METHODS: Insurance claims data for IHR occurring within 365 days of birth, in preterm infants (gestational age fewer than 37 weeks at birth), born between 2007 and 2018, were evaluated using MarketScan. Patients were stratified, based on timing of IHR, to those occurring during (early) and after (late) neonatal admission. Hernia recurrences within 1 year after IHR were identified. Crude and covariate-standardized recurrence incidence rate ratios were estimated using Poisson regression. Demographic and clinical predictors of recurrence were estimated using a multivariable Cox model. Median procedure costs were compared for early vs late IHRs using Hodges-Lehmann estimators.

RESULTS: We identified 3,662 preterm infants with IHR within 365 days of birth; 1,489 (40.7%) occurred early. Infants with early IHR were more premature (gestational age [GA] at birth ≤32 weeks: 66.2% vs 35.5%; p < 0.01), with birth weight <1,500 g (72.3% vs 39.0%; p < 0.01) compared with late IHR. Hernia recurrence rate was higher and total procedure costs lower in early IHR. Early repair (hazard ratio 1.98; 95% CI, 1.67 to 2.35), GA ≤32 weeks (hazard ratio 1.35; 95% CI, 1.14 to 1.59) and congenital anomalies (hazard ratio 1.31; 95% CI, 1.11 to 1.56) were predictors of hernia recurrence.

CONCLUSION: Using national insurance claims data, IHR performed during initial neonatal admission was associated with higher recurrence rate and lower cost compared with late repairs in premature infants.

Cost-Effectiveness of Nonoperative Management vs Appendectomy for Acute Appendicitis in a Pediatric Population
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INTRODUCTION: Nonoperative management (NOM) of acute appendicitis (AP) in the pediatric population is highly debated with uncertain cost-effectiveness. We performed a decision tree cost-effectiveness analysis of NOM vs early laparoscopic appendectomy (LA) for acute appendicitis in children.

METHODS: We created a decision tree model for a simulated cohort of the estimated annual incidence of uncomplicated pediatric AP in the US (49,000 patients) comparing NOM and LA. We included postoperative complications, recurrent appendicitis, and antibiotic-related complications. We used the payer perspective with a 1-year time horizon. Model uncertainty was analyzed using probabilistic sensitivity analysis. Event probabilities, health-state utilities, and costs were obtained from literature review, Healthcare Cost and Utilization Project, and Medicare fee schedules.

RESULTS: In the base-case analysis, NOM costs $9,823/patient, and LA costs $8,747/patient on average at 1-year; however, quality-adjusted life-year (QALY) differences slightly favored NOM compared with LA with 0.994 vs 0.986 QALYs/patient, respectively. For the entire cohort, the additional cost of NOM over LA was $52,745,070, but resulted in 370 additional QALYs, for a cost-effectiveness ratio of $142,417/QALY. Probabilistic sensitivity analysis showed NOM was 49% likely to be cost-effective at a willingness to pay threshold of $50,000/QALY and 64% likely at a willingness to pay threshold of $100,000/QALY (Fig.).

CONCLUSION: Our model demonstrated that NOM of uncomplicated AP in the pediatric population might be cost-effective at 1-year, depending on willingness to pay. Long-term follow-up data are needed in the pediatric population to assess the cost-effectiveness of NOM over longer time horizons, when recurrence rates might be higher.

Establishing a Novel 3-Dimensional Printing Model to Study Pediatric Solid Tumors
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INTRODUCTION: It has been shown that three-dimensional (3D) tumor modeling better replicates the human condition than traditional 2-dimensional monolayer culture methods, and has been used for adult cancer investigations. The application of this technology in pediatrics is limited. We aimed to create a 3D printing model for pediatric tumors that could be used for experimentation and would more accurately recapitulate the clinical condition.

METHODS: A Cellink BIOX printer was used to print layers of a sodium alginate and gelatin mixture with a suspension of tumor cells (5 × 10^6) placed in between layers. Calcium chloride was added for crosslinking. Printed tumors were stained with calcine AM and
SYTOX Orange to assess viability. Immunohistochemistry corroborated tumor morphology. Viability of printed tumors or monolayer cultures was compared after application of therapeutics or hypoxia.

RESULTS: Tumors successfully grew in the bioprint as 3D structures (Fig. 1A). After increasing doses of cisplatin, the printed tumors demonstrated less cell death than cells in monolayer culture (Fig. 1B). In hypoxia, viability of monolayer cells decreased by 50%, while 3D printed tumors were unaffected (Fig. 1C). When implanted into mice, 3D printed tumors grew (Fig. 1D) with morphology recapitulating original tumors.

CONCLUSION: We successfully established a 3D bioprinted model of pediatric solid tumors that demonstrated drug resistance and growth in hypoxia, properties seen in the human condition but diminished or absent in monolayer cultures. These models might provide infinite avenues for future studies by removing barriers associated with contrived culture conditions, mouse models, and patient-derived xenografts.

Figure 1 A). Representative images of sectioned 3D printed tumor with fluorescent imaging (left) and IHC (right). B) Increasing doses of cisplatin had a greater effect on the viability of SK-N-AS neuroblastoma in 2D than 3D culture. C) The same neuroblastoma type demonstrated resistance with little loss of viability in hypoxic conditions. D) A bioprinted patient-derived xenograft tumor was able to grow in a mouse.

Farnesoid X Receptor-Mediated Changes to Macrophage Cytokine Expression
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INTRODUCTION: Dysregulated activation of the inflammatory cascade is the hallmark of many intestinal pathologies. The Farnesoid X receptor (FXR), a nuclear bile acid receptor, has recently been shown to play a role in the inflammatory pathway. Macrophages are key drivers of intestinal inflammation that express FXR. We hypothesize that FXR activation will drive inflammatory cytokine expression.

METHODS: Bone marrow from both wild-type (WT) (C57/B6) and FXR-KO mice was harvested from femurs and cultured in RPMI with m-CSF supplementation. On day 7, macrophages were polarized to either M1 (pro-inflammatory) or M2 (anti-inflammatory) phenotypes and then treated with either the FXR agonist GW4064 or the FXR antagonist Z-guggulsterone (ZG). FXR-KO macrophages were polarized and compared with WT. TNF-α and IL1-β (for M1) and IL-10 (for M2) levels were measured via quantitative polymerase chain reaction.

RESULTS: M1-polarized macrophages treated with GW4064 showed a slight increase in IL1-β expression while treatment with ZG led to a 3-fold increase in IL1-β. TNF-α expression did not change after GW4064 but increased 50% with ZG treatment. In M2-polarized macrophages, IL-10 expression increased 300-fold with GW treatment, while ZG treatment led to a more modest increase. IL1-β levels were significantly lower in FXR-KO M1 macrophages compared with WT.

CONCLUSION: These data suggest that FXR activation is important in modulating inflammation, although not as we hypothesized. Direct pharmacologic FXR activation does not increase pro-inflammatory cytokines but does increase anti-inflammatory cytokines. However, the complete absence of FXR mitigates pro-inflammatory cytokine expression. Further investigation is needed to understand the role FXR plays in macrophage-driven inflammation.

Generation of Porcine Ileum Through Spring-Mediated Mechanical Distraction
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INTRODUCTION: Short bowel syndrome is a devastating gastrointestinal disorder in which nutritional deficiencies occur due to inadequate absorption. Current treatment options have significant morbidities, therefore, we previously proposed spring-mediated distraction enterogenesis as a method to lengthen bowel with success seen in porcine jejunum. Our current hypothesis is that spring-mediated distraction enterogenesis can be demonstrated in porcine ileum with preservation of structure and function.

METHODS: Laparotomy was performed on juvenile female mini-Yucatan pigs where a gelatin-encapsulated compressed nitinol spring was inserted into the lumen of the ileum and plicated proximally and distally. Control segments were marked with sutures. Postoperatively, pigs were placed on liquid diet and euthanized on postoperative day (POD) 7. Spring and control segments were measured. Ileum segments were formalin-fixed, paraffin-embedded, and stained by immunohistochemistry against enteroendocrine protein chromogranin-A. The density of chromogranin-A positive cells was calculated.

RESULTS: Eight pigs received ileal springs. Spring constants ranged from 4.6 to 6.5 N/m. All pigs survived to POD 7 with no adverse effects. On average, pigs gained mean ± SD 79.3 ± 59.2 g/d. Spring segments significantly lengthened mean ± SD 2.0 ± 1.5 cm with a relative change of mean ± SD 227% ± 48% increase (p < 0.001). The mean ± SD density of chromogranin-A cells in control