### Automated, Real-Time Fresh Gas Flow Recommendations Alter Isoflurane Consumption During the Maintenance Phase of Anesthesia in a Simulator-Based Study

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#### BACKGROUND:
The Low Flow Wizard (LFW) provides real-time guidance for user optimization of fresh gas flow (FGF) settings during general inhaled anesthesia. The LFW can continuously inform users whether it determines their FGF to be too little, efficient, or too much, and its color-coded recommendations respond in real time to changes in FGF performed by users. Our study objective was to determine whether the LFW feature, as implemented in the Dräger Apollo workstation, alters FGF selection and thereby volatile anesthetic consumption without affecting patient care.

#### METHODS:
To reduce potentially confounding variables, we used a human patient simulator that consumes and exhales volatile anesthetics. Standard monitoring was provided for the patient initially with invasive arterial blood pressure added after anesthetic induction. In this within-group study, each of 17 participants acted as his or her own control. Each participant was asked to anesthetize an identical simulated patient twice using a Dräger Apollo workstation, first with the LFW feature disabled and subsequently enabled. The volatile anesthetic was isoflurane. Both simulation runs were set up to have similar time durations for the different phases of anesthesia: induction, incision, and maintenance. Emergence was not simulated. The isoflurane vaporizer was weighed before and after each simulation run on a digital scale to verify total computed volatile liquid anesthetic consumption. In addition, the product of FGF (reported by the Apollo) times the isoflurane volumetric concentration (sampled by a multigas analyzer at the equivalent of the FGF hose for the Apollo) was integrated over time to obtain isoflurane consumption rate (on-the-fly anesthetic consumption rate measurement).

#### RESULTS:
The maintenance isoflurane consumption rate and FGF were significantly lower with the LFW display enabled than without (P = 0.005). The mean reduction in FGF was 53.6% (95% confidence interval, 39.2%–67.9%). There was no significant difference in alveolar isoflurane concentration (P = 0.13 for differences <0.1%). The isoflurane consumption measurement closely matched the consumption measured via the digital scale.

#### CONCLUSIONS:
Our data in a simulated anesthetic suggest that enabling the display of FGF efficiency data by the LFW results in a median percent reduction in volatile liquid anesthetic consumption rate of 53.2%. Since the lower limit of the 95% confidence interval for the median is 39.4%, this finding is likely to translate into cost savings and less waste anesthetic gas generated in the clinical setting and released into the atmosphere. (Anesth Analg 2013;117:1139–47)
phase of anesthesia, which is generally the longest lasting and relatively steady-state portion of a typical operation, without altering patient care.

METHODS
In this study, a Dräger Apollo anesthesia workstation (Dräger, Lübeck, Germany; Software ver. 4.30.05) with the Low Flow Wizard (LFW) software and display was used. According to Dräger, the LFW compares inspiratory flow and inspired drug concentration with expiratory flow and end-tidal drug concentration to determine a volume of vapor taken up by the patient and uses inspired drug concentration and total FGF to determine a volume of drug vapor delivered (Hans Ulrich Schüler, Dräger Medical Inc., Lübeck, Germany, e-mail communication to Isaac Thomas Luria [University of Florida], Dräger internal presentation explaining in general terms how the Low Flow Wizard calculates its flow recommendation, January 23, 2012). By comparing the volume delivered with the volume taken up by the patient, the LFW calculates a minimum FGF value required to deliver at least as much drug vapor volume as the patient is taking from the circuit. The LFW similarly monitors oxygen and nitrous oxide. The Dräger Apollo’s user instructions specifically recommend against using the LFW during preoxygenation and during induction when the patient and circuit are not in equilibrium. Also, when trying to lighten or deepen anesthesia, the recommendations of the LFW will not be applicable because its algorithm calculates how much flow is needed to maintain the current level of drug uptake without considering that the user may be trying to change it. The LFW is not intended to supplant good clinical judgment and careful monitoring of inspired and end-tidal drug concentrations by the anesthesia provider, but to provide FGF recommendations for an otherwise stable patient during maintenance of anesthesia and patient/circuit equilibrium. The monitor presents in a display box on the anesthesia machine screen (Fig. 1) the FGF status using a red “too little” indicator when FGF is below the recommended minimum, a yellow “too much” indicator when FGF is >1 L/min over the minimum, and a green “efficient” indicator if FGF is within 1 L/min of the minimum FGF recommended by the LFW.

After IRB approval (UFIRB #2011-U-0532) and written informed consent, 17 study participants were recruited randomly from clinical staff available on that particular day with the goal of equally representing nurse anesthetists/anesthesia assistants, residents, and faculty. Of 17 enrolled participants, 6 were midlevel provider anesthetists (Certified Registered Nurse Anesthetists or anesthesiologist assistants), 6 were residents or fellows, and 5 were attending physicians. Years of experience in anesthesia practice ranged from <1 to 31 and age span was 25 to 66 years. Our random

![Dräger Apollo main display with the 3 possible Low Flow Wizard recommendations demonstrated.](image-url)
Each simulation run was ended 5 minutes after incision. Preparation and drape before incision would occur and the anesthesiologist declared that he or she was ready for the simulation scenario, we allowed exactly 10 minutes after Y-piece. On expired drug concentrations at the breathing circuit space of the patient directly rather than relying only on the HPS to measure drug concentrations in the simulated lung. Measure of “alveolar drug concentration” which allowed addition, the HPS’ internal gas analysis system provides a measurement of inhaled drug concentration and consumes and exhales volatile anesthetic drug. In oxygen, produces CO₂, responds to anesthetic drugs, intensity, and interpatient variability. The HPS consumes such as fat compartment volume, surgical procedure pain and consumes and exhales volatile anesthetic drug. In oxygen, produces CO₂, responds to anesthetic drugs, intensity, and interpatient variability. The HPS consumes such as fat compartment volume, surgical procedure pain and consumes and exhales volatile anesthetic drug. In oxygen, produces CO₂, responds to anesthetic drugs, intensity, and interpatient variability. The HPS consumes such as fat compartment volume, surgical procedure pain and consumes and exhales volatile anesthetic drug. In oxygen, produces CO₂, responds to anesthetic drugs, intensity, and interpatient variability. The HPS consumes such as fat compartment volume, surgical procedure pain and consumes and exhales volatile anesthetic drug. In oxygen, produces CO₂, responds to anesthetic drugs, intensity, and interpatient variability. The HPS consumes such as fat compartment volume, surgical procedure pain and consumes and exhales volatile anesthetic drug. In oxygen, produces CO₂, responds to anesthetic drugs, intensity, and interpatient variability. The HPS consumes such as fat compartment volume, surgical procedure pain and consumes and exhales volatile anesthetic drug. In oxygen, produces CO₂, responds to anesthetic drugs, intensity, and interpatient variability. The HPS consumes such as fat compartment volume, surgical procedure pain and consumes and exhales volatile anesthetic drug.

Figure 2. A timeline of each participant’s activity during the collection of data. The timeline is depicted in this configuration to highlight the consistent timing of simulation events in the control and Low Flow Wizard (LFW) portions of the study.

The HPS was also programmed to exhibit a consistent and repeatable increase in arterial blood pressure and heart rate (HR) (mean arterial blood pressure 40% and HR 20% both wearing off over 4 minutes) during laryngoscopy and in response to surgical incision. Before each scenario was ended, participants were told to expect no significant surgical or hemodynamic changes in the patient or procedure and allowed to make any adjustments they wanted to the anesthesia machine, IV drugs, patient airway, etc. The scenario and data collection were ended approximately 1 minute after each participant declared they were satisfied with the status of patient care. Each participant performed this simulated anesthetic induction twice, the second time after the LFW was enabled. Participants were instructed about the meaning of the LFW indications, that the LFW is for information only and does not raise alarms or adjust ventilation variables, and that the minimum flow recommendations are based on equilibrium conditions in the breathing circuit which may not be relevant when altering depth of anesthesia. The LFW was presented as extra information available to the anesthesiologist, and participants were instructed that it was at their discretion whether or not to use the LFW. After completing both a control (without LFW) and a LFW display-enabled scenario, each participant was given a questionnaire to assess their level of experience, typical FGF during maintenance of anesthesia, satisfaction (or lack thereof) with the recommendations of the LFW, and possible reasons for not using lower FGF in their daily procedures. A timeline of a participant’s involvement in the study can be seen in Figure 2.

A clinically realistic scenario was created to make the anesthesiologist go through all the usual steps of induction and preparation for surgery to allow the anesthesiologist time to naturally settle into the flow and vapor settings that they thought appropriate. Simply asking an anesthesiologist what their typical flow and vapor settings are during maintenance anesthesia would have imparted a bias about why we were asking and what answer might make them appear most responsible. In the simulated anesthetic, many parts of a real anesthetic were included even if they were not directly relevant to our study to ensure that participants did not know what we were looking for and would conduct themselves as closely as possible to their usual practice. Sampling of anesthesia providers was 4 women to 13 men. Five participants acknowledged some previous experience using the Dräger Apollo anesthesia workstation but, of those 5, only 1 had enough experience with the LFW to remember how it worked and had a preexisting opinion about its use. The other 4 either had no recollection of the LFW in their use of the Apollo or acknowledged seeing it as part of the display but not knowing what it did or considering it during use of the machine. Two participants acknowledged never having used a simulated patient before their participation in this study.

A preintervention/postintervention design with each participant functioning as their own control was chosen; the intervention was an in-service on the LFW and activation of the LFW on the workstation display. Because the Dräger Apollo was not used at our institution at the time of the study, each participant was initially given an in-service style introduction to the Apollo excluding any mention of the LFW. The participant was then asked to perform a routine anesthetic induction and maintenance on a full body mannequin patient simulator (Human Patient Simulator [HPS], version B, CAE Healthcare/Medical Education Technologies Inc., Sarasota, FL) for an otherwise healthy 64-year-old, 70-kg individual for a laparoscopic removal of a pancreatic head mass with the stipulation that isoflurane be used with a 1.0 minimum alveolar concentration (MAC) target. We used the HPS rather than human patients to simplify study data collection and remove confounding patient variables such as fat compartment volume, surgical procedure pain intensity, and interpatient variability. The HPS consumes oxygen, produces CO₂, responds to anesthetic drugs, and consumes and exhales volatile anesthetic drug. In addition, the HPS’ internal gas analysis system provides a measure of “alveolar drug concentration” which allowed us to measure drug concentrations in the simulated lung space of the patient directly rather than relying only on expired drug concentrations at the breathing circuit Y-piece.

In an effort to keep a consistent time scale for each simulation scenario, we allowed exactly 10 minutes after the anesthesiologist declared that he or she was ready for preparation and drape before incision would occur and each simulation run was ended 5 minutes after incision.
Participants were also instructed to not discuss the study with colleagues.

Data collection for the simulated anesthetic scenarios described above was conducted via the serial data outputs of the Apollo and a multigas analyzer (Capnomac Ultima ULT-I.09.EN, Datex/GE Healthcare, Waukesha, WI), the scenario logs of the HPS, and manual recording of pre- and postsimulation run vaporizer weights. The flow of information into the data collection system is detailed schematically in Figure 3. Starting with an unmodified Dräger Apollo, the common FGF hose that connects the flowmeters and vaporizers to the patient circuit was cut in 2 places and reconnected with a barbed fitting featuring additional Luer lock connections. The multigas analyzer was connected to this fresh gas line such that both the analyzer inlet and exhaust lines were spliced in, with the inlet tee connector upstream of the exhaust tee. This configuration allowed for measurement of isoflurane concentration directly from the common FGF outlet without possible contamination from patient exhalation and circuit mixing. The fresh gas isoflurane concentration closely matched the vaporizer setting and was treated as a reliable proxy measurement for the vaporizer setting. Using technical documentation provided by Dräger, software was developed to interface with the Apollo’s internal computer via serial communication and provide recordable information about the state of the Apollo. This information included individual gas flow settings, volatile drug concentrations at the Y-piece, ventilator settings as well as the Apollo’s own internally calculated approximation of liquid drug consumption rate (with a resolution of 1 mL of liquid anesthetic).

By multiplying drug gas concentration percentage and FGF rate and integrating over time, drug consumption in liters of anesthetic vapor can be calculated. This calculated consumption was verified by weighing the vaporizer on a digital scale (Model EK-12Ki, 12,000 g × 1 g, A&D Engineering, San Jose, CA) before and after each usage and comparing the consumption based on change in vaporizer weight with analysis of FGF and composition via the gas analyzer. This allowed us to cross-validate our own on-the-fly measurements against the Apollo’s reported consumption and the mass of consumed drug as read by the digital scale.

A multiparameter physiological monitor (Merlin M1094B/M1046A, Hewlett-Packard Company, Palo Alto, CA) placed on top of the Apollo displayed the electrocardiogram, HR, pulse oximeter oxygen saturation (SpO2), and first noninvasive and subsequently invasive arterial blood pressures. Exhaled CO2, ventilator variables, and inhaled and expired gas concentrations were displayed on the Dräger Apollo workstation’s main screen.

**Statistical Methods**

We had 3 research questions related to the change in outcomes after the introduction of LFW: (1) Is there a significant change in FGF settings during maintenance of anesthesia?; (2) Is there a significant change in anesthetic consumption rate during maintenance of anesthesia?; (3) Is the difference in the amount of anesthetic drug provided to the patient simulator, for example, alveolar drug concentration, >0.1%? The null hypothesis for the first 2 research questions is:

\[ H_0 : \theta_{CTRL} - \theta_{LFW} = 0 \]

where \( \theta \) is the population parameter.

For the last research question, we considered a difference more than 0.1% meaningful and tested this as the null value:

\[ H_0 : \theta_{CTRL} - \theta_{LFW} > 0.1 \]

For FGF settings, directly measured values were compared. For anesthetic consumption rate, directly measured values of FGF and vaporizer setting were multiplied and corrected for liquid to vapor volume

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**Figure 3.** This schematic diagram depicts the flow of data from each source to the data acquisition computer. Drug consumption rate is actually calculated after collection, but is depicted this way for clarity. HPS = Human Patient Simulator; ECG = electrocardiogram; NIBP = noninvasive arterial blood pressure; ABP = arterial blood pressure; SpO2 = pulse oximeter oxygen saturation; FGF = fresh gas flow; HR = heart rate; BP = blood pressure; \( P_{iso} \) = partial pressure of alveolar isoflurane vapor.
conversion and then compared. In the case of drug provided to the patient simulator, mean values of alveolar isoflurane concentration as reported by the patient simulator’s internal gas analysis system during maintenance were compared for a difference >0.1%.

The study was planned for a dependent samples (paired) $t$ test with target power = 0.80 assuming a 2-tailed test with significance level $\alpha = 0.05$ and a moderate correlation ($\rho = 0.25$–0.50) between the dependent measures (control and LFW conditions) to detect a moderate to large effect size (i.e., effect size $= 0.80$ in standard deviation units). The power analysis determined that a sample size of 17 was sufficient.

After data collection, we checked for normality by evaluating skewness and kurtosis, normal probability plots (P-P plots), and the Shapiro-Wilk test for normality (at $P > 0.05$). Based on these diagnostic measures for the 3 primary outcomes, FGF at maintenance, liquid drug consumption rate at maintenance, and alveolar isoflurane concentration at maintenance, only alveolar isoflurane concentration at maintenance can be considered to be normally distributed. This was largely due to 1 participant who had extremely large FGF values for the control condition (without LFW) which in turn produced large difference scores for the 3 outcome variables. We tested the difference in alveolar isoflurane concentration using the paired $t$ test and the difference in FGF and liquid drug consumption using the Wilcoxon signed-rank test.

We also evaluated the difference in outcome measures first without the LFW and then with it enabled using robust estimators (medians and 20% trimmed means) and 95% confidence intervals (CIs) for these point estimates. Both the median and trimmed mean are less susceptible to sampling fluctuation than the arithmetic mean especially in the case of skewed distributions. For these data, the median and the trimmed mean provide more useful measures of central tendency.

We used the bias-corrected and accelerated (BCa) bootstrap method to construct CIs for the medians. Resampling methods, such as the bootstrap, do not require that distributions be normal or that sample sizes be large. The bootstrap uses the data and computer processing power to estimate the unknown sampling distribution. In this case, each bootstrap sample is a simple random sample of 15 values selected with replacement from the original observations, and the statistic is estimated for each bootstrap sample.

BCa bootstrap 95% CI for the trimmed means and medians were estimated using 50,000 bootstrap samples. The BCa bootstrap adjusts for both bias and skewness in the bootstrap distribution. This approach is accurate in a wide variety of settings, has reasonable computation requirements, produces reasonably narrow intervals, and can estimate standard errors when there is not an obvious formula as is the case for the sample median. CIs were then examined to determine whether the hypothesized difference was contained within the lower and upper limits of the interval. Statistical analysis was produced using SAS (v.9.3; SAS, Cary, NC) and SPSS (v. 21.0; IBM Corp, Armonk, NY) software packages.

RESULTS

Of the 17 enrolled participants, 2 were subsequently excluded. Our first participant was treated as a pilot of our study protocol, and we ended up talking openly about the purpose of the study in front of the participant and making changes to the protocol. A second participant was excluded due to a period of missing data. A box and whisker plot of these data

Figure 4. Box and whisker plots of liquid isoflurane consumption rate during maintenance of anesthesia (left), total fresh gas flow rate during maintenance of anesthesia (middle), and alveolar isoflurane concentration during maintenance of anesthesia (right). The midline represents the 50th percentile, boxes the 25th and 75th percentiles, and whiskers the 5th and 95th percentiles. LFW = Low Flow Wizard.
Table 1. Outcome Variables: Arithmetic Means, Trimmed Means, and 95% Confidence Intervals

<table>
<thead>
<tr>
<th>Outcomes (all measures taken at maintenance)</th>
<th>Mean ± SE</th>
<th>20% trimmed mean ± SE</th>
<th>95% CI for the trimmed mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar isoflurane volumetric concentration (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (no LFW)</td>
<td>1.14 ± 0.12</td>
<td>1.06 ± 0.08</td>
<td>0.87–1.24</td>
</tr>
<tr>
<td>LFW</td>
<td>0.93 ± 0.08</td>
<td>0.89 ± 0.07</td>
<td>0.73–1.04</td>
</tr>
<tr>
<td>Difference (control – LFW)</td>
<td>0.21 ± 0.07</td>
<td>0.20 ± 0.06</td>
<td>0.06–0.34</td>
</tr>
<tr>
<td>Fresh gas flow (L/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (no LFW)</td>
<td>2.95 ± 0.42</td>
<td>2.58 ± 0.21</td>
<td>2.11–3.06</td>
</tr>
<tr>
<td>LFW</td>
<td>1.27 ± 0.27</td>
<td>1.02 ± 0.12</td>
<td>0.78–1.26</td>
</tr>
<tr>
<td>Difference (control – LFW)</td>
<td>1.68 ± 0.44</td>
<td>1.41 ± 0.21</td>
<td>0.92–1.90</td>
</tr>
<tr>
<td>Liquid drug consumption rate (mL/h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (no LFW)</td>
<td>19.86 ± 4.06</td>
<td>15.99 ± 1.15</td>
<td>13.16–18.48</td>
</tr>
<tr>
<td>LFW</td>
<td>9.93 ± 1.84</td>
<td>7.42 ± 0.79</td>
<td>5.62–9.21</td>
</tr>
<tr>
<td>Difference (control – LFW)</td>
<td>10.83 ± 4.72</td>
<td>7.87 ± 1.35</td>
<td>4.76–10.97</td>
</tr>
</tbody>
</table>

CI = confidence interval; LFW = Low Flow Wizard.

can be seen in Figure 4. Our analyses of the data using the Wilcoxon signed rank test show a significant decrease in the median maintenance FGF from 2.50 to 0.98 L/min (W = 58, P < 0.001) leading to a decrease in the median maintenance liquid isoflurane consumption rate from 16.21 to 8.08 mL/h (W = 47, P = 0.005). The difference in mean alveolar isoflurane concentration during maintenance was tested with a dependent samples (paired) t test. Although the estimated difference between control and LFW conditions was 0.21% (SD = 0.27), this result was not statistically significant (t0.05,13 = 1.62, P = 0.06; absolute isoflurane volumetric concentration, not 0.1% of measured range). Therefore, there is insufficient evidence to reject the null hypothesis that the difference is >0.1%. During induction, the LFW monitor did not significantly impact drug consumption.

In addition, Table 1 presents the means and 20% trimmed means with their estimated standard errors and the 95% CI for the trimmed mean. Trimming 20% of the data eliminates 3 observations in each tail of the distribution and eliminates the influence of extreme observations. In Table 2, we present the medians, the interquartile range (the difference between the upper and lower quartiles), and CIs. CIs were calculated using the BCa bootstrap. With small samples, the actual coverage probability may not be equal to the nominal coverage probability, so we also report exact distribution-free CIs based on order statistics. This interval does not “undercover.”

We also calculated the average percent reduction in FGF and drug rate consumption after the introduction of the LFW for each participant (CTRL – LFW/CTRL, where CTRL represents data from the control simulation scenario and LFW is the simulation scenario with the LFW enabled). The mean reduction in FGF was 53.6%, and the 95% CI assuming normality (Shapiro-Wilk: W = 0.93, P = 0.31) was 39.2% to 67.9%. The median percent reduction in FGF was 55.1%, and the 95% BCa bootstrap CI for the median was 45.2% to 69.6%. Both the mean and the median reduction in drug consumption rate are calculated as (CTRL–LFW)/CTRL for each participant and then the mean (or median) of this distribution is computed. The mean percent reduction in drug consumption rate was 42.9%; however, this variable was not normally distributed (W = 0.73, P = 0.001). The median percent reduction in drug consumption rate was 53.2% (39.4%–56.4%).

Questionnaire responses indicated the potential influence of concern about compound A on the anesthesia providers’ thoughts concerning maintenance FGF rates during sevoflurane use. Eight of 15 participants answered that their typical FGF rates during maintenance were 2 L/min or more, the recommended minimum FGF when using sevoflurane. In the comments section of the questionnaire and through talking in person during the study, many participants mentioned their fears of compound A specifically as a reason to use 2 L/min FGF with sevoflurane. Questionnaire answers (shown as histograms in Fig. 5) also demonstrated that the participants all agreed that reducing anesthetic drug consumption is important to them. Participants also

Table 2. Outcome Variables: Medians, Interquartile Range, and Confidence Intervals

<table>
<thead>
<tr>
<th>Outcomes (all measures taken at maintenance)</th>
<th>Median (IQR)</th>
<th>BCa Bootstrap 95% CI</th>
<th>ADF 96.48% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar isoflurane concentration (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (no LFW)</td>
<td>1.04 (0.41)</td>
<td>0.87–1.18</td>
<td>0.87–1.28</td>
</tr>
<tr>
<td>LFW</td>
<td>0.96 (0.36)</td>
<td>0.72–0.96</td>
<td>0.72–1.08</td>
</tr>
<tr>
<td>Difference (control – LFW)</td>
<td>0.20 (0.34)</td>
<td>0.14–0.24</td>
<td>0.04–0.38</td>
</tr>
<tr>
<td>Fresh gas flow (L/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (no LFW)</td>
<td>2.50 (1.05)</td>
<td>2.05–3.10</td>
<td>2.11–3.06</td>
</tr>
<tr>
<td>LFW</td>
<td>0.98 (0.55)</td>
<td>0.76–1.29</td>
<td>0.75–1.30</td>
</tr>
<tr>
<td>Difference (control – LFW)</td>
<td>1.34 (1.19)</td>
<td>1.13–1.81</td>
<td>0.80–1.99</td>
</tr>
<tr>
<td>Liquid drug consumption rate (mL/h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (no LFW)</td>
<td>16.21 (5.83)</td>
<td>13.18–18.41</td>
<td>12.66–18.49</td>
</tr>
<tr>
<td>LFW</td>
<td>8.08 (4.07)</td>
<td>6.68–8.55</td>
<td>5.16–9.23</td>
</tr>
<tr>
<td>Difference (control – LFW)</td>
<td>7.66 (6.95)</td>
<td>4.76–10.97</td>
<td>4.11–11.06</td>
</tr>
</tbody>
</table>

IQR = interquartile range; CI = confidence interval; LFW = Low Flow Wizard.

*The bias-corrected and accelerated (BCa) bootstrap with 50,000 replications was used to compute 95% confidence intervals for medians.

*The asymptotically distribution-free (ADF) CIs are based on order statistics, that is, rank ordering of the observed data.
all agreed that keeping FGFs low when patient conditions permit is something that they routinely consider.

**DISCUSSION**

Concern for interference of varied user perceptions about compound A associated with sevoflurane as a function of FGF suggested that isoflurane would be more appropriate for this study investigating FGF rates. Desflurane would have been the most attractive and financially relevant drug to study but is not supported by the HPS used in this study. No published data specifically validating the drug uptake model of the HPS could be found. However, the drug uptake behavior was found to be reasonable for a healthy patient by an experienced anesthesiologist and compared favorably with the behavior exhibited by the Gas Man™,

Figure 5. Summary of agreement/disagreement with statements presented in the questionnaire. Five indicates strong agreement and 0 strong disagreement. Simulation run, a more important consideration for this study. Test runs with the HPS demonstrated that collecting additional data for 30 minutes during the maintenance phase made almost no difference in the circuit and alveolar concentrations. The HPS’ comparatively rapid equilibration was likely a contributing factor in this observation.

The data most critical to the conclusions drawn from this study were vaporizer settings and FGF rates during the designated steady-state maintenance phase of anesthesia. Since the presence of the LFW monitor did not significantly impact drug consumption during induction, nor is it intended to, real-world reductions in consumed drug will depend on the duration of an institution’s typical case and the ratio of time spent inducing versus maintaining anesthesia. Longer cases will tend toward a total drug reduction closer to the median of 53.2% that we observed for maintenance of anesthesia, while in shorter cases anesthetic drug consumption may be dominated by the induction phase and thus exhibit less reduction in drug use. The possible savings associated with lower FGFs are even more relevant for desflurane. Desflurane costs more per milliliter than isoflurane, has a higher MAC, has a greater impact as a greenhouse gas, and has the lowest blood/gas solubility coefficient of any potent inhaled anesthetic drug in common use.7,8 The latter characteristic

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makes for the most rapid equilibration (steady state) between inspired and expired drug concentration.

The goal of a potent inhaled drug-based anesthetic is to achieve clinically relevant alveolar concentrations of drug to supplement the other medications given in the course of an anesthetic. A typical potent inhaled drug-based anesthetic target would be between 0.7 and 1.3 MAC. Review of the data reveals that the end anesthetic result, that is, alveolar isoflurane concentration achieved was clinically similar between the control and LFW conditions (1.13% and 0.93%, respectively, \( P = 0.13 \) for a difference of <0.1%). This reflects an average 1.0 MAC for the control and 0.8 MAC for the LFW phase. The slightly higher vaporizer setting (1.91% vs 1.73%, \( P = 0.07 \)) observed during “maintenance” with the LFW enabled is in keeping with clinical practice and the longer time constant and higher vaporizer settings needed to overcome the greater dilution of the inspired gas by the correspondingly expected greater rebreathing of the expired gases in the lower flow condition. This observation is reassuring because the LFW is not intended to supplant good clinical judgment or careful monitoring of inspired and end-tidal drug concentrations. The fact that participants on average increased their vaporizer settings to maintain a safe anesthetic depth with lower flows suggests that they understood the information the LFW was providing and that they did not let it distract them from more fundamental anesthetic care.

The use of identical patient simulator scenarios provided an opportunity for a basic cost-minimization analysis. Using point estimates for median liquid drug consumption rate during maintenance of 16.21 mL/h without the LFW vs 8.08 mL/h with the LFW, and a median drug consumption during induction of 4.0 mL with or without the LFW, we estimated the cost savings for an average procedure length of 2.5 hours (assuming 15 minutes of induction/equilibration and 2.25 hours of maintenance). A total of 40.5 mL isoflurane would be used without the LFW vs 22.2 mL with the LFW. With isoflurane at $10 per 100 mL bottle, the costs would be $4.05 vs $2.22 for similar outcomes. Applying these calculations to the limits of the bootstrap 95% CI for the difference in median drug consumption (4.76–10.97), estimated cost savings range from a low of $1.07 to a high of $2.47.

Costs associated with an equivalent anesthetic using desflurane were estimated, based on 1.0 MAC of desflurane having a drug concentration 5.22 times higher than 1.0 MAC of isoflurane and 1 mL liquid desflurane producing 7.2% more vapor volume than 1 mL liquid isoflurane. For the same 2.5-hour procedure, an estimated 197 mL liquid desflurane would be consumed without the LFW and 108 mL with the LFW. With desflurane at $151 per 240 mL bottle, the cost would be $240.00 (without LFW) vs $67.95 (with LFW). Applied to the limits of the 95% CI the estimated cost savings range from a low of $32.81 to a high of $56.05 per average procedure using desflurane. For the same 2.5-hour procedure using desflurane can reach substantial values even if administered as part of a fraction of the 200 million total anesthetics. Even with the cost of desflurane declining after generic products arrive in the U.S. market, the major environmental impact of venting an excess 18.7 L desflurane vapor (assuming 209.7 mL vapor from 1 mL liquid) into the atmosphere per average procedure is a pressing concern. Our poststudy survey data suggest that many of the anesthesia providers involved in this study consider 2 L/min to be a “default” FGF setting which may be due in part to out of context fears about compound A, even when the drug used was isoflurane. As all of our simulation exercises were conducted with isoflurane and not sevoflurane, this suggests that FGF habits from using sevoflurane, which is routinely used in our institution, can carry over to other drugs for which compound A is not as relevant. This carry over behavior may also become more archaic and wasteful as CO2 absorbents that produce little or no compound A (because they have zero or greatly reduced amounts of KOH and NaOH) become commonplace. These new CO2 absorbent materials offer an FGF rate independent solution to compound A fears, and thus legacy habits about FGF rates for sevoflurane should occur under the same waste prevention scrutiny as with other drugs.

If anesthesia providers consider saving drug important and also routinely think about decreasing their flows, this would seem to indicate that FGF is routinely higher than necessary because many anesthesia providers are unsure of how low they can decrease their FGF. The questionnaire provided more support for this notion with 14 of 15 participants agreeing that they would be more comfortable using lower flows if they had a monitor indicating that they could safely go lower. Our study design limits our ability to make causal inferences (i.e., small sample, no control groups). While increased vaporizer settings with the LFW enabled and survey answers are suggestive, we have no way of knowing directly whether the information content of the LFW helped users decrease their FGF or simply acted as a visible reminder to practice drug-conservative anesthesia. We consider it likely that both factors play a role in the measured effect of reduced drug consumption.

**Conclusion**

The results of this simulation study revealed a significant reduction in maintenance FGF and thus volatile drug consumption during a simulated anesthetic when the Dräger LFW is present. Participants agreed that objective information and monitoring of breathing circuit gases help them feel more confident in reducing flows when patient care permitted. Others have reported similar decreases in drug consumption using different devices that provide anesthetic flow information. In summary, our results suggest that additional information and a continuous reminder to optimize flows, like that provided to anesthesia providers from the LFW, can have a significant impact on reducing the cost of drugs to an anesthesia department or practice and also the negative environmental impacts associated with venting excess volatile drugs into the atmosphere.

**DISCLOSURES**

Name: Isaac Luria, MS.

Contribution: This author helped design and conduct the study, analyze the data, and write the manuscript.
Attestation: Isaac Luria has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

Conflicts of Interest: The author has no conflicts of interest to declare.

Name: Samsun Lampotang, PhD.
Contribution: This author helped design the study, analyze the data, and write the manuscript.
Attestation: Samsun Lampotang has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.

Conflicts of Interest: Samsun Lampotang received royalties from Medical Education Technologies Inc. Royalties are collected on sales of the METI Human Patient Simulator, the one used in this study.

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Conflicts of Interest: The author has no conflicts of interest to declare.

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Attestation: Nikolaus Gravenstein has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.

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