Appendix 1 (as supplied by authors): Methods

We performed a systematic review on the management of hyponatremia through searches of Ovid Medline (1946 through June 2011), EMBASE (1947 through July 2011), and the Cochrane database. The initial search identified terms relevant to hyponatremia and included "Hyponatremia",or "Inappropriate ADH Syndrome" or "Water intoxication", or "Schwartz Barter syndrome". In order to identify relevant study designs we searched the terms randomized controlled trials (RCTs) and initially included the search terms 'cohort study' and 'case-control study' out of interest to see what the number of non-RCT based studies existed in the literature. We conducted our search with the assistance of a librarian who specialized in literature searches. Citations were included if they were written in English, the patient population was 18 years or older, and the diagnosis of hyponatremia was established based on volume status and laboratory assessment with a serum sodium level less than 135 mEq/L. Papers that were excluded with the initial search included expert opinions, literature reviews, and if the studies utilized medications that are not used in North America. The titles and abstracts of the studies from the literature search were screened for eligibility by two independent reviewers (KY and JJL) based on our inclusion and exclusion criteria. Papers were then screened in full text and reviewed if eligibility was inconclusive based on initial abstract screening. All papers that were considered eligible from the initial screening were retrieved in full text and reviewed to confirm eligibility. Eligible articles that were reviewed in this stage included RCT's and quasi random RCT's. Randomized crossover studies were included if they included pharmacologic or nonpharmacologic interventions for hyponatremia. Eligible cross-over studies had to have serum sodium concentration as one of the outcomes. At this stage we also excluded all papers that were deemed to be traditional cohort or case-control studies. Each reviewer assessed pre-defined aspects of study quality related to the definition of hyponatremia, type of participants, study design, randomization, allocation concealment, blinding, outcome measures, analysis type(specifically, was intention to treat utilized) and, loss to follow up. Disagreements between the two reviewers were resolved through joint consensus. The primary outcome was change in serum sodium level. The secondary outcomes were death or adverse reactions to the intervention. We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement as closely as possible (7).

Appendix to: Lee JJY, Kilonzo K, Nistico A, et al. Management of hyponatremia. *CMAJ* 2013.
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