

Influenza Vaccination in Perioperative Settings: A Teachable Moment

To the Editor:

Although influenza vaccination is recommended for all children 6 months of age and older, American vaccination rates are well below U.S. Department of Health and Human Services (Washington, D.C.) target goals.^{1,2} To increase vaccination rates, the Centers for Disease Control and Prevention (Atlanta, Georgia) and the American Academy of Pediatrics (Itasca, Illinois) recommend influenza vaccination during all healthcare-seeking opportunities including the perioperative period.^{1,3}

No longer limited to the primary care setting, we hypothesized that the perioperative period would be an ideal setting to increase influenza vaccination in children. In the United States, approximately 6 million children under the age of 18 yr undergo general anesthesia annually.⁴ Because general anesthesia is so fraught with fear and anxiety, it is a “teachable moment,”—that is, an event that “motivates individuals to spontaneously adopt risk-reducing health behaviors” and would help overcome resistance to vaccination.^{5–7} Further, to “sweeten the pot,” vaccination under general anesthesia provides several benefits, including patient comfort, expedited care, and leveraging existing workflows and processes that we also believed would increase vaccination rates.⁴ Additionally, in the fall of 2020, we were faced with the prospect of a combined influenza epidemic and COVID-19 pandemic.

Thus, we implemented a standardized process to actively offer influenza vaccination to all our patients undergoing elective general anesthesia. We sought to increase the number of vaccines given under general anesthesia and understand patient factors associated with vaccine acceptance. We conducted multivariate multilevel mixed logistic regression analyses, accounting for repeat procedures per patient within a given season, to determine if the intervention was associated with the outcome of perioperative vaccination, while controlling for all patient- and procedure-level data that yielded statistical significance when examined at a bivariate level. All analyses were conducted using Stata 17.0 (StataCorp LP, USA).

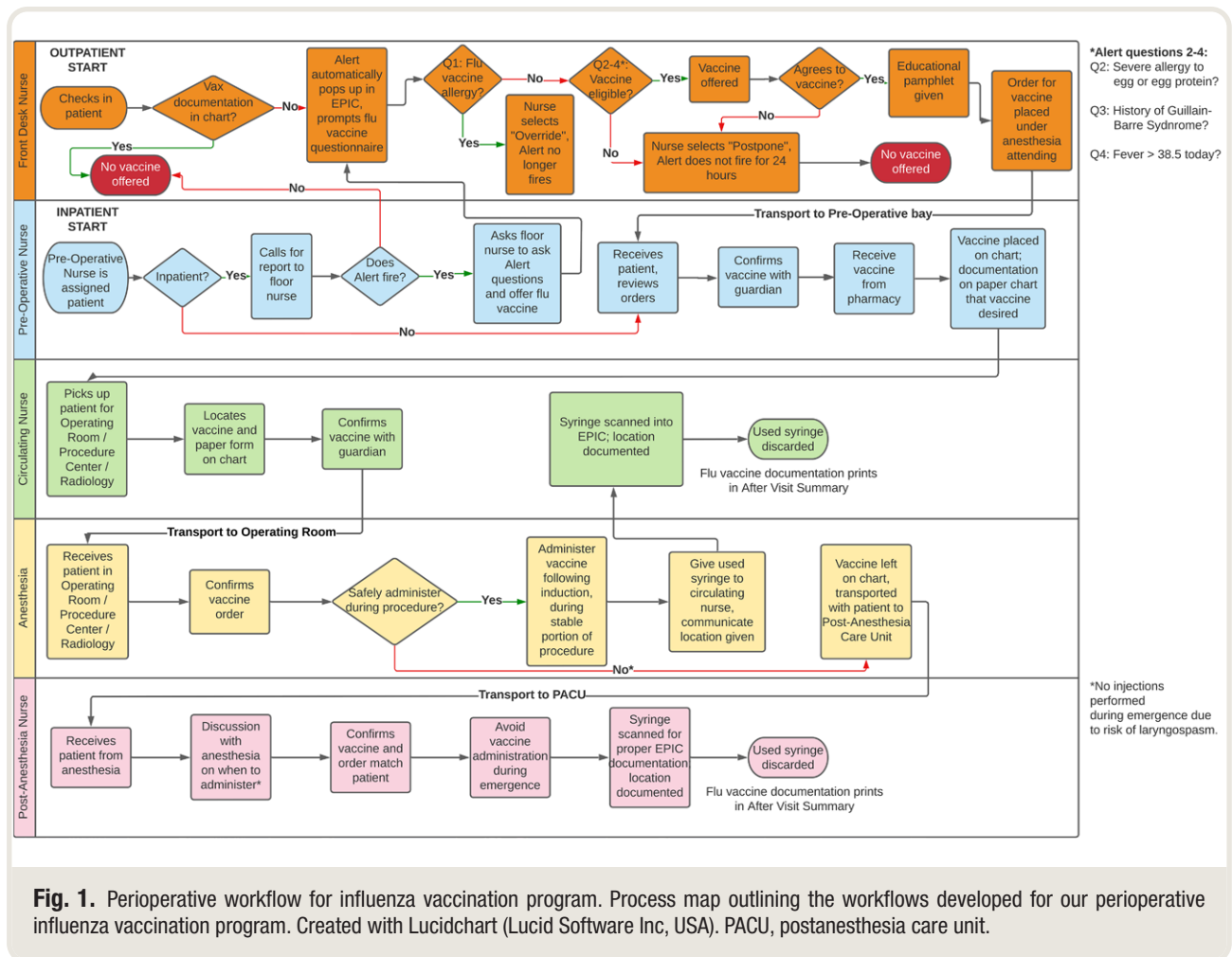
Our quality improvement process included forming a multidisciplinary team, modifications to the electronic

health record, nurse standing order utilization, data analytics, and development of a best practice workflow (fig. 1). Specifically, during preoperative registration, a best practice advisory in the electronic health record specific to perioperative areas prompted nursing staff to (1) determine and document influenza vaccination status, (2) determine eligibility for vaccination, and (3) order inactivated influenza vaccine using existing hospital standing orders if consent/assent for vaccination was obtained. The vaccine was then sent from pharmacy and placed on the patient’s chart to be given after induction of anesthesia by the anesthesia team or circulating nurse. The vaccine was documented in the electronic health record, populated in the state immunization registry, and included in the after-visit/discharge summary (fig. 1).

After obtaining approval by the Organizational Research Risk and Quality Improvement Review Panel for Children’s Hospital Colorado (Aurora, Colorado), parental consent, and when applicable, patient assent, we offered the influenza vaccine to all patients undergoing elective general anesthesia at our tertiary care, freestanding children’s hospital between October 2020 to March 2021. Additionally, Colorado Multiple Institutions Review Board (Aurora, Colorado; No. 21-2654) approval was obtained to review the data. The number of patients receiving the vaccine in this intervention was compared to the previous year’s nonstandardized process.

There were 6,841 and 6,858 perioperative visits (children younger than 18 yr) in our preintervention and intervention periods, respectively. Our standardized process significantly increased influenza vaccinations by sixfold. Specifically, in the preintervention period, only 140 patients (2%) were vaccinated compared to 930 (13.6%) during the intervention period (odds ratio, 0.1509; 95% CI, 0.1259 to 0.1808; $P < 0.001$). There were minor and likely unimportant differences in the demographics between the reference and intervention years. In the intervention year, children who were vaccinated under anesthesia were more likely to be older (median, 98.5 vs. 91 months), Hispanic (33% vs. 26.8%), and discharged after the procedure (86.8% vs. 81.2%). Further, in multivariate multilevel mixed logistic regression analyses, factors associated with perioperative vaccination included the intervention season (odds ratio, 15.49; 95% CI, 9.58 to 25.05), Hispanic ethnicity (odds ratio, 1.39; 95% CI, 1.11 to 1.75), and vaccination in October and November (odds ratio, 3.38; 95% CI, 2.30 to 4.96; and odds ratio, 2.40; 95% CI, 1.72 to 3.36, respectively). Of the 127 patients who were vaccinated and scheduled for postoperative admission to the hospital, only one developed a temperature greater than 38.4°C in the first 48 h postoperatively. On the other hand, 6 of 1,251 nonvaccinated patients admitted during the same time period developed a fever. Additionally, there

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were no reports in our hospital's safety reporting system of adverse or serious safety events related to vaccination (seizures, anaphylaxis, or injection site pain, swelling, or erythema) in either ambulatory patients or those admitted to the hospital postoperatively. Finally, this was an observational cohort study with all its inherent limitations.

In conclusion, low influenza vaccination rates require novel, alternative strategies to promote influenza vaccination. We developed "best practice" workflows with key stakeholders and end users and recognized the need for an organized processes system change, rather than individual change, which confirms other studies on the importance of collaboration and teamwork in process improvement.^{8,9} This standardized process substantially increased the number of perioperative vaccinations, particularly among Hispanic children, without increasing postoperative vaccine-related adverse events. Our intervention is sustainable and generalizable outside the COVID-19 pandemic. During the 2021 to 2022 influenza season, we had even greater success and vaccinated 3,166 patients perioperatively. While still a small percentage of the overall population presenting for anesthesia, we provided a reliable, expedited process with improved patient comfort to administer the influenza vaccine. Thus,

our findings that the perioperative period is a novel health-care opportunity to create a teachable moment and increase vaccination rates may have important implications for not only influenza vaccination, but also potentially for other childhood vaccinations, including COVID-19 vaccines.

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Competing Interests

Dr. Rao has previously received research support from Biofire (Salt Lake City, Utah) and GSK (Rockville, Maryland). The other authors declare no competing interests.

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Ketamine Pharmacodynamics Entangled: Comment

To the Editor:

We read with interest the study of ketamine psychedelic and analgesic effects by Olofsen *et al.*¹ and

the accompanying editorial by Mashour.² In both articles, the authors refer to the “dissociative” effects of ketamine. Corssen and Domino³ originally used the term “dissociative” in 1966 to describe “patients and subjects who, during recovery from CI-581 [ketamine], felt as though they were in outer space, or had no arms or legs.” This term has been used ever since, although we know considerably more about the subjective effects of ketamine than we did in the 1960s. Olofsen *et al.* measured the subjective effects of ketamine using a subset of items from a previously validated rating scale (Bowdle Visual Analogue Scale).¹ We first used this rating scale in its entirety in 1998,⁴ along with the Hallucinogen Rating Scale,⁵ to establish the relationship between plasma concentrations and the subjective effects of ketamine. The Bowdle Visual Analogue Scale and the Hallucinogen Rating Scale are intended to measure the overall psychedelic effects, not specifically dissociative effects. We would suggest that the term “dissociative” may no longer be the best descriptor of the subjective effects of ketamine.

Numerous terms have been used to describe the mind-altering effects of ketamine, including “dissociative,” “psychotomimetic,” “hallucinogenic,” “emergence reaction,” and “psychedelic.” Parsing these terms can be difficult because there is no universal agreement about their meaning. Dissociative experiences as described by Corssen and Domino can occur under the influence of a variety of psychedelic drugs and are not specific to ketamine. Psychotomimetic implies a psychotic state, lacking in insight; psychosis is not typical of psychedelic drug experiences because subjects are usually able to reflect on the nature of the experience. Hallucinogenic effects can occur under the influence of psychedelic drugs but are not an essential or universal element of the psychedelic experience. Emergence reaction refers to mind-altering experiences that occur after awakening from anesthesia with ketamine, and so does not apply to subanesthetic doses of ketamine. Psychedelic, meaning “mind manifesting,” was originally proposed by Osmond in 1957⁶ to describe the effects of a variety of mind-altering drugs, including hashish. Subsequently, the term psychedelic has been applied to diverse mind-altering drugs, although some authors have used the term psychedelic more specifically to refer to lysergic acid diethylamide-like serotonergic receptor agonists.^{7,8}

Our current understanding of the psychedelic effects of ketamine and other psychedelic drugs comes primarily from narrative descriptions related by subjects who have experienced the effects, or from rating scales constructed to capture the experiences in a standardized fashion. Although scales are useful for measuring drug effects, the results depend on the nature of the items chosen for inclusion in them.

Beyond ketamine, a small group of drugs that produce psychedelic experiences, analgesia, and anesthesia has been referred to as “dissociative anesthetics,” implying a similarity to ketamine. This group usually includes phencyclidine, ketamine analogues, dextromethorphan, salvinorin A (produced by the plant, *Salvia divinorum*),⁹ and nitrous oxide. The term “dissociative anesthetics” suggests that the mechanisms of action and the