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1 **TITLE**

2 Diagnosis and treatment of dehydration after stroke: A synthesis of existing evidence.

3 **Commentary on:**

4 Bahouth, M. N., Gottesman, R. F., & Szanton, S. L. (2018). Primary 'dehydration' and acute stroke: a
5 systematic research review. *Journal of neurology*, 265(10), 2167–2181.

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22 AM sits on the Editorial Board. The remaining authors do not have any conflict of interest to disclose.

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27

28

29 **TITLE**

30 Diagnosis and treatment of dehydration after stroke: A synthesis of existing evidence.

31 **KEY POINTS**

- 32 1. There is currently no gold standard of measurement of dehydration. Multiple definitions and
33 diagnostic criteria have been used across a range of study designs.
- 34 2. Although there are limited studies investigating the effects of dehydration after acute stroke
35 there appears to be an association with poorer outcomes.
- 36 3. Best practice remains unclear and further research exploring diagnostic criteria and rehydration
37 therapies associated with stroke would improve the evidence base.
- 38 4. Dehydration is common at the time of stroke, often as a complication associated with
39 swallowing difficulties (dysphagia), and management of hydration status is a crucial element of
40 acute stroke care.

41 **ABSTRACT**

42 Dehydration after stroke is associated with poor health outcomes, increased mortality, and poses a
43 significant economic burden to health services. Yet research suggests that monitoring and
44 assessment of hydration status is not routinely undertaken. In this commentary, we critically
45 appraise a systematic review which aimed to synthesise the existing evidence regarding diagnosis
46 and treatment of dehydration after stroke. The review discusses common measures of dehydration,
47 describes studies evaluating rehydration treatments, and highlights the link between dehydration
48 and poorer health outcomes in both human and animal studies. The reviewers suggest, future
49 research should focus on determining a single, validated, objective measure to clinically diagnose
50 dehydration in stroke patients. Research designs should include clearly defined patient
51 characteristics, type and severity of stroke, and type and time point of dehydration measurement, to
52 enable comparison between studies. Management of hydration status is a crucial element of acute
53 stroke care which should be routinely practiced.

54 **Key Words**

55 Stroke; Dehydration; Diagnosis; Assessment; Management; Systematic Review.

56 **Word Count (Excluding Title, Abstract, Tables and References)**

57 1861

58 **INTRODUCTION**

59 Globally, there are around 80 million individuals who have experienced a stroke, and it is estimated
60 that over 13 million new cases of stroke occur each year (Johnson et al. 2019). It is estimated that
61 around 36% of stroke patients are dehydrated upon admission, and 62% will become dehydrated
62 during their hospital stay (Rowat et al. 2012). Dehydration after stroke is associated with increased
63 mortality, poor health outcomes, and poses a significant economic burden to health services
64 (Edmonds et al. 2021; Bhalla et al. 2000; Kelly et al. 2004). Ensuring sufficient hydration during (and
65 following) the acute phase of a stroke offers benefits in that it can mitigate complications including
66 infections, constipation, delirium, and venous thromboembolism (Kelly et al. 2004; Miller et al. 2023;
67 Stotts and Hopf 2003; Visvanathan et al. 2015).

68 Despite the importance of adequate hydration after stroke being emphasised in international clinical
69 practice guidelines (Intercollegiate Stroke Working Party 2023; Powers et al. 2018; Stroke
70 Foundation 2023), research suggests that monitoring and assessment of hydration status is not
71 routinely completed, and consequently dehydration is often recognised as a result of tests for other
72 clinical conditions and complications (Watkins et al. 2017; Mullins, 2021). The reasons for this
73 disparity between guidelines and practice are not completely understood but may be explained in
74 part by a lack of consensus regarding definitions, diagnosis, and treatment of dehydration (Lacey et
75 al. 2019). In the most recent systematic review on this specific topic, Bahouth and colleagues aimed
76 to identify and synthesise the existing evidence regarding diagnosis and treatment of dehydration
77 after stroke to inform future research and practice (Bahouth et al. 2018).

78 **Aim of commentary**

79 This commentary aims to critically appraise the methods used within the review by Bahouth et al.
80 (2018) and to expand on the review findings in the context of clinical practice.

81 **METHODS OF BAHOUTH ET AL (2018)**

82 Multiple databases were used in the review including PubMed, CINAHL, Cochrane and Scopus.

83 Search terms included “hydration”, “dehydration”, “blood viscosity”, “volume contraction”,

84 “hypertonicity”, “thirst” and “haemodilution”. Studies were included if they were published

85 between the years 1997 and 2017. The authors chose to commence the search from 1997 as this

86 marked a significant transformation in the treatment of acute stroke (thrombolytic therapy for acute

87 stroke patients) (Bahouth et al. 2018). In addition to these, the reviewers conducted backward

88 citation searches, as well as including a pre-1997 seminal study which investigated dehydration and

89 stroke.

90 Only studies which examined hydration status in hospitalised patients with first time ischaemic

91 stroke were included. The study team only reviewed papers written in English and excluded both

92 research around dehydration linked to difficulties with swallowing, and studies focusing on

93 dehydration occurring beyond the acute phase of stroke, defined by the authors as “the immediate

94 post-stroke period”.

95 The authors did not indicate how many reviewers were involved in the title/abstract and full-text

96 screening or in the data extraction. One reviewer used the Quality Assessment Tool for Quantitative

97 Studies (Bahouth et al. 2018; Ciliska et al. 1998) to investigate the potential bias of the included

98 studies. No indication was provided on the method of synthesis.

99 **RESULTS**

100 There was variation between the review aims and the reported results, but this may be due to the

101 difficulties in combining the varied literature around this topic. There were several inconsistencies in

102 the reporting of the total number of studies included across the review and more details are

103 provided in the relevant results sections. Quality assessment was only reported for the 23 studies
104 included in the data tables, of which 7 (30%) were reported as moderate, with the remaining 16
105 (70%) weak indicating an overall low quality of evidence (Bahouth et al. 2018).

106 **Studies measuring dehydration**

107 Nineteen studies measuring dehydration in an acute stroke population were included, however
108 results were discussed from 20 studies, and only 18 were included in the data tables. Most studies
109 used laboratory values as objective indirect diagnostic criteria, with blood urea nitrogen to
110 creatinine ratio (BUN/Cr) and serum osmolarity being the most common laboratory markers used;
111 only one study used patient weight as a measure. Within the twelve studies that used BUN/Cr there
112 were three different definitions of dehydration. Overall rates of dehydration in the acute stroke
113 population ranged from 29 to 70%.

114 **Studies evaluating treatments of dehydration**

115 Two comprehensive Cochrane reviews (Chang and Jensen, 2014; Visvanathan et al. 2015) exploring
116 this research area were published shortly before this review was completed. The reviewers
117 therefore included only five studies published after the Cochrane papers. Although four studies (Lin
118 et al. 2015; Lin et al. 2015; Lin et al. 2016; Mucke et al. 2012) suggested that treatment of
119 dehydration could improve function and lower death rate, the remaining study (Dharmasaroja,
120 2016) suggested that high volumes of rehydration in patients with large strokes may increase
121 cerebral oedema.

122 **Outcomes after stroke in dehydrated patients.**

123 Outcome measures across the studies varied but included death, dependency, early neurological
124 deterioration (END), stroke in evolution (SIE), hemispatial neglect, and discharge to nursing home.
125 The review stated that all clinical studies of dehydration measures at the time of stroke reported
126 worse clinical outcomes in dehydrated patients. However, not all studies included in the review
127 measured patient outcomes. Nevertheless, where patient outcomes were assessed, the majority
128 were found to be poorer in those classified as dehydrated (see Table 1).

129 **Table 1:** Characteristics of studies included in Bahouth et al. 2018 systematic review. (This table was amalgamated from analysis and/or narrative)

| Author, year, country | Review Ref. No. | Review Table | Inclusion reason | Measure | % Dehydrated | Patient outcomes measured | Effect of dehydration | Observations |
|---|-----------------|--------------|----------------------|---------------------------|---------------|---------------------------------|-----------------------|--|
| Akimoto et al, 2011, Japan | 13 | 1 | Measures Dehydration | BUN/Cr >25 | 29% (28/97) | No | N/A | Dehydration on admission is associated with higher prevalence of cardioembolic stroke |
| Bahouth et al, 2016, USA | 35 | 1 | Measures Dehydration | BUN/Cr >15 USG > 1.010 | 57% (114/201) | NIHSS Hemispatial neglect | Negative | Dehydration on admission is associated with more severe hemispatial neglect |
| Bhalla et al, 2000, UK | 14 | 1 | Measures Dehydration | pOsm >296mOsm/kg | NR | Death or dependency | Negative | Dehydration on admission is associated with increased mortality |
| Bhatia et al, 2015, India | 15 | 1 | Measures Dehydration | BUN/Cr >15 USG > 1.010 | 39% (45/114) | NIHSS END | Negative | Dehydration on admission is associated with early neurological deterioration |
| Chang et al, 2014, USA | 42 | Not in Table | Cochrane Review | - | - | - | - | Review showed no clear evidence of benefit of haemodilution therapy for ischaemic stroke |
| Chang et al, 2016, Taiwan | 16 | 1 | Measures Dehydration | BUN/Cr ≥15 | 70% (61/87) | NIHSS Collateral development | Negative | Dehydration on admission is associated with poor collateral flow development |
| Crary et al, 2013, USA | 36 | 1 | Measures Dehydration | BUN/Cr ≥15 | 53% (36/67) | No | N/A | Dehydration on admission with dysphagia is associated with worsened hydration status at discharge |
| Dharmasaroja, 2016, Thailand | 30 | 2 | Hydration Therapy | - | - | - | - | Higher volume of fluid intake is associated with increased brain oedema in cerebral infarction |
| Dehghani Firoozabadi, et al, 2013, Iran | 17 | 1 | Measures Dehydration | Increased BUN/Cr | NR | Death | Negative | Dehydration is associated with increased mortality |
| Furukawa et al, 2016, Japan | 18 | 1 | Measures Dehydration | Blood viscosity | NR | No | N/A | Dehydration is associated with the onset of ischaemic stroke (small artery occlusion SAO) |
| Gross et al, 2005, USA | 39 | Not in Table | Biological Model | - | - | - | - | Animal study: Many brain regions have depressed metabolism in chronic severe dehydration |
| Hyodo et al, 1989, USA | 40 | Not in Table | Biological Model | - | - | - | - | Animal study: Cerebral blood flow is increased by haemodilution in dogs with ischaemic stroke |
| Kafri et al, 2013, UK | 29 | Not in Table | Measures Dehydration | Bioelectrical Impedance | 22% (6/27) | No | N/A | Bioelectrical Impedance Assessment appears ineffective at diagnosing water-loss dehydration after stroke |
| Lin CJ et al, 2016, Taiwan | 31 | 2 | Hydration Therapy | - | - | - | - | BUN/Cr based hydration therapy in ischemic stroke is associated with improved discharge outcomes |
| Lin LC et al, 2011, Taiwan | 19 | 1 | Measures Dehydration | BUN/Cr >15 | 15% (30/196) | NIHSS SIE | Negative | Dehydration on admission is associated with early clinical deterioration |
| Lin LC et al, 2011, Taiwan | 20 | 1 | Measures Dehydration | USG >1.010 | 56% (177/317) | NIHSS SIE | Negative | Dehydration on admission is associated with early clinical deterioration |
| Lin LC et al, 2014, Taiwan | 32 | 2 | Hydration Therapy | - | - | - | - | BUN/Cr based hydration therapy in ischemic stroke is associated with reduced occurrence of SIE |

| | | | | | | | | |
|-----------------------------------|----|--------------|----------------------|----------------------------|-----------------|-------------------------|----------|--|
| Lin WC et al, 2015, Taiwan | 33 | 2 | Hydration Therapy | - | - | - | - | BUN/Cr based hydration therapy in ischemic stroke is associated with decreased infections and LOS |
| Lip et al, 2002, UK | 21 | 1 | Measures Dehydration | Blood viscosity | NR | No | N/A | Explored haemorheology alterations in acute stroke. Abnormalities could not be linked to hydration status |
| Liu et al, 2014, Taiwan | 22 | 1 | Measures Dehydration | BUN/Cr ≥ 15 | 48% (1229/2570) | mRS BI | Negative | Dehydration on admission is associated with poor discharge outcomes |
| Lourbopoulos et al, 2017, Germany | 37 | Not in Table | Biological Model | - | - | - | - | Animal study: Ischaemic stroke mortality in mice is associated with inadequate food and/or water intake |
| Morris et al, 1999, USA | 38 | Not in Table | Biological Model | - | - | - | - | Animal study: Results demonstrate a differential response to dehydration in mice lacking AT1a receptors |
| Mucke et al, 2012, Germany | 34 | 2 | Hydration Therapy | - | - | - | - | Fluid intake > 2000 ml per day may prevent secondary stroke |
| Murray et al, 2015, Australia | 23 | 1 | Measures Dehydration | BUN/Cr >20 | 44% (35/79) | Adverse health outcomes | Unclear | Rehab patients, with and without dysphagia, with mobility issues may be at risk of dehydration |
| O'Neill et al, 1992, UK | 24 | 1 | Measures Dehydration | pOsm AVP | NR | Death or dependency | Negative | Increased AVP is associated with poor outcomes |
| Ott et al, 1974, Austria | 46 | Not in Table | Biological Model | - | - | - | - | Dehydration with atherosclerotic disease associated with high blood viscosity and may contribute to stroke |
| Rodriguez et al, 2009, USA | 3 | Not in Table | Measures Dehydration | Calculated pOsm | | No | N/A | Dehydration is a potential contributing factor to the onset of ischaemic stroke |
| Rowat et al, 2011, UK | 25 | 1 | Measures Dehydration | U:C >60 Urine Colour >4 | 45% (9/20) | No | N/A | Further research is needed to develop a practical tool for the prevention, detection, and treatment of dehydration |
| Rowat et al, 2011, UK | 26 | 1 | Measures Dehydration | U:C >80 | 62% (1606/2591) | Death or dependency | Negative | Dehydration at any point during hospital stay is associated with poor discharge outcomes and death |
| Schrock et al, 2012, USA | 27 | 1 | Measures Dehydration | BUN/Cr >15 | 43% (138/324) | Death or dependency | | Dehydration on admission is associated with poor discharge outcomes and death |
| Song et al, 2017, Korea | 28 | 1 | Measures Dehydration | Blood viscosity | NR | No | N/A | Dehydration is associated with the onset of ischaemic stroke (small artery occlusion SAO) |
| Visvanathan et al, 2015, UK | 41 | Not in Table | Cochrane Review | - | - | - | - | no evidence to guide the best volume, duration, or mode of parenteral fluid delivery for people with acute stroke |

130 *AVP = Arginine vasopressin; BI = Barthel Index; BUN/Cr = Blood Urea Nitrogen to Serum Creatinine ratio; END = Early Neurological Deterioration; LOS = Length of stay; mRS = Modified

131 Rankin Scale; NIHSS = NIH Stroke Scale; NR = Not reported; pOsm = plasma osmolality; SIE = Stroke in evolution; Table 1: Studies measuring dehydration in acute stroke (N=18); Table 2:

132 Studies including recommended hydration therapies for acute stroke patients (N=5); U:C = Urea creatinine ratio; USG = Urine Specific Gravity

133 **Biological mechanisms using animal models to investigate the relationship**
134 **between dehydration and stroke.**
135 The review concluded, based on four animal studies which were not reported in the tables of
136 included studies but discussed in the narrative results section, that poor hydration status is
137 associated with worse outcomes. One animal study showed that supported access to food and drink
138 was independently associated with decreased mortality regardless of infarct size (Lourbopoulos et
139 al. 2017).

140 **COMMENTARY**

141 **Critical appraisal**

142 Using the Joanna Briggs Institute Critical Appraisal tool for systematic reviews (Aromataris et al.
143 2015), we determined that 5 of the 11 criteria were deemed satisfactory (see Table 2). The review
144 provides a satisfactory overview of the research to date, but this must be interpreted within the
145 context of the six quality criteria that were not met or lacked clarity. While the critical appraisal
146 criteria chosen by the review's authors were appropriate, only one reviewer appraised the eligible
147 studies. Best practice in conducting a systematic review requires two or more reviewers to
148 undertake critical appraisal, neglecting this introduces the potential for error and reduces
149 confidence in the review findings. No methods to minimise errors in data extraction were reported
150 and the likelihood of publication bias was not discussed. Finally, while the recommendations for
151 research were extensive, the recommendations for practice, such as utilising hydration therapy with
152 isotonic fluids, were not supported by the reported data, limiting interpretability for healthcare
153 practitioners.

154 Based on the critical appraisal, the review did not comprehensively attempt to minimise bias in the
155 study selection, data extraction process or critical appraisal of included studies. Consequently, the
156 validity and reliability of the synthesis may be limited in its implications for practice.

157 **Table 2.** Critical appraisal of Bahouth et al. 2018 using the JBI Checklist for Systematic Reviews and
 158 Research Syntheses.

| JBI Critical Appraisal Checklist | Appraisal response |
|---|---|
| 1. Is the review question clearly and explicitly stated? | No, the review question was not clearly stated. |
| 2. Were the inclusion criteria appropriate for the review question? | Yes, the review stated a broad inclusion criteria. |
| 3. Was the search strategy appropriate? | No, there was insufficient detail reported to assess the appropriateness of the strategy. |
| 4. Were the sources and resources used to search for studies adequate? | Yes, a systematic literature search was conducted from three bibliographic databases |
| 5. Were the criteria for appraising studies appropriate? | Yes, appraisal was conducted using a validated tool (QATQS). |
| 6. Was critical appraisal conducted by two or more reviewers independently? | No, critical appraisal of included studies was undertaken by only one reviewer. |
| 7. Were there methods to minimize errors in data extraction? | No, the process of data extraction was not clearly stated. |
| 8. Were the methods used to combine studies appropriate? | Yes, it appears a narrative synthesis was conducted on heterogenous literature. |
| 9. Was the likelihood of publication bias assessed? | No, the review did not explore publication bias. |
| 10. Were recommendations for policy and/or practice supported by the reported data? | No, the recommendations for policy and/or practice were not clear. |
| 11. Were the specific directives for new research appropriate? | Yes, the review makes clear recommendations for future research. |

159

160 **Implications for practice**

161 Overall, the findings of the review highlight that dehydration may be a substantial problem
 162 impacting 29% to 70% of stroke patients (Bahouth et al. 2018). This variation in the rates of
 163 dehydration reported in the included studies may be partially explained by the variety and range of
 164 measurement techniques utilised in the study designs. The heterogenous nature of the evidence
 165 base limits the opportunity for comparisons to be made across studies, and therefore the
 166 development of meaningful recommendations to improve practice.

167 Although the review aimed to standardise terminology and identify gaps in the literature, these
168 were not covered within the results section. This omission in reporting may be due to the limited
169 number of studies, and the heterogeneity of those that exist, resulting in a lack of data to achieve
170 the review aims. Despite the inconsistencies in the review overall, the findings suggest an
171 association between dehydration and poor outcomes in acute stroke.

172 In relation to clinical practice, the review highlights the detrimental effects of dehydration on patient
173 outcomes (Bahouth et al. 2018). Although the interpretation of this evidence is limited by the
174 review's methodological limitations, the findings increase awareness of the impact of dehydration
175 among this population for healthcare practitioners. This increased awareness may allow for early
176 identification and prompt management of dehydration in these patients. That said, further research
177 is needed to recommend a specific clinical assessment given that there is a dearth of evidence in this
178 area (Oates and Price 2017). To minimise the acknowledged detrimental effects of dehydration,
179 healthcare practitioners could incorporate routine screening for dehydration into their clinical
180 assessments for patients presenting with acute stroke (Guastafarro et al. 2018; Miller et al. 2023).

181 The association between dehydration and poor outcomes in stroke may also prompt the
182 development of educational initiatives and training programs for healthcare professionals (McCotter
183 et al. 2016). Recent evidence suggests that continuing education programs, workshops, and
184 conferences should emphasise the importance of hydration in acute stroke management (McCotter
185 et al. 2016; Mullins 2021). By enhancing healthcare professionals' knowledge and skills in this area,
186 they may be better equipped to identify and address dehydration more promptly and effectively
187 (Miller 2023; Mullins 2021).

188 While the review highlights evidence suggesting rehydration therapies may improve clinical
189 outcomes and functional independence (Lin et al. 2016), further robust research evidence is
190 required to inform best practice in this area.

191 **Implications for future research**

192 Bahouth et al. (2018) suggest that future research should focus on determining a single, validated,
193 objective measure to clinically diagnose dehydration in stroke patients. They further recommend
194 that the reporting of future research findings should include more detailed information about the
195 type and severity of stroke, type and time point of dehydration measurement, and more clearly
196 defined patient characteristics. An under researched area highlighted by the review was that of
197 patient experience of dehydration after stroke, as no previous studies have explored this important
198 aspect of care.

199 Further research could also investigate the underlying mechanisms linking dehydration and poor
200 stroke outcomes, identify specific patient populations at higher risk, and evaluate the impact of
201 hydration interventions on clinical outcomes. This research could contribute to an expanded
202 evidence base, further informing clinical practice guidelines and fostering continuous improvement
203 in stroke management.

204 **CPD reflective questions**

- 205 1. What do you think the key take-away messages from the review are and why?
- 206 2. Are you satisfied with the way the authors conducted and reported the review? Justify
207 your answer.
- 208 3. The authors concluded that a hydration therapy based on isotonic fluids could be
209 promising. Do you agree based on the evidence presented? Justify your answer.

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