Reanalyses of case-control studies examining the temporal association between sudden infant death syndrome and vaccination

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A B S T R A C T

In this paper we examine different time periods after vaccinations and investigate whether the risk of sudden infant death is different during the post-vaccination period than at other times. Three already published case-control studies are re-examined in this context. Several evaluation approaches are presented. The recently developed self-controlled case series (SCCS) method for terminal events, which only takes the cases into account, is used in addition. There is no increased or reduced risk of sudden infant death during the period after the vaccination. The previously reported protective effect seen in case control studies is based on the inclusion of unvaccinated cases. The results of the case-control analysis of one study is affected by two confounders. The SCCS method for terminal events, in which all time-independent confounders are eliminated, is an alternative to case-control analysis when it comes to the temporal association between exposed time periods and SIDS after vaccination.

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1. Introduction

Although several studies on different vaccines established that vaccination does not increase the overall risk of sudden infant death (SIDS) [see [11]], there is still some discussion on whether the risk may be increased or reduced in the early post-vaccination period [see [10,12]]. To address this issue, we examined three published case-control studies which analyse the potential temporal association between SIDS and vaccinations. Case-control studies often yield large protective effects, which have usually been ascribed to methodological bias. For example, Ref. [4] showed that such protective effects could be induced by delaying vaccination during periods of ill-health. Other unmeasured fixed confounders could have an impact on the estimated effect in the case-control studies which for example results in an over-representation of unvaccinated SIDS cases compared to controls. We used different evaluation strategies and investigated different time periods after vaccination. The different evaluation models are introduced in detail in Section 2. The three case-control studies were then re-analysed. The three studies were the German study on sudden infant death (GeSID) study [see [9]], the Confidential Enquiry into Still Births and Deaths in Infancy (CESDI) study [see [5]], and the New Zealand Cot Death (NZCD) study [see [8]].

2. Evaluation models

First, we introduced different evaluation concepts for case-control studies and defined different models. The study questions usually examined in case-control studies are:

1. Is there an overall association between vaccination and the risk of SIDS?
2. Is there a temporal association between vaccination and the risk of SIDS?

Question 1 has been sufficiently analysed in the three case-control studies and in the meta-analysis of Ref. [11]. We will focus on a possible temporal association between vaccination and SIDS.

Fig. 1 shows a general three-phase model. To explain the concepts, we stratify the study period into 3 different phases. Phase 1 includes study participants (cases and controls) who are unvaccinated at the time of event (cases) or the reference date (controls). Phase 2 includes study participants with an event during the risk period, and phase 3 includes all vaccinated study participants with...
an event outside of phase 2. The time after the respective risk period
(which needs to be defined) is regarded as the control period.

Four evaluation strategies are listed in Table 1. Let model 1
denote the first evaluation concept to examine an overall associa-
tion between vaccination and SIDS. In model 1, subjects with an
event (cases) or reference date (controls) in phase 2 or phase 3 are
merged and compared with subjects who experienced the event
(cases) or reference date (controls) during phase 1. This model
corresponds to the original case-control approach and has been
applied in several case-control studies, see Ref. [11]. The second
approach (model 2) deals with the temporal association between
vaccination and SIDS. Subjects with an event (cases) or reference
date (controls) in phase 1 or phase 3 are merged and compared
with subjects who experienced the event (cases) or reference date
(controls) during phase 2. This model was applied in Refs. [8,10].
It has to be assumed that the probability of an event in phase 1
is equivalent to the probability of an event in phase 3. The third
evaluation approach (model 3) compares subjects of phase 3 with
subjects of either phase 1 or phase 2 (one by one). The necessary
assumption for model 2 (i.e. whether phase 1 and phase 3 can be
merged) can be checked by means of model 3b. Model 3a is
proposed to compare the estimates with the self-controlled case
series method (SCCS). The SCCS method [see 1] is an alternative
case-control analyses (only model 3a) and investigates the tem-
poral association between vaccination and SIDS. The basic idea of
the case series method is that only individuals with an event are
considered and that these cases act as their own controls. The mul-
plicative effect of any time-independent confounder is eliminated
by the SCCS method’s design. Any potential bias caused by time-
constant variables can therefore be ignored. In the SCCS method, the
ratio between the probability of an event during the risk period and
the probability of an event during the control period is expressed
by the relative incidence (RI). The main limiting assumption of
the standard SCCS method is that both the exposure distribution
and the observation period must be independent of the time of
event. This assumption is clearly violated when death is con-
cided as event. A simple modified SCCS method is proposed by
Ref. [7] which is applicable for examining a temporal association
between multiple exposures and terminal events such as death.
This method requires that successive vaccine doses are separated
by a known minimum time-interval. This additional assumption
about the vaccination schedule is not necessary in the further de-
veloped adjusted SCCS method for terminal events, described in Ref.
[2]. For our analysis we used the R package adSCCS (can be down-
loaded from http://statistics.open.ac.uk/sccs/r.htm) to calculate the
adjusted SCCS method for terminal events according to Ref. [2].

2.1. Comparison between model 3a and the SCCS method

We can show that the effect estimates of a case-control study
(model 3a) and the SCCS method are basically identical. Let us
define an observation period O of duration I and a risk period of
duration r that is included in the observation period. We assume
that the event rate is low and that the probability of an event during
the risk periods and the control period is uniformly distributed (no
age effects). We also assume that the probability of an event during
the risk period is RI times higher than the probability of an event
during the control period. With these assumptions we can describe
the conditional probability of an event during the risk periods as:

\[
P_{\text{case}}(T \in \text{Risk} | T \in O) = \frac{RI \times r}{RI \times r + I-r}, \tag{1}
\]

and the conditional probability of an event during the control
period is given as:

\[
P_{\text{case}}(T \notin \text{Risk} | T \in O) = \frac{l-r}{RI \times r + I-r}, \tag{2}
\]

where \(T\) is the time of the event. In this setting, the controls have
the same probability for an event during the risk and control period
\((RI = 1)\). The Odds Ratio (OR) is defined as

\[
OR = \frac{P_{\text{case}}(T \in \text{Risk} | T \in O) \times P_{\text{control}}(T \notin \text{Risk} | T \in O)}{P_{\text{case}}(T \notin \text{Risk} | T \in O) \times P_{\text{control}}(T \in \text{Risk} | T \in O)} = \frac{RI \times r}{I-r} \times \frac{1}{RI \times r + I-r} = RI. \tag{3}
\]

We have thus proven under the assumption of no age effect that
the OR is equivalent to the RI for rare events.

However, it is known that the incidence of SIDS is not equally
distributed during the first year of life, as assumed in the proof. The
age distribution of SIDS is considered in the case-control analysis
by including the matching criterion age (region,...) in the model. To
analyse this, we apply conditional logistic regression. Age must also
be taken into account for the SCCS analysis. We have defined age
classes for each study as shown in Appendix A.
Table 2
GeSID study: numbers and proportions of cases and controls by time period (days) after the last vaccination prior to event.

<table>
<thead>
<tr>
<th>Period in days</th>
<th>Unvaccinated</th>
<th>1–3</th>
<th>4–7</th>
<th>8–14</th>
<th>15–21</th>
<th>22–28</th>
<th>29–max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>179</td>
<td>9</td>
<td>15</td>
<td>17</td>
<td>16</td>
<td>13</td>
<td>84</td>
</tr>
<tr>
<td>Overall in %</td>
<td>53.8</td>
<td>2.7</td>
<td>4.5</td>
<td>5.1</td>
<td>4.6</td>
<td>3.9</td>
<td>25.2</td>
</tr>
<tr>
<td>Vaccinated cases in %*</td>
<td>5.8</td>
<td>9.7</td>
<td>11.0</td>
<td>10.4</td>
<td>8.4</td>
<td>54.5</td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>413</td>
<td>45</td>
<td>51</td>
<td>87</td>
<td>56</td>
<td>80</td>
<td>266</td>
</tr>
<tr>
<td>Overall in %</td>
<td>41.4</td>
<td>4.5</td>
<td>5.1</td>
<td>8.7</td>
<td>5.6</td>
<td>8.0</td>
<td>26.7</td>
</tr>
<tr>
<td>Vaccinated controls in %*</td>
<td>7.7</td>
<td>8.7</td>
<td>14.9</td>
<td>9.6</td>
<td>13.7</td>
<td>45.5</td>
<td></td>
</tr>
<tr>
<td>Reference date</td>
<td>497</td>
<td>27</td>
<td>31</td>
<td>87</td>
<td>53</td>
<td>49</td>
<td>254</td>
</tr>
<tr>
<td>Overall in %</td>
<td>49.8</td>
<td>2.7</td>
<td>3.1</td>
<td>8.7</td>
<td>5.3</td>
<td>4.9</td>
<td>25.5</td>
</tr>
<tr>
<td>Vaccinated controls in %*</td>
<td>5.4</td>
<td>6.2</td>
<td>17.4</td>
<td>10.6</td>
<td>9.8</td>
<td>50.7</td>
<td></td>
</tr>
</tbody>
</table>

* Related to model 3a.

3. The GeSID study

3.1. Data of the GeSID study

The GeSID study was conducted in Germany between 1998 and 2001 [see [9]]. Members of 333 SIDS families were interviewed. For each case, three controls – matched for gender, age, and region – were recruited via the local residents registration offices. The controls had to be born 4–6 weeks later than the index case, so by the time the interview with the control family took place the control infants had the same age as the index case. A detailed description on case and control recruitment was reported in Ref. [3]. Table 2 shows the numbers and proportions of cases and controls by time period (days) relative to the last vaccination prior to event. For the controls, the interview date counts as the reference (nominated) date and is called an “event” in the following. The percentages are based on the number of all subjects (model 2) and the number of all vaccinated subjects (model 3a).

3.2. Results of the GeSID study

Fig. 2 shows the results of case-control analyses of the aggregate relative risk i days after vaccination according to model 2 and model 3a and, in addition, the results of the SCCS analysis, which includes only cases. Each point corresponds to the OR/RR for the risk period (phase 2) from the date of vaccination to the i-th day thereafter (i = 1, ..., 40). See Appendix A for a definition of the age classes included in the SCCS model.

According to model 2, there is a constantly reduced risk of SIDS for each time period after vaccination. Risk reduction is less pronounced by applying model 3a to the data. The difference between the two models can be explained by the proportion of unvaccinated subjects, which differs between cases and controls. Unvaccinated subjects are not included in model 3a. The estimated RIs for the time periods up to day 15 are slightly higher when calculated by the SCCS method than according to model 3a. From day 15 up to the final day, the two approaches result in quite similar estimates.

3.3. Potential confounders of the GeSID study

Some confounding can be introduced by controls being older than the corresponding cases. Table 3 shows that 15.6% of controls were imperfectly matched to cases that were more than 21 days younger. Older controls are more likely to have received some vaccinations, especially at the age of 61–150 days.

A second source of confounding could be parents who were contacted two weeks before the interview and asked to participate in the study: this enquiry may have reminded these parents about preventive medical checkups and vaccinations that have been missed. We can verify this by applying the SCCS method to GeSID controls. In this analysis, the date of the interview (the “event”) is related to the time of vaccination. Fig. 3 shows an analysis of the aggregate relative risk i days after vaccination according to the SCCS method that includes only GeSID controls. It reflects the temporal association between the dates of interview and vaccination. The RI is greater than 1 during the first 15 days. This means that a vaccination is more probable during these periods before the interview than in previous time periods. In the time period 11 days before the interview date, there is a statistically significant accumulation of vaccinations compared to the control period (phase 3).

![Fig. 2. Analyses of the aggregate relative risk of an event i days after vaccination; model 2 + model 3a + SCCS method with cases (data from the GeSID study).](image-url)
Table 3
Numbers and proportions of controls by age of matched case.

<table>
<thead>
<tr>
<th>Age category in days</th>
<th>Case is younger than 21 days</th>
<th>21–6 days</th>
<th>Same age as case</th>
<th>Case is older than 6–21 days</th>
<th>&gt;21 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–60</td>
<td>32 (23.5%)</td>
<td>53 (39.0%)</td>
<td>40 (29.4%)</td>
<td>11 (8.1%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>61–90</td>
<td>32 (17.7%)</td>
<td>48 (26.5%)</td>
<td>82 (45.3%)</td>
<td>19 (10.5%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>91–150</td>
<td>38 (13.1%)</td>
<td>117 (40.3%)</td>
<td>113 (39.0%)</td>
<td>16 (5.5%)</td>
<td>6 (2.1%)</td>
</tr>
<tr>
<td>151–210</td>
<td>23 (13.5%)</td>
<td>54 (31.8%)</td>
<td>85 (50.0%)</td>
<td>8 (4.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>211–365</td>
<td>31 (14.0%)</td>
<td>68 (30.8%)</td>
<td>104 (47.1%)</td>
<td>18 (8.1%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>156 (15.6%)</td>
<td>340 (34.1%)</td>
<td>424 (42.3%)</td>
<td>72 (7.2%)</td>
<td>6 (0.6%)</td>
</tr>
</tbody>
</table>

3.4. Improved age adjustment: changing the nominated date of controls

In order to reduce the influence of these two confounders, we changed the event time (interview date) of the controls. First, we set the reference date 12 days before the interview date, so that any changes in the parents’ behaviour after being invited to take part in the study would no longer influence the analysis. We chose the number of 12 days because of results presented in Fig. 3. In addition, we set the reference date according to the age of the matched case if the control was older. Vaccinations after the new nominated date were not considered. The last three lines of Table 2 show the numbers and proportions of controls in the individual time periods with the new reference date. Fig. 4 shows the analysis of the aggregate relative risk of vaccination within $i$ days before the reference date according to the SCCS method with an adjusted reference date. By contrast to Fig. 3, the RI oscillates randomly around 1.

3.5. Individual time periods

Table 4 shows the comparison of risk estimates (OR) for individual time periods according to models 3a and 3b and the corresponding risk estimate from the SCCS analysis (RI). Some differences depend on the choice of the nominated date. The differences are quite evident for the time period of 4–7 days. In this period, the OR estimator increases from 1.35 to 1.83 if the nominated date is changed. The comparison between case-control analysis and the SCCS method reveals the impact of the controls. In the first time period we observe no clustering of cases (RI = 1.01). The OR is slightly smaller than 1 (0.85). For the cases this indicates a slightly reduced risk of an event during the first time period. The reason is probably a clustering of vaccinations in controls within the three days before the interview; see Fig. 3.

In model 3b, phase 3 is compared with phase 1. It is shown that the assumption of model 2 is not tenable, since there are significant differences between phase 1 and phase 3. However, the odd ratios are consistently and significantly smaller than one, indicating a higher level of risk for unvaccinated cases than vaccinated cases.

4. CESDI study

4.1. Method and data of the CESDI study

The study called Confidential Enquiry into Still Births and Deaths in Infancy (CESDI) study was conducted in England between 1993 and 1996 [see 6]. A detailed description of this study is available in Ref. [5]. For each case, four controls were recruited, matched for age, and region. Table 5 shows the numbers and proportions of cases and controls by time period (days) relative to the last vaccination prior to event. The proportion of vaccinations in the cases is markedly higher than controls in the time interval of 15–21 days before the event.

In the CESDI study, only the first and last vaccinations were recorded. This procedure is sufficient for the analysis of a case-control study, as only the last vaccination is decisive for allocating a subject to either the ‘exposed’ or ‘not exposed’ class. However, the full vaccination history prior to the event must be known in order to apply the SCCS method. If not all vaccinations are observed, the total time at risk is underrepresented. The probability of an event, during the risk period is therefore overestimated, as is the RI.

The national immunization programme in the United Kingdom was accelerated during the field phase 1993–1996, with immunization against diphtheria, tetanus and pertussis, and oral poliomyelitis given at ages 2, 3, and 4 months respectively. Since three vaccinations are recommended, we imputed a vaccination 29 days after the first one when the time interval between first and last...
was more than 60 days. This approach probably overrepresented the total time at risk, since not all children are vaccinated according to recommendations.

4.2. Results of the CESDI study

Fig. 5 shows the result of analyses of the aggregate relative risk \( i \) days before the event according to model 2 and model 3a and the results of the SCCS analysis (cases only). See Appendix A for a definition of the age classes included in the SCCS model. Like the GESID study, the same characteristic between model 2 and model 3a can also be observed here. In contrast to the case-control analysis (model 2) no constant reduced risk can be shown. The OR in model 3a rises to a value of 1.65 \((P\text{-value}=0.031)\) from the 15th to the 30th day. The SCCS analysis of the CESDI cases leads to smaller \( \text{RI} \) estimates compared to the OR of model 3a. As expected, the RI with the additional (imputed) vaccination is smaller than the RI with the original data. It can be assumed that the graph of the true \( \text{RI} \) would be located between the two \( \text{RI} \) graphs. Both graphs of \( \text{RI} \) are located below 1 until the 17th day and increased continuously from the 15th until the 30th day.

4.3. Individual time periods

Table 6 shows the comparison of risk estimates (OR) for individual time periods according to models 3a and 3b and the corresponding risk estimate from the SCCS analysis (RI). The risk estimators from the first and third time period show no increased or reduced risk. The risk estimators of model 3a and the SCCS analysis are below 1 during the second time period, whereas the risk

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### Table 4

<table>
<thead>
<tr>
<th>GeSID study; individual time periods; reference category for model 3a: time after vaccination without risk period; and for model 3b: time before first vaccination.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
</tr>
<tr>
<td>3a</td>
</tr>
<tr>
<td>3b</td>
</tr>
<tr>
<td>3a</td>
</tr>
<tr>
<td>3b</td>
</tr>
<tr>
<td>3a</td>
</tr>
<tr>
<td>3b</td>
</tr>
<tr>
<td>3a</td>
</tr>
<tr>
<td>3b</td>
</tr>
<tr>
<td>3a</td>
</tr>
<tr>
<td>3b</td>
</tr>
</tbody>
</table>

* With adjusted reference date.
* 1 case is removed because a vaccination falls within the risk period of previous vaccination.
* 4 cases are removed because a vaccination falls within the risk period of previous vaccination.
* 8 cases are removed because a vaccination falls within the risk period of previous vaccination.
* 13 cases are removed because a vaccination falls within the risk period of previous vaccination.

### Table 5

<table>
<thead>
<tr>
<th>CESDI study; numbers and proportions of cases and controls by time period (days) relative to the last vaccination prior to event; the vaccination data are missing in 22 cases and 66 controls.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period in days</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Cases</td>
</tr>
<tr>
<td>Overall in %</td>
</tr>
<tr>
<td>Vaccinated cases in %</td>
</tr>
<tr>
<td>Controls</td>
</tr>
<tr>
<td>Overall %</td>
</tr>
<tr>
<td>Vaccinated controls in %</td>
</tr>
</tbody>
</table>

* Related to model 3a.
estimators were above 1 in the GeSID study. The risk estimator from model 3a indicates a 1.73-fold (P-value = 0.036) increase in the risk for the cases of an event in the time period 15–21 days after vaccination. The estimators of the SCCS analysis also show a significantly increased risk during the fourth time period. Except for the first and third time periods, the estimators of the OR are within the interval between the two SCCS estimators, where we expect the true value.

5. New Zealand Cot Death (NZCD) study

5.1. Method and data of NZCD study

A description and evaluation of the New Zealand Cot Death (NZCD) study is published in Ref. [8]. It was a large, nationwide case-control study that covered 78% of all live births in New Zealand over a three-year study period (1987–1990). We have access to vaccination data on the 393 cases of the study. The exact day of the last vaccination was unknown in 84 cases. Table 7 shows the numbers and proportions of cases by time period (days) relative to the last vaccination prior to event. The proportion of unvaccinated cases is low (at 29.1%) compared to the other two studies. Otherwise, the proportion of cases with a missing last date of vaccination is very high at 21.4%.

The same difficulties as in the CESDI study also occur also here, because the exact dates of all vaccinations were not collected. The question asked was whether the vaccination was given according to recommendation (yes/no). The vaccination schedule in New Zealand was made up of a BCG vaccination at birth, a DTP after 6 weeks, and DTP and polio after 3 and 5 months. The BCG vaccination is not considered in this analysis. Where it was evident that several vaccinations were given, the date of the first vaccination was set at day 42 of life (day 90 for the second vaccination).

5.2. Results according to the SCCS method

Fig. 6 shows the results of analyses of the aggregate relative risk i days before the event according to the SCCS analysis. See Appendix A for a definition of the age classes included in the SCCS model. The risk estimates of the aggregated risk are below 1 up to day 10 and increase up to day 20 (RI_{20th} = 1.43, P value = 0.024) after vaccination, a pattern that can also be observed in the CESDI study. Table 8 shows the risk estimates for the defined time periods obtained by a
SIDS analysis. The estimates of risk rise slightly during the first four time periods. The risk estimator from the last time period shows a marginally significant reduced risk.

6. Discussion

Vaccination is one of the most important and effective preventive measures in medicine. One should bear in mind that studies on SIDS and vaccination specifically examine only cases of unexplained sudden death. The protective effects of vaccination on infant mortality from explained death (e.g., lethal Haemophilus influenzae- or pertussis infections) are not investigated and not reflected in the calculated risk estimates. The statistics produced by the studies and analyses mentioned above do not provide an overall estimate of vaccination’s effect on infant mortality. In addition, the above calculations (model 3a and SCCS analyses) are only related to a possible temporal association of SIDS with vaccination. However, the development of the SCCS method for investigating of a possible temporal association between adverse events and vaccination led to more detailed insights into the methodological pitfalls of such analyses using conventional case-control methods.

The temporal association between vaccinations and SIDS has been examined in Refs. [8,10], among others. Model 2 was used in both papers. It was shown that the risk of SIDS is reduced in all investigated time periods after vaccination. However, as we have shown, the risk in phase 1 and 3 differs significantly (see model 3b in Table 4 and Table 6). Phase 1 and phase 3 cannot, therefore, be straightforwardly merged.

If only the vaccinated cases and controls are considered according to the model 3a and in the SCCS analysis, then it cannot be proven that vaccination already has a protective effect during the early post-vaccination period. Besides periods of slightly reduced risk, varying time periods with slightly increased risk were identified in the studies. These are the period from the 4th day until the end of the 7th day in the GeSID study and the period from the 15th day until the end of the 21st day in the CESDI and NZCD studies.

However, these results were gained by multiple tests, and no correction for multiple tests was carried out. We performed 39 statistical tests for each of the four charts (see Figs. 2, 5, and 6). At least two significant results with significance level of 5% would be expected from 40 statistical tests. Therefore, no conclusive statement can be based on these large number of tests. However, it was important to present the trend of the risk and thus to be able to compare results between the studies and identify risk periods which might be prone to bias if analysed conventionally.

The small number of cases is a problem with the three case-control studies, particularly in view of the short time periods under investigation. This problem is illustrated by the very broad confidence intervals of estimates that are only related to the events of the first few days (see Fig. 6).

For the SCCS analysis it was a problem that not all vaccination data were observed in the CESDI and NZCD studies. However, the timing of all but the last vaccination has little influence over the results obtained using the adjusted SCCS method. In case of analysis of terminal events, only the last vaccination determines whether the case is allocated to the risk or the control period. The length of the time period under risk influences the results of the adjusted SCCS method: if the time under risk is underrepresented (when we do not observe all the vaccinations), then the relative incidence will overestimate the true relative risk. The possible source of over- or underestimation introduced by imputation or assumed non-vaccination was illustrated with the data of CESDI study. At first, we included only the observed vaccinations and in second step we imputed assumed vaccinations. For the 137 vaccinated cases of the CESDI study we imputed 34 vaccinations at time points for which the second vaccine dose was recommended in the respective vaccination schedule. An alternative could be to evaluate the CESDI study without the 34 cases. However, we would loose 25% of the vaccinated cases thus study power decreases. Subtly differentiated analyses could be carried out if the vaccination data were collected completely for future studies.

6.1. Conclusion

The detailed re-analyses show that the risk of SIDS in vaccinated cases and controls is neither increased nor reduced during the early post-vaccination period. This result of case-control analyses restricted to vaccinated cases and controls is similar to the results

<table>
<thead>
<tr>
<th>Table 8 NZCD study; individual time periods.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time period</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>1–3 days</td>
</tr>
<tr>
<td>4–7 days</td>
</tr>
<tr>
<td>8–14 days</td>
</tr>
<tr>
<td>15–21 days</td>
</tr>
<tr>
<td>22–28 days</td>
</tr>
</tbody>
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Fig. 6. Analysis of the aggregate relative risk of an event within i days after vaccination; NZCD study.
of the SSCS method. The risk of SIDS in unvaccinated cases and controls is higher than the risk to infants in the late post-vaccination period. An additional protective effect of vaccinations in the early post-vaccination period (as indicated by conventional case-control analyses) is derived from differences between vaccinated and not vaccinated subjects.

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Appendix A.

See Table 9 for the definition of the age classes (in days).

References


