Using Real World Evidence to Guide Clinical Outcomes and Reduce Costs of Care

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Background

- Pharmacy and Therapeutics committees can be challenged to analyze and act on care variation in inpatient prescribing practices due to:
  - Limited insights from traditional electronic data warehouses
  - Insufficient anecdotal insights from clinical practice
  - Burdensome manual chart review
- Stanford Health Care experienced marked increases in high-cost perineural liposomal bupivacaine use from 2015 to 2021 (Figure 1) and in rifaximin addition to lactulose monotherapy initial therapy for hepatic encephalopathy for first episode of hepatic encephalopathy from 2018 to 2021 (Figure 2)
- We hypothesized that real world evidence from the Stanford EHR (electronic health record) would:
  - Confirm a recent meta-analysis showing high-cost perineural liposomal bupivacaine for procedural analgesia did not lead to improved outcomes[1]
  - Assess clinical value of dual rifaximin/lactulose versus lactulose monotherapy for first episode of hepatic encephalopathy in hospitalized patients

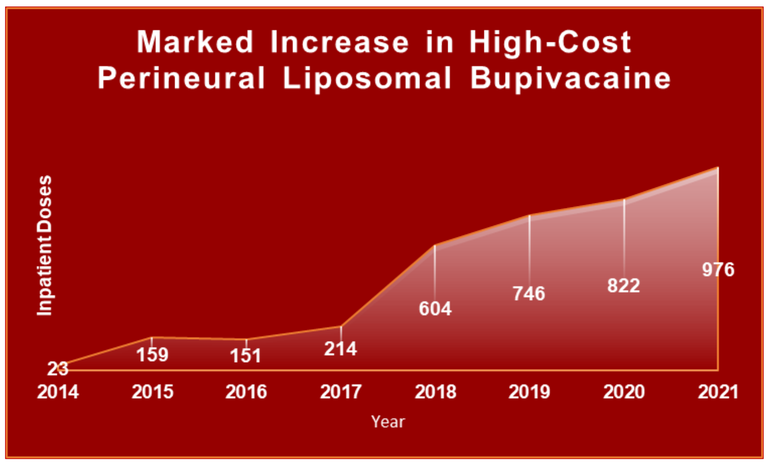

Figure 1. Perineural liposomal bupivacaine use by year

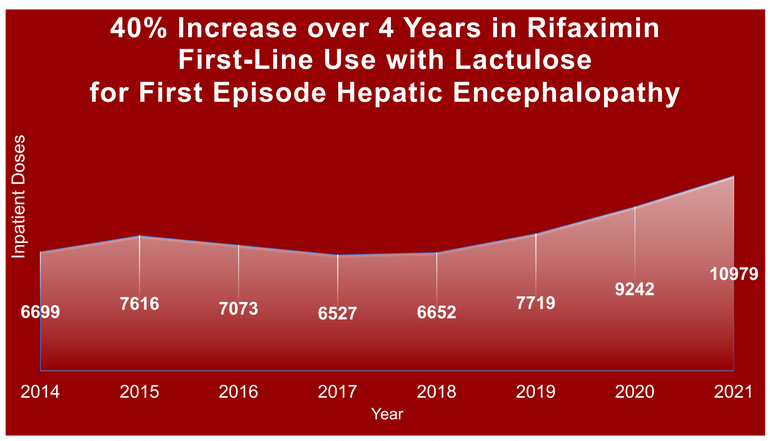

Figure 2. Perineural liposomal bupivacaine use by year

Methods

- Primary Outcomes:
  - Liposomal Bupivacaine: Cohort comparisons for subsequent opiate use, subsequent local anesthetic use, length of stay
  - Rifaximin: Cohort comparisons for hospital length of stay, mortality over 6 years
  - Primary outcomes: Cohort comparisons for hospital length of stay, mortality over 6 years
- Secondary Outcomes:
  - Projected drug cost savings from retiring liposomal bupivacaine from the formulary
  - Projected drug cost savings from restricting rifaximin initiation to 48 hours after lactulose

Methods

- Data Collection: Data were collected from the electronic medical record on patients undergoing procedures 2015-2022 using Stanford Green Button Informatics Consult
- Statistical analysis: Cohorts were built and analyzed by Atropos Health, a real-world evidence generation company originating at Stanford using high dimensional propensity score (HdPS) matching to control for observational study confounding

Results: Liposomal Bupivacaine Clinical Outcomes

	Hydromorphone	Liposomal Bupivacaine	SMD
N	15876	1358	
Female (%)	8811 (55.49)	922 (67.89)	< 0.01
Mean age (sd)	56.5 (17.5)	62.6 (13.5)	0.48
Race and ethnicity (%)			
White	9300 (58.57)	949 (69.88)	< 0.01
Other	3937 (24.80)	196 (14.43)	< 0.01
Hispanic	2686 (16.92)	146 (10.75)	<0.01
Asian	1900 (11.97)	164 (12.08)	0.91
Black	739 (4.65)	49 (3.61)	0.08
Charlson comorbidity index (sd)	4.5 (4.1)	3.8 (2.9)	0.11
Orthopedic procedure (%)	12784 (80.52)	817 (60.16)	< 0.01

Table 1. Patient and intervention characteristics

	Hydro-Morphone	Liposomal Bupivacaine	OR or SMD (CI)
Opiates in next 96 hrs (%)	365 (32.44)	615 (54.67)	2.51 (2.12, 2.98)
Local anesthetics in next 96 hrs (%)	325 (28.90)	380 (33.78)	1.26 (1.05, 1.48)
Length of inpatient stay (sd)	2.1 (1.5)	2.4 (1.2)	0.20 (0.08, 0.32)
Mortality at 30 days (%)	8 (0.71)	1 (0.89)	0.12 (0.00, 1.93)

Table 2. Primary outcomes by HdPS matching

Results: Rifaximin + Lactulose Clinical Outcomes

	Lactulose	Lactulose + Rifaximin	SMD
N	1833	569	
Female (%)	738 (40.3)	243 (42.7)	0.05
Mean age (sd)	58.4 (12.8)	58.0 (11.2)	0.03
Race and ethnicity (%)			
White	862 (47.1)	294 (51.7)	0.09
Other	650 (35.5)	223 (39.2)	0.08
Hispanic	546 (29.8)	204 (35.9)	0.22
Asian	255 (13.9)	38 (6.7)	0.06
Black	66 (3.6)	14 (2.5)	0.13
Charlson comorbidity index (sd)	8.8 (3.8)	7.9 (3.1)	0.26

Table 1. Patient Characteristics

	Lactulose	Lactulose + Rifaximin	SMD or HR (CI)
Length of inpatient stay in Yr 1 (sd)	14.0 (26.8)	16.8 (24.3)	0.11 (0.00, 0.28)
Death in next 6 years (%)	132 (26.83)	159 (32.12)	1.24 (0.98, 1.56)

Table 2. Primary outcomes

Results: Cost-Effectiveness Outcomes

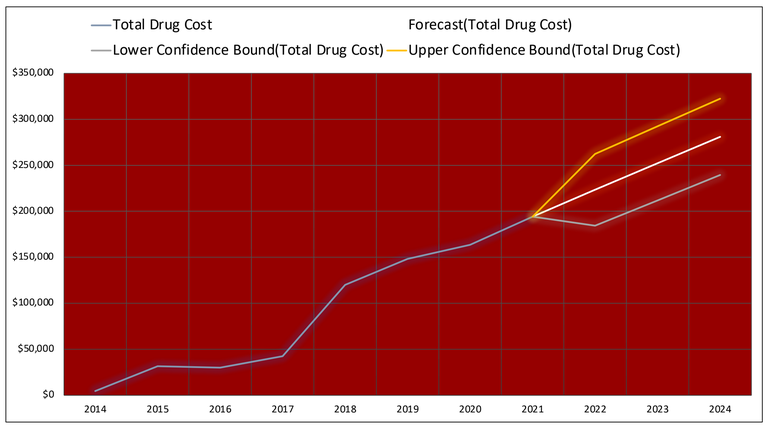

Figure 3. **$193,883** projected annualized cost savings from retiring liposomal bupivacaine from Stanford drug formulary

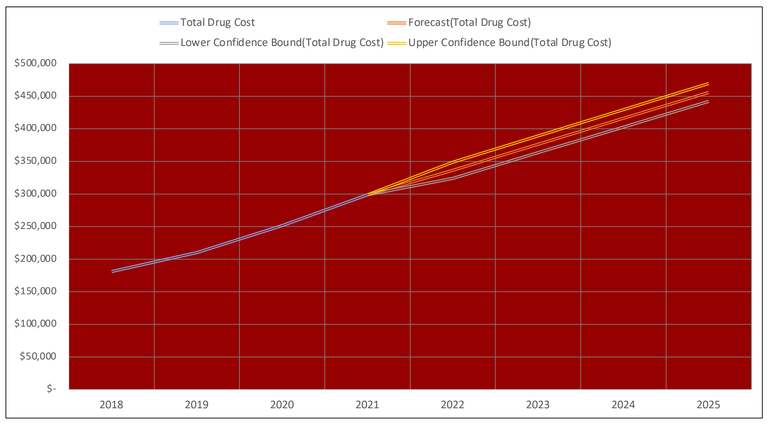

Figure 4. **$224,136** projected annualized cost savings from restricting 75% of first episode hepatic encephalopathy treatment with rifaximin

Discussion

- Stanford Health Care real world evidence findings of non-superior clinical outcomes with high-cost liposomal bupivacaine consistent with recent meta-analysis (Table 2, Figure 2)
- Liposomal bupivacaine was retired from the Stanford drug formulary after presentation by Pharmacy and Therapeutics Committee to stakeholders including real world evidence findings for an annualized cost savings in Year 1 at **$193,883** (Figure 3)
- Stanford Health Care is evaluating restriction of inpatient rifaximin to after 48 hours lactulose monotherapy for first episode of hepatic encephalopathy for a projected annualized cost savings in Year 1 at **$224,136** (Figure 4)
- **>$400,000** realized and potential P&T savings achieved without reliance on manual chart review

Conclusion

- Real world evidence generation from health system electronic records such as the Stanford Green Button Informatics consult provides acceleration of valuable insights on health outcomes when comparing high and low-cost drugs
- Pharmacy and Therapeutics committees can increase cost-effective care through use of rapid and repeatable real world evidence comparative effectiveness studies

References

1. Dinges, H.-C, Wiesmann, T, et al (2021). The analgesic efficacy of liposomal bupivacaine compared with bupivacaine hydrochloride for the Prevention of Postoperative Pain: A systematic review and meta-analysis with trial sequential analysis. *Regional Anesthesia & Pain Medicine*, *46*(6), 490–498. https://doi.org/10.1136/rapm-2020-102427