

Supplement 1: Relevant historical perspective on COVID-19 vaccine and menstrual disturbances

In the Spring of 2021, shortly after the introduction of the novel COVID-19 vaccine, public reports of menstrual cycle disturbances began appearing both through formalized passive surveillance systems (e.g., US Centers for Disease Control Vaccine Adverse Event Reporting System; VAERS) and via social media (e.g., Twitter; now X). Individuals reported a range of potential vaccine-related menstrual cycle changes including but not limited to shorter and longer cycles, heavier, lighter or no flow during menses, more or fewer days of menses, and intermenstrual bleeding. These reported menstrual cycle disturbances also raised concerns regarding future fertility given menstrual health is a general indicator of health and fertility. A 2021 Kaiser family foundation poll reported that two-thirds of parents were concerned that COVID-19 vaccines will impact their child's future fertility. Women in the US make approximately 80% of health care decisions for their families and thus play a key role in household vaccination decisions, thereby highlighting the need to better understand any links between menstrual health and vaccines.

This universal knowledge deficit, the extent to which vaccines influence menstrual health, limited the ability to counsel menstruating individuals and their families about what to expect with vaccination at a critical time in the COVID-19 pandemic when infection rates were high, pandemic 'panic' was rampant, health care capacity was overtaxed, and there was growing mistrust of the medical system. It also drew attention to long-standing sex-specific research inequities especially around menstrual health, as well as the adverse patient experiences within the healthcare system when reporting concerns around menstrual health. The National Institutes of Health responded with a rapid-response funding opportunity in order to support further research (NOSI NOT-HD-21-035 COVID-19 Vaccination and Menstruation). The grant funding had strict inclusion criteria (reproductive-age, naturally cycling US-based individuals) as its purpose was to identify a causal relationship among healthy menstruating

individuals not using exogenous hormones. Here, we take the opportunity to report on both the latest research supported by this NIH funding as well as additional research from the scientific community that helps create a foundation of understanding of the effects of vaccination on menstrual health.