# Major Adverse Events and Relationship to *Nil per Os* Status in Pediatric Sedation/Anesthesia Outside the Operating Room

## *A Report of the Pediatric Sedation Research Consortium*

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## ABSTRACT

**Background:** Studies that have attempted to define the incidence of aspiration or pulmonary complications during sedation/anesthesia of children with respect to *nil per os* (NPO) status or other factors are difficult because of the relatively infrequent rate of these complications.

**Methods:** The Pediatric Sedation Research Consortium consists of 42 participating institutions with elective sedation services that submit consecutive patient encounter information to a central database. The authors evaluated aspiration episodes and a combined outcome of major adverse events (defined as aspiration, death, cardiac arrest, or unplanned hospital admission) with respect to NPO status, American Society of Anesthesiologists physical status, age, propofol use, procedure types, and urgency of the procedure.

**Results:** A total of 139,142 procedural sedation/anesthesia encounters were collected between September 2, 2007 and November 9, 2011. There were 0 deaths, 10 aspirations, and 75 major complications. NPO status was known for 107,947 patients, of whom 25,401 (23.5 %) were not NPO. Aspiration occurred in 8 of 82,546 (0.97 events per 10,000) *versus* 2 of 25,401 (0.79 events per 10,000) patients who were NPO and not NPO, respectively (odds ratio, 0.81; 95% CI, 0.08 to 4.08; $P = 0.79$). Major complications occurred in 46 of 82,546 (5.57 events per 10,000) *versus* 15 of 25,401 (5.91 events per 10,000) (odds ratio, 1.06; 95% CI, 0.55 to 1.93; $P = 0.88$). Multivariate adjustment did not appreciably impact the effect of NPO status.

**Conclusions:** The analysis suggests that aspiration is uncommon. NPO status for liquids and solids is not an independent predictor of major complications or aspiration in this sedation/anesthesia data set. **(ANESTHESIOLOGY 2016; 124:80-8)**


FOR many years, researchers have sought to define the link between various factors relating to pediatric sedation practice and rare but dangerous outcomes. Notable among these issues has been the importance of the *nil per os* (NPO) interval, American Society of Anesthesiologists (ASA) physical status, age, and relative urgency of the procedure. Specifically, questions have been raised as to exactly how much each of these factors adds to the risk of aspiration or major adverse events that could be linked to aspiration for a given procedural sedation/anesthesia encounter. Unfortunately, to date, individual studies published on pediatric procedural sedation/anesthesia have been underpowered to allow analysis of these adverse outcomes because these events occur on the order of one in hundreds (or thousands) of procedural sedation/anesthesia encounters. Because of this, it has been necessary for professional organizations to publish guidelines and recommendations concerning issues (such as NPO status) based on "consensus" of experts rather than data.[1,2]

### What We Already Know about This Topic

- The relationship between the incidence of aspiration and related complications during sedation/anesthesia of children with respect to *nil per os* status is difficult to establish because of the relatively infrequent rate of these complications

### What This Article Tells Us That Is New

- Using a large database obtained from the Pediatric Sedation Research Consortium (139,142 patients), the authors have shown that the incidence of aspiration was low in this patient population (less than 1 event per 10,000 patients) and that *nil per os* status for liquids and solids was not an independent predictor of aspiration or other related major complications.

To address these issues, we used the database developed by the Pediatric Sedation Research Consortium (PSRC) to investigate the link between patient and procedure factors and adverse pulmonary outcomes that occur during procedural sedation/anesthesia. This database has been described

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in peer-reviewed studies.[3] For this investigation, we evaluated the largest cohort to date (approximately 140,000 procedural sedation/anesthesia encounters) to evaluate possible links between aspiration, pulmonary adverse events, major adverse events, and NPO status as well as several distinct factors that have been thought to impact the safety of pediatric procedural sedation/anesthesia.

## Materials and Methods

This study was approved by the institutional review board (IRB) at each institution participating in the PSRC. These institutions are listed in the appendix. The need for written informed consent was waived. Clinical trial registration is not required because there was no change in any patient's plan of care.

Research associated with the PSRC has published our methodology for this study when we reported adverse events in the first 35,000 procedural sedation/anesthesia encounters we cataloged. Subsequently, we published our overall complication rate in 49,000 sedation/anesthesia encounters using propofol as the primary sedative/anesthetic agent collected by the PSRC.[4,5] For the purposes of this project, we considered any pharmacological intervention made to facilitate an invasive procedure or test in a pediatric-age patient outside of the operating room environment under the heading of "procedural sedation/anesthesia." The database includes a wide variety of "depths" of sedation, medications used, environments, provider types, monitoring arrays, and many more. Because of the inherent difficulty in defining exact depths of sedation, we have not attempted to define the specific depth of sedation and correlate *that* data with outcomes. Having noted this, examination of the data from the PSRC reveals that these encounters are essentially never performed with an endotracheal tube or laryngeal mask airway. The vast majority of these are natural airway elective sedations performed with varying depths of sedation/anesthesia by a range of sedation providers.

Forty institutions, including large children's hospitals, children's hospitals within hospitals, and general/community hospitals, obtained IRB approval for participation in the PSRC data-sharing group. Each of the participating institutions was required to identify a primary investigator and agreed to a standardized methodology for data collection and quality oversight from sedation/anesthesia sites at their location. As a condition of participation, all participants agreed to perform periodic audits of records to ensure data accuracy and integrity. Investigators involved in this project include anesthesiologists, pediatric medical subspecialists, general pediatricians, emergency physicians, pediatric intensivists, nurses, physician assistants, and healthcare research personnel who seek to continuously improve the quality, safety, effectiveness, and cost of pediatric sedation practice. The IRBs of all participating centers approved this study. No alteration of procedural sedation/anesthesia practice was made at any participating institution for the purposes of this study. Data collection is prospective and observational.

### Complication Data

Our Internet-based data collection tool has a specific "screen" related to complications during sedation. This screen includes data on "complications during the procedure." All the question sets or "screens" include logic that drives the generation of "pop-ups" in response to any answer to clarify the nature of the "complications" selected. For example, if "Desaturation" were selected, a pop-up would be activated to define the level and duration of desaturation involved in a given incident. Additionally for all complication options, an online resource text was available to all participants that defined the nature of what we meant by each "complication" entry. In addition, one of the primary investigators was available during all working hours to answer any question that arose concerning data entry. All primary investigators were required to perform data audits on 10 charts every 6 months and report accuracy of the data transmitted. In addition, these investigators were required to review total counts of sedations performed in their institution (independently recorded) *versus* the number of records submitted to the PSRC. Any discrepancies in numbers provided *versus* sedations performed at the institution require a complete review of the data-gathering methodology at the institution. Before starting this data collection effort, 510 records were discarded from the database because of lack of data audit reports or difficulties with IRB reapproval. No such deviations were present for the data set used in this investigation. The data for this study were collected by the PSRC between September 2, 2007 and November 9, 2011.

For the purposes of this study, we considered a subset of our complication list—that of aspiration (alone) and major complications—and related them to NPO interval as well as other factors. We defined an aspiration episode as an event where emesis was noted or food material was found in the oral/pharyngeal cavity—associated with any or the following: new cough, wheeze, increase in respiratory effort, change in chest radiograph indicative of aspiration, or new need for oxygen therapy after recovery from sedation. The combined outcome of "major adverse events" was defined as aspiration, death, cardiac arrest, or unplanned admission to a hospital. In all of the categories of data collection, participants were allowed to write in any additional complications that occurred during the course of the procedure that are not accounted for by our standard list. The data collection tool asks for the duration of time each patient was NPO for clear liquids, nonclear liquids, and solids. The question does not delineate the nature of the solid food intake (*i.e.*, toast *vs.* hamburger).

### Statistical Analysis

We defined two primary dichotomous outcomes: aspiration and the occurrence of a major adverse event. The primary independent variable was NPO status defined as no solid foods for at least 8 h, no nonclear fluids for at least 6 h, and no clear fluids for at least 2 h. In addition, we considered a

subset of patients who were NPO except liquids defined as no solid foods for at least 8 h, no nonclear fluid for at least 6 h, and clear liquids less than 2 h. To guard against the possibility of confounding affecting our conclusions about NPO status, we considered a variety of models to test the robustness of the lack of an NPO effect using logistic regression. The limited number of complications restricted the complexity of these models, but we considered age, ASA physical status greater than II, emergent status, provider, and propofol use. Variables were entered alone and in combination both with and without interactions. Because the unadjusted analysis did not show a statistically significant association between NPO status and major complications, we investigated the extent to which any of these models might alter that conclusion. Model fit was assessed by using Hosmer–Lemeshow goodness-of-fit statistic.[6] Because missing data on NPO status represented a significant portion of the data, we used multiple imputation with chained equations.[7] More specifically, we imputed NPO status, ASA physical status greater than II, and emergency status using major event, age, provider, and propofol use. Because aspirations and major complications were rare, we considered the possibility that logistic regression models were misspecified by repeating the analysis using penalized likelihood models as suggested by Firth.[8] We report odds ratios (ORs) and 95% CIs without adjustment for multiple comparisons and consider *P* value less than 0.05 to indicate statistical significance. All analyses were performed using STATA[9] (Stata Press, USA).

## Results

Data were collected on 139,142 patients. A list of all procedures performed on patients in this cohort and the percentages of patients who met NPO criteria and did not meet these criteria are listed in table 1. The frequency of these procedures did not differ substantially depending on NPO status. A list of the medications used for sedation in these procedures can be found in table 2, which demonstrates a similar distribution for patients who were NPO and not NPO. The medications listed are not "exclusive"—multiple medications or techniques may be listed for a given sedation encounter. No sedation encounter was included unless some sedative medication was given. Data entered into this PSRC database indicate that all of these procedural sedation cases were performed without endotracheal tube placement or laryngeal mask airway placement as the initial strategy. Care after aspiration event varied.

Table 3 lists the NPO status and complications for patients in this cohort. NPO status was known for 107,947 (77.6%), of whom 25,401 (23.5%) were not NPO. Although we restricted our analysis to those patients for whom NPO status was known, it is not necessary in all cases to have complete information to determine NPO status. To be specific, a patient who was not NPO for liquids would be classified as "not NPO" even if NPO for solids data were missing, whereas a patient who was described as NPO for solids would be considered "missing data" if NPO for nonclears was missing. Most (93.8%) of the violations could be accounted for by violations in NPO intervals for solids. Table 3 also provides detail on the 31,195 of patients (22.4%) for whom we could not determine NPO status. In the majority of these cases, NPO information for nonclears was not available. Importantly, there were no aspirations in this cohort.

We consider the subset of 83,231 patients who were NPO for solids and nonclears and for whom NPO status for clear liquids was known as a secondary exposure variable. This allowed us to investigate the risk of complication for patients who are NPO for solids and nonclears but who are not NPO for clear liquids. Violation for clear liquid alone occurred in 685 of these patients (0.82%).

There were 75 major complications defined as unplanned admission, aspiration, cardiac arrest, or death. There were

**Table 1.** Procedures Performed by NPO Status

| | NPO | Not NPO | Missing NPO |
|---|---|---|---|
| | N = 107,947 | N = 82,546 | N = 31,195 |
| Airway (bronchoscopy) | 713 (0.86) | 202 (0.80) | 369 (1.18) |
| Bone (fracture reduction) | 1,699 (2.06) | 949 (3.74) | 554 (1.78) |
| Cardiac (catheterization or echocardiogram) | 966 (1.17) | 303 (1.19) | 480 (1.54) |
| Dental | 485 (0.59) | 70 (0.28) | 94 (0.30) |
| Foreign body removal (nose, ear, or skin) | 9 (0.01) | 5 (0.02) | 9 (0.03) |
| Gastrointestinal (upper or lower endoscopy) | 9,794 (11.86) | 638 (2.51) | 2,619 (8.40) |
| Oncology (lumbar puncture or bone marrow) | 14,226 (17.23) | 2,199 (8.66) | 4,254 (13.64) |
| Neurology (EEG) | 4,623 (5.60) | 1,476 (5.81) | 1,923 (6.16) |
| Ophthalmology examination | 68 (0.08) | 30 (0.12) | 31 (0.10) |
| Radiology (MRI or CT scan) | 44,168 (53.51) | 17,963 (70.72) | 18,789 (60.23) |
| Sexual abuse examination | 15 (0.02) | 3 (0.01) | 8 (0.03) |
| Surgical (minor procedure) | 6,881 (8.34) | 1,914 (7.54) | 2,548 (8.17) |

Entries in each cell are the counts and column percentages stratified by NPO status. For example, airway procedures comprised 0.86% of the 107,947 procedures for which NPO status is known. Examples are given in parentheses for some procedures and are not meant to be an exhaustive classification.
CT = computed tomography; EEG = electroencephalogram; MRI = magnetic resonance image; NPO = *nil per os*.

**Table 2.** Medications Used during Sedation

| | NPO | Not NPO | Missing NPO |
|---|---|---|---|
| | N = 107,947 | N = 82,546 | N = 31,195 |
| Analgesics | 15,837 (19.19) | 3,941 (15.52) | 5,665 (18.16) |
| Anticholinergics | 5,718 (6.93) | 1,663 (6.55) | 2,114 (6.78) |
| Antiemetics | 2,294 (2.78) | 104 (0.41) | 616 (1.97) |
| Distraction | 6,538 (7.92) | 1,267 (4.99) | 2,666 (8.55) |
| Inhaled anesthetics | 1,762 (2.13) | 621 (2.44) | 428 (1.37) |
| Inhaled medications | 345 (0.42) | 61 (0.24) | 111 (0.36) |
| Local anesthesia | 18,780 (22.75) | 3,861 (15.20) | 4,789 (15.35) |
| Muscle relaxants | 170 (0.21) | 36 (0.14) | 59 (0.19) |
| Sedatives | 81,948 (99.28) | 24,998 (98.41) | 30,972 (99.29) |
| Reversal agents | 15 (0.02) | 3 (0.01) | 3 (0.01) |
| Ativan | 40 (0.05) | 18 (0.07) | 20 (0.06) |
| Chloral hydrate | 3,126 (3.79) | 1,729 (6.81) | 1,923 (6.16) |
| Dexmedetomidine | 6,130 (7.43) | 744 (2.93) | 1,855 (5.95) |
| Etomidate | 108 (0.13) | 57 (0.22) | 70 (0.22) |
| Ketamine | 5,305 (6.43) | 2,050 (8.07) | 2,252 (7.22) |
| Methohexital | 409 (0.50) | 194 (0.76) | 139 (0.45) |
| Midazolam | 18,133 (21.97) | 6,021 (23.70) | 8,931 (28.63) |
| Pentobarbital | 3,701 (4.48) | 837 (3.30) | 4,006 (12.84) |
| Propofol | 62,779 (76.05) | 18,685 (73.56) | 19,447 (62.34) |
| Thiopental | 328 (0.40) | 174 (0.69) | 239 (0.77) |
| Valium | 11 (0.01) | 7 (0.03) | 4 (0.01) |

Entries in each cell are the counts and column percentages stratified by NPO status. For example, propofol was used in 76.05% of the 107,947 sedations procedures for which NPO status is known.

NPO = *nil per os*.

**Table 3.** Classification of NPO Status and Complications

| Category | Patients (N = 139,142) | Aspiration (N = 10) | Major Complication (N = 75)* |
|---|---|---|---|
| NPO | 82,546 | 8 | 46 |
| Not NPO† | 25,401 | | |
| Solids | 23,817 | 2 | 14 |
| Nonclears | 899 | 0 | 1 |
| Liquids | 685 | 0 | 0 |
| Unable to determine NPO‡ | 31,195 | | |
| Missing solids | 2,507 | 0 | 2 |
| Missing nonclears | 28,184 | 0 | 12 |
| Missing liquids | 504 | 0 | 0 |

* Major complications defined as death, cardiac arrest, aspiration, or unplanned admission. † Reflects primary reason for NPO violation, solids < 8 h, nonclears < 6 h, and liquids < 2 h. For example, patients not NPO for nonclears are NPO for solids; patients not NPO for liquids are NPO for nonclears and solids. ‡ Patients for whom NPO status can be determined are not included. For example, a patient missing NPO status for nonclears would still be not NPO if not NPO for solids.

NPO = *nil per os*.

0 deaths, 3 cardiac arrests, 10 aspirations, and 62 admissions for other reasons. Table 4 gives the unadjusted relationship for aspiration and major complications by NPO status. Unadjusted rates per 10,000 for aspiration were 0.97 and 0.79 for patients who were NPO and not NPO respectively (OR, 0.81; 95% CI, 0.08 to 4.08; $P = 0.79$). Rates per 10,000 for major complications were 5.57 and 5.91 (OR, 1.06; 95% CI, 0.55 to 1.93; $P = 0.88$).

Because the unadjusted comparison did not reveal a relationship between NPO status and complications, we undertook a multivariate exploration to better understand the observational nature of the data. Variables associated with major complications are given in table 5. As expected, infants had a higher risk of a major complication by threefold, from 3.88 per 10,000 to 11.66 per 10,000 (OR, 3.01; 95% CI, 1.45 to 6.50; $P < 0.01$). Similarly, ASA physical statuses of III or IV, gastroenterology diagnosis, and airway or gastroenterology procedure were also associated with an increased risk of a major complication. Factors associated with a higher risk of not being NPO included patients younger than 1 yr, those undergoing emergency surgery, those who were posttrauma, those who carried a neurologic diagnosis, and those undergoing a radiology procedure (results not shown).

Adjusting for age, ASA physical status greater than II, propofol use, provider, and emergent status did not change our finding of a lack of an association of NPO status and major complication (OR, 0.75; 95% CI, 0.40 to 1.39; $P = 0.36$). Similarly, no other combination of variables produced a statistically significant effect. There were too few aspirations to perform a similar multivariate analysis for this outcome. Refitting the data using penalized likelihood models to account for rare outcomes did not significantly change the result (OR, 0.76; 95% CI, 0.41 to 1.41; $P = 0.39$). A similar penalized likelihood multivariate model for aspiration was also not statistically significant (OR, 1.07; 95% CI, 0.26 to 4.51; $P = 0.92$).

The impact of missing NPO data has the potential to alter our conclusions. On the assumption that the missing data can be predicted by other variables in the model, multiple imputation techniques again do not demonstrate an association of NPO status on major complications (OR, 0.73; 95% CI, 0.39 to 1.35; $P = 0.31$). If the assumptions about the multiple imputation model are violated, we would require at least 10 (71%) of the 14 patients to have violated NPO guidelines (compared with 23% for nonmissing data) to get a statistically significant result. We also calculated unadjusted ORs under the extreme assumption that all patients with missing NPO data were in fact not NPO. In this case, the OR for major complications would decrease to 0.92 (95% CI, 0.56 to 1.50; $P = 0.72$) and the OR for aspiration would decrease to 0.36 (95% CI, 0.04 to 1.83; $P = 0.18$). A similar analysis assuming all patients with missing NPO data were NPO gives an unadjusted OR for major complications of 1.12 (95% CI, 0.59 to 2.00; $P = 0.70$) and an OR for aspiration of 1.12 (95% CI, 0.12 to 5.62; $P = 0.89$).

Although the data on patients who met NPO criteria except for liquids are limited, there were no aspirations and no major complications for the 685 patients in this group (table 5). The unadjusted OR for aspiration was 0 (95% CI, 0 to 57.9; $P = 0.80$) and for major complication was also 0 (95% CI, 0 to 10.1; $P = 0.53$).

**Table 4.** Rates for Major Complications/Aspiration and NPO Status

| | Rate per 10,000 (95% CI) | Events | N | Odds Ratio (95% CI for Odds Ratio) | *P* Value |
|---|---|---|---|---|---|
| Major complications* | | | | | |
| NPO | 5.57 (4.08–7.43) | 46 | 82,546 | Reference | |
| Not NPO† | 5.91 (3.31–9.74) | 15 | 25,401 | 1.06 (0.55–1.93) | 0.88 |
| Not NPO for liquids‡ | 0.00 (0–79.2) | 0 | 464 | 0.00 (0.00–14.86) | 1.00 |
| Aspiration | | | | | |
| NPO | 0.97 (0.42–1.91) | 8 | 82,546 | Reference | |
| Not NPO† | 0.79 (0.10–2.84) | 2 | 25,401 | 0.81 (0.08–4.08) | 0.79 |
| Not NPO for liquids‡ | 0.00 (0–79.2) | 0 | 464 | 0.00 (0.00–85.57) | 0.83 |

* Major complications defined as death, aspiration, cardiac arrest, or unplanned admission. † Defined as solids < 8 h or nonclears < 6 h or liquids < 2 h. ‡ Defined as NPO for solids and nonclears but not NPO for liquids (< 2 h).
NPO = *nil per os*.

Finally, we present details of the 10 cases of clinical aspiration in table 6.

## Discussion

Adverse pulmonary outcomes such as aspiration are (appropriately) rare during pediatric sedation encounters. As such, the relationship between these events and various factors associated with patients or their procedures is extremely difficult to study unless extremely large numbers of patient encounters are evaluated. In this study, we wished to investigate the relationship between NPO intervals for solids and liquids and the incidence of aspiration and (more generally) major adverse outcomes. Although this issue has been the topic of several guidelines and innumerable reports and editorials, there have been relatively little useful data presented to help guide practice for pediatric sedation providers. The ASA has maintained that (largely because of the uncertainty of depth of sedation/anesthesia) pediatric patients undergoing sedation for procedures should adhere to the guidelines for perioperative fasting. These consensus-based guidelines were intended for patients undergoing elective surgery, and their application to sedation activity has been the subject of some controversy for many years.[1] Existing guidelines recommend fasting times that consider types of oral intake and the duration of fast (*i.e.*, 2 h for clear fluids, 8 h for full meals, and so on). Recently, the American College of Emergency Physicians has published its own practice advisory for periprocedural fasting for patients receiving sedation.[2] These guidelines take a different approach with specific consideration given to the acuity of the procedure for which sedation is required and has shorter NPO intervals accepted for more urgent interventions.

Previous studies of NPO safety have used different definitions for what is considered an aspiration event. In our study, we defined such an event as one where emesis is observed during the periprocedural period and was accompanied by a change in the respiratory status of the patient—or a new radiograph finding. Because aspiration can occur and not result in pulmonary symptoms, our study almost certainly underestimates its frequency. We felt it was necessary to combine the observation of emesis with new pulmonary findings to be certain we were following events of importance. In addition, without the requirement for new "signs" associated with aspiration, it would be very hard to be consistent with the data definition.

In the anesthesia literature, a retrospective study examining aspiration incidence (and outcomes) in adults and children was reported by Warner *et al.* in 1999.[10] This study looked at a series of 63,180 anesthetics using a definition of aspiration as "direct visualization of bilious or particulate matter in the tracheobronchial tree or new findings on a chest radiograph consistent with aspiration." They found an overall incidence of aspiration at 3.79 per 10,000 anesthetics; however, only 1.25 per 10,000 developed any signs or symptoms of respiratory difficulty. Frequency of aspiration was higher for patients who underwent emergency procedures, but there was no relationship to age. The authors did not evaluate the incidence of aspiration with respect to NPO status; however, they did comment the majority of their patients with aspiration had bowel obstruction. Of the children who aspirated and were under 3 yr of age, 91% had bowel obstruction as a primary pathology.

Another difficulty in studying NPO intervals and outcomes in children relates to the difficulty in defining "sedation" *versus* "anesthesia." We have used the phrase "sedation/anesthesia" for this investigation because we readily recognize that many of the cases (performed by a variety of specialists) would meet the definition of "anesthesia" *versus* the various depths of "sedation." Few of the studies in the collective literature, such as the study of Vespasiano *et al.*,[11] offer exacting assessment of patient "state" during each procedure. We believe in this era of sedation that (using potent sedative hypnotics and analgesics such as propofol and various combinations of ketamine) sedation depths vary during the course of a given sedation and it is difficult to differentiate where the line between deep sedation and anesthesia exists. We believe that it is best to consider all of these cases as sedation/anesthesia (with natural airway) aimed at accomplishing tests or procedures in children/young adults and evaluate the outcomes globally. With this caveat in mind,

**Table 5.** Predictors of Major Complications for Patients with Known NPO Status

| | Rate per 10,000 | Events | N | Odds Ratio (95% CI for Odds Ratio) | *P* Value |
|---|---|---|---|---|---|
| Age | | | | | |
| Neonate (< 1 month) | 50.76 | 1 | 197 | 13.14 (0.31–88.25) | 0.08 |
| Infant (1 month to 1 yr) | 11.66 | 22 | 18,869 | 3.01 (1.45–6.50) | < 0.01 |
| 1–5 yr | 4.48 | 30 | 67,003 | 1.15 (0.58–2.41) | 0.75 |
| 6–11 yr | 3.88 | 13 | 33,488 | Reference | |
| 12–18 yr | 4.60 | 9 | 19,585 | 1.18 (0.45–2.99) | 0.67 |
| ASA physical status | | | | | |
| I or II | 4.61 | 52 | 112,787 | Reference | |
| III or IV | 9.10 | 21 | 23,073 | 1.97 (1.13–3.34) | 0.01 |
| Elective classification | | | | | |
| Routine | 5.35 | 72 | 134,549 | Reference | |
| Emergency | 7.63 | 1 | 1,311 | 1.43 (0.04–8.21) | 0.51 |
| Provider | | | | | |
| Anesthesiologist | 3.39 | 4 | 11,814 | Reference | |
| Emergency physician | 3.66 | 11 | 30,089 | 1.08 (0.32–4.65) | 1.00 |
| Intensivist | 6.58 | 49 | 74,511 | 1.94 (0.71–7.41) | 0.23 |
| Pediatrician | 4.31 | 7 | 16,260 | 1.27 (0.32–5.92) | 0.77 |
| Radiologist | 7.33 | 2 | 2,727 | 2.17 (0.20–15.13) | 0.31 |
| Other | 5.35 | 2 | 3,741 | 1.58 (0.14–11.02) | 0.64 |
| Propofol used | | | | | |
| No | 5.49 | 21 | 38,231 | Reference | |
| Yes | 5.35 | 54 | 100,911 | 0.97 (0.58–1.70) | 0.90 |
| Diagnosis categories | | | | | |
| Gastrointestinal | | | | | |
| No | 4.20 | 50 | 118,999 | Reference | |
| Yes | 12.41 | 25 | 20,141 | 2.96 (1.75–4.87) | < 0.001 |
| Neurologic | | | | | |
| No | 6.14 | 49 | 79,783 | Reference | |
| Yes | 4.38 | 26 | 59,358 | 0.71 (0.43–1.17) | 0.20 |
| Obstructive sleep apnea | | | | | |
| No | 5.22 | 72 | 138,048 | Reference | |
| Yes | 27.47 | 3 | 1,092 | 5.28 (1.06–16.08) | 0.02 |
| Respiratory (lower) | | | | | |
| No | 5.22 | 67 | 128,458 | Reference | |
| Yes | 7.49 | 8 | 10,683 | 1.44 (0.60–3.00) | 0.28 |
| Respiratory (upper) | | | | | |
| No | 5.04 | 66 | 130,877 | Reference | |
| Yes | 10.89 | 9 | 8,263 | 2.16 (0.95–4.36) | 0.04 |
| Posttrauma | | | | | |
| No | 5.31 | 73 | 137,449 | Reference | |
| Yes | 11.83 | 2 | 1,691 | 2.23 (0.26–8.35) | 0.23 |
| Procedure | | | | | |
| Airway (bronchoscopy) | | | | | |
| No | 5.01 | 69 | 137,858 | Reference | |
| Yes | 46.73 | 6 | 1,284 | 9.38 (3.32–21.51) | < 0.001 |
| Gastroenterology (endoscopy) | | | | | |
| No | 4.68 | 59 | 126,091 | Reference | |
| Yes | 12.26 | 16 | 13,051 | 2.62 (1.41–4.62) | < 0.01 |
| Radiology | | | | | |
| No | 6.35 | 37 | 58,222 | Reference | |
| Yes | 4.70 | 38 | 80,920 | 0.74 (0.46–1.19) | 0.20 |
| Surgical | | | | | |
| No | 5.09 | 65 | 127,799 | Reference | |
| Yes | 8.82 | 10 | 11,343 | 1.73 (0.79–3.40) | 0.13 |

Variables presented in this table are unadjusted for other covariates. Rates are for the 139,140 patients except for ASA physical status and elective classification with missing information for some patients.

ASA = American Society of Anesthesiologists; NPO = *nil per os*.

**Table 6.** Descriptive Data on Aspiration Episodes

| Age | Diagnosis | Procedure | NPO Status | Setting | ASA | Type of Provider | Primary Sedative | Airway Technique |
|---|---|---|---|---|---|---|---|---|
| 21 months | Gastric reflux | Endoscopy | 6 h: solids<br>6 h: liquids<br>6 h: clears | Intensive care unit | II | Intensivist | Propofol | Natural airway |
| 26 months | Dehydration | Central line | 8 h: solids<br>8 h: liquids<br>8 h: clears | Sedation unit | II | Intensivist | Propofol | Oral airway with jaw thrust |
| 12 yr | Hoarse voice | Bronchoscopy | 8 h: solids<br>8 h: liquids<br>4 h: clears | Sedation unit | II | Intensivist | Propofol | Natural airway with jaw thrust |
| 6 yr | Renal failure | Renal biopsy | 8 h: solids<br>8 h: liquids<br>2 h: clears | Radiology | II | Intensivist | Propofol | Natural airway |
| 15 yr | Lymphoma | LP-chemo | 8 h: solids<br>8 h: liquids<br>8 h: clears | Sedation unit | III | Intensivist | Propofol | Natural airway with jaw thrust |
| 10 months | Right-side weakness | MRI scan | 6 h: solids<br>6 h: liquids<br>6 h: clears | Radiology | II | Pediatric anesthesiologist | Propofol | Natural airway with chin lift |
| 6 yr | Leukemia/acute respiratory illness | Bronchoscopy | 8 h: solids<br>8 h: liquids<br>4 h: clears | Sedation unit | III | Intensivist | Propofol | Natural airway with chin lift |
| 5 yr | Brain tumor | MRI | 8 h: solids<br>8 h: liquids<br>4 h: clears | Radiology | II | Intensivist | Propofol | Natural airway |
| 3 yr | Leukemia | CT scan | 8 h: solids<br>8 h: liquids<br>8 h: clears | Radiology | II | Intensivist | Propofol | Natural airway with chin lift |
| 3 yr | Status postvisceral transplant | Upper endoscopy | 8 h: solids<br>8 h: liquids<br>8 h: clears | Sedation unit | III | Intensivist | Propofol and ketamine | Natural airway with chin lift |

ASA = American Society of Anesthesiologists; CT = computed tomography; LP-chemo = lumbar puncture with or without intrathecal chemotherapy; MRI = magnetic resonance imaging; NPO = *nil per os*.

evaluations of NPO studies categorized as "pediatric sedation" have been too small to determine relationships between aspiration and this type of care. Roback *et al.*[12] performed a retrospective analysis of aspiration in a cohort of emergency medicine patients. In their study of 1,555 patients undergoing procedural sedation in the emergency department, they found no aspiration events and "no relationship" between the adherence (or nonadherence) to ASA NPO recommendations and adverse pulmonary outcomes. A careful reading of this article reveals that few of the patients sedated were NPO for less than 4 h and almost none of the patients were NPO for less than 2 h.

Our study describes the results of the largest cohort of prospectively collected sedation encounters ever reported. These cases come from a variety of care settings using standard definitions for adverse events. The results are similar to previous studies while offering two orders of magnitude larger numbers of patients. The relative incidence of aspiration is low at 1 per 10,000. This could be explained by our high "bar" for the diagnosis of aspiration—specifically our requirement for changes in respiratory status to qualify for the diagnosis. In a large database involving a very heterogeneous group of patients, we needed to define the event in a manner that would not be equivocal. Although our outcome analysis did not extend beyond the immediate periprocedural time frame, it is unlikely we missed many aspiration episodes as previous investigators have shown that aspiration events invariably are clinically evident within 2 h of the aspiration event if they are going to result in clinical findings at all.[10]

The limitations to our study are clear. This is a prospective observational database that contains no controls. The difficulties in determining cause and effect that are present in any such study apply to this article. In addition, we must recognize that the providers of the sedation in this particular study were working in high-performance sedation teams. The fact that they participate in our research consortium indicates a serious commitment to following outcomes and improving sedation quality. We recognize the bias built into our study favoring highly trained sedation professionals. We do not propose that our data indicate the outcomes that would be found in a more diverse group of sedation providers working under different conditions using different medications, monitors, and others.

Although anesthesiologists had the lowest rate of major complications, our data do not allow us to distinguish between different types of providers. We have endeavored to be as honest and descriptive about the type of practice we have been able to evaluate with this study. We also recognize that the definition of "major adverse event" or "complication" is arbitrary. For example, we considered unanticipated intubation or an emergency anesthesia consult as part of a major complication but recognized the provider bias resulting from such a definition. We sought consensus among the members of our consortium to define problem states. There is no doubt that our events vary greatly in their importance or gravity. With these limitations in mind, we were not able to determine a relationship between our defined adverse events and the intake of solids or liquids. Unfortunately, the nature of our database does not allow us to differentiate the type of solid food eaten (*i.e.*, hamburger *vs.* toast), so uncertainty remains as to whether or not some of these solid food aspirations met ASA criteria or not. In addition, our database does not capture patients who may have had care transferred to an anesthesiologist in the operating room for intubation because either the risk of aspiration was deemed to be high or because the NPO status was grossly violated (hamburger 30 min prior).

One may question the validity of this analysis based on the large number of patients with missing data for NPO status, but the impact on our conclusions is likely limited. A multiple imputation analysis showed little change in our estimates. Assigning all patients with missing data to either the NPO group or to the not NPO group also did not affect the statistical significance.

Finally, even in this large database, the number of aspirations is very small and the relationship to NPO status is therefore unlikely to be established. Because of this, we chose to investigate the relationship with other adverse events that might be proxy measures for significant risk. Yet even here, the number of major complications affects the width of the CIs and limits the ability to detect small but possibly important differences.

In consideration of these limitations, we do not believe our data should be interpreted as an indictment of the ASA NPO criteria. Rather we would point out that the specific relationship between NPO status and patient injury is uncertain.

## Conclusions

Our investigation into a large prospective database of pediatric sedation practice revealed little association between NPO status and aspiration or major adverse outcomes. There was a positive correlation with other factors such as ASA physical status, emergency sedation status, age, and specific procedures.

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## Competing Interests

The authors declare no competing interests.

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## Appendix: Pediatric Sedation Research Consortium Participating Institutions

American Family Children's Hospital, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin; Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois; Arizona Children's Center at Maricopa Medical Center, Phoenix, Arizona; Avera Mckennan Hospital, Sioux Falls, South Dakota; Blank Children's Hospital, Iowa Methodist Medical Center, Des Moines, Iowa; Brenner Children's Hospital, Wake Forest Baptist Health, Winston-Salem, North Carolina; Cape Fear Valley Medical Center, Fayetteville, North Carolina; Children's Healthcare of Atlanta Egleston Campus, Atlanta, Georgia; Children's Healthcare of Atlanta Scottish Rite Campus, Atlanta, Georgia; Children's Hospital at the Medical Center of Central Georgia, Macon, Georgia; Children's Hospital Medical Center of Akron, Akron, Ohio; Children's Hospital of The King's Daughters, Norfolk, Virginia; Children's Memorial Hospital, Emergency Department, Chicago, Illinois; Children's Mercy Hospital, Emergency Department, Kansas City, Missouri; Children's of Alabama, Birmingham, Alabama; Chris Evert Children's Hospital, Fort Lauderdale, Florida; Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; East Tennessee Children's Hospital, Knoxville, Tennessee; Eastern Maine Medical Center, Bangor, Maine; Florida Hospital for Children, Orlando, Florida; Gundersen Lutheran, LaCrosse, Wisconsin; Helen DeVos Children's Hospital, Grand Rapids, Michigan; Holtz Children's Hospital at the University of Miami/Jackson Memorial Medical Center, Miami, Florida; Joe DiMaggio Children's Hospital, Hollywood, Florida; Kentucky Children's Hospital, Lexington, Kentucky; Kosair Children's Hospital, University of Louisville, Louisville, Kentucky; Medical University of South Carolina, Charleston, South Carolina; Memorial University Medical Center, The Children's Hospital at Memorial, Savannah, Georgia; Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, Tennessee; Nationwide Children's Hospital, Columbus, Ohio; Nemours/Alfred I. DuPont Hospital for Children, Wilmington, Delaware; North Central Baptist Hospital, San Antonio, Texas; Palmetto Health Richland Memorial Hospital, Columbia, South Carolina; Rainbow Babies and Children's Hospital, Cleveland, Ohio; St. Vincent Hospital, Green Bay, Wisconsin; The Children's Hospital at Providence, Anchorage, Alaska; UMass Memorial Medical Center, Worcester, Massachusetts; UNC Healthcare, Chapel Hill, North Carolina; UVA Children's Hospital, Charlottesville, Virginia; Yale New Haven Children's Hospital, New Haven, Connecticut (institutional review board approval was obtained at each institution).