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Original Research

Total Hip Arthroplasty Complications in Patients With Sickle Cell Disease: A Comparison Study

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ABSTRACT

Background: Total hip arthroplasty (THA) is one of the most common orthopaedic procedures performed in the United States, but there are rare complications which can be devastating. Sickle cell disease (SCD) can lead to avascular necrosis of the femoral head, often necessitating THA. This article seeks to better characterize the complication risks in patients undergoing THA with SCD when compared to osteoarthritis (OA) using a large database from the National Inpatient Sample.

Methods: National Inpatient Sample data from 2006 through the third quarter of 2015 were analyzed using International Classification of Diseases, Ninth Revision codes. A weighted frequency of 4,350,961 THAs were recorded for OA and 4279 for SCD. These were compared using a Rao-Scott chi-squared test, and the prespecified complications were given sampling weights to approximate national estimates.

Results: The following complications were found to occur at a significantly increased frequency in patients with OA with SCD vs OA only: wound infection (0.69% vs 0.36%), dislocation (1.68% vs 0.80%), and urinary complications (3.61% vs 2.35%). SCD, when evaluated independent of avascular necrosis, was reported with higher frequency wound infection (0.86% vs 0.36%), and overall complications (7.25% vs 5.06%). Additionally, multiple comorbidities were significantly more prevalent in the SCD population compared to OA patients.

Conclusions: This study illustrates that patients with SCD have increased complication rates when compared to OA patients. This information benefits orthopaedic surgeons in preoperative and postoperative planning and counseling patients for realistic expectations. Furthermore, this study provides data that could benefit decision-making on bundled reimbursement for this specific patient population.

Introduction

Total hip arthroplasty (THA) is one of the most common orthopaedic procedures performed in the United States annually, with an estimated 400,000 primary total hips to occur in 2022 [1]. The most common indication for the operation is osteoarthritis (OA), followed by osteonecrosis, and rheumatoid arthritis [2]. Additionally, the demand for these procedures is expected to increase substantially due to an increasing elderly population and increased public awareness of the improved quality of life resulting from the procedure [3,4]. With continued advancement and increased utilization of THA in the United States, it is imperative that orthopaedic surgeons understand and identify patient risk factors that may lead to a complicated postoperative course. Several risk factors, which are well documented in the literature, include obesity, chronic kidney disease, rheumatologic disease, and diabetes mellitus [5-7]. One critical risk factor, which is not as highly discussed in the literature, is sickle cell disease (SCD). In fact, one recent meta-analysis recognized SCD as the leading risk factor for a higher revision rate in patients undergoing THA for avascular necrosis (AVN) of the femoral head [8].

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SCD is a common autosomal recessive disorder with a prevalence that varies from 5%-25% in different parts of the world. The disease is caused by a point mutation in the beta globin chain of hemoglobin 1, and the association of 2 normal alpha globin subunits with 2 mutant beta globin subunits forms hemoglobin S. This hemoglobinopathy affects red blood cell shape under low oxygen tension making them susceptible to sickling, which impedes blood supply to human tissues [9]. As a result, these patients deal with a multitude of medical problems and suffer higher mortality rates [10].

A common problem SCD patients face is AVN of the femoral head. This occurs from sickled red blood cells creating vascular congestion, venostasis, and thrombosis in the microvasculature of the bone. The resulting ischemia compounded by an increase in pressure secondary to medullary hyperplasia causes bone infarction and necrosis [11]. The incidence of AVN has been reported to occur in up to 50% of patients based on specific genotype [11-14]. The AVN often develops at a young age, and it has been noted that approximately 25%-30% of SCD patients will undergo THA before the age of 50 [15]. The range of complications in the SCD population resulting from THA varies from 11.5% to 67% [16-19]. These data highlight the increased complexity of the SCD population when undergoing THA, and this study aims to provide key information to aid orthopaedic surgeons in decision-making while managing these patients.

There are limited data directly comparing patients with SCD vs patients with OA undergoing THA. One way to evaluate the relationship between the 2 populations is to use a large national database spanning several years to develop a large enough sample size to create statistical significance. The National Inpatient Sample (NIS) is the largest publicly available all-payer database, which has shown to be effective in analyzing risk factors, comorbidities, and outcomes associated with total joint arthroplasty [20,21]. The purpose of this study is to use the NIS database to determine if there is a difference in complication rates or comorbidities between patients with SCD undergoing THA and patients with OA undergoing THA. Specifically, the complications under investigation include wound seroma, wound infection, cardiac complications, dislocation, urinary complications, and pulmonary complications. The comorbidities being evaluated span a wide range of medical diagnoses including heart failure, renal disease, liver disease, hypertension, and others noted below.

Materials and methods

The NIS is the largest all-payer inpatient care database in the United States that is made available to the public. Unweighted, it contains data from more than 7 million hospital stays annually. Weighted, it estimates more than 35 million hospitalizations nationally. The advantage derived from a database of this magnitude is the ability to analyze specific patient populations, complications, and rare conditions. Due to the wide breadth of coverage the database contains, it gives us the power to make both regional and national estimates regarding specific areas of interest. The data were developed through a Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality. The data were developed for the Healthcare Cost and Utilization Project to help make evidence-based decisions at the national, community, and state level [22].

The NIS data from 2006 through the third quarter of 2015 were selected for analysis in this study. We omitted fourth-quarter data from 2015 because of the transition from International Classification of Diseases, Ninth Revision (ICD-9) to ICD, 10th Revision. In this study, we used ICD-9 codes and Clinical Classifications Software (CCS) codes to identify and include our groups of interest and specific diagnoses. We did not exclude any patients who were identified from the ICD-9 and CCS codes. CCS codes were developed by the Healthcare Cost and Utilization Project to provide a way of classifying diagnoses and procedures into a limited number of categories. This was accomplished by aggregating individual ICD-9 Clinical Modification and Current Procedural Terminology codes into broad diagnosis and procedure groups to facilitate statistical analysis and reporting. The following ICD-9 codes were used: SCD (282.60-282.69, 282.41-282.49, and 282.5), OA (715.16, 715.36, and 715.96), osteonecrosis (733.4), wound seroma or hematoma (998.1), wound infection (996.6, 998.5, and 998.53), dislocation (835 and 996.42), cardiac complications (997.1), urinary complications (584.5-584.9 and 997.5), deep vein thrombosis (453.40, 453.41, and 453.42), and pulmonary complications (518.81-518.85 and 997.3). The CCS code used for the primary THA procedure was 153. These data were analyzed year by year within the variables of interest. Additionally, we used the Elixhauser Comorbidity Software, which is a tool that identifies 29 common medical comorbidities within the NIS database for further comparison and identification of pertinent differences.

For each patient group, descriptive statistics on selected complications relating to THA (including a derived variable indicating presence of 1 or more of the listed complications) are summarized in the tables provided. *P* values comparing complication rate by patient group were computed using Rao-Scott chi-squared tests accounting for the sampling design. Additionally, marginal comparisons by AVN and SCD alone are reported below. The "AVN" group may include SCD and non-SCD patients, and the "SCD group" may include AVN and non-AVN patients. To assess whether presence of either AVN or SCD, regardless of the other, was associated with increased odds of complications, a series of logistic models were fitted using a derived variable set to "yes" in the presence of either AVN or SCD or both, and "no" for "OA only" patients. For the prespecified complications, sampling weights were used to produce national estimates. Statistical significance was set at a P value of $< .05$.

Results

Between the years 2006 and 2015, the NIS database accounted for a weighted frequency of 4,350,961 THA procedures for OA and 4279 procedures for SCD (Table 1). Based on the Rao-Scott chi-squared tests, the following complications were found to occur at a

Table 1
THA cases performed for OA, AVN, and SCD.

Sickle cell disease	Freq.	Weighted freq.	SE of weighted freq.	Percent	SE of percent
No	878,546	4,346,682	60,870	99.9017	0.005
Yes	870	4279	226	0.0983	0.005
Total	879,416	4,350,961	60,927	100.0000	

AVN	Freq.	Weighted freq.	SE of weighted freq.	Percent	SE of percent
No	829,151	4,102,566	58,745	94.291	0.0050
Yes	50,265	248,395	3252	5.709	0.0050
Total	879,416	4,350,961	60,927	100.000	

Patient group	Freq.	Weighted freq.	SE of weighted freq.	Percent	SE of percent
OA only	828,602	4,099,886	58,698	94.2294	0.0615
OA + AVN only	49,944	246,796	3231	5.6722	0.0610
OA + SCD only	549	2680	177	0.0616	0.0039
OA + AVN + SCD	321	1599	136	0.0367	0.0031
Total	879,416	4,350,961	60,927	100.0000	

SE, standard error.

Table 2
Complication rates following THA for SCD, AVN, and OA.

Complication	OA only		OA + AVN		OA + SCD		OA + AVN + SCD		*P* value
	N[a]	Percent	N	Percent	N	Percent	N	Percent	
Wound hematoma	31,358	0.765	2336	0.946	15	0.541	36	2.237	**.0012**
Wound infection	14,944	0.364	598	0.242	18	0.686	18	1.148	**.0002**
Dislocation	32,624	0.796	1093	0.443	45	1.676	0	0.000	[b]
Cardiac issues	26,841	0.655	1574	0.638	13	0.482	0	0.000	[b]
Urinary complications	96,179	2.346	6765	2.741	97	3.605	81	5.061	**<.0001**
Pulmonary complications	21,914	0.535	1743	0.706	9	0.346	0	0.000	[b]
Any of the above	207,020	5.049	13,052	5.289	175	6.528	135	8.446	**.0423**

Bold values indicate statistical significance ($P < .05$).
[a] Sample sizes based on weighted frequencies.
[b] Rao-Scott tests could not be conducted due to small cell counts.

statistically significant increased frequency in patients with OA + SCD vs OA only (Table 2): wound infection (0.69% vs 0.36%; $P < .0002$), dislocation (1.68% vs 0.80%, Table 2), and urinary complications (3.61% vs 2.35%; $P < .0001$).

Independently of SCD, AVN was reported with a higher frequency of wound hematoma (0.96% vs 0.76%; $P = .0006$), urinary complications (2.74% vs 2.35%; $P < .0001$), and pulmonary complications (0.71% vs 0.54%; $P = .0004$) (Table 3). In contrast, a statistically significant decrease was observed in the rates of wound infection (0.24% vs 0.36%; $P = .0002$) and dislocation (0.44% vs 0.80%; $P < .0001$) in the AVN group compared to those who underwent THA for OA.

SCD, when independent of AVN, was reported with higher frequency wound infection (0.86% vs 0.36%; $P = .0204$), and overall complications (7.25% vs 5.06%; $P = .0293$) (Table 4). Furthermore, when analyzing patients with AVN and/or SCD together compared to OA only, these patients were associated with significantly higher odds of wound hematoma, urinary complications, and pulmonary complications, and lower odds of infection or dislocation. AVN and/or SCD were associated with marginally higher odds of any complication post THA (Table 5).

The prevalence of the following comorbidities was significantly higher in patients with SCD when compared with OA patients (Table 6): congestive heart failure, pulmonary circulation disease, paralysis, chronic pulmonary disease, renal failure, liver disease, acquired immune deficiency syndrome, coagulopathy, weight loss, fluid and electrolyte disorders, and drug abuse. The following comorbidities had a significantly higher prevalence in patients with OA when compared with SCD patients (Table 6): hypertension, diabetes without chronic complications, hypothyroidism, peptic ulcer disease, obesity, and depression.

Discussion

In this study, the incidence of postoperative complications and preoperative comorbidities were compared between patients with ICD-9 diagnoses of OA, AVN with or without associated SCD, and SCD alone who underwent THA. Our results demonstrated statistically significant increased odds for postoperative wound infection, urinary complications, and overall complications in patients with SCD. If patients were associated with ICD-9 codes for AVN and SCD, their odds of the above complications were increased, but also associated with wound hematoma. Additionally, we found a higher prevalence of various comorbidities including hypertension, hypothyroidism, diabetes, peptic ulcer disease, and depression. To our knowledge, this is the first study to objectively show these suspected differences in surgical outcomes and preoperative comorbidities in a comparative fashion between OA patients and SCD patients using the nationwide NIS database.

SCD has previously been shown in the literature to be a risk factor for perioperative complications [8,10,23-27]. These complications can arise intraoperatively, immediately postoperatively, or in the chronic postoperative period. A meta-analysis by Kenanidis et al. showed an overall complication rate of 14.3% with the most common being transfusion reactions, sickle cell crises, and acute chest syndrome [28]. One suggested cause of perioperative complications in this patient population is the surgically induced intracellular dehydration increasing hemoglobin concentration and sickling [23]. This can be especially precipitated by recent alcohol binges, ascents to high altitude, and prolonged airplane flights. Standard maintenance fluids should be applied to these patients to help avoid this situation and maintain appropriate blood volume status.

A strength of our study is the ability of our data from the NIS, the largest all-payer database in the United States, to directly compare SCD and OA patient complication rates following THA, as well as their preoperative medical comorbidities. Many studies in the literature have focused on surgical outcomes and complications for SCD patients, but these are not comparative in nature [16-19,29-31]. Additionally, many of these studies have a limited number of patients (less than 50), which hinders their ability to be generalized. Our study includes 4279 patients from the NIS database with

Table 3
Postoperative complications following THA in patients with or without SCD.

Complication	No AVN		AVN		*P* value
	N	Percent	N	Percent	
Wound hematoma	31,372	0.765	2371	0.955	**.0006**
Wound infection	14,962	0.365	616	0.248	**.0022**
Dislocation	32,669	0.796	1093	0.440	**.0000**
Cardiac issues	26,854	0.655	1574	0.634	.6759
Urinary complications	96,276	2.347	6846	2.756	**<.0001**
Pulmonary complications	21,924	0.534	1743	0.702	**.0004**
Any of the above	207,195	5.050	13,187	5.309	.0797

Bold values indicate statistical significance ($P < .05$).

Table 4
Postoperative complications following THA in patients with or without SCD.

Complication	No SCD		SCD		*P* value
	N	Percent	N	Percent	
Wound hematoma	33,694	0.775	50	1.175	.3309
Wound infection	15,541	0.358	37	0.859	**.0204**
Dislocation	33,717	0.776	45	1.050	.5060
Cardiac issues	28,415	0.654	13	0.302	.2792
Urinary complications	102,945	2.368	178	4.149	**.0137**
Pulmonary complications	23,657	0.544	9	0.217	.1786
Any of the above	220,072	5.063	310	7.245	**.0293**

Bold values indicate statistical significance ($P < .05$).

Table 5
Odds ratios from series of logistic models showing effects of AVN and/or SCD on postoperative THA complications vs patients with only OA.

Complication	Comparison	OR	95% lower confidence limit	95% upper confidence limit	*P* value
Wound hematoma	**AVN ± SCD vs OA only**	**1.245**	**1.095**	**1.416**	**.0008**
Wound infection	*AVN ± SCD vs OA only*	*0.693*	*0.543*	*0.884*	*.0031*
Dislocation	*AVN ± SCD vs OA only*	*0.567*	*0.453*	*0.711*	*<.0001*
Cardiac issues	AVN ± SCD vs OA only	0.966	0.829	1.125	.6535
Urinary complications	**AVN ± SCD vs OA only**	**1.184**	**1.093**	**1.282**	**<.0001**
Pulmonary complications	**AVN ± SCD vs OA only**	**1.309**	**1.124**	**1.523**	**.0005**
Any of the above	***AVN ± SCD vs OA only***	***1.057***	***0.997***	***1.121***	***.0643***

OR, odds ratio.
Italic = lower odds of particular complication in AVN ± SCD group. Bold = higher odds of particular complication in AVN ± SCD group.

SCD who underwent THA (Table 1). This tremendous sample size increases the power of our results, and we believe it will give orthopaedic surgeons confidence when delineating patient expectations. Another strength of our study is the different statistical methods we employed to isolate the true effect of SCD on THA complications, mainly by controlling for OA as seen in Table 2 and by controlling for AVN by itself in Tables 3 and 4.

Classically, surgical approaches have found to impact outcomes for THA specifically in relation to dislocation. However, this has recently been brought into contention by a recent large-scale review of literature revealing no association between approach and dislocation rates [32]. Due to the absence of documented approach of this database study, we were unable to analyze approaches. However, overall, we found a significant increase in dislocation with patients with SCD. This is critical to highlight because postoperative dislocation following THA has a significant deleterious effect on patient outcomes and, when required, revision procedures are extremely expensive to the healthcare system [33,34].

Recent decades have provided significant advances in the understanding of osteonecrosis, which has led to improvements in treatments specifically for the pathology of AVN. There has been a widespread increase in implementation of second-generation and third-generation implant designs, with authors demonstrating a positive influence on the survivability of total hip implants in patients with AVN [35]. For instance, Steinberg et al. recently looked at THA performed in patients with AVN (203 hips) and OA (300 hips) and found a failure rate of 10% for AVN vs 4% for OA at a mean follow-up of 14 years [36]. However, when the study was limited to the newer generation uncemented acetabular cup, they found only one revision in 111 hips with AVN and no failure in 124 hips with OA. Additionally, Johannson et al. conducted a systematic review showing a greatly diminished revision rate (3% vs 17%) in patients who underwent THA after 1990 (second-generation cementless components) compared to prior to 1990 [8]. This information is promising for the SCD population as the vast majority of the population undergoes THA for AVN. However, both previously

Table 6
Comorbidities associated with SCD and OA patients.

Comorbidities	Overall (N = 4,355,240)	SCD (N = 4279)	OA (N = 4,350,961)	*P* value
Congestive heart failure	118,190 (2.7%)	234 (4.4%)	117,957 (2.7%)	.0103
Valvular disease	176,167 (4.0%)	187 (3.5%)	175,980 (4.0%)	.5206
Pulmonary circulation disease	38,441 (0.9%)	223 (4.2%)	38,218 (0.9%)	<.0001
Peripheral vascular disease	104,058 (2.4%)	78 (1.5%)	103,980 (2.4%)	.0922
Hypertension	2,595,145 (59.6%)	1491 (28.2%)	2,593,654 (59.6%)	<.0001
Paralysis	15,333 (0.4%)	84 (1.6%)	15,249 (0.4%)	<.0001
Other neurological disorders	167,190 (3.8%)	254 (4.8%)	166,937 (3.8%)	.2056
Chronic pulmonary disease	604,407 (13.9%)	975 (18.4%)	603,433 (13.9%)	.0040
Diabetes without chronic complications	571,138 (13.1%)	270 (5.1%)	570,868 (13.1%)	<.0001
Diabetes with chronic complications	51,879 (1.2%)	36 (0.7%)	51,843 (1.2%)	.1791
Hypothyroidism	593,684 (13.6%)	271 (5.1%)	593,413 (13.6%)	<.0001
Renal failure	178,816 (4.1%)	334 (6.3%)	178,482 (4.1%)	.0087
Liver disease	42,464 (1.0%)	149 (2.8%)	42,314 (1.0%)	<.0001
Peptic ulcer disease × bleeding	699 (0.0%)	0 (0.0%)	699 (0.0%)	<.0001
Acquired immune deficiency syndrome	3932 (0.1%)	31 (0.6%)	3902 (0.1%)	<.0001
Lymphoma	14,188 (0.3%)	30 (0.6%)	14,159 (0.3%)	.4361
Metastatic cancer	6829 (0.2%)	6 (0.1%)	6823 (0.2%)	.6834
Solid tumor without metastasis	19,794 (0.5%)	16 (0.3%)	19,778 (0.5%)	.4468
Rheumatoid arthritis/collagen vas	163,229 (3.7%)	205 (3.9%)	163,024 (3.7%)	.8594
Coagulopathy	96,506 (2.2%)	203 (3.8%)	96,303 (2.2%)	.0080
Obesity	668,995 (15.4%)	300 (5.7%)	668,695 (15.4%)	<.0001
Weight loss	23,487 (0.5%)	106 (2.0%)	23,381 (0.5%)	<.0001
Fluid and electrolyte disorders	393,078 (9.0%)	730 (13.8%)	392,349 (9.0%)	<.0001
Chronic blood loss anemia	76,033 (1.7%)	119 (2.2%)	75,914 (1.7%)	.3054
Deficiency anemia	588,662 (13.5%)	769 (14.5%)	587,893 (13.5%)	.4821
Alcohol abuse	63,841 (1.5%)	74 (1.4%)	63,767 (1.5%)	.9076
Drug abuse	30,069 (0.7%)	157 (3.0%)	29,913 (0.7%)	<.0001
Psychoses	82,256 (1.9%)	127 (2.4%)	82,129 (1.9%)	.3982
Depression	493,538 (11.3%)	403 (7.6%)	493,135 (11.3%)	.0044

mentioned studies did not focus on AVN cases in the sickle cell population, which means the unique complexities of the sickle cell diagnoses could lead to less successful operative outcomes.

In our evaluation of patients with SCD, the following comorbidities were found to be more prevalent compared to OA patients: congestive heart failure, pulmonary circulation disease, paralysis, chronic pulmonary disease, renal failure, liver disease, acquired immune deficiency syndrome, coagulopathy, weight loss, fluid and electrolyte disorders, and drug abuse. These must be considered simultaneously while assessing complication rates, as many of them have been previously linked to hospital readmission in patients undergoing THA [37].

The importance of this information is multifactorial, with preoperative counseling and planning at the forefront. This study illustrates that patients with SCD have an increased risk for complications, which could serve patients in their understanding of risk to proceed with elective joint replacement or to simply understand expected postoperative course. The importance of this information is underlined by the substantial SCD patient population and the overall rising incidence of THA as management for hip pathology. Furthermore, as bundled payments use information such as comorbidities in the evaluation of risk for complications and adjusted bundled payment, this study could serve as objective evidence of the increased risk for complication increasing with presence or absence of SCD. For example, the risk of overall complications rises from 5.05% in OA patients to 6.53% in SCD patients. This could be useful in the consideration of payment modifiers for the Comprehensive Care for Joint Replacement Model in this specific payment population.

There are limitations to this study that must be addressed. The primary limitation of this study involves the nature of using a large national database. A large database could potentially have data entry errors that would lead to bias in our results. ICD-9 codes used to conduct this study were unable to completely isolate AVN of the femoral head and SCD from AVN of other locations and sickle cell trait or thalassemia, respectively, and could represent possible confounders, although symptomatic osteonecrosis affecting the femoral head and necessitating surgical management represents the most frequent major complication of SCD [38]. In this way, causality cannot be confirmed by this study, as the study design included a breadth of ICD-9 codes that does not allow isolation of AVN due to purely SCD as the indication for THA in this patient population.

Furthermore, patients with AVN of the femoral head alone could be susceptible to postoperative complications due to other systemic conditions. As such, providers should be aware of and prepared to counsel patients based on these additional risk factors on a patient-specific basis.

Additionally, the database is limited to inpatient procedures. The lack of outpatient data could lead to our results predicting more negative outcomes following THA, because inpatients are typically more physically disabled and more prone to complications. This may mean these results are not applicable to the outpatient setting or a joint-specific hospital. Also, we are only able to assess perioperative complications. Postoperative functional information and survivorship data were not available in the database. Finally, coding errors or omissions may be the cause for the decreased sample size seen in the OA, AVN, and SCD group, as the low population value could result in data misrepresentation.

Conclusions

This study uses a large database to further characterize complication risk for patients undergoing THA with SCD compared to patients undergoing THA with OA. As current technology continues to advance, this increased complication risk may improve with longer survivability of implants and improving medical management of SCD. However, this study highlights the need for special consideration when choosing an optimal treatment strategy for patients with SCD. Additionally, the comorbidities which are more common in SCD patients should be considered as possible complicating factors throughout their treatment influencing preoperative discussion and perioperative multidisciplinary care. This could also have implications in the realm of bundled reimbursements for difficult patient populations undergoing certain procedures, such as THA.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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Research ethics statement

This study met Institutional Review Board criteria for exemption from full review due to the absence of patient identifiers and the blinded nature of the National Inpatient Sample database.

CRediT authorship contribution statement

Christian DeMaio: Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation. **Conner Patrick:** Writing – original draft, Methodology, Investigation, Data curation. **Grayson Domingue:** Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Jake Fox:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Justin Dvorak:** Software, Methodology, Formal analysis, Data curation. **Rishi Thakral:** Visualization, Supervision, Resources, Project administration, Investigation, Conceptualization.

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