Integrated Pulmonary Index during procedural sedation and analgesia: a cluster-randomized trial

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# Abstract

## Aim

To evaluate the effectiveness of utilizing the Integrated Pulmonary Index for capnography implementation during sedation administered by nurses.

## Design

Cluster-randomized trial

## Methods

Participants were enrolled from the interventional radiology department at an academic hospital in Canada. Nurses were randomized to either enable or disable the Integrated Pulmonary Index feature of the capnography monitor. Procedures were observed by a research assistant to collect information about alarm performance characteristics. The primary outcome was the number of seconds in an alert condition state without an intervention being applied.

## Results

The number of seconds in an alarm state without intervention was higher in the group that enabled the Integrated Pulmonary Index compared to the group that disabled this feature but this difference did not reach statistical significance. Likewise, the difference between groups for the total alarm duration, total number of alarms and the total number of appropriate alarms was not statistically significant. The number of inappropriate alarms was higher in the group that enabled the Integrated Pulmonary Index, but this estimate was highly imprecise. There was no difference in the odds of an adverse event (measured by the Tracking and Reporting Outcomes of Procedural Sedation tool) occurring between groups. Desaturation events were uncommon and brief in both groups but area under the SpO2 90% desaturation curve scores were lower for the group that enabled the Integrated Pulmonary Index.

## Conclusion

Enabling the Integrated Pulmonary Index during nurse-administered procedural sedation did not reduce nurses’ response times to alarms. Therefore, integrating multiple physiological parameters related to respiratory assessment into a single index did not lower the threshold for intervention by nurses.

## Implications for the profession and/or patient care

The time it takes to respond to capnography monitor alarms will not be reduced if the Integrated Pulmonary Index feature of capnography monitors is enabled during nurse-administered procedural sedation.

## Impact

Results do not support the routine enabling of the Integrated Pulmonary Index when nurses use capnography to monitor patients during procedural sedation as a strategy to reduce the time it takes to initiate responses to alarms.

## Reporting method

CONSORT

## Patient or Public Contribution

There was no patient or public contribution.

## Keywords

Nursing, sedation, procedural sedation, physiological monitoring, capnography, alarm management, alarm fatigue, integrated pulmonary index

## What does this paper contribute to the wider global clinical community?

There was a large number of alarms triggered in both groups where there was either a prolonged period before an intervention was applied or prolonged periods without any intervention. It is possible that clinical interventions taken in response to alarms in the Integrated Pulmonary Index group mediated the reduction in severity of oxygen desaturation events, which potentially signals a safety benefit for using this approach for capnography alarm management. Further research is needed to evaluate this potentially beneficial impact on patient safety.

## Trial Registration

This study was registered at ClinicalTrials.gov (ID: NCT05068700)

# Introduction

The medications used for nurse-administered procedural sedation are central nervous system depressants. As such, all patients who receive nurse-administered procedural sedation are at risk of sedation-induced respiratory depression. Nurses must continually analyze and integrate information from multiple different individual parameters to make an assessment of respiratory status and implement interventions to restore normal function if indicated (Conway et al., 2013).

Physiological monitor alarms are used to alert clinicians to changes in physiological parameters that may indicate a deterioration in respiratory function. However, the high number of alarms that are triggered by physiological monitors can lead to alarm fatigue, which is a desensitization to alarms that can result in delayed or missed responses to clinically significant events (Sendelbach & Funk, 2013). Alarm fatigue is a recognized patient safety issue that has been associated with adverse events and patient deaths (Sendelbach & Funk, 2013). Capnography can detect even minor abnormalities in breathing patterns, so it is essential when using this device during nurse-administered sedation that the alarm conditions set will not result in unnecessary disruptions to procedures. Ideally, every alarm that gets triggered from a capnography monitor during a procedure should be important enough to trigger an intervention. In addition, the intervention should be initiated as soon as possible after the alarm is triggered, to both minimize the duration of the alarm and to ensure that the patient is not exposed to a prolonged period of respiratory compromise.

The Integrated Pulmonary Index (IPI) is a smart alarm that can be enabled in some models of capnography monitors, which shows promise as a tool to assist clinician’s with the process of respiratory assessment. It is a mathematically-derived index based on a fuzzy-logic inference model, which combines physiological parameters related to respiratory function, such as end-tidal carbon dioxide, oxygen saturation, respiration rate, and heart rate (Ronen et al., 2016). By assigning clinical responses to specific IPI scores, it simplifies the interpretation of continuous oxygenation and ventilation monitoring. It uses a numerical scale from 1 to 10 to represent different respiratory states, with 1 indicating severe respiratory dysfunction and 10 indicating optimal respiratory status. Specifically, it aims to reduce the cognitive load of synthesizing multiple sources of physiological monitoring data and lower the threshold for intervention by clinicians to support respiration. An IPI score of four had over 90% sensitivity and specificity for detecting clinically significant events in a clinical validation study (Ronen et al., 2016). This study aimed to determine whether using the IPI during nurse-administered sedation achieves its intended effect of reducing the threshold for intervention by measuring the time it takes for nurses to respond to capnography monitor alarms.

# Background

The use of capnography for ventilation monitoring (without the IPI) has been shown to improve safety, evidenced by a reduction in episodes of hypoxemia in a meta-analysis (Conway et al., 2016). As a result, capnography monitoring is recommended for use during sedation in many clinical practice guidelines (Conway et al., 2013; Dobson et al., 2018). The IPI has been evaluated in a number of different studies across multiple clinical settings, including the intensive care unit (Kaur et al., 2021), emergency department(Gurlu et al., 2021; Karaarslan et al., 2023) and post-operative recovery (Kuroe et al., 2021). For the procedural sedation context specifically, there has been two randomized trials that compared the use of capnography monitoring with the IPI enabled against no capnography monitoring. One of the trials, which recruited patients undergoing sedation for percutaneous endoscopic gastrostomy, found that the odds of hypoxia was increased more than 4-fold when capnography with the IPI was not used (Michael et al., 2020). In contrast, an earlier study reported that using capnography with the IPI did not reduce the maximum decrease of oxygen saturation or rates of oxygen desaturation below 90% in patients who received sedation for interventional upper GI-endoscopy(Riphaus et al., 2017). In both of these trials, patients included in the ‘usual care’ comparison groups were not monitored with capnography. Therefore, there is a lack of evidence about the unique contribution of enabling the IPI when capnography is used during nurse-administered procedural sedation.

# The Study

## Aim

The aim of this study was to evaluate the effectiveness of utilizing the IPI for capnography implementation during sedation administered by nurses.

## Objectives

The primary objective was to determine whether enabling the IPI during nurse-administered sedation reduced the time between the onset of a capnography monitor alarm and the initiation of an intervention. Additionally, the study investigated the effect of the IPI on:

* The total alarm burden
* The number of appropriate alarms
* The number of inappropriate alarms
* The total duration of alert conditions
* The choice of alarm settings
* The number and severity of adverse sedation events

# Methods

## Design

A parallel cluster randomized trial was conducted, guided by the hybrid effectiveness-implementation approach (Curran et al., 2012). The hybrid effectiveness-implementation framework was appropriate because evidence for the safety and efficacy of using capnography exists and implementation of this monitoring device for sedation is recommended in clinical guidelines (Conway et al., 2013, 2014; Dobson et al., 2018). A detailed description of this trial was reported in the published protocol (Conway et al., 2022). Briefly, this implementation-effectiveness study involved an initial ‘establishment’ period, where the research team facilitated the implementation of capnography monitoring for procedures performed with sedation by providing education and assistance using the devices. All nurses in the department were permitted to use capnography, regardless of participation in the randomized controlled trial component of the study. Nurses who participated in the study were randomized to either enable or disable the IPI feature of the capnography monitor. In a subsequent ‘stability’ period, an audit and feedback process was undertaken, with the aim of optimizing capnography alarm conditions. Nurses either enabled or disabled the IPI depending on randomization. Alarm performance was compared between nurses randomized to use capnography with the IPI enabled or disabled in the ‘evaluation’ period. The results of this ‘evaluation’ period are reported in this paper.

## Study Setting

Participants were enrolled from the interventional radiology department at an academic hospital in Canada.

## Inclusion Criteria

All nurses who administer and monitor sedation were eligible to be randomized. Adult patients who were scheduled to undergo elective procedures with sedation administered by the nursing staff were eligible for inclusion in the analysis.

## Exclusion Criteria

Patients were excluded if a preference against the presence of a research assistant observer during their procedure was expressed.

## Sample size calculation

We used cluster randomized trial sample size calculation software to determine the sample size required for the primary outcome (Hemming et al., 2020). Based on a type I error rate of 5%, and estimating that the intra-cluster correlation would be 0.02, 40 clusters with a cluster size of 10 would achieve >80% power to detect a standardized effect size of 0.3. As such, we targeted a sample size of 400 patient-participants in the evaluation period, based on estimates for the number of nurses (40) and the cluster size (10).

## Randomization

Concealed random allocation of nurses to either enable or disable the IPI was undertaken. The redcapAPI package in R was used to upload a stratified (by department) randomized sequence to REDCapTM. The research assistant retrieved the allocation from REDCAPTM for each consecutive nurse who choose to participate.

## Study interventions

Nurses randomized to enable the IPI were instructed to enable this feature when they used the Capnostream 35p monitor. Nurses randomized to disable the IPI were instructed to disable this feature. Alarm thresholds for the Capnostream 35p monitors were not pre-specified in the protocol. Nurses were encouraged to select suitable thresholds for alarms based on their clinical judgement. Additional details were provided in the published protocol about the methods used to optimize alarm settings (Conway et al., 2022).

## Data collection

A research assistant observed all procedures to collect information about participant and procedure characteristics, alarm performance and adverse sedation events. The research assistant was not blinded to the randomization allocation of the nurse because it was not practical to obscure the monitor from their view without also impeding the nurses own use of the device.

## Outcomes

The primary outcome was the number of seconds in an alert condition state without an intervention being applied. For nurses who were randomized to enable the IPI, an alert condition state was triggered if the index fell below the lower limit threshold selected for this parameter in the Capnostream 35p monitor. For nurses who were randomized to disable the IPI, an alert condition state was triggered if any one of the physiological parameters measured by the Capnostream 35p monitor fell outside of the lower and upper limit thresholds selected for each parameter. Parameters measured included the pulse rate, respiratory rate, end-tidal carbon dioxide, and oxygen saturation. An alarm was also triggered if the ‘no breath’ criteria had been met for a specified minimum amount of time. An intervention was defined as a response to an alert condition state by a nurse.

The secondary outcomes for the study were the following:

* Alarm burden (total number of Medtronic Capnostream 35p monitor alarms).
* Number of appropriate alarms (defined as an alarm that triggered an intervention).
* Number of inappropriate alarms (defined as alarms that were triggered but manually dismissed by silencing the alarm).
* Total duration of alert conditions (defined as the total time that an alert condition was active inclusive of the time to an intervention and the time until the alert conditions are resolved).
* TROOPS adverse sedation events (Roback et al., 2018).
* Area under the curve of oxygen desaturation, calculated by taking the difference between a threshold (SpO2 90%) and current oxygen saturation summed each second while oxygen saturation was below the threshold (Ward et al., 2018).

## Data analysis

An intention-to-treat approach was used. Patients were included in the analysis if their procedure was observed by the research assistant during the evaluation period of the study, provided that sedation was administered. Patients who did not receive sedation during their procedure for any reason were not included. The primary outcome was a count of the total number of seconds from initiation of an alarm to implementation of an intervention by a nurse, so we used a mixed effects negative binomial model. The fixed effect in the model was the randomization and the random effect was the cluster. The secondary outcome measures that were counts of the duration or number of alarms were analyzed using zero-inflated mixed effects models that accounted for the large number of zero scores from patients who had no alarms. The two parts of the zero-inflated model we used were a logit model to model which of the two processes the zero outcome was associated with, and a negative binomial model for the count process. This analysis was conducted using the mixed\_model function from the GLMMadaptive R package (Rizopoulos, 2023). A hurdle lognormal model was used for the area under the curve of oxygen desaturation outcome because it follows the same general approach as zero-inflated models but where the outcome is not a count variable. A mixed effects logistic regression model was used for the binary adverse events outcome.

## Differences between the protocol and this report

We initially planned to collect data from four departments that use procedural sedation in the health service in which this study was conducted. Three of these four departments did not participate, because significant challenges associated with workforce shortages arose at the time of data collection and it was decided that staff did not have the capacity to take on participation in research. We pre-specified in the protocol that a process evaluation of alarm performance over time during the establishment and stability phases would be conducted. The process evaluation will be reported separately.

## Ethical considerations

The hospital Research Ethics Board (REB) approved the trial (REB 21-5249). Additional information has previously been published in the protocol (Conway et al., 2022).

# Results

Data collection for this study took place from June 2022 to June 2023. A total of 11 nurses chose to participate in the study and were randomized. There were 401 patients monitored by the nurses participating in the study. The flow of participants through the study is presented in Figure 1. All nurses who were randomized monitored patients with their assigned intervention and cluster sizes ranged from 7 to 69. There were two patients monitored by nurses assigned to the IPI-enabled group who did not receive the allocated intervention. The pulse oximeter was not working for one participant and the capnography line malfunctioned during the procedure for the other participant. Data from 11 patients was not included in the final analysis because they did not receive sedation during their procedure.

## Sample characteristics

A summary of characteristics for patients included in the analysis is provided in Table 1. Demographic data about nurse participants was not collected. Patients received small doses of midazolam and fentanyl for a variety of different radiology procedures, with an average duration of 30 minutes. Oxygen supplementation was delivered for most patients using nasal cannula. Nurses participating in the study elected to use the default settings displayed in Table 2 for all patients they monitored.

## Alarm performance

The incidence rate ratio for the primary outcome, which was the number of seconds in an alarm state without an intervention, was 1.71 (95% CI 0.96 to 3.06). The intra-cluster correlation coefficient for the primary outcome was 0.03. Figure 2A displays a breakdown of the proportion of participants who had any any alarms between groups and 2B further presents the number of seconds an alarm was triggered without intervention.

A summary of results for both components of the zero-inflated negative binomial models used to compare differences in alarm performance between the IPI-enabled and IPI-disabled groups is presented in Table 3. There was no difference between groups for the secondary outcomes of total alarm burden, the total alarm duration and number of appropriate alarms. The effect estimate (IRR 13.13) for the negative binomial component of the model for the number of inappropriate alarms was statistically significantly but highly imprecise (95% CI 1.4 to 122.95).

## Clinical outcomes

Desaturation events were not common in either group. Area under the SpO2 90% desaturation curve scores for participants who had a desaturation event were lower for the IPI-enabled group (𝛽 -0.73; 95% CI -1.32 to -0.14). There was one intermediate severity respiratory adverse event observed in the IPI disabled group. There were two intermediate-severity adverse events related to sedation quality in the IPI enabled group. The remaining 13 adverse events were minor severity related to breathing where oxygen desaturation was addressed with minor interventions. There were no serious adverse events observed in either group. The odds ratio for the occurrence of an adverse event in the IPI enabled group compared to the IPI disabled group was 1.43 (95% CI 0.51 to 4.01).

# Discussion

This study investigated the impact of using the IPI feature of capnography monitors on alarm performance during nurse-administered sedation procedural sedation. We found that the use of the IPI did not reduce the number of seconds that alarms were triggered without intervention. As such, results from the study do not indicate that integrating multiple physiological parameters related to respiratory assessment into a single index will help to lower the threshold for intervention by clinicians. Total alarm duration was not different between groups, suggesting that using the IPI may not adversely impact alarm fatigue by increasing exposure to alarms.

Secondary outcomes revealed some insights that require further investigation. Of primary interest, although oxygen desaturation was not common in either group, the IPI-enabled group had lower levels of the area under the SpO2 desaturation curve. This outcome comprises an assessment of both the length and severity of an oxygen desaturation event, which has been used in multiple different studies in procedural sedation (Conway, Collins, et al., 2021; Niklewski et al., 2014; Schaik et al., 2021). It is possible that the actions taken in response to alarms in the IPI-enabled group mediated the effect on oxygen saturation, which potentially signals a safety benefit for using this approach for capnography alarm management. A previous randomized controlled trial that compared the use of IPI-enabled capnography monitoring with no capnography during deep sedation for interventional endoscopy found no difference in the average decrease in oxygen saturation (Riphaus et al., 2017). The discrepant results between this study and the previous study may be due to the different patient populations and sedation protocols. The previous study included patients who received propofol, which certainly has a more pronounced impact on respiratory function compared with the small doses of midazolam and fentanyl used in the present study (Riphaus et al., 2017). In a different clinical setting, there was evidence that using the IPI decreased the duration of respiratory events (Broens et al., 2020). A randomized trial that evaluated the use of the IPI for overnight monitoring of post-operative patients who received opioids found that the duration of low IPI events was reduced in comparison to standard monitoring (Broens et al., 2020), which, similar to our trial, suggests that nurses’ responses to IPI alarms may increase safety.

The total doses of sedative and analgesic medication for many patients was small, with a median dose of only 1mg for midazolam and 50-75mcg for fentanyl. It is unclear if different results would be observed if there was a larger dose of sedative and analgesic medication administered, which likely would also be associated with a higher number of alarms due to the increased risk of respiratory depression that has been observed in previous studies (Li et al., 2023; Wang, Shen, et al., 2023; Wang, Sheng, et al., 2023). Application of results from this study should therefore be limited to procedures where a small dose of sedative and analgesic medication are used. These doses are likely typical of many settings that use nurse-administered sedation (Conway et al., 2014). Importantly, there was no systematic difference in the doses of sedative and analgesic medication administered between groups, which suggests that the results are not confounded by differences in the sedation protocol or degree of sedation induced.

Nurses were not directed to use specific thresholds to trigger capnography monitor alarms for either the IPI-enabled or disabled group. Instead, the implementation-effectiveness design permitted nurses who participated in the study to use feedback from audits of alarm performance to identify the alarm settings that worked best for them in their setting. Some previous studies that have compared default with modified alarm management strategies have applied a prescriptive approach where the modified alarm trigger conditions were decided for the whole department rather than for individual nurses (Allan et al., 2017; Cvach et al., 2015). However, permitting nurses to alter thresholds based on feedback of alarm performance characteristics has been shown to be an effective strategy to reduce alarm burden (Ruppel et al., 2018). As such, we believe that the implementation-effectiveness design used in this study was appropriate. That said, it is possible that the broader culture and context in the department that this study was conducted impacted the nurses’ decision-making about adjusting the alarm settings. Previous research has shown that attitudes towards alarm management across the department can influence the alarm management practices of individual nurses (Ruppel et al., 2019).

## Limitations

There was a smaller number of clusters included than we had planned due to the restricted number of sites available at the time of data collection. In addition, the intra-cluster correlation for the primary outcome was also higher (0.03) than we estimated for the sample size calculation. It is therefore possible that the final sample size for this study was too small to detect a statistically significant difference between groups for the primary outcome. Nurses were not blinded to assigned allocation due to the nature of the intervention being an alarm management strategy. Likewise, the research assistant performing outcome measurement was not blinded to the allocation of the nurse because it was not practical to obscure the Capnostream monitor from their view without also impeding the nurses own use of the device.

## Recommendations for further research

There was a large number of alarms triggered in both groups where there was either a prolonged period before an intervention was applied or prolonged periods without any intervention. As such, it is clear from this study that further efforts are required to identify more effective strategies to optimize capnography alarm management. Our results indicate that simply combining multiple physiological parameters into a single index is not sufficient to improve nurses’ responses to capnography alarms. Further exploratory research would be worthwhile to investigate nurses’ decision-making process to understand the potential reasons why using the IPI was not an effective strategy to lower the threshold for intervention by nurses. For example, it is possible that the IPI does not provide sufficient information to guide nurses’ decision-making about the appropriate intervention to apply. Additionally, future research could investigate whether the use of the IPI in combination with other strategies, such as alarm escalation protocols, can improve alarm performance. Additionally, there is increasing evidence that machine learning approaches could be used to improve capnography alarm management (Conway, Jungquist, et al., 2021; Conway et al., 2023). The IPI is a mathematically-derived index, so it is possible that machine learning approaches could be used to develop a more effective index for capnography alarm management.

## Implications for policy and practice

The results do not support the routine enabling of the IPI when nurses use capnography to monitor patients during procedural sedation as a strategy to reduce the time it takes to initiate responses to alarms.

## Conclusion

Enabling the Integrated Pulmonary Index during nurse-administered procedural sedation did not reduce the number of seconds that alarms were triggered without intervention. Therefore, integrating multiple physiological parameters related to respiratory assessment into a single index did not lower the threshold for intervention by nurses.

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**Figure 2. CONSORT diagram**

**Figure 2. Number of seconds in an alert state condition without intervention**

Table 1. Sample characteristics

| **Characteristic** | **IPI disabled**, N = 1751 | **IPI enabled**, N = 2151 |
| --- | --- | --- |
| Age (years) | 63 (50, 72) | 65 (55, 71) |
| Sex |  |  |
| Female | 81 (47%) | 82 (39%) |
| Male | 93 (53%) | 129 (61%) |
| Total midazolam (mg) | 1.00 (1.00, 1.50) | 1.00 (1.00, 2.00) |
| Total fentanyl (mcg) | 50 (50, 100) | 75 (50, 100) |
| Oxygen device |  |  |
| mask | 0 (0%) | 2 (0.9%) |
| nasal prongs | 173 (100%) | 210 (99%) |
| Procedure duration (minutes) | 31 (20, 51) | 31 (17, 53) |
| Procedure type |  |  |
| Abdominal drain | 4 (2.3%) | 8 (3.7%) |
| Ablation | 0 (0%) | 6 (2.8%) |
| Angiogram | 25 (14%) | 33 (15%) |
| Angioplasty | 7 (4.0%) | 16 (7.4%) |
| Biopsy | 22 (13%) | 12 (5.6%) |
| Central venous cannula | 13 (7.4%) | 12 (5.6%) |
| Embolization | 28 (16%) | 31 (14%) |
| Fistula | 6 (3.4%) | 3 (1.4%) |
| Gastric tube | 36 (21%) | 42 (20%) |
| Hemodialysis line | 7 (4.0%) | 11 (5.1%) |
| Other | 25 (14%) | 34 (16%) |
| Percutaneous transhepatic cholangio drain | 2 (1.1%) | 6 (2.8%) |
| Pulmonary angiogram | 0 (0%) | 1 (0.5%) |
| 1Median (IQR); n (%) | | |

Table 2. Alarm settings used by nurses during the study

| Parameter | Lower threshold | Upper threshold |
| --- | --- | --- |
| Pulse rate | 40 beats per minute | 120 beats per minute |
| Respiratory rate | 6 breaths per minute | 50 breaths per minute |
| End-tidal carbon dioxide | 8 mmHg | 60 mmHg |
| Oxygen saturation | 90% |  |
| No breath detected | 30 seconds |  |
| Integrated pulmonary index | 4 |  |

Table 3. Alarm performance

|  | Negative binomial component | | | Zero component | | |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Outcome | IRR | 95% CI | p-value | OR | 95% CI | p-value | ICC |
| Total alarm duration | 1.77 | 0.96 to 3.27 | 0.068 | 0.94 | 0.56 to 1.59 | 0.83 | 0.02 |
| Number of alarms | 0.63 | 0.17 to 2.37 | 0.495 | 0.37 | 0.1 to 1.4 | 0.14 | <0.01 |
| Number of appropriate alarms | 0.63 | 0.17 to 2.37 | 0.495 | 0.37 | 0.1 to 1.4 | 0.14 | <0.01 |
| Number of inappropriate alarms | 13.13 | 1.4 to 122.95 | 0.024 | 38.04 | 0.07 to 20945.51 | 0.26 | <0.01 |
| OR = Odds ratio; IRR = Incidence rate ratio; ICC = Intra-cluster correlation | | | | | | | |