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7/30/2023

Method:

Statistical analyses were performed in R version 4.3.1. Cox regression was employed to evaluate the association between measles vaccination and all-cause mortality. The 95% confidence intervals (CI) of the hazard ratios (HR) were used to interpret the findings.

Result

Among the cohort, 1007 children were female, the median age of vaccination was 10 months (Interquartile range, 9 to 11), and 200 individuals remained unvaccinated until 30 months of age (Table1).

Table 1: Open-cohort characteristics

Characteristic	Alive, N = 1,900[1]	Dead, N = 100[1]	Overall, N = 2,000[1]
Sex			
Male	946 (50%)	47 (47%)	993 (50%)
Female	954 (50%)	53 (53%)	1,007 (50%)
Date of birth	1999-10-15 to 2002-12-13	2000-02-23 to 2002-12-28	1999-10-15 to 2002-12-28
Year - Birth			
1999	11 (0.6%)	0 (0%)	11 (0.6%)
2000	388 (20%)	30 (30%)	418 (21%)
2001	564 (30%)	38 (38%)	602 (30%)
2002	937 (49%)	32 (32%)	969 (48%)
Receive vaccine	1,746 (92%)	54 (54%)	1,800 (90%)
Date of measles vaccination	2000-09-01 to 2004-04-06	2000-11-27 to 2004-01-02	2000-09-01 to 2004-04-06
Age at vaccination (months)	10.00 (9.00, 11.00)	9.00 (9.00, 10.00)	10.00 (9.00, 11.00)
Vaccination Status			
Unvaccinated	154 (8.1%)	46 (46%)	200 (10%)
Earlier (6-8 months)	119 (6.3%)	3 (3.0%)	122 (6.1%)
On-time (9-12 months)	1,480 (78%)	47 (47%)	1,527 (76%)
Late (>12 months)	138 (7.3%)	4 (4.0%)	142 (7.1%)

Likely error (<6 months)	9 (0.5%)	0 (0%)	9 (0.5%)
Death period			
Postneonatal (1-11 months)	-	40 (40%)	40 (2.0%)
Childhood (12-59 months)	-	60 (60%)	60 (3.0%)
Age at death (months)	-	13 (9, 20)	13 (9, 20)

[1] n (%); Range; Median (IQR)

A total of 1951 individuals were included in the analysis of mortality after 12 months of age. Among them, 268 children contributed as unvaccinated and vaccinated. The median follow-up period was 552 days(interquartile range, 545 to 552). The hazard ratio after 12 weeks was 0.42 (95% CI, 0.23 to 0.75) (Figure 2).

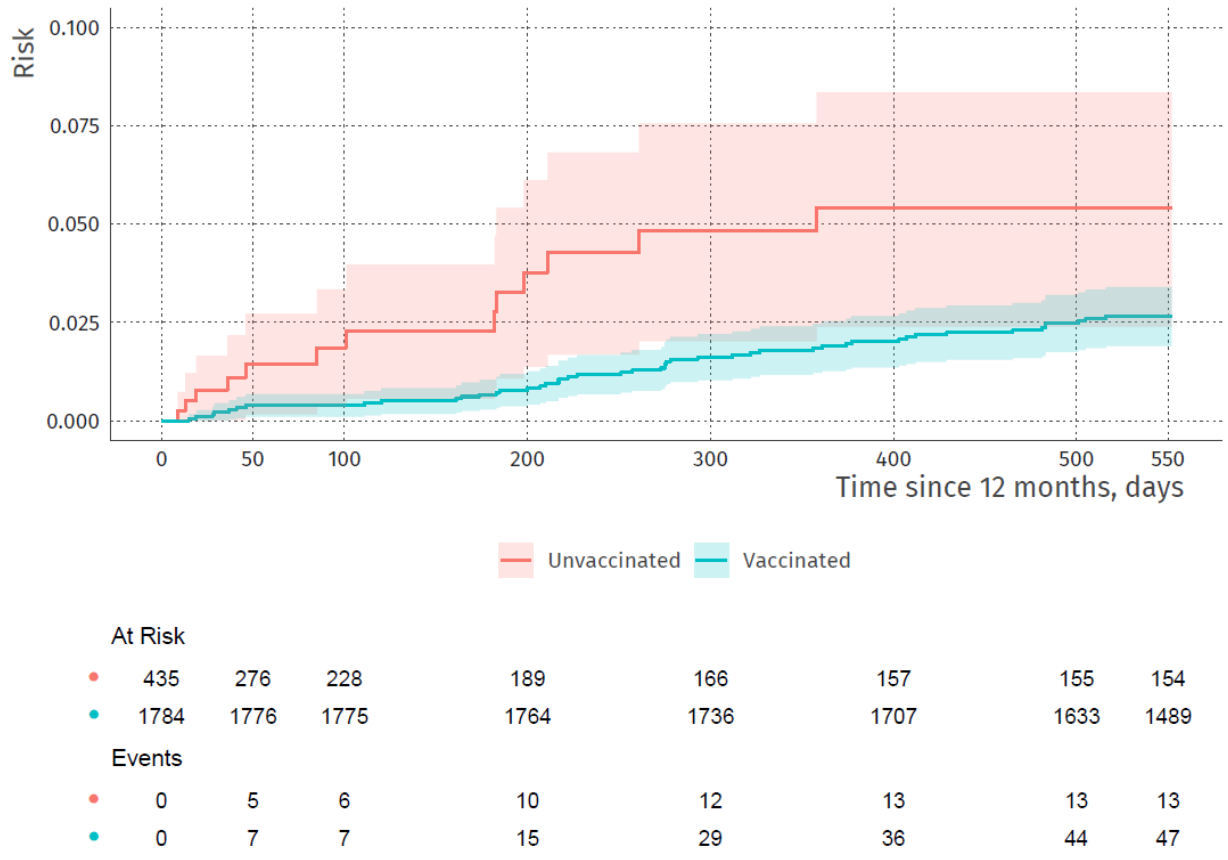

Figure 2: Cumulative incidence of death derived from adjusted Cox regression

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Discussion:

Our findings indicate a potential beneficial effect of the measles vaccine in all-cause mortality in children between 12 and 30 months. This result is subject to multiple biases; first, as an observational study, we are subject to residual confounding for unmeasured confounding; second, we did not have access to the information on the cause of death if most of the deaths occurred due to measles it can't disentangle the benefit of protection against measles from an overall benefit; third, we are subject to the healthy vaccines bias, in this case, family who decide to vaccinate their children is likely to differ from the families who didn't vaccinate in terms of health consciousness and other habits. Similar problems have been reported in observational studies evaluating the benefit of statins in reducing cancer incidence,[1] which was not replicated in randomized clinical trials designed to evaluate this association.[2,3] Of note, studies emulating a target trial with observational data yielded similar results from the randomized clinical trial.[4]

[1] Poynter, Jenny N., et al. "Statins and the risk of colorectal cancer." *New England Journal of Medicine* 352.21 (2005): 2184-2192.
[2] Trialists, Cholesterol Treatment. "Lack of effect of lowering LDL cholesterol on cancer: meta-analysis of individual data from 175,000 people in 27 randomised trials of statin therapy." *PloS one* 7.1 (2012).
[3] Kjekshus, John, et al. "Rosuvastatin in older patients with systolic heart failure." *New England Journal of Medicine* 357.22 (2007): 2248-2261.
[4] Dickerman, Barbra A., et al. "Avoidable flaws in observational analyses: an application to statins and cancer." *Nature medicine* 25.10 (2019): 1601-1606.