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End user feedback on the Revised Department of Defense (DoD) Progressive Return to Activity (PRA): Primary Care for Acute Concussion Management Clinical Recommendation (CR)

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OBJECTIVES/GOALS: The objectives of the study were to evaluate end-user feedback regarding usefulness and compliance with the revised DoD PRA-CR. The PRA-CR utilizes symptom-guided management strategies to advance service members with acute concussion through 6 stages of gradually increased activity prior to their Return to Duty (RTD). METHODS/STUDY POPULATION: Clinical providers previously trained on the PRA-CR were invited via email to participate in an online survey-based study to examine their opinions and utilization of the revised PRA-CR. Participants who responded to the initial email invitation were provided an electronic Microsoft Forms based survey. Of the 83 total responders, 36 met inclusion criteria and advanced to the end-user survey. Six items were designed to assess inclusion–exclusion criteria (i.e., credentialed medical provider trained in the PRA-CR with experience treating concussion over the previous 2 years). Four items gauging utilization required yes/no responses; 20 opinion items on a 7-point Likert scale ranged from strongly disagree to strongly agree; 5 explanatory items were multi-select; and 1 item allowed free text responses. RESULTS/ANTICIPATED RESULTS: Overall, 87% of respondents who had used the revised CR indicated that it helped them treat patients with acute concussion and 73% rated, "ease of use" favorably. Of the newly added elements to the CR, utilization of the Patient Leadership Guide (PLG) was the highest at 78%, with the majority of the providers rating the PLG as useful in communicating with patients and command. In contrast, only 35% of participants reported using the Physical RTD screening section and 22% indicated using the Cognitive RTD screening tool. Those not utilizing the Physical screening identified a lack of support staff (67%) or setting barriers (47%) as the primary reasons. Those not utilizing the Cognitive RTD screening tool identified multiple barriers to use including availability (72%), inexperience (39%), and baseline data access (33%). DISCUSSION/SIGNIFICANCE OF IMPACT: This study sought end-user (provider) feedback regarding the revised PRA-CR's usability and utility, in addition to their confidence in the tool itself. Overall results were generally positive, except for the updated Physical RTD and newly introduced Cognitive RTD screenings.

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Allogeneic recellularized lung orthotopic (ARLO) transplant research: A short-term non-survival model

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OBJECTIVES/GOALS: This study assesses the feasibility of a human-to-swine lung transplant model for the evaluation of bioengineered organs. Given the critical organ shortage, this research explores bioengineered organs as a potential solution by evaluating early lung function, immune responses, and technical aspects to develop a model for bioengineered lungs. METHODS/STUDY POPULATION: The study employs a non-survival human-to-swine left lung transplant model in an immunosuppressed Yorkshire swine. A combination of cobra venom factor pretreated with methylprednisolone and Benadryl with scheduled dosing of tacrolimus and mycophenolate over a 24-hour period will be administered. The transplanted human lung is assessed over a 24-hour post-transplant period, with hourly pulmonary vein gas sampling and lung tissue resections. The proposed model will assess the immunological response of swine to human lung tissue as well as the efficacy of the immunosuppression model. Tissue samples are taken at intervals to evaluate for signs of rejection, cellular damage, and the overall function of the transplanted lung. All tissues are preserved in formaldehyde for subsequent immunohistology evaluation. RESULTS/ANTICIPATED RESULTS: We anticipate a successful non-survival swine transplant model with pulmonary function sustained for the full 24-hour study using our proposed immunosuppression regimen. Initial testing with a standard human lung will lay the groundwork to assess the effectiveness of the human-to-swine transplant model. Hourly pulmonary vein gas analyses and tissue biopsies are expected to show minimal immune rejection, supported by the preoperative immunosuppression regimen. Early data indicate that the swine tolerates both the surgical procedure and immunosuppressive therapy well, with manageable hemodynamic stability. This model is expected to yield critical insights into lung viability and will identify areas for optimization for long-term survival studies to test the efficacy of bioengineered organs. DISCUSSION/SIGNIFICANCE OF IMPACT: This non-survival swine model offers valuable insights into the acute-phase immune response and functional viability of human-to-swine lung transplant model. The findings will support the development of long-term survival models that will allow the evaluation of bioengineered organs based solely on their functionality as engineered organs.

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Uncovering an unexpected therapeutic target for motivational deficits following early-life exposure to SSRIs

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OBJECTIVES/GOALS: Motivational deficits are associated with depression and poorly treated by current therapeutics. We sought to identify more effective therapeutics for these deficits using a mouse model of early-life exposure to SSRIs, a developmental risk factor identified for depression in humans. METHODS/STUDY POPULATION: Mice were administered the SSRI, fluoxetine (FLX), or a vehicle control from postnatal day P2-P11, a window that mimics brain development occurring during the third trimester in a human pregnancy. Motivation and hedonic perception were assessed in adulthood using the progressive ratio and lickometer tasks, respectively. Behavioral testing was repeated after chronic adult administration of either an SSRI (fluoxetine), an atypical antidepressant and mu-opioid receptor agonist (tianeptine), or a mu-opioid receptor antagonist (methocinnamox). RESULTS/ANTICIPATED RESULTS: Mice administered FLX in early-life showed motivational deficits in the progressive ratio task, while hedonic perception, as measured by the lickometer task, remained intact. Chronic

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