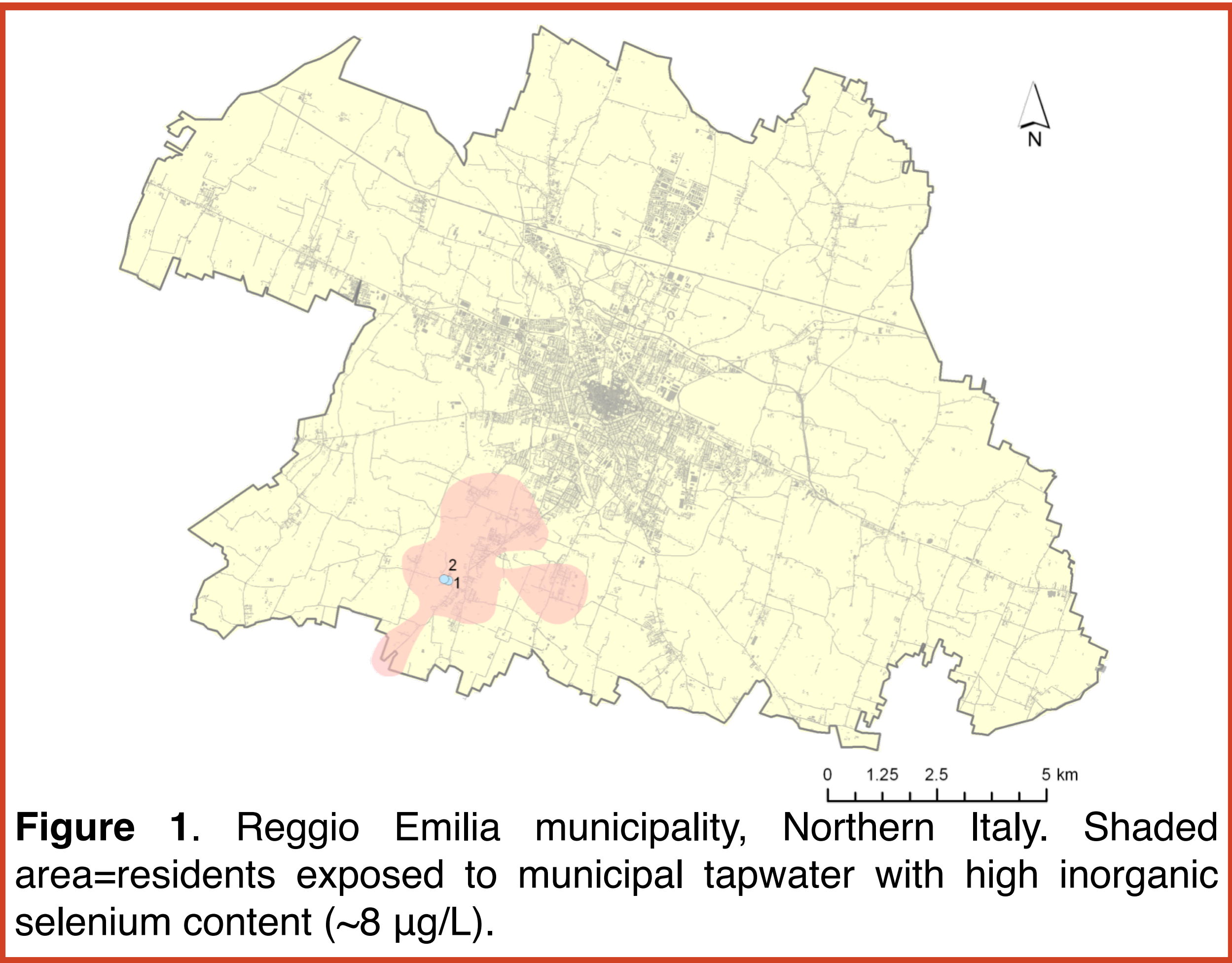


Exposure to inorganic selenium in drinking water and incidence of amyotrophic lateral sclerosis: a long-term follow-up of a natural experiment

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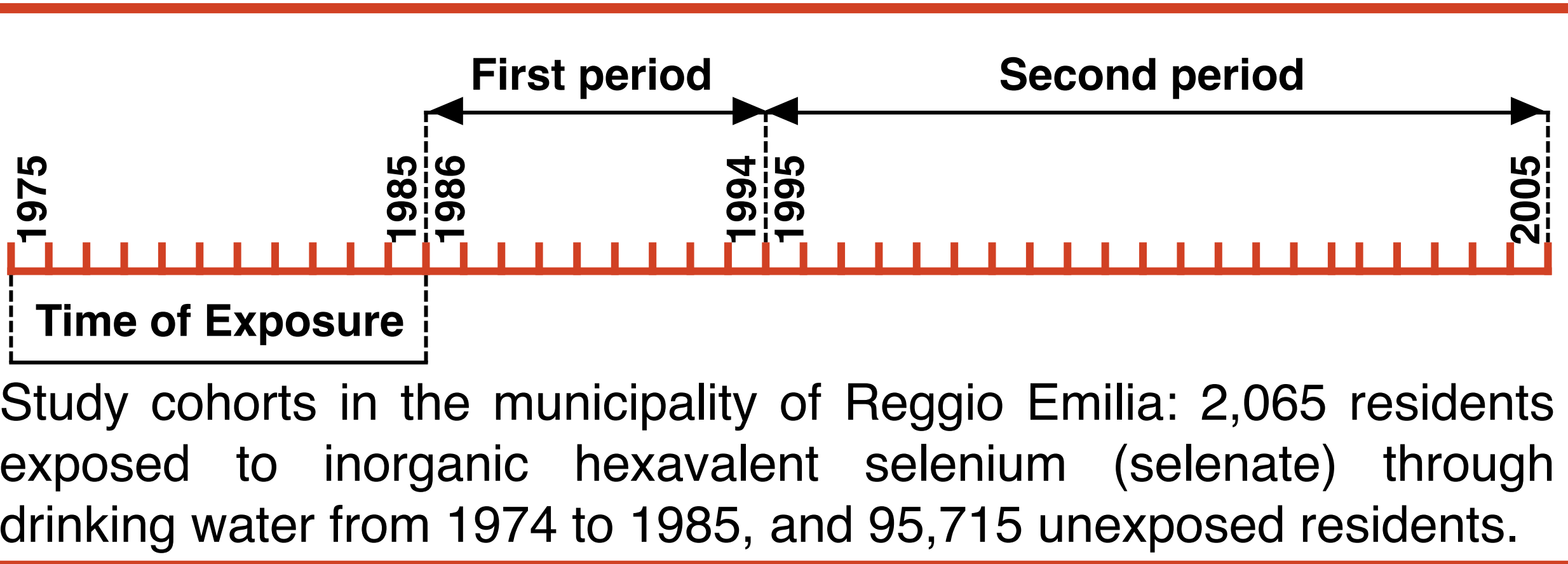
Background

Some studies have reported an association between overexposure to selenium and risk of amyotrophic lateral sclerosis (ALS), a rare degenerative disease of motor neurons. From 1986 through 2015, we followed a cohort in Northern Italy that had been inadvertently consuming tap water with unusually high concentrations of inorganic hexavalent selenium from 1974 to 1985 (**Figure 1**).



Methods

We had previously documented an excess incidence of ALS in this cohort during 1986-1994. Here, we report extended follow-up of the cohort for an additional 21 years, encompassing 50,100 person-years of the exposed cohort and 2,233,963 person-years of the unexposed municipal cohort. We assessed ALS risk using a Poisson regression analysis, adjusting for age, sex and calendar year.



Results

During follow-up, we identified 7 and 112 incident ALS cases in the exposed and unexposed cohorts, respectively, yielding crude incidence rates of 14 and 5 cases per 100,000 person-years (**Table 1**). The Poisson regression analysis produced an overall incidence rate ratio (IRR) for ALS of 2.8 (95% confidence interval (CI) 1.3, 6), with a substantially stronger IRR in 1986-1994 (8.2, 95% CI 2.7, 24.7) than in 1995-2015 (1.5, 95% CI 0.5, 4.7), and among women (5.1, 95% CI 1.8, 14.3) than men (1.7, 95% CI 0.5, 5.4) (**Table 2**).

	Selenium-exposed cohort				Unexposed cohort				Rate difference
	Cases/Non cases	Person-years	Rate	95% CI	Cases/Non cases	Person-years	Rate	95% CI	
All subjects	7/ 2,058	50,100	14.0	6.7, 29.3	112/ 95,603	2,233,963	5.0	4.2, 6.0	9.0
By sex									
Men	3/ 1,017	24,522	12.2	3.9, 37.9	73/ 44,772	1,036,533	7.0	5.6, 8.9	5.2
Women	4/ 1,041	25,578	15.6	5.9, 41.7	39/ 50,831	1,197,430	3.3	2.4, 4.5	12.4
By period									
1985-1994	4/ 2,061	17,561	22.8	8.5, 60.7	21/ 95,694	803,347	2.6	1.7, 4.0	20.2
1995-2015	3/ 1,831	32,539	9.2	3.0, 28.6	91/ 82904	1,430,616	6.4	5.2, 7.8	2.9

Table 1. Number of amyotrophic lateral sclerosis cases, person-years of observation, and incidence rates (cases per 100,000 person-years), by exposure to selenium, sex, and period of follow-up in Reggio Emilia, Northern Italy, 1985-2015.

	Crude		Adjusted ^a		Adjusted ^b	
	RR	95% CI	RR	95% CI	RR	95% CI
All subjects	2.8	1.3, 6.0	2.7	1.3, 5.8	2.8	1.3, 6.0
By sex						
Men	1.7	0.5, 5.5	1.7	0.5, 5.5	1.7	0.5, 5.4
Women	4.8	1.7, 13.4	4.6	1.7, 13.0	5.1	1.8, 14.3
By period						
1985-1994	8.7	3.0, 25.4	8.6	2.9, 25.0	8.7	2.7, 24.7
1995-2015	1.4	0.5, 4.6	1.4	0.4, 4.5	1.5	0.5, 4.7

Table 2. Incidence rate ratio (RR) with its 95% confidence interval (CI) of amyotrophic lateral sclerosis in a residential cohort exposed to inorganic selenium through drinking water, Reggio Emilia, Northern Italy, 1986-2015. ^aAdjusted for sex, calendar year, and age. ^bFurther adjusted for education and occupation.

Conclusions

Overall, these results indicate an association between high exposure to inorganic selenium, a recognized neurotoxicant, and amyotrophic lateral sclerosis incidence, with declining rates after cessation of exposure and stronger effects among women.

Keywords: selenium; amyotrophic lateral sclerosis; drinking water; cohort study; incidence



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