

Norwegian Institute of Public Health - Centre for Fertility and Health – impact case number 4

Institution: Norwegian Institute of Public Health
Administrative unit: Centre for Fertility and Health
Title of case study: Understanding potential consequences of infection with and vaccination against Covid-19 during pregnancy
Period when the underpinning research was undertaken: 2020 - 2022
Period when staff involved in the underpinning research were employed by the submitting institution: 2017 -
Period when the impact occurred: 2021 - 2024

1. Summary of the impact

During the Covid-19 pandemic, we conducted a range of studies looking into the potential consequences of infection with and vaccination against Covid-19 during pregnancy. These studies became very important in the generation and continuous update of national guidelines for vaccination of pregnant women during the pandemic and contributed to the international knowledge base on covid-19 and pregnancy. The findings were also communicated to the public through press releases and to important international stakeholder such as the World Health Organization and the European Medicines Agency.

2. Underpinning research

During the pandemic, we conducted a range of studies looking into the consequences of infection with and vaccination against Covid-19 during pregnancy. We used national health registries, and collaborated with researchers in Sweden and Denmark, to conduct high-quality studies and produce robust evidence using data from these three Nordic countries. With our unique registry linkages, we were able to perform research which is not possible in most other countries. Our work was made possible by the Emergency preparedness register for Covid-19 (BEREDT C19) at the Norwegian Institute of Public Health (NIPH). This register includes data from all the central health registries, including the Medical Birth Registry of Norway, the Norwegian Patient Registry, the Vaccination Registry, the Norwegian Surveillance System for Communicable Diseases and several other important data sources. In addition, we used rich data collected by questionnaires from participants in the Norwegian Mother, Father, and Child Cohort Study (MoBa) and the Norwegian Influenza Cohort (NorFlu). The regularly updated data in BEREDT C19 was invaluable to the conduction of this work. The research conducted within this topic at the CEFH has been funded by the Research Council of Norway and NordForsk. Some of our major findings include (the numbering of these main findings corresponds to the numbering of the references below):

- 1) In a study using information from Norwegian health registries, pregnant women were not more likely to be infected with the coronavirus SARS-CoV-2. Still, pregnant women with COVID-19, especially those born outside of Scandinavia, were more likely to be hospitalised. This supports the notion that pregnant women are at greater risk of severe disease from COVID-19 if they get infected. These findings supported vaccination of pregnant women (Oct 2020-Oct 2021)
- 2) The rate of fetal death (miscarriage and stillbirth) did not change after the implementation of COVID-19 pandemic mitigation measures in the three Nordic countries. This provided preliminary reassuring evidence that pandemic mitigation measures, or the general psychosocial stress throughout the pandemic, did not appear to impact the rate of fetal death (June 2021-Oct 2022)
- 3) Using unique population-based data on first-trimester miscarriages in Norway, we found no evidence of an increased risk of first-trimester miscarriage after Covid-19 vaccination,

which added to findings from smaller reports of more selected samples indicating no increased risk of early pregnancy loss following vaccination. (March 2021-Sept 2021)

- 4) Based on findings from a large population-based study of births in Sweden and Norway, vaccination against SARS-CoV-2 during pregnancy, compared with no SARS-CoV-2 vaccination during pregnancy, was not significantly associated with an increased risk of adverse birth outcomes, such as stillbirth, preterm birth, small-for-gestational age, low Apgar score etc. This study provided important evidence of the safety of vaccination against Covid-19 during pregnancy (July 2021-Feb 2022)
- 5) Results from Norway suggested a lower risk of a positive test for SARS-CoV-2 during the first 4 months of life among infants born to mothers who were vaccinated during pregnancy. Maternal COVID-19 vaccination may therefore provide important passive protection to young infants, for whom COVID-19 vaccines are not recommended. (Nov 2021-July 2022)
- 6) Using MoBa, we followed 70 000 participants with and without SARS-CoV-2 infection and found an excess risk of 13.6% for fatigue 12 months after infection. Two main underlying factors explained 50% of the variance in the 13 symptoms that were associated with infection (long COVID symptoms). Brain fog, poor memory, dizziness, heart palpitations, and fatigue had high loadings on the first factor, while shortness-of breath and cough had high loadings on the second factor.
- 7) Using questionnaire information from cohort participants we found that cigarette smoking, but not snus use, was negatively associated with SARS-CoV-2 infection in women. The lack of an association between snus use and SARS-CoV-2 infection in this population with prevalent snus use does not support the hypothesis of a protective effect of nicotine.

Names of key researchers

NAME OF RESEARCHER	POSITION	DATE JOINING	DATE LEAVING
Siri Eldevik Håberg	Director	Nov 1, 2017	-
Maria C Magnus	Researcher	Aug 1, 2018	-
Håkon Gjessing	Researcher	Nov 1, 2017	-
Ellen Øen Carlsen	PhD Student	Mar 4, 2019	-
Laura Oakley	Researcher	March 1, 2021	-
Jonas Minet Kinge	Researcher	Aug 1, 2018	-
Ida Caspersen	Researcher	March 1, 2021	-
Per Magnus	Deputy Director	Nov 1, 2017	-

Grants:

We have received three grants to facilitate the completion of the described research. The research has primarily come out of a Nordic research collaboration funded by NordForsk, which enabled us to study the risk of more rare pregnancy complications.

NordForsk – Scandinavian studies of Covid-19 in pregnancy (SCOPE) : 105545

NordForsk – Scandinavian studies of Covid-19 in pregnancy 2 (SCOPE 2): 135876

NordForsk – Tobrisk-Cov grant no. 105544.

Research Council of Norway – Safety of Covid-19 vaccination in pregnancy (SAFETY): 324312

2. References to the research

- 1) **Magnus MC, Oakley L, Gjessing HK**, Stephansson O, Engjom HM, Macsali F, Juliusson PB, Nybo Andersen AM, **Håberg SE**. (2022). Pregnancy and risk of COVID-19: a Norwegian registry-linkage study. *BJOG*, 129(1), 101-109. <https://doi.org/10.1111/1471-0528.16969>

- 2) **Magnus MC, Gjessing HK**, Eide HN, Wilcox AJ, Fell DB, **Håberg SE**. (2021). Covid-19 Vaccination during Pregnancy and First-Trimester Miscarriage. *N Engl J Med*, 385(21), 2008-2010. <https://doi.org/10.1056/NEJMc2114466>
- 3) **Magnus MC**, Örtqvist AK, Dahlqvist E, Ljung R, Skår F, **Oakley L**, Macsali F, Pasternak B, **Gjessing HK, Håberg SE**, Stephansson O. (2022). Association of SARS-CoV-2 Vaccination During Pregnancy With Pregnancy Outcomes. *JAMA*, 327(15), 1469-1477. <https://doi.org/10.1001/jama.2022.3271>
- 4) **Carlsen EØ, Magnus MC, Oakley L**, Fell DB, Greve-Isdahl M, **Kinge JM, Håberg SE**. (2022). Association of COVID-19 Vaccination During Pregnancy With Incidence of SARS-CoV-2 Infection in Infants. *JAMA Intern Med*, 182(8), 825-831. <https://doi.org/10.1001/jamainternmed.2022.2442>
- 5) **Caspersen IH, Magnus P**, Trogstad L. (2022). Excess risk and clusters of symptoms after COVID-19 in a large Norwegian cohort. *Eur J Epidemiol*, 37, 539-548. <https://doi.org/10.1007/s10654-022-00847-8>
- 6) **Caspersen IH, Trogstad L, Galanti MR, Karvonen S, Peña S, Shaaban AN, Håberg SE, Magnus P**. (2023). Current tobacco use and SARS-CoV-2 infection in two Norwegian population-based cohorts. *BMC Public Health*, 23, 846 <https://doi.org/10.1186/s12889-023-15822-5>

4. Details of the impact

Description of relevant stakeholders

There are several important stakeholders regarding the described research.

- 1) Government agencies responsible for developing guidelines for vaccination of pregnant women against Covid-19 and monitoring of potential side effects.
- 2) Pregnant women contemplating vaccination.
- 3) General practitioners responsible for the routine antenatal care of pregnant women.
- 4) Other researchers.

Description of dissemination activities

- 1) Meetings with government agencies. Throughout the pandemic, we have continuously informed the **advisory group at the Norwegian Institute of Public Health (NIPH)** about our findings, in order to inform their development and updated recommendations for vaccination of pregnant women against Covid-19. The evidence that we have made available has been critically important to inform the existing national recommendations for vaccination of pregnant women. Therefore, we had regular meetings with the advisory group at the NIPH and informed them about our findings. Furthermore, we have presented our findings to a sub-committee at the **World Health Organization** responsible for their official guidelines of vaccination of pregnant women against Covid-19. Together with evidence from large-scale studies originating from other countries, our findings have therefore also contributed to the official WHO recommendations. Finally, we have presented findings from our studies on vaccination for the **Norwegian and European Medicines Agencies**. These agencies are responsible for monitoring all evidence regarding potential side effects of vaccines. Our reassuring findings of no adverse effects of vaccination during pregnancy based on Nordic data has been critically important both national and internationally for this purpose.
- 2) Our findings have been of interest to the **general population of pregnant women trying** to decide whether they should get vaccinated against Covid-19. We have been able to show that pregnant women appear to be at an increased risk of severe disease, and that there is no evidence of adverse effects of vaccination, supporting the general recommendation of vaccination for pregnant women. The described research has been disseminated widely through press releases and news articles to reach the general population of pregnant women. Specifically, we have written press releases together with the NIPH

communications department which has been published on our website. Furthermore, we have contacted/and been contacted by major national newspapers, which has further contributed to the wide dissemination of our findings to the general population.

- 3) Our findings have also been of interest to **all general practitioners responsible for the antenatal care of pregnant women**. As general practitioners are those who meet pregnant women and must answer their questions about whether or not they should get vaccinated against Covid-19, it has been vitally important to have evidence from large well-conducted studies that they can lean on when communicating with pregnant women. General practitioners heavily relied on the summary of evidence and existing recommendations from the NIPH, and as our findings contributed to these, they were also vitally important for these health-care workers.
- 4) Our findings have also been important for **other researchers both nationally and internationally**. For example, our analytical strategies to minimize bias leading to spurious findings have been adopted by other researchers on other/independent datasets. This has been important as similar evidence across different populations are necessary to increase confidence in the robustness of findings.

5. Sources to corroborate the impact (indicative maximum of ten references)

1. [COVID-19: latest safety data provide reassurance about use of mRNA vaccines during pregnancy | European Medicines Agency \(europa.eu\)](#)
2. [Covid-19 vaksiner av gravide \(nhi.no\)](#)
3. [Ny studie blant gravide: – Koronavaksinen gir ikke økt risiko for komplikasjoner \(aftenposten.no\)](#)
4. [Vaksinestudie blant gravide: Ikke økt risiko for komplikasjoner \(dagensmedisin.no\)](#)
5. [Økt forekomst av menstruasjonsforstyrrelser hos unge kvinner etter vaksinasjon mot korona - FHI](#)
6. [Studie: Mors covid-19-vaksine under svangerskapet beskytter barnet etter fødsel \(dagensmedisin.no\)](#)
7. [Mors vaksine beskytter også barnet i magen - FHI](#)
8. [Covid-19 i graviditet – risiko for mor og barn | Tidsskrift for Den norske legeförening \(tidsskriftet.no\)](#)
9. Meeting with the WHO Global advisory committee on Vaccine Safety, 31 May, 2022, <https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/topics/covid-19-vaccines/subcommittee>