

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	A Retrospective, Matched Case-Control Analysis of Tick-Borne Encephalitis Vaccine Effectiveness by Booster Interval, Switzerland 2006-2020
<b>AUTHORS</b>	Zens, Kyra; Haile, Sarah; Schmidt, Axel Jeremias; Altpeter, Ekkehardt S.; Fehr, Jan S.; Lang, Phung

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Steffen, Robert University of Zurich
<b>REVIEW RETURNED</b>	27-Jan-2022

<b>GENERAL COMMENTS</b>	<p>This original research paper is relevant in the ongoing debate on the duration of protection after the last dose of TBE vaccine. Fundamentally study design, presentation of the data and conclusions are OK — I have only minor points to be reconsidered and corrected.</p> <p>2/44 It is useless to list terms included in the title as keywords as these will be recorded anyway. Strongly suggest to list other keywords, such as TBE, duration, protection, ...</p> <p>3/28 Missing ) after 96.1</p> <p>3/42-44 "complete" ... "should be": is there not a slight contradiction in this sentence? If complete —&gt; then case data ARE representative. Consider to state "almost complete" as some reporting MDs (subsequent to the lab report) may have submitted incomplete (or no) report.</p> <p>3/50 To clarify suggest: Despite a large number of TBE cases ...</p> <p>4/28 extending the Swissmedic and EMA-approved ... (addition needed)</p> <p>4/56 suggest to add that the initial notification is by the laboratory</p> <p>5/22 names of the half cantons can be deleted</p> <p>6/11-33 I find the double reporting of data in the text and again in the table unnecessary; would suggest to shorten the text just highlighting what is important in the table</p> <p>7/46 Consider also to mention the 0, 14, ... rapid scheme for FSME-Immun for the sake of completeness</p> <p>8/25 From recent publications there is more evidence that growing age does not result in decreased VE: consider to slightly expand the discussion taking into account:</p> <p>a) Schmitt HJ et al. Vaccines (Basel). 2021 Aug 21; 9(8):932.</p> <p>b) Erber W et al. Vaccine. 2022 Jan 31; 40(5):819-25.</p> <p>11/6-17 References 1 to 6 should have an author, e.g. #2 is WHO, #3, 4 either Anonymous or Swissmedic. #1, 5, 6 the author is the Swiss Federal Office of Public Health, for #1 I would suggest to indicate the general website for the Bulletin.</p>
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<b>REVIEWER</b>	Beran, J The Vaccination and Travel Medicine Center, Poliklinika II
<b>REVIEW RETURNED</b>	06-Feb-2022

<b>GENERAL COMMENTS</b>	<p>Title of the manuscript: A Retrospective, Matched Case-Control Analysis of TickBorne Encephalitis Vaccine Effectiveness by Booster Interval, Switzerland 2006-2020</p> <p>This was a retrospective, matched case-control study design to investigate TBE VE in Switzerland considers both incomplete and complete vaccination, and, among completely vaccinated individuals with different time intervals since the last vaccination.</p> <p>The authors did not observe a decrease in VE with increasing time since the last vaccine dose was received.</p> <p>VE was lower in the first 5 years following the last vaccination compared to the last vaccination 10+ years.</p> <p>Nearly half of vaccinated cases were among recipients of only 1-2 doses with VE for incomplete vaccination at 76.8%.</p> <p>VE was significantly less than that for complete vaccination (95.0%).</p> <p>Authors found that nearly 40% of the cases among incompletely vaccinated individuals occurred within 2 months of their last dose, suggesting they were exposed before they had developed a protective immune response to vaccination.</p> <p>An important limitation of our study is the relatively small number of vaccinated cases.</p> <p>I don't have any relevant comments on this manuscript and I recommend it ACCEPT.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Robert Steffen, University of Zurich

Comments to the Author:

This original research paper is relevant in the ongoing debate on the duration of protection after the last dose of TBE vaccine. Fundamentally study design, presentation of the data and conclusions are OK — I have only minor points to be reconsidered and corrected.

2/44 It is useless to list terms included in the title as keywords as these will be recorded anyway.

Strongly suggest to list other keywords, such as TBE, duration, protection, ...

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3/42-44 "complete" ... "should be": is there not a slight contradiction in this sentence? If complete —> then case data ARE representative. Consider to state "almost complete" as some reporting MDs (subsequent to the lab report) may have submitted incomplete (or no) report.

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Reviewer: 2

Dr. J Beran, The Vaccination and Travel Medicine Center, Poliklinika II

Comments to the Author:

Title of the manuscript: A Retrospective, Matched Case-Control Analysis of TickBorne Encephalitis Vaccine Effectiveness by Booster Interval, Switzerland 2006-2020

This was a retrospective, matched case-control study design to investigate TBE VE in Switzerland considers both incomplete and complete vaccination, and, among completely vaccinated individuals with different time intervals since the last vaccination.

The authors did not observe a decrease in VE with increasing time since the last vaccine dose was received.

VE was lower in the first 5 years following the last vaccination compared to the last vaccination 10+ years.

Nearly half of vaccinated cases were among recipients of only 1-2 doses with VE for incomplete vaccination at 76.8%.

VE was significantly less than that for complete vaccination (95.0%).

Authors found that nearly 40% of the cases among incompletely vaccinated individuals occurred within 2 months of their last dose, suggesting they were exposed before they had developed a protective immune response to vaccination.

An important limitation of our study is the relatively small number of vaccinated cases.

I don't have any relevant comments on this manuscript and I recommend it ACCEPT.

Reviewer: 1

Competing interests of Reviewer: Until retirement 15 years ago I worked in the same University of Zurich institution.

Reviewer: 2

Competing interests of Reviewer: No competing interests

### VERSION 2 – REVIEW

<b>REVIEWER</b>	Steffen, Robert University of Zurich
<b>REVIEW RETURNED</b>	03-Mar-2022
<b>GENERAL COMMENTS</b>	The authors have revised the manuscript as suggested; I have no further suggestions. Good work!