adults in selected counties in California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, Ohio, Oregon, New Mexico, New York, Tennessee, and Utah with a total catchment population of over 27 million people (~9% of the US population). Using this platform, we will retrospectively evaluate four influenza seasons using FluSurv-NET data to look at the timing of influenza vaccination and severity of illness among patients with influenza-related hospitalization. We will conduct a multivariate analysis to assess for differences in severe outcomes including duration of hospitalization, ICU admission, and death among patients with varying lengths of time between influenza vaccination and influenza-related hospitalization. Separate analyses will be performed among different age groups and influenza type/subtypes, as well as specific seasons as a surrogate for most common circulating strain. RESULTS/ANTICIPATED RESULTS: We hypothesize that patients with chronic medical conditions and those at the extremes of age will have a longer duration between vaccination and hospitalization as they are more likely to get vaccinated earlier. We also hypothesize that patients with longer duration between seasonal influenza vaccination and hospitalization will have a longer duration of hospitalization and a higher rate of other severe outcomes (e.g., ICU admission, death). Such data would suggest that immune protection wanes during the influenza season. DISCUSSION/SIGNIFICANCE OF IMPACT: Limited data suggest that vaccine-induced influenza immunity may wane during the influenza season. It is not known whether the impact of influenza vaccination upon severity of disease might wane with increasing time between vaccination and influenza infection. In contrast to many previous studies evaluating vaccine effectiveness which have assessed medically-attended influenza illness as a primary outcome, our dataset is a large cohort of hospitalized patients which allows us to assess rare yet critical outcomes such as ICU admission and death. This study will also have a substantially larger amount of pediatric data than previous studies, which will provide the opportunity to determine whether timing of vaccination affects children and adults differently. Improving our understanding of whether influenza vaccine-induced protection might wane over time could ultimately impact U.S. influenza vaccination policy resulting in decreased morbidity and mortality attributed to influenza each season.

3542

Torsade de pointes/QT prolongation risks with antibiotics: A contemporary analysis of the FDA Adverse Event Reporting System

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OBJECTIVES/SPECIFIC AIMS: Macrolides, linezolid, imipenem-cilastatin, fluoroquinolones, penicillin combinations, and ceftriaxone are known to be associated with Torsade de pointes/QT prolongation (TdP/QTP). Other antibiotics may also lead to TdP/QTP, but no study has systemically compared TdP/QTP risks of different antibiotics using recent data. Therefore, the objective of this study was to evaluate the association between TdP/QTP and antibiotics in recent years using the FDA Adverse Event Report System (FAERS). METHODS/STUDY POPULATION: FAERS reports from January 1, 2015 to December 31, 2017 were analyzed. The Medical Dictionary for Regulatory Activities (MedDRA) was used to identify TdP/QTP cases. We calculated the Reporting Odds Ratios (RORs) and corresponding 95% confidence intervals (95%CI) for the association between antibiotics and TdP/QTP. An association was considered to be statistically significant when the lower limit of the 95%CI was greater than 1. RESULTS/ANTICIPATED RESULTS: A total of 2,042,801 reports (including 5,221 TdP/QTP reports) were considered, after inclusion criteria were applied. Macrolides had the greatest proportion of TdP/QTP reports, representing 2.9% of all macrolide reports. TdP/QTP RORs (95%CI) for the antibiotics were (in descending order): macrolides 11.73 (9.74-14.12), linezolid 9.39 (6.45-13.68), amikacin 8.94 (4.22-18.92), imipenem-cilastatin 5.01 (2.38-10.56), fluoroquinolones 4.67 (3.96-5.52), penicillin combinations 3.52 (2.56-4.86), cephalosporins 1.90 (1.14-3.16), metronidazole 1.49 (0.74-2.99), vancomycin 1.26 (0.70-2.28), clindamycin 0.83 (0.27-2.58), trimethoprim-sulfamethoxazole 0.82 (0.31-2.18), and amoxicillin 0.57 (0.18-1.78). DISCUSSION/SIGNIFICANCE OF IMPACT: This study confirms prior evidence for TdP-QTP risks with macrolides, linezolid, imipenem-cilastatin, fluoroquinolones, penicillin combinations, and cephalosporins. This study provides new evidence for TdP-QTP risks with amikacin. Macrolides had the highest TdP/QTP ROR among the antibiotics evaluated in this study.

3317

Translating simulation-based team leadership training into patient-centered outcomes

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OBJECTIVES/SPECIFIC AIMS: The objective of this research was to assess the clinical impact of simulation-based team leadership training on team leadership effectiveness and patient care during actual trauma resuscitations. This translational work addresses an important gap in simulation research and medical education research. METHODS/STUDY POPULATION: Eligible trauma team leaders were randomized to the intervention (4-hour simulation-based leadership training) or control (standard training) condition. Subject-led actual trauma patient resuscitations were video recorded and coded for leadership behaviors (primary outcome) and patient care (secondary outcome) using novel leadership and trauma patient care metrics. Patient outcomes for trauma resuscitations were obtained through the Harborview Medical Center Trauma Registry and analyzed descriptively. A one-way ANCOVA analysis was conducted to test the effectiveness of our training intervention versus a control group for each outcome (leadership effectiveness and patient care) while accounting for pre-training performance, injury severity score, postgraduate training year, and days since training occurred. Association between leadership effectiveness and patient care was evaluated using random coefficient modeling. RESULTS/ANTICIPATED RESULTS: Sixty team leaders, 30 in each condition, completed the study. There was a significant difference in post-training leadership effectiveness [$F(1,54)=30.19$, $p<.001$, $\eta 2=.36$] between the experimental and control conditions. There was no direct impact of training on patient care [$F(1,54)=1.0$, $p=0.33$, $\eta 2=.02$]; however, leadership effectiveness mediated an indirect effect of training on patient care. Across all trauma resuscitations

team leader effectiveness correlated with patient care ($p<0.05$) as predicted by team leadership conceptual models. DISCUSSION/SIGNIFICANCE OF IMPACT: This work represents a critical step in advancing translational simulation-based research (TSR). While there are several examples of high quality translational research programs, they primarily focus on procedural tasks and do not evaluate highly complex skills such as leadership. Complex skills present significant measurement challenges because individuals and processes are interrelated, with multiple components and emergent nature of tasks and related behaviors. We provide evidence that simulation-based training of a complex skill (team leadership behavior) transfers to a complex clinical setting (emergency department) with highly variable clinical tasks (trauma resuscitations). Our novel team leadership training significantly improved overall leadership performance and partially mediated the positive effect between leadership and patient care. This represents the first rigorous, randomized, controlled trial of a leadership or teamwork-focused training that systematically evaluates the impact on process (leadership) and performance (patient care).

Commercialization/Entrepreneurship/Regulatory Science

3466

Innovative 3D Printed Intravaginal Rings: Developing AnelleO PRO, the First Intravaginal Ring for Infertility

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OBJECTIVES/SPECIFIC AIMS: The study aims to develop and test a biocompatible 3D-printed IVRs for the mechanical and release properties of a model drug, β-estradiol, then translate these methods to the target drug, progesterone. The goals include demonstrating decoupling of mechanical and release properties of the rings, release profiles driven by geometry and efficacy in sheep animal models to evaluate device safety. METHODS/STUDY POPULATION: A novel 3D-printing platform, continuous liquid interface production (CLIP), pioneered by Carbon, enables the fabrication of complex designs on a timescale that is amenable to manufacturing. The process utilizes computational-aided design (CAD), specifying shape and geometry, which is recreated via a photopolymerization process. IVRs are fabricated with CLIP using a biocompatible resin at a rate of approximately 15 min. per ring. Rings were fabricated and assessed for the release of a model drug, β-estradiol. The process was then translated to the target drug, progesterone. Rings were evaluated for radial compression and in vitro release in simulated vaginal fluid (SVF). RESULTS/ANTICIPATED RESULTS: Intravaginal rings (IVRs) were designed and fabricated to be geometrically complex in an effort to control release. Ring geometry and subsequent pore size was achieved through the use of unit cells. Several design parameters were explored including unit cell type, size, and band presence in two resins of differing mechanical properties. Through design, a wide range of radial compressive properties were achieved which spanned values covered by commercially available rings. The release of β-estradiol in SVF was found to span 57 – 115 days and resulted in near or complete release of the total loaded drug. Changing the internal geometric design of the ring was found to have minimal influence on the compression properties, thus the mechanical and release characteristics of the rings were largely decoupled. DISCUSSION/SIGNIFICANCE OF IMPACT: This is a novel approach to the design and fabrication of intravaginal rings for the treatment of infertility. The use of CAD and the decoupling of release from mechanical properties allows for us to move away from the one-size one-dose fits all approach to IVRs.

3570

The Regulatory Landscape of Products to Treat Opioid Overdose

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OBJECTIVES/SPECIFIC AIMS: Since 1971, Naloxone has been the only FDA approved opioid antagonist indicated for use after opioid overdose. New formulations of Naloxone have been introduced into the market, including an injectable, auto-injector, and nasal spray. However, Naloxone is short-acting and as such often requires multiple doses and may induce severe withdrawal symptoms. This study examines the regulatory framework to understand the evolution of products indicated to treat opioid overdose and the landscape of therapies in development. Furthermore, this study examines how the Food and Drug Administration (FDA) and other government agencies have approached the opioid crisis. METHODS/STUDY POPULATION: A PubMed search of "naloxone AND opioid overdose" with the filter "humans" was conducted to understand Naloxone's regulatory framework. The term "naloxone" was searched on the Drugs@FDA: Approved Drug Products database. Additionally, "nalmefene" was searched on ClinicalTrials.gov. To examine the opioid antagonist market landscape, a PubMed search of "opioid antagonist AND opioid overdose" with the filters "humans" and "clinical trial," and a ClinicalTrials.gov search of "opioid antagonist and opioid overdose," were conducted. Government agency reports were reviewed and cataloged. RESULTS/ANTICIPATED RESULTS: Preliminary findings suggest a lack of innovation in the development of novel opioid antagonists. Most literature review findings focused on already-marketed Naloxone products, including the original injectable approved in 1971, the 2014 Evzio Auto-Injector, and the 2015 Narcan Nasal Spray (Figure 1). For example, there were 14 results yielded from the FDA approvals database, but none of these results represented a new opioid antagonist molecule. A longer-acting opioid antagonist, Nalmefene injectable, was approved in 1995 but has since been removed from the market due to low sales. Our initial ClinicalTrials.gov search using condition "opioid overdose" and other terms "opioid antagonist",revealed no new studies being conducted on alternative opioid antagonist treatments for opioid overdose. Findings only focused on the distribution, co-dispensing, intervention, pharmacokinetics/pharmacodynamics (PK/PD) of Naloxone (Figure 2). However, a Google search yielded one new trial with an opioid antagonist by Opiant Pharmaceuticals, almost fifty years after FDA's approval of Naloxone. A ClinicalTrials.gov search was then performed using the search term "nalmefene" to find whether Opiant Pharmaceuticals' trial was in the ClinicalTrials.gov database. However, the Opiant trial is phase I, and as such does not require reporting on ClinicalTrials.gov. In 2017, the National Institutes of Health (NIH) launched an initiative for longer-acting opioid antagonist formulations. In 2018, Opiant Pharmaceuticals announced positive phase I results for intranasal Nalmefene. The potential return of Nalmefene in intranasal form