compartments, and has parameters, including half-times for helium and nitrogen, found by fit to a database ("he8n25") of air, nitrox, heliox, and a few trimix dives. In the LEM-he8n25 compartment with intermediate rate of gas exchange, the half-time for nitrogen is 52% longer than for helium (33.0 vs. 21.8 minutes), and this compartment results in prescription of deeper decompression stops for heliox than for trimix dives in the manner described above. In the fastest compartment, the half-time for nitrogen is shorter than for helium (3.29 vs. 10.5 minutes), and slower washout of helium than of nitrogen from this compartment can result in prescription of deeper stops and longer times at these stops for heliox dives than for trimix dives of sufficient bottom time for near-complete equilibration of the compartment with helium (90% equilibration of this compartment with helium occurs in 35 minutes). Figure 1A shows the difference in total decompression stop times (TST) for LEM-he8n25 schedules for a range of MK 16 MOD 1 heliox and trimix decompression schedules calculated for a target P_{DCS} of 2.3%, the target P_{DCS} of the MK 16 MOD 1 He-O_2 decompression schedules in the U.S. Navy Diving Manual. If such difference in prescribed decompression times reflects a true difference in decompression requirements arising from helium and nitrogen, then dives following identical depth/time schedules would have higher P_{DCS} if breathing heliox than if breathing trimix (of the same total inert gas content), as illustrated in Figure 1B. The present experiment compared the incidences of DCS following heliox and trimix dives with the same depth/time schedule. This design avoids confounding by differences in TST or stop depth distribution.

The principal requirements for the test schedule[b] were: 1) sufficient time on the bottom to allow time for substantive differences in helium and nitrogen uptake to occur; and 2) a P_{DCS} likely to result in a measurable incidence of DCS. In order to design a practicable and operationally relevant dive trial, there were additional desirable characteristics for a test schedule: a) a large estimated difference in P_{DCS} for trimix and heliox breathing gases so that a difference in DCS incidence might be detected in a reasonable number of man-dives; b) P_{DCS} not so high as to result in unacceptably frequent or severe DCS that would be a concern for safety of the subjects (arbitrarily, LEM-he8n25 estimated P_{DCS}<6%); c) the depth in a range where trimix diving would be useful; and d) maximum total dive time of four hours, as is typical for U. S. Navy MK 16 MOD 1 diving.

To meet these latter criteria, the test schedule was selected from a range of decompression schedules generated using the LEM-he8n25 probabilistic decompression model. Probabilistic decompression models can be used two ways: 1) to estimate the P_{DCS} of a decompression schedule and; 2) in conjunction with a search algorithm, to find the shortest decompression schedules at a target P_{DCS}.[2] Both these functions were used to generate candidate test schedules. First, LEM-he8n25 was used to generate MK 16 MOD 1 decompression schedules for trimix at target P_{DCS} of 2.3 % for dives to depths in the range 150–300 fsw (10 fsw increments) for bottom times in the range 5–60 minutes (5 minute increments). Trimix was nominally 1.3 atm constant PO_2 and equal parts helium and nitrogen (details are given in the legend for Figure 1).

[b] The terms 'depth/time schedule' or 'test schedule' indicate a schedule for which the breathing gas is not uniquely defined, as opposed to term 'decompression schedule', which has its customary meaning of a depth/time/breathing gas schedule.

Schedules included a 30-minute period of breathing 0.70 atm PO_2 on the surface before descent for operational reasons (see Diving subheading on page 10). Then, the P_{DCS} was estimated for these same depth/time schedules but conducted breathing heliox. Figure 1B shows the difference (heliox-trimix) in LEM-he8n25-estimated P_{DCS} between some of these decompression schedules. The reverse procedure, first calculating heliox decompression schedules at a relatively high P_{DCS} and then evaluating these depth/time schedules for trimix breathing, resulted in differences in P_{DCS} too small to test in a practicable number of man dives.

The depth/time schedule that best met the desirable characteristics for a test schedule was to 200 fsw with a bottom time of 40 minutes and 119 minutes of decompression stops. The schedule is given in the bottom row of Table 1. Although the test schedule was calculated for a target P_{DCS} of 2.3% using a 60 fsw/min descent rate, the schedule was dived using a 40 fsw/minute descent to minimize the incidence of ear and sinus squeezes. The LEM-he8n25-estimated P_{DCS} of the test schedule with 40 fsw/min descent rate is 2.14% with trimix diluent and 5.56% with heliox diluent. For comparison, the corresponding heliox decompression schedule calculated for a target P_{DCS} of 2.3% using 60 fsw/min descent but dived using a 40 fsw/min descent rate is given also given in Table 1, but this schedule was not used in this protocol. More details about the test schedule are given in Appendix A.

Table 1. Comparison of trimix and heliox* MK 16 MOD 1 decompression schedules

Depth (fsw)	BT	Stops (fsw, mins)								TST	P_{DCS} (%)†	
		90	80	70	60	50	40	30	20		Heliox	Trimix
200	40	5	3	3	2	3	12	11	95	134	2.14	
200	40			4	2	2	6	16	89	119	5.56	2.14

Divers breathe from MK 16 MOD 1 UBA for 30 minutes prior to starting compression.
*The heliox schedule (shaded) is given for comparison only, and was not used in this protocol
†LEM-he8n25-estimated P_{DCS} at descent rate of 40 fsw/min for indicated gas mixtures

EXPERIMENTAL DESIGN

For U.S. Navy MK 16 MOD 1 diving there are practical reasons to retain heliox instead of changing to trimix if there is not an important difference in decompression efficiency. Therefore, it is desirable to test for non-inferiority of heliox as well as superiority of trimix. Such a design requires testing for practical equivalence in, as well as for a difference in, decompression efficiency of the two gas mixtures. Practical equivalence is not established by insufficient evidence to reject a conventional null hypothesis of no difference. Instead, the experimental design tested whether or not the decompression efficiencies of trimix and heliox differ by an amount that is of practical importance. A 20% difference in TST was considered of practical importance. For the range of depths and bottom times analyzed in the preceding section (illustrated in Figure 1), shortening TST by 20% increased the estimated P_{DCS} of heliox dives by approximately 1.5%.

open-circuit emergency gas supply. Divers simultaneously performed the following procedure to purge excess nitrogen from the lungs and UBA. Divers fitted the MK 24 full face mask with the switchover handle in the open-circuit mode. Divers exhaled fully through the open-circuit exhaust then turned the switchover handle to the closed-circuit mode and inhaled a full breath from the MK 16 MOD 1. Divers repeated this procedure for the next two consecutive breaths. After the third consecutive inhalation, divers remained in closed-circuit mode breathing from the MK 16 MOD 1. Divers then completed checks of the MK 16 MOD 1. One at a time, divers entered the OSF trunk where the gas sampling tube and thermistor cable were connected to the gas sampling block on the MK 16 MOD 1, then entered the wet pot. In the wet pot divers assumed a semi-prone position on their cycle ergometer, fully submerged with mid-chest approximately three feet below the wet pot water surface.

Thirty minutes after divers began breathing from the MK 16 MOD 1 UBA, the wet pot air space, trunk, and C chamber were compressed by the introduction of compressed air, at a target descent rate of 40 fsw/min, until the pressure at diver mid chest level (chamber air pressure plus three fsw hydrostatic pressure) was equivalent to 200 fsw. Delays in descent were accommodated by adjusting the time at bottom as detailed in Appendix A. Approximately one minute after reaching bottom, the divers began exercising on the cycle ergometers. Divers pedaled at a target cadence of 60 rpm with the ergometer hysteresis brake controller (W.E. Collins; Braintree, MA) set at 50 watts so that divers' work rate (incorporating the extra power required due to submersion in this diving dress) was approximately 125 watts.[25] Divers exercised intermittently (six minutes on / six minutes off) for an estimated average diver oxygen consumption of 1.3 L/min.[26,27] Divers exercised until approximately five minutes before ascent and then rested in a seated position with mid chest level three feet below the wet pot water surface until the end of bottom time and throughout decompression. The wet pot, trunk, and C chamber were decompressed at 30 fsw/min to and between decompression stops. Decompression stops were taken as given in Table 4. Periodically throughout the dive, divers provided a self-assessment of their own thermal status on a scale of zero (comfortable) to 10 (unbearable).

Table 4. Test schedule as used in the experiment

Depth (fsw)	Time at Bottom*	Stops (fsw, mins†)						TST
		70	60	50	40	30	20	
200	35	4	2	2	6	16	89	119

Divers breathe from MK 16 MOD 1 for 30 minutes immediately prior to compression.
Descent rate 40 fsw/min. Ascent rate 30 fsw/min.
*Time at Bottom in minutes does not include the targeted five-minute descent time.
†Stop time does not include travel to stops.

After surfacing, divers were observed for two hours during which time they remained seated and at rest. A Diving Medical Officer interviewed all divers at 10 minutes and two hours after surfacing, and again the following day (19–21 hours after surfacing). The principal purpose of these interviews was to establish standard times at which divers were definitely free of signs and symptoms of DCS; this information is required for incorporating these data into the U. S. Navy decompression database. Divers were instructed to immediately report any unusual signs and symptoms that occurred outside of these interview times.

Diving took place in two phases: a five-week period and a two-week period separated by seven weeks. One dive per day was conducted, Monday through Thursday, at approximately the same time each day (the time of day of completing decompression ranged from 12:05 to 13:55). Three or four divers participated each day. Divers participated in one to eight experimental dives (median = 3). The schedule of each diver's participation in experimental dives is given in Appendix E. Divers were required to avoid any hyperbaric or hypobaric exposure for a minimum of 48 hours before and following any experimental dive. These restrictions were to avoid alterations in tissue inert gas partial pressures, gas supersaturation, and bubble growth that could influence P_{DCS} of the experimental dive. These restrictions also effectively imposed a minimum surface interval between experimental dives of about 68 hours. A 60-hour surface interval is considered to minimize acclimatization.[28] Acclimatization refers to the apparent decrease in susceptibility to DCS, by unknown mechanisms, over successive (or nearly successive) days of hyperbaric exposures.[29-31] In order to minimize confounding by any acclimatization effect persisting longer than 60 hours, all divers participated in a decompression dive 3–10 days prior to each experimental dive. This preceding 'work-up' dive was either a previous experimental dive on this protocol or a dry chamber air decompression dive specified to be 130 fsw for 15 minutes bottom time with a 30 fsw/min ascent rate and a decompression stop at 20 fsw for four minutes.

RESULTS

SCHEDULES AND DECOMPRESSION SICKNESS

Fifty man-dives were completed on the heliox schedule with no diagnosed incidents of DCS. Forty-six man dives were conducted on the trimix schedule and two divers were diagnosed with DCS by the duty Diving Medical Officer. Details of the DCS incidents are given in Appendix F. These two cases met the criteria for research outcome classification A1 (definite DCS requiring recompression). This difference in DCS incidences between trimix and heliox met a stop-high interim stopping criterion (Table 2), and diving stopped with the null hypothesis retained.

The two divers with DCS following the trimix schedule had both previously completed two dives on the heliox schedule. One of these divers had previously completed an additional trimix dive without incident. In all, 22 divers completed dives on both the heliox and trimix schedules. Four divers completed only heliox dives and six divers completed only trimix dives. The schedule of divers' participation on each test schedule is given in Appendix E. The numbers of completed man-dives on the two schedules are not multiples of the planned group size (16) because three or four man-dives were completed at a time.

The experimental protocol accommodated delays in descent of up to five minutes and some delays required modification of the time at bottom (see Appendix A). There were occasional inconsequential delays in descent to accommodate divers who were slow to equalize ear or sinus air spaces. The longest delay involved a hold for ear squeeze occurring at 21 fsw. The OSF was decompressed to the surface and the afflicted diver removed. Five minutes after the start of the first compression, the remaining three divers were again compressed, at 40 fsw/min, and completed the dive with the full 35 minutes time at bottom. On another occasion, the primary display on a diver's MK 16 MOD 1 failed during compression. There was a 4 minute 36 s delay at 148 fsw while the affected diver switched to the emergency MK 16 MOD 1. Compression was then resumed and the four divers completed the dive with the time at bottom reduced by three minutes to adjust for the hold. These seven man-dives with delays at or near the five-minute maximum were all using trimix diluent, none resulted in DCS, and are included in the 96 completed man-dives.

Fifteen man-dives were aborted, none of which are included in the 96 man-dives completed. On three occasions, compression of the OSF was aborted and all divers were returned to the surface because a diver was unable to equalize ear or sinus air spaces rapidly enough to accommodate the target compression time. On one occasion, all divers were returned to the surface soon after reaching the bottom because of an apparent failure of the emergency MK 16 MOD 1. In fact, the emergency MK 16 MOD 1 had not failed and the event is noteworthy because it involved previously undocumented behavior of the MK 16 MOD 1 UBA secondary display: the secondary display indicates "1.- -" if the maximum display value of 1.99 atm PO_2 is exceeded.[c] The PO_2 in the emergency MK 16 MOD 1 exceeded 1.99 atm during compression to 200 fsw, and the resulting, unrecognized display was interpreted as a failure of the secondary display. The PO_2 in the breathing circuit of a closed-circuit UBA can increase above the PO_2 set point during descent, and whereas it is well documented that such PO_2 overshoot in the MK 16 MOD 1 can exceed 1.99 atm, this was not expected with a 40 fsw/min descent to 200 fsw, even in the emergency MK 16 MOD 1 that was not being breathed.[20,23,32] Several factors could cause a higher than expected PO_2 overshoot in a MK 16 MOD 1 from which oxygen is not been consumed and gas is not being circulated: the PO_2 may be above the 0.75 atm set point before leaving surface; less diluent may be added during descent than expected; and added diluent may not mix completely with gas in the vicinity of the oxygen sensors.

Divers were generally thermally comfortable throughout the dives. Divers were generally warm during the work at bottom and the median thermal status score at the end of bottom time was 1 (very slight discomfort). The median thermal status score at the end of decompression was 0 (no discomfort). The highest thermal status score recorded was 3 (occasional shivering), occurring during decompression.

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[c] As a result of this event, this behavior has since been documented in: SEA 06-EXM (PMS-408(EOD)), *Technical Manual, Underwater Breathing Apparatus MK 16 MOD 1, Description, Operation and Maintenance, Revision 2*, NAVSEA SS600-AQ-MMO-010/0910-LP-028-5850 (Washington (DC): Naval Sea Systems Command, 2014)

UBA GAS COMPOSITION

UBA gas composition was analyzed for all but the one dive in which the emergency MK 16 MOD 1 was used. UBA gas compositions from typical trimix and heliox dives are illustrated in Figure 4. There was no practical difference in UBA oxygen control between heliox and trimix dives. The mean (S.D.) of the time-weighted average P_{O_2} for the trimix dives was 1.37 (S.D.=0.04, n=45) atm and for the heliox dives was 1.36 (S.D.=0.04, n=50) atm (unpaired t-test, t=1.2867, p=0.2014). The nitrogen content of the breathing gas is expressed as fraction of the inert gas: $F_{N_2}/(F_{N_2}+F_{He})$. For the trimix dives, the mean of the time-weighted average of $F_{N_2}/(F_{N_2}+F_{He})$ was 0.519 (S.D.=0.008, range 0.505–0.538, n=45). These figures indicate that the trimix the divers breathed was, as planned, composed of approximately equal fractions of nitrogen and helium. A small amount of nitrogen contaminated the UBA gas on all heliox dives, for these heliox dives the time-weighted average of $F_{N_2}/(F_{N_2}+F_{He})$ was 0.021 (S.D.=0.008, range 0.007–0.043, n=50). The maximum carbon dioxide fraction measured during each dive ranged from zero to 0.0003 and was not different between trimix and heliox dives (unpaired t-test, t=0.5632, p=0.5758). Time-weighted average P_{O_2} and $F_{N_2}/(F_{N_2}+F_{He})$ for all dives are given in Appendix G.

DISCUSSION

The present results indicate that decompression from trimix bounce dives is not more efficient than from heliox dives. This null hypothesis was retained with high power because the trial met a stop-high criterion (more DCS on the trimix than on the heliox schedule). To our knowledge, this is the first prospective comparison of trimix and heliox dives with enough man-dives on each decompression schedule for a statistically reliable comparison, and in which the same depth/time schedule was used for both trimix and heliox dives. This latter design feature avoids confounding of the results by differences in depth/time schedules. Previous programs to develop trimix decompression schedules have been premised on a greater decompression efficiency of trimix compared to heliox, and have been interpreted in that light. However, careful examination of such studies reveals that they are not in conflict with the present results.

The U. S. Navy developed and tested trimix decompression schedules for the MK 6 semi-closed circuit UBA as early as 1962, but no decompression tables and no comprehensive report of the testing were published. In two conference proceedings, Workman presented a few MK 6 trimix decompression schedules which had shorter TST than the corresponding heliox decompression schedules.[18,19] The latter schedules were promulgated in the “Helium-Oxygen Decompression Table for Mixed-Gas Scuba Using 68-32% Helium-Oxygen Supply Mixture” in NEDU TR 1-65.[33] That report documents testing of 48 single-dive heliox decompression schedules (i.e., not including no-stop dives and repetitive dive series), many with shorter TST than the schedules that appear in the final tables. These schedules were typically tested with four man-dives each, and resulted in six treated cases of DCS in 166 man-dives.[33] A search of the archived NEDU diving log books located tests of 15 decompression schedules using the MK 6 semi-closed circuit UBA supplied with trimix (34% He / 34% N_2 / 32 % O_2) that were comparable to the heliox dives reported in NEDU TR 1-65.[d] These trimix dives had on average 19 minutes less TST than (or approximately half the TST of) the corresponding heliox dives documented in NEDU TR 1-65. However, typically only two man-dives (maximum of six) were conducted per trimix schedule, for a total of 46 man dives resulting in two treated cases of DCS. These are insufficient data to assess the relative decompression efficiency of trimix versus heliox in these dives.

The Royal Navy reported sea trials of two trimix decompression schedules in the early 1980s.[15,16] These schedules were for 15-minute bottom times at 70 and 80 msw using surface-supplied trimix with oxygen decompression. Eighty-five man-dives were completed resulting in two cases of DCS. Apparently these schedules were developed on the premise of greater decompression efficiency than corresponding heliox schedules.[17] In the Royal Navy Diving manual of that era, there is a decompression table for surface-supplied heliox diving comprising schedules for 15-minute bottom times at 60, 75, and 90 msw.[34] The 75 msw heliox schedule tabulated in that manual has slightly longer TST than the 80 msw trimix schedule tested in the sea trials. However, full reports of the development and laboratory trials of the trimix schedules are not available,[e] and there is no report of a prospective comparison of trimix and heliox decompression schedules.

Trimix decompression tables using in-water oxygen decompression have recently been developed for the Canadian Underwater Mine-countermeasures Apparatus (CUMA), a semi-closed circuit UBA.[13,14] These trimix tables are an alternative to, and were calculated to have shorter decompression times than, the CUMA heliox tables.[35] Notably, both the CUMA heliox and trimix schedules are longer than the corresponding schedules in the U. S. Navy MK 16 MOD 1 He-O_2 decompression tables.[20] The success of the shorter CUMA trimix schedules is not in itself a demonstration of greater

[d] These 46 trimix dives appear in NEDU diving log books numbers 57 and 62 and occurred between September 1962 and September 1964. A further 191 trimix bounce dives, occurring over the period 1963 to 1966, are recorded in NEDU diving log books 58, 59, 62, 63, and 65. There are 22 trimix dives (1 DCS and 1 marginal DCS) to depths from 30 to 200 fsw also using MK 6 semi-closed circuit UBA, but with supply gas flows and oxygen fractions that are different from those used in NEDU TR 1-65. There are 46 trimix dives (5 DCS and 2 marginal DCS) to depths from 200 to 550 fsw using umbilical supplied MK 6 semi-closed circuit UBA with switching to 100% oxygen for decompression stops at 50 fsw and shallower. There are 25 trimix dives (6 DCS and 1 marginal DCS) to depths from 300 to 500 fsw mostly using the "Deep Sea He-O_2 rig" (a few dives used band masks) with switching to 100% oxygen for decompression stops at 50 fsw and shallower. There are 98 constant PO_2 trimix no-decompression or minimal-decompression (15 minutes TST) dives (1 DCS) to depths from 70 to 200 fsw, some of which Workman presented in a conference proceedings.[19] These dives appear in NEDU log book number 63 and include 54 dives using 1.3 atm PO_2 trimix and 44 dives using 1.6 atm PO_2 trimix. In all these log books, trimix is referred to as "multimix", and with few exceptions comprised equal fractions of helium and nitrogen.

[e] The Admiralty Marine Technology Establishment (AMTE) reports of sea trials of the trimix schedules[15,16] cite earlier reports of laboratory trials, but whereas the reports of the sea trials are listed in the U.K. National Archives, the reports of the laboratory trials are not. Inquiries at different times to the successors to ATME Physiological Laboratory (Defence Evaluation and Research Agency and QinetiQ) have also not located these reports. The original chamber logs for these dives do exist, and these trimix dives form a subset of the calibration data for LEM-he8n25.[20] That subset comprises 192 man-dives resulting in 11 cases of DCS. Sixty-eight of these dives follow similar schedules to those tested in the sea trials, and none of these 68 chamber dives resulted in DCS.

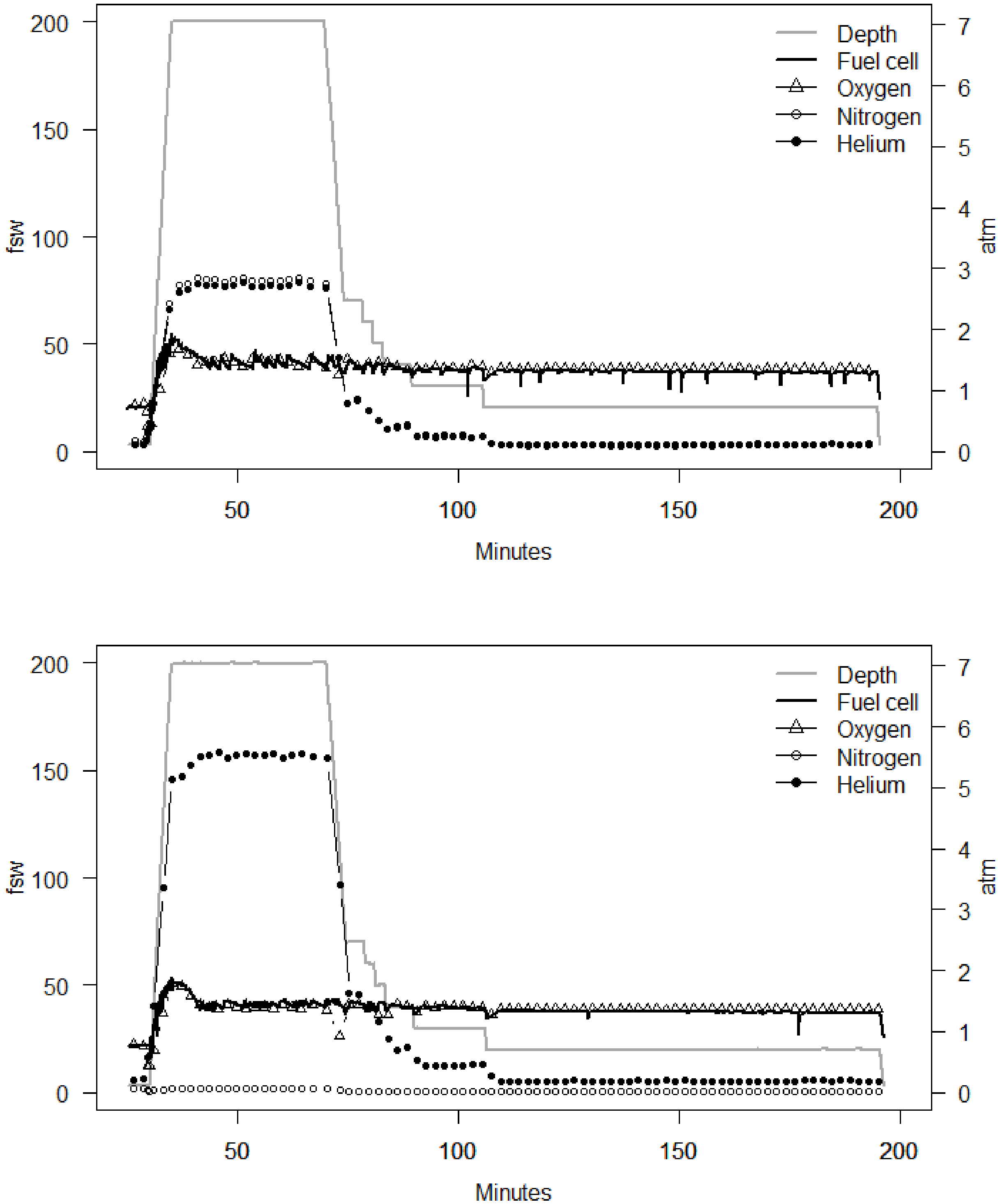

Figure 4. UBA gas composition during a trimix dive (top) and heliox dive (bottom). The depth in fsw gauge is indicated on the left axis and gas partial pressures in atmospheres are indicated on the right axis. The traces with symbols indicate oxygen, nitrogen and helium partial pressures calculated from the ambient pressure in the wet pot and the fractions of these gases analyzed with mass spectrometer. The solid black trace (Fuel cell) is oxygen partial pressure calculated from the output of the K-1D micro-fuel cell oxygen sensor.

decompression efficiency of trimix compared to heliox. Unlike the MK 16 MOD 1, the CUMA does not maintain a constant PO_2, and both the CUMA heliox and trimix decompression schedules are calculated with the conservative assumption of 1.0 atm PO_2. During testing of the CUMA decompression schedules, the time-weighted average PO_2 was substantially higher than 1.0 atm,[13,14,35] and therefore these dives do not test the limits of the underlying algorithm that prescribed shorter decompression times for trimix than for heliox. Testing of the CUMA heliox with in-water oxygen decompression schedules resulted in a low incidence of DCS: only one case of DCS in 352 man-dives.[35] The first series of CUMA trimix testing comprised 44 man-dives on four trimix schedules that had 17–55 minutes less TST (approximately 40% less TST) than the corresponding heliox schedules. No DCS occurred on three schedules, but the longest schedule, which had the greatest saving in TST compared to heliox, resulted in three definite and two possible cases of DCS in eight man-dives.[13] A revised set of 14 trimix schedules were tested which had 9–40 minutes less TST (average 23% less TST) than the corresponding heliox schedules, and these resulted in no DCS in 196 man-dives.[14] However, CUMA trimix decompression schedules with 44 minutes TST or more, which had the greatest saving in TST compared to the corresponding heliox schedules, resulted in a higher percentage of divers with high grades (≥ grade 3) of venous gas emboli than the corresponding heliox schedules.[14] The percentage of divers with high grades of venous gas emboli is used by Defence R&D Canada – Toronto as an indicator of high 'decompression stress'. Decompression stress is presumed to be positively associated with P_{DCS}.[36] This result suggests that although no DCS was observed on these trimix decompression schedules, they have a higher P_{DCS} than the corresponding heliox schedules.

The prescription of longer decompression times for heliox bounce dives than for trimix bounce dives for the same depth and bottom time arises as a result of prescription of deeper initial decompression stops for heliox than for trimix dives. The notion that heliox bounce dives require deeper initial decompression stops than trimix or nitrox dives is relatively entrenched in diving folklore, but does not appear to be based on direct, prospective comparison. The earliest U. S. Navy report on heliox diving (Momsen 1939), which promulgated the surface-supplied heliox "partial pressure" decompression table,[f] states that longer times were required at deeper decompression stops for heliox diving than for nitrogen-based diving.[39] The report provides no experimental evidence to support this statement; although the executive summary states that nearly 700 man-dives at depths up to 500 fsw were conducted, none of these dives are documented. NEDU TR 1-65 which promulgated the MK 6 heliox decompression tables, states that deeper decompression stops are required for heliox than for air dives, but the report does not describe any comparison of heliox and air dives to support this statement.[33]

The idea that heliox dives require a deeper initial decompression stop than corresponding dives conducted breathing a nitrogen-based breathing mixture appears to have arisen from theoretical consideration of how the physicochemical differences between helium and nitrogen might result in faster uptake of helium than of nitrogen

[f] The decompression tables promulgated in this report still appear, in revised form,[37,38] as the Surface Supplied Helium-Oxygen Decompression Table in the current U. S. Navy Diving Manual.

from blood into the tissues during bottom time or faster flux of helium than of nitrogen from tissue into bubbles during decompression.[39] These processes are represented by latent (unobserved) variables in decompression algorithms, in part because the exact sites of bubble-tissue interactions that result in DCS are unknown. It is possible that helium uptake into tissues and into bubbles is faster than that of nitrogen at these unknown DCS-sites, but recent in vivo experiments do not support such differences for sites with gas exchange rates relevant to bounce diving.

Faster half-times for helium than for nitrogen in some decompression algorithms cause these algorithms to prescribe deeper decompression stops for heliox dives than for trimix or nitrox bounce dives.[1] These differences in half-times represent faster tissue:blood equilibration of helium than of nitrogen. Faster tissue:blood equilibration of helium than of nitrogen will occur in tissues where the tissue solubility of helium is lower than that of nitrogen, and will also occur, owing to the higher diffusivity of helium than of nitrogen, in regions where tissue:blood equilibration is diffusion-limited. There is data to support faster washout of helium than of nitrogen in very slowly exchanging compartments.[3,4] However, direct measurement of helium and nitrogen exchange in tissues with faster gas exchange (of the same magnitudes that control decompression from bounce dives) indicate no difference in the exchange rates for nitrogen and helium.[40] These observations do not support faster half-times for helium than for nitrogen in the compartments that control the initial decompression stops from bounce dives.

Faster flux of helium than of nitrogen into bubbles could impose the requirement for deeper initial decompression stops, in order to limit bubble growth, for heliox dives than for nitrox or trimix dives. The flux of gas across the surface of a bubble is determined by the partial pressure difference of the gas across the bubble surface and the permeability (product of gas diffusivity and solubility) of that gas in the tissue at the bubble surface. Since helium has higher diffusivity than nitrogen, the permeability for helium may be higher than for nitrogen in many body tissues. Greater flux of helium than of nitrogen into bubbles is supported by experiments in gelatin, in which the permeability of helium exceeds that of nitrogen, and where the transport of gas to the bubble surface depends entirely on diffusion. In these experiments, nitrogen bubbles in gelatin saturated with nitrogen resume growth when the dissolved nitrogen is replaced by helium, and in complimentary experiments, helium bubbles shrink when the dissolved helium is replaced by nitrogen.[41] However, opposite results arise from observation of bubbles in vivo in rat tissues with intact blood supply,[42-44] and in which the diffusion region surrounding the bubble may be supplied with blood. In these experiments, following decompression from an air dive, air bubbles shrink if the animal breathes heliox, and following a heliox dive, heliox bubbles grow if the animal breathes air. Qualitatively similar results are observed in adipose tissue, where nitrogen permeability might exceed that of helium, and in aqueous tissues, where helium permeability might exceed that of nitrogen. These observations do not support faster growth of bubbles during decompression from heliox dives than during decompression from nitrox or trimix dives.

The LEM-he8n25 probabilistic decompression model behaves comparably with many deterministic decompression algorithms by prescribing deeper initial decompression stops and longer TST for heliox than for trimix dives (see Table 1 and Figure 1). Similarly, LEM-he8n25 incorrectly predicted a higher P_{DCS} for heliox dives than for trimix dives conducted using the same depth/time schedule. A better prediction may be possible with an LEM model re-parameterized with the present data. Nevertheless, the LEM-he8n25-estimated P_{DCS} of the tested trimix decompression schedule (2.14%) falls within the 95% confidence limits of the observed DCS incidence on the trimix dives (0.52%, 14.5%) and the LEM-he8n25-estimated P_{DCS} of the schedule conducted breathing heliox (5.56%) falls within the 95% confidence limits of the observed DCS incidence on the heliox dives (0%, 5.82%). That the LEM-he8n25-estimate P_{DCS} for the heliox schedule was near the upper 95% confidence limit of the observed incidence is noteworthy, because LEM-he8n25-estimated P_{DCS} are near the upper 95% confidence limit of observed incidence for a variety of heliox dives: single and repetitive MK 16 MOD 1 dives, CUMA dives with in-water or surface decompression with oxygen, and open-circuit in-water heliox dives with nitrox and oxygen decompression in the dry.[20,45] Collectively, these data indicate a trend for LEM-he8n25 to slightly over-estimate P_{DCS} for heliox dives, but provide no concern for the applicability of LEM-he8n25 for MK 16 MOD 1 heliox diving.

The present experimental dives, which found no decompression advantage of trimix over heliox, were conducted using a depth and bottom time selected from the domain covered by the U. S. Navy MK 16 MOD 1 He-O_2 decompression table – relatively short duration bounce dives, in which decompression is initially governed by relatively fast exchanging tissues. It is possible that there is a domain of depth and bottom time for which heliox dives require a deeper initial decompression stop and longer total decompression time than trimix dives. This might occur for exceptionally long, sub-saturation dives for which the deepest decompression stop is governed by tissues with slow gas exchange in which the uptake of nitrogen is slower than that of helium. Such dives, if they exist, would not be in a depth and bottom time domain where MK 16 MOD 1 or other closed-circuit self-contained trimix diving would be useful.

The present experimental trimix dives used a breathing gas mixture with approximately equal fractions of helium and nitrogen. This present mixture was chosen to have a large nitrogen fraction, so that any difference with respect to heliox could manifest. It is unlikely that a larger nitrogen fraction relative to helium would have yielded a different result, and larger nitrogen fractions are of increasingly limited practical application for deep diving. Increasing nitrogen fractions impose increasing limits on the maximum operating depths. For instance, in the MK 16 MOD 1 N_2-O_2 decompression tables in the U.S. Navy Dive Manual, all dives deeper than 150 fsw are exceptional exposure. At 150 fsw, the nitrogen partial pressure in a MK 16 MOD 1 using air diluent is 4.24 atm, and this will be used, as an example, as a maximum practical inspired nitrogen partial pressure. For a MK 16 MOD 1 using a diluent with equal fractions of helium and nitrogen, the depth at which the nitrogen partial pressure is 4.24 atm, and therefore the maximum operating depth, is 290 fsw. The maximum operating depth for the MK 16 MOD 1 He-O_2 decompression tables is 300 fsw. We are therefore confident there is not a practical trimix breathing gas that would provide a decompression advantage compared to heliox.

CONCLUSIONS AND RECOMMENDATIONS

Decompression from trimix bounce dives is not more efficient than decompression from heliox bounce dives.

Potential disadvantages of heliox with respect to cost, thermal balance, and voice communications are of limited relevance to MK 16 MOD 1 diving.

The U. S. Navy should not pursue a trimix capability for MK 16 MOD 1 or other closed-circuit self-contained diving.

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calculated using the different compartmental time constants in the LEM-he8n25 model (range 4.7–327.7 minutes) differ by only a few seconds.

Table A-2. Decrease in time at 200 fsw to accommodate holds during descent

	Hold Time (minutes)				
	1	2	3	4	5
Hold Depth*	DECREASE TIME AT BOTTOM BY:				
51–60	0	0	0	1	1
61–70	0	0	1	1	1
71–80	0	1	1	1	1
81–90	0	1	1	1	2
91–100	0	1	1	1	2
101–110	0	1	1	2	2
111–120	1	1	1	2	2
121–130	1	1	2	2	3
131–140	1	1	2	2	3
141–150	1	1	2	3	3
151–160	1	1	2	3	4
161–170	1	2	2	3	4
171–180	1	2	3	3	4
181-190	1	2	3	4	5
191–200	1	2	3	4	5

*Hold depth in fsw includes water offset.

Compression to 200 fsw at target rate of 40 fsw/min (± 5 fsw/min).The dive can be continued with delays in descent up to 5 minutes, otherwise the dive will be aborted.

If the hold occurs at 50 fsw or shallower, the dive continues with no adjustment to time at bottom. Otherwise the time at 200 fsw must be decreased by the amount shown below. Decompression will proceed according to the planned schedule.

APPENDIX B CRITERIA FOR DCS AS AN EXPERIMENTAL OUTCOME[g]

A1: DCS requiring recompression

Joint pain persisting at least as long as tabulated below (whether recompressed or not)

Severity	One joint	Multiple joints
Mild	60 min	30 min
Moderate	30 min	15 min
Severe	15 min	8 min

Skin rash or mottling in combination with joint pain of any duration
Dyspnea, unless clearly from barotrauma or anxiety hyperventilation syndrome
Any spinal neurological symptoms supported by signs
Any brain symptoms[h]
Any inner ear symptoms,[i] unless clearly from barotrauma
Any suspicious symptom leading to and relieved by recompression

A2: Marginal DCS (DCS not requiring recompression)[j]

Joint pain not persisting as long as tabulated above
Moderate or severe fatigue
Skin itch in water-immersed divers breathing air or N_2-O_2
Skin rash or mottling as only symptom
Symptoms reported as "DCS not requiring recompression" not fitting other criteria

B: Unknown outcome (data should not be used)

Headache, typical and common for this diver
Vague abdominal or chest pain, not related to trauma or barotrauma
Vague symptoms of any kind not responding to recompression or oxygen therapy attempted <18 hours after dive[k]

C: Not DCS

No signs or symptoms reported
Signs or symptoms reported 24 hours after surfacing
Mild joint pain or fatigue consistent with recent exercise
Sharp pain consistent with joint sprain or impact injury
Vague symptoms similar to Marginal DCS not responding to recompression therapy attempted >18 hours after dive[l]

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[g] Weathersby et al. 1988 criteria[21]; language reflects development for retrospective data review; not used for treatment decisions
[h] e.g., visual blurring, "mental sluggishness"
[i] e.g., unsteadiness, vertigo, hearing loss
[j] Based on perception that lack of treatment will not result in morbidity
[k] Diver may have gone on to develop DCS if not treated
[l] At which time any DCS should have occurred

APPENDIX C ACCURACY OF A GROUP-SEQUENTIAL TRIAL

In sequential trials, subjects are recruited sequentially and data are analyzed after each individual result or group of results become available. The trial stops as soon as the treatment effect first exceeds a pre-specified size. The outcome of the sequential trial is used as a test of an hypothesis in the sample collected at the point of stopping. For instance, a trial of a single decompression schedule, in which the outcome for each subject is decompression sickness (DCS) or no-DCS (Bernoulli trial), could be analyzed after each man-dive is completed (sequential trial) and stopped when the observed DCS incidence first exceeds some limiting value (stop-high) or drops below another limiting value (stop-low), and this taken as evidence that the decompression schedule has P_{DCS} greater or less than some value of interest. The trial described in this report was a comparison of two decompression schedules, and the trial was analyzed after each 16 man-dives were completed on each schedule (group-sequential) and was designed to stop if the absolute value of the difference in DCS incidences between the schedules exceeded a limiting value. This was to be taken as evidence against practical equivalence of the P_{DCS} of the two schedules.

A statistical hypothesis test in which the value of a statistic of some outcome measure in a sample from a population is classified as evidence to retain or reject a null hypothesis is an example of a binary classification test. Another example is a diagnostic test that classifies an individual as positive or negative for some disease. The fundamental measures of accuracy of a binary classification test are the sensitivity (true positive rate) and specificity (true negative rate). The sensitivity is the conditional probability of classifying an element as positive given that it truly is positive, and the specificity is the conditional probability of classifying an element as negative given that it truly is negative. The accuracy of a statistical hypothesis test is described in a complimentary way, typically by the conditional probability (α) of rejecting a null hypothesis given the null hypothesis is true (type I error, false positive) and the conditional probability (β) of retaining a null hypothesis given the null hypothesis is false (type II error, false negative). The relationship of these measures is tabulated in Table C-1.

Assessing the accuracy of hypothesis tests resulting from sequential trials is not straightforward, and we have developed a Monte Carlo simulation method for such assessments[22] that extends and corrects an earlier method.[46] Monte Carlo experiments analyze outcomes in multiple computer-generated random samples. For instance, the probability of an outcome is estimated by the proportion of samples in which the outcome occurs. Monte Carlo experiments can be used to assess the accuracy of statistical hypothesis tests by performing the test on repeated random samples from a statistical distribution that simulates the experiment, and computing the proportion of test results that equate to the conditional probabilities given in Table C-1.

Table C-1. Definition and nomenclature of measures of accuracy of binary classification tests

Trial Result	Real Condition: H_0 is True ('Negative')	Real Condition: H_0 is False ('Positive')
R_0: Retain H_0 ('Negative')	$P(R_0 \mid H_0 \text{ is true})$ Specificity $\frac{\sum TN}{\sum TN + \sum FP}$	$P(R_0 \mid H_0 \text{ is false})$ β 1-Sensitivity $\frac{\sum FN}{\sum TP + \sum FN}$
R1: Reject H_0 ('Positive')	$P(R_1 \mid H_0 \text{ is true})$ α 1-Specificity $\frac{\sum FP}{\sum TN + \sum FP}$	$P(R_1 \mid H_0 \text{ is false})$ Power=1-β Sensitivity $\frac{\sum TP}{\sum TP + \sum FN}$

TN: True Negatives; FN: False Negatives; TP: True Positives; FP: False Positives

The trial described in this report tested the null hypothesis (H_0): $P_{DCS.trimix} \geq P_{DCS.heliox}$-1.5%. The trial used the stopping rules given in Table 2 and replicated here in Table C-2. If the trial continued to 100 man dives on each profile or if the trial stopped with a positive value of x_{trimix}-x_{heliox} (stop-high), this would be evidence to retain H_0 and conclude that trimix does not afford an increase in decompression efficiency over heliox. If the trial stopped with a negative value of x_{trimix}-x_{heliox} (stop-low), this would be evidence to reject H_0 and conclude that trimix has greater decompression efficiency than heliox.

Table C-2. Stopping rules for determining difference in P_{DCS} between decompression schedules

# DCS $\lvert x_{trimix}-x_{heliox}\rvert \geq$	in # man-dives (or fewer) on each gas mixture
2	55
3	100

The stopping rules could be selected arbitrarily, but those in Table C-2 are integer values of $\lvert x_{trimix}-x_{heliox}\rvert$ and the corresponding largest number of man-dives (# man-dives) for which the proportion $\lvert x_{trimix}-x_{heliox}\rvert$/(# man-dives) has a lower 80% confidence limit>1.5%. It may seem counterintuitive that the specificity of the group-sequential trial is not simply equal to 1-α=80%, as used to generate the stopping rules, but note that the data was analyzed each time 16 man-dives were collected on each schedule, and may stop at values which represent greater differences in DCS incidence than the stopping rules (e.g. 2/16, 2/32, 2/48, 3/64, 3/80, 3/96).

Figure C-1 shows a Monte Carlo simulation of possible trial outcomes for different possible values of P_{DCS} for the trimix schedule and assuming P_{DCS}=5.56% for the heliox schedule. Each point on each of these curves is the fraction of 10,000 trial simulations with the indicated outcome. Each simulation consisted of subtracting a vector of 100 random samples from the Bernoulli distribution (possible values 0 and 1, representing no-DCS and DCS respectively), B(1,*p*) with *p*=0.0556, representing heliox dives, from a vector of 100 random samples from the Bernoulli distribution with *p* being the corresponding value of $P_{DCS.trimix}$ on the x-axis. The running, cumulative sum along the resulting vector was calculated, and each 16th value compared to the stopping rules in Table C-2.

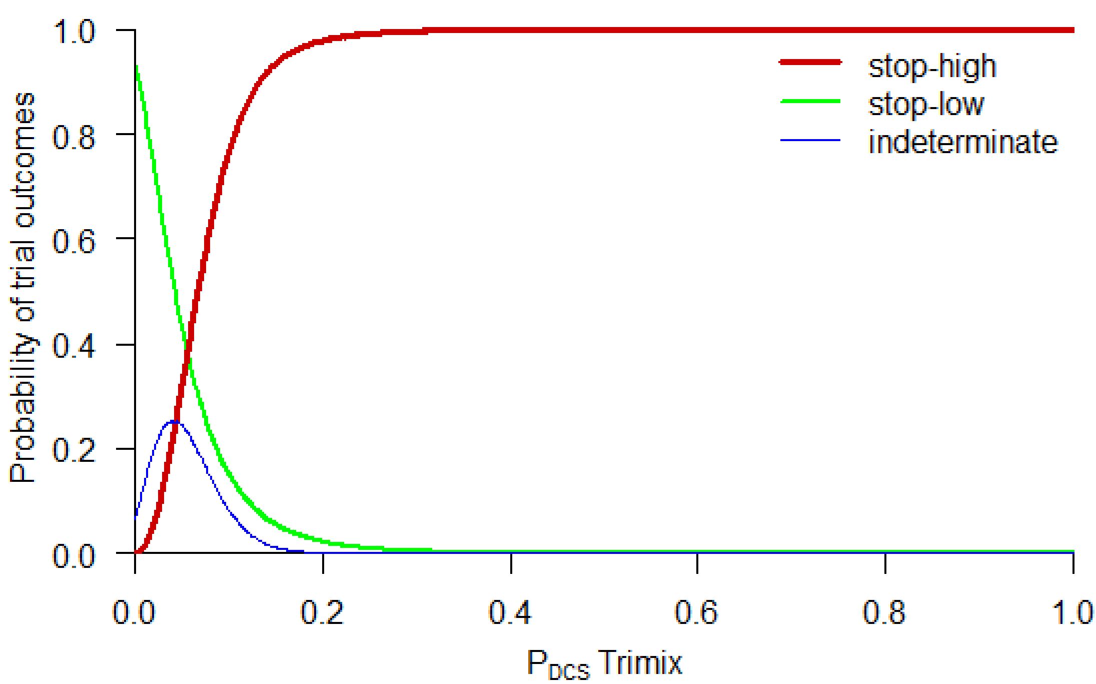

Figure C-1. Monte Carlo simulation of the proposed trial showing the probability of trial outcomes (y-axis) for different possible values of P_{DCS} of the trimix dive (x-axis) and assuming P_{DCS}=0.056 for the heliox dive. Stop-low is the outcome of stopping with a negative value of x_{trimix}-x_{heliox} (reject H_0 in favor of lower P_{DCS} for trimix). Stop-high is the reverse outcome. Indeterminate is continuing to 100 man-dives on each profile without a stop-high or stop-low.

Figures C-2 and C-3 illustrate how the accuracy of the group-sequential is estimated. In Figure C-2, the heavy line shows probability of result R_1 (rejecting H_0) for different possible P_{DCS} of the trimix dive (x-axis). This curve is the stop-low curve given in Figure C-1.The area under this curve is the $P(R_1)$ for all possible values of $P_{DCS.trimix}$. The hatched area (to the right of the vertical line at 0.0556-0.015=0.0406 and below 1) defines the domain where H_0 is true: all trial outcomes for real $P_{DCS.trimix} \geq P_{DCS.heliox}$-0.015. The un-hatched area (to the left of 0.0406 and below 1) defines the domain where H_0 is false: all trial outcomes for real $P_{DCS.trimix} < P_{DCS.heliox}$-0.015. Figure C-3 shows the corresponding information for result R_0 (retaining H_0): the heavy line is the sum of