The effect of variable pre-oxygenation endpoints on safe apnoea time using high flow nasal oxygen in comparison to standard facemask technique in pregnancy: a modelling investigation.

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Running title
Modelling apnoea: HFNO, facemask & variable $F\varepsilon'O_2$

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Abstract

Background. Studies of pulmonary denitrogenation (pre-oxygenation) in obstetric populations have shown high flow nasal oxygen therapy (HFNO) is inferior to facemask techniques. HFNO achieves median end tidal oxygen fraction (Fe'O₂) of 0.87 after 3 minutes. As HFNO prolongs safe apnoea times through apnoeic oxygenation, we postulated that HFNO would still extend safe apnoeic times despite the lower Fe'O₂ after pre-oxygenation.

Method. The Interdisciplinary Collaboration in Systems Medicine simulation suite, a highly integrated, high fidelity model of the human respiratory and cardiovascular systems, was used to study the effect of varying Fe'O₂ (60, 70, 80 and 90%) on the duration of safe apnoea times using HFNO and facemask techniques (with the airway open and obstructed). The study population consisted of validated models of pregnant women in active labour and not in labour with body mass index (BMI) of 24, 35, 40, 45 and 50 kg m⁻².

Results. HFNO provided longer safe apnoeic times in all models, with all Fe'O₂ values. Labour and increased BMI reduced this effect, in particular a BMI of 50 kg m⁻² reduced the improvement in apnoea time to 1.8–8.5 minutes (depending on the Fe'O₂), compared to an improvement of more than 60 minutes in the subject with BMI 24 kg m⁻².

Conclusions. Despite generating lower Fe'O₂, HFNO provides longer safe apnoea times in pregnant subjects. Care should be taken when use in BMI ≥50 kg m⁻² as the extension of the safe apnoea time is limited.

Keywords. Apnoea, computer simulation, high-flow nasal oxygenation, obstetrics, obesity in pregnancy.
Introduction

Achieving a safe apnoea time through adequate pre-oxygenation remains a key component of safe general anaesthesia in obstetrics. Pre-oxygenation using a standard facemask technique to an end-tidal oxygen fraction (Fe\textsubscript{E}O\textsubscript{2}) of at least 90% is recommended prior to inducing general anaesthesia.\textsuperscript{1} However, it is well recognised that several factors make this difficult to achieve in obstetric practice. Time pressure, human factors and maternal distress can all impede the optimal use of a tight fitting facemask and lead to sub-optimal pre-oxygenation.\textsuperscript{2} Even with adequate pre-oxygenation, the physiological changes of pregnancy result in more rapid deoxygenation and a shorter safe apnoea time (defined here as the time to desaturate to <90%) for labouring women.\textsuperscript{3}

Prolonging safe apnoea times through apnoeic oxygenation has grown in popularity in non-obstetric anaesthesia in recent years.\textsuperscript{4,5} During the induction of anaesthesia, apnoeic oxygenation can be achieved by continuing oxygen delivery via the application of a tight fitting facemask until airway instrumentation. This can be supplemented by the addition of nasal cannula that can also deliver oxygen during airway instrumentation. Utilising high-flow, humidified, nasal oxygen (HFNO) at ≥70 L min\textsuperscript{-1} to provide such apnoeic oxygen supplementation is appealing in obstetrics, because the handsfree nature and lack of a requirement for a tight facemask seal have clear benefits over traditional facemask pre-oxygenation. However, there have not yet been any randomised control trials of HFNO in obstetric airway management; indeed, this would present a particular challenge given the preference for regional anaesthesia and the unpredictable nature of most airway management scenarios in obstetric practice. Instead, recent work has studied the efficacy of HFNO in pre-oxygenation; three studies have demonstrated that pre-oxygenation with HFNO is inferior to a tight fitting facemask in healthy pregnant volunteers.\textsuperscript{6-8} HFNO achieved a mean Fe\textsubscript{E}O\textsubscript{2} of 87% at 3 minutes (95% confidence interval: 86.5–89%) with tidal breathing.\textsuperscript{7} Whilst in a separate study using HFNO with up to twenty vital capacity breaths,\textsuperscript{8} the median maximum Fe\textsubscript{E}O\textsubscript{2} was 82% (interquartile range [IQR] 75–86%) and 73% (IQR 63–84%) with mouth closed and mouth open respectively. These studies also identified outliers with final Fe\textsubscript{E}O\textsubscript{2} <75%. Increasing pre-oxygenation time to 8 minutes does not improve the proportion of healthy pregnant volunteers reaching Fe\textsubscript{E}O\textsubscript{2} 90 with HFNO.\textsuperscript{9} As current HFNO devices prevent measurement of Fe\textsubscript{E}O\textsubscript{2} in clinical practice, the results of the studies are potentially concerning.

Given that HFNO facilitates apnoeic oxygenation to extend safe apnoea times, we postulate that even with a lower Fe\textsubscript{E}O\textsubscript{2}, apnoeic oxygenation will extend the safe apnoea period beyond that seen with facemask techniques in obstetric airway management.

Due to the ethical and practical difficulties in addressing this question in patients, we utilised a high-fidelity computational simulation to investigate the effects of various Fe\textsubscript{E}O\textsubscript{2} values on the safe apnoea time for both HFNO and facemask pre-oxygenation for obstetric patients.
Methods

The Interdisciplinary Collaboration in Systems Medicine (ICSM) simulation suite is a high-fidelity, highly-integrated model of the respiratory and cardiovascular systems, based on the Nottingham Physiology Simulator, which has been previously described in detail. It is validated for investigation of pre-oxygenation and apnoea in adults, and specifically in pregnancy. The model has been recently extended to include cardiogenic gaseous oscillations, gas-mixing within the pulmonary deadspace and pharyngeal pressure oscillations during the use of HFNO at 70L min⁻¹. Details of the model are described in the online supplementary material.

Ten virtual subjects were created, based on published physiological data; these were similar to those used in our previous works. These subjects had body mass indices (BMI) of 24 kg m⁻² (BMI24), 35 kg m⁻² (BMI35), 40 kg m⁻² (BMI40), 45 kg m⁻² (BMI45), and 50 kg m⁻² (BMI50), and included subjects in active labour and not in labour. Where physiological data were not available, values were inferred from non-pregnant study data and established physiological theory (Table 1).

Each virtual subject underwent pulmonary pre-oxygenation via tidal breathing with FiO₂ 1.0 to reach Fe'O₂ of 60, 70, 80 and 90% before apnoea commenced. During apnoea, 100% or 21% oxygen was provided at the open glottis to simulate the continuation of HFNO or the removal of facemask during airway manipulation. Simulation runs also included a closed glottis, and in this scenario, ambient oxygen fraction was irrelevant since it did not pass the glottis. At the onset of apnoea, functional residual capacity (FRC) was reduced by 20% in the BMI24 subject and by 30% in the remaining subjects simultaneously, oxygen consumption (VO₂) was reduced by 65 ml min⁻¹ to simulate the effect on metabolic oxygen consumption of general anaesthesia and use of rocuronium as a choice of muscle relaxant. Apnoea continued until arterial haemoglobin oxygen saturation (SaO₂) reached 40%.

The SaO₂ was recorded every 5 milliseconds from the start of pre-oxygenation until termination of the protocol. Model simulations ran on a 64-bit Intel Core i7 3.7 GHz Windows 10 personal computer, running Matlab version R2018a.v9 (MathWorks Inc. MA, USA).

Results

Table 2 and Table 3 show the safe apnoea times for the various Fe'O₂ values studied in the subjects not in labour and in active labour, respectively.

Increasing the Fe'O₂ from 60% to 90% at the end of pre-oxygenation markedly extended the time to reach SaO₂ 90% and SaO₂ 40% during apnoeic oxygenation in all subjects. There is a significant increase in time to SaO₂ 90% time between Fe'O₂ 80% and 90% in all groups except BMI 24 not in labour.
The use of HFNO significantly delayed haemoglobin desaturation in all subjects in comparison to the standard facemask technique. In the BMI24 subject, who was not in active labour, the lowest SaO₂ was 82% after 120 minutes of apnoea with an open airway.

HFNO not only delayed desaturation overall, but also changed the shape of the desaturation curve with respect to time. Desaturation occurred more slowly overall and the gradient of the steep part of the curve was reduced. The decrease in SaO₂ from 90% to 40% took 12.5 minutes in the subject with the highest BMI (i.e. BMI50, in labour, Fe'O₂ 60%) with HFNO, compared to 3.7 minutes in the subject with the lowest BMI (i.e. BMI24, Fe'O₂ 90%) with facemask. For HFNO, when the Fe'O₂ was 90%, we also observed an initial plateau phase, where SaO₂ was maintained at 100%, prior to a gradual decrease to 90%. When Fe'O₂ was less than 90%, this plateau phase of the curve was very short, such that there was a slow decrease in SaO₂ after the first 1–2 minutes of apnoea. These changes are illustrated in Figure 1 for the BMI35 labouring subject, and they occurred in all models for HFNO at all Fe'O₂ values, with shorter timescales as BMI increased or end-tidal O₂ concentration decreased.

The presence of labour and/or increased BMI significantly shortened the safe apnoea time in all subjects. Despite the safe apnoic time being greatest with HFNO at all Fe'O₂ values in comparison to facemask techniques, there was a profound reduction in the observed increase in safe apnoic times for HFNO in the BMI50 subject (Table 2). In that subject, compared to the facemask models, HFNO increased safe apnoic time by only 1.8–8.5 minutes, dependent upon the Fe'O₂. This contrasts with increases of around 60 minutes in the BMI24 subject at all values of Fe'O₂.

In active labour, using HFNO with Fe'O₂ 60%, safe apnoea time was reduced by approximately 66% (from 66.9 to 22.7 minutes) in the BMI24 subject, by 42% (from 19.8 to 11.4 minutes) in the BMI35 subject, by 33% (from 12.8 to 8.6 minutes) in the BMI40 subject, by 38% in the BMI45 subject (from 7.9 to 4.9 minutes) and by 7% (from 3.9 to 3.7 minutes) in the BMI50 subject.

Figure 2 shows the difference in minutes to reach SaO₂ 90% between HFNO with the different Fe'O₂ (i.e. 60, 70, 80, 90%) and facemask with Fe'O₂ of 90% in the subjects not in labour (upper panel) and in subjects in labour (lower panel). In every configuration and every subject, HFNO offered a longer safe apnoea time, although with the increase of BMI and with the labour the gain is less marked.

**Discussion**

Our computational modelling of apnoeic oxygenation predicted that pre-oxygenation to a lower Fe'O₂ value does not prevent HFNO from providing a clinically significant increase in the safe apnoea time in obstetric populations. Even when starting with Fe'O₂ 60%, HFNO increased safe apnoea time to over 60 minutes in a non-obese parturient (similar to findings in non-obstetric populations). HFNO provided superior safe apnoeic times in all models compared to face mask pre-oxygenation with the same starting Fe'O₂. Furthermore, HFNO
provided a superior safe apnoea time from Fe’O₂ 60% than standard facemask pre-oxygenation to Fe’O₂ 90% in all modelled subjects. Greater increases in safe apnoea times were seen with higher Fe’O₂ values for HFNO, particularly when Fe’O₂ was increased from 80% to 90%. This reinforces the importance of appropriate use of HFNO to maximise patients’ Fe’O₂ — applying HFNO as soon as the patient enters the operating theatre, providing the maximum time for pre-oxygenation at the maximum tolerated flow rate.

The best initial flow rate remains an area of uncertainty, with concerns of patient tolerance of flows as high as 60–70L min⁻¹;⁹ the minimum flow rate required for pre-oxygenation remains unknown. Pre-oxygenation in HFNO studies has used a mixture of starting flow rates. Two started at 30 L min⁻¹ and either gradual ramped the flow to 60 L min⁻¹ or increased to 60 L min⁻¹ after a set time period,⁶ whilst two others started at 50 L min⁻¹.⁸,⁹ As our current model is validated for HFNO using the maximum flow rate of 70L min⁻¹, we cannot comment further on what would be the best flow rate to balance comfort and the highest generated Fe’O₂, though this an area for further research.

As our previous work demonstrated,¹⁴,¹⁹ HFNO also alters the shape of the desaturation curve, reducing the gradient of the initial decrease in SaO₂ to 90% and the subsequent steeper decrease (from 90% to 40%); this extends the available time for critical thinking and enacting airway rescue plans. Our data show that this effect is maintained regardless of the Fe’O₂ achieved during HFNO pre-oxygenation. If the Fe’O₂ achieved during pre-oxygenation is less than 90% (i.e. the likely real life scenario⁵⁻⁹), our modelling also predicted a slow decrease in SaO₂ soon after apnoea (Figure 1). Along with the relatively larger decreases in safe apnoea time with a decrease from Fe’O₂ 90% to 80%, this finding implies that the physiological mechanisms underpinning apnoeic oxygenation are more effective with a higher Fe’O₂. Clinically, this also highlights that a slight reduction in SaO₂ should be expected with HFNO after the onset of apnoea, but this may also help a clinician detect the failure of apnoeic oxygenation. Should this occur, the SaO₂ will follow the closed glottis curve (Figure 1) and a more rapid, accelerating fall in SaO₂ to 90% will be seen, rather than the slower decline to 90% with successful apnoeic oxygenation.

Increasing BMI was observed to reduce the extent of the improvement in safe apnoea time using HFNO. Increased closing capacity, lower airway collapse, atelectasis, the subsequent increase in the shunt fraction seen under the effects of GA and muscle relaxation in this cohort could explain these effects, which cannot be completely overcome.²² Being in active labour had a similar effect to increasing BMI. The greatest benefit when using HFNO for subjects in labour and high BMI were seen when Fe’O₂ reached 90%, which may be difficult to achieve.⁶⁻⁹ Our modelling in the highest BMI subjects (BMI45 and BMI50) predicts much smaller increases in safe apnoeic time with HFNO and an Fe’O₂ of less than 90% compared to facemask pre-oxygenation to an Fe’O₂ 90%. An increase of 3.4–5.2 minutes for BMI45 and 0.3–1.3 minutes for BMI50 dependent on Fe’O₂ was seen (Figure 2). Given that this cohort is at greater risk of airway obstruction, these patients are also at a greater risk of failure of apnoeic oxygenation and rapid deoxygenation. Our modelling predicts that when apnoeic oxygenation
fails, a very short safe apnoeic period ensues, especially when Fe′O₂ 90% has not been reached; this remains a concern. These patients are more likely to have difficult airway management and to desaturate rapidly after facemask pre-oxygenation; therefore, they should benefit most from HFNO. However, findings of this study suggest that they receive the least benefit. Whilst any additional increase in safe apnoea time may be lifesaving, the modest increase in safe apnoea time, particularly in the BMI50 group, combined with the risk of failure of apnoeic oxygenation may not outweigh the benefits of instant access to bag and mask ventilation, we recommend that HFNO should be used cautiously in this group.

We have utilised computational modelling to address an issue that would be extremely difficult to address using clinical methods. Of course, the quality of the data and the assumptions built into the model represent a potential weakness of this approach; however, the ICSM simulation suite has been very extensively validated in reproducing the physiological changes during apnoea in obstetric and non-obstetric populations, and it provides a suitable methodological approach given the ethical concerns with intentionally inadequate pre-oxygenation, and in studying the limits of safe apnoeic times in an obstetric population.

In contrast to our previous modelling studies,15-17 we chose to model the use of rocuronium instead of suxamethonium for muscle paralysis. This replicates the current practice in many obstetric units, and an increasing trend across obstetric practice.24 This change removes the transient increase in VO₂ seen with suxamethonium. This could be argued to extend the safe apnoeic times compared to our previous modelling studies, but this would affect each of our study subjects similarly.

HFNO offers additional benefits beyond apnoeic oxygenation for obstetrics. Theoretically, it provides a hands-free method of pre-oxygenation that does not require a tight facemask seal and can be applied as soon as the patient enters theatre, limiting the impact of the many detrimental factors which influence pre-oxygenation in obstetric general anaesthesia.3 HFNO therefore could be argued to improve the overall safety of obstetric airway management, despite concerns of a lower final Fe′O₂ after pre-oxygenation with HFNO. Apnoeic oxygenation will still extend the safe apnoeic time significantly providing an extra safety net for airway management, even with Fe′O₂ of only 60%. The additional benefits of HFNO for apnoeic oxygenation can therefore be cautiously extended to obstetric airway management. The exception maybe when the at extremes of BMI, as the gains in safe apnoeic times are significantly reduced, particularly if Fe′O₂ 90% is not achieved. Unfortunately, it is in these most obese patients where difficult airway management and rapid deoxygenation is often encountered. The advantages of the standard facemask technique to facilitate measurement of Fe′O₂, and to facilitate bag mask ventilation, if required should not be ignored in this situation. It may be that by combining nasal cannula oxygen with facemask pre-oxygenation (so called low-flow apnoeic oxygenation) will be of value in this cohort. This technique could enable the benefits of facemask pre-oxygenation, apnoeic oxygenation and easier rescue bag-mask ventilation. Further modelling work comparing lower flow nasal cannula apnoeic
oxygenation techniques to HFNO should be undertaken to help clarify the benefits of different models of apnoeic oxygen in obstetrics.

In summary, our modelling shows that HFNO provides superior safe apnoea times in pregnant subjects despite generating a lower \( \text{FeO}_2 \) after pre-oxygenation and supports cautious application to obstetric anaesthetic practice. Care should be taken when used in BMI \( \geq 50 \) kg \( m^{-2} \) as the gain in safe apnoea time is limited.

**Author's contributions**

Design of study: DS, ML, AP, JGH
Design of computational models: JGH
Simulation runs: ML
Configuration of subjects & interpretation of data: DS, ML, AP, JGH
Writing and final approval of manuscript: DS, ML, AP, JGH

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**Declaration of Interests**

JGH is the associate editor-in-chief of the British Journal of Anaesthesia. JGH accepts fees for the provision of advice to the police, crown prosecution service, coroners and solicitors.

The other authors have no conflicts to declare.

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Fisher and Paykel Healthcare (New Zealand): sponsorship of research into apnoea and mechanisms of gas exchange.

**Supplementary material**

Supplementary material is available online.


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### Tables

**Table 1.** Baseline physiological values used to configure the virtual obstetric subjects.\textsuperscript{15-17, 21, 25, 26}

<table>
<thead>
<tr>
<th></th>
<th>BMI 24</th>
<th>BMI 24 &amp; labour</th>
<th>BMI 35</th>
<th>BMI 35 &amp; labour</th>
<th>BMI 40</th>
<th>BMI 40 &amp; labour</th>
<th>BMI 45</th>
<th>BMI 45 &amp; labour</th>
<th>BMI 50</th>
<th>BMI 50 &amp; labour</th>
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<td>75</td>
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<td>94</td>
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<td>108</td>
<td>122</td>
<td>122</td>
<td>135</td>
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<td>Tidal volume (ml)</td>
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<td>690</td>
<td>900</td>
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<td>730</td>
<td>950</td>
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<tr>
<td>Respiratory rate (breaths min(^{-1}))</td>
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<td>23</td>
<td>16</td>
<td>23</td>
<td>16</td>
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<td>16</td>
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<td>Functional residual capacity (ml)</td>
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<td>1600</td>
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<td>1600</td>
<td>1600</td>
<td>1600</td>
<td>1600</td>
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<td>Deadspace (%)</td>
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<td>140</td>
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<td>Shunt fraction (%)</td>
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<td>13</td>
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<tr>
<td>Cardiac output (L min(^{-1}))</td>
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<td>8.3</td>
<td>8.0</td>
<td>9.6</td>
<td>8.6</td>
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<td>8.8</td>
<td>10.0</td>
<td>9.0</td>
<td>10.5</td>
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<tr>
<td>Heart rate (beats min(^{-1}))</td>
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<td>100</td>
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<td>100</td>
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<td>100</td>
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<td>Total blood volume (L)</td>
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<td>Haemoglobin concentration (g dl)</td>
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<td>11.3</td>
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<td>Oxygen consumption (ml min(^{-1}))</td>
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<td>338</td>
<td>404</td>
<td>388</td>
<td>464</td>
<td>439</td>
<td>524</td>
<td>450</td>
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<tr>
<td>Respiratory quotient</td>
<td>0.88</td>
<td>0.88</td>
<td>0.88</td>
<td>0.88</td>
<td>0.88</td>
<td>0.88</td>
<td>0.88</td>
<td>0.88</td>
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</tbody>
</table>

BMI 24 / 35 / 40 / 45 / 50 body mass index 24 / 35 / 40 / 45 / 50 kg m\(^{-2}\), respectively
Table 2: Times in minutes to reach SaO\textsubscript{2} 90% and 40% during apnoeic oxygenation for different end-tidal oxygen fractions in the subjects not in labour.

<table>
<thead>
<tr>
<th>End-tidal oxygen fraction (%)</th>
<th>BMI 24</th>
<th>BMI 35</th>
<th>BMI 40</th>
<th>BMI 45</th>
<th>BMI 50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Closed Glottis</td>
<td>FiO\textsubscript{2} 21%</td>
<td>HFNO</td>
<td>Closed Glottis</td>
<td>FiO\textsubscript{2} 21%</td>
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<tr>
<td><strong>Time from onset of apnoea to SaO\textsubscript{2} 90% (minutes)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>3.1</td>
<td>3.7</td>
<td>66.9</td>
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<td>4.1</td>
<td>63.9</td>
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<tr>
<td>80</td>
<td>4.5</td>
<td>4.8</td>
<td>63.8</td>
<td>3.7</td>
<td>3.9</td>
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<td>90</td>
<td>6.6</td>
<td>7.8</td>
<td>65.2</td>
<td>5.6</td>
<td>6.5</td>
</tr>
<tr>
<td><strong>Time from onset of apnoea to SaO\textsubscript{2} 40% (minutes)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>6.0</td>
<td>7.0</td>
<td>n.a.</td>
<td>6.1</td>
<td>6.7</td>
</tr>
<tr>
<td>70</td>
<td>6.7</td>
<td>7.5</td>
<td>n.a.</td>
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<td>90</td>
<td>9.8</td>
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<td>n.a.</td>
<td>9.0</td>
<td>10.6</td>
</tr>
</tbody>
</table>

SaO\textsubscript{2}: arterial oxygen saturation; BMI 24 / 35 / 40 / 45 / 50 body mass index 24 / 35 / 40 / 45 /50 kg m\textsuperscript{-2}, respectively; FiO\textsubscript{2} inspired fraction of O\textsubscript{2}; n.a.: not achieved, i.e. SaO\textsubscript{2} does not drop to 40%, but, in 120 minutes of apnoea, SaO\textsubscript{2} reaches 82%, 82%, 82% and 83% with end-tidal oxygen fractions 60%, 70%, 80% and 90%, respectively.
Table 3. Times in minutes to reach SaO$_2$ 90% and 40% during apnoeic oxygenation for different end-tidal oxygen fractions in the subjects in labour.

<table>
<thead>
<tr>
<th>End-tidal oxygen fraction (%)</th>
<th>BMI 24 &amp; Labour</th>
<th>BMI 35 &amp; Labour</th>
<th>BMI 40 &amp; Labour</th>
<th>BMI 45 &amp; Labour</th>
<th>BMI 50 &amp; Labour</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Closed Glottis</td>
<td>FiO$_2$ 21%</td>
<td>HFNO</td>
<td>Closed Glottis</td>
<td>FiO$_2$ 21%</td>
</tr>
<tr>
<td>Time from onset of apnoea to SaO$_2$ 90% (minutes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>3.1</td>
<td>3.3</td>
<td>22.7</td>
<td>2.4</td>
<td>2.6</td>
</tr>
<tr>
<td>70</td>
<td>3.6</td>
<td>3.8</td>
<td>23.7</td>
<td>2.8</td>
<td>3.0</td>
</tr>
<tr>
<td>80</td>
<td>4.1</td>
<td>4.4</td>
<td>25.4</td>
<td>3.2</td>
<td>3.4</td>
</tr>
<tr>
<td>90</td>
<td>5.8</td>
<td>6.9</td>
<td>33.9</td>
<td>4.5</td>
<td>5.4</td>
</tr>
</tbody>
</table>

| Time from onset of apnoea to SaO$_2$ 40% (minutes) |
| 60 | 6.0 | 6.6 | 45.7 | 4.6 | 5.0 | 23.8 | 4.6 | 4.9 | 19.7 | 4.4 | 4.7 | 17.9 | 4.5 | 4.7 | 16.2 |
| 70 | 6.5 | 7.1 | 46.1 | 5.0 | 5.4 | 24.8 | 4.8 | 5.2 | 20.4 | 4.6 | 4.9 | 18.5 | 4.7 | 5.0 | 16.7 |
| 80 | 7.0 | 7.8 | 47.4 | 5.4 | 5.9 | 25.8 | 4.9 | 5.3 | 21.0 | 4.8 | 5.1 | 19.4 | 4.8 | 5.1 | 16.9 |
| 90 | 8.9 | 10.5 | 52.7 | 6.8 | 8.1 | 34.3 | 6.1 | 7.1 | 28.4 | 5.6 | 6.5 | 25.5 | 5.6 | 6.6 | 24.0 |

SaO$_2$: arterial oxygen saturation; BMI 24 / 35 / 40 / 45 / 50 body mass index 24 / 35 / 40 / 45 / 50 kg m$^{-2}$, respectively; FiO$_2$ inspired fraction of O$_2$. 
Figures legend

**Figure 1.** Oxygen saturation during apnoea (SaO$_2$) in the virtual subject BMI35 kg m$^{-2}$ in labour, during HFNO, closed glottis, and open airway with FiO$_2$ 21%. Closed glottis simulates failure of HFNO whereas FiO$_2$ 21% with end-tidal oxygen fraction (FETO$_2$) of 90% simulates facemask technique.

**Figure 2.** Gain in safe apnoea times, calculated as difference in minutes to reach SaO$_2$ 90% between HFNO with end-tidal oxygen fraction (FETO$_2$) of 60, 70, 80, 90% and facemask with FETO$_2$ of 90%.