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The complex association between drinking water consumption and endemic gastrointestinal illness as shown by Swedish cohort studies

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ABSTRACT

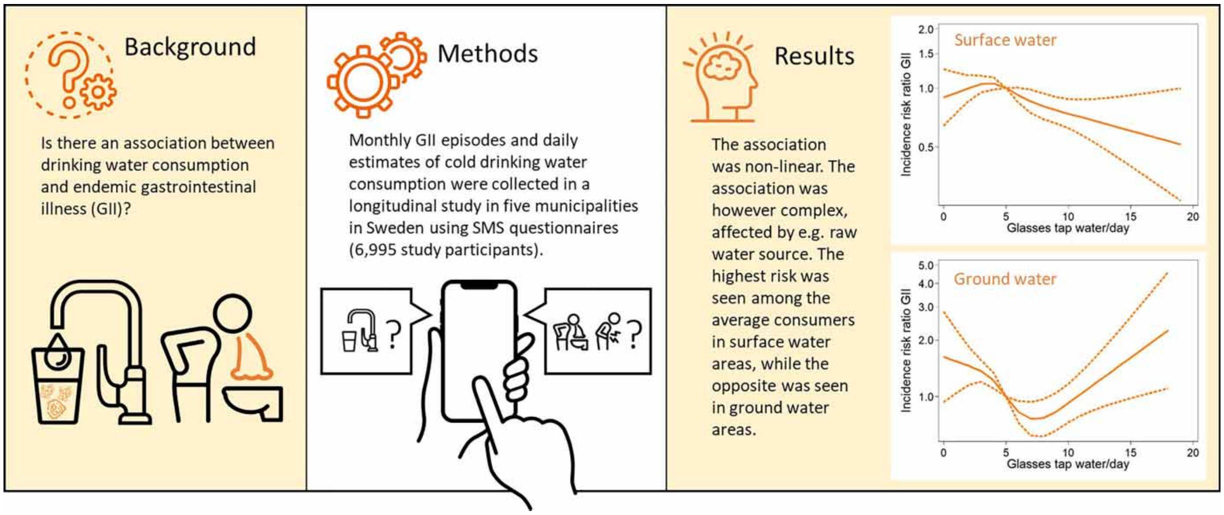
It is well known that municipal drinking water may be the cause of gastrointestinal illness (GII) outbreaks, but it is still unclear to what extent drinking water contributes to endemic GII. To explore this, we conducted a prospective cohort study among 6,955 adults in five municipalities in Sweden, collecting monthly GII episodes and mean daily cold drinking water consumption through SMS (Short Message Service). When the association between drinking water consumption and GII (all symptoms) and acute gastrointestinal illness (AGI, vomiting and/or three loose stools during a 24-h period) were assessed, there were indications that the association departed from linearity, following a unimodal shape. Among consumers in surface water areas, the highest risk of GII and AGI was generally seen among the average consumers, while the opposite was seen among groundwater consumers. The association however also seemed to be affected by neighbouring communities. The results of the study indicate that there is indeed an association between drinking water consumption and endemic GII, but the nature of this association is complex and likely affected by multiple factors, for example, water source type in the home and degree of exposure to drinking water from additional sources.

Key words: drinking water, epidemiology, gastroenteritis, gastrointestinal illness, tap water, water intake

HIGHLIGHTS

- Association between drinking water consumption and endemic GII was non-linear.
- Raw water type affected the association, with the risk of GII being higher in surface water areas.
- Association is also likely affected by exposure to drinking water from different water sources.

GRAPHICAL ABSTRACT



INTRODUCTION

Gastrointestinal illness (GII) is a major public health concern worldwide, where person-to-person transmission and food and drinking water are the most common sources of pathogen exposure (Scallan *et al.* 2011). While it is well known that municipal drinking water may be the source of GII outbreaks (Guzman-Herrador *et al.* 2015), it is still unclear to what extent drinking water contributes to the endemic GII. Several studies have indicated that drinking water may be a source of endemic GII, even when drinking water meets current drinking water quality standards (Payment *et al.* 1991, 1997; Colford *et al.* 2002, 2005, 2009; Pollock *et al.* 2008) – although some studies have reported no such indications (Hellard *et al.* 2001; Colford *et al.* 2005; Gorelick *et al.* 2011). While an ecological (population-based) exposure strategy has been common in studies assessing drinking water-related endemic GII, some studies have used individual drinking water consumption to assess the association for GII. Although some of these studies point towards a linear association between drinking water consumption and GII (Stuart *et al.* 2003; Goh *et al.* 2004, 2005; Hunter *et al.* 2004; Jones *et al.* 2007), non-linear associations have been reported as well (St-Pierre *et al.* 2009; Febriani *et al.* 2010). There have also been indications that drinking water may contribute to protective immunity (McAnulty *et al.* 2000; Frost *et al.* 2005), thus a potential association between drinking water consumption and GII may therefore potentially depart from linearity.

To explore the association between drinking water consumption and GII further, we conducted a prospective cohort study among 6,955 adults in five municipalities in Sweden during 2012–2015. A cohort study design allowed us to follow individuals over time, observing their self-reported drinking water consumption habits and GII episodes, providing longitudinal data to investigate a possible causal relationship while accounting for confounding factors. Individual information on GII episodes (28-day recall) and mean daily cold tap water consumption (24-h recall) was collected monthly during one-year periods. The collection of repeated estimates of water consumption and GII incidence from the same population, in several areas in Sweden, facilitated the assessment of a potential association in more detail.

METHODS

Study areas and source populations

We chose five municipalities across two regions of Sweden as our study areas: Falun and Borlänge in central Sweden, and Ale, Partille, and parts of Gothenburg in southwestern Sweden. The main objective of our study was to examine the relationship between tap water consumption and gastrointestinal infections (GIIs) within an endemic context. Additionally, we integrated a natural experiment into our study design due to planned improvements in water treatment by several Swedish drinking water producers during the study period. This natural experiment aimed to evaluate the impact of these planned changes on the risk of GII, and the results of these experiments have been detailed in a previous paper (Säve-Söderbergh *et al.* 2020).

Our selection of study areas was based on the types of drinking water treatment or raw water sources, as well as the planned changes in these treatments or sources, as mentioned above. In brief, these planned changes were as follows: In Partille, the water treatment plant was scheduled for an upgrade involving the addition of nanofiltration, resulting in a presumed increased pathogen reduction. Due to the discovery of indicator bacteria in the municipal water monitoring programme, the population received drinking water from a treatment plant in neighbouring city of Gothenburg during the upgrade of the Partille water treatment plant. On the other hand, Falun was transitioning its water supply from surface water to groundwater following the construction of a new groundwater treatment plant in the neighbouring town of Borlänge. This change was driven by various considerations, including economic factors and the vulnerability of water resources. No significant water-related outbreaks or events occurred in these areas, and overall quality characteristics were similar across all areas.

As the present study aims to evaluate the association between water consumption and GII, we only include the baseline data collection period to avoid the influence of changes in raw water and water treatment. Furthermore, we have only included participants connected to the public water supply, excluding those relying on private wells at their permanent residence. More comprehensive information regarding the changes in treatment or raw water source, GII incidence in the study populations, description and validation of the data collection methods, as well as validation of the findings, can be found in previous publications (Säve-Söderbergh *et al.* 2018, 2019, 2020).

The drinking water utilities assisted us in identifying the source populations. The total population in Falun and Borlänge was about 80,000 inhabitants, equally distributed between the two localities, while the total population in the selected area in Gothenburg was about 250,000 inhabitants, and the population in Partille and Ale was about 37,000 and 30,000, respectively. The source population aged 18–80 years and comprised about 75% of the total population (Statistics Sweden 2017). Surface water was used as raw water in the southern parts of Ale, and in Gothenburg, Partille and Falun, while groundwater was used in the northern parts of Ale and in Borlänge.

Recruitment

For recruitment, we used the national consumer register (Bisnode, containing contact information corresponding to 87% of the Swedish population >16 years). From the source population, a representative selection (by sex and age, 18–80 years) was contacted by professional interviewers using computer-assisted telephone interviews. Respondents residing <5 days a week at their registered home address or having chronic or recurring GII were not considered for participation. The Swedish language was used exclusively in the study and 0.3–3% of the participants, depending on the area, were unable to complete the recruitment interviews due to the language barrier. During the recruitment interview, background information on the respondent and their household was collected. The response rate ranged between 25 and 44%, depending on the area. Participation in the cohort was confirmed by informed consent. The study population characteristics had a high representability as compared to the general population in the areas. The representability of the result and the study methods were also confirmed in several validation studies (Säve-Söderbergh *et al.* 2018, 2019, 2020). The regional ethical review board in Uppsala approved the study.

SMS cohort

Data included in the present study were collected during 2012–2015, with different data collection periods for the different areas (Figure 1): Ale in March 2012–March 2013; Falun and Borlänge in November 2012–October 2013; and Ale, Partille and Gothenburg in March 2014–April 2015. Participants in each area were divided into two sub-panels, similar with respect to sex, age, water source and daily water consumption as reported at recruitment. Each sub-panel received monthly SMS questionnaires either around the turn of, or in the middle of each month. The questionnaires were sent out according to a pre-set schedule, ensuring an even distribution of the send-out dates between days of the week during the study period. The questionnaires (Supplementary material, Table S1) were sent at 10 AM, with a pre-reminder SMS being sent out 24 h earlier. The participants were asked to report the number of glasses of cold tap water consumed during the last 24 h (one glass equalling 200 mL) and the number of self-defined GII episodes during the last 28 days (Supplementary material, Table S1). In the case of illness, the participants were asked to report the number of self-defined GII episodes during the last 14 days and the duration and symptoms of the last GII episode. In case of non-response SMS reminders were sent after 6 and 24 h. To minimise reporting of traveller's diarrhoea, the participants were instructed to reply with the word 'travel' if they had been travelling abroad for at least a 7-day period during the past 28 days. Participants replying so did not receive SMS-questions about a 28-day recall of GII in that particular wave. The exception to this was data collection in Ale during 2012–2013, where

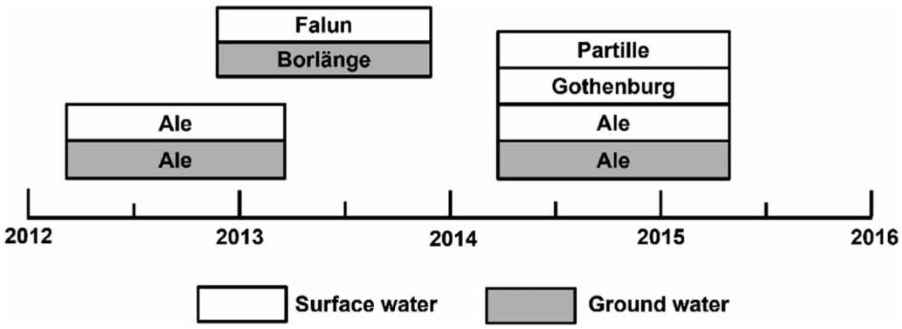


Figure 1 | Data collection periods and water source in the cohort in the Swedish municipalities Ale, Partille, Gothenburg, Falun and Borlänge, 2012–2015.

participants were simply instructed not to answer the SMS questionnaires at all in case of travel for at least a 7-day period during the past 28 days. The respondents received a lottery scratch card every, or every second month.

Case definition

Based on the symptoms reported by the participants we used GII (any symptoms) and acute gastrointestinal illness (AGI, vomiting and/or three loose stools during a 24-h period) as case definition. If a respondent had replied only to the first SMS question on water consumption, we assumed that the respondent had not suffered from GII during the last 28 days.

Statistical analysis

χ^2 tests were used to assess differences in population characteristics. The GII or AGI incidence, for each case definition, was calculated as (number of GII/AGI episodes/SMS responses)*(28 days/365.25 days). When multiple episodes of GII or AGI during a 28-day period were reported, this was included in all analyses.

Based on the distribution of the data, Poisson regression was used to assess the association, incidence risk ratio (IRR) and 95% confidence interval (CI), between the individual mean daily consumption of unheated tap water and 28-day incidence of GII or AGI. The individual mean daily consumption was categorised as $\leq$2, >2 to $\leq$4, >4 to $\leq$6, >6 to $\leq$8 and >8 glasses. The 4–6 glasses category was used as a reference in the regression analyses, representing the average consumption. To further assess the relationship between the average individual water consumption, calculated from all 24-h consumption estimates for each participant, and GII and AGI, we plotted the data using restricted cubic splines (Orsini & Greenland 2011). When plotting the data, four knots were placed at the 5th, 35th, 65th and 95th percentile (default for four knots) and five glasses were used as reference. In the models, all reported events of GII or AGI were summed and the total number of SMS responses from each respondent was treated as offset. Participants replying to fewer than two SMS questionnaires were excluded from the analyses (excluding 4% of the participants). Confounders were selected based on prior knowledge of potential risk factors, thus the final model was adjusted for age ($\geq$55/ < 55), sex (male/female) and having children aged 0–5 years (yes/no). Extreme water consumption was reported at random on a few occasions, and therefore, single self-reports exceeding 30 glasses/24 h (6 l/24 h) as well as individuals with an average daily cold tap water consumption exceeding 20 glasses (4 l/24 h) were excluded. To assess potential raw water-related differences, we stratified the data by raw water source and area in a sensitivity analysis. Statistical analysis was performed using Stata 14.2 (StataCorp, Texas, USA) and the significance level was set at 0.05.

RESULTS

The study included 6,955 cohort participants who responded to – in total – 75,875 SMS questionnaires during the data collection periods (91% of all SMS questionnaires sent out among these participants were answered). Of the participants, 4,612 and 2,343 received drinking water produced from surface water and groundwater, respectively. We observed some differences in the baseline characteristics between the exposure categories, with a significant difference for age and sex (Table 1). The proportion of females was lowest in the lowest consumption category and increased in the higher consumption categories. The highest consumption category had the lowest proportion of the population $\leq$35 years and the highest proportion of the population $\geq$55 years, consequently the population was older in this category compared to other consumption categories.

Table 1 | Population characteristics of the study participants, by quartiles of average individual consumption in glasses, stratified by water source

Water source	Variables		≤ 2 glasses	> 2– ≤ 4 glasses	> 4– ≤ 6 glasses	> 6– ≤ 8 glasses	> 8 glasses	*p*-value
All								
(*n* = 6,955)	Total	*n*	493	1,956	2,323	1,335	849	
	Age	≤35 years	102	390	438	244	161	0.001
		36–54 years	210	812	1,015	654	409	
		≥55 years	181	754	870	437	279	
	Sex	Male	322	1,174	1,173	581	335	<0.001
		Female	171	782	1,150	754	514	
	Children 0–5 y	No	444	1,738	2,068	1,195	767	0.8
		Yes	49	218	255	140	82	
	Areas	Ale	223	708	803	486	293	<0.001
		Partille	74	310	373	189	114	
		Gothenburg	40	206	251	148	113	
		Falun	92	392	412	248	152	
		Borlänge	64	340	484	264	177	
	Average consumption	Glasses	1.3	3.1	4.9	6.8	10	
Surface water								
(*n* = 4,612)	Total	*n*	335	1,342	1,516	865	555	
	Age	≤35 years	74	273	324	173	115	0.1
		36–54 years	140	582	652	426	252	
		≥55 years	121	487	540	266	188	
	Sex	Male	224	795	743	366	211	<0.001
		Female	111	547	773	499	344	
	Children 0–5 y	No	296	1,171	1,317	754	495	0.7
		Yes	39	171	199	111	60	
	Areas	Ale	129	434	480	280	176	0.07
		Partille	74	310	373	189	114	
		Gothenburg	40	206	251	148	113	
		Falun	92	392	412	248	152	
	Average consumption	Glasses	1.3	3.1	4.9	6.8	10	
Ground water								
(*n* = 2,343)	Total	*n*	158	614	807	470	294	
	Age	≤35 years	28	117	114	71	46	<0.001
		36–54 years	70	230	363	228	157	
		≥55 years	60	267	330	171	91	
	Sex	Male	98	379	430	215	124	<0.001
		Female	60	235	377	255	170	
	Children 0–5 y	No	148	567	751	441	272	0.9
		Yes	10	47	56	29	22	
	Area	Ale	94	274	323	206	117	<0.001
		Borlänge	64	340	484	264	177	
	Average consumption	Glasses	1.4	3.0	4.9	6.8	9.8	

Note: χ^2 tests were used to assess *p*-value and significant level was set at $p < 0.05$.

The average incidence of GII and AGI were 0.69 and 0.48 episodes/person-year, respectively (Table 2). The incidence among the population receiving surface water was higher as compared to the population receiving groundwater, corresponding to 0.75 and 0.54 episodes of GII/person-year and 0.51 and 0.41 episodes of AGI/person-year for surface and groundwater, respectively. For GII the highest incidence (0.80 episodes/person-years) was seen in the >2 to ≤4 glasses consumption category, while for AGI the highest incidence (0.50 episodes/person-year) was in the >4 to ≤6 glasses consumption category.

When all data were included, a significantly increased risk of GII in the lower consumption categories (≤2 glasses: IRR 1.16, 95% CI: 1.02–1.31; >2– ≤ 4 glasses: IRR 1.20, 95% CI: 1.12–1.30, Table 3), while an inverse association were seen in the highest consumption category (>8 glasses: IRR 0.87, 95% CI: 0.78–0.98), as compared to the average. For AGI, no significant association was seen. When the model was stratified by raw water source, consumption of surface water indicated

Table 2 | Incidence (cases/person-year) of GII and AGI (i.e. vomiting and/or at least three loose stools during 24 h) by quartiles of average individual consumption in glasses, stratified by water source

	Cases/person-year					
Outcome and water source	**Total**	**≤2 glasses**	**>2–≤4 glasses**	**>4–≤6 glasses**	**>6–≤8 glasses**	**>8 glasses**
GII						
All ($n = 5,683$)	0.69	0.76	0.80	0.66	0.60	0.59
Surface water ($n = 3,729$)	0.75	0.80	0.82	0.77	0.70	0.59
Ground water ($n = 1,954$)	0.54	0.67	0.76	0.44	0.41	0.53
AGI						
All ($n = 5,683$)	0.48	0.44	0.49	0.50	0.47	0.45
Surface water ($n = 3,729$)	0.51	0.45	0.49	0.55	0.53	0.47
Ground water ($n = 1,954$)	0.41	0.42	0.48	0.39	0.34	0.41

Table 3 | Incidence risk ratio (IRR) and 95% confidence interval (CI) of GII and AGI (vomiting and/or at least three loose stools during 24 hours) by quartiles of average individual consumption in glasses, stratified by water source

Outcome and water source	**≤2 glasses IRR (95% CI)**	**>2–≤4 glasses IRR (95% CI)**	**>4–≤6 glasses IRR (95% CI)**	**>6–≤8 glasses IRR (95% CI)**	**>8 glasses IRR (95% CI)**
GII					
All ($n = 6,955$)	1.16 (1.02–1.31)	1.20 (1.12–1.30)	1.00 (ref)	0.94 (0.86–1.04)	0.87 (0.78–0.98)
Surface water ($n = 4,612$)	1.05 (0.91–1.22)	1.06 (0.97–1.16)	1.00 (ref)	0.95 (0.86–1.06)	0.77 (0.67–0.88)
Ground water ($n = 2,343$)	1.50 (1.18–1.91)	1.72 (1.48–2.00)	1.00 (ref)	0.91 (0.75–1.10)	1.22 (0.99–1.50)
AGI					
All ($n = 6,955$)	0.90 (0.77–1.06)	0.99 (0.90–1.08)	1.00 (ref)	0.96 (0.86–1.06)	0.90 (0.79–1.02)
Surface water ($n = 4,612$)	0.84 (0.69–1.01)	0.91 (0.82–1.02)	1.00 (ref)	0.99 (0.88–1.12)	0.85 (0.73–0.99)
Ground water ($n = 2,343$)	1.13 (0.84–1.51)	1.22 (1.02–1.45)	1.00 (ref)	0.87 (0.70–1.07)	1.01 (0.80–1.28)

Note: Poisson model analyses adjusted for sex (male/female), children age 0–5 year (yes/no), age (<36/36–55/≥55 years).

no association in the lower consumption categories, while a significantly lower risk of GII and AGI was seen in the highest consumer category IRR 0.77 (95% CI: 0.67–0.88) and 0.85 (95% CI: 0.73–0.99), respectively, compared to the average consumer category. A significantly higher risk of GII and AGI in the lowest consumer categories in the groundwater areas (GII ≤2 glasses: IRR 1.50, 95% CI: 1.18–1.91; GII >2–≤4 glasses: IRR 1.72, 95% CI: 1.48–2.00; AGI ≤2 glasses: IRR 1.13, 95% CI: 0.84–1.51; >2–≤4 glasses: IRR 1.22, 95% CI: 1.02–1.45), while no association were seen in the highest consumer categories, compared to the reference category.

When the model was plotted using a restricted cubic spline, there were clear indications that the association between drinking water consumption and GII and AGI departed from linearity, indicating a unimodal shape (Figure 2). The shape, however, differed depending on the raw water source, where the highest risk of GII and AGI was seen among the average consumers in surface water areas (Figure 3), while the highest and lowest consumer categories indicated the highest risk in groundwater areas (Figure 4). After additional stratification by municipalities, both municipalities receiving groundwater indicated similar associations, with the lowest risk of GII and AGI among the average drinking water consumers (Supplementary material, Figures S1 and S2). Two of the surface water areas – neighbouring to the groundwater communities – also indicated the lowest risk of GII and AGI among the average drinking water consumers (Supplementary material, Figures S3 and S4), while the two other surface water areas indicated an inverse association, with the highest risk of GII and AGI among the average consumers.

DISCUSSION

In this large-scale prospective cohort, comprising almost 7,000 participants, we observed indications that the association between drinking water consumption and GII and AGI seems to depart from linearity, and instead indicate a unimodal

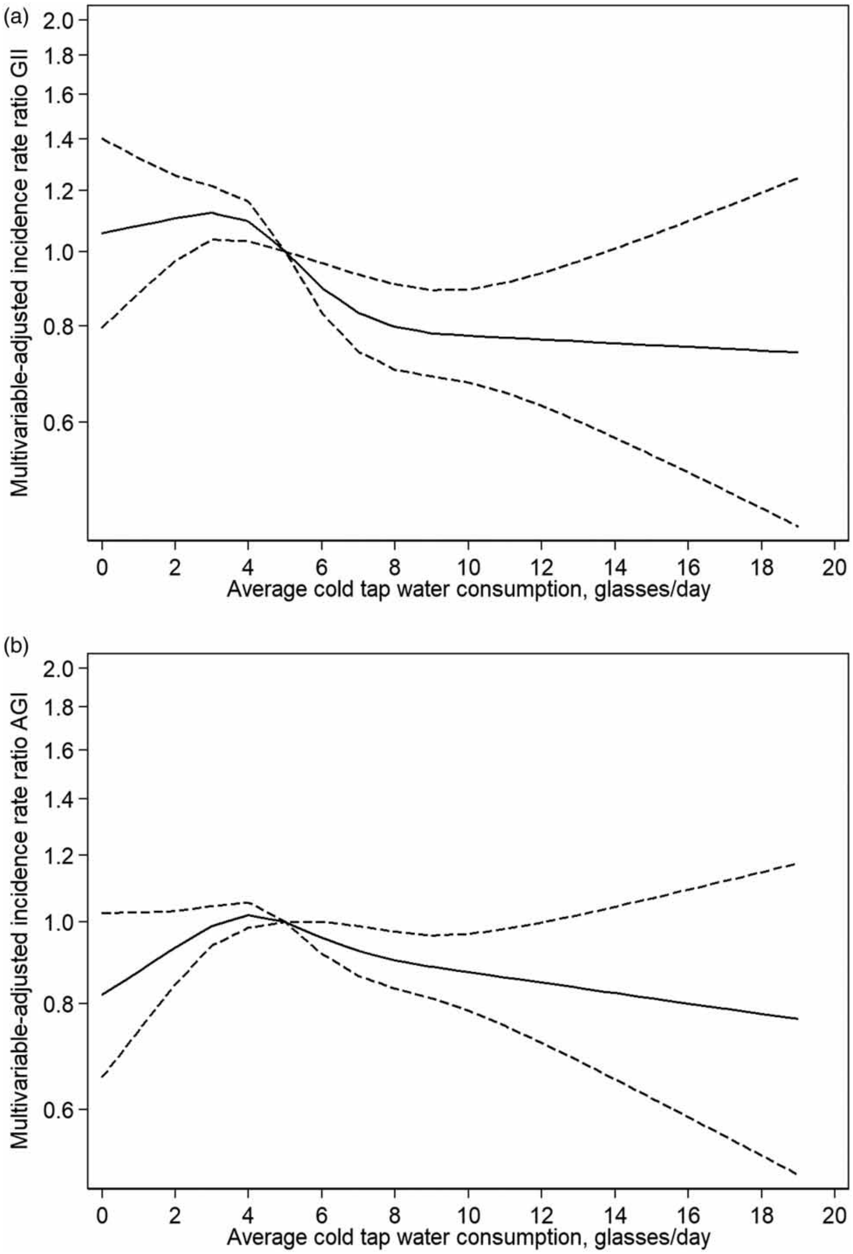


Figure 2 | Multivariable-adjusted incidence rate ratio (IRR) and 95% confidence intervals (CIs) of the average water consumption in glasses/day for all raw water types and the risk of gastrointestinal illness (GII; a) and acute gastrointestinal illness (AGI; b) using restricted cubic splines with four knots. Splines (solid line) and 95% CI (dashed lines).

shape. The association also seems to be affected by raw water sources, as the risk of GII and AGI was highest among the average consumers of surface water, while the opposite was seen among groundwater consumers. While similar associations were seen for both GII and AGI, the association was more pronounced for GII.

As mentioned, the evidence of an association between drinking water consumption and endemic GII is inconsistent, as some studies indicate an association (Stuart *et al.* 2003; Goh *et al.* 2004, 2005; Hunter *et al.* 2004; Jones *et al.* 2007) while others do not (St-Pierre *et al.* 2009; Febriani *et al.* 2010), despite most of these studies having been made in fairly similar settings, including population characteristics, study design and statistical approach. We found indications that the association was affected by area and raw water type between drinking water consumption for both GII and AGI, indicating that the raw water to some extent may explain the inconsistency seen previously. Previous studies have generally indicated that drinking

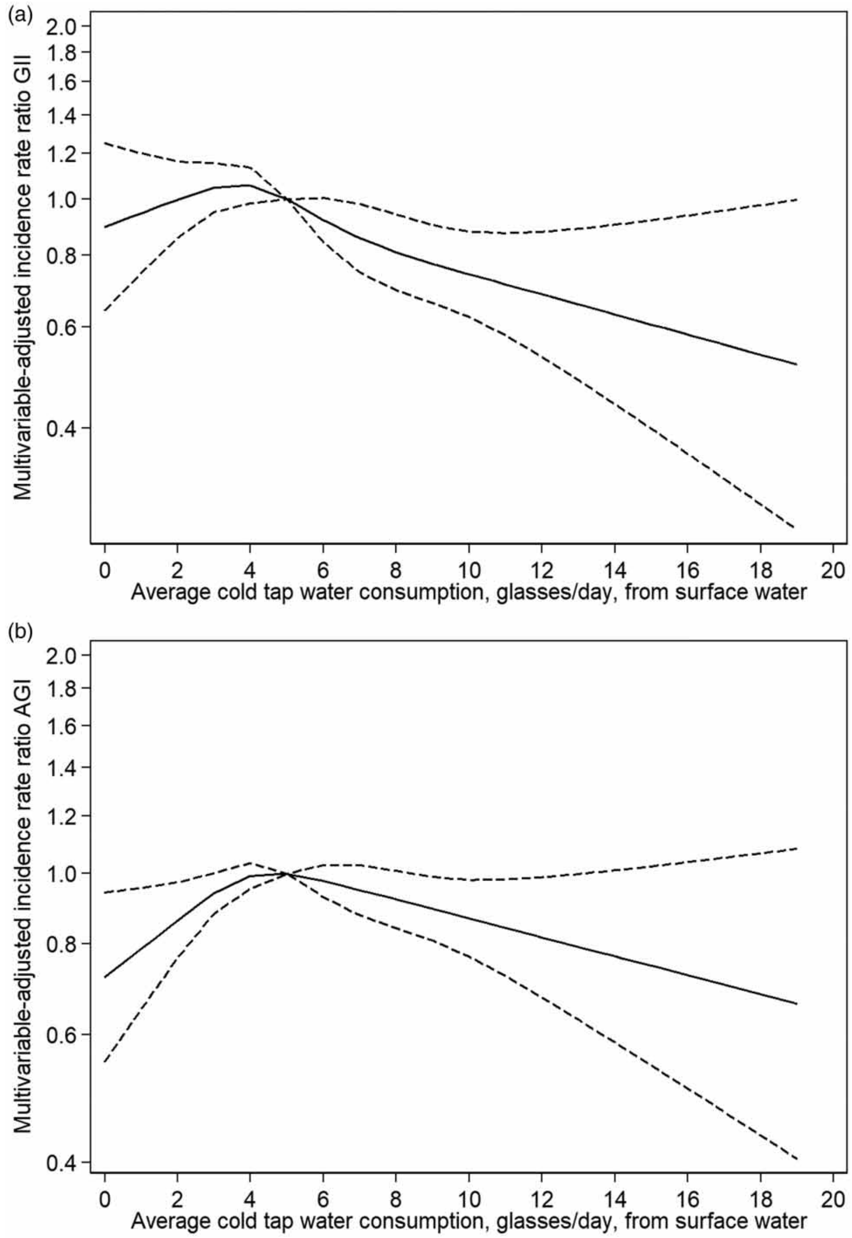


Figure 3 | Multivariable-adjusted incidence rate ratio (IRR) and 95% confidence intervals (CIs) of the average water consumption in glasses/day for surface water and the risk of gastrointestinal illness (GII; a) and acute gastrointestinal illness (AGI; b) using restricted cubic splines with four knots. Splines (solid line) and 95% CI (dashed lines).

water originating from surface water is associated with a higher risk of endemic GII, as compared to groundwater (Odoi *et al.* 2004; Uhlmann *et al.* 2009; Kabore *et al.* 2010) and that endemic GII is related to the reduction potential of the drinking water treatment efficiency and the type of raw water source (Tornevi *et al.* 2016). In the present study, the incidence of GII and AGI was lower in the groundwater areas as compared to surface water areas. We also saw indications of raw water-related differences in the relationship between drinking water consumption and GII and AGI, where the groundwater areas exhibited a more homogenous relationship between areas, while some of the surface water areas indicated an inverse relationship. As surface water naturally harbours a higher concentration of microorganisms and is also more exposed to contamination, there is an elevated risk of pathogens ending up in the drinking water. This could account for the higher incidence of GII and AGI among individuals residing in areas supplied with surface water compared to those supplied with

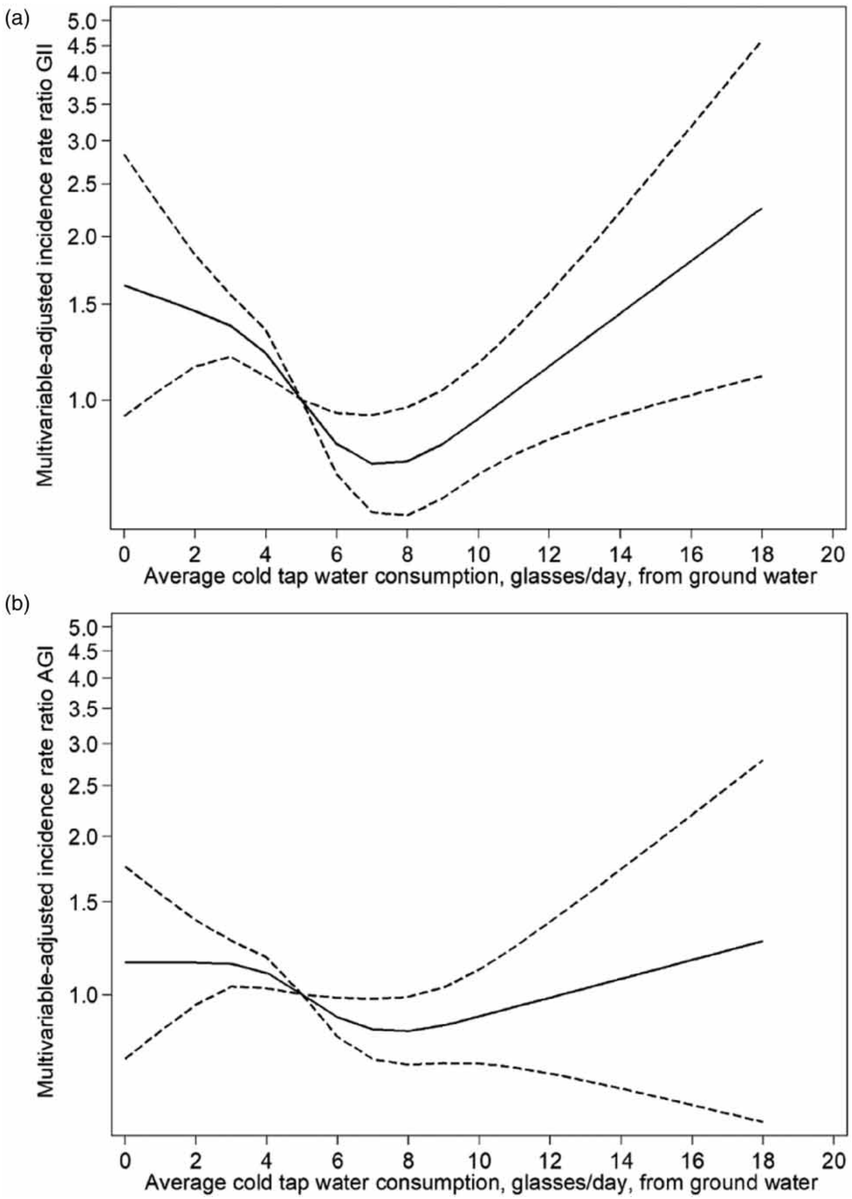


Figure 4 | Multivariable-adjusted incidence rate ratio (IRR) and 95% confidence intervals (CIs) of the average water consumption in glasses/day for ground water and the risk of gastrointestinal illness (GII; a) and acute gastrointestinal illness (AGI; b) using restricted cubic splines with four knots. Splines (solid line) and 95% CI (dashed lines).

groundwater. It is worth noting however that studies have identified pathogens, such as viruses (Borchardt *et al.* 2012), in groundwater utilised for municipal drinking water, suggesting that consumers relying on groundwater may also face some level of risk of pathogen exposure through their drinking water. Supporting this, Tornevi *et al.* (2016) demonstrated an association between telephone calls about AGI symptoms to the Swedish National Healthcare Guide and the theoretical log-reduction capacity of the drinking water treatment in 20 cities. Overall, AGI-calls decreased by 4% with each unit log-reduction. While the relationship was more pronounced in cities using surface water, there was however a statically significant effect in cities using groundwater, indicating that drinking water produced by groundwater also contributed to AGI.

While we have several hypotheses regarding the variance in association between raw water sources and the apparent deviation from linearity, we acknowledge the intricate nature of this potential association and recognise that multiple factors are likely to interact. These factors include that closely neighbouring areas exhibited similar relationships between drinking water consumption and GII and AGI, even when the drinking water originated from different raw water sources. This may to some extent be due to commuting to a neighbouring community. In a previous study, we showed that on average one-third of cold tap water is consumed outside of the home (Säve-Söderbergh *et al.* 2018), supporting the hypothesis that other water sources may influence the association. For future research, an improvement in the study design would be to only collect estimates on water consumed at home, or alternatively, ask study participants to record their water consumption at home and away from home separately. Apart from the two areas, the lowest risks of GII and AGI were seen among consumers with an average drinking water consumption. This could indicate that a higher consumption could result in a higher exposure to pathogens, but also that acquired immunity to waterborne pathogens due to moderate exposure may play a role in the association, which possibly could explain why low consumer categories are at high risk of GII and AGI. The case definition may also contribute to inconsistent findings of an association between drinking water consumption and GII in previous studies. Some of the previous studies detecting an association between drinking water consumption and GII employed a strict case definition like medically confirmed cryptosporidiosis (Goh *et al.* 2004, 2005; Hunter *et al.* 2004) and giardiasis (Stuart *et al.* 2003). Using a stricter case definition will increase the sensitivity of the outcome, but the generalisability might be compromised due to country or region-specific differences in the incidence or pathogen transmission pathways. One of the studies which detected an association between drinking water consumption and cryptosporidiosis, was in fact assessing the association during an outbreak setting, before and after the introduction of membrane filtration in the water treatment, which is a highly efficient water treatment method (Goh *et al.* 2005). Consequently, the results are unlikely to be applicable in countries like Sweden, which has a low incidence of domestic endemic cryptosporidiosis. Furthermore, during the study period, most drinking water treatment plants included in the present study already were highly efficient against waterborne protozoa. To our knowledge, only one previous study has used self-reported AGI as the outcome (Jones *et al.* 2007), but the study did not assess the shape of the association between drinking water consumption and AGI. In another study drinking water consumption and diarrhoea were assessed and they reported indications of a non-linear inverse association when comparing non-consumers to consumers of 1–3 glasses of water, OR 0.68 (95% CI: 0.49–0.93) (St-Pierre *et al.* 2009). Based on the findings seen in the present study and previous studies, future studies should focus on assessing the indicated non-linear relationship between drinking water consumption and GII more in detail, especially when it comes to factors which may influence the association – like raw water-related differences that may affect the pathogen exposure and community-related differences – but also to explore the indication of a potential acquired immunity among those with the lowest consumption.

Some limitations in the present study should be addressed. First, it is relevant to highlight the low response rate for participating in the study, a common challenge in all epidemiological studies (Galea & Tracy 2007). As the study was designed to progress for several years, it is likely that some declined to participate due to the long-term commitment. Great effort was made to increase the representability of the study population and the results were validated towards the general population (Säve-Söderbergh *et al.* 2018, 2019, 2020). Second, another limitation is the self-defined case definition of GII. Using self-defined GII may introduce a recall bias, compromising the sensitivity, since non-pathogen related GII may be included in the analysed data. While a more strict case definition – or even laboratory-confirmed cases – may be preferred, only a fraction of all GII cases will seek medical care, potentially introducing another bias, that is not relevant in the present study (Scallan *et al.* 2006). However, we used AGI as our main case definition, resulting in mainly more severe cases of GII being included and minimising the inclusion of non-pathogen related GII. Third, we used a 14- and 28-day recall, which may have introduced a recall bias due to the long recall time, commonly known as telescoping. While studies have indicated that a shorter recall time may be preferred (Muller *et al.* 2012; Viviani *et al.* 2016), in a validation of our study we concluded that a 7-day estimate yielded only a 10–15% higher GII estimate as compared to using a 14-day recall (Säve-Söderbergh *et al.* 2018), thus any underreporting of GII in the present study is expected to be low. Finally, with the exception of travel-related illness, we had limited information on the aetiology behind the GII. However, to avoid the risk of introducing an information bias, we did not collect additional information linked to aetiology.

The study also has several strengths that should be highlighted. To this date, this is one of the largest longitudinal cohort studies to assess the association between drinking water consumption and GII. Due to the extensive data collection, we were able to assess the association between drinking water consumption and GII more in detail by plotting the data to assess the shape of the association. Using SMS was an efficient method for a longitudinal cohort, and while the response rate for participating in the study was fairly low, the response rate among the participants was high throughout the study period. Thanks to the longitudinal study design we were also able to collect drinking water consumption estimates through all weekdays throughout the year and GII estimates during the entire year, limiting any bias linked to seasonal differences or differences between days of the week. It should also be mentioned that extensive validation of the data collection method was done in a previous paper – including nation-wide validation (Säve-Söderbergh *et al.* 2018, 2019).

CONCLUSIONS

In conclusion, in this large-scale cohort in Sweden, there were indications of a non-linear association between consumption of municipal drinking water for both GII and AGI. The highest risk of GII and AGI was generally seen among the average consumers among consumers in surface water, whereas indications of the opposite were seen among groundwater consumers. Still, the association seemed to be affected by neighbouring communities and the indicated differences between raw water should therefore be interpreted with caution. In other words, the results of the study indicate that there is indeed an association between drinking water consumption and endemic GII, but the nature of this association is complex and likely affected by multiple factors, for example, water source type in the home and the degree of exposure to drinking water from additional sources.

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DATA AVAILABILITY STATEMENT

Data cannot be made publicly available; readers should contact the corresponding author for details.

CONFLICT OF INTEREST

The authors declare there is no conflict.

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