# Evidence map and interactive real-time meta-analyses to present results of a living systematic review (LSR) of COVID-19 vaccines during pregnancy

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### Background

The COVID-19 pandemic demanded real-time evidence to inform decision-making. We conducted a LSR to evaluate safety and effectiveness of COVID-19 vaccines administered to pregnant persons. The great amount of evidence, the number of outcomes, and the subgroups of interest allow a large number of meta-analyses. Therefore, it is useful to have an interactive tool that allows tailored meta-analyses by selecting filters according and subgroups for each outcome.

### **Objectives**

To present the evidence map and the tool developed for interactive real-time meta-analyses using the shiny R library and developmental challenges.

### **Methods**

We describe the online evidence map and the main features of the tool developed for interactive realtime meta-analyses using the shiny R library.

### Results

The evidence map and the meta-analysis tool are available at <u>https://www.safeinpregnancy.org/living-systematic-review/</u>. The evidence map is automatically generated from a Redcaps database (**Figure 1a**). From the values selected in the menu, dynamic texts are generated with interpretations, graphs, and tables that summarize the information. The greatest difficulties of programming in R are the long list of

filters to perform the meta-analysis (random effect model) and the need for conditional panels and monthly input updating. The filters available for comparing studies include type of outcome; outcome; subgroup; type of vaccine; schema received; pregnancy trimester; dominant variant and effect measure analyzed. Once the values of each filter/variable are chosen (**Figure 1b**), the outputs for the selected outcome are:

- # studies (+ links to studies) reporting adjusted measures and # studies that were included in the meta-analysis.
- Countries of residence of patients
- Forest- plot using the R meta package with the following information:
  - o by study: country, # of patients, first author, effect measure (95%CI), weight, quality of the study,
  - $\circ~$  by subgroup: combined effect (95%CI) and I^2.
- Text with the summary of filters chosen by the user.
- Summary table with information on all studies in the meta-analysis.

## Conclusions

The presented interactive tool is useful for health decision-makers since it allows them to obtain relevant and specific evidence according to their specific needs of information regarding the effects of COVID-19 vaccines during pregnancy.

#### Figure 1a Evidence Map Ð W HYIEN CON CHARITÉ ECS Tulane University SCHOOL OF PHARMACY SCHOOL OF PUBLIC HEALTH World Health Organization COVID-19 Vaccines for Pregnant Persons: A Living Systematic Review and Meta-Analysis Last update was made on 10/31/2023 About This is a regularly updated, comprehensive dulatese and synthesis of published Marature retailing to CCV/D-19 vacores in pregnancy. To start your search, click on any given country on the map to sea all collected studies or click on the Outcomes tab for details on studies reporting on Maternal Pregnancy Dutcomes. Maternal Adverse Events Following Immunication. Intant Safety Dutcomes, Vaccine Efficacy/Effectiveness Outcomes, and Immunogenicity. For more information on the Living Systematic Review ILSRI and inclusion criteria. click the Methodology and About tabs. Filters applied: None 177 638.825 21 41 11 Collected Studies Vaccinated Population Published in the Last 6 Months Vaccine Products Number of Countries Outcomes Studies Collected per Country Studies by Vaccine Type/Platform Methodology AN AN Summary Tables nber of Studies 100 Filters PUBLICATION DATE COUNTRY / REGION :50 STUDY OUTCOM World Health Organization POPULATION RNA Viral-vector 2023. All rights VACCINE Vaccine Type/Platform Figure 1b. Interactive meta-analysis interface COVID-19 Vaccines for Pregnant Persons: A Living Systematic Review and Meta-Analysis Analysis Methodology Summary About 음 Home WUNIVERSITY () WASHINGTON WASHINGTON Analysis parameters ECS Outcome type Efficacy/Effectiveness Infant safety outcomes following Forest Plot / Meta-analysis Summary table COVID-19 vaccination during pregnancy O Maternal-Adverse events We identified 32 studies reporting this outcome. Based on the methodology described, only 4 studies reported adjusted effect measures for this outcome: Dick, A (2022) (a), Fell, D.B. (2022), Magnus, M.C. (2022), Hui, L 2023. Finally, 4 were following immunizations included in the meta-analysis based on the selected filters. The meta-analysis included a total of 113,250 patients Maternal-Pregnancy related exposed to the vaccine in 5 countries: Australia, Canada, Israel, Norway and Sweden. outcomes Maternal safety of COVID-19 vaccines during pregnancy versus unvaccinated pregnant population: Stillbirth. Outcome Stillbirth Subgroup analysis Trimester IV, Random, 95% CI Weigh Subgroup Dominant variant oup = 2nd 1.12 [0.52: 2.40] 100.0% 2 AD:NS Dick. A 2022 (a) Vaccine type O Dose 0.25 [0.08; 0.80] 100.0% Dick, A 2022 (a Vaccine type Inactivated virus Hul L 2023 0.17 [0.07: 0.43] 100.0% -Z RNA 1:2 0:0 Viral vector subgroup = 2nd;3rd BNA 2 23 AD NS Israel 2305 Dick & 2022 (a) 0.78 (0.42: 1.44) 100.0% Dose **V** 1 2 G RNA;W 2 1;2;3 NS Sweden, Norway 28506 Magnus, M.C. 2022 0.86 [0.63; 1.17] 35.2% RNA 2 1:2:3 0:0 17365 Hul L 2023 0.18 [0.09; 0.36] 28.9% Booster RNA NS 1;2;3 A;D;0 43099 Fel, D.B. 2022 0.65 [0.51; 0.83] 35.8% Canada Not specified Total (95% CI) 0.49 [0.20; 1.19] 100.0% c. Ch<sup>2</sup> = 15.0, d<sup>2</sup> = 2 (P < 0.01); I</p>

0.1 0.5 1 2 10 Favors COVID-19 vaccination Unfavorable COVID-19 vaccination

Delta
Omicron

**Dominant Variant** 

✓ Alpha✓ Beta