Marra et al.	LTC	United	132	Cross-sectional	83 years (SD 11)	Cognitive impairment	298.9 mOsm/kg (SD 8.8)
(2016) (51)		States		study		76%	
						Renal impairment 22%	
						Diabetes 29%	
*McKenna et	Commu	Republic	24	Non-randomised	HONK gp: 71 years	Diabetes 67%	HONK gp: 293.5 (SD 2.8) mmol/kg
al. (1999)	nity	of		experimental	Diabetes gp:		Diabetes gp: 286.8 mmol/kg (SD
(52)		Ireland		study	71 years		2.0)
					Control gp: 70 years		Control gp: 287.3 mmol/kg (SD 2.5)
*Morgan et	Commu	United	35	Cross-Sectional	77 years (SD 8)	NR	286.56 mOsm/kg (SD 6.87)
al. (2003)	nity	States		study			
(53)							

Author	Setting	Country	Sample	Study Design	Mean Age	Health Conditions	Mean Osmolality
			size				
*Nagae et al.	LTC	Japan	89	Prospective,	88 years (SD 6)	Cognitive impairment	288.5 (SD 6.1) mOsm/kg
(2020) (54)				observational		56%	
				study		Renal impairment	
						Diabetes 11%	
*O'Neill et al.	LTC	United	39	Cross-Sectional	83 years	Cognitive impairment	302 mOsm/kg (SD or SE 8)
(1989) (55)		Kingdom		study			
*O'Neill et al.	LTC	United	58	Cohort study	81 years (SD 7)	Renal impairment 2%	304 mOsmol/kg (SD 8)
(1990) (56)		Kingdom				Diabetes Mellitus 2%	
*O'Neill et al.	LTC	United	12	Cross-sectional	Gp A: 83 years	NR	Gp A: 294.2 mOsmol/kg
O Neill et al.	LIC	United	١Z	CIUSS-Sectional			
				study	Gp B: 80 years		Gp B: 293.8 mOsmol/kg

Author	Setting	Country	Sample	Study Design	Mean Age	Health Conditions	Mean Osmolality
			size				
*Phillips et al.	Commu	United	7	Non-randomised	71 years	NR	288.4 mOsmol/KgH ₂ 0
(1984) (58)	nity	Kingdom		experimental			(SE 1.3)
				study			
Phillips et al.	Commu	Australia	7	Non-randomised	70 years	NR	Pre-isotonic infusion gp: 283
(1991) (59)	nity			experimental			mOsm/kg
				study			Pre-hypertonic infusion gp: 279
							mOsm/kg
*Phillips et al.	Commu	Australia	10	Non-randomised	NR (Range: 64-76	NR	290.4 mOsmol/kgH ₂ 0 (SE 3.1)
(1993) (60)	nity			experimental	years)		
				study			
	.=						
*Simmons et	LTC	United	28	Non-randomised	Intervention gp: 89	Renal impairment	Intervention gp: 303.6 (SD 9.1)
		States		experimental	years (SD 7)		Control gp: 303.4 (SD 8.5)
al. (2001)							

Author	Setting	Country	Sample	Study Design	Mean Age	Health Conditions	Mean Osmolality
			size				
					Control gp: 86 years		
					(SD 6)		
*Sri-On et al.	Commu	Thailand	704	Cohort study	NR (Median age: 72	Renal impairment 0%	NR
(2023) (62)	nity				years).	Diabetes 25.1%	
*Stachenfel	Commu	United	6	Non-randomised	72 years (SE 2)	Renal impairment 0%	286mOsm/kg (SE 1.5)
d et al.	nity	States		experimental			
(1996) (63)				study			
Stachenfeld,	Commu	United	6	Cross-sectional	70 years (SD 2)	NR	Time Control gp: 293 mOsmol-kg-1
et al. (1997)	nity	States		study			H ₂ 0
(64)							Head out water Immersion gp: 294
							mOsmol-kg-1 H ₂ 0
Takamata et	Commu	Japan	9	Non-randomised	70 years (SE 3)	NR	294 mOsm/kg H ₂ 0
al. (1999)	nity			experimental			
(65)				study			

Author	Setting	Country	Sample	Study Design	Mean Age	Health Conditions	Mean Osmolality
			size				
*Wu et al.	LTC	Taiwan	111	Cross-sectional	75 years	Cognitive impairment	287.85 mmol/kg (SD 10.51)
(2011) (66)				study		18%	
*Zappe	Commu	United	6	Non-randomised	67 years (SD 1)	NR	292 mOsmol/kgH ₂ 0 (SE 2)
(1996) (67)	nity	States	U	experimental			
				study			

Table 1: Brief characteristics of included studies reporting serum or plasma osmolality [* included in meta-analysis]

Table 1 Glossary: LTC: long term care, Gp: group, SD: standard deviation, SEM: standard error of mean, SE: standard error, NR: not reported, U/L: units per litre, HONK: Hyperglycaemic hyperosmolar non-ketotic coma, CKD: Chronic kidney disease

The 29 included studies reporting directly-measured serum or plasma osmolality (shown in Table 1) were from a total of 12 countries. Twenty studies (17, 35, 41-47, 49-50, 52-53,58-60, 62-65, 67) recruited community-dwelling older adults (mean age range: 67-82 years) and nine (1, 48, 51, 54-57, 61, 66) included those living in long-term care settings (mean age range: 75-88 years). The prevalence of cognitive impairment was reported in eight studies (1, 35, 41, 51, 52, 54, 55, 66), but unreported in 18

studies (42, 45, 47-50, 53, 56-57, 59-65, 67). The prevalence of renal impairment was reported in eleven studies (1, 35, 46, 49, 52, 54, 58, 59), but unreported in 12 studies (41, 44-46, 49-50, 53, 55, 57, 59, 60, 65). The prevalence of diabetes was reported in eight studies (1, 35, 47, 51-52, 54, 56, 62), but unreported in 18 studies (41, 42, 44, 45-46, 48-50, 55, 57, 59-61, 63-67). Nine studies specifically excluded participants who had cognitive impairment, and/or renal impairment, and/or diabetes (42, 43, 46, 53, 57-58, 62, 66-67).

Six studies reported including participants with mixed functional dependency (1, 51, 54, 57, 62, 66), fourteen only included participants who were functionally independent (42-43, 45-46, 49-50, 52, 58-60, 63-64, 65, 67), while functional dependency of participants was unclear or unreported in seven studies. Although some authors reported functional dependency using assessment scales such as the Barthel Index or the Dependency in Activities of Daily Living from the Minimum Dataset (MDS-ADL), most authors did not report the method used to assess functional dependency. The characteristics of studies using other methods of assessment of dehydration are summarised in Appendix 6.

3.3 Risk of bias of included studies

Risk of bias assessments for all 61 included studies are shown in the supplementary material (Appendix 7), of which 30 were assessed as being at low risk of bias. Of the 29 included studies reporting serum or plasma osmolality, we assessed 15 as being at low risk of bias, and 14 as high risk of bias.

3.4 Meta-Analysis and Narrative Synthesis

We initially conducted a quality-effects weighted meta-analysis including all 44 studies eligible for meta-analysis, subgrouped by hydration measure, with each study represented only once. Dehydration prevalence assessed using directly-measured serum or plasma osmolality was 0.26, 95% CI 0.107-0.46, I²=97%, using 24-hour oral fluid intake: 0.77, 95% CI 0.56-0.95, I²=97%, and using calculated osmolarity: 0.26, 95% CI 0.00-1.00, I²=100% (Figure 2). As the mean prevalence was different between subgroups by more than 0.2, further analyses were conducted using studies providing data on serum or plasma osmolality only, as this was the most robust measure.

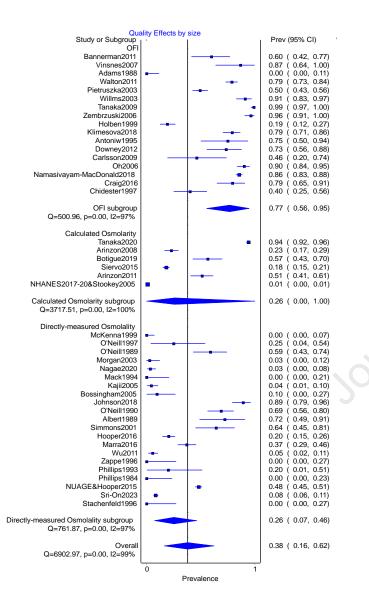


Figure 2: Forest plot of studies reporting serum or plasma osmolality, oral fluid intake, and calculated serum or plasma osmolarity (n=44)

3.5 What is the prevalence of dehydration assessed using osmolality?

The prevalence of low-intake dehydration, assessed using 21 studies reporting serum/plasma osmolality, the reference standard, was 26% (95% CI: 0.07, 0.46). The proportions of dehydrated older adults between individual studies was highly heterogeneous (I²=96%) and ranged from zero to 0.89 (Figure 2). The prevalence of low-intake dehydration (assessed using any dehydration measure) was stable to sensitivity analyses of studies only at low risk of bias (27%, 95% CI: 0.06,0.53, I² 99%, 23 studies), as well as osmolality studies combined with calculated osmolarity studies using the Khajuria and Krahn (40) equation (23%, 95% CI: 0.10,0.41, I² 97%, 22 studies) (Appendix 8). This suggests that the prevalence of low-intake dehydration varies in different groups of older adults and is very high in many groups.

We are aware of some data missing from the meta-analyses. Data from eight community-based studies, which assessed dehydration using serum or plasma osmolality (43-47, 59, 64-65), could not be included because they either did not report the number of participants dehydrated from their study, nor provided relevant data for us to estimate this number. Numbers of participants in these eight studies were relatively small, the largest study had 211 participants (47). The funnel plot for the quality-effects meta-analysis (Appendix 9) was asymmetrical, which could be explained by publication bias or by the many small studies

with high heterogeneity across studies (68). We explored factors that may influence prevalence and cause heterogeneity in subgroup analyses (Table 2).

3.6 Which groups of older people are most at-risk?

Within community settings, 19% of older people were dehydrated (95% CI: 0.00, 0.48, I² 98%), and within long-term care settings, 34% were dehydrated (95% CI: 0.09, 0.61, I² 97%). While subgroup analyses revealed a lower prevalence of dehydration in community groups, there was no statistically significant difference between these two subgroups, and study means differed by less than 20% (Figure 3).

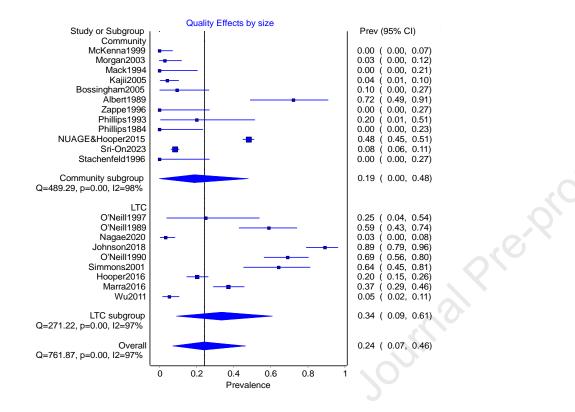


Figure 3: Forest plot of the prevalence of low-intake dehydration measured by directly-measured serum or plasma osmolality, subgrouped by care setting. LTC: long-term care.

Similarly, no clear relationship was found between prevalence of dehydration and mean age, dependency, diabetes, renal impairment, cognitive impairment, or sex. Effects differed between subgroups by less than 20%, our prespecified limit. However, participants with more health conditions were at greater risk of dehydration, and those with renal impairment were not significantly more at risk than those without, but very close (Table 2).

	Subgroups	Prevalence % (95%	Heterogeneity (I ²)	# Studies (participants)
		CI)		
Mean Age Group	65-74 years	29 (0.00, 0.66)	95%	10 (1,070)
	75-84 years	38 (0.17, 0.60)	96%	10 (745)
	85+ years	17 (0.00, 0.51)	96%	3 (234)
Cognitive Impairment	Cognitively able	31 (0.06, 0.60)	94%	13 (1,418)
	Low cognitive	50 (0.00, 1.00)	99%	2 (166)
	impairment			
	Medium cognitive	17 (0.00, 1.00)	98%	2 (117)
	impairment			

	High cognitive	16 (0.00, 0.78)	98%	4 (249)
	impairment			
Renal Impairment	Low renal impairment	23 (0.03, 0.47)	97%	18 (2,205)
	High renal impairment	42 (0.23, 0.61)	93%	3 (376)
Diabetes	Low diabetes	24 (0.03, 0.49)	95%	15 (1496)
	High diabetes	25 (0.03, 0.53)	99%	5 1,082)
# of Health Conditions	<2 conditions	15 (0.00, 0.43)	94%	16 (1,155)
	≥2 conditions	37 (0.14, 0.62)	98%	5 (1,555)
Functional	Fully independent	5 (0.02, 0.09)	0%	8 (153)
Dependency	Mixed dependency	13 (0.02, 0.27)	94%	6 (1,236)
Sex	Male	26 (0.00, 0.59)	97%	7 (793)
	Female	24 (0.01, 0.53)	99%	4 (1,257)

Table 2: Summary of subgroup analyses

We were unable to conduct meta-regression analyses, to explore the relationship between serum or plasma osmolality and secondary outcomes (such as renal impairment and cognitive impairment), because we did not have sufficient continuous data, relating to studies assessed due to inconsistent methods of reporting.

3.7 GRADE assessment of quality of evidence

GRADE assessment of the body of evidence from this systematic review was low quality, irrespective of care setting or any other subgroup. It is unsurprising that the prevalence estimation has low certainty given the wide range of prevalence rates reported amongst included studies.

No of			Certa	Prev	Certainty					
Studies	Study	Risk	Inconsistency ⁵	⁵ Indirectness ⁶	Imprecision ⁷	Other	Proportion	95%	Range	-
	design ³	of				considerations		CI		
		bias ⁴								
29 (2,955	_	_	Ļ	4	Ļ	N/A	0.24	0.07,	0-0.89	Low
participants)					v			0.46		

Table 3: Summary of Findings Table showing GRADE assessment of certainty of the evidence

³ Study design was not downgraded, because observational studies are seen to be appropriate for inclusion in prevalence and prognosis systematic reviews.

⁴ Risk of bias was not downgraded, because sensitivity analyses using risk of bias assessment showed little variation to the prevalence.

⁵ Inconsistency was downgraded once because there was large heterogeneity, as demonstrated by the high l², and also downgraded for imprecision, which is related.

⁶ Indirectness was not downgraded, because the population was specific, and serum or plasma osmolality is a robust measure of low-intake dehydration.

⁷ Imprecision was downgraded due to the wide confidence intervals, showing large variance in prevalence rates.

4. Discussion

How many older people are dehydrated?

This is the first robust systematic review to methodically seek studies reporting highquality measures of dehydration in non-hospitalised older adults and using metaanalysis to summarise low-intake dehydration prevalence in a variety of settings in 12 upper-middle and high-income countries. We found that older adults are at high risk of low-intake dehydration, with point prevalence of nearly a quarter (24%, 95% CI: 0.07, 0.46, using the reference standard directly measured serum or plasma osmolality, >300mOsmk/kg)). There was no statistically significant difference between prevalence of low-intake dehydration in long-term care settings (34%, 95% CI: 0.09, 0.61, range: 5-89%) or the community (19%, 95% CI: 0.00, 0.48, Range: 0-72%). The prevalence was very different across individual studies, irrespective of setting.

A recent systematic review reported that 0.8-38.5% of older people living in nursing homes were dehydrated (26), lower than our findings of 34% (range 3-89%) of older adults living in long-term care. They suggested (but did not assess) that the wide range of prevalence rates within their systematic review, might be explained by the variance in how dehydration was measured (26). However, our more comprehensive systematic review suggests that heterogeneity exists even when assessment is limited to the reference standard measure for older adults, directly-measured serum or plasma osmolality, at the cut-off of >300mOsm/kg (14). We discuss possible explanations for this high heterogeneity below.

Explanations for high heterogeneity in these studies

We conducted subgroup analyses to investigate the heterogeneity of the prevalence of low-intake dehydration amongst older adults. While prevalence was higher in older adults with more pre-existing health conditions, and appeared higher though not statistically significantly so in older adults in care settings or with renal impairment, other factors such as age, sex, diabetes, and cognitive function did not explain the heterogeneity.. It is likely that this heterogeneity reflects individual differences within the older adult population, with regards to variance in factors such as opportunities for social drinking, degrees of drinks provision, support, encouragement and assistance by others to drink, and cultural factors such as usual drinks patterns, routines, quantities, and concerns over continence, which needs to be investigated at individual study level. Mentes (2006) discusses the variation of hydration habits in her typology of hydration for nursing-home residents as to those who "can drink", "can't drink" and "won't drink" (69). Mentes (2006) discussed individual barriers to drinking, which included fear of incontinence, dysphagia, appropriate drinking vessels, effective communication between staff and residents, knowledge of the recommended fluid intake guidelines, drinking socially and verbal prompts to drink (69).

Additionally, hydration risk may be a balance between a composite of cognitive and physical frailty and support, where support partially or fully compensates for frailty, and frailty is a composite of factors such as age, functional status, renal, diabetic and cognitive function, number of pre-existing conditions etc. For example, low-intake dehydration may be more common in older people who have more pre-existing conditions, cognitive impairment or renal failure, but are receiving less support for drinking. It would be less common in those who are less frail and in frail individuals

receiving high quality support (which is more likely to be in place as frailty worsens), creating a U-shaped curve with individual frailty indicators such as age or renal failure. Such complex relationships are difficult to see in subgroup analysis but these conflicting influences may be driving some of the patterns of dehydration risk with age and cognitive status (Table 2). We had insufficient data to conduct meta-regression, within this systematic review, and so this issue needs to be addressed at individual study level. The timing of blood draw might have also contributed to the heterogeneity, as older people are more dehydrated in the morning, and this effect may increase if they also fasted (and limited drinks as a result) overnight. Only 8 (46, 50, 52, 55, 57-58, 62, 64) of the 29 serum or plasma osmolality studies reported timing of the blood draw, which varied between early morning to afternoon blood collections.

Which older adults are at most risk of low-intake dehydration?

While meta-analytic subgrouping found that dehydration is more prevalent in those with more pre-existing conditions, we found only a suggestion of higher prevalence in older adults with renal impairment compared to those with no renal impairment and no relationship with diabetes. Previous studies have reported associations between directly measured osmolality and both diabetes and renal impairment (assessed by estimated glomerular filtration rate (eGFR) and blood urea nitrogen (BUN)) (1, 51, 54). However, our ability to see any relationships was limited by small numbers of studies available for subgrouping and little information on severity.

Our meta-analysis found no clear difference in prevalence between older adults living with cognitive impairment and those who were cognitively able. In contrast to our findings, in other research, higher serum or plasma osmolality has been

associated with increased dementia (54), poor mental status (51) and lower MMSE score (1). Our findings might contrast with this existing literature, due to variation in how cognitive impairment was assessed and measured within the included studies, and the confounding issue of support resulting in the presence of a U-shaped curve.

We also found no clear differences in prevalence between age subgroups. Despite some previous studies demonstrating an increased risk of low-intake dehydration with increasing age (70, 71), our findings are more consistent with the findings of the DRIE study where no association was found between age and serum osmolality (1). The evidence is therefore inconsistent regarding whether ageing increases the risk of low-intake dehydration. As people age, they are more likely to require more assistance with activities of daily living and face more barriers to drinking, which will lead to low-intake dehydration. However, if people receive appropriate support and assistance with drinking as they age, then this might be enough to disrupt any association between ageing and low-intake dehydration.

We found no clear differences in prevalence between male and female older adults, which is consistent with existing literature (1, 51).

What are the limitations of this study?

We encountered several issues which might have affected the findings. Directlymeasured serum or plasma osmolality is used in included studies, only to provide point prevalence of low-intake dehydration, and dehydration status may vary over short time periods. When authors did not provide raw data for the proportions of their sample who were dehydrated, we estimated the number of dehydrated participants based on normal distribution of osmolality, which will have introduced small errors. We applied the stricter >300mOsm/kg cut-off for directly-measured serum or plasma

osmolality to indicate low-intake dehydration (as recommended by the European Society for Clinical Nutrition and Metabolism, ESPEN) (14)), prevalence would be higher if we had applied the less stringent >295mOsm/kg cut-off for impending dehydration. Although we focussed on studies which assessed dehydration using the reference standard (serum or plasma osmolality), these varied in terms of whether participants were fasted prior to blood draws and a lack of reporting of collection, storage, laboratory processing and calibration methodology. Authors also sometimes confused, or interchangeably used the terms, directly-measured "osmolality" with calculated "osmolarity".

5. Conclusion

This is the first robustly conducted, high quality and comprehensive assessment of the prevalence of low-intake dehydration in non-hospitalised older people worldwide. We included 61 studies from 12 countries and conducted a meta-analysis of 44 of those studies which assessed dehydration using directly measured osmolality, the reference standard.

Our meta-analysis suggested that while approximately a quarter of older people are dehydrated (so needing to drink more) the proportion varies a great deal between different groups of older adults (prevalence ranged from zero to 89% across included osmolality studies). This heterogeneity highlights that dehydration is not inevitable with age, but preventable and avoidable. Subgroup analyses suggested higher prevalence of dehydration in those with more pre-existing diseases, and possibly also in those with poorer renal function or living in care, but did not suggest

significant differences in low-intake dehydration prevalence by sex, functional dependency, diabetes, cognitive impairment, or age. Therefore, the heterogeneity is likely to result from individual differences in drinking behaviours, a generic measure of frailty, and the levels of care and support provided to older people. We suggest that a cohort study would be useful to measure more specifically the individual differences which might affect low-intake dehydration. The findings from our systematic review and meta-analysis are also important for raising public awareness of the high prevalence of low-intake dehydration to the older adult population globally, which can be prevented by sufficient drinking.

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Conflict of Interest

Ellice Parkinson: None

Lee Hooper: Hooper led some of the included prevalence studies. She was not involved in data extraction or risk of bias assessments on these studies, though did provide additional data where requested. Judith Fynn: None

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Author Contributions

Ellice Parkinson: Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization, Project administration Lee Hooper: Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Writing - Review & Editing, Supervision, Funding acquisition Judith Fynn: Investigation, Writing - Review & Editing Stephanie Howard Wilsher: Investigation, Writing - Review & Editing Titilopemi Oladosu: Investigation, Writing - Review & Editing Fiona Poland: Conceptualization, Writing - Review & Editing, Supervision, Funding acquisition Simone Roberts: Investigation, Writing - Review & Editing Elien Van Hout: Investigation, Writing - Review & Editing Diane Bunn: Conceptualization, Methodology, Investigation, Writing - Review & Editing, Supervision, Funding acquisition

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