

DEPARTMENT OF OBSTETRICS & GYNECOLOGY

20th Annual RESIDENT RESEARCH DAY
& JOHN ROCK LECTURE



MAY 19, 2023

FLYERS/76ERS SURGERY THEATRE
HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

Welcome

20TH ANNUAL RESIDENT RESEARCH DAY & JOHN ROCK LECTURE

Welcome to the 20th Annual John Rock Lecture and Department of

Obstetrics and Gynecology Resident Research Day. Resident Research Day is an opportunity for our trainees to present their research projects to their colleagues with the goal of challenging current thinking to improve reproductive health care. We believe this experience inspires our young physicians to engage in basic science, translational and clinical research opportunities in their future careers in order to benefit patients and advance our specialty.

We are honored to welcome our speaker Dr. William Grobman, Professor of Obstetrics and Gynecology and Vice Chair of Clinical Operations in the Department of Obstetrics and Gynecology, Ohio State University College of Medicine, Wexner Medical Center.

A special thank you to the Women's Health Clinical Research Center, The Penn Ovarian Cancer Research Center, The Center for Research on Reproduction and Women's Health and all mentors for supporting our trainees.

We thank you all for your attendance today and hope you will join us in congratulating all of today's participants on their achievements.

RESEARCH LEADERSHIP TEAM

Anuja Dokras, MD, MCHI, PhD
Director, Resident Research Program

Stefanie Hinkle, PhD
Associate Director, Resident Research Program

Catherine R. Salva, MD, MEd
Director, Residency Program

Elizabeth A. Howell, MD, MPP
Chair, Department of Obstetrics and Gynecology

JOHN ROCK LECTURER



William Grobman, MD, MBA

Professor of Obstetrics and Gynecology
Vice Chair, Clinical Operations — Obstetrics and Gynecology
The Ohio State University
Wexner School of Medicine

After receiving his BA from Amherst College and his MD from Harvard Medical School, Dr. Grobman completed residency training in Obstetrics and Gynecology as well as fellowship in Maternal-Fetal Medicine at Northwestern. During fellowship, he completed an MBA in Health Services Administration and Decision Sciences at

Northwestern's Kellogg School of Management. Dr. Grobman continued as faculty at the Feinberg School of Medicine, Northwestern University, until 2021. At the Ohio State University Wexner School of Medicine he is a Professor with tenure in the Department of Obstetrics and Gynecology and serves as Vice Chair of Clinical Operations for the department. He is the Past President of the Society for Maternal-Fetal Medicine and he serves on the Board of Directors of the American Board of Obstetrics and Gynecology. His research is focused on the prediction and prevention of adverse obstetric outcomes; he has been principal investigator on multiple NIH and foundation grants, has authored over 460 peer-reviewed publications, and is a member of the National Academy of Medicine.

AGENDA

7:30 - 8:00 am

CONTINENTAL BREAKFAST

8:00 - 8:05 am

WELCOME REMARKS

Elizabeth A. Howell, MD, MPP

8:05 - 8:10 am

INTRODUCTION

Anuja Dokras, MD, MCHI, PhD

8:10 - 10:10 am

RESIDENT RESEARCH PRESENTATIONS

Adaptations to COVID:

Analysis of National Abortion Clinic Survey Data.....Page 5

Elizabeth Kravitz, MD | Mentor: Sarita Sonalkar, MD, MPH

The Shock Index and the Surgical Management

of Ectopic PregnancyPage 6

Camille J. McCallister, MD, MPP | Mentor: Kathleen E. O'Neill, MD, MTR

Barriers to Enrollment in Gynecologic Oncology

Clinical TrialsPage 7

Erin McMinn, MD, MPH | Mentor: Emily M. Ko, MD, MSCR

Patient Consent for Exam Under Anesthesia

by Medical Students: A Single Institution Review.....Page 8

Lakeisha Mulugeta-Gordon, MD | Mentor: Mary DeAgostino-Kelly, MD, MPH

Postoperative Epidural Anesthesia Use in

Gynecologic Surgery: Worth the pain?Page 9

Margaret A Rush, MD | Mentors: Nawar Latif, MD, MSCE and Stefan Gysler, MD, MHS

The Experience with a Standardized Protocol for Labor Induction:

A Qualitative Evaluation of the Patient Perspective.....Page 10

Rosa Speranza, MD | Mentor: Rebecca F. Hamm, MD, MSCE

Medication Discontinuation and Associations with

Non-persistence among Patients with Interstitial Cystitis/Bladder Pain SyndromePage 11

Hunter L. Terry, MD | Mentor: Lily A. Arya, MD, MS

EPDS Screening at Delivery Discharge as a

Predictor of Postpartum Depression.....Page 12

Kelly Zafman, MD, MSCR | Mentor: Sindhu Srinivas, MD, MSCE

10:10 - 10:30 am

BREAK

10:30 - 11:10 am

JOHN ROCK LECTURE

The ARRIVE Trial: Interpretation and Implication

William Grobman, MD, MBA

11:10 am - 12:30 pm

RESIDENT (PGY2) RESEARCH PROPOSALS

Improving Health Disparities in Access to Minimally Invasive Hysterectomy

Annie Apple, MD | Mentor: Abike James, MD, MPH

A Calculator to Predict Latency in PPRM

Kira Bromwich, MD | Mentors: Rebecca Hamm, MD, MSCE and Nadav Schwartz, MD

Disparities in Access to Gynecologic Oncology Care – a SEER-Medicare Study

Clare Cutri-French, MD | Mentor: Emily M. Ko, MD, MSCR

Perceived Discrimination in Medical Settings by Pregnant Patients with Opioid Use Disorder

Karampreet Kaur, MD | Mentor: Nia Bhadra-Heintz, MD, MS

Determining Efficacy of Combined Cervical Ripening with Increasing BMI

Jacqueline Thompson, MD, MPH | Mentor: Rebecca Hamm, MD, MSCE

Peripartum Counseling Around Maternal Health Disparities: A Qualitative Study of Patient and Clinician Perspectives

Eileen Wang, MD | Mentor: Rebecca Hamm, MD, MSCE

12:30 pm

RESIDENT LUNCH

MFM Conference Room, 2 Silverstein



ADAPTATIONS TO COVID: ANALYSIS OF NATIONAL ABORTION CLINIC SURVEY DATA

Authors Elizabeth Kravitz, MD | Jessica Chen, MD | Jessica Wu, MD | Nathanael Koelper, MPH
Arden McAllister, MPH | Sarita Sonalkar, MD, MPH

Background COVID-19 exacerbated both existing inequities and barriers to accessing abortion services and introduced new unique challenges. The objective of this study was to analyze changes in national abortion clinic practices and telehealth utilization during the COVID-19 pandemic.

Methods We conducted descriptive analyses of nationwide abortion service trends utilizing a longitudinal survey distributed by the Society of Family Planning. The dataset was comprised of 3 surveys: T1: February-March 2020, T2: May-July 2020, T3: August-October 2020. Demographic characteristics including region (Northeast, Midwest, South, Midwest, West) and type of clinic site (academic/hospital affiliated, Planned Parenthood, independent) were provided in the survey data. Wilcoxon rank sum and Kruskal-Wallis tests were utilized for statistical analysis.

Results There was no difference in the volume of abortion services provided nationwide over T1-T3. However, there was a significant increase in the proportion of medical abortions as compared to procedural abortions from T1-T3 (26.7% to 40.0%, $p < .05$). Planned Parenthood/independent sites performed a significantly greater proportion of medical abortions than academic/hospital affiliated clinic sites ($p < .05$) across all three time periods. There was no difference in utilization of telehealth across the time periods, even when controlling for type of site and region. Sites offering telehealth services did not experience changes in volume of abortions or in distribution of abortion services provided (medical versus procedural).

Conclusion An increase in proportion of medical abortions over procedural abortions may suggest increasing access to medical abortions as clinics adapted to limitations of COVID-19 pandemic. Utilization of telehealth did not appear to decrease the availability of operative procedures or volume of services, suggesting telemedicine as a favorable care delivery option for clinics hoping to limit face-to-face interaction as the pandemic continues.



THE SHOCK INDEX AND THE SURGICAL MANAGEMENT OF ECTOPIC PREGNANCY

Authors Camille J. McCallister, MD, MPP | Nathanael C. Koelper, MPH
Kathleen E. O’Neill, MD, MTR

Background The shock index (SI), the ratio of heart rate to systolic blood pressure, has previously been reported as a tool useful in identifying acute hemorrhage. Additional studies have shown a possible relationship of shock index with ruptured ectopic pregnancy (EP).

Objectives To characterize the timeline for patients presenting to the emergency department (ED) who required surgical management for an ectopic pregnancy, and to assess the temporal trend of the SI and its relationship to the patient’s therapeutic course.

Methods This is a retrospective cohort study of patients who required surgical management for EP after presenting to the ED at two tertiary-care teaching hospitals from March 1, 2019, to March 31, 2022. The SI was calculated based on presenting vital signs (VS) and last VS documented before surgical incision. Chart review was used to construct a timeline of their hospital course. The diagnosis of ruptured EP was based on operative report findings or the pathology report with disruption of the fallopian tube serosa. SI values were then compared across patient demographics, diagnostic and therapeutic courses.

Results 204 patients underwent surgical management for EP. Included in the analysis were 117 patients with ruptured EP and 83 patients with non-ruptured EP. The average time from triage to surgical incision was 7.7 hours (range 1.4 - 36.0). The average time to surgical incision did not differ between individuals with a SI < 0.8 and SI ≥ 0.8 at triage (7.5 vs 8.1 hours respectively, $p = 0.45$). Additionally, the average time to surgical incision did not differ between individuals with a SI < 0.8 and SI ≥ 0.8 at the start of the procedure (8.0 vs 6.7 hours respectively, $p = 0.12$).

Ruptured EP was associated with time to surgical incision, with those diagnosed with ruptured EP having a shorter time to surgical incision ($p = 0.00$). Although SI ≥ 0.8 at triage and the start of the procedure was not associated with the finding of ruptured EP ($p = 0.07$, $p = 0.23$ respectively), the need for blood transfusion was found to be associated with SI ≥ 0.8 at triage ($p = 0.02$), SI ≥ 0.8 at procedure start ($p = 0.001$), and time to surgical incision ($p = 0.00$).

Conclusion The time to surgical incision was associated with ruptured ectopic pregnancy. SI ≥ 0.80 was not associated with ruptured ectopic pregnancy or time to surgical incision. However, it was associated with the need for blood transfusion. The relationship between SI and hemodynamic instability suggests SI may be a useful parameter to factor into a patient’s therapeutic course.



BARRIERS TO ENROLLMENT IN GYNECOLOGIC ONCOLOGY CLINICAL TRIALS

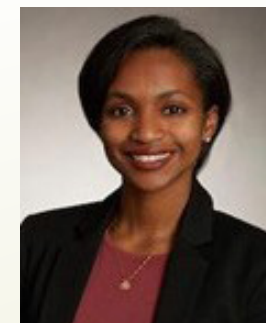
Authors Erin McMinn, MD, MPH | Emily M. Ko, MD, MSCR

Background Racial and ethnic minorities are underrepresented in clinical trials, including gynecologic oncology trials. We sought to evaluate factors associated with, and potential barriers to, enrollment, among patients considered for gynecologic oncology clinical trials at a tertiary care center to inform future participant recruitment.

Methods We conducted a retrospective cohort study at the University of Pennsylvania Abramson Cancer Center. We included patients discussed at weekly gynecologic oncology multi-disciplinary treatment planning conferences (TPC) from 1/1/2022-12/31/2022. A separate cohort of patients referred for clinical trial screening outside of the TPC pathway (non-TPC) was also included. Patients were further classified as ‘referred/not referred’ for screening for trials, and ‘enrolled/not-enrolled’ on to trial. We collected socio-demographic, cancer, trial screening, and enrollment data from electronic medical records. For patients referred for trial screening, we collected reasons for non-enrollment and ineligibility. We compared patient factors across 5 subgroups: 1) TPC not-referred, 2) TPC referred not-enrolled, 3) TPC referred enrolled, 4) non-TPC referred not-enrolled, 5) non-TPC referred enrolled. We performed descriptive analyses including univariable and bivariable non-parametric testing as appropriate.

Results In total 234 unique patients were included in this study. Median age was 66 years (IQR 58.2-73.6 years). 67.5% of patients were White, 23.1% Black, and 9.4% Other/unknown. 96% spoke English. The majority were insured by Medicare (51.5%), followed by Private (34.3%) and Medicaid (12.5%). From TPC, 128 patients were never referred for trial, 123 were referred but not enrolled, and 12 were referred and enrolled, with an overall enrollment rate of 4.7%. From the non-TPC screening pathway, 33 out of 41 referred patients were enrolled (80.5%). Across the five subgroups, there was no difference in age (p=0.107). Virtually all enrolled patients were white (10/12 TPC; 29/33 non-TPC) and had Medicare or private insurance (66% TPC; 59% non-TPC Medicare; 25% TPC; 37.5% non-TPC private). Only 8% of enrolled TPC and 3% of enrolled non-TPC patients had Medicaid, compared to 21% of those discussed at TPC and not referred to trial (p=0.012). Only 23% of patients referred from TPC but not enrolled had a documented exclusion criteria, compared to 87% of non-TPC non-enrolled, (p<0.001). Reasons for trial ineligibility were most commonly medical comorbidity and patient refusal.

Conclusion The vast majority of patients referred for clinical trial screening through TPC do not enroll in a clinical trial; those referred through other mechanisms had a high enrollment rate. Disparities by race and insurance status were apparent between enrolled and non-enrolled patients.



PATIENT CONSENT FOR EXAM UNDER ANESTHESIA BY MEDICAL STUDENTS: A SINGLE INSTITUTION REVIEW

Authors Lakeisha Mulugeta-Gordon, MD | Leigh Ann Humphries, MD | Hannah Ryles, MD Catherine Salva, MD, MEd | Jesse Chittams, MA | Ryan Quinn, MPH Mary DeAgostino-Kelly, MD, MPH

Background Medical student involvement in a pelvic exam under anesthesia (EUA) remains to be a challenge during their OB/Gyn clerkship. A consent process that addresses exams by medical students is necessary to protect patient autonomy. The aim of this study was to evaluate the presence of an exam under anesthesia consent and evaluate factors associated with a patient’s response to the EUA consent.

Methods This retrospective study included all patients who underwent a scheduled gynecologic procedure at the Hospital of the University of Pennsylvania and the Perelman Center for Advanced medicine from 7/1/2019 to 12/31/2019. Patient characteristics, clinical characteristics and practice attributes were collected and stored in a REDCap database. Statistical analyses were performed using SAS 9.4 for Windows. Significant associations were reported as odds ratios and 95% confidence intervals. Chi-square, Fischer’s exact and Wilcoxon Rank Sum tests were applied when appropriate. Logistic regression analyses were performed to estimate the effects of patient characteristics and practice attributes on the odds of consent being pursued and the odds of patient consenting to an EUA.

Results Out of 865 total patients, 46% (n=401) were offered the opportunity to consent to an EUA. Of those 401 patients, n=355 (89%) agreed to have the examination performed by a medical student. Bivariate analysis showed that all covariates had statistically significant associations with EUA consent status in the overall sample. Black patients had 0.58 times the odds of being consented for EUA (CI: 0.4404 – 0.7640; p<0.001), compared to non-black patients. Patients who received care from generalist practices had 5.86 times the odds of being consented when compared to patients who were seen in subspecialty practices (CI: 4.36 – 7.87; p<0.001). Compared to patients using private or commercial health insurance, patients on government-issued insurance had 0.73 the odds of being consented for EUA (CI: 0.55 – 0.97; p=0.082). After controlling for confounding, fellows and residents had 83% greater odds of consenting a patient to undergo EUA when compared to attending physicians (OR: 1.83 CI: 1.12 – 2.99 p=0.02).

Conclusion Although not all patients are routinely offered and consented for an EUA by a medical student, when consent is discussed, an overwhelming majority of patients consent to EUA by medical students. Our data offers support for all providers to feel empowered to discuss an EUA with their patients.



POSTOPERATIVE EPIDURAL ANESTHESIA USE IN GYNECOLOGIC SURGERY: WORTH THE PAIN?

Authors Margaret A. Rush, MD | Nayla Labban, MD | Clare Cutri-French, MD
Markoline Forkpa, MPH | Jesse Chittams, MA | Nawar Latif, MD, MSCE
Stefan Gysler, MD, MHS

Background Epidural anesthesia for post-operative pain management has been associated with improved patient-reported pain scores and decreased rate of opioid medication use. However, evidence also suggests that epidural use is associated with adverse post-operative outcomes, including an increased rate of hypotension necessitating transfer to intensive care and post-operative hospital readmission. Many studies evaluating the benefit of epidural anesthesia were performed prior to the widespread adoption of the Enhanced Recovery after Surgery (ERAS) pathways, which prioritize decreased opioid use and limit post-operative hospital length of stay. Therefore, the objective of this study was to evaluate the role of epidural anesthesia in the ERAS era.

Methods We conducted a retrospective cohort study using data collected from patients undergoing open gynecologic surgery within the University of Pennsylvania Health system for either malignant or benign pathology between 2016 and 2019. Patients included in this study underwent gynecologic surgery via midline laparotomy for any indication. Propensity score matching was performed with a 3:1 ratio of control group to intervention group based on age, race, malignancy, and number of procedures performed. Data was abstracted on demographics, post-operative pain medications, and pain scores. The primary outcome of interest was length of hospital stay.

Results Propensity score matching yielded 1072 patients, 339 (31.6%) with epidural placement at time of surgery, and 733 (68.4%) in the control group. There was no difference in race, ethnicity, or BMI between groups. After propensity score matching, patients who had an epidural placed at the time of their surgery had significantly longer operating room time (319 minutes vs. 271 minutes, $p < 0.01$) and median length of hospital stay (4 days vs. 3 days, $p < 0.01$) compared to patients who did not have an epidural placed. Mean pain scores were improved on post-operative days 1 (3.2 vs 4.4, $p < 0.01$) and 2 (4.4 vs. 4.8, $p < 0.01$) for patients with epidural anesthesia compared to those without. However, this difference was not observed on post-operative day 3 (4.5 vs 4.6, $p = 0.6$).

Conclusion Epidural anesthesia use for post-operative pain control is associated with increased time in operating room and length of hospital stay, with modest improvements in average pain scores for patients on the first and second postoperative day. The role of this pain modality must be carefully considered to ensure net benefit to post-operative patients.



THE EXPERIENCE WITH A STANDARDIZED PROTOCOL FOR LABOR INDUCTION: A QUALITATIVE EVALUATION OF THE PATIENT PERSPECTIVE

Authors Rosa Speranza, MD | Lisa D. Levine, MD, MSCE | Rebecca F. Hamm, MD, MSCE

Background A standardized protocol for induction of labor (IOL) was implemented at the Hospital of the University of Pennsylvania in October 2020 with the aim of decreasing cesarean rate and maternal morbidity, as well as reducing racial disparities in those outcomes. This protocol includes recommendations regarding cervical ripening, frequency of cervical exams, timing of amniotomy, and Pitocin initiation. Yet, prior research describes IOL as a risk factor for decreased birth satisfaction and limited data define the specific patient experience or acceptability of the various parts of IOL. In this study, we aimed to characterize the patient perspective of a standardized protocol for IOL.

Methods This qualitative study enrolled English-speaking, postpartum patients at our institution who underwent IOL for a term, singleton gestation with intact membranes and an unfavorable cervix. Enrollment occurred until thematic saturation was achieved with purposive sampling by parity, race/ethnicity, and mode of delivery in order to obtain diverse perspectives. Semi-structured interviews were performed exploring the experience of: (1) the overall standardized IOL, and (2) each IOL protocol component. Interviews were coded using a structured approach by two coders with high inter-rater reliability ($k=0.8$).

Results Eleven patient interviews were conducted between Nov 2022 and March 2023. Most of the participants (73%) were nulliparous and identified as Black (73%). Most patients did not have reservations regarding IOL. When concerns were expressed, they primarily centered around pain, the baby, and the possibility of cesarean delivery. When considering the individual components, many had never heard of misoprostol or Foley catheters prior to IOL. Misoprostol placement sparked little concern (“fine with it”). While Foley catheter placement caused apprehension, most patients felt placement wasn’t as painful as expected, describing primarily “pressure”. Many participants expressed concerns with Pitocin originating from outside sources (friends, social media) related to pain, but appreciated its ability to “speed up labor”. Conversely, for AROM, most patients reported neutrality (“doesn’t matter”), but a similar appreciation that AROM “moved labor along”. For cervical exams, participants noted wide variation in expectations – from “every hour” to “one and done”, but primarily found them to be less frequent than expected.

Conclusion When considering the patient perspective surrounding IOL with a standardized protocol, the primary sentiment was positive with a focus on prioritizing pain management, detailed counseling regarding steps of IOL, and speeding up labor. Future work should optimize patient counseling around IOL components in the prenatal care setting.



MEDICATION DISCONTINUATION AND ASSOCIATIONS WITH NON-PERSISTENCE AMONG PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

Authors Hunter L. Terry, MD | Edward K. Kim, MD, MPH | Lily A. Arya, MD

Background Our primary objective was to estimate the discontinuation rates of medications used for the treatment of Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS). The secondary objective was to identify variables associated with non-persistence.

Methods We conducted a retrospective cohort study of women with IC/BPS, ICD N30.10, who were treated in the University of Pennsylvania Health System (UPHS) from January 2019 to July 2021. Data were extracted from UPHS electronic medical record. Inclusion criteria were women over 18 years or older, confirmed by pharmacy records to have initiated amitriptyline, cimetidine, hydroxyzine, or pentosan polysulfate (PPS) by the departments of Urogynecology or Urology during the study interval. Exclusion criteria were prior treatment with the aforementioned medications or the diagnosis of genitourinary malignancy. Covariates examined included associated comorbid conditions, age, BMI and race. Discontinuation was defined as 90 days after the last prescribed dose of medication or order cancellation. Persistence was defined as receiving a prescription for greater than 1 year of treatment. Persistent and non-persistent cohorts were compared in regards to medication type and covariates.

Results Out of 176 women who met inclusion criteria, 103 (51%) were prescribed amitriptyline, 51 (25%) hydroxyzine, 40 (20%) PPS, and 8 (4%) cimetidine. A portion of this population underwent trials with multiple medications. The rates and average time to discontinuation for amitriptyline were 65% and 8.2 months, 75% and 8.5 months for hydroxyzine, 98% and 9.5 months for PPS, and 75% and 7.8 months for cimetidine. Of the population followed for greater than 1-year, 122 patients were non-persistent and 46 patients were persistent with treatment. While there was no significant relationship between non-persistence and the covariates examined, younger women showed a higher rate of non-persistence (p=0.11) and women who were prescribed amitriptyline had a lower rate of non-persistence (OR 0.559, CI 0.28-1.11).

Conclusion Although the discontinuation and non-persistence rates were lowest among women who were prescribed amitriptyline, overall discontinuation rates for medication prescribed for IC/BPS are high. Our findings suggest a discrepancy between what clinicians and patients consider to be appropriate and acceptable treatment. Future studies should investigate the reasons for discontinuation and non-persistence.



EPDS SCREENING AT DELIVERY DISCHARGE AS A PREDICTOR OF POSTPARTUM DEPRESSION

Authors Kelly Zafman, MD, MSQR | Melissa Riegel, MD | Sindhu Srinivas, MD, MSCE

Background Early identification of postpartum depression (PPD) is critical in order to identify at-risk patients and provide timely interventions and referrals. In September 2020, our institution implemented universal Edinburgh Postpartum Depression Scale (EPDS) screening for all patients prior to delivery discharge (DC) We sought to determine if screening with the EPDS at DC is predictive of postpartum depression (PPD).

Methods This was a retrospective cohort study of all patients who delivered at a single large urban academic medical center from 6/2021-6/2022. A score of ≥ 9 was considered at risk for PPD. Patients were re-screened at 2-6 weeks postpartum (PP). The primary outcome was mean EPDS score at 2-6 weeks PP. Secondary outcomes included the change in EPDS score from delivery DC to 2-6 weeks PP (paired t-test) and the positive and negative predictive value (PPV, NPV) of the DC score.

Results Of 4194 deliveries, 1603 (38.2%) completed EPDS screening at both timepoints. Patients were predominantly Black (64.2%) and publically insured (61.6%). 219 (13.7%) patients scored ≥ 9 at DC and 37(2.3%) endorsed self-harm at DC. There was a moderate positive correlation between scores at delivery DC and PP ($r=0.51, p < 0.001$). Mean EPDS score at the PP visit was significantly higher for patients who had an elevated EPDS at delivery DC compared to those with a score < 9 (7.9 vs. 2.7, $p < 0.001$). Of patients who had an EPDS ≥ 9 at delivery DC, 42.0% (92/219) continued to score ≥ 9 PP, representing the PPV. Most patients who scored < 9 at delivery DC continued to score low PP (1270/1384, NPV 91.8%). A small proportion of patients who had a low score at delivery DC scored ≥ 9 at the PP visit (114/1384, 8.2%). Patients who had a low-risk EPDS at DC and then scored high PP were more likely to be privately insured compared to those who continued to have a low risk score (OR=1.38, $p=0.001$). There was no difference by age, race, or mode of delivery.

Conclusion Immediate PP EPDS screening is feasible and captures patients at risk of PPD. Interventions should target patients with an elevated EPDS score at delivery DC, as many patients will continue to score high at their PPV. Further investigation is needed to determine which patients will develop symptoms of PPD despite a low-risk score at delivery DC.

RESIDENT RESEARCH PUBLICATIONS 2022-23

PGY-1

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Jung WF, Pollie MP, Ho KK, Mauer EA, Newman LA, Otterburn DM. Does the Type of Reconstruction Matter? A Propensity Score Matched Analysis of Immediate Post-mastectomy Implant and Flap Reconstruction. *Plast Reconstr Surg*. 2023 Feb 27:e010319. doi: 10.1097/PRS.00000000000010319. Epub ahead of print. PMID: 36827476.

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PGY-2

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Umeukeje EM, Koonce TY, Kusnoor SV, Ulasi II, Kostelanetz S, Williams AM, Blasingame MN, Epelbaum MI, Giuse DA, Apple AN, Kaur K, González Peña T, Barry D, Eisenstein LG, Nutt CT, Giuse NB. Systematic review of international studies evaluating MDRD and CKD-EPI estimated glomerular filtration rate (eGFR) equations in Black adults. *PLoS One*. 2022 Oct 18;17(10):e0276252. doi: 10.1371/journal.pone.0276252. PMID: 36256652; PMCID: PMC9578594.

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PGY-3

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PGY-4

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