

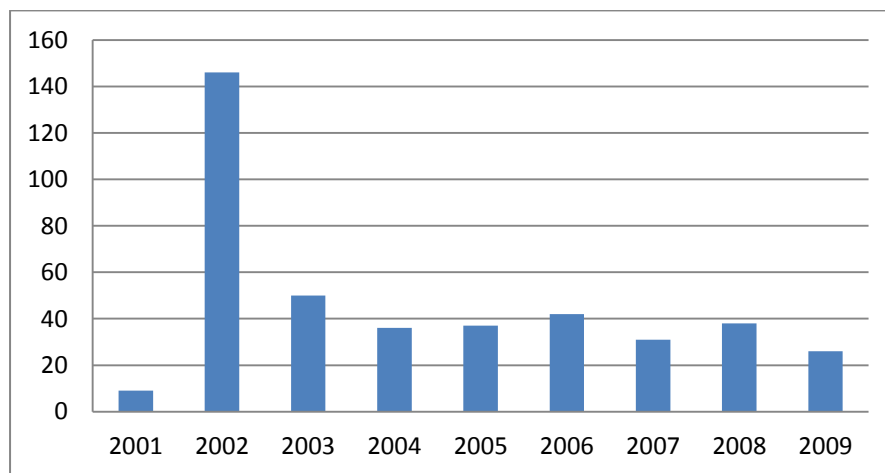
Appendix – Sensitivity analyses

A) Alternative outcome definitions

Start of follow-up (sensitivity a, b)

The follow-up period for the main analysis presented in this paper started January 1, 2003 and ended December 31, 2009, allowing 2-year period of wash-out for the Outpatient Register. Based on the distribution of new cases per year in the Outpatient Register (Figure App-1 below) we considered this period sufficient to eliminate prevalent cases of RA.

Figure App-1: Frequency of new RA cases identified through the Outpatient Register between 2001 and 2009.



However, we also performed sensitivity analyses using longer wash-out periods (Figure App-2 below).

Figure App-2: Timeline to illustrate starts of follow-up according to the main analysis and to the different sensitivity analyses performed.

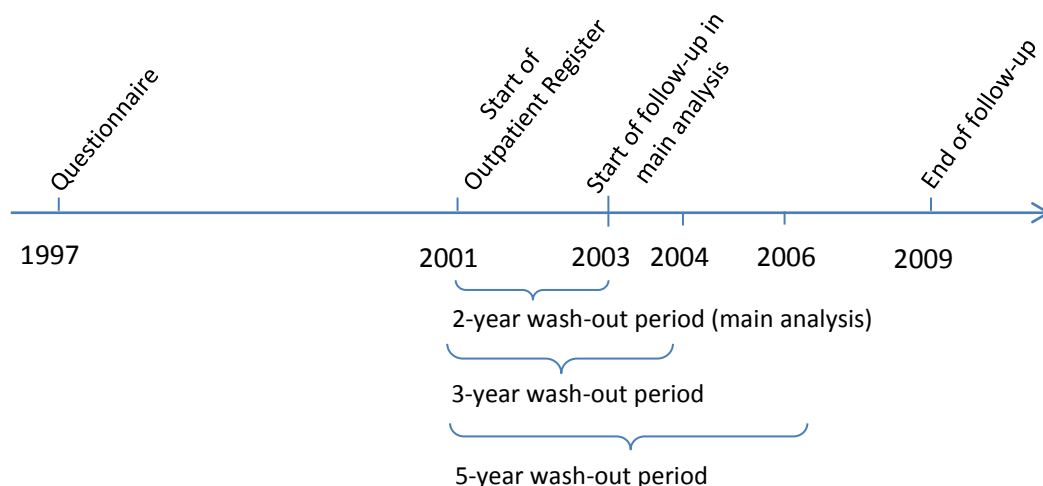


Table A shows results for sensitivity analyses for 3-year (a) and 5-year (b) wash-out periods. Risk estimates were very similar to results from the main analysis, with slightly wider confidence intervals due to smaller number of cases.

Use of Inpatient Register (sensitivity c, d)

We performed two further sensitivity analyses (Table A, c and d) additionally including the newly diagnosed RA cases identified in the Inpatient Register. In the main analysis we did not include subjects identified solely through this register since RA is not a disease that usually lead to hospitalization in the first stages and therefore those subjects were likely to be prevalent RA cases.

TABLE A. Multivariable adjusted relative risk[‡] and 95 percent confidence interval (in parenthesis) for four additional alternative case definitions (different time of follow-up and exclusion/inclusion of the Inpatient Register) by alcohol status and number of glasses of alcohol per week in the Swedish Mammography Cohort.

	Main		Sensitivity a		Sensitivity b		Sensitivity c		Sensitivity d	
	Cases	Analysis	Cases	Follow-up	Cases	Follow-up	Cases	Follow-up	Cases	Follow-up
		2-years w-o*		2004-2009		2006-2009		2003-2009		2004-2009
				3-year w-o*		5-year w-o*		+ Inpatient Reg.		+ Inpatient Reg.
Number of cases	197		151		86		265		212	
Glasses/week										
<1 or never	73	1.00	56	1.00	36	1.00	101	1.00	81	1.00
1-2	30	0.86	26	0.97	17	1.06	41	0.90	35	0.95
		(0.56 to 1.33)		(0.61 to 1.56)		(0.59 to 1.92)		(0.62 to 1.30)		(0.64 to 1.42)
2-4	45	0.99	33	0.94	19	0.93	55	0.96	43	0.93
		(0.67 to 1.46)		(0.61 to 1.47)		(0.52 to 1.65)		(0.68 to 1.35)		(0.64 to 1.37)
≥4	37	0.63	29	0.64	14	0.53	48	0.67	39	0.67
		(0.42 to 0.96)		(0.40 to 1.02)		(0.27 to 1.02)		(0.47 to 0.97)		(0.45 to 1.01)

[‡] Adjusted for age (continuous) and smoking status (categorized as never, former, current ≤10 cigarettes/day or >10 cigarettes/day).

*w-o = wash-out period

B) Exclusion of potential prevalent cases

We performed a probabilistic sensitivity analysis to evaluate in which direction our results would change if some prevalent cases were not excluded in the main analysis. Instead of using a deterministic sensitivity analysis, where the percentage of prevalent cases is fixed to a certain value, we assumed an a priori probability distribution that captures our uncertainty about the amount of prevalent cases in the cohort. We assumed that the a priori probabilistic density function of the percentage of prevalent cases among the identified RA cases is a uniform with values between 0 and 20. We then performed simulations with 200 draws from this distribution to obtain the percentages of cases that should be excluded. After excluding randomly the cases, we calculated the corresponding RR for glasses of alcohol per week. We obtained the distributions of the RR estimates according to three hypotheses (median and standard deviation of the obtained distributions are reported in table B):

1. Prevalent cases did not changed their drinking habits (prevalent cases were excluded randomly from all categories of glasses of alcohol per week)
2. All prevalent cases stopped drinking alcohol (prevalent cases were excluded only from the lower category)
3. All prevalent cases increased their alcohol consumption (prevalent cases were excluded from the upper category).

Results from these sensitivity analyses were very similar to the results from the main analysis presented in the paper.

TABLE B. Median values‡ and standard deviation of the distributions of RA relative risks by glasses of alcohol per week according to three alternative hypothesis about the behaviour of prevalent cases among incident cases (1. Prevalent cases did not changed drinking habits; 2. Prevalent cases stopped drinking; 3. Prevalent cases increased drinking).

Glasses/week	Hypothesis 1	Hypothesis 2	Hypothesis 3
<1 or never	1.00	1.00	1.00
1-2	0.86 ± 0.06	0.95 ± 0.03	0.87 ± 0.003
2-4	0.98 ± 0.05	1.09 ± 0.04	0.99 ± 0.004
≥4	0.63 ± 0.04	0.70 ± 0.03	0.58 ± 0.03

‡ Adjusted for age (continuous) and smoking status (categorized as never, former, current ≤10 cigarettes/day or >10 cigarettes/day).