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## **Increased Water Intake to Reduce Headache: Learning From a Critical Appraisal**

**Title:** Increased Water Intake to Reduce Headache: Learning from a Critical Appraisal

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# Increased Water Intake to Reduce Headache: Learning From a Critical Appraisal

## Increased Water Intake to Reduce Headache: Learning From a Critical Appraisal

### Critically Appraised Topic (CAT): Water Intake to Reduce Headache

#### Clinical Bottom Line

Water intake is a cost effective, non-invasive and low-risk intervention to reduce or prevent headache pain. Rationale: Chronic mild dehydration may trigger headache. Increased water intake could help. A small trial shows modest benefit; however, a larger methodologically sound randomized controlled trial is needed to confirm efficacy.

#### Critically Appraised Paper

Spigt, M., Weerkamp, N., Troost, J., van Schayck, C. P., & Knottnerus, J. A. (2012). "A randomized trial on the effects of regular water intake in patients with recurrent headaches." *Family practice*, 29(4), 370–5. Doi: 10.1093/fampra/cmr112

#### Clinical scenario

Patients from primary care registered as 'headache', 'tension headache' and/or 'migraine' for more than one year who suffer at least two episodes of moderately intense headache or more than four mildly intense episodes of headache per month with a daily fluid intake of less than 2.5 litres per day.

#### PICO (M)

Patient/Problem = Headache > 1 year with 2 moderately intense or 4 mildly intense episodes per month  
Intervention= 1.5 litres water per day + stress control and sleep hygiene  
Comparison/Control = stress control and sleep hygiene  
Outcome = Reduce or eliminate headache  
Methodology = Therapy RCT

#### Table 1: Final Search Terms

|                                                                                                       |                                                             |                                   |
|-------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|-----------------------------------|
| <b>TRIP Data Base:</b> hits = 517 used filter<br>Extended Primary research 4 found 1 paper applicable | "Water intake "[MeSH Terms]<br>AND "Headache "[All Fields]" | Best match to PICO,<br>(2012) RCT |
|-------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|-----------------------------------|

#### Selection Criterion and Overall Results

102 headache patients in 16 primary care clinics were randomized into control (n=50) and intervention groups (n=52) Inclusion criteria = two > episodes of moderately intense headache or five > mildly intense headaches per month and total fluid intake > 2.5 litres per day, Follow-up @ 3 months. 79% intervention and 66% of controls completed RCT. Drinking more water resulted in a statistically significant improvement of 4.5 (confidence interval: 1.3–7.8) points on Migraine-Specific Quality of Life (MSQOL). 47% in the intervention (water) group self-reported improvement (6 > on a 10-point scale) against 25% in controls. Drinking water did not reduce headache days.

#### Comments

The transparency from the author of this critically appraised paper enables others to use this study as a teaching tool and to learn from the shortcomings in the trial. The study was underpowered and contains methodological shortcomings. Participants were partially un-blinded during the trial increasing the risk for bias. Only the subjective measures are statistically significant and attrition was significant. The intervention is low risk and of negligible cost. A methodologically sound RCT is recommended to evaluate if the intervention has beneficial effects.

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### Rationale

“Does increased water intake help prevent or relieve headaches?” was a question identified as of interest to the public and prioritised for answering by ThinkWell’s *Citizens’ Research – Identifying and Setting Priorities* panel (CRISP)<sup>1</sup>. ThinkWell<sup>2</sup> is a charity dedicated to helping the public make informed health choices and undertake research into the self-management of health. ThinkWell identifies questions of interest to the public, prioritises those to be addressed, looks for a systematic review and if there is no high quality up-to-date systematic review or the findings of the review are equivocal registers the uncertainty with UK DUETS<sup>3</sup> and adds the uncertainty to the questions for systematic review or primary research. Following this ThinkWell will use PLOT-IT<sup>4</sup> the online randomised controlled trials platform to run a clinical trial with citizen collaborators. The process used for engagement is illustrated in figure 1

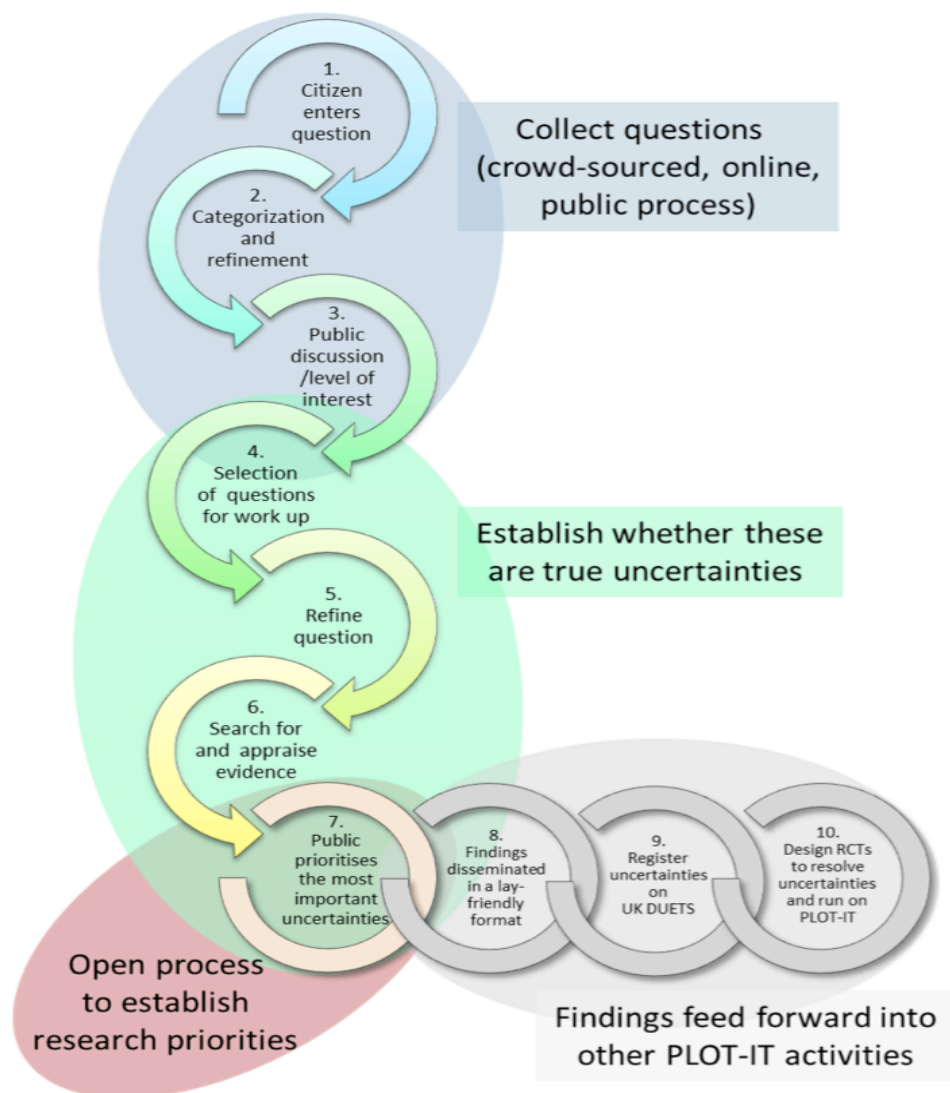


Figure 1 ThinkWell Priority setting for an online trial

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There is growing awareness of the trend towards collaborative engagement, health self management, data ownership by patients and the need for shared decision making in clinical care<sup>5,6</sup>, however it is still unusual for patient citizens, clinicians and researchers to co-create and prepare for all aspects of an clinical trial collaboratively<sup>7</sup>. This critical appraisal report may serve as an exemplar for initiating this process.

Health websites, internet sites and leaflets advocate drinking extra water to reduce headaches, for example, the BUPA website<sup>8</sup> includes drinking water to reduce headaches as a self help intervention. A Google search “Is drinking water good for headaches?” brought up 861,000 results. Although headaches can result from mild dehydration, drinking too much water<sup>9</sup>, or drinking cold water quickly<sup>10</sup>, may also trigger headaches. The prevalence for headache from a meta-analysis of studies including 205,000 participants is estimated at ~60% per year and person<sup>11,12</sup>. The indirect costs of headache in Europe is estimated at £112-173 billion annually<sup>13</sup>. Added to the complexity of gathering evidence we found bottled water is not entirely harmless as it can: contain contaminants; waste natural resources; contribute to excessive energy consumption; and entail excessive packaging<sup>14</sup>. Spending on bottled water has increased dramatically in recent years and some people make considerable effort to drink extra water to avoid headaches. A trial of water intake to reduce headaches may decrease the uncertainty about the value or effectiveness of using water for headaches and may contribute to health knowledge<sup>15,16</sup>.

### Is this a genuine uncertainty?

The 6S system<sup>17</sup> was used to search available literature for the efficacy of drinking water to reduce headaches and to identify conditions that could make drinking additional water harmful. The 6S strategy is designed for efficiency, with searches beginning at the top and stopping when an answer is found. Systems and summaries were reviewed to identify clinical directives, current opinion and research evidence. Clinical synopses were used to identify relevant issues, MeSH terms and keywords to improve the sensitivity and specificity of our searches. We found no systematic reviews or RCTs that conclusively established effectiveness or harm.

### Clinical Questions

1. What are the benefits of drinking additional water to reduce or eliminate headache frequency, duration or intensity?
2. What time is required for water to have an effect and how much water is needed?
3. Will drinking additional water increase nocturnal urination and what is the relationship to volume or timing?
4. Does drinking extra water improve quality of life or sleep?

### Foreground Question

*“For otherwise healthy adults with headache, does drinking water help prevent, reduce or eliminate headaches?”*

The question was put into PICO format (table1) to facilitate searching.

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| POPULATION                 | INTERVENTION | CONTROL                                             | OUTCOME                                  |
|----------------------------|--------------|-----------------------------------------------------|------------------------------------------|
| <b>Adults AND headache</b> | Water intake | Placebo or usual practice or lesser volume of water | Headache (incidence, severity, duration) |

### Search Strategy

The search revealed one RCT closely matching the PICO but no systematic reviews. Using a PICO with items on separate lines with additional descriptors yielded descriptive information but no RCTs. Search results after de-duplication and filtering by title and abstracts are presented in (table 2).

**Table 2** Detailed PICO search\* Additional searches completed separating outcome variables included in the PICO yielded no further applicable studies.

| Database                                  | Terms                                                                                                                                                                                     | Studies Found | Appraisal RCT? |
|-------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|----------------|
| <b>PubMed &gt;2007</b>                    | ("Headache"[MeSH Terms] OR "headache"[All Fields]) AND ("drinking"[MeSH Terms] OR "drinking"[All Fields] OR ("water"[All Fields] AND "intake"[All Fields]) OR "water intake"[All Fields]) | 9/260         | Yes            |
| <b>Scopus</b>                             | Human water intake AND headache<br>Dehydration AND headache                                                                                                                               | 7/354         | Yes            |
| <b>Google Scholar</b>                     | Water intake OR headache, Dehydration OR headache                                                                                                                                         | 1/200         | Yes            |
| <b>ClinicalTrials.gov</b>                 | Headache AND water intake                                                                                                                                                                 | 0/3           | No             |
| <b>UKCTG - UK Clinical Trials Gateway</b> | Headache OR water intake                                                                                                                                                                  | 0/0           | No             |
| <b>DUETS</b>                              | Headache OR Water                                                                                                                                                                         | 1/1           | No             |
| <b>PLOS</b>                               | Water intake OR headache (Clinical trials)                                                                                                                                                | 0/0           | No             |
| <b>NHS Guidelines</b>                     | Public Information<br>Drinking water AND Headache                                                                                                                                         | 1/6           | No             |
| <b>Trip Data Base</b>                     | Water intake OR headache OR migraine (Clinical trials) (Primary research) (Systematic reviews)                                                                                            | 8/227         | Yes            |
| <b>Mendeley</b>                           | Water and headache, cost of headache                                                                                                                                                      | 4/30          | Yes            |

Expanding the search to blogs, patient forums, and personal contact with experts in the field yielded no additional studies but did confirm how widespread advice is to increase water intake to avoid headache. The searches yielded case reports, pilot studies, opinions, non-systematic reviews, an un-blinded feasibility trial and the unregistered randomised controlled trial we critically appraised.

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Spigt, M., Weerkamp, N., Troost, J., van Schayck, C. P., & Knottnerus, J. A. (2012). "A randomized trial on the effects of regular water intake in patients with recurrent headaches." *Family practice*, 29(4), 370–5, Doi: 10.1093/fampra/cmr112

### Critical Appraisal

The question to address was *"Does drinking water reduce headache duration, frequency or intensity?"*

The evidence to support water intake to reduce headache pain is sparse. The 2012 trial by Spigt et al. was the only RCT to address the PICO question. The trial protocol was unregistered as confirmed by the authors. In non-registered trials publication and selection bias is a concern<sup>1819</sup> The research strengths include a clear CONSORT<sup>20</sup> flowchart and the transparency in the discussion. The authors reported confidence intervals and they communicated transparently in their assessment of the trial. The transparency points out the complexities researchers face when initiating an RCT. Our appraisal consisted of an initial assessment using the free tool, Critical Appraisal Skills Programme (CASP) checklist for RCTs (table 3).

Table 3 CASP Analysis for SPIGT et al ©CASP.

| Question                                                                | Response   | Comment                                                                                                                                                                                                                                                                                           |
|-------------------------------------------------------------------------|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Clearly Focused Question?                                               | Yes        | (See PICO above)                                                                                                                                                                                                                                                                                  |
| Randomized                                                              | Yes        | Participants were independently allocated by a computer generated list of random numbers.                                                                                                                                                                                                         |
| Patients accounted for?                                                 | Can't tell | Losses to follow up left out of analysis                                                                                                                                                                                                                                                          |
| Were patients, health workers and study personnel 'blind' to treatment? | No         | Participants were un-blinded ½ through study.                                                                                                                                                                                                                                                     |
| Group similar demographics?                                             | Can't tell | Age & sex yes, Authors claim heterogeneity of headache type. The authors did not report social or economic demographics like education, income, ethnicity or baseline blood pressure or weight                                                                                                    |
| Groups treated equally?                                                 | No         | The research was un-blinded. This can lead to unplanned/unconscious potential differences and in fact the authors referred to the lack of blinding in their earlier pilot trial as a potential difference in the outcomes. Active group was informed of intervention results from the pilot trial |
| How large was the effect?                                               | Small      | Outcomes measures = increase of 4.5 MSQOL CI= 1.3-7.8 (5.7 ± 2.2 versus 3.7 ± 2.7; P value 0.001) to favour intervention group. Effects on headache frequency and duration NS. Intervention group reported reduced pain/medication use                                                            |
| How precise estimate of treatment effect? CI?                           | Can't tell | Subjective measures improved, objective did not. Study claims it was underpowered and compliance was limited to ½ of expected water intake                                                                                                                                                        |
| Results apply to                                                        | Can't tell | Small effect, headache prone may be different, onset                                                                                                                                                                                                                                              |

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|                                                    | intention to treat analysis |                                                                                                                                                                                                                                                                                                                                |
|----------------------------------------------------|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Were all clinically important outcomes considered? | No                          | Not considered: Outcomes of overconsumption and electrolyte balance risk. Low blood pressure, dizziness, and headache effects from increased water intake. Used <i>post hoc</i> sample size calculation for days without headache rather than <i>a priori</i> . Inadequate consideration of all outcomes increases uncertainty |
| Are the benefits worth the harms and costs?        | Not Sure                    | Water is inexpensive, however and benefits were small. Media reported the study as evidence for water as an effective intervention and may impede people from seeking appropriate medical care                                                                                                                                 |

### Results

102 headache patients in 16 primary care clinics were randomized into control (n=50) and intervention groups (n=52). Inclusion criteria = two > episodes of moderately intense headache or five > mildly intense headaches per month and total fluid intake > 2.5 litres per day, Follow-up @ 3 months. 79% intervention and 66% of controls completed RCT. Drinking more water resulted in a statistically significant improvement of 4.5 (confidence interval: 1.3–7.8) points on Migraine-Specific Quality of Life (MSQOL). 47% in the intervention (water) group self-reported improvement (6 > on a 10-point scale) against 25% in controls. Headache days remained constant.

### Discussion

Spigt et al<sup>21</sup> report self-reported quality of life improvement reached statistical significance after following three months of increased water intake by participants. Participants in the intervention (extra water) reported better quality of life with 47% of them reporting less headache pain. The extra water group experienced reduced frequency and shorter duration of headache pain and a modest decrease in medication use. They report more headache-free days although the results of these changes were small and did not reach statistical significance. The authors state the sample size was inadequate to measure the objectives.

It is also possible that with chronic severe pain a decrease of medication or a full headache free day was an unrealistic expectation. The authors chose a heterogeneous headache population. They indicate this led to their statistical undoing but neglected to mention that an effect that is statistically non-significant could still be clinically significant for those grateful for any pain reduction<sup>22</sup>. Curiously although authors noted the study was under-powered and the direction of the effect favoured the intervention this was not highlighted as the principal failure to realise statistical significance even though the principal investigator reports successful results in an earlier non-blinded feasibility trial of student participants<sup>23</sup>. In the present trial participants are confirmed chronic recurrent headache patients for greater than one year. It may be the heterogeneity between chronic severe headache patients and profiles of student headache sufferers differ<sup>24</sup>. They may represent separate conditions responding differently to the same intervention<sup>24</sup>. Exclusive enrolment of participants who report minimum one-year histories of severe, frequent chronic headaches could eliminate the population that may benefit from increased water intake such as casual, uncomplicated, infrequent or newly diagnosed headache sufferers. Long-term headaches can be accompanied by co-morbid conditions or chronic inflammation and

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There were significant compliance problems in the active water group as the average daily intake was just over  $\frac{1}{2}$  (842ml) of the 1.5 litres the intervention required. Only 35% of the participants in the intervention group increased their water intake by more than 1 litre.

The authors cited fear of contamination as support for their decision to un-blind participants midway through the trial when in reality the balancing of treatment allocations by a clinician or treatment center in a randomized trial could facilitate unacceptable levels of treatment prediction<sup>22</sup>. Authors stated they were surprised with the failure to obtain the same results as in their earlier un-blinded pilot study<sup>23</sup>. They report blinding to be “a ‘difficult’ aspect for non-pharmaceutical interventions” and shared concerns about contamination as a threat to internal validity.

*“Patients in the control group could decide to drink more water, if they knew this was the hypothesis of the study. We solved this problem by partially informing the patients about the goal of our study. In that way, we successfully prevented contamination. However, not being able to blind the interventions possibly also leads to differences in placebo effects” (Spigt et al.)<sup>21</sup>.*

The authors report informing previously blinded participants of the goals of the trial to stave off attrition in an ill-fated attempt to reduce crossover contamination however their actions potentially removed the benefits accrued by the randomisation to reduce selection bias<sup>19</sup>. The authors were concerned the control group could decide to drink more water to accrue benefits. Although authors perceived un-blinding as reducing inner validity conflicts, such measures could introduce increased placebo effects and could introduce unplanned/unconscious potential differences<sup>19</sup> and introduce potential selection bias<sup>25</sup>. Interestingly the authors referred to the lack of blinding in their earlier pilot trial as a potential difference in the outcomes and state the pilot trial outcomes confirmed their hypothesis. The authors did measure expected effect in both groups, and the intervention group reported greater positive expectations but expectations failed to match objective outcome measures.

In addition, the authors state the study was underpowered for objective measures, stating they would need “a minimum of 19.433 patients per group to have sufficient power for an effect on days with at least moderate headache (with an standard deviation of 6 and effect size of 0.17)”. It appears they did not calculate headache-free days against those of the general population in their *a priori* sample size estimate.

*“Measuring the effect of a drug as the difference between an outcome and a baseline established after the start of treatment is like measuring how high an athlete can jump from the top of his head. It gives midgets a sporting chance but it is no way to run the Olympics.” (S. Senn)<sup>26</sup>*

The authors discuss negative objective findings and report calculation errors in sample size, high attrition, and choosing non-specific headache types as culprits. Existing medication changes are tracked as an outcome. This may produce unpredictable treatment effects as the baseline is initiated prior to randomisation<sup>26</sup>. Spigt et al. mentioned markers chosen for the trial were not sensitive enough to detect

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results would vary by exchanging markers. The authors stated their goal was to run a pragmatic rather than explanatory study and to later study the results of water intake on headache subtypes.

In comments following the publication of the trial the authors were criticized for the way they handled missing values but countered there was no way to make attrition right except to declare it and discuss the implications<sup>27,28</sup>. They reasoned attrition was balanced between controls and interventions indicating interpretation could take either direction. Participant feedback pointed to the rationale that those who dropped out of the study felt the intervention was ineffective.

The authors rightly stated that imputation of values by last available measurement or other means could introduce additional bias and thus compound the problem<sup>29</sup>. Altman and Bland<sup>27</sup> suggest planning at pre-trial stage to avoid attrition, making provision to collect data post-withdrawal in order to preserve the intention to treat population, to investigate, document and anticipate the reasons for missing data and to prepare for this by pre-specification of primary and sensitivity assessment with which to support the conclusions based on a planned analysis<sup>27</sup>.

The Migraine-Specific Quality of Life (MSQOL)<sup>23,30</sup> was migraine validated; however, in this study it was used for a mixed headache population. McKenna (2011)<sup>31</sup> argues for appropriate use of the validation process in PROMS (patient reported outcome measures) by stating that PROMS are built to measure the value of specific concepts or constructs via questionnaire in a standardised way rather than offering tick boxes to opinion. When we use standardized mechanisms for the purposes for which they are validated, they provide an avenue to quantify qualitative information in ways that can be replicable<sup>31</sup>.

### Other Considerations

Critical appraisal serves to filter reliable health care research. The literature rationale is that mild dehydration may trigger headache pain. One counter argument is that bodies self-regulate to retain homeostasis with the exception of the very ill<sup>32</sup>. Additional concerns are the escalation of financial interests beyond reasonable science and the lack of evidence for extra water as a lifestyle intervention<sup>32</sup>.

The authors recommend drinking extra water to reduce headaches because it is cheap, safe, and non-invasive and might be effective based on earlier pilot research. This presents a problem to health science research<sup>33</sup>. When cited by others in healthcare, this disseminates a non-validated hypothesis that is untested and subject to bias<sup>34,35</sup>.

The study is promoted as a medical and scientific source of evidence for increasing water intake to combat headache frequency and pain. For example, a Google search using terms “drink water for headache 2012” brings up multiple first page results citing the study. Even without cited research, NHS evidence provides a patient advice sheet from BUPA<sup>8</sup> that suggests drinking extra water may reduce headaches. It would be better public health practice to base patient advice on the results that could come from a methodologically sound clinical trial.

Other points to consider are:

- Multiple medications and health conditions can interfere with body

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individuals to be insensitive to hydration needs. They may “overheat” or be unable to differentiate between hunger and thirst. This may create the potential for harm from what would normally be an innocuous behavioural change<sup>36</sup>.

- The majority of individuals over 50 are on at least two prescription medications for long-term conditions<sup>37</sup>. It is possible these interventions could interfere with hydration or cause hypervolaemic hyponatraemia<sup>36</sup>.
- Individuals may sustain trauma, brain or cervical injuries where the endocrine system is compromised leaving them with a susceptibility to mild dehydration<sup>38</sup>.
- Older adults may have decreased mobility, cognition, organ function or other chronic conditions that reduce hydration awareness<sup>3936</sup>.
- Athletes or weekend warriors may rehydrate sub-optimally and not to pre-workout status<sup>3640</sup>.

### Conclusion

The existing research leaves the research question unanswered but the materials increases awareness of areas that can go wrong in research. Negoianu and Goldfarb<sup>34</sup> state:

*“There is no clear evidence of benefit from drinking increased amounts of water. Although we wish we could demolish all of the urban myths found on the Internet regarding the benefits of supplemental water ingestion, we concede there is also no clear evidence of lack of benefit. In fact, there is simply a lack of evidence in general. Given the central role of water not only in our bodies but also in our profession, it seems a deficit worthy of repletion”*

The absence of evidence is not “proof”<sup>41</sup>. In the instance of headache and water intake, it is a research question that begs to be answered with a large randomised controlled trial that is methodologically sound. Headache pain may be experienced by 77% of the population<sup>1112</sup>. Families of headache sufferers and society at large are indirectly affected by headache; no one wants to see others in pain<sup>1112</sup>.

Only a few years ago an RCT investigation with extra water intake as an intervention would carry an impossible price tag and would bring significant security, attrition and validity concerns. Recent advances in online security, science and medical technology make ThinkWell’s public led online trials (PLOT)<sup>4</sup> a feasible and accessible option to explore the question “*Does drinking measured amounts of additional water reduce headache pain?*” This is a research question the public can join together to answer in the upcoming ThinkWell PLOT feasibility trial. Online platforms could be good news for clinicians as well who are at the forefront of patient treatment. They are well situated to observe gaps in treatment and consider ways to meet these needs. The lower cost and methodological support offered by a well-managed online platform could make trials run by clinicians a trend in future research and medicine.

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