USE OF SEDATIVE GUMMY BEARS COMPARED TO ORAL SYRUPS IN PEDIATRIC DENTAL PATIENTS

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DISCLOSURES/ CONFLICT OF INTEREST

- I have no potential conflicts of interest to report. I am not endorsing any specific product.
- This presentation is not a representation of the American Academy of Pediatric Dentistry.

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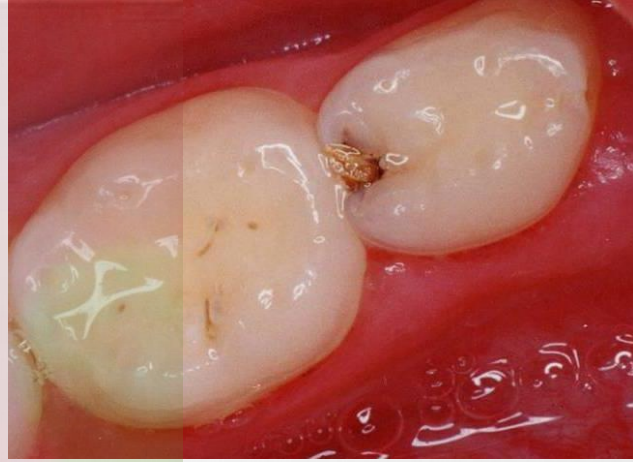


DENTAL CARIES = CAVITIES

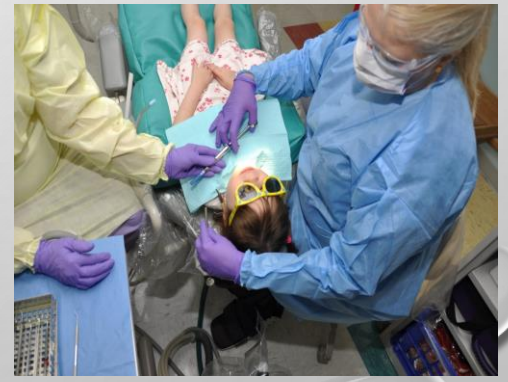
- In the United States prevalence of caries for children:
  - 23% of children age 2-5 have cavities in their baby teeth
  - >50% of children age 6-8 have a cavity in at least 1 baby tooth
  - >50% of children age 12-19 have a cavity in at least 1 adult tooth
- 1 in 36 children have autism
- As a pediatric dentist, we see children, teenagers & special needs adults

https://www.cdc.gov/oralhealth/basics/childrens-oral-health/index.html
https://www.nidcr.nih.gov/research/data-statistics/dental-caries/children
https://www.nimh.nih.gov/health/statistics/autism-spectrum-disorder-asd

all accessed Oct. 15, 2023

SAFETY & BEHAVIOR GUIDANCE

- **Safety is our #1 concern.**
- Treatment follows recommended national safety standards by the American Academy of Pediatric Dentistry, American Academy of Anesthesiologists & American Academy of Pediatrics.
- We evaluate the patient's attributes, parental influences, societal constructs & norms.
- We always start with non-pharmacologic options such as: positive reinforcement, distraction, tell-show-do, desensitization, etc.



American Academy of Pediatric Dentistry. Behavior guidance for the Pediatric Dental Patient. The Reference Manual of Pediatric Dentistry. Chicago, IL.: American Academy of Pediatric Dentistry.2022:321-39.

PHARMACOLOGIC TREATMENT OPTIONS

- Mild sedation= laughing gas/ nitrous oxide, pt. awake
- Moderate sedation= RX medications, pt. awake
- Deep sedation or general anesthesia= RX medications, pt. has significant altered consciousness or asleep.
  - Current wait list for hospital operating room nationally for dental cases range from 7 months - 24 months. Average is 12 months.
  - Very expensive & higher safety risk

Coté CJ, Wilson S. American Academy of Pediatric Dentistry, American Academy of Pediatrics. Guidelines for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures. Pediatr Dent 2019;41(4):E26-E52.

Ashok M, Lumsden C, Myers A, Yoon R. Emergency dental treatment among patients waitlisted for the operating room. J Clin Ped Dent. 2023; 47(3): 54-58.

CURRENT LIMITATIONS

There are 2 major limitations to using oral sedatives in children:

Aversion to Taste: bitter taste of midazolam is difficult to mask

Aversion to Administration:

- Children often have difficulty with tablets & capsules because they cannot swallow properly & lack experience.
- Medicine cup or oral syringes are anecdotally associated with anxiety and apprehension.
- Several studies have reported a positive correlation between the patient's willingness to take the medication, and the outcome of the sedation.

Lenahan M, Wells M, Scarbecz M. A Retrospective Study of 248 Pediatric Oral Sedations Utilizing the Combination of Meperidine and Hydroxyzine for Dental Treatment. J Clin Pediatr Dent. 2015;39(5):481-487.

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MODERATE CONSCIOUS SEDATION

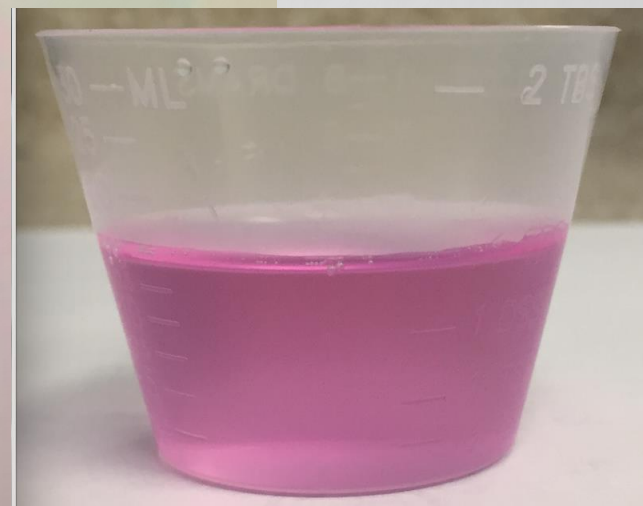
- Nationally there are a variety of safe sedation prescription medications that can be used.
- Oral sedation medications have challenges of large volume & bitter taste.
- Midazolam is ultimately the drug of choice for sedations at Nova Southeastern University (NSU). It very safe compared to other alternatives.
- Hydroxyzine is used if the desire is to increase the length of the sedation. Hydroxyzine however requires a much larger volume to be consumed making it harder for the patient to ingest.

Chen, N. and T. Tanbonliong, Comparison of Two Morphine-Benzodiazepine-Hydroxyzine Combinations for the Oral Sedation of Pediatric Dental Patients: A Retrospective Study. Pediatr Dent, 2018. 40(1): p. 43-48.
Lenahan, M., M. Wells, and M. Scarbecz, A Retrospective Study of 248 Pediatric Oral Sedations Utilizing the Combination of Meperidine and Hydroxyzine for Dental Treatment. J Clin Pediatr Dent, 2015. 39(5): p. 481-7

MIDAZOLAM

PROPERTIES

- Belongs to the Benzodiazepine family
- It is a selective CNS depressor
- Acts by opening GABA mediated chloride channels
- Rapid onset of action= 5-15 minutes
- Short-acting= 20-30 minutes
- Bitter taste
- Anxiolytic
- Amnesic properties
- Muscle relaxant
- Anticonvulsant
- Hypnotic
- Reversed via flumazenil



Bagheri M. The Use of Midazolam in Paediatric Dentistry: A review of Literature. Razavi Int. J Med. 2014 Aug 2(3):e16913. p 1-6.

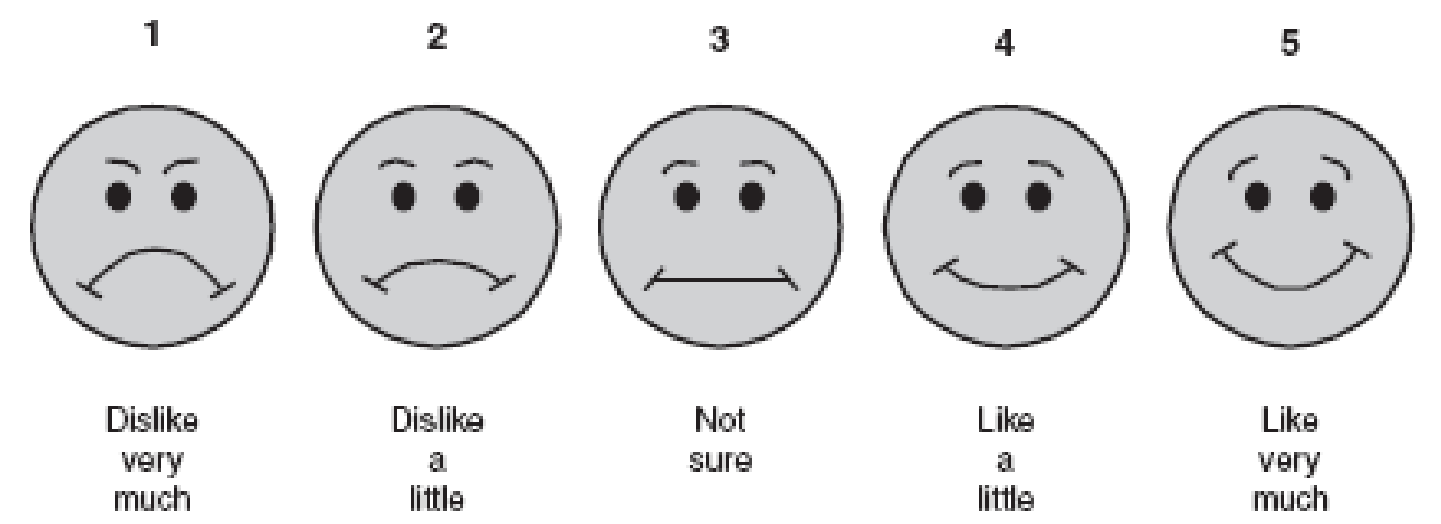
HYDROXYZINE

- PROPERTIES
  - Histamine H1 receptor antagonist
  - Sedative
  - Antihistamine: commonly prescribed for allergies
  - Antiemetic
  - Antispasmodic
  - Anticholinergic effects xerostomia
  - Medium onset of action= 15-25 minutes
  - Long-acting= 30-60 minutes
  - No reversal medication
  - Tastes good but large volume needed

Kim T, Kim K, Kim S, Kim J. Safety of hydroxyzine in the sedation of pediatric dental patients. J Dent Anesth Pain Med. 2022 Dec; 22(6):395-404.

3 SPECIFIC AIMS FOR MIDAZOLAM & HYDROXYZINE GUMMY BEARS

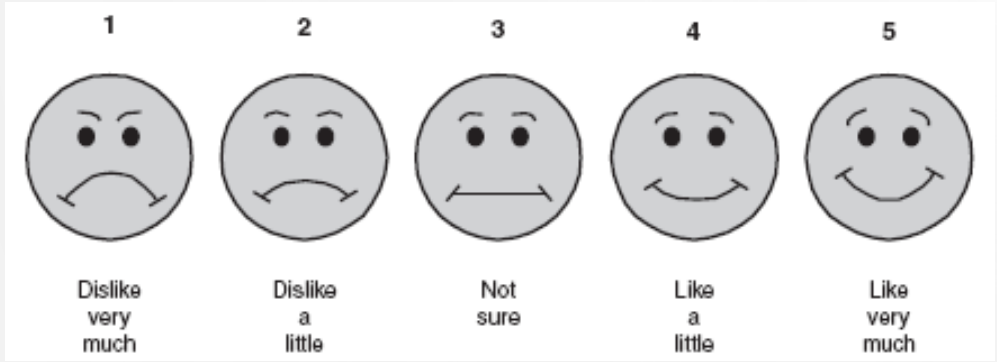
1: formulate small sized gelatin gummies with optimized taste masking techniques
2: determine if children like the taste of sedation gummies
3: measure sedation parameters after administration



METHODS

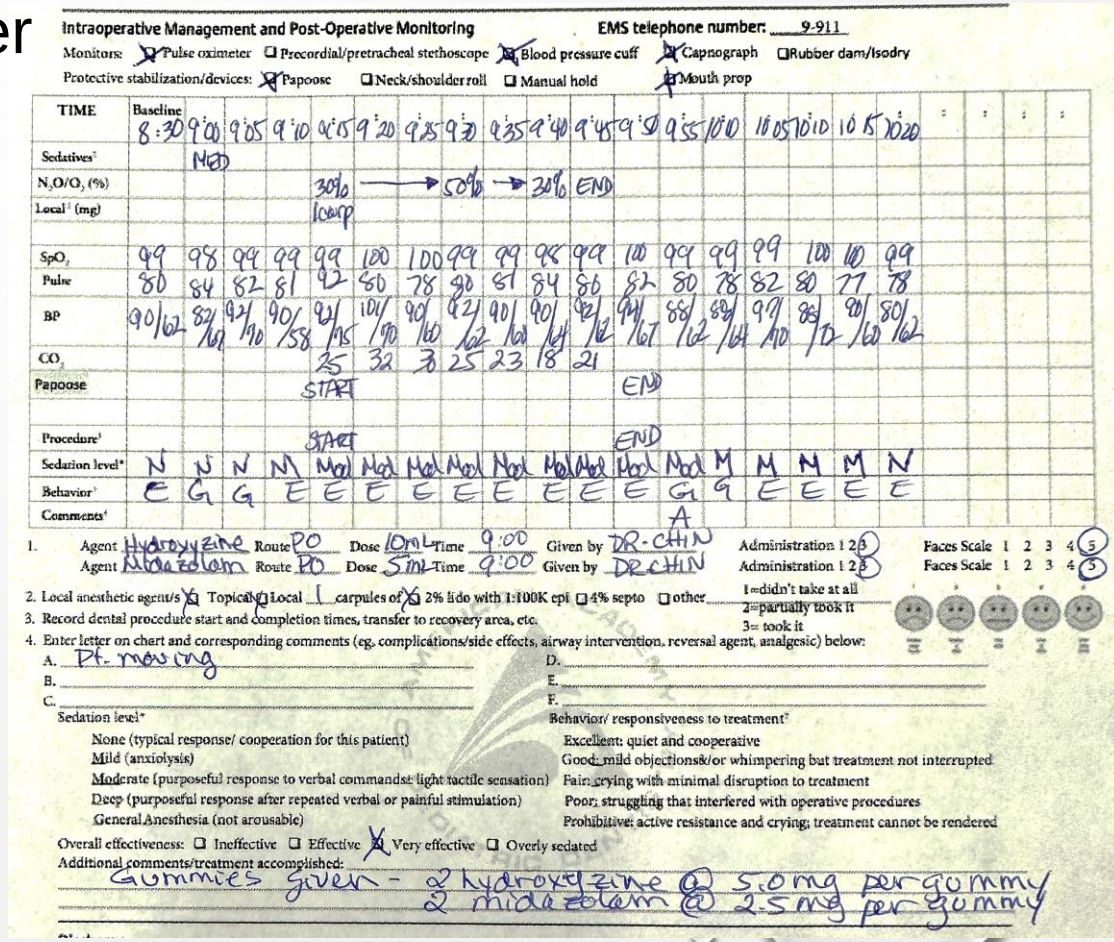
DEPENDENT VARIABLES:

- **Acceptance** of the midazolam and hydroxyzine liquid/ gummies using the 5-point hedonic scale
- **Effectiveness** of the sedation with liquid and gummies using onset time



INDEPENDENT VARIABLES:

- # of previous sedations
- # of gummies taken
- gender
- age



Mistry P, et. al. Evaluation of patient-reported outcome measurements as a reliable tool to measure acceptability of the taste of paediatric medicines in an inpatient paediatric population BMJ Open. 2018; 8(7): e021961

METHODS

- IRB approvals obtained & all study subjects chosen met all sedation safety standards
- Total 80 subjects: grouped into 40 with autism & 40 neurotypical

CONTROL SAMPLE USING LIQUID

Autism
- ❖10 midazolam suspension
- ❖10 midazolam + hydroxyzine

Neurotypical
- ❖10 midazolam suspension
- ❖10 midazolam + hydroxyzine

STUDY SAMPLE USING GUMMIES

Autism
- ❖10 midazolam suspension
- ❖10 midazolam + hydroxyzine

Neurotypical
- ❖10 midazolam suspension
- ❖10 midazolam + hydroxyzine

RESULTS

- Total 80 subjects: grouped into 40 subjects with autism & 40 neurotypical
- **Currently completed 67 study subjects**

CONTROL SAMPLE USING LIQUID

COMPLETED

Autism
- ❖10 midazolam suspension
- ❖10 midazolam + hydroxyzine

Neurotypical
- ❖10 midazolam suspension
- ❖10 midazolam + hydroxyzine

STUDY SAMPLE USING GUMMIES

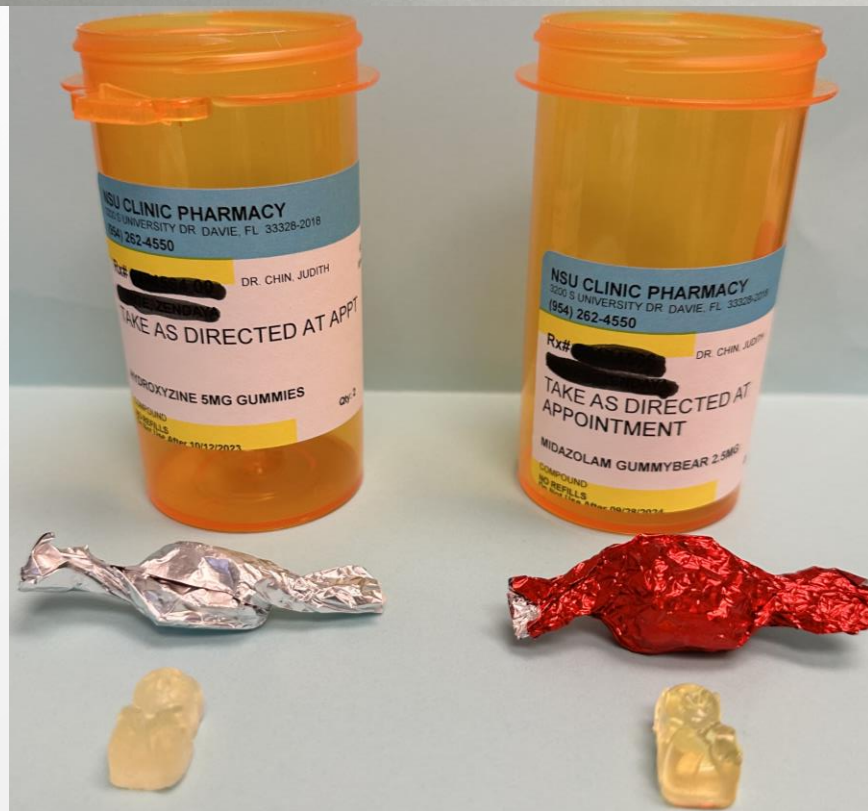
ONGOING

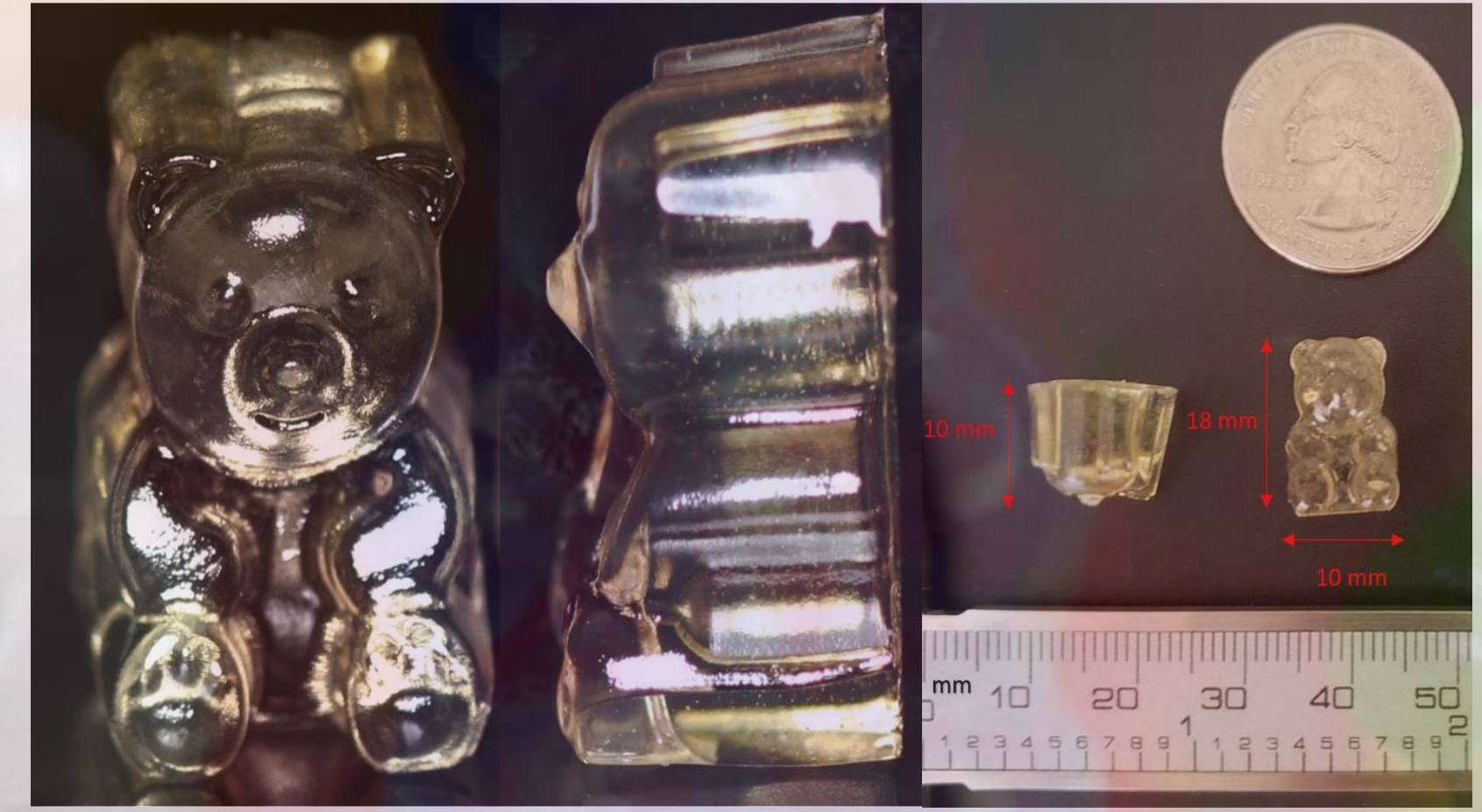
Autism
- ❖10 midazolam suspension
- ❖**10 midazolam + hydroxyzine = 3 remain**

Neurotypical
- ❖10 midazolam suspension
- ❖**10 midazolam + hydroxyzine = 10 remain**

AIM 1 RESULTS: PREPARATION OF SEDATION GUMMIES

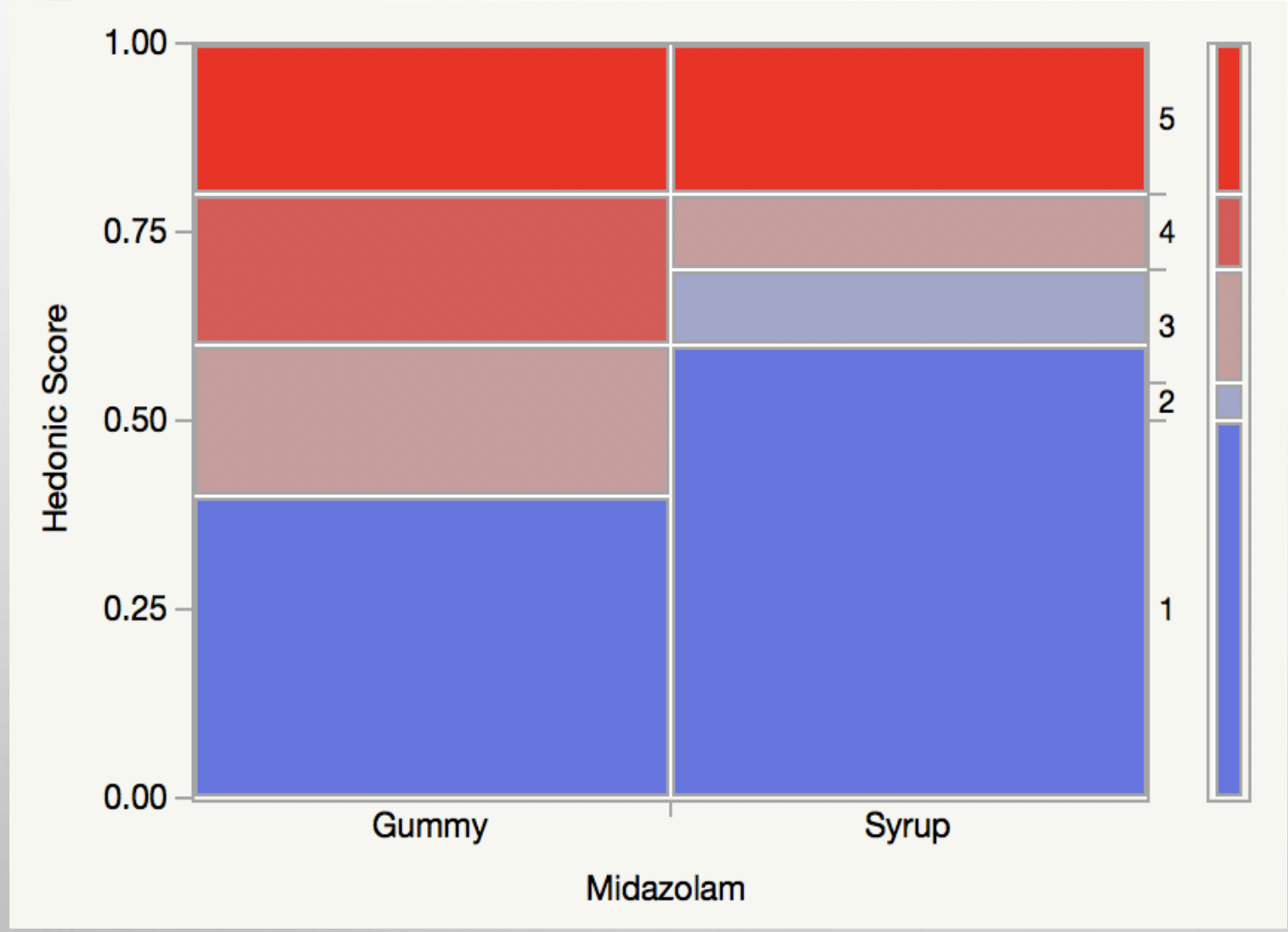
- Cultural and Society influences considered- no artificial colors or preservatives, gelatin used is bovine derivative
- Compounded at the NSU Pharmacy: lasts 14 days
- Chewable gummy base consisted of gelatin, simple syrup, flavoring, & sucralose
- Bitter masking optimized using bitter suppressing agents, organic acids, sodium salt
- Flavors used: fruit punch, tangerine marshmallow, tutti fruity
- Doses standardized in each gummy
  - 2.5 mg for midazolam
  - 5.0mg for hydroxyzine



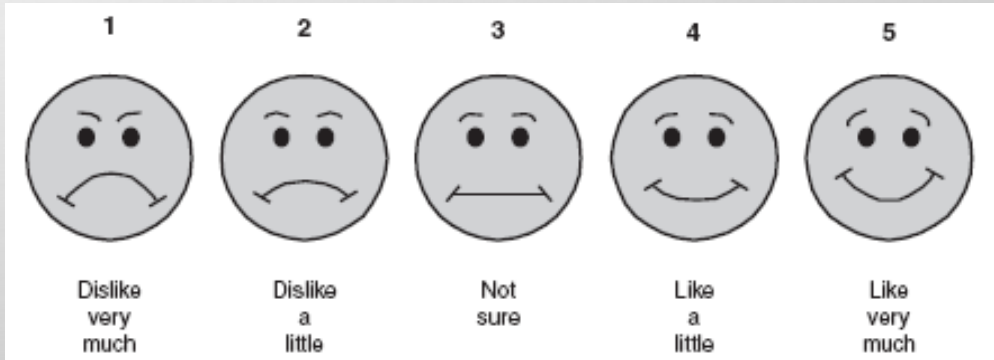


The final product was gummy bear approximately 18mm in length, 10mm in width, and 10mm in thickness

AIM 2 RESULTS : TASTE/LIKEABILITY

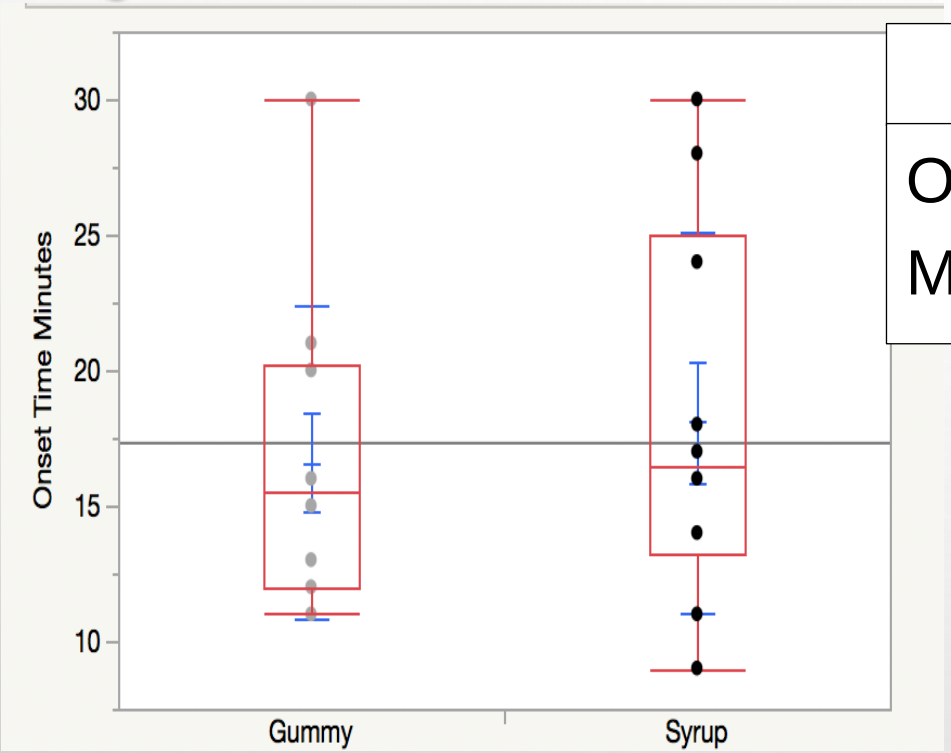


- Independent samples t-test
- Overall gummy groups had high ratings of taste versus syrup/s
- One 1 subject spit gummy out.



Graph 1. Mosaic plot of the hedonic score of gummy versus syrup groups

AIM 3 RESULTS : SEDATION ONSET TIME

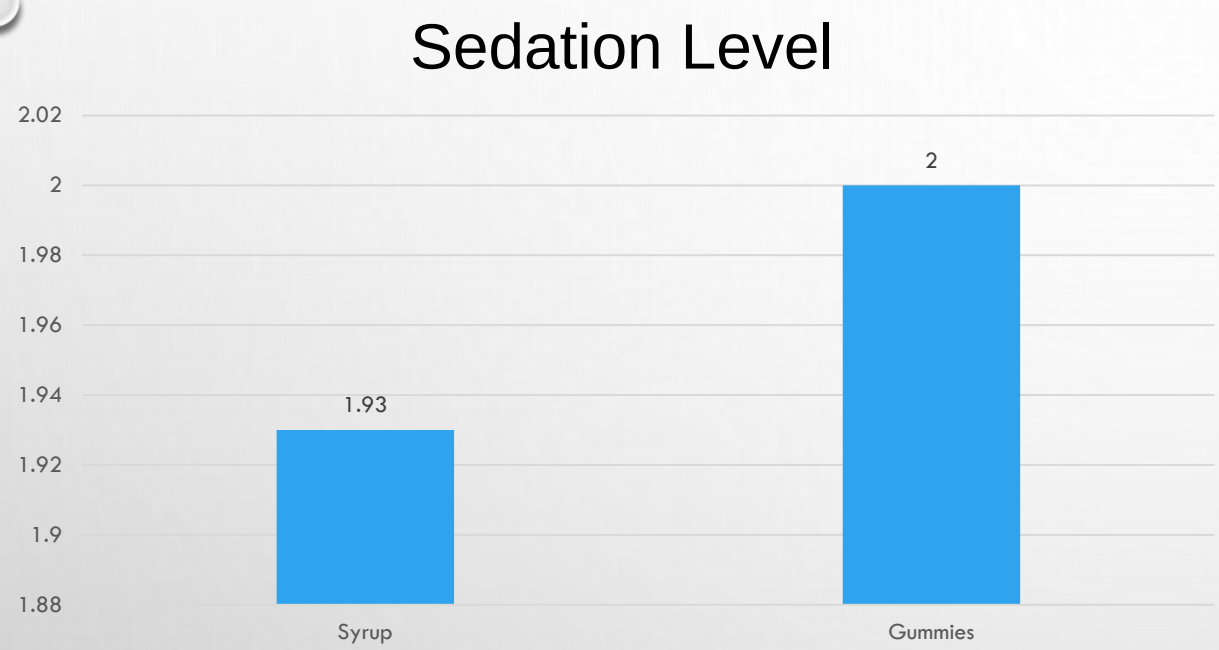


		Syrup	Gummy	*p* value
ONSET TIME MEAN		18.10	16.60	0.6639
MINUTES	SD	7.05	5.78	

- Gummies had quicker onset of sedation although current *p* value not statistically significant.

Onset time versus form of sedation medication

AIM 3 RESULTS : SEDATION LEVEL



- There were no significant differences found in sedation level (P=0.33).
- A sedation score of 2 meant the moderate sedation was effective and not too deep or too light.
- Syrups had a mean sedation score of 1.93 (SD=0.26) versus medications administered in gummy form (2.00, SD=0.00).
- All Gummy sedations considered effective
- No adverse events reported

DISCUSSION

Observations:

- Trend of patients liking the gummy bears more than the syrup
- Participants also showed more enthusiasm and compliance PRIOR to ingesting the gummy bears in comparison with the syrup
- Easier to salvage and re-administer if the patient spits it out
- Clinical trial continuing to complete double drug combination of midazolam and hydroxyzine. 13 study subjects remain. Expected completion date Feb. 2024.
- Future clinical trials and development could streamline the process of ordering, making, and transporting the gummies.

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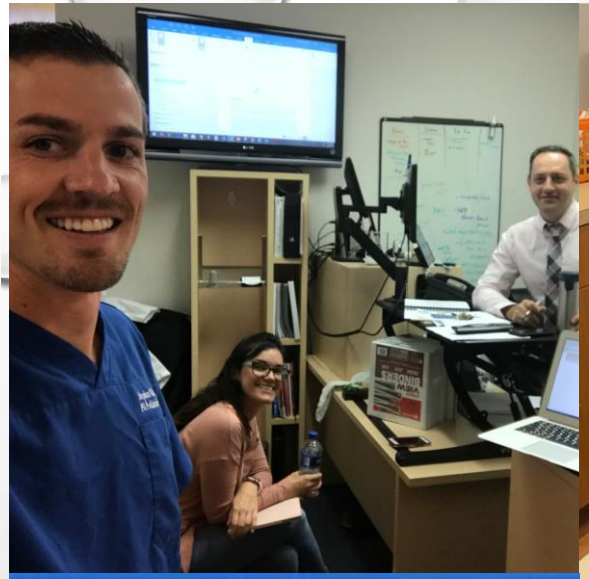

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