VON Grand Rounds

Evidence to Practice: Oxygen in the NICU

August 6th, 2025

Vermont Oxford NETWORK

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2025 VON Grand Rounds Date: 08/6/2025

Planners: Roger Soll MD; Denise Zayack RN, MPH; Danielle Ehret MD, MPH; Debra Sims PhD, RNC-NIC

Speaker(s): Roger Soll MD, Danielle Ehret MD, MPH, Wendy Timpson MD

Purpose Statement/Goal of this Activity: Review of evidence, summary of current practice guidelines, synthesis of evidence in practice and interactive discussion with expert faculty – Oxygen Therapy

The following have relevant financial relationships with ineligible companies (all have been mitigated):
None

All other speakers/planners/CMIE reviewers do not have any relevant financial relationships.

This activity did not receive any support for ineligible companies (grants or in-kind).

All recommendations involving clinical medicine made during this talk were based on evidence that is accepted within the profession of medicine as adequate justification for their indication and contradictions in the care of patients.

In support of improving patient care, this activity ahs been planned and implemented by The Robert Larner College of Medicine at the University of Vermont and Vermont Oxford Network. The University of Vermont is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialling Center (ANCC), to provide continuing education for the healthcare team.

The University of Vermont designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extend of their participation in the activity.

This program has been reviewed and is acceptable for up to 1.0 Nursing Contact Hours.

This activity was planned by and for the healthcare team, and learners will receive 1 Interprofessional Continuing Education (IPCE) credit for learning and change.

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Moderators

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Roger F. Soll, MD
H. Wallace Professor of Neonatology,
University of Vermont
Coordinating Editor, Cochrane Neonatal
Director, VON Institute for Evidence Based Practice, Vermont Oxford Network

Danielle Ehret, MD, MPH
Asfaw Yemiru Green and Gold Professor,
University of Vermont
Chief Medical Officer, Director, Global Health,
Vermont Oxford Network

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Discussants

Vermont Oxford NETWORK

Wendy L. Timpson, MD. MEd
Associate Professor of Pediatrics
Clinical Chief, Neonatology Division
UMass Chan Medical School. UMass Memorial Medical Center
Worcester, MA

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Evidence to Practice: Eat, Sleep, Console

Disclosures

Danielle Ehret MD, MPH is the Director of Global Health and Chief Medical Officer at Vermont Oxford Network (VON) and receives salary support to UVM for non-clinical time dedicated to her leadership roles.

Roger F. Soll, MD is the H. Wallace Professor of Neonatology at the Larner College of Medicine at the University of Vermont, Vice President of the Vermont Oxford Network, Director of the VON Institute for Evidence Based Practice, and Coordinating Editor of Cochrane Neonatal.

Wendy L. Timpson, MD. Med is Associate Professor of Pediatrics and Clinical Chief, Neonatology Division at the UMass Chan Medical School, UMass Memorial Medical Center. She has no relevant financial issues to disclose.

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How to Participate in Today's Webinar

- Chat questions and comments to "Everyone" during the presentations and discussion.
- Use Poll Everywhere to answer questions posed during the session. Please do not respond to polls in the Chat.

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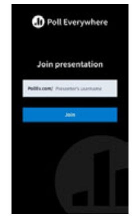
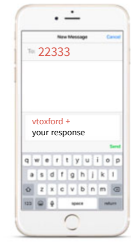
Three ways to use Poll Everywhere

Option 1: Web
Go to "pollev.com/vtoxford"

Option 2: App
Poll Everywhere app: Enter username "vtoxford" and click "Join".



Option 3: Text
Text "vtoxford" to 22333, then send your response.



Please do not respond to polls in the Chat.

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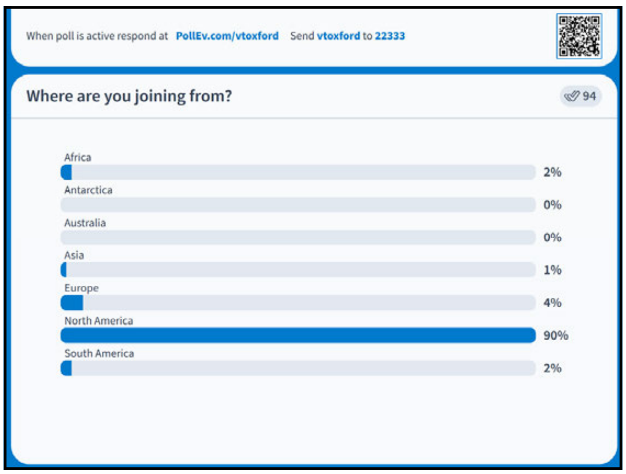

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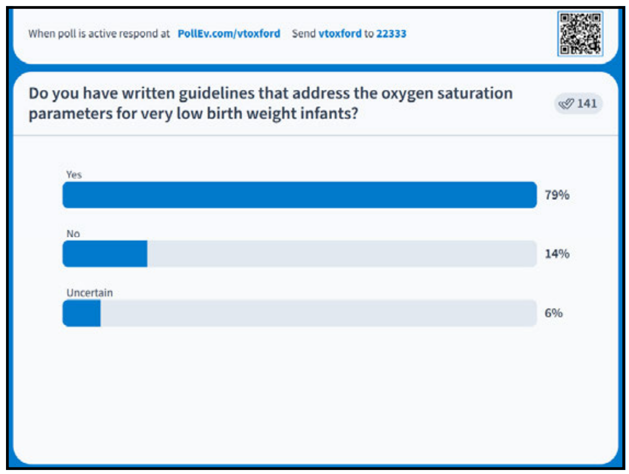

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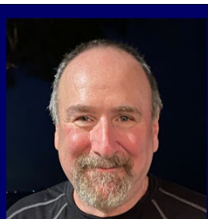

Evidence to Practice: Oxygen in the NICU

Roger F. Soll, MD
H. Wallace Professor of Neonatology, University of Vermont
Coordinating Editor, Cochrane Neonatal
Director, VON Institute for Evidence Based Practice, Vermont Oxford Network

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Cochrane Neonatal

Oxygen in the NICU

We will review the evidence from randomized trials and meta-analyses and discuss the different approaches that teams around the world are using regarding the use of oxygen in critically ill preterm infants

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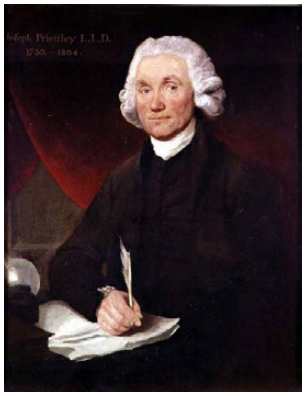

Joseph Priestley
(1733–1804)

Reported the discovery of oxygen and described some of its extraordinary properties

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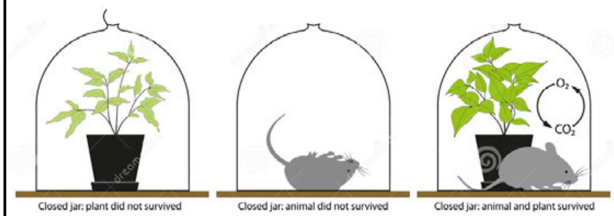
Priestley's experiment



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Neonatology
Fetal and Neonatal Research

Oxygen was used in neonatal resuscitation from 1780… within 5 years of its detection.

It rapidly gained general acceptance and infiltrated delivery rooms and, a century later, neonatal special care units.

After 217 years without scientific evidence, the use of oxygen for neonatal resuscitation has recently been questioned.

Obladen M. History of neonatal resuscitation. Part 2: oxygen and other drugs. Neonatology. 2009;95(1):91-6. doi: 10.1159/000151761.

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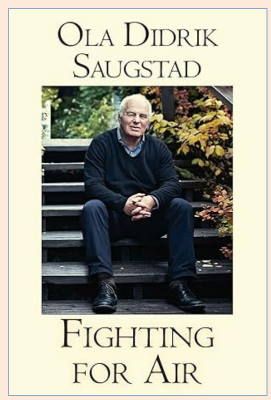

Saugstad demonstrated that hypoxanthine, a purine metabolite, accumulates during hypoxia.

Introducing oxygen in the aftermath of hypoxia could lead to an explosive generation of oxygen-free radicals.

These studies represent the basis for understanding the hypoxia–reoxygenation or ischemia-reperfusion injury that has puzzled medicine far beyond neonatology.

Saugstad 2010

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Oxygen in the Preterm Infant

"In the 1940s, Wilson and colleagues observed that periodic breathing in premature infants was nearly eliminated with the use of 70% oxygen.

Although Wilson cautioned against unrestricted use of oxygen, other investigators and the American Academy of Pediatrics advocated its liberal use…."

Polin NEJM 2013

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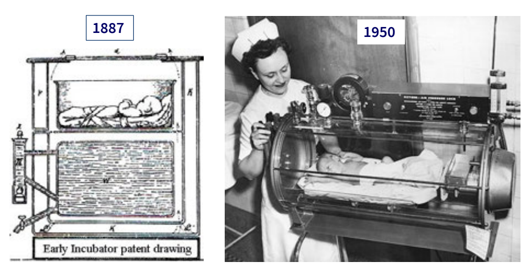
Retinopathy of Prematurity is in many ways the story of oxygen use in the preterm newborn….



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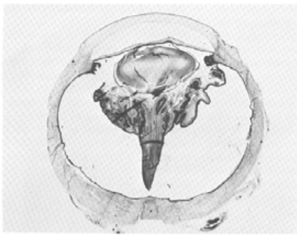
Retinopathy of Prematurity (Retrolental Fibroplasia)



First described in 1942:

"Grayish white opaque membrane behind each crystalline lens"

Terry 1942

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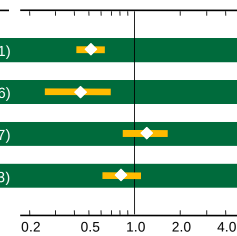
Cochrane Neonatal

Effect of Restricted Oxygen on Retrolental Fibroplasia

Overview of 3 Randomized Controlled Trials

Outcome	Typical Risk Difference
ACTIVE RLF	-0.30 (-0.39,-0.21)
CICATRICIAL RLF	-0.13 (-0.20,-0.06)
DEATH	0.03 (-0.02, 0.07)
DEATH OR CICATRICIAL RLF	-0.07 (-0.16, 0.03)



Watts 1992

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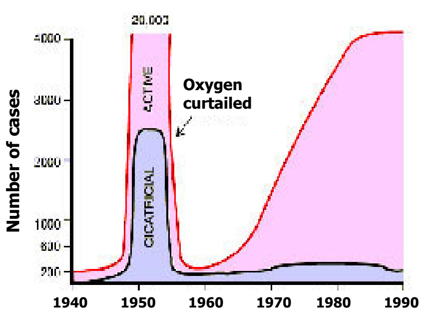
Epidemic of ROP



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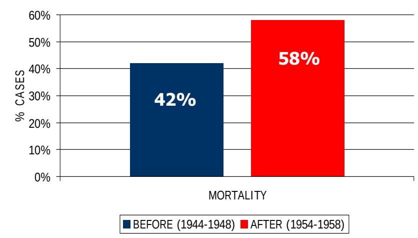
Effect of Restricted Oxygen on Mortality

Mortality before (1944-1948) and after (1954-1958) introduction of a policy of oxygen restriction in infants birth weight 1000-1499 grams



AVERY et al. Recent increase in mortality from hyaline membrane disease. J Pediatrics 1960

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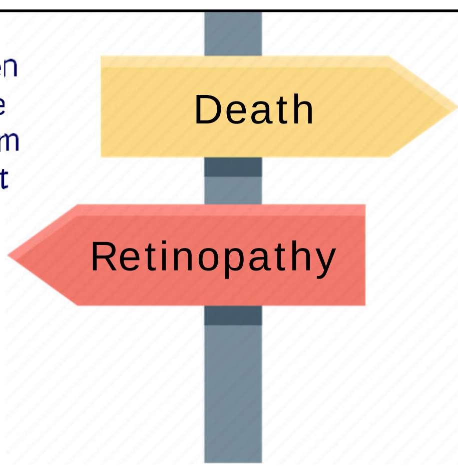
Oxygen in the Preterm Infant



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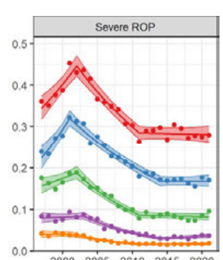
Severe retinopathy of prematurity (ROP)



Observed severe retinopathy of prematurity (ROP) rate (dot) and fitted trend with 95% CI (shaded area) by gestational age at birth among infants born at 24 to 28 weeks' gestational age from 1997 to 2021.

Horbar et al. Trends in mortality and morbidities for infants born 24 to 28 weeks in the US: 1997 to 2021. Pediatrics, 2023

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Oxygen Monitoring and Retinopathy of Prematurity

Use of Oxygen and Retinopathy of Prematurity

- Blood gases
- Transcutaneous Monitoring
- Policies/guidelines to decrease oxygen exposure
- Recent multicenter trials (NeoProM)

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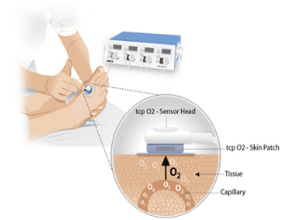
Transcutaneous oxygen monitoring



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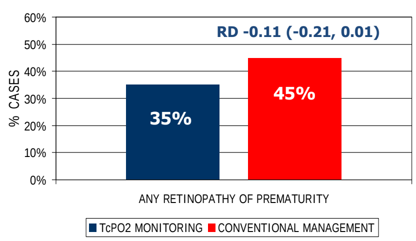
Continuous TcPO2 Monitoring Compared to Intermittent PaO2 Monitoring

Retinopathy of prematurity
All Study Infants BW 500-1300 grams



BANCALARI et al. Influence of transcutaneous oxygen monitoring on the incidence of retinopathy of prematurity. Pediatrics 1987; 79: 663-669

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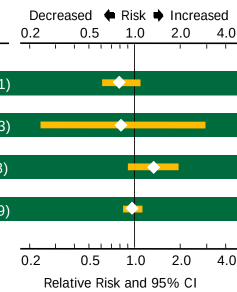
Continuous TcPO2 Monitoring Compared to Intermittent PaO2 Monitoring

BANCALARI AND COWORKERS 1987

Outcome	Risk Difference (95% CI)
ANY ROP	-0.11 (-0.21, 0.01)
CICATRICIAL ROP	-0.01 (-0.05, 0.03)
DEATH	0.08 (-0.02, 0.18)
DEATH OR ROP	-0.02 (-0.13, 0.09)



BANCALARI et al. Influence of transcutaneous oxygen monitoring on the incidence of retinopathy of prematurity. Pediatrics 1987; 79: 663-669

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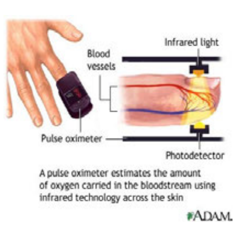
Oxygen saturation monitoring



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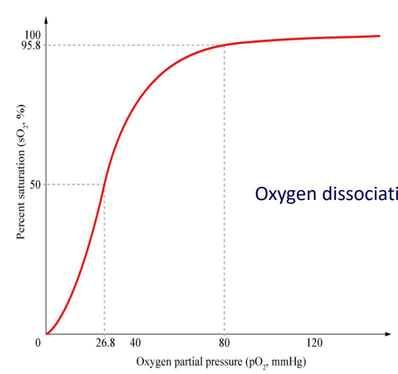

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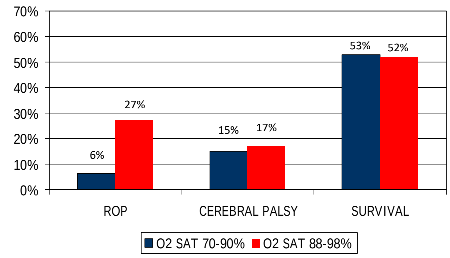
Lower Oxygen Saturation and the Impact on Retinopathy of Prematurity



Tin W et al. Pulse oximetry, severe retinopathy, and outcome at one year in babies of less than 28 weeks gestation. Arch Dis Child Fetal Neonatal Ed 2001;84:F106-110

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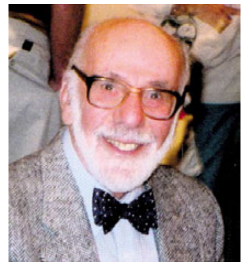
A cautionary tale about supplemental oxygen



William A. Silverman, MD.

A Cautionary Tale About Supplemental Oxygen: The Albatross of Neonatal Medicine. Pediatrics 2004; 113: 394 -396.

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A cautionary tale about supplemental oxygen

In the 1970s, transcutaneous O_2 electrodes arrived and were replaced in the 1980s by pulse oximeters, but these technologic advances provided a misleading sense of newly found accuracy.

To put it bluntly, there has never been a shred of convincing evidence to guide limits for the rational use of supplemental oxygen in the care of extremely premature infants.

For decades, the optimum range of oxygenation (to balance 4 competing risks: mortality, ROP blindness, chronic lung disease, and brain damage) was, and remains to this day, unknown.

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Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Cochrane

Askie LM, Darlow BA, Davis PG, Finer N, Stenson B, Vento M, Whyte R.

Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011190. DOI: 10.1002/14651858.CD011190.pub2.

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Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Objectives:

1. What are the effects of targeting lower versus higher oxygen saturation ranges on death or major neonatal and infant morbidities, or both, in extremely preterm infants?

2. Do these effects differ in different types of infants, including those born at a very early gestational age, or in those who are outborn, without antenatal corticosteroid coverage, of male sex, small for gestational age or of multiple birth, or by mode of delivery?

Askie and colleagues. Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011190. DOI: 10.1002/14651858.CD011190.pub2.

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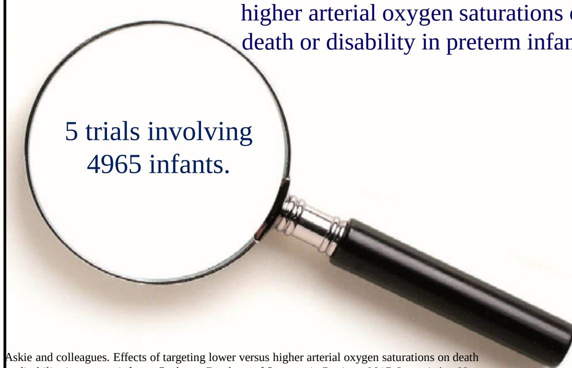
Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants



Askie and colleagues. Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011190. DOI: 10.1002/14651858.CD011190.pub2

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The investigators of these five trials had prospectively planned to combine their data as part of the NeOProM (Neonatal Oxygen Prospective Meta-analysis) Collaboration.

Askie et al. BMC Pediatrics 2011, 11:6
http://www.biomedcentral.com/1471-2431/11/6

BMC Pediatrics

STUDY PROTOCOL Open Access

NeOProM: Neonatal Oxygenation Prospective Meta-analysis Collaboration study protocol

Lisa M Askie[1*], Peter Brocklehurst[2], Brian A Darlow[3], Neil Finer[4], Barbara Schmidt[5,6], William Tarnow-Mordi[7,8], for the NeOProM Collaborative Group[1]

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Characteristics of randomized trials included in the NeoProM Collaboration

Trial acronym	BOOST II-Australia	BOOST II-UK	BOOST-NZ	SUPPORT	COT
Registration number	ACTRN12605000055606	ISRCTN00842661	ACTRN12605000253606	NCT00233324	ISRCTN62491227
Planned sample size	1200	1200	320	1310	1200
Countries of recruitment	Australia	United Kingdom	New Zealand	United States	Canada, USA, Argentina, Germany, Israel, Finland
Participants	Infants < 28 wks gestation inborn or outborn < 24 hrs old	Infants < 28 wks gestation < 12 hrs old (24 hrs if outborn)	Infants < 28 wks gestation inborn or outborn < 24 hrs old	Infants 24-27 wks gestation < 2 hrs old	Infants 23 0/7-27 6/7 wks gestation < 24 hrs old
Masked?	Yes	Yes	Yes	Yes	Yes
Intervention	Lower oxygen saturation (85%-89%)	Lower oxygen saturation (85%-89%)	Lower oxygen saturation (85%-89%)	Lower oxygen saturation (85%-89%)	Lower oxygen saturation (85%-89%)
Comparator	Higher oxygen saturation (91%-95%)	Higher oxygen saturation (91%-95%)	Higher oxygen saturation (91%-95%)	Higher oxygen saturation (91%-95%)	Higher oxygen saturation (91%-95%)
Intervention & comparator duration	Oximeter applied asap after admission to NICU, continued for minimum 2 wks. Thereafter continued until 36 wks corrected age or SpO_2 > 96% in room air for 95% of time over 3 days.	Oximeter applied from randomisation until postmenstrual age (PMA) of 36 wks or until baby is breathing air. All monitoring at any time prior to 36 wks to be done using study oximeter. BPD defined at 36 wks using a physiological test.	Oximeter applied asap after admission to NICU, continued for minimum 2 wks. Thereafter continued until 36 wks corrected age or SpO_2 > 96% in room air for 95% of time over 3 days.	Oximeter applied within 2 hrs following admission to NICU until infant has been in room air for 72 hrs or until 36 wks corrected age, assessed by physiologic oxygen test.	Oximeter applied from day of birth until a minimum 36 wks PMA. If breathing room air without any form of respiratory assistance from 35 wks PMA onward, study oximetry discontinued at a 36 wks PMA. If receiving any form of respiratory assistance and/or oxygen therapy from 35 wks PMA onward study oximetry continues until 40 wks PMA. Study oximetry stopped at any time before 40 wks PMA if baby discharged home (with or without respiratory assistance and/or oxygen).

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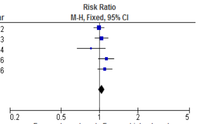
Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Death or Major Disability to 18 to 24 months

Study or Subgroup	Lower oxygen saturation Events	Lower oxygen saturation Total	Higher oxygen saturation Events	Higher oxygen saturation Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Vaucher 2012	363	613	374	624	31.7%	0.99 [0.90, 1.08]	2012
Schmidt 2013	298	578	283	569	24.4%	1.04 [0.92, 1.16]	2013
BOOST NZ 2014	65	167	76	168	6.5%	0.86 [0.67, 1.11]	2014
BOOST-II Australia 2016	247	549	217	545	18.6%	1.13 [0.98, 1.30]	2016
BOOST-II UK 2016	245	473	220	468	18.9%	1.10 [0.97, 1.25]	2016
Total (95% CI)		**2380**		**2374**	**100.0%**	**1.04 [0.98, 1.10]**	
Total events	1218		1170				

Heterogeneity: Chi² = 5.50, df = 4 (P = 0.24); I² = 27%
Test for overall effect: Z = 1.35 (P = 0.18)



Typical RR 1.04 (95% CI 0.98 to 1.10)

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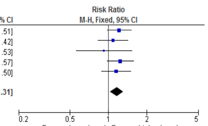
Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Death to 18 to 24 months

Study or Subgroup	Lower oxygen saturation Events	Lower oxygen saturation Total	Higher oxygen saturation Events	Higher oxygen saturation Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Vaucher 2012	140	633	118	648	27.9%	1.21 [0.98, 1.51]
Schmidt 2013	97	585	88	577	21.2%	1.09 [0.83, 1.42]
BOOST NZ 2014	25	170	27	170	6.5%	0.93 [0.56, 1.53]
BOOST-II UK 2016	122	484	98	483	23.5%	1.24 [0.98, 1.57]
BOOST-II Australia 2016	100	561	87	562	20.8%	1.15 [0.89, 1.50]
Total (95% CI)		**2433**		**2440**	**100.0%**	**1.16 [1.03, 1.31]**
Total events	484		418			

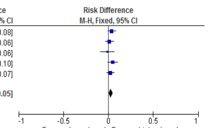
Heterogeneity: Chi² = 1.51, df = 4 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.50 (P = 0.01)



Typical RR 1.16 (95% CI 1.03 to 1.31)

Study or Subgroup	Lower oxygen saturation Events	Lower oxygen saturation Total	Higher oxygen saturation Events	Higher oxygen saturation Total	Weight	Risk Difference M-H, Fixed, 95% CI
Vaucher 2012	140	633	118	648	26.3%	0.04 [-0.00, 0.08]
Schmidt 2013	97	585	88	577	23.8%	0.01 [-0.03, 0.06]
BOOST NZ 2014	25	170	27	170	7.0%	-0.01 [-0.09, 0.06]
BOOST-II UK 2016	122	484	98	483	19.8%	0.05 [-0.00, 0.10]
BOOST-II Australia 2016	100	561	87	562	23.0%	0.02 [-0.02, 0.07]
Total (95% CI)		**2433**		**2440**	**100.0%**	**0.03 [0.01, 0.05]**
Total events	484		418			

Heterogeneity: Chi² = 2.41, df = 4 (P = 0.66); I² = 0%
Test for overall effect: Z = 2.50 (P = 0.01)



Typical RD 0.03 (95% CI 0.01 to 0.05)

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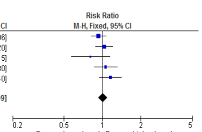
Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Major Disability to 18 to 24 months

Study or Subgroup	Lower oxygen saturation Events	Lower oxygen saturation Total	Higher oxygen saturation Events	Higher oxygen saturation Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Vaucher 2012	223	473	256	506	33.5%	0.93 [0.82, 1.06]
Schmidt 2013	201	488	195	489	26.4%	1.03 [0.89, 1.20]
BOOST NZ 2014	40	142	49	141	6.7%	0.81 [0.57, 1.15]
BOOST-II UK 2016	123	351	122	370	16.1%	1.06 [0.87, 1.30]
BOOST-II Australia 2016	147	449	130	458	17.4%	1.15 [0.95, 1.40]
Total (95% CI)		**1903**		**1964**	**100.0%**	**1.01 [0.93, 1.09]**
Total events	734		752			

Heterogeneity: Chi² = 5.13, df = 4 (P = 0.27); I² = 22%
Test for overall effect: Z = 0.25 (P = 0.80)



Typical RR 1.01 (95% CI 0.93 to 1.09)

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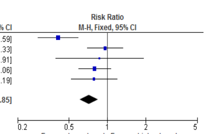
Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Severe Retinopathy of Prematurity

Study or Subgroup	Lower targeting Events	Lower targeting Total	Higher targeting Events	Higher targeting Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Vaucher 2012	36	482	93	514	29.9%	0.41 [0.29, 0.59]
Schmidt 2013	63	500	66	503	21.9%	0.96 [0.70, 1.33]
BOOST NZ 2014	11	158	12	150	4.1%	0.87 [0.40, 1.91]
BOOST-II UK 2016	67	395	86	403	28.3%	0.79 [0.60, 1.06]
BOOST-II Australia 2016	37	487	48	497	15.8%	0.79 [0.52, 1.19]
Total (95% CI)		**2022**		**2067**	**100.0%**	**0.72 [0.61, 0.85]**
Total events	214		305			

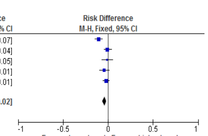
Heterogeneity: Chi² = 12.90, df = 4 (P = 0.01); I² = 69%
Test for overall effect: Z = 3.97 (P < 0.0001)



Typical RR 0.72 (95% CI 0.61 to 0.85)

Study or Subgroup	Lower targeting Events	Lower targeting Total	Higher targeting Events	Higher targeting Total	Weight	Risk Difference M-H, Fixed, 95% CI
Vaucher 2012	36	482	93	514	24.3%	-0.11 [-0.15, -0.07]
Schmidt 2013	63	500	66	503	24.5%	-0.01 [-0.05, 0.04]
BOOST NZ 2014	11	158	12	150	7.5%	-0.01 [-0.07, 0.05]
BOOST-II UK 2016	67	395	86	403	19.5%	-0.04 [-0.10, 0.01]
BOOST-II Australia 2016	37	487	48	497	24.1%	-0.02 [-0.06, 0.01]
Total (95% CI)		**2022**		**2067**	**100.0%**	**-0.04 [-0.06, -0.02]**
Total events	214		305			

Heterogeneity: Chi² = 15.10, df = 4 (P = 0.004); I² = 74%
Test for overall effect: Z = 4.03 (P < 0.0001)



Typical RD -0.04 (95% CI -0.06 to -0.02)

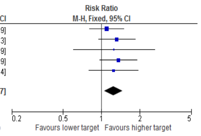
42

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Necrotizing Enterocolitis

Study or Subgroup	Lower oxygen saturation Events	Lower oxygen saturation Total	Higher oxygen saturation Events	Higher oxygen saturation Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Vaucher 2012	76	641	70	649	31.2%	1.10 [0.81, 1.49]
Schmidt 2013	74	602	56	599	25.2%	1.31 [0.95, 1.83]
BOOST NZ 2014	15	170	12	170	5.4%	1.25 [0.60, 2.59]
BOOST-II UK 2016	71	484	52	480	23.4%	1.35 [0.97, 1.89]
BOOST-II Australia 2016	41	567	33	567	14.8%	1.24 [0.80, 1.94]
Total (95% CI)		**2464**		**2465**	**100.0%**	**1.24 [1.05, 1.47]**
Total events	277		223			

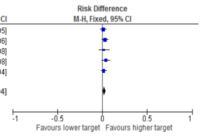
Heterogeneity: Chi² = 0.98, df = 4 (P = 0.91); I² = 0%
Test for overall effect: Z = 2.55 (P = 0.01)



Typical RR 1.24 (95% CI 1.05 to 1.47)

Study or Subgroup	Lower oxygen saturation Events	Lower oxygen saturation Total	Higher oxygen saturation Events	Higher oxygen saturation Total	Weight	Risk Difference M-H, Fixed, 95% CI
Vaucher 2012	76	641	70	649	26.2%	0.01 [-0.02, 0.05]
Schmidt 2013	74	602	56	599	24.4%	0.03 [-0.01, 0.06]
BOOST NZ 2014	15	170	12	170	6.9%	0.02 [-0.04, 0.08]
BOOST-II UK 2016	71	484	52	480	19.6%	0.04 [-0.00, 0.08]
BOOST-II Australia 2016	41	567	33	567	23.0%	0.01 [-0.01, 0.04]
Total (95% CI)		**2464**		**2465**	**100.0%**	**0.02 [0.01, 0.04]**
Total events	277		223			

Heterogeneity: Chi² = 1.47, df = 4 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.56 (P = 0.01)



Typical RD 0.02 (95% CI 0.01 to 0.04)

43

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Author's Conclusions:

In extremely preterm infants, targeting lower (85% to 89%) SpO_2 compared to higher (91% to 95%) SpO_2 had no significant effect on the composite outcome of death or major disability or on major disability alone, including blindness, but increased the average risk of mortality by 28 per 1000 infants treated.

Askie and colleagues. Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011190. DOI: 10.1002/14651858.CD011190.pub2.

44

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

"The tradeoff between the potential benefits and risks of lower versus higher saturations may not be the same in each nursery."

Schmidt B, Whyte RK, Roberts RS. J Pediatr. 2014;165:6-8 .

45

46

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Outcome of concern	Appropriate choice of saturation range (SpO_2)
Composite outcome of death or major disability	lower (85% to 89%) *or* higher (91% to 95%)
Death	higher (91% to 95%)
Retinopathy of Prematurity	lower (85% to 89%)
Necrotizing Enterocolitis	higher (91% to 95%)

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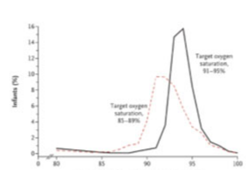
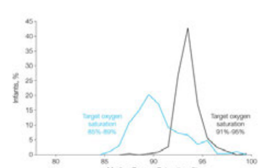
Median Oxygen Saturation with Oxygen Supplementation in the Low Target and High Target Groups

SUPPORT Trial



COT Trial

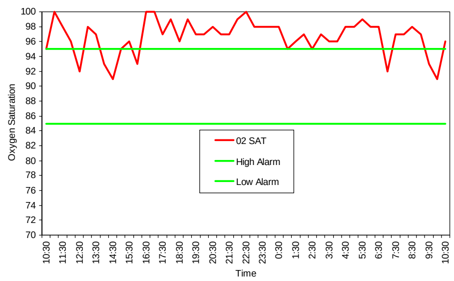


N Engl J Med. 2010 May 27;362(21):1959-69.

JAMA. 2013;309(20):2111–2120. doi:10.1001/jama.2013.5555

48

Hitting our targets is easier said then done!



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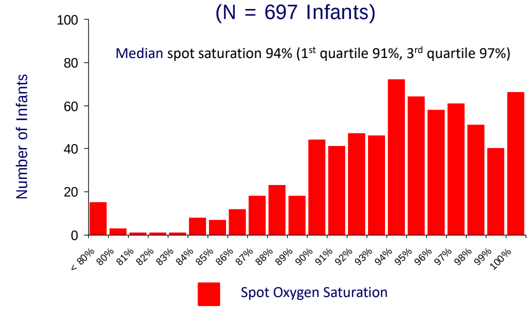
VON Day Oxygen Monitoring Audit
Spot Oxygen Saturation

Infants on Oxygen and Respiratory Support
(N = 697 Infants)

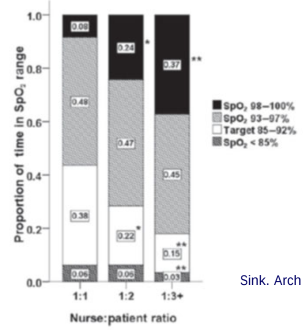


50

What's missing from this discussion?

51

Nurse/patient ratio and achievement of oxygen saturation goals in premature infants



Sink. Arch Dis Child Fetal Neonatal Ed. 2011

Mean proportion of time in specified oxygen saturation range

52

Compliance with alarm limits for pulse oximetry in very preterm infants

Dependent on:

- Staff knowledge of unit policies and guidelines
- Nurse / patient ratio
- Patient acuity
- Patient age

53

Intermittent Hypoxemia in Preterm Infants.

Intermittent hypoxemia (IH) events are common during early postnatal life, particularly in preterm infants.

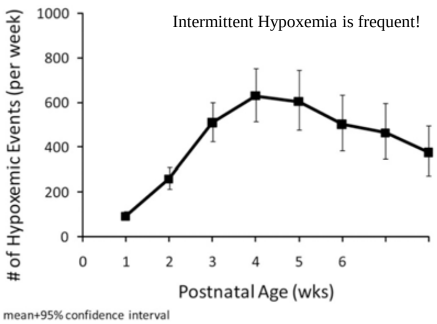
These events have been associated with multiple morbidities including retinopathy of prematurity, sleep disordered breathing, neurodevelopmental impairment, and mortality.

The relationship between IH and poor outcomes may be dependent on the patterns (frequency, duration, and timing) of the IH events.

Current treatment modalities used in the clinical setting have been only partially successful in reducing the incidence of apnea and accompanying IH but the risks and benefits of more aggressive interventions should include knowledge of the relationship between IH and morbidity.

Di Fiore and colleagues. Intermittent Hypoxemia in Preterm Infants. Clin Perinatol. 2019 Sep;46(3):553-565. doi: 10.1016/j.clp.2019.05.006.

54



The progression of intermittent hypoxemic events (IH) during early postnatal life. Preterm infants exhibit relatively few IH during the first week of life followed by an increase during weeks 2–4 and a decrease thereafter.

From Di Fiore JM, Bloom JN, Orge F, et al. A higher incidence of intermittent hypoxemic episodes is associated with severe retinopathy of prematurity. The Journal of pediatrics. Jul 2010;157(1):69–73

55

Intermittent Hypoxemia in Preterm Infants.

Objective: To test the hypothesis that preterm infants randomized to a low vs high O_2 saturation target range have a higher incidence of intermittent hypoxemia.

Study design: A subcohort of 115 preterm infants with high resolution pulse oximetry enrolled in the Surfactant, Positive Pressure, and Oxygenation Randomized Trial were randomized to low (85%-89%) or high (91%-95%) O_2 saturation target ranges. Oxygen saturation was monitored until 36 weeks postmenstrual age or until the infant was breathing room air without respiratory support for ≥ 72 hours.

Results: The low target O_2 saturation group had a higher rate of intermittent hypoxemia (≤ 80% for ≥10 seconds and ≤ 3 minutes) prior to 12 days and beyond 57 days of life ($P < .05$).

Di Fiore and colleagues. Low oxygen saturation target range is associated with increased incidence of intermittent hypoxemia. J Pediatr. 2012 Dec;161(6):1047-52. doi: 10.1016/j.jpeds.2012.05.046.

56

Better ways to monitor our use of oxygen in critically ill newborns?

57

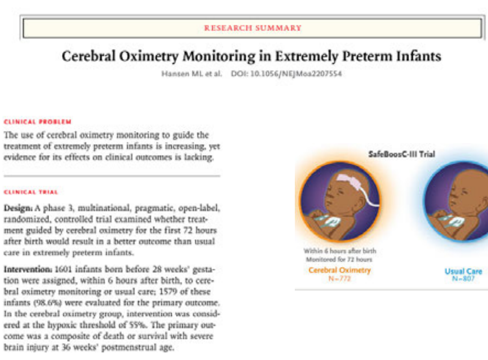
The NEW ENGLAND JOURNAL of MEDICINE

Cerebral Oximetry Monitoring in Extremely Preterm Infants

Hansen ML, Pellicer A, Hyttel-Sørensen S, Ergenekon E, Szczapa T, Hagmann C, Naulaers G, Mintzer J, Fumagalli M, Dimitriou G, Dempsey E, Tkaczyk J, Cheng G, Fredly S, Heuchan AM, Pichler G, Fuchs H, Nesargi S, Hahn GH, Piris-Borregas S, Širc J, Alsina-Casanova M, Stocker M, Ozkan H, Sarafidis K, Hopper AO, Karen T, Rzepecka-Weglarz B, Oguz SS, Arruza L, Memisoglu AC, Del Rio Florentino R, Baserga M, Maton P, Truttmann AC, de Las Cuevas I, Agergaard P, Zafra P, Bender L, Lauterbach R, Lecart C, de Buyst J, El-Khuffash A, Curley A, Vaccarello OO, Miletin J, Papathoma E, Vesoulis Z, Vento G, Cornette L, Lopez LS, Yasa B, Klamer A, Agosti M, Baud O, Mastretta E, Cetinkaya M, McCall K, Zeng S, Hatzidaki E, Bargiel A, Marciniak S, Gao X, Huijia L, Chalak L, Yang L, Rao SA, Xu X, Gonzalez BL, Wilinska M, Yin Z, Sadowska-Krawczenko I, Serrano-Viñuales I, Krolak-Olejnik B, Ybarra MM, Morales-Betancourt C, Korček P, Teresa-Palacio M, Mosca F, Hergenhan A, Koksal N, Tsoni K, Kadri MM, Knöpfli C, Rafinska-Wazny E, Akin MS, Nordvik T, Peng Z, Kersin SG, Thewissen L, Alarcon A, Healy D, Urlesberger B, Baş M, Baumgartner J, Skylogianni E, Karadyova V, Valverde E, Bergon-Sendin E, Kucera J, Pisoni S, Wang L, Smits A, Sanchez-Salmador R, Rasmussen MI, Olsen MH, Jensen AK, Gluud C, Jakobsen JC, Greisen G.

N Engl J Med. 2023 Apr 20;388(16):1501-1511. doi: 10.1056/NEJMoa2207554.

58


RESEARCH SUMMARY

Cerebral Oximetry Monitoring in Extremely Preterm Infants

Hansen ML et al. DOI: 10.1056/NEJMoa2207554

CLINICAL PROBLEM

The use of cerebral oximetry monitoring to guide the treatment of extremely preterm infants is increasing, yet evidence for its effects on clinical outcomes is lacking.

CLINICAL TRIAL

Design: A phase 3, multinational, pragmatic, open-label, randomized, controlled trial examined whether treatment guided by cerebral oximetry for the first 72 hours after birth would result in a better outcome than usual care in extremely preterm infants.

Intervention: 1601 infants born before 28 weeks' gestation were assigned, within 6 hours after birth, to cerebral oximetry monitoring or usual care; 1579 of these infants (98.6%) were evaluated for the primary outcome. In the cerebral oximetry group, intervention was considered at the hypoxic threshold of 55%. The primary outcome was a composite of death or survival with severe brain injury at 36 weeks' postmenstrual age.

Hansen and colleagues. Cerebral Oximetry Monitoring in Extremely Preterm Infants. N Engl J Med. 2023 Apr 20;388(16):1501-1511. doi: 10.1056/NEJMoa2207554.

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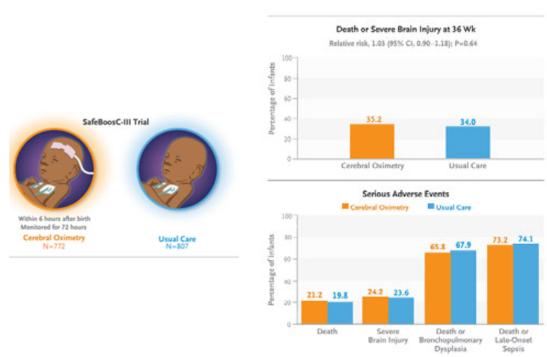

Hansen and colleagues. Cerebral Oximetry Monitoring in Extremely Preterm Infants. N Engl J Med. 2023 Apr 20;388(16):1501-1511. doi: 10.1056/NEJMoa2207554.

60

Better ways to adjust oxygen in critically ill newborns?

61

Current Opinion in
Pediatrics

Automated control of fraction of inspired oxygen: is it time for widespread adoption?

Mitra S, McMillan D.

Curr Opin Pediatr. 2021 Apr 1;33(2):209-216. doi: 10.1097/MOP.0000000000000993. PMID: 33394746.

62

Automated control of fraction of inspired oxygen: is it time for widespread adoption?

Over the past two decades, numerous algorithms for automated control of the fraction of inspired oxygen (FiO_2) have been developed and incorporated into contemporary neonatal ventilators and high-flow devices in an attempt to optimize supplemental oxygen therapy in preterm infants.

Recent findings
To date, 15 studies have compared automated versus manual control of FiO_2 in preterm infants on respiratory support. This includes four new randomized cross-over trials published in the last 2 years.

Available evidence consistently demonstrates a significant improvement in time spent within the target saturation range with automated FiO_2 control.

There are fewer episodes of severe hypoxemia and fewer manual FiO_2 adjustments with automated oxygen control. Nursing workload may be reduced. However, no currently completed studies report on clinical outcomes, such as chronic lung disease or retinopathy of prematurity.

Summary
Automated oxygen control appears to be a reasonable option for FiO_2 titration in preterm infants on respiratory support, if resources are available, and might substantially reduce nursing workload.

Further randomized clinical trials to explore its effects on clinical outcomes are required.

Mitra S, McMillan D. Automated control of fraction of inspired oxygen: is it time for widespread adoption? Curr Opin Pediatr. 2021 Apr 1;33(2):209-216. doi: 10.1097/MOP.0000000000000993.

63

Trials have now shown us the appropriate range to maintain oxygen saturation.

Maintaining appropriate oxygen saturation is a complex task that includes oxygen targets, alarm settings and staff response and unit culture.

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Vermont Oxford NETWORK

Discussants

Wendy L. Timpson, MD. MEd
Associate Professor of Pediatrics
Clinical Chief, Neonatology Division
UMass Chan Medical School. UMass Memorial Medical Center
Worcester, MA

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Optimizing Oxygenation

66

When poll is active respond at PollEv.com/vtoxford Send vtoxford to 22333

In your practice, alarm settings are... 140

Response	%
Standardized in all patients (one size fits all)	14%
Individualized based on factors including gestational age, chronological age and disease severity	78%
Variable depending on provider	6%
Unsure	1%

67

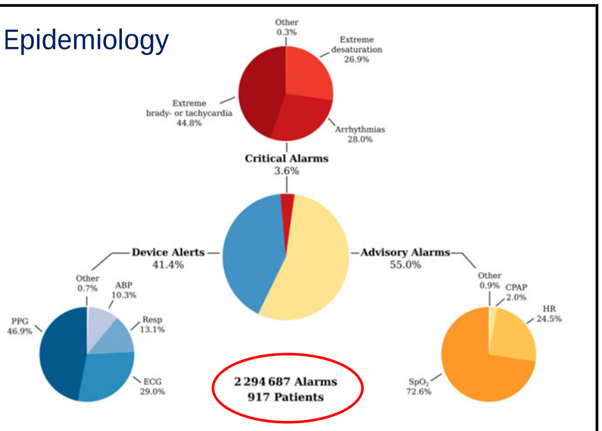
When poll is active respond at PollEv.com/vtoxford Send vtoxford to 22333

In our unit, responding to alarms is *primarily* the responsibility of... 165

Response	%
Nurses	70%
Respiratory therapists	1%
Providers	1%
Everyone	28%

68

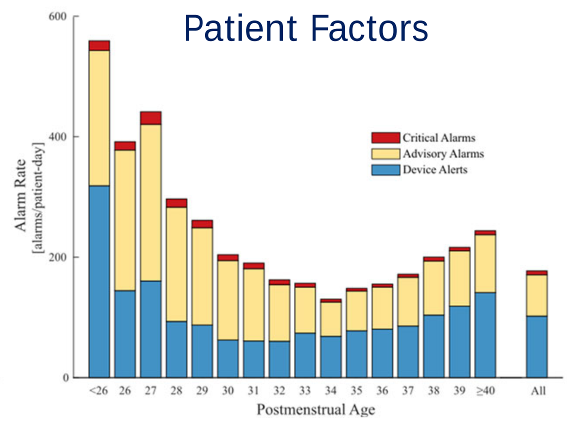
Epidemiology



Li, Timpson, Heldt, et al. J Perinatol. 2018 Aug; 38(8): 1030-1038

69

Patient Factors



Li, Timpson, Heldt, et al. J Perinatol. 2018 Aug; 38(8): 1030-1038

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Alarm Fatigue: Impact on Safety

- Workflow disruptions
- Distraction errors
- Delayed response
- Missed alarms

- Impact on oxygenation?

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PEDIATRICS

Council on Quality Improvement and Patient Safety| August 01, 2019

Responding to an Alarming Problem: Decreasing Alarm Burden & Increasing Safety in the NICU

Wendy L. Timpson, MEd, MD; Thomas Heldt, PhD; Munish Gupta, MD; Susan Young, RN; Karen Waldo, RN

Pediatrics (2019) 144 (2_MeetingAbstract): 155.

72

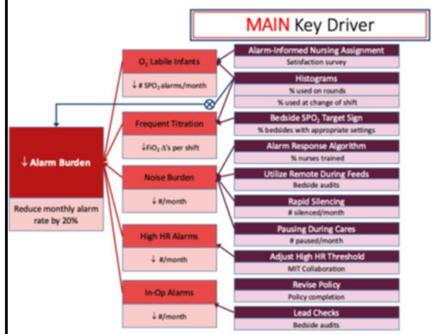
PEDIATRICS

Key Aims

- Reduce audible CR alarm burden for all NICU patients by 20% between September 2015 and December 2017
- Increase proportion of time VLBW infants spend within their target saturation range by 20%

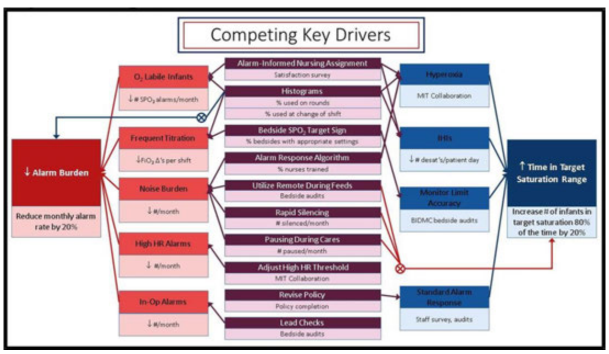
Timpson and colleagues. *Pediatrics* (2019) 144 (2_MeetingAbstract): 155.

73



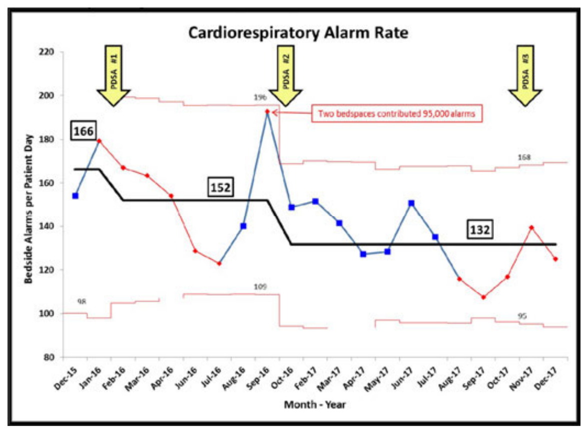
Timpson and colleagues. *Pediatrics* (2019) 144 (2_MeetingAbstract): 155.

74



Timpson and colleagues. *Pediatrics* (2019) 144 (2_MeetingAbstract): 155.

75



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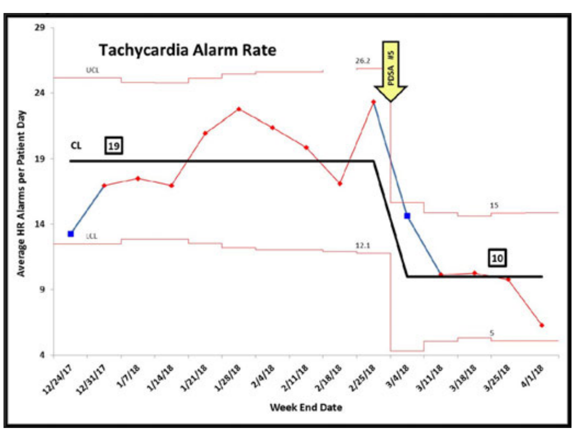

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Lessons Learned

- Immense alarm burden
- Patient factors drive variation
- Modest impact of education
- Big impact of hard-wired changes

Timpson and colleagues. *Pediatrics* (2019) 144 (2_MeetingAbstract): 155.

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Practical Interventions

- Know your limits
  - Narrow vs. wide
  - Averaging time, latching, escalation
  - Partner with Clinical Engineering
- Focus on the noise
  - Utilizing silence & pause features
- Deploy balancing measures
- Share the burden

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The Washington Post

Health & Science

'Every 30 seconds another alarm is going off': Neonatal ICUs can take their toll on parents

"An orchestra of alarms beeps incessantly….

"…the nurses may grab your baby from you to get her to start breathing…."

"…. It's just relentless."

Amialya Durairaj: February 23, 2019

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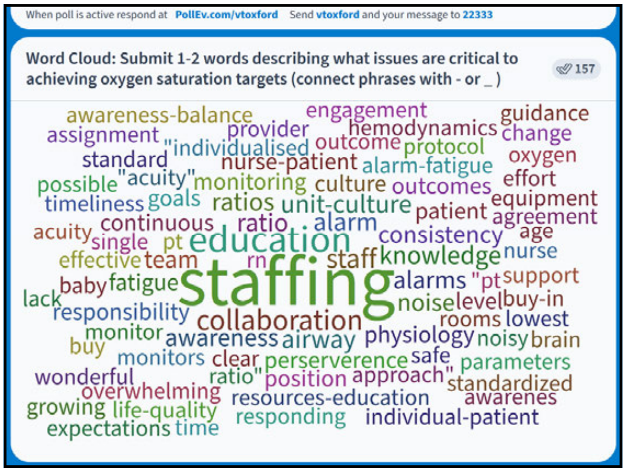

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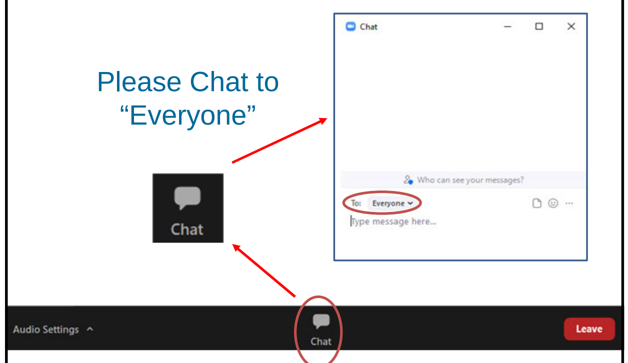
Questions? Comments? Ideas to Share?

Please Chat to "Everyone"



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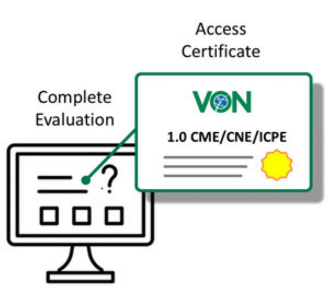
Continuing Education Credit



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Future sessions

November 12th 2025 – Evidence to Practice: The NICU environment

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NICQ
All Care is Brain Care
iNICQ
All Care is Brain Care
All Care is
Brain Care
VON Vermont Oxford
NETWORK

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