INPLASY PROTOCOL

To cite: Peng et al. Effect of vaccine approaches on influenza in travelers: A study protocol of meta-analysis and systematic review. Inplasy protocol 202140137. doi: 10.37766/inplasy2021.4.0137

Received: 28 April 2021

Published: 28 April 2021

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Support: Chongqing Education Commission.

Review Stage at time of this submission: The review has not yet started.

Conflicts of interest: None declared.

Effect of vaccine approaches on influenza in travelers: A study protocol of meta-analysis and systematic review

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Review question / Objective: To evaluate the incidence of clinical influenza infections among travelers and the efficiency of influenza vaccination among travelers.

Condition being studied: Influenza is an acute viral respiratory infection that can cause significant morbidity and mortality. Many studies suggest that vaccination is a way that is the most effective and economical way to prevent influenza virus infections and complications. The present systematic review and meta-analysis aim to provide an up-to-date evaluation of influenza vaccination effectiveness in travelers all over the world and findings will inform existing and new clinical guidelines. In light of increasing tourism tremendously, an upto-date synthesis of evidence on the possible association of the prevalence of clinical influenza in travel is needed. Furthering existing reviews, a broadened scope to better reflect effectiveness in a global context is also important. Our proposed meta-analysis integrates multiple statistical techniques for a comprehensive assessment of influenza vaccination effectiveness. This systematic review and metaanalysis will enhance our understanding of the effectiveness of influenza vaccination in travel populations all over the world.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 April 2021 and was last updated on 28 April 2021 (registration number INPLASY202140137).

INTRODUCTION

Review question / Objective: To evaluate the incidence of clinical influenza infections among travelers and the efficiency of influenza vaccination among travelers. Condition being studied: Influenza is an acute viral respiratory infection that can cause significant morbidity and mortality. Many studies suggest that vaccination is a way that is the most effective and economical way to prevent influenza virus infections and complications. The present systematic review and meta-analysis aim to provide an up-to-date evaluation of influenza vaccination effectiveness in travelers all over the world and findings will inform existing and new clinical guidelines. In light of increasing tourism tremendously, an up-to-date synthesis of evidence on the possible association of the prevalence of clinical influenza in travel is needed. Furthering existing reviews, a broadened scope to better reflect effectiveness in a global context is also important. Our proposed meta-analysis integrates multiple statistical techniques for a comprehensive assessment of influenza vaccination effectiveness. This systematic review and meta-analysis will enhance our understanding of the effectiveness of influenza vaccination in travel populations all over the world.

METHODS

Participant or population: Studies on travelers who made short-term, holiday trips, long-term will be included.

Intervention: We will include studies that report the incidence of influenza and other clinical influenza symptoms among travelers, with or without a comparison group. We will exclude studies of a single case.

Comparator: Refer to the above section.

Study designs to be included: We will include prospective study, retrospective study and other observational studies.

Eligibility criteria: We will include studies with no language restrictions which meet the criteria, written material (grey literature) other than peer-reviewed journal articles (e.g., technical reports, proceedings, case reports and government publications) and will screen the reference lists of systematic reviews identified by the search for relevant studies. We will include prospective study, retrospective study and other observational studies. Full text research from databases and other sources will be included, but abstracts without full text will be excluded. There will be no language restrictions. We will include studies from the date of database inception to January 2021.

Information sources: As to electronic databases, we will search for the following electronic databases: MEDLINE, Embase, Cochrane Library, Web of Science, and additional sources will be used. Our search strategy will combine index terms (e.g. MeSH) and text words for influenza or flu. The MEDLINE search strategy will be peerreviewed by a second researcher. Search results will be limited to human studies published from the date of database inception to January 2021. There will be no language limitations. Refer to the online supplementary appendix 2 for MEDLINE search strategy. As to additional sources, we will also perform a hand search of the reference lists of articles selected to supplement the electronic search and. We will also search the grey literature such as Baidu and Google. Furthermore, We will contact the authors to obtain more information if necessary. Conference proceedings will be included considered in our search for Embase and Web of Science (which includes the Conference Proceedings Citation Index). Finally, we will hand-search reference lists of relevant systematic reviews, and included studies will also be conducted. Search results will be exported to Endnote X9 for preliminary screening.

Main outcome(s): The primary outcomes will include vaccination in the pre-travel setting, the attack rate of influenza infection while traveling and after traveling.

Additional outcome(s): The secondary outcomes will be the types, frequency, and impact of health problems occurring during and after travel as well as respiratory illness.

Quality assessment / Risk of bias analysis: Individual studies Two authors will assess the methodological quality of each preliminary study based on the study design independently. The risk of bias assessment will be conducted using the RoB 2.0 tool developed by the Cochrane

CollaborationFor randomized controlled trials, we will use the Cochrane Risk of Bias tool.16 For cohort and case-control studies, we will use the Newcastle-Ottawa Scale.17 Disagreements will be resolved through discussion with the third author. Body of evidence Two authors will independently assess the certainty of the body of evidence for each outcome according to the Grading of **Recommendations** Assessment **Development and Evaluation (GRADE) tool** from the GRADE Handbook. The assessment will be conducted in five domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The quality score can be classified as high, medium, low, or very low. Ethics and dissemination There is no need for ethical approval because the publications included in our study do not involve patient's privacy. The main data will be from published literature. Our protocol will be submitted for peer review presentation and publication.

Strategy of data synthesis: Descriptive analysis will be used for studies and population characteristics. Demographic and travel characteristics were evaluated by chi-square test for categorical and Wilcoxon rank-sum test for continuous variables. If data can be pooled together, the validity data will be imported into Revman (Revman v.5.3 Cochrane). Due to the expected differences between the included studies, we will use a random effect model and use the I2 statistics to measure the heterogeneity of studies. Values higher than 75%, 50%, and 25% are considered to be very high, high, and moderate, respectively. We will use Egger's test will also be used to determine the publication bias.

Subgroup analysis: Subgroup analyses will be conducted based on population group of interest and in the narrative and forest plot synthesis if it is possible. The following subgroups will be identified: sex, country, type of travel.

Sensitivity analysis: If a meta-analysis is performed, a sensitivity analysis will be

conducted. We will perform sensitivity analyses based on study design, including example prospective studies versus retrospective studies and risk of bias.

Country(ies) involved: China.

Keywords: influenza vaccine, travelers, meta-analysis protocol.

Contributions of each author: Author 1 - Zhao Peng.

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