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DEVELOPMENT OF A PULMONARY OXYGEN TOXICITY RISK CALCULATOR FOR REPEATED DIVES WITH PO_2 = 1.3 ATM

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14. ABSTRACT
A two-part residual oxygen time model predicts the probability of detectible pulmonary oxygen toxicity (P[O_2tox]) after dives with oxygen partial pressure (PO_2) approximately 130 kPa, and provides a tool to plan dive series with selected risk of P[O_2tox]. Data suggest that pulmonary oxygen injury at this PO_2 is additive between dives. Recovery begins after a delay and continues during any following dive. A logistic relation expresses P[O_2tox] as a function of dive duration (T_{dur}) [hours]

$$P[O_2tox] = 100 / [1+\exp (3.586–0.49 \cdot T_{dur})]$$

This expression maps T_{dur} to P[O2tox] or, in the linear mid-portion of the curve, P[O_2tox] to T_{dur}. For multiple dives or during recovery, it maps incidence of signs or symptoms to an equivalent dive duration, T_{eq}.

T_{eq} was found after second dives of duration $T_{dur\ 2}$. Residual time from the first dive $t_r = T_{eq} – T_{dur\ 2}$. With known t_r, t and T_{dur}, a recovery model was fitted.

$$t_r = T_{dur} \cdot \exp [– k\cdot((t–5)/T_{dur})^2], \text{ where}$$

k = 0.149 for resting, and 0.047 for exercising divers, and t represents time (hours) after surfacing. An electronic implementation of the equations is presented.

The fits were assessed for 1352 man-dives. Standard deviations of the residuals were 8.5% and 18.3% probability for resting or exercise dives, respectively. This model and its calculators apply only to dives with PO_2 of 1.3 to 1.4 atm and with T_{dur} ≤8 hours.

15. SUBJECT TERMS
model, pulmonary oxygen toxicity, risk, rebreather, calculator, UBA, technical diving

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INTRODUCTION

The set point for the MK 16 Mod 1 underwater breathing apparatus (UBA) is PO_2 = 1.3 atm. This is also the prevalent PO_2 in the MK 25 UBA with normal purging at depths near 20 feet, the depth of transit swims. Dives with this PO_2 have low risk of central nervous system oxygen toxicity. However, long or repeated dives at PO_2 = 1.3 atm may cause pulmonary oxygen toxicity. That is the exposure considered in the model presented here.

Divers may wish to know the risk of incurring signs or symptoms of pulmonary oxygen toxicity after an exposure. They may also want to know the cumulative effects of multiple dives with various surface intervals (SI). Navy Experimental Diving Unit (NEDU) has performed more than 1350 IRB-approved in-water man-dives with PO_2 = 1.3 to 1.4 atm (1–13), a total of more than 5,500 man-hours of diving. Risk of and recovery from the pulmonary oxygen toxicity resulting from these exposures have been addressed through modelling based on those data. Calculation algorithms have resulted; they are the “risk calculator” mentioned in the title of this report.

In the model development, any exposure to elevated PO_2 was assumed to begin a process of pulmonary injury that increases with exposure time. Symptoms or changes in pulmonary function, specifically in flow – volume parameters (ΔFV), indicate detectable pulmonary oxygen toxicity, but pulmonary oxygen toxicity can be present without signs or symptoms.

The probability of signs and symptoms of pulmonary oxygen toxicity (P[O_2Tox]) is extremely low if the exposure to the elevated PO_2 is short, is close to unity if the exposure is very long, and is approximately proportional to exposure time for intermediate exposures. The incidence of symptoms or ΔFV estimates the probability. Thus, in the midrange the incidence can be mapped to the exposure duration (T_{dur}). Further, after a composite exposure to or during recovery from exposure to PO_2 = 130 kPa, the incidence of symptoms or signs can be mapped to an equivalent oxygen time (T_{eq}) defined as the single exposure duration with the same probability of pulmonary function changes or of symptoms.

Recovery begins sometime after the end of exposure. The probability that a diver has symptoms or measurable changes in pulmonary function decreases with time as symptoms and signs resolve. The reduced incidence translates to a lower T_{eq}. T_{eq} remaining during recovery is called the residual oxygen time (t_r), and the exposure times of later dives are assumed simply to add to t_r.

In the description that follows, the term “dive” refers to similar exposures of multiple people. The full model is a composite of an incidence – time model which translates dive duration or equivalent dive time at PO_2 = 1.3 to 1.4 atm to P[O_2tox], and a recovery model which expresses remaining pulmonary oxygen insult as residual oxygen time. Immediately after any dive T_{eq} is the sum of duration of the current dive and any t_r from previous dives.

METHODS

Model Building

Incidence-Time Model

The incidence-time model was developed based on the single dive data described in Table 1 and shown in Figure 2. Incidences of overt pulmonary oxygen toxicity after a total of 529 man-dives in eight distinct exposures were fitted by logistic regression for an expression of the form,

$$P[O_2tox]\ (\%) = 100 / [1+\exp(b - m \cdot T_{dur})], \qquad [1]$$

where m = the slope, and b = the intercept of a linear relation between T_{dur} and the log-transformed probability of pulmonary oxygen toxicity. The odds ratio would be that probability divided by the probability of similar ΔFV or symptoms after an air exposure. Data after air exposures are available for only some of the dive profiles (Table 2). The overall probability of apparent pulmonary toxicity after an air dive is 6%.

The presence of one or more respiratory symptoms or flow-volume deficits (ΔFV) after a dive indicated overt pulmonary oxygen toxicity. The symptoms considered were inspiratory burning, cough, chest tightness, and dyspnea. A flow-volume deficit was defined as a parameter value depressed from baseline beyond the 95% confidence bounds of day-to-day, non-diving variability previously measured at NEDU (1). Specifically, decreases from baseline were called deficits if the average of three consistent measurements was below baseline (a three- to six-value average) by more than 7.7% for FVC, 8.4% for FEV_1, or 17% for $FEF_{25–75}$. Note that the use of multiple criteria, each with less than 5% possibility of a false positive, leads to an overall probability of a false positive that is greater than 5%. However, false positives for ΔFV were considered safer than false negatives.

The estimate used for $P[O_2tox]$ was the number of divers with symptoms and/or ΔFV divided by the number of divers exposed. When a dive profile had been investigated in more than one dive series, the information was combined as the total number of divers who reported symptoms or showed ΔFV, divided by the total number of divers exposed to the condition. The assumption that the populations could be pooled was tested using Tarone's Z (14).

Table 1. Sources for single dive data, PO_2 = 1.3 atm

Dive duration	n (person dives)	Breathing conditions	References
4 hours , rest	75	MK 20, test pool	1, 2, 5, 10
6 hours, rest	72	MK 20, test pool	1, 4, 10, u
8 hours, rest	79	n=62: MK 20, test pool n=17: MK 16, BBAT(tower)	1, 3, 7
3 hours, exercise	38	n=23: MK 20, test pool n=15: MK 25, test pool	8, 9
3.5 hours, exercise	68	MK 20, test pool	13
4 hours, exercise	84	MK 20, test pool	6, 11
6 hours, exercise	25	MK 20, test pool	u
6, 6.5, and 7 hours, some exercise	88	MK 16 for exercise, MK 25 at rest; OSF	12
	Total = 529		

Reference “u” means unpublished dives from the MULLET protocol. “OSF” is the ocean simulation facility, a pressure chamber with a large wet-pot. The BBAT tower was 50 feet deep. The test pool is 15 feet deep.

The counts include single dives and the first dives of series.

MK 20 divers were supplied with humidified 100% O_2. MK 16 divers in the BBAT ascended once in the middle of the 8-hour dive for a rig change-out.

Divers breathing the MK 20 at rest in the test pool sat in chairs for a chest depth about 12 feet (3.7 m) and a hydrostatic load similar to head-out immersion, but they sometimes moved about or even lay on the bottom. Divers breathing the MK 25 lay prone on the bottom during their rest periods.

Divers exercising while breathing the MK 20 or MK 25 were semi-prone on cycle ergometers with chest depth similar to that when seated. They cycled against a brake load that kept heart rate between 95 and 110 beats/min, estimated to be 30 to 40% $\dot{V}O_{2\ max}$. (Oxygen consumption measurements in the water were not available.) Work periods of 30 minutes were alternated with 30 minute rest periods. Divers exercising with the MK 16 (6, 6.5, and 7 hours) performed periodic underwater weight-lifting.

For the four-hour MK 25 dives, purge procedures gave at least 90% oxygen at the beginning of dives. Purge procedures for the 6- to 7-hour dives gave about 80% O_2 and divers were at 20 fsw, for PO_2 initially approximately 1.3 atm.

Table 2. Sources of single "air dive" data

Dive duration	n (person dives)	Breathing conditions	References
4 hours , rest	8	MK 20, test pool	1
6 hours, rest	70	MK 20, test pool	1, u
8 hours, rest	8	MK 20, test pool	1
4 hours, exercise	70	MK 20, test pool	u
6 hours, exercise	83	MK 20, test pool	u
	Total = 239		

Counts include single dives and dives repeated daily for up to five days with surface intervals of 18 hours (six-hour dives) or 20 hours (four-hour dives). Later days were included as independent single dives because there was no evidence of cumulative effect.

The conditions are as described for Table 1, except that the breathing gas was air.

The incidences of detectable pulmonary oxygen toxicity recorded after single dives at PO_2 = 1.3 atm (Table 1) are shown as a function of dive duration in Figure 1. The error bars are the Agresti-Coull binomial 95% confidence intervals on the measured values,

$$95^{th}\ \%\ CI = \tilde{p} \pm 1.96 \cdot (\tilde{p}^{0.5}) \cdot (1 - \tilde{p})^{0.5} \cdot \tilde{n}^{-0.5} \qquad [2]$$

where $\tilde{p} = (X+1.96) / \tilde{n}$, $\tilde{n} = n+1.96^2$, X= number of "hits", and n = number of observations.

The Agresti-Coull confidence intervals are similar in form to, but more reliable than, the commonly used Walsh formulation for binomial distributions (15). They indicate the ranges of the true values of $P[O_2tox]$ for each dive duration.

Pulmonary signs and symptoms following open-circuit **air** dives were also available for 4-, 6-, and 8-hour resting dives and 4- and 6-hour dives with exercise (Table 2, Figure 1). The air dive conditions were identical to those of the open circuit dives with 100% oxygen in all ways except for the breathing gas, which provided PO_2 approximately 30 kPa. The resulting low incidence of signs and symptoms (Figure 1) can largely be ascribed to effects of breathing underwater from the MK 20 UBA. The number of divers with symptoms or ΔFV remained consistent as the number of repeated air dives increased, and values were too low for an equivalent oxygen exposure time to be assigned.

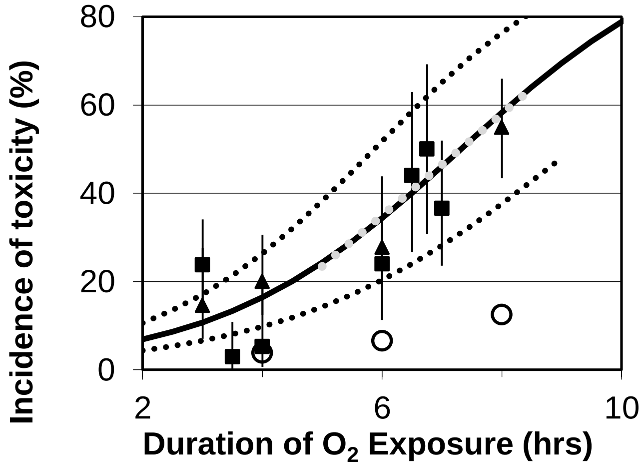

Figure 1. P[O_2Tox] as a function of dive duration, and the corresponding incidence – exposure time model. PO_2 = 1.3 atm data of Table 1: ▲ are resting dives; ■ are dives with exercise, means and Agresti-Coull binomial 95% confidence intervals. The solid line represents the logistic regression (RESULTS Equation 7), and the dashed lines show one standard error on the fitted parameters. The broken portion of the regression curve is the linear range from which T_{eq} was read from incidence to permit the determination of recovery parameters. **o** are the air dive (PO_2 = 0.3 atm) data of Table 2. Air dive error bars are omitted for clarity, but confidence intervals are tabulated here:

Confidence intervals on incidences of evident pulmonary oxygen toxicity after dives with PO_2 approximately 0.3 atm (air dives in the test pool).

Duration	lower 95th CI	upper 95th CI
4-hours	0.92	11.3
6-hours	3.49	11.8
8-hours	0.50	49.5

Resting and exercise dives were combined in the incidence-exposure time models; within two hours after surfacing, incidences after single four hour resting dives were statistically indistinguishable from those after single four-hour dives with exercise (8).

The binary outcome, overt evidence of pulmonary toxicity or no evidence of overt toxicity, was fitted by logistic regression of P[O_2Tox] vs. T_{dur}. This was the only fitting of binary or binomial data in the modeling process. The regression gives a one-to-one mapping between exposure duration and probability of overt pulmonary oxygen toxicity.

More importantly, the mid-range mapping can be inverted, allowing mid-range incidence to be mapped to equivalent exposure duration T_{eq}.

Recovery

$P[O_2tox]$ within two hours of surfacing is that from the previous hyperoxic exposure. That observed on the following day, though, represents partial recovery. In principle, the equivalent exposure time at any stage of recovery can be found from looking at the incidence of overt pulmonary oxygen toxicity on the y-axis of Figure 1 and reading the corresponding time. In practice, because of the local slope of the incidence – time curve, only incidences in the approximate range of 20 to 60% yield equivalent exposure times with any reasonable certainty. These criteria were satisfied for data obtained 18 hours after surfacing from single, 8-hour dives at rest, 18 hours after single 6-hour dives with exercise, and 22 hours after single dives 6.75-hour dives with exercise. For those dives, the equivalent dive durations were found by inversion of the incidence-time relation, and the residual time at the recovery time points equaled the equivalent times (**Bold** in Table 3).

Incidences during the recovery period after shorter single dives were low enough that they fell on the nearly-horizontal part of the logistic curve, the part of the curve where a small difference in assessment of pulmonary oxygen toxicity causes a very large difference in estimated T_{eq}, and thus the part of the curve where T_{eq} cannot be read with any precision. This difficulty in assessing recovery from most single dives was solved by using the incidence of signs and symptoms after a second exposure and finding the equivalent exposure duration that corresponded to the pair of dives. If the incidence after a second exposure was also below approximately 20%, the data were not used in the determination of model coefficients, but only in later assessment of the model.

A second exposure to oxygen was assumed to add injury directly to that remaining from the first exposure with no changes in susceptibility. T_{eq} for the combination of the two exposures and the surface interval between them was found by inverting the incidence – duration relationship for the incidence assessed within two hours of surfacing from the second dive. T_{eq} for the pair of dives was considered to be the sum of the second exposure duration (T_{dur2}) and t_r from the first exposure. Thus, t_r for the first dive was found by subtracting T_{dur2} from the T_{eq} for the pair of dives. The corresponding recovery time was the total time after surfacing from the first dive, that is, the sum of the surface interval and the duration of the second dive. Values are shown in Table 3.

The binomial incidence ($P[O_2Tox]$) data thus were transformed to the continuous variable t_r by inverting the logistic regression equation. The probability distribution of t_r is inverse logit, but logit and probit functions are similar in their middle (approximately linear) ranges, the portion of the curve from which the t_r data were drawn for parameter fitting. The inverse of the probit function is the normal distribution. To confirm that the selected values of t_r could be assumed to be normal variates, quartile plots were inspected. They showed no significant deviations from a normal distribution.

Table 3. Calibration data used to fit the recovery model, T_{dur} and T_{eq}

Dive duration, SI	Recovery time t after 1st dive (hrs)	P[O_2 tox] after 2nd dive (%)	T_{eq} after 2nd dive (hrs)	t_r (hrs)
Rest				
3 hrs, SI = 2 hrs	5	41.7	6.58	3.58
3 hrs, SI = 4 hrs	7	25.0	5.14	2.14
3 hrs, SI = 6 hrs	9	33.3	5.86	2.86
4 hours, SI = 20 hrs	24	12.9	4.09	0.09
6 hours, SI = 18 hrs	24	42.5	6.66	0.66
6 hrs, SI = 42 hrs	42	21.4	4.83	–1.17
8 hours, one dive	**18**	**31.4**	**5.70**	**5.70**
Exercise				
3 hrs, SI = 4 hrs	7	12.5	4.05	1.05
4 hrs, SI = 15 hrs	19	31.3	5.68	1.68
4 hrs, SI = 20 hrs	24	35.7	6.07	2.07
6 hrs, SI = 18 hrs	24	23.8	5.03	2.03
6 hrs, one dive	**18**	**58.3**	**8.03**	**8.03**
6.75 hrs, one dive	**22**	**26.0**	**5.23**	**5.23**

T_{eq} was obtained from the inversion of the incidence – time model of Figure 1. For single dives (**bold face**), $t_r = T_{eq}$. For pairs of dives, $t_r = T_{eq} – T_{dur2}$. For model fitting, the negative value was set to zero, and $t_r > T_{dur}$ was set to T_{dur}. The sources of data are listed in Table 4.

Based on inspection of the data, a delay t_d between surfacing and the start of recovery was introduced into the model. From a total of 620 man-dives, seven combinations of dive duration, recovery time, and t_r were available for parameter fitting after resting dives, and six after dives with exercise (Table 3, Figure 1). These constitute the recovery model calibration data. For fits of the exercise data, an extra value, $t_r = T_{dur}$ when $\boldsymbol{t} = 0$, where $\boldsymbol{t} = t – t_d$, was included to anchor the start of the fit.

Recovery was formulated as the decrease in t_r after diving.

$$t_r = T_{dur} \cdot e^{-f(\boldsymbol{t},\, T_{dur})}, \quad \boldsymbol{t} > 0$$

$$t_r = T_{dur}, \quad \boldsymbol{t} \le 0 \qquad [3]$$

where t is the recovery time (t = 0 at the end of the exposure of duration T_{dur}) and f($\boldsymbol{t}$, T_{dur}) means a function of $\boldsymbol{t}$ and T_{dur}.

Table 4. Sources of calibration data used to fit the recovery model. Dive pairs were used unless otherwise noted.

Dive duration	n (person-dives or -dive pairs)	Breathing conditions	References
Rest			
3 hrs, SI = 2 hrs	12	MK 20, test pool	4, 10
3 hrs, SI = 4 hrs	24	MK 20, test pool	4, 10
3 hrs, SI = 6 hrs	12	MK 20, test pool	4, 10
4 hours, SI = 20 hrs	49	MK 20, test pool	2, 5, 10
6 hours, SI = 18 hrs	40	MK 20, test pool	4, 10, u
6 hrs, SI = 42 hrs	14	MK 20, test pool	4, 10
8 hrs, single dive	71	n=23: MK 20, test pool n=31: MK 20, OSF n=17: MK 16, BBAT	1, 3, 7
	Total = 221		
Exercise			
3 hrs, SI = 4 hrs	25	n=12: MK 20, test pool n=13: MK 25, test pool	9
4 hrs, SI = 15 hrs	28	MK 20, test pool	6, 11
4 hrs, SI = 20 hrs	16	MK 20, test pool	6, 11
6 hrs, SI = 18 hrs	12	MK 20, test pool	u
6 hrs, one dive	13	MK 20, test pool	u
6, 6.5, and 7 hours, grouped as 6.75 hrs. single dive	73	MK 16, exercise, then MK 25 at rest, OSF	12
	Total = 167		

Conditions are described in the legend of Table 1.

Two forms were considered for the recovery exponent f(t, T_{dur}), one to yield exponential recovery:

$$f(t,T_{dur}) = -(c + g / T\mathrm{dur}) \cdot \mathbf{t} \qquad [4]$$

and, after inspection of the data (Figure 2), one that gives sigmoidal recovery:

$$f(t,T_{dur}) = -[(h \cdot \mathbf{t}^2 + k \cdot (\mathbf{t} / T\mathrm{dur})^2] \,. \qquad [5]$$

Parameters of the recovery exponents given by Equations 4 or 5 were fitted by non-linear regression of Equation 3 using the Gauss-Newton algorithm (SYSTAT10, SPSS Inc., Chicago, IL, USA). For normally distributed errors, weighted non-linear least squared error fitting is equivalent to maximum likelihood estimation (16). For fitting, each value of t_r was weighted by multiplying by the number of dives for the specific condition divided by the total number of dives and dividing that result by the variance of the value. The variance for each value of t_r was estimated as the square of the corresponding standard deviation of the logistic regression. The extra anchor point was given an arbitrary weight of one.

A set of six models, specifically, three exponential (Equation 4) and three sigmoidal (Equation 5) formats, in each case with dependence on $\boldsymbol{t}$ only, on $\boldsymbol{t}/T_{dur}$ only, or on both $\boldsymbol{t}$ and $\boldsymbol{t}/T_{dur}$, was considered for each of rest and exercise. Figure 2 shows the data with the four single-variable fits, the functions of either $\boldsymbol{t}$ or $\boldsymbol{t}/T_{dur}$, for Equations 4 and 5.

<u>Model selection</u>

The best fit for each of rest and exercise was selected by applying Akaike's information criterion with small sample adjustment, AIC_c. For normally distributed error and models fitted by minimizing the sum of squares, AIC_c can be written

$$AIC_c = n \cdot \ln(RSS/n) + 2 \cdot m + (2 \cdot m \cdot [m+1])/(n-m-1), \qquad [6]$$

where RSS is the residual sum of squares from the regression fit, n indicates the number of data in the fit and m is the number of parameters in the model.

If $AIC_{c\ min}$ denotes the smallest value of AIC_c obtained among the models under consideration for a data set, and $\Delta_i = AIC_{c\ i} - AIC_{c\ min}$, then, given the data, the relative likelihood of model i is proportional to $\exp(-0.5 \cdot \Delta_i)$. That relative likelihood divided by the sum of the relative likelihoods for all the candidate models gives the probability that, given the data, the specific model is the best of the candidates. (17) The null model (the mean of the data) was also considered.

Once the best-fit models for rest and exercise were selected, their performance was examined in more detail using all available data. The data sources are described in Table 5. For each dive, T_{eq} was computed from recovery time t and T_{dur}, and the incidence- time model was used to translate from the continuous T_{eq} value to the binomial predicted incidence. Predicted and measured incidence values were then compared.

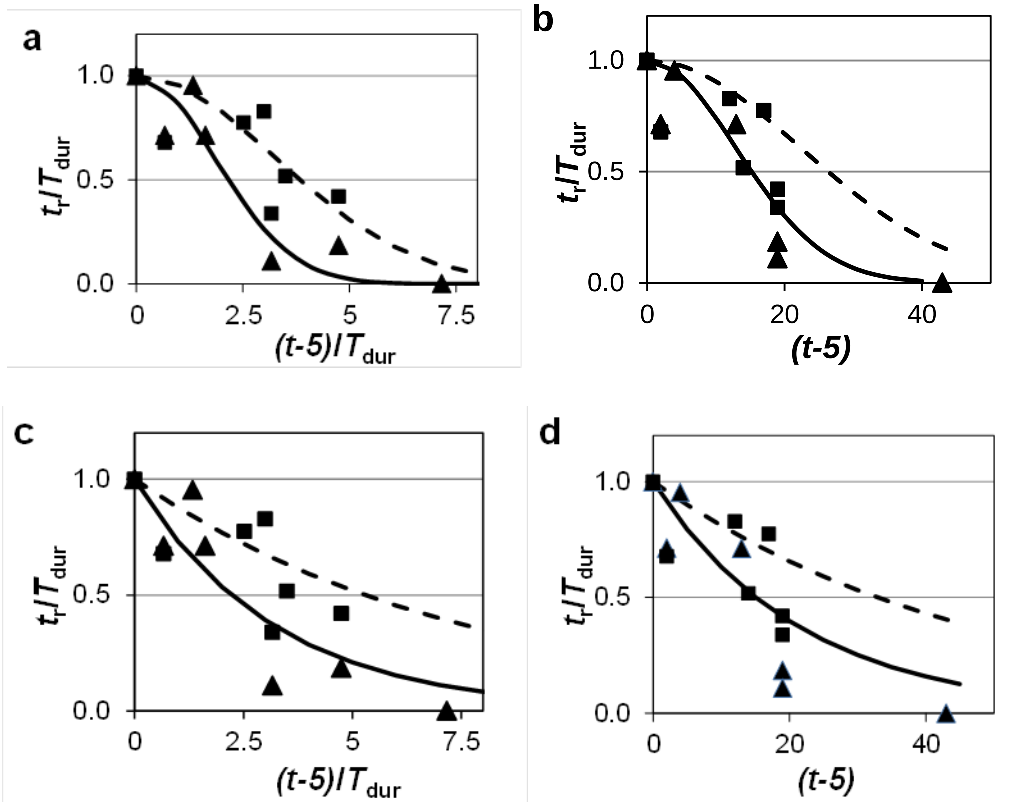

Figure 2. Values of t_r/T_{dur} used in parameter fitting for the recovery models. (Table 4). A delay of 5 hours is included, representing the time before recovery is seen to begin. The symbols indicate values obtained from the incidence of pulmonary oxygen toxicity after long single dives and pairs of shorter dives (Table 3). After resting dives: ▲ (7 dives or dive pairs, 221 person dives or person dive pairs). After dives with exercise: ■ (6 dives or dive pairs; 167 person dives or person dive pairs). The lines are the best fit single-parameter models fitted to the data: ——— for resting dives, – – – for dives with exercise.

Panels a) and b): sigmoidal recovery (Exponent from Equation 4).a) t_r/T_{dur} plotted against $\boldsymbol{t}/T_{dur}$, with lines $t_r/T_{dur} = \exp[-k\,(\boldsymbol{t}/T_{dur})^2]$, k = 0.149, 0.047; b) t_r/T_{dur} plotted against $\boldsymbol{t}$, with lines $t_r/T_{dur} = \exp(-h\,\boldsymbol{t})^2$, h = 0.003, 0.002.

Panels c) and d): exponential recovery (Exponent from Equation 3). c) t_r/T_{dur} plotted against $\boldsymbol{t}/T_{dur}$, with lines $t_r/T_{dur} = \exp(-a\,\boldsymbol{t}/T_{dur})$, a = 0.313, 0.179; and d) t_r/T_{dur} plotted against $\boldsymbol{t}$, with lines $t_r/T_{dur} = \exp(-b\,\boldsymbol{t})$, b = 0.046, 0.028.

The model in panel (a) was selected.

Three data groupings were considered. The calibration set (Table 3) is that used to find the recovery parameters. The grouping of all data (Table 5) included the calibration set. Because a number of individual dives produced identical values of T_{eq}, a third data set was constructed in which all dives with a particular T_{eq} were combined using the total number of episodes of overt pulmonary oxygen toxicity divided by total number of divers. This resulted in 16 pooled resting dives and 15 pooled exercise dives, but some of the pooled dives represented repeated dives by the same individual on successive days.

Table 5. All data used to test model performance

a) Resting dives

<table>
<tr><th>Dive duration, SI</th><th colspan="2">n
(person dives)</th><th>Breathing conditions</th><th>References</th></tr>
<tr><td colspan="5">Rest, single dives</td></tr>
<tr><td>4 hrs</td><td colspan="2">8</td><td>MK 20, test pool</td><td>3</td></tr>
<tr><td>6 hrs</td><td colspan="2">18</td><td>MK 20, test pool</td><td>3, u</td></tr>
<tr><td>8 hrs</td><td colspan="2">71</td><td>n=23: MK 20, test pool
n=31: MK 20, OSF
n=17: MK 16, BBAT</td><td>3, 5, 9</td></tr>
<tr><td colspan="5">Rest, two dives only</td></tr>
<tr><td>4 hrs, SI = 20 hrs</td><td colspan="2">17</td><td>MK 20, test pool</td><td>4</td></tr>
<tr><td>4 hrs, SI = 44 hrs</td><td colspan="2">18</td><td>MK 20, test pool</td><td>4</td></tr>
<tr><td>6 hrs, SI = 18 hrs</td><td colspan="2">13</td><td>MK 20, test pool</td><td>6</td></tr>
<tr><td colspan="5">Rest, multiple dives</td></tr>
<tr><th>Dive duration, SI</th><th>Frequency</th><th>n</th><th>Conditions</th><th>References</th></tr>
<tr><td>3 hrs, SI = 2,
16 hrs overnight</td><td>Twice daily,
2 days</td><td>12</td><td>MK 20, test pool</td><td>6</td></tr>
<tr><td>3 hrs, SI = 4
14 hrs overnight</td><td>Twice daily,
2 days</td><td>24</td><td>MK 20, test pool</td><td>6</td></tr>
<tr><td>3 hrs, SI = 4
12 hrs overnight</td><td>Twice daily,
2 days</td><td>12</td><td>MK 20, test pool</td><td>6</td></tr>
<tr><td>4 hrs, SI = 20 hrs</td><td>5 dives</td><td>16</td><td>MK 20, test pool</td><td>4</td></tr>
<tr><td>4 hrs, SI = 20 hrs days,
weekend off between</td><td>10 dives</td><td>16</td><td>MK 20, test pool</td><td>7</td></tr>
<tr><td>6 hrs, SI = 18 hrs</td><td>5 dives</td><td>27</td><td>MK 20, test pool</td><td>6, u</td></tr>
<tr><td>6 hrs, SI = 42 hrs</td><td>6 dives</td><td>14</td><td>MK 20, test pool</td><td>6</td></tr>
</table>

Conditions are described in the legend of Table 1. The number of divers listed is the number to start the series. Individuals dropped out during some of the longer dives series.

b) Dives with underwater exercise

Dive duration, SI	n (person dives)		Breathing conditions	References
Exercise, single dives				
3.5 hrs	68		MK 20, test pool	15
4 hrs	40		MK 20, test pool	8
4 hrs	23		MK 25, test pool	11
6 hrs	13		MK 20, test pool	u
6.75 hrs	88		MK 16 for exercise, MK 25 at rest, OSF	14
Rest, two dives only				
4 hrs, SI = 15 hrs	28		MK 20, test pool	8
Rest, multiple dives				
Dive duration, SI	**Frequency**	**n**	**Conditions**	**References**
3 hrs, SI = 4, 14 hrs overnight	Twice daily, 2 days	22	MK 20, test pool	11
3 hrs, SI = 21 hrs	5 dives	16	MK 20, test pool	10
4 hrs, SI = 20 hrs	5 dives	16	MK 20, test pool	8
6 hrs, SI=18 hrs	5 dives	12	MK 20, test pool	u

Conditions are described in the legend of Table 1. The number of divers listed is the number to start the series. Individuals dropped out during some of the longer dives series.

RESULTS

Incidence-exposure time model

The combined model for occurrence of either symptoms or ΔFV within two hours of surfacing is

$$P[O_2tox]\ (\%) = 100 / [1+\exp(3.586-0.490 \cdot T_{dur})] \qquad [7]$$

The fitted curve is shown with the data in Figure 1.

The incidence-time model predicts that with $T_{dur} = 0$, that is, that with no exposure to elevated PO_2, symptoms or signs normally considered to represent pulmonary oxygen toxicity will be apparent in 2.7% of divers. The 95% confidence limits for this extrapolation to an exposure of zero length extend from 0.8% to 4.9%.

Separate models for the occurrence of symptoms (Sx) only or of ΔFV only (Figure 4) were

$$P[O_2 tox\ Sx]\ (\%) = 100 / [1+\exp(3.758–0.469 \cdot T_{dur})] \qquad [8]$$

$$P[O_2\ tox\ \Delta FV]\ (\%) = 100 / [1+\exp(4.912–0.417 \cdot T_{dur})] \qquad [9]$$

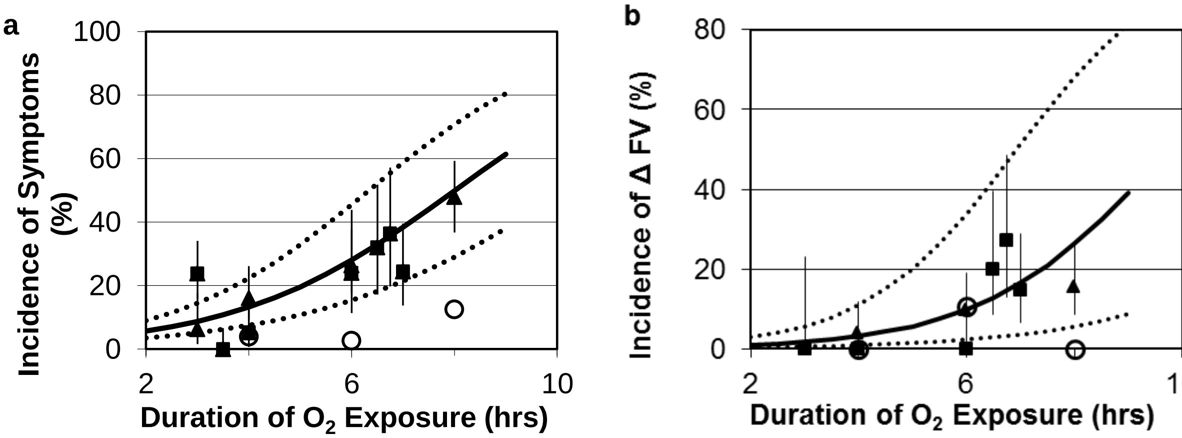

Figure 3. Incidence – time models separated into a) symptoms and b) changes in pulmonary function (flow-volume parameters). Symbols and line types match those in Figure 1.

Air dives

Data were available for 239 shallow air dives, PO_2 = 0.30 atm (Table 2). Both resting dives and dives with in-water exercise were included, and durations were 4, 6, and 8 hours. The overall combined incidence of symptoms or ΔFV immediately after diving was 5.9%. There was no significant effect of duration from 4- to 8-hours (Figures 1, 3), and no accumulation of effects across days

Recovery model parameter fitting

Data for estimation of the delay t_d were thin. The value of 5 hours was chosen somewhat arbitrarily, with the choice motivated by the results after two three-hour dives separated by a two-hour surface interval where there was no evidence that recovery had occurred (6). For resting data, r^2 between fitted t_r and estimated t_r (the square of the correlation coefficient) increased as delay was increased from 0 to 5 hours but changed very little between 5 and 5.5 hours.

Fitted parameters for all of the candidate models with delay a = 5 hours are listed in Table 6. For resting dives the Akaike criteria strongly favored the $(\boldsymbol{t}/T_{dur})^2$ model; its probability (Akaike weight) was 70%, that of the two-term sigmoidal recovery model, was 19%, and that for all others was less than 5% (Table 7). For exercise dives, the model selection was not as clear as it was for resting dives; the most likely $(\boldsymbol{t}/T_{dur})^2$ model had an Akaike weight of 46%, only slightly more than twice that for the $\boldsymbol{t}/T_{dur}$ model (Table 7). However, the choice of the $(\boldsymbol{t}/T_{dur})^2$ model for recovery after dives with exercise was bolstered by analogy to the resting dive condition.

The selected models are

$$\text{resting } t_r = T_{dur} \cdot \exp\left[-\,0.149 \cdot (\boldsymbol{t}/T_{dur})^2\right], \quad r^2{=}0.90; \text{ and} \qquad [10]$$

$$\text{exercise } t_r = T_{dur} \cdot \exp\left[-0.047 \cdot (\boldsymbol{t}/T_{dur})^2\right], \quad r^2{=}0.59; \qquad [11]$$

where $\boldsymbol{t} = t - 5$ hours, r^2 is the square of the correlation coefficient between fitted t_r and t_r estimated from the calibration data, and “resting” or “exercise” refer to the conditions of exposure, not of recovery time. (Activity levels during surface intervals were neither controlled nor monitored.)

Table 6. Coefficients of model fits from the calibration set (Data of Table 3).

Equation		$t_r = T_{dur} \cdot \exp(c + g / T_{dur}) \cdot t$				$t_r = T_{dur} \cdot \exp[(h \cdot t^2 + k \cdot (t/T_{dur})^2]$			
	MEAN	***c***	***g***	r^2 ***RSS***	***No recovery after***	***h***	***k***	r^2 **RSS**	***No recovery after***
Rest n=7	r^2 = 0 Mean = 0.50 RSS = 1.527		–0.313 0.062	0.85 0.374			**–0.149** 0.024	0.90 0.159	
		–0.046 0.012		0.66 0.668		–0.003 0.001		0.81 0.348	
		0.115 0.072	–1.148 0.559	0.86 0.227	10 hrs	0.003 0.003	–0.333 0.167	0.93 0.126	10.5 hrs
Exercise n = 7	r^2 = 0 Mean = 0.73 RSS = 0.370		–0.131 0.025	0.48 0.194			**–0.047** 0.008	0.59 0.155	
		–0.021 0.005		0.17 0.318		–0.001 0.000		0.18 0.324	
		0.037 0.025	–0.361 0.162	0.66 0.128	9.8 hrs	0.000 0.001	–0.056 0.029	0.61 0.593	

For parameters *c*, *g*, *h*, and *k,* the second row entry is the asymptotic standard error of the estimate. Time is expressed in hours. For rest, seven dive profiles were used. For exercise, six dive profiles were used, augmented with a value of $t_r = T_{dur}$ at $\boldsymbol{t} = 0$. RSS represents Residual Sum of Squares, and r^2 is the square of the correlation between observed and predicted values.

Table 7. Akaike criteria for model selection. Models are arranged in order from smallest to largest AIC_c.

a) Resting data (n=7)

model	m	RSS	AIC_c	Δ_i	relative likelihood	Akaike weights
squared, t/T_{dur}	1	0.159	-23.693	0.000	1.000	0.697
squared, both	2	0.126	-21.122	2.572	0.276	0.193
squared, t	1	0.348	-18.210	5.483	0.064	0.045
linear, t/T_{dur}	1	0.374	-17.706	5.987	0.050	0.035
linear, both	2	0.227	-17.001	6.692	0.035	0.025
linear, t	1	0.668	-13.646	10.048	0.007	0.005
average (null)	0	1.527	-10.658	13.035	0.001	0.001

b) Exercise data (n=7, six dive sets plus one arbitrary anchor point: $t_r = T_{dur}$ at $\boldsymbol{t} = 0$, weight = 1)

model	m	RSS	AIC_c	Δ_i	relative likelihood	Akaike weights
squared, t/T_{dur}	1	0.155	-23.872	0.000	1.000	0.460
linear, t/T_{dur}	1	0.194	-22.301	1.571	0.456	0.210
linear, both	2	0.128	-21.011	2.860	0.239	0.110
average (null)	0	0.37	-20.581	3.291	0.193	0.089
squared, both	2	0.152	-19.808	4.063	0.131	0.060
linear, t	1	0.318	-18.841	5.030	0.081	0.037
squared, t	1	0.324	-18.710	5.161	0.076	0.035

Models with relative likelihood ≤ 5%, those unlikely to be useful to explain the data, are greyed out. "Squared" or "linear" refers to the exponent. "Squared" gives a sigmoidal recovery, and "linear", a simple exponential.

Here, n is the number of data (number of sets of second or long dives) used in fits; m is the number of parameters in the model; RSS is the residual sum of squares from the regression fits; AIC_c is the "Akaike Information Criterion" corrected for small sample size; Δ_i is the difference of the AIC_c of the model from the smallest AIC_c found; relative likelihood = exp (-0.5 Δ_i) is the relative likelihood, given the models and the data, that a particular model is the best of the set; and the Akaike weight is the probability that the model is the best in the set, given the data.

Comparison of sigmoidal and exponential recovery

The models were selected using only the calibration data. The relative performance of the sigmoidal and the best fitting of the simple exponential models, the functions of $\boldsymbol{t}/T_{dur}$ only, (Tables 6, 7) was checked also on the entire available data set. Results are tabulated (Table 8). The standard deviations of the sigmoidal residuals for resting and exercise dives, respectively were 31% and 29% smaller than those of the exponential fits. The mean bias of the sigmoidal fit was –3% for resting dives and 1% for exercise dives, in contrast to 7% and 13% for the exponential. Finally, the increases in bias with increasing incidence for the sigmoidal fit were 0.04 and 0.26 for rest and exercise dives, respectively, while for the exponential fit, bias increased with incidence with slopes of 0.43 and 0.53 for rest and exercise respectively.

Table 8. Comparison of residuals of sigmoidal and exponential fits with parameter $\boldsymbol{t}/T_{dur}$, all available data.

Residuals Model - Measured	**Sigmoidal, t/T_{dur}**		**Exponential, t/T_{dur}**	
	Rest	**Exercise**	**Rest**	**Exercise**
Mean	–2.7	0.8	7	13
Standard deviation	11.6	15.3	16	22
Median	–2.6	0.2	5	6
Minimum	–42	–42	–42	–17
Maximum	20	36	45	65
Correlation, residuals to measured	–0.40	–0.04	–0.20	0.08
Fraction of residuals >0	52%	52%	64%	74%
slope, residuals vs. measured	–0.33	0.04	–0.23	0.09
slope, residuals vs. average(measured, modeled)	0.04	0.26	0.43	0.53

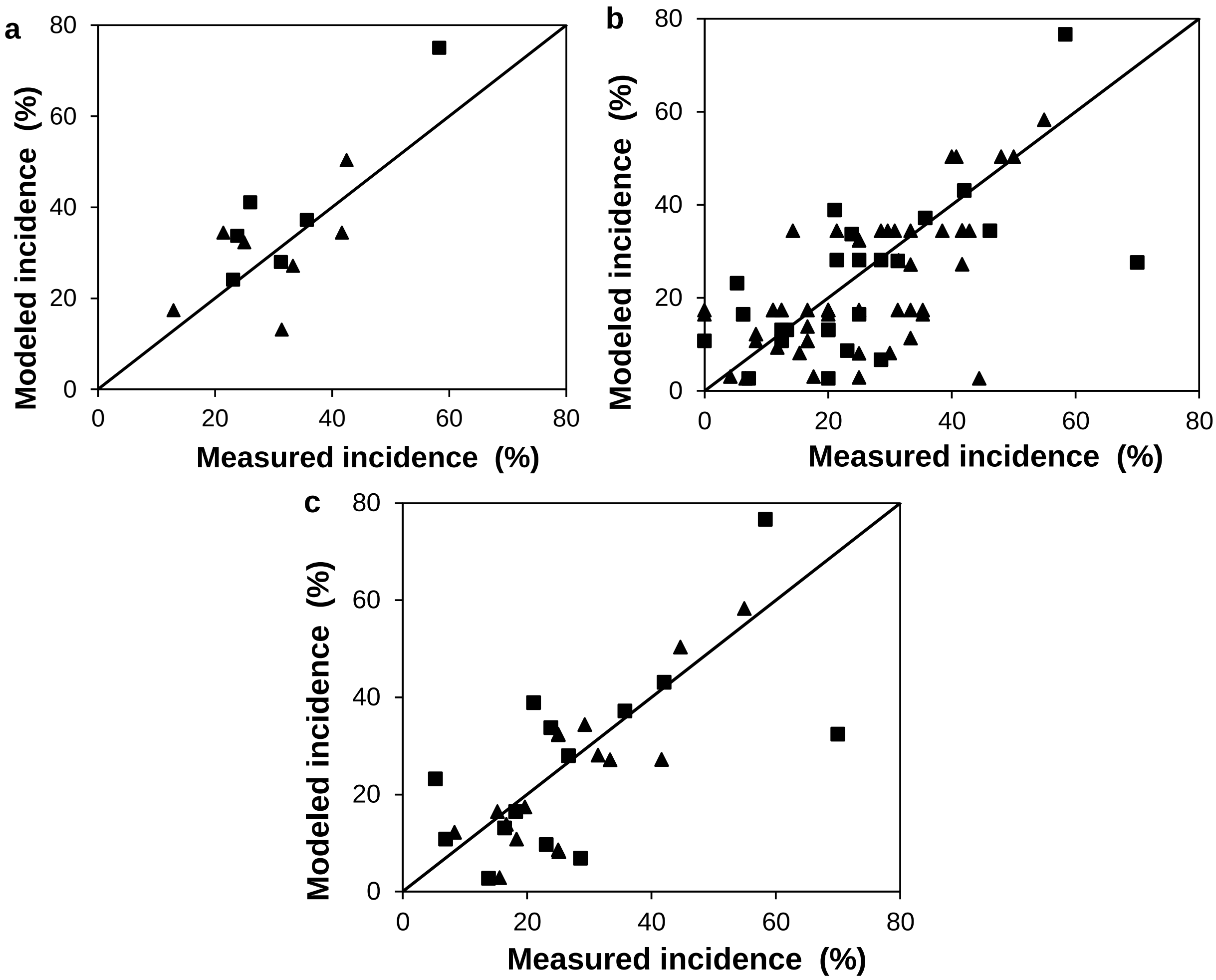

Figure 4. Incidences of pulmonary oxygen toxicity after dives with PO_2 = 130 kPa, modeled vs. measured. Resting dives: ▲, dives with exercise: ■. The identity line is shown. a) Calibration data used to fit the recovery models. Best fit slopes through the origin are 0.97 for resting dives and 1.04 for dives with exercise. b) All available data. Best fit slopes through the origin are 0.84 for resting dives and 1.00 for dives with exercise**.** Data with identical modeled values but different observed incidence are evident as horizontal lines. c) All available data, but the dives with identical modeled incidence have been pooled and are shown against the corresponding total number of occurrences measured divided by the total number of person-dives. Best fit slopes through the origin are 0.91 for resting dives and 0.88 for dives with exercise.

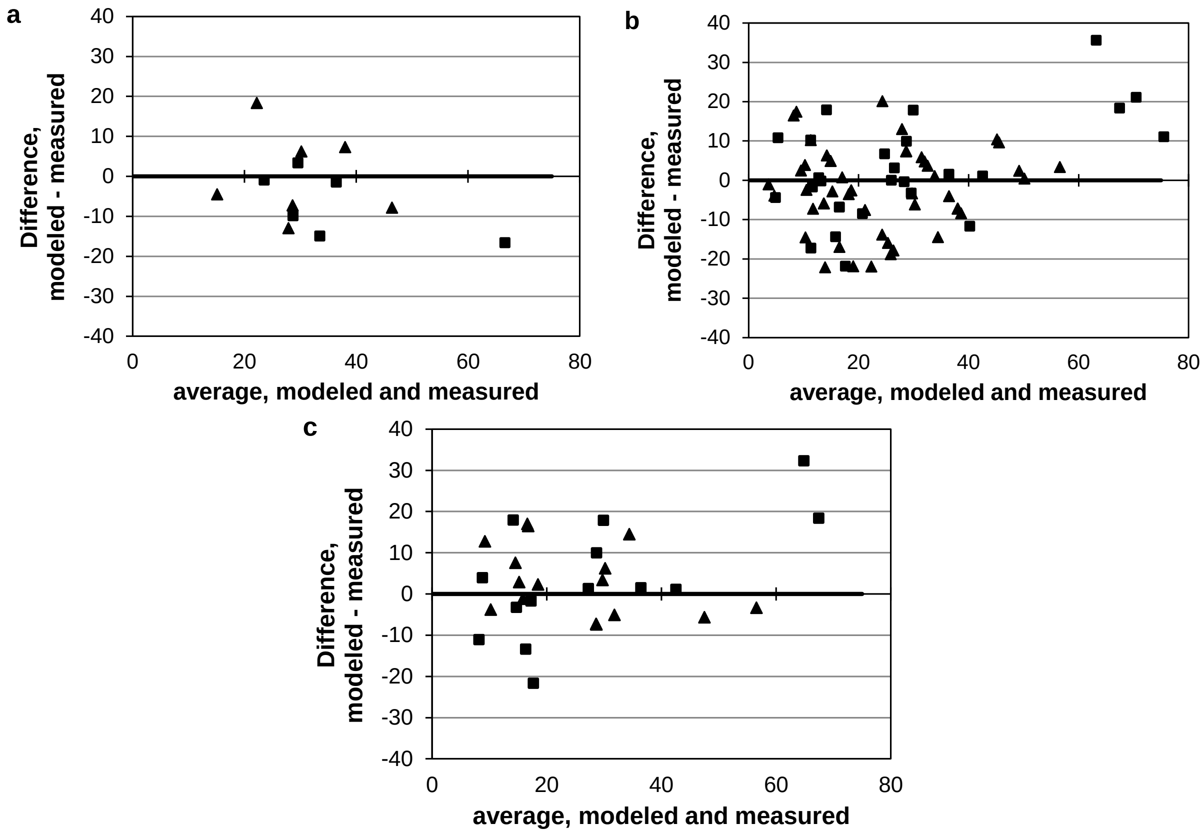

Figure 5. Bland Altman plots of probability for any evidence of pulmonary oxygen toxicity. The difference between model and measured incidences is plotted against the mean of the two estimates. Resting dives: ▲, dives with exercise: ■. a) Calibration data used to fit the recovery models. b) All available data. Dives with identical modeled values but different observed incidence are evident as linear runs with slopes of –2. (See text.) c) All available data, but the dives with identical modeled incidence have been pooled, as described above.

<u>Goodness of fit assessment</u>

The composite model, Equations 10 or 11 and Equation 7, was applied to the calibration data, to the full data set, and to pooled data to predict P[O_2Tox] for each dive. The observed incidences of detected pulmonary oxygen toxicity were compared to the model predictions dive by dive. Correspondence of model and data can be assessed in Figures 4 and 5. In Figure 4, fitted values are plotted against observed incidences, while in Figure 5, the difference between the two estimates of probability are plotted against the average of the two (Bland Altman plots) (18). Panels “a” show only the calibration data (Table 3). Panels “b” represent all available dives (Table 5), with each dive represented individually. Panels “c” include all the data with the dives of matching modeled incidence pooled as was described above.

The multiple dives where several observed values correspond to a single model prediction are evident as horizontal lines on Figure 4b and as linear trends in Figure 5b. The constant (horizontal) lines of Figure 4b become the diagonal lines on Figure 5b as follows: if the modeled value is called k and the measured values m_i, the graph shows k-m_i against 0.5 (k+m_i), a line with slope –2. The lines disappeared with pooling of those results (Figures 4c, 5c).

For the calibration data, the slopes through the origin of modeled vs. observed (measured) incidence are 1.03 and 1.16 for rest and exercise data, respectively, and the overall correlation between modeled and measured probabilities is 0.86 (Figure 5a). The modeled values are slightly lower than those observed, (Figure 5a) with an increase in bias (offset from zero) with exercise for greater incidence (Table 9, "slope, residuals vs. average"), though elimination of a single outlier would decrease the differences. For all available dives considered individually, the slopes of the best fit lines through the origin are 0.84 for resting data and 1.01 for exercise data, and the overall correlation between measured and modeled incidences of pulmonary oxygen toxicity (either sign or symptom) is 0.71 (Figure 4b). The differences between modeled and measured values (Figure 5b) scatter generally about zero except for the four exercise-dive outliers at high incidence. Bias and slope of the residuals vs. the average are low, but the standard deviation of the residuals is high (Table 9). For the grouped dives, the slopes through the origin are 0.91 and 0.96 for rest and exercise data, respectively, (Figures 4c) while the overall correlation between modeled and measured probabilities remains 0.71. The Bland Altman plot of the grouped data (Figure 5c) has similar bias to that of the ungrouped data, and the standard deviation of the differences is not reduced (Table 9).

Correspondence between model and observation improved when dives of identical modeled outcomes were pooled. The magnitudes of the differences between model and observed incidences (the residuals) were approximately proportional to $n^{-0.5}$, where n is the number of man-dives for each point (Figure 6). Note that uncertainty in a binomial estimation of probability also is proportional to $n^{-0.5}$ (Equation 2).

Table 9. Statistics for residuals of the composite model, Sigmoidal, t/T_{dur}

P[O_2Tox] Residuals Model - Measured	Calibration		All data		All data, pooled	
	Rest	Exercise	Rest	Exercise	Rest	Exercise
Mean	–2.3	–4	–2.7	0.8	3	0.7
Standard deviation	8	8	12	15	9	18
Minimum	–13	–18	–42	–42	–7	–42
Maximum	7	3	20	36	17	32
Correlation, residuals to measured	0.46	–0.71	–0.38	–0.04	–0.10	–0.12
Fraction of residuals ≥0	43%	50%	52%	52%	60%	60%
slope, residuals vs. measured	0.34	–0.45	–0.33	0.04	–0.07	–0.19
slope, residuals vs. average (measured, modeled)	0.09	–0.42	0.04	0.26	0.09	0.42

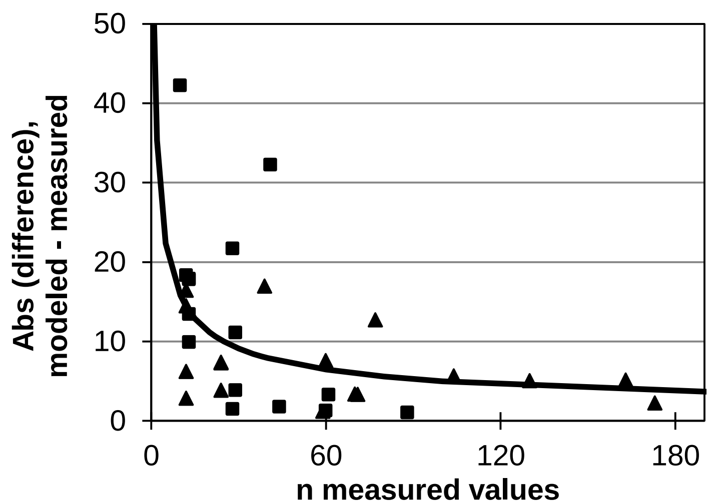

Figure 6. Magnitudes of the differences, model to observation, of incidences of observable pulmonary oxygen toxicity vs. the number of observations. Data are for the pooled data set (see text).

An electronic calculator provides the numbers for up to four dives at rest or with exercise, with PO_2 = 1.3 to 1.4 atm, duration ≤8 hours, and any surface intervals. (See CD)

To select a surface interval between two dives, one chooses an acceptable P[O_2tox] for the end of the second dive. The corresponding T_{eq} is found from the Incidence-time model, and t_r is computed by subtracting $T_{dur\,2}$ from it. The necessary recovery time to yield that t_r is then computed from the model using equations 12 and 13, rearranged forms of equations 10 and 11.

After resting exposures, recovery time $\boldsymbol{t}$ for a chosen t_r is given by

$$\boldsymbol{t}/\mathrm{T}_{dur} = [6.71 \cdot \mathit{ln}\,(T_{dur}/t_r)]^{0.5} \qquad [12]$$

and after exposures with exercise, by

$$\boldsymbol{t}/\mathrm{T}_{dur} = [21.3 \cdot \mathit{ln}\,(T_{dur}/t_r)]^{0.5}. \qquad [13]$$

Here, *ln* represents the natural logarithm.

Recall that $\boldsymbol{t} = t - 5$ hours, that $t = 0$ at the end of the dive, and that t_r after a second dive is assessed at the end of that dive. Thus, the SI is $t_r - T_{dur\,2}$. Table 10 shows some sample values.

Table 10. Sample calculations of recovery times

a) Resting dives (times in hours:minutes)

1	2	3	4	5
t_r/T_{dur}	A= $\boldsymbol{t}/T_{dur}$ ($\boldsymbol{t} = t$–5)	If T_{dur} =	$t = A \cdot T_{dur} + 5$ [decimal hours] Hours after surfacing	SI to add t_r to 2nd dive $t - T_{dur\,2}$
0.5	2.16	2	[9.32] 9:19	7:19
		4	[13.64] 13:38	9:38
		6	[17.96] 17:58	11:58
0.25	3.05	2	[11.10] 11:06	11:06
		4	[17.20] 17:12	13:12
		6	[23.30] 23:18	17:18

b) Dives with exercise (all times in hours:minutes)

1	2	3	4	5
t_r/T_{dur}	A= $\boldsymbol{t}/T_{dur}$ ($\boldsymbol{t} = t$–5)	If T_{dur} =	$t = A \cdot T_{dur} + 5$ [decimal hours] Hours after surfacing	SI to add t_r to 2nd dive $t - T_{dur\ 2}$
0.5	3.84	2	[12.68] 12:41	10:41
		4	[20.36] 20:22	16:22
		6	[28.04] 28:02	22:02
0.25	5.43	2	[15.86] 15:52	13:52
		4	[26.76] 26:43	22:43
		6	[37.58] 37:35	31:35

DISCUSSION

This residual oxygen time plus incidence-time model provides a method to plan repeated dives at PO_2 of 1.3 to 1.4 atm with a risk of pulmonary oxygen toxicity that is acceptable under the circumstances. The model 1) describes the progress of recovery after exposure to this PO_2 (Equations 10 and 11) to answer the question of how long after a dive deleterious effects remain; 2) determines the minimum necessary surface interval for a chosen residual oxygen time (Equations 12 and 13); and 3) describes the risk of signs and symptoms of pulmonary oxygen toxicity associated with any oxygen exposure time, residual oxygen time, or the sum of the two (Equations 7 – 9). Thus, the model predicts how likely it is that someone will have noticeable pulmonary oxygen toxicity after a particular combination of dives and surface intervals.

Unlike a number of other pulmonary oxygen toxicity models (19–22), this model attempts no association between exposure duration and either the magnitude of ΔFV or the severity of symptoms. It is worth noting, however, that in the extensive NEDU data set for exposure to PO_2 = 1.3 to 1.4 atm, almost all measured changes or reported have been mild to moderate. Moderately severe symptoms were reported only in conjunction with more than two dives with exercise in series of four-hour (6, 11) or six-hour dives (unpublished) and 20– or 18-hour SI, respectively. The experiments cited in this work also have shown that either symptoms or ΔFV may be present without the other, but that symptoms are more common than ΔFV.

The model treats recovery from one exposure as continuing even as injury from the next dive accumulates. This is based on experimental evidence: divers beginning a dive with symptoms or mild ΔFV are often without symptoms or ΔFV when they leave the water (2, 5, 10), and symptoms or measureable ΔFV early in a dive series may clear by later in the week (10, 11). Recovery is modeled to begin five hours after surfacing from a dive, and thus usually not to begin during the dive when the injury is incurred. This is consistent with a two-phase process, for example, a primary oxidative injury followed by fluid incursion and inflammation that take time to resolve and that can continue to heal even as new oxidative damage may be occurring. A better delay term would be timed from the start of the oxygen exposure, but our data cannot support a more detailed analysis of the time at which recovery begins.

The incidence- time model and air dives

Dives with PO_2 = 0.3 atm resulted in non-zero incidences of signs and symptoms, as did the incidence-time model with T_{dur} = 0. Although the signs and symptoms considered are associated with pulmonary oxygen toxicity, at low incidence they also can be associated with underwater breathing and hydrostatic load in general.

Calculation method

The effective exposure time at the end of a second or later dive in a series is the duration of the dive just completed plus the sum of residual times from any previous dives. Residual time is calculated at the **end** of the latest dive, the same time at which the exposure to the new dive is assessed. Each component of residual time must be computed with its own $T_{dur,}$ and from the end of the dive to which it relates, as described in Equation 14, below.

$$t_{\mathrm{r\,tot}} = \sum_i^n T_{\mathrm{dur\,i}} \cdot \exp\left[-\ \mathrm{k} \cdot (t - t_{e\,i} - t_d)^2 / T_{dur\,i}\right] \qquad [14]$$

where $t_{r\ tot}$ is the total residual time after n dives, $T_{dur\ i}$ is the duration of the i^{th} dive, $t_{e\ i}$ is the time at the start of the i^{th} dive relative to the first dive (where $t_{e\ i}$ = 0), and t_d is delay time for start of healing, here 5 hours.

Even with identical dive durations and conditions, because the functions of time are squared the calculation must be

$$t_{r\ tot} = T_{dur} \cdot \exp\left[-\ \mathrm{k} \cdot \boldsymbol{t}^2 / T_{dur}^2\right] + \exp\left[-\ \mathrm{k} \cdot (\boldsymbol{t} - t_{e\ 2})^2 / T_{dur}^2\right]\ . \qquad [15]$$

Recovery from a long dive is slower than from a short dive, as indicated by the dependence of the recovery exponent on T_{dur}. Additionally, the initial insult from a long dive is greater than that from a shorter one; the probability of symptoms or pulmonary function deficits increases with T_{dur}. Thus, assuming that recovery time is essentially unlimited after the completion of the entire job, the more efficient use of time for the same pulmonary risk is to complete a shorter dive before a longer one.

For two dives of the same duration, one with exercise and one at rest, the initial injury after the dives does not differ, but recovery is slower after the dive with exercise; for recovery rate alone, an exercise dive is equivalent to a resting dive with the duration multiplied by a factor, $[0.149/\ 0.047]^{0.5}$ = 1.8. In other words, recovery from a four-hour dive with exercise takes approximately as long as does recovery from a seven-hour resting dive. The more time-efficient order of two dives of the same length is rest before exercise.

The maximum rates of recovery, the inflection points of equations 9 and 10, occur when $(t–5)^2/T_{dur} = 2 \cdot k$, where t, in hours, is measured from the end of the dive. Thus, for resting dives, the maximum recovery rate is reached after 8.7 and 9.5 hours for four- and six-hour dives, respectively. Similarly, for dives with exercise, the maximum recovery rate is reached after 11.5 and 13.0 hours for four- and six-hour dives, respectively.

The sigmoidal recovery pattern is a departure from the functional form of other published recovery models, (19, 22–24) models in which physical healing or chemical clearance were expected to follow first-order reaction kinetics despite the cascade of probable processes. The sigmoidal pattern was proposed based on observed values of P[O_2tox] rather than on putative mechanisms. The format was selected instead of an exponential because the Akaike criterion method and the magnitude of the residuals indicated that it better fit the data. Subjectively, the sigmoidal fit is tighter than the exponential during the initial slow recovery and during the steep recovery in the middle time range of the calibration data (Figure 3).

When Akaike criteria are used for model selection, models with Akaike weight greater than 5% are often combined (17). However, for the resting data here, the second most likely model was the combination of the most likely and the third-most likely (Table 7). In other words, addition of the third most likely model to the most likely one reduced its probability. Further combination of the resting models seemed illogical, and the pattern was carried over to the exercise models.

Goodness of fit assessment

The measured data, low-incidence samples from a binomial process, have inherently high variance. Thus, not all of the difference between model and data should be ascribed to the model; the uncertainty of the difference is the sum of the uncertainties of the two estimates. All of the large deviations from the line of identity in Figure 5c represent data sets with size less than or equal to the median n = 28. Most of them represent cohorts of nine to 13 divers where one diver with a different outcome would change the incidence by close to 10%. In other words, a single false positive may have skewed the measured value. Where the residuals, model to measurement, are large, so is the uncertainty of the measurement.

Limitations of ROT and its development

The incidence-time relation does not show zero incidence at zero duration. The non-zero starting point represents a very low probability but also is counterintuitive. However, symptoms typical of pulmonary oxygen toxicity were reported after exposures to PO_2 = 0.3 atm (air dives), that is, after dives where the duration of exposure to elevated PO_2 was zero.

The model developed here assumes simple additive effects of dives on the factors driving probability of symptoms and signs. The varied recovery rates after dives of differing duration are assumed not to affect the recovery rate from previous dives. No physiological mechanism is proposed. Rather, the acceptability of the assumption is based on model correspondence to data. It is important to note, though, that the additivity assumption does not appear to carry over to exposures to PO_2 of 2 atm. (26)

After dives, ΔFV and symptoms of pulmonary oxygen toxicity are sometimes delayed in onset. This model has no explicit injury-onset delays, though the sigmoidal recovery function provides for slow initial healing after the somewhat arbitrary 5-hour recovery delay. Data were unavailable for true fitting of the recovery delay, and the possibility of optimizing by varying the delay and refitting the entire model was not explored. Further, the evidence of pulmonary oxygen toxicity used in model building was that manifest within two hours after pairs of dives or evident a day after single long dives. In other words, the sampling interval was coarse.

The data from third and later dives of series that were used to check the model were serially correlated with the data used to fit the model; they came from the same individuals, included the same individual confounding factors, and were compared to the same baselines. Even though errors of measurement after one dive could not affect values after any other dive, any errors in baseline (consisting in general of two sets of three reproducible values) would affect all the data from that diver.

Many of the NEDU data are from dives with PO_2 that varies around 1.35 atm because it was set by water depth with divers free to move near the bottom of the pool. This is a good representation of diving, where rebreather PO_2 varies around the set-point. Those variations of PO_2 are within the level of precision of the data.

Exercise was treated as an all or nothing condition. Most dives with exercise involved moderate aerobic work on cycle ergometers for half the dive (alternating 30 minutes work, 30 minutes rest). Resting dives had divers either stationary or moving about freely in the pool, but without organized work. Clearly, open-water dives represent a continuum of effort from fish watching or scooter riding to swimming hard against a current.

Residual oxygen times developed here are based only on pulmonary data. Any predictions related to non-pulmonary or “whole body” symptoms, for example finger numbness (25), hyperoxic myopia (4, 27, 28), and exercise intolerance, would require different data and a separate model. Nevertheless, an estimate of pulmonary residual oxygen time and thus of pulmonary oxygen toxicity risk is a step forward in planning.

The 5-hour delay time may be shorter than optimal, in that the change observed in r^2 was a plateau, not a maximum, and it was seen only in the resting data. Further work could better define this parameter, but more data from pairs of dives with short surface intervals might be needed.

CONCLUSIONS

The question of pulmonary risk after a single dive with PO_2 = 1.3 atm is answered by the incidence – time model, a simple logistic regression on data. The question of cumulative effects has been answered through the residual time model. A calculator for estimating the risk of pulmonary oxygen toxicity of up to four dives is presented here. The calculator permits easy manipulation of dives length, order, and SI to see the effects on pulmonary oxygen toxicity risk. It could be used to plan a mission with the least possible projected pulmonary risk. The equations of the model which are incorporated into the calculator have also been presented.

The entire background of the model is laid out to indicate its strengths and limitations. The model corresponds closely to most, but not to all, measured data.

This model and the calculator that implements it apply only to exposures to the specified partial pressures and to dives not longer than 8 hours. Its accuracy for equivalent oxygen times longer than 10 hours is unknown.

RECOMMENDATIONS

1) This calculator should be made available on dive planning computers and/or on an internet-accessible site.

2) More pulmonary oxygen toxicity data should be accumulated in conjunction with other experimental dives to permit future refinement of at least the incidence-time model.

3) A mechanism for feedback from fleet divers should be considered for “field testing” the calculator and the model.

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Appendix A

Table A1. Probability of pulmonary oxygen toxicity after repeated dives of durations (T_{dur}) one to eight hours, and surface intervals (SIs) from 1 hour to the time necessary for approximately no residual time between dives

T_{dur} 1 hour	Probability of any detectable pulmonary oxygen toxicity (%)							
	Rest				**Exercise**			
SI (hrs)	1st dive	2nd dive	3rd dive	4th dive	1st dive	2nd dive	3rd dive	4th dive
1	4	7	11	16	4	7	11	16
2	4	7	10	11	4	7	11	13
3	4	7	8	8	4	7	9	10
4	4	7	7	7	4	7	8	8
5	4	6	6	6	4	7	7	7
6	4	6	6	6	4	6	6	6
7	4	5	5	5	4	6	6	6
8	4	5	5	5	4	5	5	5
9	4	4	4	4	4	5	5	5
12					4	4	4	4

T_{dur} 2 hours	Probability of any detectable pulmonary oxygen toxicity (%)							
	Rest				**2 hours**			
SI (hrs)	1st dive	2nd dive	3rd dive	4th dive	1st dive	2nd dive	3rd dive	4th dive
1	7	16	34	47	7	16	34	54
2	7	16	29	32	7	16	32	45
3	7	16	23	23	7	16	29	36
4	7	16	18	18	7	16	25	28
5	7	15	15	15	7	16	22	22
6	7	13	13	13	7	15	18	19
7	7	11	11	11	7	14	16	16
8	7	10	10	10	7	13	14	14
9	7	9	9	9	7	12	13	13
10	7	8	8	8	7	11	11	11
12	7	7	7	7	7	10	10	10
15					7	8	8	8

T_{dur} **3 hours**	**Probability of any detectable pulmonary oxygen toxicity (%)**							
	Rest				**3 hours**			
SI (hrs)	1st dive	2nd dive	3rd dive	4th dive	1st dive	2nd dive	3rd dive	4th dive
1	11	34	65	79	11	34	68	87
2	11	34	58	65	11	34	66	82
3	11	34	50	53	11	34	62	75
4	11	32	42	42	11	34	57	66
5	11	30	35	35	11	33	52	57
6	11	27	29	29	11	32	46	49
7	11	24	25	25	11	30	41	42
8	11	22	22	22	11	29	36	37
10	11	17	17	17	11	26	29	29
12	11	14	14	14	11	22	23	23
14	11	12	12	12	11	19	20	20
16					11	17	17	17
18					11	15	15	15
24					11	12	12	12

T_{dur} **4 hours**	**Probability of any detectable pulmonary oxygen toxicity (%)**							
	Rest				**Exercise**			
SI (hrs)	1st dive	2nd dive	3rd dive	4th dive	1st dive	2nd dive	3rd dive	4th dive
1	16	58	87	94	16	58	90	97
2	16	58	83	88	16	58	88	96
3	16	57	77	80	16	58	86	94
4	16	55	70	71	16	57	84	91
5	16	52	62	63	16	56	81	87
6	16	48	55	55	16	55	77	82
7	16	45	48	48	16	53	73	76
8	16	41	43	43	16	52	68	70
10	16	34	34	34	16	48	58	59
12	16	28	28	28	16	44	49	50
14	16	23	23	23	16	39	42	42
16	16	20	20	20	16	35	36	36
18	16	19	19	19	16	31	32	32
20	16	18	18	18	16	28	28	28
22	16	17	17	17	16	25	25	25
36					16	17	17	17

T_{dur} 5 hours	Probability of any detectable pulmonary oxygen toxicity (%)							
	Rest				**Exercise**			
SI (hrs)	1st dive	2nd dive	3rd dive	4th dive	1st dive	2nd dive	3rd dive	4th dive
1	24	79	96		24	79	97	
4	24	75	88		24	78	95	
6	24	70	79	79	24	76	93	
8	24	64	68	68	24	74	89	
10	24	56	58	58	24	71	84	
12	24	48	49	49	24	68	78	78
14	24	41	42	42	24	64	71	71
16	24	36	36	36	24	59	64	64
18	24	32	32	32	24	55	57	57
20	24	29	29	29	24	50	52	52
22	24	27	27	27	24	46	47	47
24	24	26	26	26	24	42	43	43
26	24	25	25	25	24	39	39	39
30					24	34	34	34
36					24	28	28	28
48					24	25	25	25

T_{dur} 6 hours	Probability of any detectable pulmonary oxygen toxicity (%)							
	Rest				**Exercise**			
SI (hrs)	1st dive	2nd dive	3rd dive	4th dive	1st dive	2nd dive	3rd dive	4th dive
1	34	90			34	91		
4	34	88			34	90		
6	34	85			34	89		
8	34	81			34	88		
10	34	76	79	79	34	87		
12	34	70	71	71	34	85		
14	34	63	64	64	34	82		
16	34	57	57	57	34	80		
18	34	51	51	51	34	77	81	81
20	34	46	46	46	34	73	76	76
22	34	43	43	43	34	70	72	72
24	34	40	40	40	34	66	67	67
26	34	38	38	38	34	62	63	63
30	34	36	36	36	34	55	55	55
36	34	35	35	35	34	46	46	46
48					34	37	37	37
60					34	35	35	35

***T*dur** **7 hours**	**Probability of any detectable pulmonary oxygen toxicity (%)**							
	Rest				**Exercise**			
SI (hrs)	1st dive	2nd dive	3rd dive	4th dive	1st dive	2nd dive	3rd dive	4th dive
4	46	95			46	96		
8	46	92			46	95		
12	46	85			46	94		
16	46	76	77	77	46	91		
20	46	66	66	66	46	88		
24	46	58	58	58	46	84	86	86
36	46	47	47	47	46	67	67	67
48					46	54	54	54
60					46	48	48	48

***T*dur** **8 hours**	**Probability of any detectable pulmonary oxygen toxicity (%)**							
	Rest				**Exercise**			
SI (hrs)	1st dive	2nd dive	3rd dive	4th dive	1st dive	2nd dive	3rd dive	4th dive
4	58	98			58	98		
8	58	97			58	98		
12	58	94			58	97		
16	58	89			58	97		
20	58	82			58	95		
24	58	75	75	75	58	93		
36	58	61	61	61	58	83		
48	58	59	59	59	58	71	71	71
60					58	63	63	63
72					58	60	60	60

- No additional dives (next column to the right) are listed when the probability of detectable pulmonary oxygen toxicity after a dive exceeds 80%. Probabilities greater than 60% are extrapolations from the data.
- When the 2nd through 4th dives yield the same probabilities, t_r remains from only one dive. When the 3rd and 4th dives give the same probability and the value differs from that after the 2nd dive, t_r is present from two prior dives. When the 2nd dive has the same probability as that after the 1st dive, no t_r remains with the selected SI. No further probabilities are given; they will be that after a single dive.
- Values for mixed T_{dur}, SI, and presence or absence of exercise can be determined using the electronic calculator.

Table A2. Recovery time (hrs:min) needed to reduce t_r to specified levels

Resting dives	t for $t_r \leq$ given value					
T_{dur}	6 hrs	5 hrs	4 hrs	3 hrs	2 hrs	1 hr
2					0	9:25
3				0	10:05	13:20
4			0	10:40	13:50	17:30
5		0	11:15	14:25	17:40	21:45
6	0	11:45	15:05	18:10	21:35	26:15
7	12:15	15:45	18:50	22:00	25:40	30:50
8	16:20	19:30	22:35	26:00	30:00	35:25

Exercise dives	t for $t_r \leq$ given value					
T_{dur}	6 hrs	5 hrs	4 hrs	3 hrs	2 hrs	1 hr
2					0	12:40
3				0	13:50	19:30
4			0	15:00	20:25	27:00
5		0	16:00	21:30	27:05	34:20
6	0	16:50	22:45	28:05	34:00	42:00
7	17:45	23:45	29:10	34:45	41:15	50:00
8	24:50	30:20	35:45	41:40	48:30	58:50

See Figure 1 (main test) for the relation between t_r and probability of pulmonary oxygen toxicity.