

Does COVID-19 Vaccination Status Shape Avoidable and Non-Avoidable Mortality? Insights from a Czech Population-Based Study (2022–2024)

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Background and aims of the research

The COVID-19 pandemic caused a global mortality crisis, yet also led to rapid scientific progress, including the development of vaccines (vaccination began in general in early 2021) and highlighted the importance of data-driven approaches. However, societal differences and opinions widened, with distrust and vaccine refusal [1,2]. Specifically targeted studies have mapped the effect of vaccination in reducing mortality and severe impacts due to the COVID-19 disease itself [3–6], and vaccine hesitancy [7] has begun to manifest as a problem that potentially endangers public health and resilience [1]. In this aspect, much less is known about the indirect effects of vaccination, i.e., differences in mortality risks not directly related to vaccination itself [8], but rather to factors underlying the decision to resist vaccination. Several previous studies have mapped the different average characteristics of the general population and the population refusing vaccination (e.g., flu or other vaccinations), which include, among other things, trust in medical recommendations, prevention, and lifestyle [9–14].

A generally higher risk of death in the non-vaccinated population could signal a need for better-targeted health and preventive campaigns or better-formulated medical recommendations [2,9,10]. Additionally, it can identify more vulnerable target groups where the effort to increase health literacy should be concentrated. Vaccine or prevention hesitancy, lack of trust in health system officials, science, or government, psychological factors, minimisation of the pandemic's importance and severity, as well as inefficiently targeted preventive or informational campaigns, or even conspiracy theories, could be considered key systemic risks during any health crisis. To evaluate the potential indirect effects of vaccination, this study applies the concept of avoidable mortality, which distinguishes between deaths that could be prevented through adequate healthcare or preventive measures (preventable, treatable, and partially preventable and treatable) and those that are largely unavoidable [15]. It can be assumed that avoidable causes of death, in particular, should reflect the specific behavioural factors associated with vaccination refusal, mentioned above.

This study aims to address the knowledge gap on the differential risk of death by vaccination status through three steps:

- (1) compare mortality risk from selected non-COVID-19 causes by vaccination status,
- (2) assess avoidable and non-avoidable mortality differences by vaccination status, and
- (3) analyse trends of the mortality differences over time to verify their stability, reflecting behavioural or lifestyle differences behind vaccine hesitancy or acceptance.

Data and Methods

The Czech population was chosen for the analysis due to its severe impact from the COVID-19 pandemic and relatively lower vaccine acceptance compared to other EU countries, providing a unique context for studying vaccination-related mortality differences. By the end of 2021, in Czechia, around 64% of the total population (more than 72% in EU countries) and slightly more than 86% of the population aged 60 and older (91% in EU countries) received at least one vaccination dose [16].

The analysis is based on individual data from the Czech National COVID-19 Infection and Vaccination Registry (ISIN) and the database of deaths for the years 2020–2024. The analysis includes almost 7.5 million records of adults (aged 18 and older) who underwent at least one PCR test for the presence of COVID-19 or received at least one dose of vaccination against this disease (in the years 2020–2024). The starting population for the analysis refers to the number of people as of January 1, 2022, i.e., one year after the start of vaccination, when all adults had the opportunity to receive a complete vaccination series.

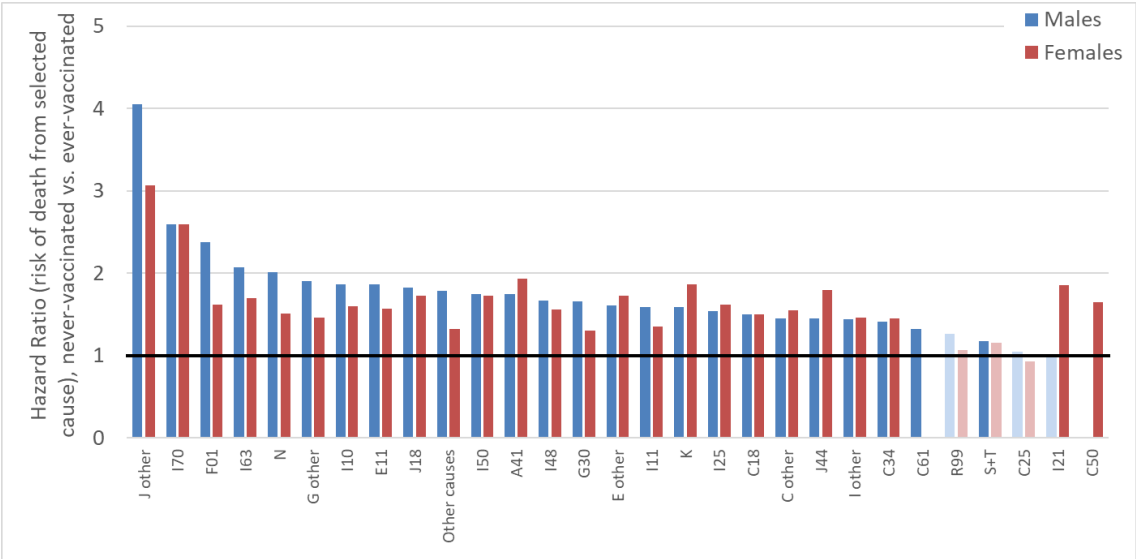
The analysis is based on Cox regression with competing risks (specific causes of death). The model was conducted separately for males and females. Results related to vaccination status (never-vaccinated versus ever-vaccinated individuals) were adjusted for age, health status (measured by the DCCI comorbidity index), and the number of previous registered COVID-19 infections. Results are presented as hazard ratios along with their levels of significance (p-values). The hazard ratios indicate the relative risk of death from a specific cause for the never-vaccinated group compared to the ever-vaccinated group.

In the first step, the model included 30 competing causes or groups of causes of death, each of which covered, on average, at least 1% of the annual number of deaths. For the second step, the avoidable mortality concept was used to aggregate the data (based on the Eurostat-OECD definition [15]). The third step involves analyses applied to specific calendar years, and it is currently in progress.

Results

This extended abstract presents results only for the first and second steps of analysis, and only for the year 2022. The results confirm a roughly 18-fold higher risk of death due to COVID-19 for the never-vaccinated population compared to the ever-vaccinated people. This specific result will not be repeated in particular steps of the analysis, where the focus is on non-COVID-19 causes specifically.

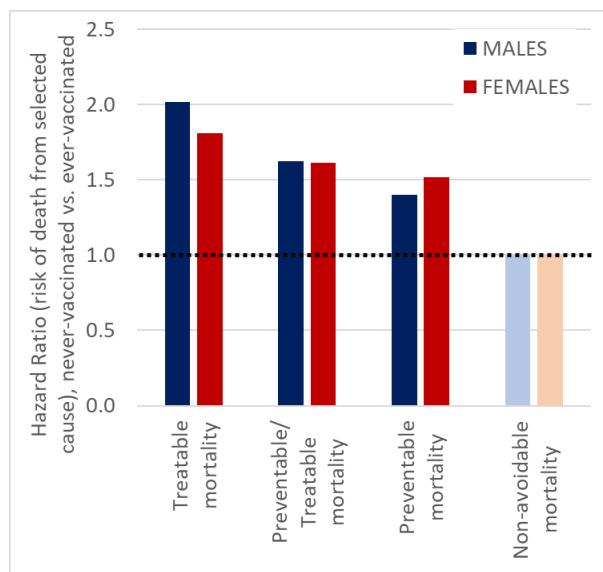
Figure 1: Hazard ratio – relative risk of death from selected causes of death for the never-vaccinated population compared to the ever-vaccinated, Czechia, males, females, 2022ⁱ



Note: 18-fold higher risk of death due to COVID-19 for the never-vaccinated population compared to the ever-vaccinated population is not included in the figure. Lighter colours represent values not statistically significant at the 5% level of significance. Results are adjusted for control variables included in the model. See the list of abbreviations at the end of the document.

Figure 1 presents the different levels of mortality risk for specific causes or groups of causes of death for the never- and ever-vaccinated subpopulations (first step of the analysis). The differences are smaller compared to those of COVID-19; however, most of them remain statistically significant. A three- to four-fold risk was confirmed for other respiratory diseases, a significant difference is for some types of dementia, cerebral infarction, hypertension or diabetes. On the other hand, more minor differences (below or approaching the threshold of statistical significance) are shown in the case of selected types of malignant neoplasms (neoplasm of pancreas) or in external causes of death in the case of women.

Figure 2 Hazard ratio – relative risk of death from avoidable (preventable, treatable) and non-avoidable causes of death for the never-vaccinated population compared to the ever-vaccinated, Czechia, males, females, 2022



When applying the avoidable mortality concept (Figure 2, second analytical step), differences in mortality were confirmed for all types of avoidable mortality (1.5-2.0-fold risk of death for people without vaccination when adjusted for age and other control variables). In the case of non-avoidable mortality, on the other hand, no difference in the risk of death between ever- and never-vaccinated subpopulations was confirmed. The results do not differ fundamentally when applied to lower age groups (up to 80 years, in accordance with the definition of the concept of avoidable mortality) and to the entire age spectrum, including the oldest individuals.

This corresponds to the assumption that different behavioural factors underlie vaccination decisions and are associated with

trust in expert recommendations, the use of preventive measures, or a risky lifestyle. Differences by gender are manifested mainly in specific causes.

Conclusion

The analysis confirmed significant differences in COVID-19 mortality between never- and ever-vaccinated groups, an expected direct effect of vaccination. However, it mainly examined indirect effects, such as differing risks from non-COVID causes. These mortality differences likely stem from factors that influence vaccination decisions, such as trust in healthcare, science, health habits, lifestyle, and preventive measures. Selected causes of death showed differences in mortality between never- and ever-vaccinated groups. The risk difference was only confirmed for avoidable causes, which are preventable or treatable. For harder-to-prevent or treat diseases (non-avoidable), no risk differences were found linked to vaccination.

While further research is needed, the mortality differences likely reflect differences in healthcare approach and trust, which in turn influence vaccination use. Initial results suggest these differences persist over time, indicating that willingness to take preventive measures during the health crisis is linked to long-term healthcare and lifestyle choices. Clearly, the population defined by vaccine hesitancy is, on average, at a higher risk of mortality. Targeting appropriately formulated information campaigns specifically at this population group can help reduce the overall level of mortality and mortality inequalities in society. The finding that the

never-vaccinated population has a higher risk of death from avoidable causes should lead to strategies that help to improve trust in the health system, health literacy, and prevention.

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ⁱ **Abbreviations:** U=COVID-19; J other=Other causes of Diseases of the respiratory system; I70=Atherosclerosis; F01=Vascular dementia; I63=Cerebral infarction; N=Diseases of the genitourinary system (N00-N99); G other=Other causes of Diseases of the nervous system; I10=Essential (primary) hypertension; E11=Type 2 diabetes mellitus; J18=Pneumonia, unspecified organism; Other causes=Other causes not included elsewhere; I50=Heart failure; A41=Other sepsis; I48=Atrial fibrillation and flutter; G30=Alzheimer's disease; E other=Other causes of Endocrine, nutritional and metabolic diseases; I11=Hypertensive heart disease; K=Diseases of the digestive system (K00-K95); I25=Chronic ischemic heart disease; C18=Malignant neoplasm of colon; C other=Other malignant neoplasms; J44=Other chronic obstructive pulmonary disease; I other=Other causes of Diseases of the circulatory system; C34=Malignant neoplasm of bronchus and lung; C61=Malignant neoplasm of prostate; R99=Ill-defined and unknown cause of mortality; S+T=External causes; C25=Malignant neoplasm of pancreas; I21=Acute myocardial infarction; C50=Malignant neoplasms of breast