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Association between naturally occurring lithium in drinking water and suicide rates: systematic review and meta-analysis of ecological studies

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Figure S1. Search strategy used for EMBASE in Ovid

1. Lithium.mp or exp Lithium/
2. drinking water.mp or exp Drinking Water/
3. public water.mp
4. exp Water/ or water.mp
5. tap water.mp
6. 2 or 3 or 4 or 5
7. suicide.mp or exp Suicide/
8. mortality.mp or exp Mortality/
9. violent.mp
10. violence.mp or exp Violence
11. 7 or 8 or 9 or 10
12. 1 and 6 and 11

Figure S2

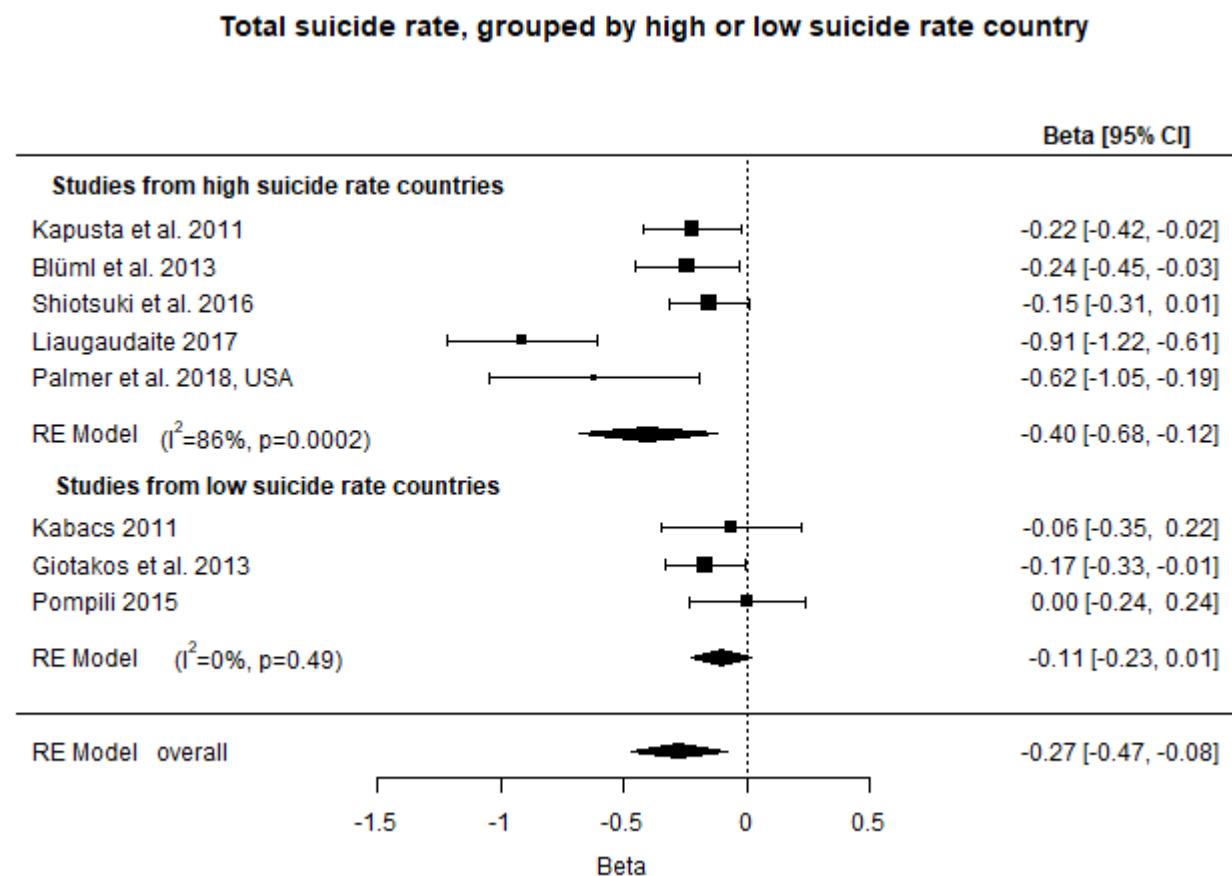


Figure S3

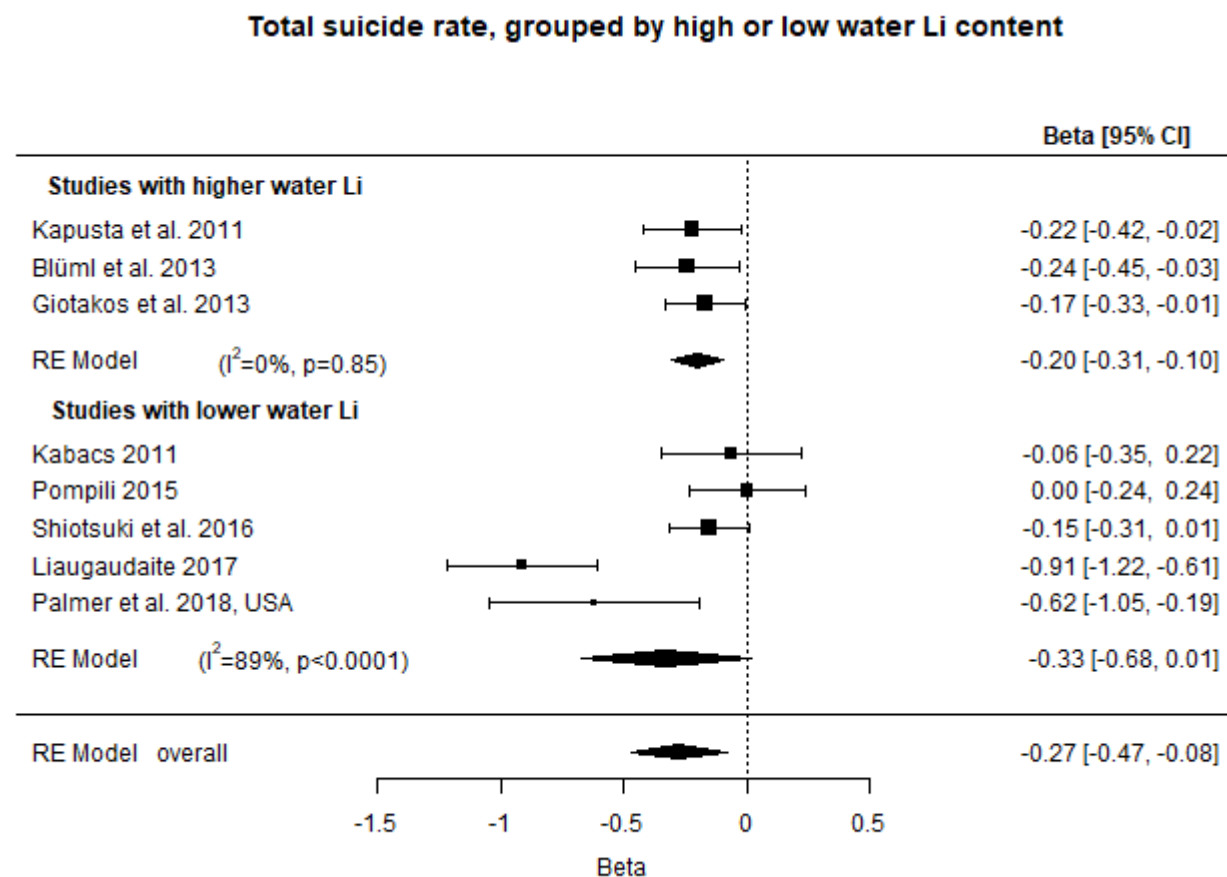


Table S1. Quality assessments of included studies

Evaluation criteria	Sugawara et al (2013)(1)	Shiotsuki et al. (2016)(2)	Kabacs et al (2011)(3)	Kapusta et al. (2011)(4)	Giotakos et al (2013)(5)	Pompili et al (2015)(6)	Liaugaudaite et al 2017(7)	Bluml et al (2013)(8)	Palmer et al. 2018(9)
Are the subjects in the study representative of conclusions being drawn?	✓	✗	✓	✓	✓	✓	✓	✓	✓
Were the statistical methods used appropriately?	✓	✓	✓	✓	✓	✓	✓	✓	✓
Were confounders adjusted for appropriately?	✓	✓	✗	✓	✗	✓	✗	✓	✗
Do the authors present and justify key elements of the study design?	✓	✓	✓	✓	✗	✓	✓	✓	✓
Discussion of limitations (e.g. ecological fallacy)	✓	✓	✓	✓	✗	✗	✓	✓	✗

Table S2. Studies included in the narrative review

Study	Region and number of locations	Population data	Number of lithium samples, dates and methods of collection and analysis	Lithium levels in µg/l Mean (range)	Mean suicide rate (per 100,000/y)	SMR mean (range)	Covariates	Results
Schrauzer and Shrestha 1990(10)	USA, Texas, 27 counties	All suicides from 1978 – 1987 in counties with high (70-160µg/l), medium (13-60 µg/l) and low (1-12 µg/l) water lithium	2-5 samples per county, local tap water collected in 1968 as part of Texas Nutrition Survey, analysed using spectrophotometry	NR (0 – 160)	High Li counties 8.7 (sd 0.85) Medium Li counties 14.8 (sd 2.9) Low Li counties 14.2 (sd 1.3) or 13.9 (sd 1.2) on excluding counties with high population density	NR	Adjusted for population density by repeating analysis excluding counties with high population density	T test comparing suicide rate of high and low lithium counties found higher rate in low lithium counties, $p < 0.005$
Ohgami et al. 2009(11)	Japan, Oita prefecture, 18 municipalities	All suicides from 2002 – 2006, total population 1,206,174	NR, samples, analysed using ion chromatography or mass spectrometry	NR (0.7 – 59)	NR	T: 105 (60 – 181)	None	In population weighted least squares regression of SMR on Log Li (µg/l) T: $\beta = -0.65$, $p < 0.004$ M: $\beta = -0.61$, $p < 0.008$ F: $\beta = -0.46$, $0.05 < p < 0.06$
Helbich et al. (2012)(12)	Austria, 99 districts	All suicides 2005-2009 (total population 8,297,964)	6460; 2005-2010; samples of local drinking water, analysed by inductively coupled plasma optical emission spectrometry	11.3 (sd 27)	T: 16.5 [†] M: 26.4 [†] F: 7.00 [†]	T: 0.790 ^{†,‡} M: 0.821 ^{†,‡} F: 0.673 ^{†,‡}	Proportion of Roman Catholics, density of psychiatrists	Spearman correlation: T: -0.26, $p = 0.009$ Global spatial regression of SMR (with ref 1.00) on Li (mg/l) T: $\beta = -4.844$, $p < 0.001$
Helbich et al. 2013(13)	Austria, 99 districts	All suicides 2005-2009 (total population 8,297,964)	6460; 2005-2010; samples of local drinking water, analysed by inductively coupled plasma optical emission spectrometry	10 (sd 11)	T: 16.5 [†] M: 26.4 [†] F: 7.00 [†]	T: 0.802 [‡] (sd 0.198)	Covariate: altitude Controls considered: population density, income per capita, Roman Catholics, psychiatrist density, GP density, psychotherapist density, unemployment rates	Linear regression model of SMR [‡] on Li (mg/l) T: β (se) = -9.407 (2.218), $p < 0.001$
Helbich et al. 2015(14)	Austria	All suicides in the period 2005-2009 (total population 8,297,964)	6460 samples; 2005-2010; local drinking water, analysed by inductively coupled plasma optical emission spectrometry	10 (SD 10)	T: 16.5 [†] , M: 26.4 [†] , F: 7.00 [†]	NR	Proportion of Roman Catholics, population density, Li prescriptions, income, density of psychiatrists, GPs, psychotherapists, unemployment rates	Multivariate spatial Bayesian hierarchical models (without prescription interaction) of SMR (with ref 1.00) on log Li T: β (95%CI) = -0.080 (-0.136 to -0.124) M: β (95%CI) = -0.092 (-0.157 to -0.026)

Study	Region and number of locations	Population data	Number of lithium samples, dates and methods of collection and analysis	Lithium levels in µg/l Mean (range)	Mean suicide rate (per 100,000/y)	SMR mean (range)	Covariates	Results
								F: β (95%CI) = -0.044 (-0.148 to 0.059)
Ishii et al. 2015(15)	Japan, Kyushu Island, 274 municipalities	All registered suicides in 2011. Total population: 14,646,121	434 samples, 2010-2013; collected from rail station or municipal office; analysed by mass spectrometry	4.2 (0 – 130)	T: 23.8 M: 35.3 F: 13.4	T: 114 (0 - 729) M: 120 (0 – 1082) F: 101 (0 - 644)	Proportion of elderly people, 1 person households, yrs in college education, primary industry, unemployment rate, marriage rate, mean temperature, postal savings.	Population weighted least squares regression of SMRs on Log Li Unadjusted analyses T: β = -0.175, p = 0.031 M: β = -0.228, p = 0.005 F: β = 0.004, p = 0.957 Adjusted analyses T: β = -0.122, p = 0.094 M: β = -0.169, p = 0.019 F: β = 0.031, p = 0.706

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