



# Electronic health record associations in patients self-reporting to be difficult to anesthetize

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**Background:** Patients who report to be difficult to anesthetize for dental procedures are commonly encountered. Determining their frequency and shared characteristics could improve understanding of pain management failures.

**Methods:** Categorical and continuous variables of 24 demographic, medical history, and dental history variables were compared in a deidentified cross-sectional study using electronic health records (EHR) of patients at the University of Iowa College of Dentistry. Individuals who self-reported to be difficult to anesthetize in their dental health history form were compared to those who reported no complications with local anesthesia. Descriptive, univariate regression, and multivariable regression statistical analyses were completed on the demographic, medical history, and dental history EHR variables.

**Results:** A total of 12,400 deidentified patient records met the inclusion criteria with a 11.4% (n = 1,411) prevalence of difficult to anesthetize self-reports. Eight categorical variables were found to have statistically significant (95% confidence interval [CI]) adjusted odds ratios (AOR) in the multivariable regression of difficult to anesthetize reporting patients: female gender (AOR = 1.61, 95% CI: 1.32-1.96, P < 0.001), dental fear (AOR = 3.60, 95% CI: 3.01-4.31, P < 0.001), mental health disorders (AOR = 1.21, 95% CI: 1.00-1.46, P < 0.045), problems with general anesthesia (AOR = 1.46, 95% CI: 1.11-1.89, P = 0.005), neurological/nerve disorders (AOR = 1.30, 95% CI: 1.05-1.60, P = 0.015), temporomandibular joint clicking/popping (AOR = 1.31, 95% CI: 1.08-1.60, P = 0.006), needle anxiety (AOR = 29.03, 95% CI: 23.80-35.52, P < 0.001), and history of root canal treatment (AOR 0.82, 95% CI: 0.68-0.99, P = 0.035).

**Conclusion:** A clinically relevant percentage of patients self-reported being difficult to anesthetize for dental procedures. The relationship between local anesthesia inadequacies and variables such as female gender, dental fear, mental health, and neurological disorders requires further investigation. The use of evidence-based local anesthesia approaches and communication practices is suggested to minimize pain experienced and subsequent fear of dental care.

**Keywords:** Anesthesia, Local; Dental Anxiety; Epidemiology; Electronic Health Records.



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## INTRODUCTION

The practice of dentistry is dependent on controlling

procedural pain, given the invasive nature of dental procedures performed in conscious patients. Adequate pain control is commonly achieved through local anesthesia [1,2]. However, local anesthetic inadequacies and failures

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in medicine and dentistry are not well understood and are commonly attributed to anatomical variations, anxiety, acute inflammatory conditions, and provider errors, though their frequency in the overall patient population remains unknown [1,2].

Pain typically results from the stimulation of peripheral nociceptors that relay noxious stimuli to the cerebral cortex [2]. Local anesthetics work by blocking the sensory neuronal conduction of these stimuli [3]. Determining the etiology of a local anesthetic failure is challenging due to the subjective nature of pain and the complexity of accurately assessing the chain of nerve impulses in patients [2]. Due to the lack of large-scale investigations into the effectiveness of local anesthesia across populations, causal influence on failures during routine dental procedures remains anecdotal.

The mass adoption of electronic health records (EHR) has enhanced screening and surveillance of conditions/diseases in healthcare. A retrospective review of EHR data provides an ideal means for screening potential overlapping pathophysiologic conditions impacting pain. This study was designed to find clinically relevant associations in demographic, medical histories, and dental histories in patients who self-reported as difficult to anesthetize.

## METHODS

Medical history forms with a selectable option to denote difficult to numb (i.e., anesthetize) were updated at the University of Iowa College of Dentistry in January 2022. Inclusion criteria included an EHR form entered between January 2022 and January 2024 and a reported history of receiving local anesthesia for a dental procedure. Categorical and continuous variables of demographic, medical history, and dental history variables were compared in individuals reporting to have had local anesthesia for dental procedures with and without difficulty becoming profoundly anesthetized. Medical history variables were left as broad categories

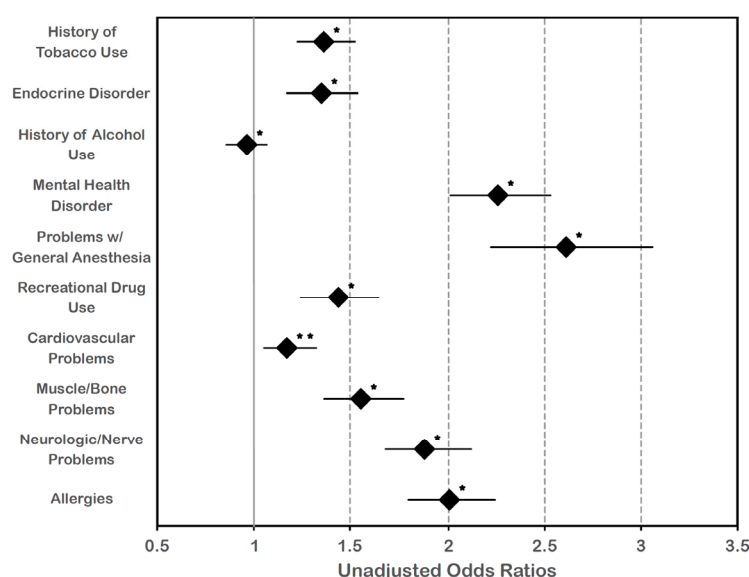
that included current or historical substance use of tobacco, alcohol, or recreational drugs. The presence or absence of a medical diagnosis under the following categories was assessed: endocrine, mental health, cardiovascular, muscle/bone, and neurological. Additionally, any history of food or pharmaceutical allergy or problems with general anesthesia were assessed as a binary variable. This was necessary given the patients' ability to write specific diagnoses under each of these categories, which presents challenges in standardizing data for analysis. For example, a diagnosis of Ehlers-Danlos Syndrome could not be analyzed from the larger subcategory of "Muscle/Bone Problems". Dental history reports assessed included: dental fear preventing a patient from seeking care previously, clenching/grinding/bruxism, history of tooth extractions and root canal treatments, presence of dental pain (at time of form entry), sensitive teeth, being unhappy with their smile, experiencing problems with previous treatment, click/popping of their temporomandibular joint(s), and anxiety of needles related to dental injections. To avoid including incomplete EHR records, the sole exclusion criterion was any EHR missing >20% of the variable entries of consideration. The University of Iowa IRB (#202212202) reviewed and approved the investigation protocol involving a deidentified EHR query from the institution's dental practice management software (axiUm, Exan Software, Las Vegas, NV).

Descriptive, univariate, and multivariable regression statistical analyses were completed on the investigated variables comparing patients reporting to have received local anesthesia with and without difficult to anesthetize notations. Measures for central tendency and variance were used for continuous variables, and ratios and frequencies for categorical variables. Univariate analysis was performed to find any predictive variables of the difficult to anesthetize outcome using a Wald Chi-square test (CI = 95%,  $P < 0.05$ ). Multivariable logistic regression was performed using the R function general linear model (GLM). The final logistic regression model was developed whereby variables were selected with an

**Table 1.** Univariate analysis of demographic variables

Characteristics	Total (N = 12,400) (%)	Difficult to anesthetize (N = 1,411) (%)	Control (N = 10,989) (%)	Unadjusted OR (CI)	P-value
Gender					
Female	7,393 (59.9)	1,038 (14.0)	6,355 (86.0)	2.08 (1.83-2.36)	< 0.001
Male	4,954 (40.1)	361 (7.3)	4,593 (92.7)	1.00	
Insurance					
Medicaid	5,082 (41.0)	707 (13.9)	4,375 (86.1)	1.52 (1.36-1.70)	< 0.001
Other	7,318 (59.0)	704 (9.6)	6,614 (90.4)	1.00	

Results of univariate logistic regression for the prediction of difficult to anesthetize. CI, 95% confidence interval; N, number; OR = The odds ratio estimate is the estimated change in the odds ratio resulting from an increase of 1 unit in the corresponding independent variable, and “1.00” indicates the reference category of the independent variable.



**Fig. 1.** Unadjusted odds ratios of difficult-to-anesthetize patients of the univariate analysis for medical history variables assessed. CI = 95% confidence interval listed. \*,  $P < 0.001$ ; \*\*,  $P < 0.01$ .

Akaike information criterion (AIC) method. Multicollinearity among the predictor variables was evaluated by calculating the Variance Inflation Factors (VIF). Hosmer-Lemeshow goodness-of-fit test along with Nagelkerke R-Square were used to evaluate goodness of fit in the logistic regression models. All tests employed a significance level of 0.05. Statistical analysis was performed using the R statistical package.

## RESULTS

A total of 12,400 deidentified patient records met the inclusion criteria for the study. The prevalence of difficult to anesthetize reports was 11.4% ( $n = 1,411$ ). The mean age was lower in difficult to anesthetize patients (41.6

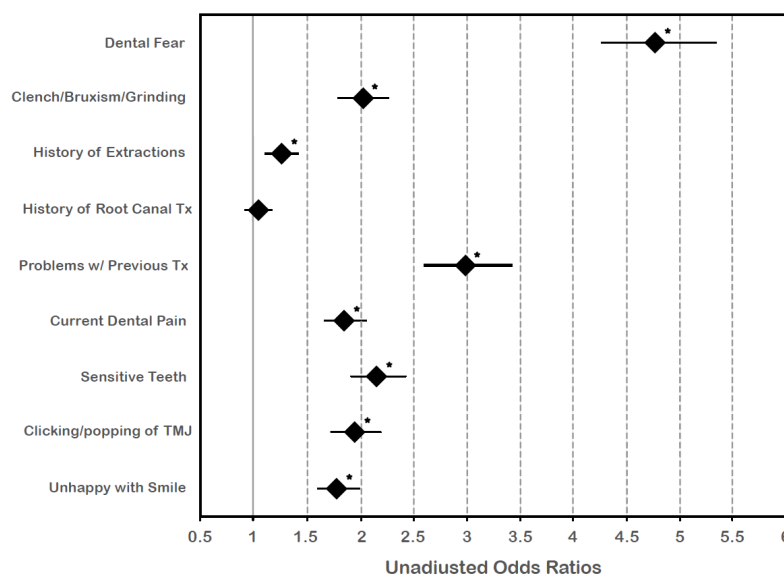
vs 44.2 years,  $P < 0.001$ ) and there was a greater proportion of total females (59.9%) than males (40.1%), with a statistically significant ( $P \leq 0.05$ ) higher unadjusted odds ratio (UOR) observed in females reporting to be difficult to anesthetize (UOR = 2.08, 95% CI: 1.86-2.36,  $P < 0.001$ ). Patients who were on Medicaid dental insurance had a higher frequency of reporting to be difficult to anesthetize in comparison to those who were self-pay or privately insured (UOR = 1.52, 95% CI: 1.36-1.70,  $P < 0.001$ ). Table 1 contains the results of the descriptive and univariate analysis of the demographic variables assessed.

Descriptive and univariate analyses indicating UORs of medical history items queried are displayed in Figure 1 and Table 2. Eight statistically significant associations ( $P \leq 0.05$ ) were found in the univariate analysis of

**Table 2.** Univariate analysis for medical history variables

Variables	Total (N = 12,400) (%)	Difficult to anesthetize (N = 1,411) (%)	Control (N = 10,989) (%)	Unadjusted OR (CI)	P-value
History of tobacco use					
Yes	5,192 (41.9)	687 (13.2)	4,505 (86.8)	1.36 (1.22-1.53)	< 0.001
No	7,191 (58.1)	723 (10.1)	6,468 (89.9)	1.00	
Endocrine disorder					
Yes	2,206 (18.0)	308 (14.0)	1,898 (86.0)	1.35 (1.17-1.54)	< 0.001
No	10,077 (82.0)	1,085 (10.8)	8,992 (89.2)	1.00	
History of alcohol use					
Yes	5,139 (41.5)	572 (11.1)	4,567 (88.9)	0.96 (0.86-1.07)	0.454
No	7,238 (58.5)	837 (11.6)	6,401 (88.4)	1.00	
Mental health disorder					
Yes	5,068 (41.3)	824 (16.3)	4,244 (83.7)	2.26 (2.01-2.53)	< 0.001
No	7,216 (58.7)	572 (7.9)	6,644 (92.1)	1.00	
Problem with general anesthesia					
Yes	998 (8.8)	224 (22.4)	774 (77.6)	2.61 (2.22-3.07)	< 0.001
No	10,675 (91.5)	1,064 (10.0)	9,611 (90.0)	1.00	
Recreational drug use					
Yes	1,944 (15.7)	286 (14.7)	1,658 (85.3)	1.43 (1.24-1.65)	< 0.001
No	10,413 (84.3)	1,121 (10.8)	9,292 (89.2)	1.00	
Cardiovascular problems					
Yes	1,408 (33.5)	509 (12.4)	3,599 (87.6)	1.17 (1.05-1.32)	0.007
No	8,140 (66.5)	875 (10.7)	7,265 (89.3)	1.00	
Muscle/bone problems					
Yes	1,981 (16.2)	308 (15.5)	1,673 (84.5)	1.55 (1.36-1.78)	< 0.001
No	10,271 (83.8)	1,088 (10.6)	9,183 (89.4)	1.00	
Neurologic/nerve problems					
Yes	2,527 (20.6)	432 (17.1)	2,095 (82.9)	1.88 (1.67-2.13)	< 0.001
No	9,716 (79.4)	959 (9.9)	8,757 (90.1)	1.00	
Allergies					
Yes	4,874 (40.3)	760 (15.6)	4,114 (84.4)	2.01 (1.79-2.25)	< 0.001
No	7,219 (59.7)	609 (8.4)	6,610 (91.6)	1.00	

Results of univariate logistic regression for the prediction of difficult to anesthetize. CI, 95% confidence interval; N, number; OR = The odds ratio estimate is the estimated change in the odds ratio resulting from an increase of 1 unit in the corresponding independent variable, and "1.00" indicates the reference category of the independent variable.



**Fig. 2.** Unadjusted odds ratios of difficult-to-anesthetize patients of the univariate analysis for dental history variables assessed. CI = 95% confidence interval listed. \*, P < 0.001. Note: Needle Anxiety (UOR = 31.60, 95% CI:27.21-36.69, P < 0.001) was not listed due to the scale of difference from other variables.

**Table 3.** Univariate analysis values for dental history variables

Variables	Total (N = 12,400) (%)	Difficult to anesthetize (N = 1,411) (%)	Control (N = 10,989) (%)	Unadjusted OR (CI)	P-value
Tooth count	22.3	21.0	22.5	0.98 (0.97-0.99)	< 0.001
Dental fear					
Yes	2,955 (24.3)	757 (25.6)	2,198 (74.4)	4.77 (4.25-5.36)	< 0.001
No	9,185 (75.7)	618 (6.7)	8,567 (93.3)	1.00	
Clench/bruxism/grinding					
Yes	4,781 (42.7)	729 (15.2)	4,052 (84.8)	2.01 (1.78-2.26)	< 0.001
No	6,415 (57.3)	528 (8.2)	5,887 (91.8)	1.00	
History extractions					
Yes	8,479 (70.1)	1,015 (12.0)	7,464 (88.0)	1.25 (1.10-1.42)	< 0.001
No	3,616 (29.9)	354 (9.8)	3,262 (90.2)	1.00	
History of root canal Tx					
Yes	5,438 (45.3)	625 (11.5)	4,813 (88.5)	1.05 (0.93-1.17)	0.448
No	6,568 (54.7)	726 (11.1)	5,842 (88.9)	1.00	
Problems with previous Tx					
Yes	1,298 (10.7)	309 (23.8)	989 (76.2)	2.98 (2.59-3.44)	< 0.001
No	10,788 (89.3)	1,023 (9.5)	9,765 (90.5)	1.00	
Current dental pain					
Yes	5,610 (46.2)	818 (14.6)	4,792 (85.4)	1.84 (1.64-2.06)	< 0.001
No	6,521 (53.8)	555 (8.5)	5,966 (91.5)	1.00	
Sensitive teeth					
Yes	6,669 (55.4)	970 (14.5)	5,699 (85.5)	2.15 (1.90-2.43)	< 0.001
No	5,367 (44.6)	394 (7.3)	4,973 (92.7)	1.00	
Clicking/popping of TMJ					
Yes	2,671 (22.1)	457 (17.1)	2,214 (82.9)	1.94 (1.72-2.19)	< 0.001
No	9,389 (77.9)	903 (9.6)	8,486 (90.4)	1.00	
Unhappy with smile					
Yes	5,124 (43.4)	750 (14.6)	4,374 (85.4)	1.77 (1.58-1.99)	< 0.001
No	6,691 (56.6)	590 (8.8)	6,101 (91.2)	1.00	
Needle anxiety					
Yes	1,062 (8.6)	715 (67.3)	347 (32.7)	31.60 (27.21-36.69)	< 0.001
No	11,336 (91.4)	694 (6.1)	10,642 (93.9)	1.00	

Results of univariate logistic regression for the prediction of difficult to anesthetize. CI, 95% confidence interval; N, number; OR = The odds ratio estimate is the estimated change in the odds ratio resulting from an increase of 1 unit in the corresponding independent variable, and "1.00" indicates the reference category of the independent variable; TMJ, Temporomandibular joint; Tx, treatment.

medical history reports. The highest unadjusted odds ratios in the univariate analysis associated with difficult to anesthetize patients were a medical history report of problems with general anesthesia (UOR = 2.61, 95% CI: 2.22-3.07,  $P < 0.001$ ) and a mental health-related disorder (UOR = 2.26, 95% CI: 2.01-2.53,  $P < 0.001$ ).

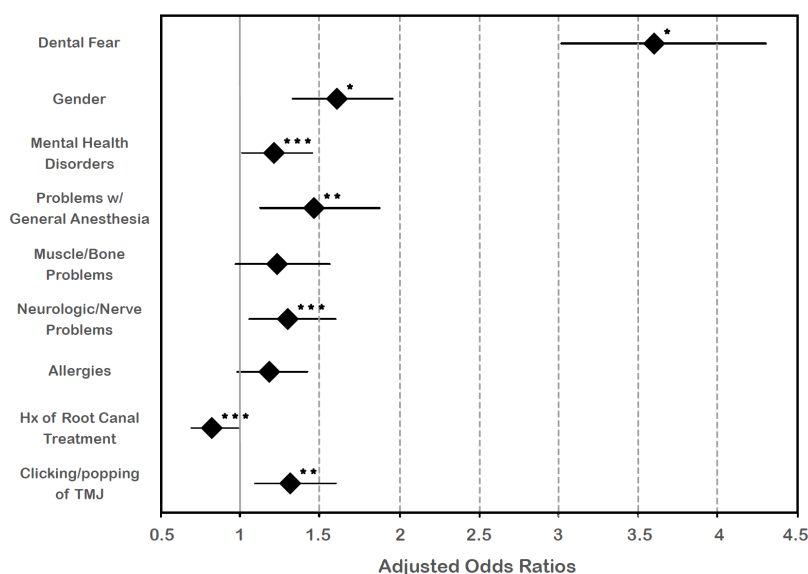
Descriptive and univariate analyses of dental history items queried are listed in Figure 2 and Table 3. Nine statistically significant associations ( $P \leq 0.05$ ) were found. The highest odds ratios in the univariate analysis associated with difficult to anesthetize patients were needle anxiety (UOR=31.60, 95% CI: 27.21-36.69,  $P < 0.001$ ) and dental fear (UOR = 4.77, 95% CI: 4.25-5.36,  $P < 0.001$ ).

Eight variables from demographic and history-reported

categories were found to be statistically significant in difficult to anesthetize patients in the multivariable regression analysis (Figure 3, Table 4). The highest adjusted odds ratios were dental history reports of needle anxiety (AOR = 29.03, 95% CI: 23.80-35.52,  $P < 0.001$ ) and dental fear (AOR = 3.60, 95% CI: 3.01-4.31,  $P < 0.001$ ). Female gender was a statistically significant demographic influence (AOR = 1.61, 95% CI: 1.32-1.96,  $P < 0.001$ ).

## DISCUSSION

Epidemiological studies and management of dental pain-related conditions/disorders have primarily focused on chronic orofacial pain conditions such as



**Fig. 3.** Adjusted odds ratios of difficult-to-anesthetize patients following multivariable regression analysis of all EHR assessed variables. CI = 95% confidence interval listed. \*,  $P < 0.001$ ; \*\*,  $P < 0.01$ ; \*\*\*,  $P < 0.05$ . Note: Needle anxiety (AOR = 29.03, 95% CI:23.80-35.52,  $P < 0.001$ ) was not listed due to the scale of difference from other variables.

**Table 4.** Odds ratios observed in difficult to anesthetize reporting patients in the Akaike information criterion (AIC) multivariable regression model of all investigated variables (demographic, medical history, and dental history)

Predictors	Odds ratios	Standard error	Confidence interval	P-value
Dental fear	3.6	0.33	3.01 – 4.31	< 0.001
Gender	1.61	0.16	1.32 – 1.96	< 0.001
Mental health disorder	1.21	0.12	1.00 – 1.46	0.045
Problems with general anesthesia	1.46	0.2	1.11 – 1.89	0.005
Muscle/bone problem	1.23	0.15	0.96 – 1.57	0.101
Neurologic/nerve problem	1.3	0.14	1.05 – 1.60	0.015
Allergies	1.18	0.11	0.98 – 1.42	0.079
History of root canal treatment	0.82	0.08	0.68 – 0.99	0.035
Clicking/popping of TMJ	1.31	0.13	1.08 – 1.60	0.006
Needle anxiety	29.03	2.96	23.80 – 35.52	< 0.001

Multivariable logistic regression was performed using the R function general linear model (GLM). The final logistic regression model was developed whereby variables were selected with an Akaike information criterion (AIC) method. Multicollinearity among the predictor variables was evaluated using Variance Inflation Factor (VIF). Hosmer-Lemeshow goodness-of-fit test along with Nagelkerke R-square were used to evaluate goodness of fit in the logistic regression models. All tests employed a significance level of 0.05. TMJ, Temporomandibular joint.

temporomandibular joint disorder (TMJD) and trigeminal neuralgia or acute management of post-operative pain following dental procedures [4-7]. The etiology of pain experienced by patients during conscious dental procedures is less understood. Our results demonstrate reports of being difficult to anesthetize (11.4%) were relatively low but clinically relevant. Numerous demographic, medical history, and dental history associations were found to have statistically significant associations to being difficult to anesthetize.

## 1. Demographic associations

Several demographic associations in difficult to anesthetize reporting patients overlap with findings from other categorical types of pain. Our study found a higher UOR in the univariate analysis in Medicaid-insured patients in comparison to self-pay and privately insured patients, although it was not significant in the multivariable regression. This finding is suggested to compound on social, economic, and healthcare access challenges that many individuals on Medicaid encounter

[8, 9]. For example, Medicaid-insured patients are more likely to face social barriers such as limited support systems and higher stress, which can exacerbate pain perception [10]. In addition, Medicaid-insured patients face financial and access barriers that may limit their ability to access routine care, leading to unmanaged pain [11]. Efforts to improve and understand Medicaid-insured patient pain management concerns may improve future appointment and routine care compliance [12,13].

A plethora of dental local anesthesia efficacy studies have been conducted, although with minimal reference to the influence of patient sex on achieving profound anesthesia. The frequency of females to males of difficult to anesthetize reports was approximately two-fold, aligning with the profile of other pain disorders [14]. Differences in pain thresholds, tolerance, expressed experience, and response to treatment have been noted in the literature [14]. A biological explanation for sex-based differences has been a focus of pain research related to the effects of hormones (e.g., testosterone, estrogen) or endogenous pain modulation on pain perception [15-17]. Psychosocial factors related to gender roles have suggested higher masculinity relative to femininity is associated with higher pain thresholds and tolerances in both sexes [14]. Dentin hypersensitivity has been noted to occur in higher frequencies in female patients, presumably tied to sex-based biological pain responses rather than differences in dental pathologies [18,19]. Inevitably, the differences observed between males and females in relation to pain are complex, with several potential explanatory variables. Deliberately designed investigations relating to sex and gender differences in pain have grown over the past three decades to improve understanding and address disparities observed in females [14,20].

Several demographic factors that warrant investigation were not assessed in the current study, including natural hair color, ethnicity, and race. However, the axiUm EHR database at the University of Iowa College of Dentistry does not collect these demographic variables making deidentified collection impossible. These demographic

variables have been suggested to influence pain perception and tolerance with a potential impact on local anesthetic efficacy. Further large-scale data analysis to better define their association with pain, including their influence regarding difficult to anesthetize reports, would be of benefit [21-24].

## 2. Medical history associations

The univariate analysis found statistically significant associations in difficult to anesthetize patients with the generic mental health variable, which encompasses many mental health disorders. Anxiety and depression, the most prevalent mental health conditions in the United States, have been previously associated with lower pain thresholds and thus an anticipated difficult to anesthetize status [25-27]. Each mental health disorder has a different underlying pathophysiology, making correlation of the findings difficult. Needle phobia, tangentially related to mental health, had the highest adjusted odds ratio in patients reporting to be difficult to anesthetize. This finding aligns with the commonly referenced influence that anxiety plays related to pain, in which a patient's fear of dental injections is disproportionate to the experienced pain. The associations observed demonstrate the significant role that the central nervous system plays in difficult to anesthetize reports despite local anesthetics in dentistry acting on the peripheral nervous system. The relative effect of mental health disorder management on pain perception and tolerance would benefit from further investigation in dentistry.

Patients presenting with joint hypermobility syndromes (JHS), specifically Ehlers Danlos Syndrome (EDS), are often cited in association with local anesthesia failures in both medicine and dentistry [28-30]. The statistically significant association of increased muscle/bone problems reported by difficult to anesthetize patients in the univariate analysis was an expected finding given past knowledge relating to local anesthesia failures with JHS/EDS patients. However, the association was not statistically significant in the multivariable regression analysis. The odds ratio related to this finding would be



quantifiable if JHS/EDS were a selectable sub-option under muscle/bone problems in the health history forms used in the current study. The pathophysiology of local anesthesia failures in JHS/EDS patients warrants further investigation given the mechanism seems unintuitive as these disorders are primarily collagen-based. Genetic mutations in these individuals may also impact the molecular function of local anesthetics, including binding to sodium channel receptors or transport through nerve membranes. Determining the etiology of the commonly encountered local anesthesia inadequacies experienced by JHS/EDS patients may provide new insights into the disorder's pathophysiology as well as potential solutions to improve their procedural pain outcomes.

Endocrine disorders were found to have significantly higher odds ratios in difficult to anesthetize patients in the univariate analysis. There may be overlap in various medical factors given painful neuropathies and joint disorders have been noted to have increased prevalence in hypothyroidism patients, which correlates well with the findings of the current study [31,32]. Although endocrine disorders encompass a large umbrella of conditions, our study's findings on difficult to anesthetize reports are consistent with Weitz et al.'s findings, in which diabetics reported procedural pain failures at nearly a 5-fold higher odds ratio than patients not reporting a history of diabetes [33].

### 3. Dental history associations

The second highest odds ratio found in difficult to anesthetize patients was reported dental fear. High dental fear and anxiety (DFA) affects approximately 15 percent of the general population [34]. The difficult to anesthetize reports were slightly less than this rate. This is understandable given the multitude of influential factors relating to DFA. A high level of DFA was reported in our study, with both groups totaling 24.3%. Over half of the difficult to anesthetize patients reported having DFA, suggesting the significance of procedural pain management influencing these reports. Increased efforts to prevent painful experiences, especially early in life,

along with the utilization of evidence-based local anesthesia practices are expected to assist with lowering DFA reports in the future.

A common report associated with TMJD, clicking/popping of a patient's temporomandibular joint, was noted in the multivariable regression analysis to have a statistically significant higher adjusted odds ratio in difficult to anesthetize patients. Clicking/popping is indicative of anterior disk displacement with reduction, a condition in which the motion of the disk sliding anterior to the head of the condyle of the mandible is responsible for the noise a patient observes [35]. Clicking/popping has also been frequently observed to be asymptomatic in individuals [35]. It is important to note that TMJD is not solely indicative of clicking/popping sounds when a patient opens and closes, as TMJD is diagnostically driven by subjective discomfort and can also be associated with an anterior disk displacement without clicking/popping (i.e., without reduction) or a muscular-based etiology [35]. Given this consideration, a potential cognitive influence of catastrophizing personality traits when clicking/popping sensations are experienced likely influenced the association with difficult to anesthetize reporting patients. Despite the complex and controversial diagnostic criteria limitations related to diagnosing TMJD, there was a similar overlap with the clicking/popping reports, and many of the previously discussed factors found in higher association with the difficult to anesthetize patients such as female sex/gender, mental health disorders, and JHS/EDS [36,37].

Statistically significant findings of other dental-related reports included current dental pain (at the time of health history entry), sensitive teeth, and being unhappy with their smile. These may be influenced by DFA through routine care avoidance. It would be beneficial to determine whether sensitive teeth reports were more representative of generalized sensitivity to cold stimulus or causative factors such as untreated caries. If the former, it would indicate a link between pre-anesthesia pain thresholds or tolerances and the probability of achieving



profound anesthesia with local anesthetics. Interestingly, a history of root canal treatment, a procedure in which profound anesthesia is often challenging to achieve, was found to be statistically significant in the multivariable regression to decrease the odds of reporting being difficult to anesthetize. We hypothesize this may indicate that difficult to anesthetize patients elected not to undergo root canal treatment due to fear of pain.

#### 4. Limitations

The data analyzed in this investigation were self-reported by patients on written health history forms and subsequently manually entered into their EHR by one of the dental auxiliary staff or dental students at the University of Iowa College of Dentistry. The degree to which data entry error occurred is unknown, and medical and dental history self-reports were not confirmed diagnoses. These potential inconsistencies are expected to be weighed towards underreporting [38]. Given the difficult to anesthetize report was not able to be confirmed, the true incidence of local anesthetic inadequacies in patients is still in question. False positives are likely in this study, given the possibility that an individual's past dental care involved substandard pain management practices. The influence of practitioner experience and the management of common local anesthesia failures, such as the high degree of failure in the inferior alveolar nerve block injection, are likely to have caused false positives [33,39]. Additionally, several independent variables in this analysis may be correlated with each other risking multicollinearity. Finally, this study was conducted at a single center, which may limit its external validity if the characteristics of patients seeking care at a dental school or in our geographic region demonstrate selection bias.

#### 5. Suggested management of difficult to anesthetize patients

Dental professionals should encourage patients, regardless of responses to local anesthesia, to address medical or mental health imbalances before completing

elective dental treatment. Unfortunately, many associations found are non-modifiable, leaving pain management primarily in the hands of dental professionals. Cold or electric pulp testing can be completed before initiating treatment on teeth with vital pulps to verify if profound anesthesia is present instead of referencing patient soft tissue anesthesia or waiting for the patient to report pain during treatment [1,2]. A provider's management of pain during injections to help with a patient's needle anxiety (e.g., topical anesthetic, gate-control theory distractions) and exhibiting compassion can build trust with a patient and play a potential psychological role in raising or lowering pain thresholds during treatment. Dental professionals should be knowledgeable of supplemental pain management practices to implement in challenging patient scenarios to help obtain profound anesthesia, including intraosseous anesthesia and the utilization of nitrous oxide. Furthermore, ensuring proper communication when situation-specific inflammation, swelling/infection, or anatomical variation/technical errors are encountered is suggested to help minimize perpetual dental fear and care avoidance. In the case of complete local anesthetic resistance, estimated to be extremely rare [40], general anesthesia may be indicated to complete surgical dental treatment.

#### 6. Conclusion

The complex interplay between each associated demographic, medical history, and dental history variable identified requires further investigation to better understand their impact on pain associated with dentistry. Given that modifiable traits such as dental fear and needle anxiety had significantly higher adjusted odds ratios observed compared to other medical conditions, practitioners may reduce the number of "tough to numb" reports by implementing the reviewed pain control practices. Further extrapolation of the other associative variables found in this study is suggested in patients with clinically confirmed local anesthesia resistance/inadequacies. Enhanced understanding of the pathophysiology of pain and the

respective development of testable treatments can then be focused on improving the comfort and safety of dental and medical surgeries in the cohort of patients who experience reduced efficacy with local anesthetics.

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