Clinical question.

In neonates receiving resuscitation or stabilization (P), when attempting to match blood oxygenation to that of an uncompromised full term baby undergoing normal transition (C), is pulse oximetry (I) beneficial (O)?

Is this question addressing an intervention/therapy, prognosis or diagnosis? Diagnosis
State if this is a proposed new topic or revision of existing worksheet: new

Conflict of interest specific to this question
Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No

Search strategy (including electronic databases searched).
Strategy 1: Ovid Medline 1950 to present – Oxygen monitoring/Oximetry
resuscitation/ or exp cardiopulmonary resuscitation/ or heart massage/ or respiration, artificial/ OR resuscitati:.ti.
AND *Oxygen/an, bl, du [Analysis, Blood, Diagnostic Use] OR exp Oximetry/ OR oximet:.tw.
AND exp Infant, Newborn/ OR neonat:.tw.
Limits for strategy 3: Humans
Yield = 180

Strategy 2: Additional references from key papers
Review abstracts and appropriate papers of references from recently-published key papers
Yield = 15

Strategy 3: The Cochrane Library (including DARE)
Oximet* or Oxygen in the title AND Neonat* in the text
Yield = 1

Number of articles/sources meeting criteria for further review: 51

Summary of evidence

Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
<th>Level of evidence</th>
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<tbody>
<tr>
<td></td>
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<td></td>
<td>A = Return of spontaneous circulation</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>B = Survival of event</td>
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<td>C = Survival to hospital discharge</td>
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<td>D = Intact neurological survival</td>
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<td>E = Other endpoint</td>
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<td>Italics = Animal studies</td>
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### Evidence Neutral to Clinical question

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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  

*Italics = Animal studies*

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### Evidence Opposing Clinical Question

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<th>1</th>
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<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  

*Italics = Animal studies*
REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

There are now numerous reports of oximetry data following delivery. When using technology available from the early 2000s, a reliable reading can be obtained from > 90% of normal term births, approximately 80% of those born preterm, and 80-90% of those requiring resuscitation, within 2 minutes from birth. (Dawson, LOE4 2009, pF87) Uncompromised babies born at term at sea level have SaO2 ~60% during labor (Dildy, LOE4 1994, p679), and increases to >90% by 10 minutes (Mariani, LOE4 2007, p418). The 25th percentile is approximately 40% at birth and increases to ~80% at 10 minutes (Dawson, LOE4 2009, in press). Values are lower for those born by cesarean section (Rabi, LOE4 2006, p590) and those born at altitude (Gonzales, LOE4 2005, p46). Those born preterm may take longer to reach >90% (Dawson, Pediatrics, LOE4 in press). Those given supplemental oxygen had a higher incidence of SaO2>95%, even when a protocol to decrease the FiO2 was implemented, although the extent of this was restricted by insufficient power and the particular protocols used in the studies (Escrig LOE5 2008, p875; Wang LOE5 2008, p 1083).

Acknowledgements:
Thanks to Ms. Elaine Attridge from the University of Virginia Health Sciences Library for assistance with literature search.

Citation List of articles reviewed in depth and found to be relevant


Level of Evidence: 4
Quality of Evidence: Good
Reviewer’s Comments: 200 healthy term infants had pre-ductal pulse oximetry immediately following birth. 25% were c-sections. None received supplemental oxygen. 92% achieved reliable values by 1 minute following birth. Median values were 71, 92, and 98% at 1, 5, and 10 minutes, respectively, in vaginal deliveries and 70, 79, and 96% in cesarean deliveries. SpO2 was significantly lower in the cesarean group, preterm lower than term.


Level of Evidence: 4
Quality of Evidence: Fair
Reviewer’s Comments: Small RCT of oximetry performed at birth with 30 uncompromised babies born at term and randomized to oropharyngeal suctioning or not. Pre-ductal oximetry showed lower SpO2 between 1 and 6 minutes after birth.


Level of Evidence: Not included in worksheet
Quality of Evidence: Not included in worksheet
Reviewer’s Comments: Review article. Notes that preductal readings were significantly higher than postductal, c-section values lower than vaginal, neither Saugstadt nor Vento found any difference in O2Sat increase following birth, whether babies were resuscitated with oxygen or air, and values were lower at altitude than at sea level. A good review, but no new data here.

Level of Evidence: 4  
Quality of Evidence: Good  
Reviewer’s Comments: Prospective observational convenience study of 125 infants < 30 weeks gestation undergoing neonatal resuscitation during 2006 and 2007. For the 1st 6 months, use of 100% oxygen was the routine (n=20). For the next 18 months 21% oxygen was used, backed up by 100% oxygen guided by pre-ductal oximetry, aiming for 80-90% (n-105). During both periods, CPAP was given via T-piece to spontaneous breathing infants. 92% during the 21% O2 received supplemental oxygen at a median of 5 minutes. The median heartrate was slightly lower in the 21% group over the first 5 minutes, but was >100 in both groups by 2 minutes. There appeared to be more low outliers in the 21% group over 10 minutes, but this wasn’t tested in the article. There were not measurable differences in mortality or morbidity in this small series, but there was insufficient power to draw implications about equivalence.


Level of Evidence: 4  
Quality of Evidence: Good  
Reviewer’s Comments: 468 infants from 3 different databases had oximetry measured immediately following birth. 308 were born at term and 160 were preterm. None received oxygen at birth, but the clinicians have previously shown a bias for withholding the use of supplemental oxygen. At least one data group came from a randomized study where oxygen use was restricted by protocol. Results showed that the a reliable oximeter reading was obtained at a mean of 74 seconds following birth. Preterm babies had slightly lower SpO2 than those at term.

<table>
<thead>
<tr>
<th>Minutes from birth</th>
<th>SpO2 (%) Preterm infants</th>
<th>SpO2 (%) Term infants</th>
<th>SpO2 (%) All infants</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62 (47 - 72)</td>
<td>68 (60 - 77)</td>
<td>66 (55 - 76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>68 (58 - 78)</td>
<td>76 (65 - 84)</td>
<td>73 (63 - 82)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>76 (67 - 83)</td>
<td>81 (71 - 90)</td>
<td>76 (69 - 88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>81 (72 - 86)</td>
<td>88 (78 - 94)</td>
<td>85 (76 - 93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5</td>
<td>86 (80 - 92)</td>
<td>92 (83 - 96)</td>
<td>89 (82 - 95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6</td>
<td>90 (81 - 95)</td>
<td>94 (86 - 97)</td>
<td>92 (85 - 96)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>7</td>
<td>92 (85 - 96)</td>
<td>95 (90 - 97)</td>
<td>94 (88 - 97)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>8</td>
<td>92 (87 - 96)</td>
<td>96 (92 - 98)</td>
<td>95 (90 - 98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>9</td>
<td>93 (87 - 96)</td>
<td>97 (94 - 98)</td>
<td>96 (92 - 98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10</td>
<td>94 (81 - 97)</td>
<td>97 (84 - 98)</td>
<td>96 (92 - 98)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are median (interquartile range)
This paper reinforces the observations that a reliable signal can be obtained within 2 minutes following birth. The data are not very helpful for defining the “normal” range of oxygenation for preterm oxygenation, since the range will be affected by the degree of prematurity any associated lung immaturity, as well as the possible restrictions being imposed on oxygen use. Data for term babies are somewhat lower than data of others [e.g., Rabi (2009) and Mariani (2007)], again perhaps because of the investigators’ bias for restricting the use of supplemental oxygen. Also, since some of the data came from randomized studies of babies at risk for needing resuscitation, they may not be representative of babies undergoing normal transition.


Level of Evidence: 4
Quality of Evidence: Good
Reviewer’s Comments: 291 fetuses at 3 centers over a wide altitude range received pulse oximetry during labor. There was a gradual but significant decrease as labor progressed. There was no difference at different altitudes.


Level of Evidence: 5
Quality of Evidence: Good
Reviewer’s Comments: Prospective randomized trial of 42 neonates < 29 weeks “bradycardic (heart rate [HR]<80 beats per minute), hypotonic or hyporeactive, and unable to sustain active and/or effective respiration” randomized to 30% vs 90% FiO2 with FiO2 increased for bradycardia (<100 bpm) or decreased for preductal sats > 85%. Conducted in 2 hospitals in Spain. Mean times to achieve adequate reading were 86 and 88 seconds. Sats had reached target at 5-7 minutes in both groups and there was no difference in sats between the groups at 4 minutes. There were no differences in short term morbidity or mortality, although there was insufficient power to determine equivalence.
Gonzales GF, Salirrosas A. Arterial oxygen saturation in healthy newborns delivered at term in Cerro de Pasco (4340 m) and Lima (150 m). Reproductive Biology and Endocrinology. 3:46, 2005

**Level of Evidence:** 4  
**Quality of Evidence:** Good  
**Reviewer’s Comments:** Pulse oximetry of 37 term babies born at altitude of 4340 M and 131 term babies born at 150 M, from 1 through 60 minutes following birth.

Head circumference and Apgar scores were similar, but saturations were 15% lower and took longer to reach plateaus at altitude. Plateau was reached by 15 minutes at low altitude (similar to other studies) and 30 minutes at altitude. Birthweights were lower at altitude suggesting fetal effects of low oxygen. Neurological scores were lower at 24 hours at altitude and correlated with saturations at 1 minute of age.


**Level of Evidence:** Not included in worksheet  
**Quality of Evidence:** Not included in worksheet  
**Reviewer’s Comments:** 26 neonates on supplemental O2 and/or mechanical ventilation in the NICU had oximetry determined with 2 different oximeters. The Massimo more reliably identified bradycardias than did the Nellcor, Phillips, or Novametrix. The patient population (stable NICU subjects, not during resuscitation) and outdated technology render this study non-contributory to the hypothesis.
Harling (Still attempting to locate article)  
**Level of Evidence:** Not included in worksheet  
**Quality of Evidence:** Not included in worksheet  
**Reviewer's Comments:** 63 newborns < 31 weeks were randomized to 50% or 100% FiO2. 1/3rd of those in the 50% group actually received >50%. Oximetry was not used. Cytokine levels in bronchoalveolar lavage was not different between the groups.

**Level of Evidence:** 4  
**Quality of Evidence:** Good  
**Reviewer's Comments:** 205 infants >=31 weeks gestation who did not require supplemental oxygen or resuscitation were evaluated by Masimo pulse oximetry as soon as possible and until 5 minutes after birth. 15% were excluded for data acquisition problems. The purpose was to evaluate the normal state of O2 saturation following birth. 53% had reliable data by 60 sec. The median quartile range was 53-68% at 1 minute and rose to 79-91% by 5 minutes of age. Mean time to reach >90% was 5.8 minutes, with some taking as long as 20 minutes. Gestational age and presence of labor were significant confounding variables, both resulting in longer times to achieve neonatal values.

Kopotic RJ, Lindner W. Assessing high-risk infants in the delivery room with pulse oximetry. Anesth Analg 2002;94:S31-6: randomized babies to oximeter and not and found oximeter babies were admitted to NICU less. (Still attempting to locate article)  
**Level of Evidence:** 4  
**Quality of Evidence:** Fair  
**Reviewer's Comments:** This is a small study, but shows that oximetry can be applied quickly and improves the management of babies requiring resuscitation.

**Level of Evidence:** 4  
**Quality of Evidence:** Good  
**Reviewer's Comments:** 110 healthy term newborns were evaluated by Masimo pulse oximetry as soon as possible after birth. The purpose was to evaluate the normal pre and post ductal O2 saturations following birth. Median (interquartile range) time to get accurate readings was 3 minutes (2.4-4.1). At 5 minutes, the mean pre-ductal SpO2 level was 89%, and the mean post-ductal SpO2 level was 81%. Pre- and post-ductal SpO2 levels were significantly different during the first 15 minutes after birth.

Level of Evidence: 5  
Quality of Evidence: Good  
Reviewer's Comments: The investigators studied the difference in time to acquire a reliable signal if the probe is (1) to the cable first, (2) to the cable then the investigator then the subject, or (3) to the subject first. 40 babies were evaluated in the NICU (i.e., not immediately following birth). Method 3 was quicker by an average of 10 seconds.


Level of Evidence: 5  
Quality of Evidence: Fair  
Reviewer's Comments: 27 clinicians assessed videos of 20 infants (mean gestation 31 weeks) and scored them for color (“pink” or “not pink”) and timing of when turned pink. Oximetry data were available at a mean of 66 seconds after birth. 17/22 had supplemental oxygen, 11/20 had CPAP and 4 were intubated. 81% of the observers judged 19/20 babies to never become pink, although sats achieved >90% in 17/19. There was considerable variation in the judgement of “pink” among observers. It is quite possible that technological limitations influenced the outcome of this study (i.e., there was no comparison of actual visualization to visualization of the video, or of actual assessment of color by viewing the baby as compared to saturation measurements). Nevertheless, the study suggests that assessment of color is an unreliable sign.


Level of Evidence: Not included in worksheet  
Quality of Evidence: Not included in worksheet  
Reviewer's Comments: The investigators studied 115 babies requiring resuscitation following birth. Range of gestation was 23-42 weeks and 52% were < 1500 gms birthweight. 75% received 100% oxygen by PPV or blow-by and no oximetry data were reported. The primary purpose of the study was to evaluate the feasibility of using oximetry to guide neonatal resuscitation and the optimum technique for application of the probe. 91% had reliable data acquired and all had data by 81 seconds from birth, if the oximeter was placed on the baby before being connected to the machine. Otherwise, the paper is not helpful for addressing the hypothesis.


Level of Evidence: 4  
Quality of Evidence: Fair  
Reviewer's Comments: CO2 production was measured during the course of resuscitations and shown to correlate with SPO2. VCO2 was satisfactory only when pre-ductal O2 sat was > 70%. This confirms a relationship of VCO2 to SPO2 and to degree of compromise, but provides no evidence of superiority to SPO2.


Level of Evidence: 4  
Quality of Evidence: Good  
Reviewer's Comments: 115 newborns >= 35 weeks gestation who did not require supplemental oxygen were evaluated by Masimo pulse oximetry as soon as possible after birth. The purpose was to evaluate the normal state of O2 saturation following birth. At 5 minutes of age, median SpO2 values (interquartile range) were 87%
(80% to 95%) for infants delivered vaginally and 81% (75% to 83%) for those delivered through cesarean section. The median SpO2 did not reach 90% until 8 minutes of age in either group.


Level of Evidence: 4
Quality of Evidence: Fair
Reviewer's Comments: 186 newborns were examined with pulse oximetry following birth. 70 received supplemental oxygen, either by blow-by, under CPAP, or by IPPV, while 116 received no supplemental O2 or positive pressure. Those receiving positive pressure increased SaO2 more rapidly than those receiving supplemental oxygen by free-flow, perhaps because of more rapid establishment of FRC and the higher concentration used during PPV. Those receiving free-flow oxygen increased slower than those receiving no supplement, probably related to the existence of lung disease in those supplemented. Data were smoothed and extrapolated to the time of birth, with variance not reported. The time from birth to acquisition of signal was not reported. This study contributes little to other studies regarding our knowledge of the normal increase in SaO2 following birth, and is inconsistent with the study of Wang et al, which showed rapid development of hyperoxia when positive pressure is delivered with 100% supplemental oxygen.


Level of Evidence: 5
Quality of Evidence: Good
Reviewer's Comments: 95 infants > 1000 gms requiring resuscitation were compared to 30 control newborns using pulse oximetry, but with older technology (Novametrix 515A). 10.5% of resuscitated and 6.7% of controls were unable to acquire a signal and 6.3, 36.5, 63.1, and 80% of the resuscitated babies had a signal acquired by 1, 3, 5, and 10 minutes of age respectively. >90% saturation was achieved at a median time of 300 and 170 seconds, respectively in resuscitated infants and controls, respectively. Supplemental oxygen use was not specifically defined.


Level of Evidence: 4
Quality of Evidence: Good
Reviewer's Comments: Re-analysis of the ReAir-2 study from 199 in which 591 babies requiring resuscitation were randomized into RA (n=311 and 100% FiO2 (280). Only 22% and 34% had readable sats at 1 and 5 minutes, but there was no significant difference in those treated with oxygen versus air, even when separated by high and low Apgars. Approximately half of the babies in both groups were < 90% at 10 minutes. It should be noted that these data were collected with older technology oximeters.
Table II. SaO2 according to Apgar score and group in the first 10 min of life

<table>
<thead>
<tr>
<th>Group</th>
<th>1</th>
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<tr>
<td>All, room air</td>
<td>68</td>
<td>85</td>
<td>90</td>
<td>90</td>
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<tr>
<td>All, oxygen</td>
<td>63</td>
<td>85</td>
<td>90</td>
<td>92</td>
</tr>
<tr>
<td>Apgar 1 min ≥6, room air</td>
<td>68</td>
<td>85</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Apgar 1 min ≥6, oxygen</td>
<td>75</td>
<td>90</td>
<td>92</td>
<td>93</td>
</tr>
<tr>
<td>Apgar 1 min &lt;4, room air</td>
<td>65</td>
<td>82</td>
<td>87</td>
<td>90</td>
</tr>
<tr>
<td>Apgar 1 min &lt;4, oxygen</td>
<td>58</td>
<td>78</td>
<td>86</td>
<td>90</td>
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</tbody>
</table>


Level of Evidence: Not included in worksheet  
Quality of Evidence: Not included in worksheet  
Reviewer's Comments: 78 preterm and term neonates had left-foot SpO2 compared with UAC and UVC oxyhemoglobin blood saturation at 1-4 days after birth. They showed that accuracy of the SpO2 was close to that seen in adults in the 95-98% range (+/- 2.5-3%) if one wants to maintain PaO2 in the 50-75 mmHg range. However, the error becomes much more dependent on the quantity of fetal hemoglobin and error may reach 6% during desaturation episodes. This article is not very helpful for the PICO question being asked, except that the SpO2 may tend to overestimate the true saturation in the lower range, particularly in the presence of high fetal hemoglobin (e.g., ELBW).


Level of Evidence: 4  
Quality of Evidence: Fair  
Reviewer's Comments: 50 healthy term newborns were assessed for pre- and post-ductal oxygen saturations following birth. Values were obtained in all by 2 minutes. The instruments used in this study have been improved since the study.


Level of Evidence: 4  
Quality of Evidence: Fair  
Reviewer's Comments: This was evidently an expanded version of the trial reported by Escrig, et al (Pediatrics, 2008, p 875), now with 37 randomized to 30% FiO2 and 41 randomized to 90% FiO2, for a total of 78, as opposed to 42. Again, the times to reach the target SpO2 (75% at 5 minutes and 85% at 10 minutes) were similar.
However, biochemical markers were less in the 30% group at 3 and 6 days of age and chronic lung disease was dramatically less in the 30% group. The low-oxygen group needed fewer days of oxygen supplementation (6 vs 22 days) and fewer days of mechanical ventilation (13 vs 27 days) and had a lower incidence of BPD at discharge (15.4% vs 31.7%). The implications of this and the Escrig study are limited by the caretakers not being blinded to group assignment. This is also the only group to have demonstrated such dramatic differences in outcome from such brief exposure to high FiO2 for less than 5 minutes in the presence of equal SpO2.


**Level of Evidence:** 5  
**Quality of Evidence:** Good  
**Reviewer’s Comments:** This was a 2-center prospective, randomized, control trial of 41 infants of 23-32 weeks gestation who required “any resuscitation” at birth. The babies were randomized to 21% or 100% oxygen and subsequent oxygen concentration was guided by pulse oximetry with a pre-ductal oximeter probe. In the 100% group, FiO2 was weaned if after 5 minutes the sats were > 95%. In the RA group, FiO2 was increased to 100% if HR<100 at 2 minutes, <60 for 30 seconds, or chest compressions required; or in 25% increments if sats < 70 at 3 minutes or <85% at 5 minutes. All infants in the RA group required an increase in FiO2. More infants in the 100% O2 group had sats >95% (significant at 4 and 5 minutes only, probably because of being underpowered).

The authors concluded that room air not be used for resuscitation of babies <=32 weeks because their target goals were not achieved. However, it should be noted that the strategy they used also resulted in hyperoxemia in the 100% group. This paper supports the discontinuance of using either RA or 100% in the VLBW baby, but does not help to define the optimum percentage to use between 21% and 100%.