

# Reducing Variation in the Use of Inhaled Nitric Oxide

**AUTHORS:** Janet M. Simsic, MD,<sup>a</sup> Sheilah Harrison, CPHQ,<sup>b</sup> Laura Evans, RRT-NPS,<sup>c</sup> Richard McClead, MD,<sup>b</sup> and Douglas Teske, MD<sup>a</sup>

<sup>a</sup>The Heart Center, <sup>b</sup>Department of Quality Improvement Services, and <sup>c</sup>Department of Respiratory Therapy, Nationwide Children's Hospital, Columbus, Ohio

## KEY WORDS

congenital heart disease, guidelines, inhaled nitric oxide, outcomes, pulmonary hypertension, quality improvement

## ABBREVIATIONS

CTICU—cardiothoracic ICU

IHI—Institute of Healthcare Improvement

iNO—inhaled nitric oxide

SMART—specific, measurable, achievable, realistic, timely

Dr Simsic contributed to the concept and design, supported the quality initiative, conducted the initial and continued analyses, and wrote the first draft and all revisions; Ms Harrison and Dr McClead conceptualized, designed, and instituted the quality initiative, conducted the initial and continued analyses, and reviewed and revised the manuscript; Ms Evans conceptualized, designed, and instituted the quality initiative, conducted the initial analysis, and reviewed and revised the manuscript; Dr Teske contributed to the concept and design as well as supported the quality initiative, conducted the initial and continued analyses, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

[www.pediatrics.org/cgi/doi/10.1542/peds.2013-4011](http://www.pediatrics.org/cgi/doi/10.1542/peds.2013-4011)

doi:10.1542/peds.2013-4011

Accepted for publication Jan 29, 2014

Address correspondence to Janet M. Simsic, MD, The Heart Center, T2292, Nationwide Children's Hospital, 700 Children's Dr, Columbus, OH 43205. E-mail: [janet.simsic@nationwidechildrens.org](mailto:janet.simsic@nationwidechildrens.org)

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2014 by the American Academy of Pediatrics

**FINANCIAL DISCLOSURE:** The authors have indicated they have no financial relationships relevant to this article to disclose.

**FUNDING:** No external funding.

**POTENTIAL CONFLICT OF INTEREST:** The authors have indicated they have no potential conflicts of interest to disclose.

## abstract

**BACKGROUND AND OBJECTIVE:** Decreasing practice variation and following clinical guidelines improve patient outcomes and reduce costs. Inhaled nitric oxide (iNO) is an effective but expensive treatment of pulmonary hypertension and right heart failure in patients with congenital or acquired heart disease. Our objective was to implement standardized initiation and weaning guidelines for iNO usage in the cardiothoracic ICU (CTICU) to reduce variation in use while maintaining quality patient care.

**METHODS:** All CTICU patients who received iNO from January 2011 to December 2012 were retrospectively reviewed. Standardized iNO initiation and weaning guidelines were implemented in January 2012. Variables before and after guideline implementation were compared.

**RESULTS:** From January to December 2011, there were 36 separate iNO events (6% of CTICU admissions;  $n = 547$ ). Mean  $\pm$  SD iNO usage per event was  $159 \pm 177$  hours (median: 63 hours; range: 27–661 hours). From January to December 2012, there were 47 separate iNO events (8% of CTICU admissions;  $n = 554$ ). Mean iNO usage per event was  $125 \pm 134$  hours (median: 72 hours; range: 2–557 hours). Initiation guideline compliance improved from 83% to 86% ( $P = .9$ ); weaning guideline compliance improved from 17% to 79% ( $P < .001$ ). Although mean iNO usage per event decreased, there was no significant reduction in utilization of iNO ( $P = .09$ ).

**CONCLUSIONS:** Implementation of standardized iNO initiation and weaning guidelines in the CTICU was successful in reducing practice variation supported by increasing guideline compliance. However, decreasing practice variation did not significantly reduce iNO utilization and does not necessarily reduce cost. *Pediatrics* 2014;133:e1753–e1758

Clinical practice guidelines have been touted as methods to reduce practice variation, improve quality of care, and contain cost.<sup>1</sup> Guidelines require re-design of work processes, communication strategies, and infrastructure, as well as sustained measurement and vigilance. According to the Institute of Healthcare Improvement (IHI) strategy for designing systems, the first step is to create a simple, standardized approach or guideline that is minimally controversial.<sup>2</sup> The second step is to evaluate adherence to the guideline. The next steps use strategies of standard order sets, checklists, education, and training. Once the standardized process is in place, compliance is reviewed to identify failures to use the process to help identify barriers and understand the failures. This process leads to improvement of the guidelines. Inhaled nitric oxide (iNO) is an effective but expensive treatment of pulmonary hypertension and right heart failure in patients with congenital or acquired heart disease. Pulmonary hypertension may be due to increased flow, increased resistance, or a combination of the 2 factors.<sup>3</sup> Examples of congenital cardiac defects associated with pulmonary hypertension after cardiac surgery include atrioventricular canal defects, total anomalous pulmonary venous return, truncus arteriosus, aortopulmonary window, and double outlet right ventricle. Pulmonary hypertension is a process of pathologic changes to the pulmonary vascular bed, including vasoconstriction, vascular remodeling, endothelial dysfunction, and thrombus formation. Postoperative pulmonary hypertension has been associated with longer duration of mechanical ventilation, ICU stay, and hospital stay.

iNO is a selective pulmonary vasodilator that diffuses across the alveolar-capillary membrane into the pulmonary artery smooth muscle, resulting in local vasodilation.<sup>3,4</sup> It reduces vascular tone by

activating soluble guanylate cyclase, which converts guanosine triphosphate into cyclic guanosine monophosphate. Increased intracellular concentrations of cyclic guanosine monophosphate relax the smooth muscle of the pulmonary vessels. iNO has few effects on the systemic vasculature.

Review of iNO utilization in the cardiothoracic ICU (CTICU) of our institution revealed inconsistency in the starting dose of iNO, inconsistency in the timely discontinuation of iNO when not clinically effective, and inconsistency in the method of weaning of iNO. These issues led to a quality initiative to create standardized guidelines for iNO initiation and weaning. We used the IHI strategy to develop experience-based guidelines for initiation and weaning of iNO in the CTICU. Our objective was to implement standardized initiation and weaning guidelines for iNO usage in the CTICU to reduce variation in use while maintaining quality patient care.

## METHODS

### Ethical Issues

This quality improvement work involved development of experience-based guidelines for initiation and weaning of iNO in the CTICU. No interventions involved comparison of multiple devices or therapies, and patients were not subjected to randomization. Medical records were accessed by quality improvement team members as part of their normal responsibilities. No personal health information was shared outside of our institution. Therefore, a waiver for consent for this study was provided by the institutional review board at our institution.

### Setting

Nationwide Children's Hospital is an academic, nonprofit, freestanding children's hospital located in Columbus, Ohio. The CTICU is a 20-bed unit with

>500 admissions per year. Its current electronic medical record system (Epic Systems Incorporated, Verona, WI) and computerized practitioner order entry system are fully integrated with clinical decision support.

### Planning the Intervention

Retrospective review of all patients in the CTICU who received iNO therapy in 2011 revealed inconsistencies in the following: the starting dose of iNO, the timely discontinuation of iNO when not clinically effective, and the method of weaning iNO. These issues led to a quality initiative to develop and implement standardized guidelines for iNO initiation and weaning.

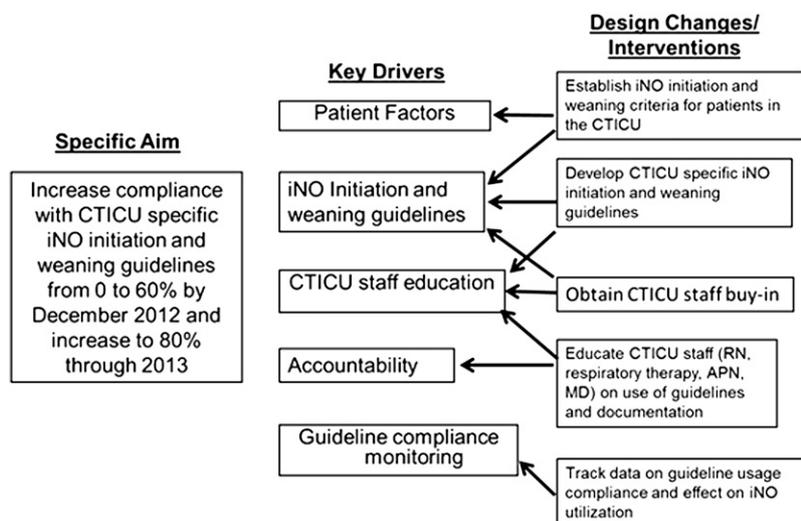
We began by creating a SMART (specific, measurable, achievable, realistic, timely)-specific objective statement and key driver diagram<sup>2</sup> (Fig 1). Patient factors, lack of guidelines, staff education, staff accountability, and measurable outcome were identified as our key drivers.

### Intervention

The interventions or process changes that were introduced included establishment of patient criteria for iNO initiation that were simple and minimally controversial; development of standardized initiation and weaning guidelines for iNO that were also simple and minimally controversial; creation of electronic medical record SMART phrases for the initiation and weaning guidelines to simplify use; education and training of the CTICU staff regarding the guidelines and goals; obtaining CTICU staff buy-in and accountability; and development of outcome and compliance measures. Standardized initiation and weaning guidelines were implemented in January 2012 (Table 1).

### Method of Evaluation and Analysis

Data on guideline usage compliance and effect on iNO utilization were tracked. We used a Plan-Do-Study-Act cycle to review



**FIGURE 1** Key driver diagram. APN, advanced practical nurse; MD, medical doctor; RN, registered nurse.

guideline compliance. Compliance was initially measured by searching for physician documentation of iNO initiation and weaning in the physician progress notes in the electronic medical record. After the first quarter following implementation, we found that physician documentation in the medical record was lacking with respect to justification for weaning or not weaning. iNO weaning remained inconsistent and difficult to track. Therefore, we shared these findings with the CTICU staff and reeducated them on the importance of the guidelines and the SMART phrases developed for our electronic medical record system to facilitate usage of the guidelines.

We also altered the way we tracked compliance. Instead of measuring documentation of iNO initiation and weaning justification or plan in the physician progress notes, we elected to track the usage of the iNO initiation and weaning SMART phrases in our electronic medical record. This method was a more consistent and easily obtainable plan of tracking compliance with initiation and weaning guidelines.

**Statistical Analysis**

Retrospective review of iNO usage and outcome variables was performed with

comparison of patients from 2011 (before the standardization guidelines) and from 2012 (after the standardization guidelines). Data are expressed as mean ± SDs; median and interquartile ranges are also supplied where appropriate. Statistical analysis was performed by using Fisher's exact test or  $\chi^2$  tests where appropriate. Statistical significance was defined as a *P* value < .05.

**RESULTS**

Overall trend in iNO utilization over time is displayed as a run chart in Figure 2. Shortly after guideline implementation, our baseline mean iNO hours per event decreased, although this change was not statistically significant (*P* = .09). There were still outliers; however, they were less frequent postguideline implementation. We were able to sustain our new baseline with continued staff engagement and routine e-mails updating progress and outcomes.

**Patients**

Patient characteristics were similar before and after guideline implementation and are shown in Table 2. Overall, more than one-half of our patients who underwent ventricular assist device

placement were treated with iNO therapy postprocedure to decrease right ventricular afterload and improve right ventricular function. Twenty-five percent of our patients were treated with iNO after comprehensive stage II palliation (bidirectional Glenn shunt and Norwood arch reconstruction) for cyanosis. One-third of our patients with atrioventricular septal defects were treated with iNO therapy postoperatively. In 2012, seven patients with human rhinovirus were treated with iNO. (Of note, the test for human rhinovirus only became available in our institution in 2012.)

**Compliance**

Initiation guideline compliance improved from 83% to 86%. This change was not a significant increase because most of the CTICU staff already had indicated buy-in regarding patient and clinical scenarios in which iNO may be useful. Once the literature was reviewed, there was also a buy-in regarding the recommended starting dose of iNO (20 ppm). Weaning guideline compliance improved from 17% to 79% after the Plan-Do-Study-Act cycle, staff reengagement, education, and alteration of the compliance tracking method. CTICU practitioners were more apt to use the SMART phrases developed for our electronic medical record once the practitioners were shown the inconsistency in the timely discontinuation of iNO when not clinically effective and the inconsistency in the method of weaning iNO. In-depth review of fourth quarter weaning compliance data demonstrates that the most frequent reason for noncompliance was weaning faster than guidelines would indicate.

**DISCUSSION**

High health care costs, practice variation, and demands for quality medical care have stimulated health professionals to develop practice

**TABLE 1** Patient Clinical Criteria for Initiation of iNO Trial and Standardized Initiation and Weaning Guidelines Implemented in January 2012

---

Two-ventricle patients (1 of the following)

- Evidence of pulmonary hypertension or elevated pulmonary vascular resistance defined by 1 of the following: (1) estimated right ventricular pressure according to ECHO of >50%; or (2) right to left shunting at atrial septum
- Right ventricular dysfunction defined by 1 of the following: (1) moderate to severe right ventricular dysfunction according to ECHO; or (2) elevated central venous pressure >12 mm Hg
- Disease process with V/Q mismatch defined by systemic saturations <88% on 100% FiO<sub>2</sub>
- Reperfusion injury defined by using Pao<sub>2</sub>/FiO<sub>2</sub> ratio <150 to 200 and radiographic infiltrates

Single-ventricle patients (1 of the following)

- Concerns for pulmonary hypertension or elevated pulmonary vascular resistance defined by any of the following: (1) Pao<sub>2</sub> <35; (2) systemic saturations <70% on 100% FiO<sub>2</sub>; (3) bidirectional Glenn pressure >15 mm Hg; (4) mean pulmonary artery pressure >15 mm Hg; or (5) transpulmonary gradient (mean pulmonary artery pressure – left atrial pressure) >8 mm Hg

Initiation of iNO

- Obtain baseline blood gas, vital signs, systemic saturation, cerebral oximetry, and methemoglobin
- Start iNO at 20 ppm
- Obtain blood gas, vital signs, cerebral oximetry, and systemic saturations in 30 minutes. If systemic saturations, cerebral oximetry, or Pao<sub>2</sub> do not improve by >10%, discontinue iNO; trial unsuccessful/patient did not respond
- If systemic saturations or Pao<sub>2</sub> improve by >10%, continue iNO
- Monitor blood gases minimum of once daily while on iNO
- Monitor methemoglobin every day while on iNO. If methemoglobin >5%, wean iNO. Monitor nitrogen dioxide levels; if >3%, wean iNO
- Wean FiO<sub>2</sub> to <50%, maintaining acceptable blood gas and systemic saturation parameters per APN or MD

Weaning guidelines

- For patients on iNO secondary to right heart failure, criteria for weaning will be at the discretion of APN or MD
- For all other patients, criteria for weaning (FiO<sub>2</sub> at <50% with acceptable blood gas or systemic saturations per parameter) provided by APN or MD
- iNO weaning attempt must occur daily if patient meets criteria for weaning or weaning guideline. Reason for not weaning must be documented in the chart if patient meets parameters and is not weaned

Weaning

- Obtain baseline blood gas (if appropriate, per MD or APN order), vital signs, and systemic saturation before iNO weaning
- Wean iNO by 50% every 4 to 6 hours until reaching 5 ppm; then wean by 1 ppm every 4 to 6 hours until off
- Monitor vital signs and systemic saturation 30 minutes after each wean attempt
- Continue to wean to off as long as systemic saturations are within acceptable parameters provided by the APN or MD
- If systemic saturations are not within parameters, notify APN or MD

---

APN, advance practice nurse; FiO<sub>2</sub>, fraction of inspired oxygen; MD, medical doctor; ECHO, Echocardiogram.

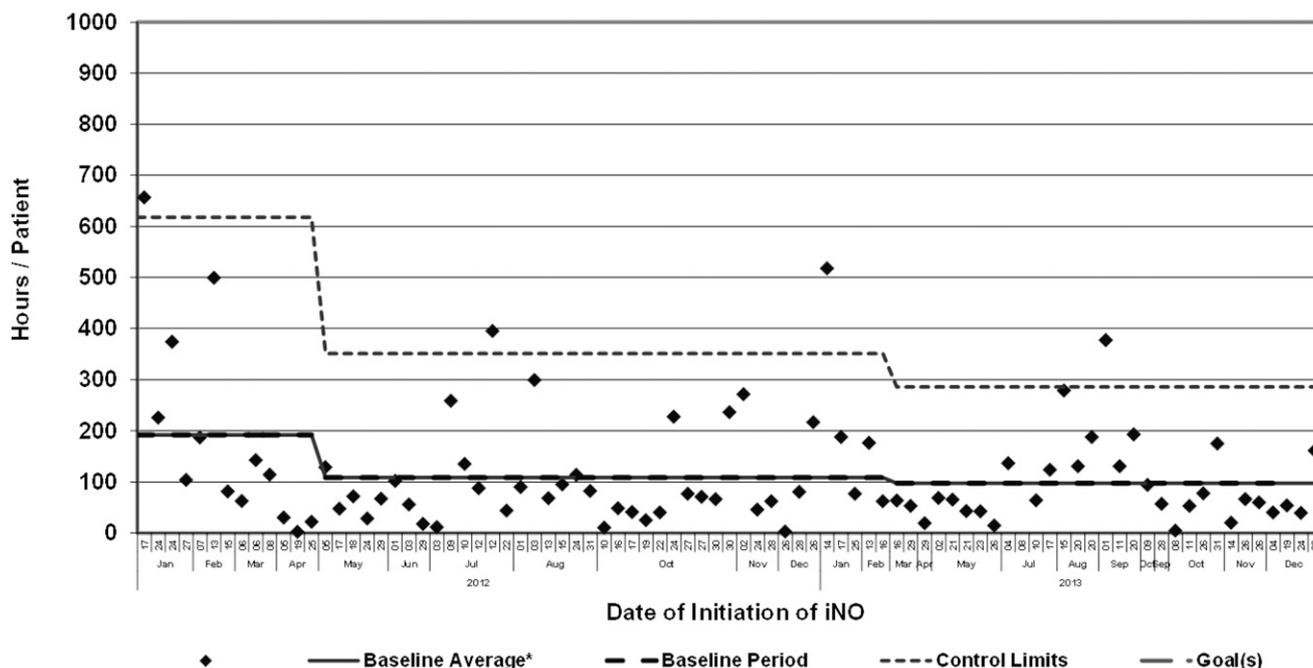
guidelines.<sup>5</sup> Practice guidelines are systematically developed statements intended to assist with decisions regarding appropriate care for certain medical situations.<sup>6</sup> These guidelines are intended to improve decision-making and optimize patient outcomes while reducing costs.<sup>1</sup> iNO is an effective but expensive treatment of pulmonary hypertension and right heart failure in patients with congenital or acquired heart disease. Our objective was to implement standardized initiation and weaning guidelines for iNO usage in the CTICU to reduce variation in use while maintaining quality patient care.

Our initiation and weaning guidelines were based on evidence from the literature. iNO therapy in pediatric patients after surgery for congenital heart disease has been reported in a variety of clinical trials, including case reports, pilot studies, prospective and retrospective investigations, randomized controlled clinical studies, and crossover studies.<sup>3,7–18</sup> The recommended dose of iNO is 20 ppm for the approved indication of hypoxic respiratory failure associated with pulmonary hypertension in term and near-term neonates.<sup>3,19</sup> iNO may also be beneficial in patients with right ventricular dysfunction because it

selectively decreases right ventricular afterload and improves right ventricular function.<sup>20</sup> Abrupt withdrawal from iNO may lead to rebound pulmonary hypertension, secondary to down-regulation of endogenous nitric oxide production and increased levels of endothelin-1, a potent vasoconstrictor.<sup>21,22</sup> In pediatric patients who failed to be weaned from iNO after surgery for congenital heart disease, sildenafil has been shown to facilitate weaning.<sup>23</sup>

Our first step toward obtaining CTICU staff buy-in for iNO initiation and weaning guidelines was review of the patients and iNO usage from the previous year. The inconsistent initiation and weaning (or not weaning) was obvious. The awareness of CTICU practitioner variation in usage of iNO, coupled with a hospital-wide initiative to reduce variation of iNO usage in all units, improved individual practitioner buy-in and accountability. This improvement was reinforced by periodic review of usage, patient outcomes, and compliance throughout the year at staff meetings and via e-mail communications. With 8 CTICU physicians, it became obvious who was and was not using the guidelines consistently, and individual coaching was at times necessary.

The patients who received iNO in 2011 and 2012 were similar in terms of overall number (percentage of total CTICU admissions), number of post-operative patients, categorization according to underlying heart disease, and mortality to hospital discharge. We believe this similarity supports our continued delivery of quality patient care despite reducing variation and utilization. The 2 major differences in the patients who received iNO in 2011 and 2012 were age and human rhinovirus infection. The patients in 2012 were older than the patients in 2011. We surmise this is secondary to our case mix, with increasing numbers of heart and lung transplant patients and our



**FIGURE 2** Run chart of individual iNO hours per event hours from January 2011 to December 2012.

**TABLE 2** Comparison of Patient Characteristics Before and After Institution of Standardized Guidelines for Initiation and Weaning of iNO

Characteristic	January 2011	December 2012	P Value
CTICU admissions	547	554	
No. of iNO events (% of total admissions)	36 (6%)	47 (8%)	.3
Age, mean ± SD (range), mo	15 ± 42 (0.1–228)	44 ± 91 (0.1–444)	<.001
Postoperative patients	30 (83%)	35 (74%)	.4
Cardiac defect			
Single ventricle, normal arch	6 (18%)	9 (22%)	.9
Single ventricle, abnormal arch	9 (26%)	8 (20%)	.4
Two ventricle, normal arch	17 (50%)	22 (53%)	.9
Two ventricle, abnormal arch	2 (6%)	2 (5%)	.9
Mean ± SD hours of iNO per event (median; interquartile range)	159 ± 177 (63; 27–661)	126 ± 136 (72; 2–557)	.1
Mortality to hospital discharge	26%	12%	.3

screening process for human rhinovirus in which high-risk patients, defined as those with single-ventricle physiology or atrioventricular septal defects, were screened preoperatively and cardiac surgery postponed if positive for human rhinovirus.

Average nitric oxide utilization (in hours) per event decreased in 2012. Initiation of iNO was not a significant issue after review of the literature and agreement that 20 ppm was the recommended starting dosage. Most practitioners agreed up front with the clinical indications for therapy. Indications for

continued treatment and weaning guidelines provided a consistent method of defining response to iNO and providing a consistent method of weaning for both responders and nonresponders, as well as accountability for weaning when meeting criteria, thus eliminating past issues that may have slowed down the weaning process. In fact, the most common cause for noncompliance with the weaning guidelines at the end of 2012 was weaning too fast rather than not weaning.

This study did have some limitations. They included a small patient population

and patient heterogeneity. Only 6% of our total CTICU patient population received iNO therapy. This quality initiative involves only a single, free-standing children’s hospital system. Limitations also include those inherent to any retrospective data review.

Key components that we believe contributed to our successful process include involving a multidisciplinary team to question and explore our current practice variability; developing and implementing simple guidelines to reduce variation and change the practice pattern; holding appropriate staff accountable for implementation and outcomes; monitoring to ensure the intervention was successful; and sharing the results with the staff of the CTICU.

Based on our compliance data, one of the reasons for noncompliance with the guidelines is the physician desire to wean faster than the guideline recommendations. Therefore, our next step is to reevaluate our weaning guidelines and adjust our weaning frequency to allow for a more flexible weaning strategy if warranted.

## CONCLUSIONS

Implementation of standardized initiation and weaning guidelines for iNO in

the CTICU was successful in reducing variation in iNO usage and overall CTICU iNO utilization (from a mean of  $159 \pm$

177 hours per event to  $126 \pm 136$  hours per event) while maintaining quality patient care.

## REFERENCES

1. Berg M. Problems and promises of the protocol. *Soc Sci Med.* 1997;44(8):1081–1088
2. Institute for Healthcare Improvement. How to Improve - Improvement Methods at: [www.ihl.org/IHI/Topics/Improvement/ImprovementMethods/HowToImprove/](http://www.ihl.org/IHI/Topics/Improvement/ImprovementMethods/HowToImprove/)
3. Checchia PA, Bronicki RA, Goldstein B. Review of inhaled nitric oxide in the pediatric cardiac surgery setting. *Pediatr Cardiol.* 2012;33(4):493–505
4. Ichinose F, Roberts JD Jr, Zapol WM. Inhaled nitric oxide: a selective pulmonary vasodilator: current uses and therapeutic potential. *Circulation.* 2004;109(25):3106–3111
5. Institute of Medicine. *Guidelines for Clinical Practice: From Development to Use.* Washington, DC: National Academies Press; 1992
6. Woolf SH. Practice guidelines: a new reality in medicine. I. Recent developments. *Arch Intern Med.* 1990;150(9):1811–1818
7. Beghetti M, Habre W, Friedli B, Berner M. Continuous low dose inhaled nitric oxide for treatment of severe pulmonary hypertension after cardiac surgery in paediatric patients. *Br Heart J.* 1995;73(1):65–68
8. Curran RD, Mavroudis C, Backer CL, Sautel M, Zales VR, Wessel DL. Inhaled nitric oxide for children with congenital heart disease and pulmonary hypertension. *Ann Thorac Surg.* 1995;60(6):1765–1771
9. Day RW, Hawkins JA, McGough EC, Crezéé KL, Orsmond GS. Randomized controlled study of inhaled nitric oxide after operation for congenital heart disease. *Ann Thorac Surg.* 2000;69(6):1907–1912, discussion 1913
10. Göthberg S, Edberg KE. Inhaled nitric oxide to newborns and infants after congenital heart surgery on cardiopulmonary bypass. A dose-response study. *Scand Cardiovasc J.* 2000;34(2):154–158
11. Haydar A, Malhere T, Mauriat P, et al. Inhaled nitric oxide for postoperative pulmonary hypertension in patients with congenital heart defects. *Lancet.* 1992;340(8834–8835):1545
12. Journois D, Pouard P, Mauriat P, Malhère T, Vouhé P, Safran D. Inhaled nitric oxide as a therapy for pulmonary hypertension after operations for congenital heart defects. *J Thorac Cardiovasc Surg.* 1994;107(4):1129–1135
13. Journois D, Baufreton C, Mauriat P, Pouard P, Vouhé P, Safran D. Effects of inhaled nitric oxide administration on early postoperative mortality in patients operated for correction of atrioventricular canal defects. *Chest.* 2005;128(5):3537–3544
14. Miller OI, Tang SF, Keech A, Pigott NB, Beller E, Celermajer DS. Inhaled nitric oxide and prevention of pulmonary hypertension after congenital heart surgery: a randomised double-blind study. *Lancet.* 2000;356(9240):1464–1469
15. Morris K, Beghetti M, Petros A, Adatia I, Bohn DF. Comparison of hyperventilation and inhaled nitric oxide for pulmonary hypertension after repair of congenital heart disease. *Crit Care Med.* 2000;28(8):2974–2978
16. Russell IA, Zwass MS, Fineman JR, et al. The effects of inhaled nitric oxide on postoperative pulmonary hypertension in infants and children undergoing surgical repair of congenital heart disease. *Anesth Analg.* 1998;87(1):46–51
17. Shimpo H, Mitani Y, Tanaka J, et al. Inhaled low-dose nitric oxide for postoperative care in patients with congenital heart defects. *Artif Organs.* 1997;21(1):10–13
18. Wessel DL, Adatia I, Giglia TM, Thompson JE, Kulik TJ. Use of inhaled nitric oxide and acetylcholine in the evaluation of pulmonary hypertension and endothelial function after cardiopulmonary bypass. *Circulation.* 1993;88(5 Pt 1):2128–2138
19. INOmax [package insert]. Clinton, NJ: INO Therapeutics; 2010
20. Fullerton DA, Jones SD, Jagggers J, Piedalua F, Grover FL, McIntyre RC Jr. Effective control of pulmonary vascular resistance with inhaled nitric oxide after cardiac operation. *J Thorac Cardiovasc Surg.* 1996;111(4):753–762, discussion 762–763
21. Miller OI, Tang SF, Keech A, Celermajer DS. Rebound pulmonary hypertension on withdrawal from inhaled nitric oxide. *Lancet.* 1995;346(8966):51–52
22. Pearl JM, Nelson DP, Raake JL, et al. Inhaled nitric oxide increases endothelin-1 levels: a potential cause of rebound pulmonary hypertension. *Crit Care Med.* 2002;30(1):89–93
23. Lee JE, Hillier SC, Knoderer CA. Use of sildenafil to facilitate weaning from inhaled nitric oxide in children with pulmonary hypertension following surgery for congenital heart disease. *J Intensive Care Med.* 2008;23(5):329–334

## Reducing Variation in the Use of Inhaled Nitric Oxide

Janet M. Simsic, Sheilah Harrison, Laura Evans, Richard McClead and Douglas Teske

*Pediatrics* 2014;133:e1753

DOI: 10.1542/peds.2013-4011 originally published online May 12, 2014;

<b>Updated Information &amp; Services</b>	including high resolution figures, can be found at: <a href="http://pediatrics.aappublications.org/content/133/6/e1753">http://pediatrics.aappublications.org/content/133/6/e1753</a>
<b>References</b>	This article cites 20 articles, 2 of which you can access for free at: <a href="http://pediatrics.aappublications.org/content/133/6/e1753#BIBL">http://pediatrics.aappublications.org/content/133/6/e1753#BIBL</a>
<b>Subspecialty Collections</b>	This article, along with others on similar topics, appears in the following collection(s): <b>Critical Care</b> <a href="http://www.aappublications.org/cgi/collection/critical_care_sub">http://www.aappublications.org/cgi/collection/critical_care_sub</a> <b>Administration/Practice Management</b> <a href="http://www.aappublications.org/cgi/collection/administration:practice_management_sub">http://www.aappublications.org/cgi/collection/administration:practice_management_sub</a> <b>Quality Improvement</b> <a href="http://www.aappublications.org/cgi/collection/quality_improvement_sub">http://www.aappublications.org/cgi/collection/quality_improvement_sub</a>
<b>Permissions &amp; Licensing</b>	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://www.aappublications.org/site/misc/Permissions.xhtml">http://www.aappublications.org/site/misc/Permissions.xhtml</a>
<b>Reprints</b>	Information about ordering reprints can be found online: <a href="http://www.aappublications.org/site/misc/reprints.xhtml">http://www.aappublications.org/site/misc/reprints.xhtml</a>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



# PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## **Reducing Variation in the Use of Inhaled Nitric Oxide**

Janet M. Simsic, Sheilah Harrison, Laura Evans, Richard McClead and Douglas Teske

*Pediatrics* 2014;133:e1753

DOI: 10.1542/peds.2013-4011 originally published online May 12, 2014;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/133/6/e1753>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2014 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

