Large US study confirms most mRNA COVID-19 vaccine side effects are mild and temporary

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A review of adverse events following vaccination against COVID-19 with mRNA vaccines in the U.S. confirms that most side effects were mild and decreased substantially after one day. The new study, published in *The Lancet Infectious Diseases* journal, suggests that for more than

298 million vaccine doses administered between December 2020 and June 2021, 92% (313,499/340,522) of reported adverse events were not serious, and less than 1% of v-safe participants reported seeking any medical care following vaccination.

In December 2020 two mRNA COVID-19 vaccines—Pfizer-BioNTech (BNT162b2) and Moderna (mRNA-1723) – were authorised for emergency use in the U.S.. Both vaccines involved two primary doses and have shown good safety profiles in clinical trials, with mild effects such as injection site pain, fatigue, and headache being reported as the most common adverse events.

As is the case for all vaccines in the U.S., anyone can report adverse events using the Vaccine Adverse Event Reporting System (VAERS), a long-standing reporting system run jointly by US Centers for Disease Control and Prevention (CDC) and the US Food and Drug Administration (FDA). With VAERS, US residents, their healthcare providers, or vaccine manufacturers can submit any event experienced following receipt of a vaccine. These reports are categorised as non-serious, serious, or death. The v-safe system, managed by CDC, was developed specifically for the COVID-19 vaccination programme, and consists of smartphone-based surveys sent daily for the first week after vaccination (and at longer time intervals in the months following) to monitor adverse reactions.

"Vaccines are the most effective tool to prevent serious COVID-19 disease outcomes and the benefits of immunisation in preventing serious illness and death strongly favour vaccination," says study author, Dr. Hannah Rosenblum, U.S. Centers for Disease Control and Prevention (CDC). "COVID-19 vaccine safety monitoring is the most robust in US history and the two complementary surveillance systems used in this study should bolster confidence that mRNA COVID-19 vaccines are safe."

This study looked at available VAERS and v-safe self-reported data between December 2020 and June 2021 following both doses of either the Pfizer-BioNTech or Moderna mRNA vaccines. During the study period, over 298 million doses of mRNA vaccines were administered (132 million Moderna and 167 million Pfizer).

VAERS received over 340,000 reports of adverse effects with more than 313,000 (92%) registered as non-serious, including headache (64,064/340,522 or 20%), fatigue (52,048/340,522 or 17%), fever (51,023/340,522 or 16%), chills (49,234/340,522 or 16%) and pain (47,745/340,522 or 15%). Of the more than 22,000 (6.6%) side effects registered as serious, the most common was shortness of breath (4,175/340,522 or 15%). Of 340,522 adverse events reported to VAERS during the study period, approximately 4500 (1.3%) were deaths, with more than 80% of these deaths among people ages 60 years or older. Because COVID-19 vaccines have been authorised under emergency use, healthcare providers are required to report all deaths following vaccination, regardless of the potential direct association. The study authors note that no unusual patterns were detected in cause death reports.

"The rapid pace at which COVID-19 vaccines were administered under emergency use, especially among older populations, was unprecedented. Due to their age, this group already has a higher baseline mortality rate than the general population and our results follow similar patterns of deaths rates for people in this age group following other adult vaccinations," says study author Dr. David Shay, also of the CDC.

Of the nearly 8 million v-safe participants, over half reported local (4.6 million) and systemic (3.6 million) reactions post-vaccination, occurring more frequently after dose two than dose one. Side effects were most frequently reported the day after vaccination and were nearly all mild, with the most common being fatigue (2,295,205/6,775,515 or 34% after

dose one, 3,158,229/5,674,420 or 56% after dose two), headache (1,831,471/6,775,515 or 27% after dose one, 2,623,721/5,674,420 or 46% after dose two), and injection site pain (4,488,402/6,775,515 or 66% after dose one, 3,890,848/5,674,420 or 69% after dose two).

More v-safe reports of being unable to work, perform normal activities, or seeking medical care were reported after dose two (1,821,421/5,674,420 or 32%), than after dose one (808,963/6,775,515 or 12%). Less than 1% of participants (56,647 after dose one and 53,077 after dose two) reported seeking medical care after either vaccine dose.

Study author Dr. Tom Shimabukuro (US CDC) says: "VAERS and v-safe are important tools CDC can use when evaluating vaccine safety and to help identify any unexpected or unusual events. These data are reassuring that reactions to both mRNA vaccines are generally mild and subside after one or two days—confirming reports from clinical trials and post-authorization monitoring."

The authors acknowledge some limitations with this research. Firstly, the VAERS system relies on spontaneous reporting and is not representative of the entire population. This also means that while it can monitor for potential safety signals, it cannot define a causal relationship between vaccination and adverse events. This limitation lies with the surveillance system and not the study design. In addition, the need for smartphone access to participate in v-safe excludes populations without access to these devices. Finally, although trends in differences in adverse reactions have emerged among the Pfizer-BioNTech and Moderna mRNA vaccines, neither VAERS nor v-safe can definitively measure the safety differences between the two vaccines.

Writing in a linked comment, Elizabeth Phillips, Vanderbilt University Medical Center U.S., who was not involved in the study, said: "Reassuringly, the six-month VAERS data supports that, although

approximately one in 1,000 individuals vaccinated may have an adverse effect, most of these are non-serious. No unusual patterns emerged in the cause of death or serious adverse effects among VAERS reports… For adverse events of special interest, it is reassuring that there were no unexpected signals other than myopericarditis and anaphylaxis, already known to be associated with mRNA vaccines."

More information: Safety of mRNA vaccines administered during the initial 6 months of the US COVID-19 vaccination programme: an observational study of reports to the Vaccine Adverse Event Reporting System and v-safe, *The Lancet Infectious Diseases* (2022). www.thelancet.com/journals/lan … (22)00054-8/fulltext

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