Acute traumatic ischaemia (crush injury, compartment syndrome)

Hyperbaric oxygen (HBO2) added to surgery: evidence overview

SA ICD-10: T04.7-T04.9, S47, S57.0, S57.8, S57.9, S67.0, S67.8, S77.0-S77.2, S87.0, S87.8, S97.0-S97.8, T79.6
UHMS accepted indication · PMB DTP 147H (treatment: surgical management, ventilation, acute renal dialysis)

Evidence developing **HBO2 probably reduces infection and late complications after severe limb trauma; certainty is low**

Three randomised trials (36, 117 and 60 patients) all point the same way, but none is large, blinding is partial, and the largest missed its primary endpoint: composite necrosis or infection 43% vs 58% (OR 0.55, 0.25-1.18; p=0.12) while tissue necrosis (29% vs 53%) and late complications (6/53 vs 18/52) were significantly lower [2, 1, 3]. The pooled analysis of 7 studies (3 randomised) found lower wound infection (OR 0.31, 0.22-0.45; randomised trials alone OR 0.46, 0.23-0.93) but no difference in healing time or hospital stay, with GRADE low to very low for every outcome [8]. Observational studies are consistent but confounded [9, 10]. Not shown: any effect on healing time or hospital stay in the pooled analysis, or on amputation; fewer repeat operations appeared only in one historical series (none vs 5 of 12) [10]. Surgery, revascularisation and fasciotomy within 24 hours remain the treatment.

OCEBM 1 (Choi 2026 systematic review, 3 RCTs) **GRADE** Low (published: wound infection, Choi 2026)
Published ECHM Type 1, Level B (open fracture with crush injury) · SAUHMA Level B · UHMS no class stated

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Order:** surgery first, including fasciotomy within 24 hours in compartment syndrome [12]. All trials gave HBO2 after surgery.
- **When:** early. HOLLT started at a median 21.6 h after injury [2]; Matos started within 72 h in all but two [13]; the UHMS chapter advises at least three sessions in the first 72 hours [18].
- **Pressure and course:** 2.0-2.5 ATA, 60-120 min, once or twice daily, at least 6 sessions. Used: 2.5 ATA, 90 min twice daily for 6 days [1]; 243 or 284 kPa for 80-100 min, at least 6 sessions in 85% [2]; 2.36 ATA, 90 min [13]; 2.5 bar, 120 min, 10 sessions over about 10 days, first within 48 h of surgery [11]; 2 ATA, 60 min daily [10].
- **Selection:** the one trial subgroup (post hoc) that gained most was patients over 40 with grade III soft-tissue injury [1]. Skin oxygen measured at 2.5 ATA predicted amputation in 23 patients (ratio under 0.20 always amputation) [19].

Synthesised from the studies below; no trial has compared doses. HBO2 is added to, never instead of, debridement, fixation, revascularisation and fasciotomy.

RANDOMISED TRIALS

Ref	Trial	n	Design and regimen	Result	Quality
1	**Bouachour 1996**	36	Limb crush, Gustilo II-III; HBO2 2.5 ATA 90 min twice daily x6 days vs air at 1.1 ATA; double-blind	Complete healing 17/18 vs 10/18 (printed p=0.009; Fisher 0.018); repeat surgery 1 vs 6 (printed p=0.03; Fisher 0.088); gain concentrated in a post hoc subgroup	RoB 2: some concerns
2	**Millar 2022** HOLLT	120 enrolled, 117 analysed	Open tibial fracture; HBO2 243 or 284 kPa, 80-100 min, median start 21.6 h; open label, blinded adjudication; target cut from 250	Necrosis or infection 43% vs 58% (OR 0.55, 0.25-1.18); necrosis 29% vs 53% (OR 0.35); late complications 6/53 vs 18/52 (OR 0.22); 12% intolerant	RoB 2: some concerns
3	**Raj 2023**	60	Open fractures, Gustilo II-III; up to 12 sessions at about 2.4 ATA; lottery allocation, blinding not reported	Smaller, less severe wounds and shorter stay; further surgery not significantly different	RoB 2: high
4	**Lindström 1998**	20	Simple tibial fractures after nailing; 2.5 atm 90 min daily x5	Posterior tibial artery Doppler peak signal higher than controls (dorsalis pedis not); skin oxygen rose within the HBO2 group; no clinical outcome	RoB 2: some concerns

SYSTEMATIC REVIEWS AND POOLED ANALYSES

Ref	Analysis	Scope	Finding	Appraisal
5	**Garcia-Covarrubias 2005**	9 studies, about 150 patients	8 of 9 favourable, one major complication; mostly uncontrolled series; the one randomised trial poorly designed	AMSTAR-2: critically low
6	**Eskes 2013** Cochrane	acute wounds, 4 trials, 229 patients	Too varied to pool; evidence low quality	AMSTAR-2: high
7	**Kwee 2024**	7 studies, 229 patients (2 randomised)	A signal of benefit in severe leg crush injury	AMSTAR-2: critically low
8	**Choi 2026**	7 studies (3 randomised, 4 observational)	Infection OR 0.31 (0.22-0.45); randomised alone 0.46 (0.23-0.93). Necrosis 0.23 (0.12-0.45) but randomised alone 0.17 (0.02-1.26). Healing time MD -1.44 days (-6.70 to 3.82); stay MD -3.39 days (-14.74 to 7.97); GRADE low to very low	AMSTAR-2: low

COHORTS AND UNCONTROLLED SERIES

Ref	Study	n	Result	Quality
9	**Roje 2008**	388, war wounds	With HBO2 (99) vs without: deep infection 35% vs 68%, graft loss 23% vs 52%, flap necrosis 15% vs 51%; not randomised	ROBINS-I: serious
10	**Yamada 2012**	15 vs 12 (historical)	No infection with HBO2 vs 6 of 12 earlier patients	ROBINS-I: serious
11	**De Francesco 2020**	179 mangled arms	HBO2 added in complicated cases: better wound closure and less pain; groups not comparable	ROBINS-I: serious
12	**Kilinc 2025**	145, earthquake	Fasciotomy within 24 h essential; HBO2 went with better function	ROBINS-I: serious
13	**Matos 1999** (abstract)	23, Gustilo III	20 (87%) kept the limb with HBO2 (2.36 ATA, 90 min) plus surgery	JBI case series

ANIMAL EXPERIMENTS (LIMB ISCHAEMIA AND CRUSH)

Ref	Study	Model	Result
14	**Strauss 1983**	dogs, compartment syndrome, 2 atm x3	Less muscle swelling and cell death than dogs from an earlier study
15	**Nylander 1987**	rats, 3 h tourniquet	Muscle ATP about 50% of normal vs about 10% without treatment at 5 h; at 12 h three sessions needed
16	**Haapaniemi 1995**	rats, 3 or 4 h ischaemia	One session preserved glutathione and energy stores and reduced swelling after 3 h; nothing after 4 h
17	**Nelson 1994**	36 rabbits, calf crush, started 16-18 h	No better than air for muscle strength or enzymes; mild crush, no early-treatment arm; 6 of 36 died

WHY THE BENEFIT IS UNCERTAIN

- **Surrogates and subgroups:** the sham-controlled trial's repeat-surgery gap is not significant by Fisher exact test (0.088) and its biggest effect is a post hoc subgroup of 8 vs 10 patients [1].
- **Power and blinding:** HOLLT was cut from 250 to 120 patients, was open label, and 67% vs 56% needed further surgery, though with fewer procedures overall (96 vs 114; 2.5 vs 3.3 per operated patient) [2].
- **Timing in animals:** no benefit when treatment began 16-18 h after a mild crush (no early arm, so delay is the authors' inference) [17]; benefit when ischaemia lasted 3 h but not 4 h, with HBO2 started at reperfusion in both [16].

GAPS IN THE EVIDENCE

- No trial large enough for amputation, healing time or hospital stay; no dose or timing study; compartment syndrome has no randomised data.

MECHANISM

- **Proposed:** HBO2 raises tissue oxygen and reduces swelling and cell death; in animals it reduced muscle swelling and necrosis in dogs [14], preserved about half of normal muscle ATP in rats [15] and reduced swelling after 3 h of ischaemia [16]. The clinical trials measure infection, necrosis and complications, not these mechanisms.

Arterial and cerebral gas embolism

Hyperbaric oxygen (HBO2) recompression: evidence overview

SA ICD-10: T79.0, T80.0, T81.7, T88.9, O88.0
UHMS accepted indication · NRPL 2006 recognised (SA §4.8a) · PMB DTP 627E

Accepted standard of care **Benefit of recompression is unproven by controlled data, but it is the accepted treatment and a trial is not ethical**

No randomised trial of recompression against none exists in people, and Cochrane found none [19]. Observational series point the same way: earlier treatment goes with better outcomes, in an individual-patient meta-analysis of iatrogenic cerebral embolism [1] and in four cohorts [2–5], but delay is confounded by severity, and in the French inception cohort delay was not associated with mortality, only with neurological sequelae [7]. Animal work is mixed: in randomised cats 2.8 ATA oxygen recovered more than no treatment [11], but in swine oxygen started at 2 or 4 hours did not help, in an underpowered study [12]. UHMS rates it Class I, level of evidence C [21], and Germany's hospital committee funded it because no randomised trial exists, it is regarded as the standard, and no alternative exists [24].

OCEBM 4 (case series and cohorts) **GRADE** Not rated (no controlled data) **Published** ECHM Type 1, Level C · SAUHMA Level C · UHMS Class I, level C

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **First aid:** 100% oxygen; supine, or lateral if unconscious, not head-down; isotonic fluids, not dextrose; low-altitude transport [23]. Stop nitrous oxide [21].
- **Who:** sudden neurological or cardiovascular change within minutes of a gas-introducing event; a normal CT is not a reason to withhold treatment; late referrals are still treated [21]. Recovery has been reported after 15 to 60 hours [10].
- **First treatment:** 100% oxygen at 2.82 ATA (US Navy Table 6 or equivalent); starting at 6 ATA is not routinely recommended [21]. In cats a 6 ATA air-then-oxygen profile gave no more than 2.8 ATA oxygen [11].
- **Repeat:** until no further improvement, usually 1-2 sessions, occasionally 5-10, review after 10 [21]. A chest tube first for any pneumothorax in a monoplace [21], ultrasound may aid earlier diagnosis (expert opinion) [16]; ventilators need their own checks [17].

UHMS and the review in the wiki; no trial has tested this protocol. Do not delay referral for imaging.

HUMAN OUTCOME STUDIES (OBSERVATIONAL)

Ref	Study	n / design	Result	Quality
1	**Fakkert 2023**	263 patients, individual data on 126 from 8 studies	Time to HBO2 predicted a good outcome (p=0.013, adjusted 0.041); about 65% good at once, 30% at 15 hours	AMSTAR-2: critically low
2	**Beevor 2016**	45 patients, Melbourne	Time to treatment the only univariate predictor of good outcome: OR 0.94 per unit time (0.89-0.99)	ROBINS-I: critical
3	**Blanc 2002**	86 patients, same HBO2 course	Treatment within 6 hours did better in venous but not arterial embolism; venous 67% vs arterial 35% recovered	ROBINS-I: serious
4	**Tekle 2013**	36 patients	Treatment within 6 hours and no established infarct predicted a good early response	ROBINS-I: high risk
5	**Leitch 1986**	140 pulmonary barotrauma cases; 89 treated gas embolism cases	Cure 65% of the 89; longer delay lowered the chance of cure	ROBINS-I: high risk
6	**Kizer 1987**	42 cases, Hawaii	Complete recovery in 61% of 35 symptomatic; no clear difference between 6 ATA and 2.8 ATA tables or with steroids	moderate
7	**Bessereau 2010**	119 treated, French inception cohort	12% died by ICU discharge, 21% by one year; delay linked to sequelae, not mortality; authors favour HBO2 within 7 hours	JBI: 8 of 10
8	**Fakkert 2025**	22 patients, prospective	23% died; about a third fully recovered at 6 months	JBI: 9 of 10
9	**McCarthy 2017**	67 cases over 25 years	14 of 67 (21%) treated with HBO2; mortality 54% with cardiac arrest vs 13.5% without; HBO2 14.3% vs no HBO2 22.6%, p=0.72	ROBINS-I: high risk
10	**Bitterman 1993** (abstract)	5 patients treated at 15-60 hours	3 recovered partly or fully, 1 no response, 1 died	JBI: high risk

ANIMAL EXPERIMENTS

Ref	Study	Model	Result
11	**McDermott 1992**	26 cats, cerebral air embolism	2.8 ATA oxygen recovered 62% of evoked potential vs 29% untreated; 6 ATA air then oxygen gave 49%, not significantly better than untreated
12	**Weenink 2013**	swine	One Table 6 session at 2 or 4 hours: no significant gain in brain function measures; 6 per group, unblinded, method of random assignment not reported
13	**Dutka 1992**	dogs	Dexamethasone after the embolism added nothing to recompression; given before, a slight borderline effect

CASE REPORTS, LETTERS AND TECHNICAL PAPERS

Ref	Source	Topic	Content	Quality
14	**Bothma 2012**	case report	Cerebral venous air embolism treated with HBO2	JBI: case report
15	**Bothma 2013** (letter)	reply to the swine study	HBO2 remains the treatment of choice despite animal data	letter
16	**Bothma 2015** (letter)	pneumothorax in the chamber	Ultrasound allows earlier diagnosis of a pneumothorax	letter
17	**Bothma 2009**	hyperbaric ventilator	One model delivered tidal-volume surges of 30-100% when oxygen fraction changed	technical report
18	**Kanga 2026**	case report	Fatal cerebral air embolism 7 hours after central-line removal	JBI: case report

REVIEWS, CONSENSUS AND GUIDANCE

Ref	Source	Scope	Position	Quality
19	**Bennett 2012** (Cochrane)	decompression illness	Recompression is standard care; no randomised trial of recompression	AMSTAR-2: see appraisal
20	**Hatling 2019**	264 case reports	Central lines, cardiopulmonary bypass, lung biopsy the main causes, then ERCP and haemodialysis	AMSTAR-2: high risk
21	**UHMS 15th ed, ch 1**	indications manual	Class I, level C; first treatment 2.82 ATA; review after 10	AGREE II: see appraisal
22	**ECHM 2016** (Mathieu 2017)	consensus conference	Gas embolism recommended (Type 1, Level C)	AGREE II: 4 of 7
23	**Mitchell 2018**	pre-hospital consensus	Supine position, highest oxygen concentration, fluids, low-altitude transport	AGREE II: see appraisal

WHY THE EVIDENCE IS WEAK

- **No controlled trial:** recompression has never been compared with none in people [19, 21].
- **Confounding by severity:** the sickest patients reach a chamber fastest, and in the French cohort delay did not predict mortality but did predict sequelae, over a narrow delay range [7]; cardiac arrest carried the worst outcome [9].
- **Selection:** only 21% of patients in one hospital series were treated, so, by inference, treated series may exclude early deaths [9]; the venous form may allow more time [14], and air can enter hours after line removal [18].

GAPS IN THE EVIDENCE

- No published registry analysis of treated and untreated cases, no table comparison in people, and a swine study with no early-treatment control that found no significant gain at 2 to 4 hours, answered by the argument that HBO2 remains the treatment of choice [12, 15].

MECHANISM

- **Bubble and tissue:** pressure shrinks the bubble (Boyle's law: about 36% of its volume at 2.8 ATA, calculated); in cats recompression with oxygen recovered more evoked potential than no treatment [11].

Evidence labels, OCEBM level and GRADE are defined on the reference sheet. Evidence base held for this indication: 678 appraised records (13 systematic reviews; 12 non-randomised studies; 493 case reports and series; 71 narrative reviews; 56 animal and laboratory). Shown: the highest-certainty studies. Full references, PMIDs and DOIs: https://www.hbo.co.za/cards/refs/air-gas-embolism.html

Avascular necrosis of the femoral head

Hyperbaric oxygen (HBO2) for early (pre-collapse) osteonecrosis: evidence overview

SA ICD-10: M87.05, M87.15, M87.25, M87.35, M87.85, M87.95; dysbaric: M90.35 with T70.3
UHMS accepted indication · not on the NRPL 2006 §4.8 list · no PMB code

Evidence developing **Benefit of HBO2 for early femoral-head necrosis is unproven: pain relief is shown, joint preservation is not**

One assessor-blinded trial of 20 patients (19 analysed) found less pain with HBO2 than hyperbaric air in Ficat stage II disease [1]; a 2005 conference abstract appears to report the same trial [2]. No trial shows that HBO2 prevents collapse or hip replacement: a 2025 pooled analysis of two studies (125 hips) found no difference against controls, with a very wide interval (RR 1.83, 0.37-9.09) [5], and in a network analysis no treatment reduced conversion to hip replacement, though HBO2-based treatment ranked highest for pain with very large, imprecise effects [6]. Older pooled analyses report odds ratios of 3.8 to 5.0 from mostly non-randomised controlled studies [3, 4]. UHMS and the European consensus accept it mainly for early disease [9, 10]; the German guideline advises against it [11]. Uncontrolled series report good hip function, but with large losses to follow-up [18, 20].

OCEBM 2 (one RCT, 20 patients) **GRADE** Low (published: hip replacement and pain, Niu 2026)
Published ECHM Type 2, Level B · SAUHMA 'Level 1' as printed · UHMS adopts ECHM 2B, no class of its own

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** early, pre-collapse disease (Ficat I-II); UHMS recommends including HBO2 among the possible options [9]. Benefit is not expected after subchondral collapse [8]; for Ficat IIIA or worse UHMS offers a cost-benefit option only [9].
- **Dose:** stage I: 30-40 sessions at 2.0-2.5 ATA for 60-70 min; stage II: 30-40 sessions, a pause of 20-30 days, then 20 more [9]. Used: 30 sessions at 2.5 ATA for 80 min in the randomised trial [2].
- **Review:** after 40 treatments, with repeat MRI at least a month later [9].

UHMS staged schemes; no trial has compared schemes. HBO2 is an adjunct to offloading and multidisciplinary care.

RANDOMISED TRIALS

Ref	Study	n / design	Result	Quality
1	**Camporesi 2010**	20 randomised, 19 analysed; assessor-blinded; HBO2 vs hyperbaric air, 30 sessions; Ficat II	Pain score fell about 5.9 to 1.4 with HBO2, unchanged with air; extension, abduction, adduction improved, flexion did not	RoB 2: some concerns
2	**Vezzani 2005** (abstract)	20, Ficat II; stopped early; apparently the same trial as above	Hip movement, balance load and pain better with HBO2; no numbers given	RoB 2: see appraisal

POOLED ANALYSES, GUIDELINES AND CONSENSUS

Ref	Study	Scope	Result	Quality
3	**Li 2017**	9 studies, mostly observational	Clinical effect OR 4.95 (3.24-7.55)	AMSTAR-2: critically low
4	**Paderno 2021**	10 cohort studies, 721 patients	Clinical benefit OR 3.84 (2.10-7.02); authorship overlaps with Camporesi	AMSTAR-2: critically low
5	**Cao 2025**	10 studies, 568 patients	Pain fell after HBO2 (VAS -2.94); vs controls, 2 studies, 125 hips: RR 1.83 (0.37-9.09), I2 89%, uninformative	AMSTAR-2: low
6	**Niu 2026** (network)	29 studies, 2,177 hips	HBO2-based treatment ranked highest for pain, with very large imprecise effects; no treatment reduced hip replacement	AMSTAR-2: low
7	**Uzun 2016**	8 studies, small	HBO2 helped early disease in small studies; no pooling	AMSTAR-2: critically low
8	**Osmani 2017**	16 studies, conservative options	HBO2 benefit confined to pre-collapse disease	AMSTAR-2: critically low
9	**UHMS 15th ed, ch 15**	indications manual	Recommends including HBO2 among options for early disease; Ficat IIIA+ cost-benefit; authors overlap with the trial	AGREE II: 3 of 7
10	**ECHM 2016** (Mathieu 2017)	consensus conference	Femoral head necrosis accepted (Type 2, Level B)	AGREE II: 4 of 7
11	**German S3 guideline 2015**	non-traumatic necrosis	HBO2 should not be used: eases pain early, no evidence of delayed collapse	AGREE II: not scored

COHORTS AND UNCONTROLLED SERIES

Ref	Study	n / design	Result	Quality
12	**Reis 2003**	12 patients, 16 hips, Steinberg I; historical controls	MRI normal in 13 of 16 hips, 9 of 12 like-for-like	ROBINS-I: critical
13	**Moghamis 2021**	19 patients, 23 stage II hips; HBO2 vs core decompression	Similar results; 8 of 23 hips progressed radiologically in a year	ROBINS-I: serious
14	**Bozkurt 2022**	80 hips; HBO2 alone vs with core decompression	Both improved; combination improved more (pain fall 5.4 vs 4.1); allocation by clinic	ROBINS-I: serious
15	**Hsu 2009**	63 analysed (98 hips, ARCO I-III); ESWT, HBO2 and alendronate vs ESWT; odd/even allocation	Hip replacement 10% vs 10.4% of hips; HBO2 not separable	ROBINS-I: serious
16	**Bernbeck 2004**	27 children with leukaemia or lymphoma; 19 had HBO2	MRI differences not statistically significant	ROBINS-I: critical
17	**Scherer 2000** (abstract)	20 children; 12 added HBO2 to weight-bearing relief	No significant difference in MRI scores	ROBINS-I: serious
18	**Koren 2015**	68 patients, 78 joints, all treated	93% joint survival at 11 years, of 58 joints traced; 20 lost	ROBINS-I: critical
19	**Ansari 2025**	28 patients, 44 hips, 35 sessions, all treated	Hip score 68 to 81, pain 9 to 3.4 over 2 years; one hip replacement	JBI: 9 of 10
20	**Chandrinou 2020**	73, Steinberg I-II, all treated	Scores improved; only 44 completed the protocol	JBI: high risk

WHY THE EVIDENCE IS WEAK

- **Trial size:** one randomised trial of 20 patients, reported twice, by authors who co-wrote the UHMS chapter [1, 2, 9].
- **Wrong endpoint:** the trial measured pain and movement [1]; no treatment reduced conversion to hip replacement [6], and the German guideline found no evidence of delayed collapse [11].
- **Follow-up and controls:** the series have no comparator and lose 10-40% of patients [18, 20, 19]; the two paediatric comparisons found no significant overall MRI difference [16, 17].

GAPS IN THE EVIDENCE

- No adequately powered randomised trial with hip survival or collapse as the outcome.

MECHANISM

- **Necrotic bone:** HBO2 is thought to raise oxygen tension in necrotic bone, reduce intraosseous pressure and oedema, and promote angiogenesis [9].

Carbon monoxide poisoning

Hyperbaric oxygen (HBO2) versus normobaric oxygen (NBO): evidence overview

SA ICD-10: T58 (toxic effect of carbon monoxide)
UHMS accepted indication · PMB DTP 316S (toxic effect of gases, fumes and vapours)

Evidence developing **Benefit of HBO2 over normobaric oxygen is unproven**

Ten randomised trials (nine reports) disagree: the three sham-controlled, double-blind trials split (Weaver 2002 positive [6], Scheinkestel 1999 null with a harm signal [5], Weaver 2023 dose comparison null [9]). Four pooled analyses find no significant overall benefit [10–13]. Certainty of benefit: low to very low (GRADE, Fujita 2026 [13]). Signals that keep HBO2 in use: fewer cognitive sequelae at 6 weeks in the one sham-controlled, double-blind trial that favoured it (25.0% vs 46.1%; stopped early, RoB 2: some concerns) [6]; memory impairment favoured HBO2 in pooled data (RR 0.67) [11]; earlier treatment did better in a propensity-matched registry analysis of 706 patients [14].

OCEBM 1 (Buckley 2011 Cochrane, 6 RCTs) **GRADE** Low to very low (published: Fujita 2026, Table 2) **Published** ECHM Type 1, Level B · SAUHMA Level A · UHMS Class I, level B-R

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **When:** as early as possible, ideally within 6 h of CO exposure: in a registry of 706 HBO2-treated patients analysed with propensity matching, treatment within 6 h of CO exposure gave fewer poor 6-month outcomes than 6-24 h (p=0.027; dose-response p=0.008; observational) [14]. The positive trials enrolled symptomatic patients [3, 6].
- **Sessions:** one. A second session was not better (more memory impairment [11]; worse on three outcomes in a severity-confounded comparison [12]; worse in the one trial of initial coma [7]); three did not differ from one in an underpowered trial [9].
- **Pressure and time:** 2.4-3.0 ATA for 90-120 min. Tested: 2.5 ATA 90 min [4]; 2.8 then 2.0 ATA, 120 min [3]; 2.4 and 3.0 ATA showed no significant difference in an underpowered pilot [8].
- **Comatose or ventilated:** no adequately powered trial; in the one trial of initial coma, two sessions (2 ATA) did worse than one, so do not routinely add a second [7]. Exclude pneumothorax first. Use laboratory CO-oximetry, not pulse oximetry [17].

Synthesised from the trials below; no trial has tested this exact protocol. A starting point for clinical judgement.

RANDOMISED TRIALS

Ref	Trial	n	Regimen and comparator	Result	Quality
1	**Raphael 1989** RCT, 2 strata	629	HBO2 2 ATA, 1 h at pressure (2 h session) vs NBO 6 h; loss-of-consciousness stratum (brief LOC or coma): 1 vs 2 sessions	No LOC: recovery at 1 mo 68% vs 66%. LOC stratum: 54% (1 session) vs 52% (2); brief LOC alone 60% vs 54%	RoB 2: some concerns; open-label
2	**Ducasse 1995** RCT	26	HBO2 2.5 ATA, 2 h vs NBO; non-comatose, treated ~53 min after rescue	Abnormal signs at 2 h 2/13 vs 9/13; abnormal EEG at 3 wk 0/8 vs 6/10 (surrogates)	RoB 2: high (3-wk data on 18/26)
3	**Thom 1995** RCT, open-label	60	HBO2 2.8 ATA 30 min then 2.0 ATA 90 min vs NBO; mild-moderate	Delayed neurological sequelae 0/30 vs 7/30 (p<0.05)	RoB 2: some concerns
4	**Mathieu 1996** RCT, interim abstract	575	HBO2 2.5 ATA 90 min (1 session) vs NBO 12 h; non-comatose	Persistent symptoms 3 mo 9.5% vs 15%; at 1 yr 4.3% vs 5%	Abstract only; interim; blinding not reported
5	**Scheinkestel 1999** RCT, double-blind, sham	191	HBO2 2.8 ATA 60 min daily x3-6 d vs sham; all grades, 65-72% suicide attempts	No benefit; extra treatments 28% vs 15%; all 5 DNS relapses in the HBO2 arm (p=0.03)	RoB 2: high; mean delay 7.5 h (HBO2) vs 6.6 h
6	**Weaver 2002** RCT, double-blind, sham	152	3 HBO2 sessions in 24 h vs 1 NBO + 2 sham	Cognitive sequelae 6 wk 25.0% vs 46.1% (p=0.007; aOR 0.45, 0.22-0.92); 12 mo p=0.04 (ITT; complete-case p=0.08; post hoc endpoint)	RoB 2: some concerns; stopped early
7	**Annane 2011** 2 RCTs	385 of 970 planned	A: transient LOC, +1 HBO2 session (2 ATA, 1 h) vs NBO. B: coma, 2 vs 1 session	A: full recovery 58% vs 61% (OR 0.90, 0.47-1.71). B: 47% vs 68% (OR 0.42), stopped for harm (p=0.007)	GRADE low; retrospective registration
8	**Hampson 2006** Pilot RCT	30	Single HBO2 session 2.4 ATA (90 min) vs USAF table (3.0 ATA 2 x 23 min, then 2.0 ATA 2 x 25 min)	Abnormal screen straight after treatment 22% (4/18) vs 17% (2/12), p=0.71; at 14-21 days 6% vs 9%, p=0.75; feasibility only	RoB 2: some concerns
9	**Weaver 2023** RCT, double-blind	72 of 150 planned	3 HBO2 vs 1 HBO2 + 2 sham; intubated excluded; 28% LOC	Sequelae 6 wk 50% (1 session) vs 55% (3), p=0.80; 6 mo 42% vs 46%	GRADE low; stopped for slow enrolment

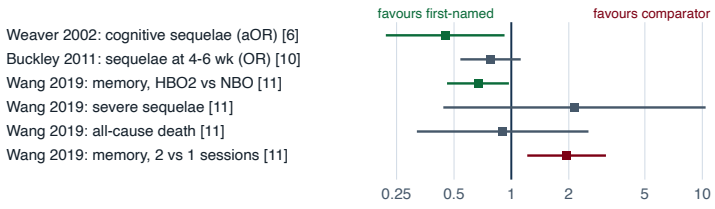
POOLED ANALYSES

Ref	Analysis	Scope	Finding	Appraisal
10	**Buckley 2011 (Cochrane)**	6 RCTs, 1,361 analysed	Neurological symptoms or signs at 4-6 weeks: pooled OR 0.78 (0.54-1.12), not significant; trials too heterogeneous and flawed to conclude	AMSTAR-2: low
11	**Wang 2019**	7 RCTs, 2,023 patients	Recovery RR 0.92 (0.78-1.08; HBO2 vs NBO subgroup 1.01); severe sequelae 2.15 (0.44-10.40); death 0.90 (0.32-2.53); memory impairment HBO2 vs NBO 0.67 (0.46-0.97, p=0.035); 2 vs 1 sessions 1.95 (1.21-3.13, worse)	AMSTAR-2: low
12	**Ho 2022 (network)**	8 RCTs, 1,785 patients	HBO2 no better than NBO; two sessions worse than one for fatigue (RR 1.29), memory (1.80), concentration (1.85), but the two-session arms were sicker at baseline (Annane: 104 of 105 comatose), so the comparison is confounded	AMSTAR-2: critically low
13	**Fujita 2026 (Japan Resuscitation Council)**	6 RCTs	No significant benefit on mortality or neurological outcome, including the 2.5 ATA or higher subgroup; GRADE mostly very low to low	AMSTAR-2: critically low

WHO BENEFITS, AND PROGNOSIS

- **Who benefits is not settled.** Raphael: nothing without loss of consciousness [1]; Thom (mild-moderate) [3] reported fewer delayed sequelae; Mathieu (non-comatose) [4], fewer at 3 months only (interim abstract; none at 1 year); Ducasse [2], faster early recovery and fewer abnormal EEGs at 3 weeks (no clinical sequelae); Weaver enrolled all symptomatic grades [6]; Scheinkestel (mostly severe suicide attempts) found none [5].
- **Delayed encephalopathy:** small trials adding a drug or stimulation to HBO2 reported better remission or cognitive scores; none tested HBO2 itself [20–23].
- **Prognosis:** a low initial Glasgow Coma Score raised the odds of delayed neurological sequelae (OR 2.98, 2.10-4.23; 10 studies, 2,328 patients) [15]; early MRI flagged about 71% of later sequelae at about 84-85% specificity [16]. Neither has been tested as a rule for choosing HBO2.

ADVERSE-OUTCOME RATIOS (95% CI, LOG SCALE)



HARMS AND LIMITS

- **Harms seen in trials:** ear barotrauma 7 and 1 oxygen-toxicity seizure among 104 HBO2 patients [5].
- **Pulse oximetry is unreliable:** it read falsely normal (SpO2 above 90%) in all 30 patients with COHb above 25% (mean overestimate 31.9 points, 95% CI 28.3-35.5, n=15 with arterial CO-oximetry) [17].
- **Cardiac arrest:** of 980 severely poisoned patients treated with HBO2, 18 had been resuscitated first; all 18 died, 10 of them treated within 3 h [18].
- **Ventilated (conference abstract):** 76 of 80 (95%) reached arterial PO2 above 760 mmHg at 2.8-3.0 ATA [19].

MECHANISM

- **Clearance:** at 1.58 ATA oxygen the carboxyhaemoglobin half-life was about 26-29 min vs about 71-87 min on non-rebreather mask oxygen (12 healthy volunteers, smoking-induced COHb about 1.0-1.2 g/dl) [24].
- **Beyond clearance (rats):** HBO2 at 3 ATA for 45 min, even 45 min after poisoning, blocked neutrophil beta-2 integrin adherence and brain lipid peroxidation; 1 ATA oxygen did not stop lipid peroxidation, and 3 ATA at normal oxygen partial pressure did nothing [25].
- **Cellular:** CO disturbs mitochondrial oxidative phosphorylation in humans [26]; HBO2 lowers inflammatory mediators, often only briefly [27]. Faster clearance is mechanism, not proof of better outcome.

GAPS IN THE RANDOMISED EVIDENCE

- No adequately powered randomised trial in comatose, ventilated or pregnant patients [7], or of one early session at 2.5 ATA or more.
- Endpoints differ: delayed sequelae in 7 of 30 NBO controls in Thom [3], none in Scheinkestel [5].

Evidence labels, OCEBM level and GRADE are defined on the reference sheet. Evidence base held for this indication: 640 appraised records (19 randomised trials; 14 systematic reviews; 149 non-randomised studies; 273 case reports and series; 67 narrative reviews; 54 animal and laboratory). Shown: the highest-certainty studies. Full references, PMIDs and DOIs: https://www.hbo.co.za/cards/refs/carbon-monoxide-poisoning.html

Central retinal artery occlusion

Hyperbaric oxygen (HBO2) for acute retinal artery occlusion: evidence overview

SA ICD-10: H34.1 (also H34.0, H34.2, H34.9)
UHMS accepted indication · PMB DTP 906B (its treatment component names laser, not HBO2)

Clinical consensus **Benefit of HBO2 for retinal artery occlusion is unproven**

There is no randomised trial of HBO2. Controlled comparisons are non-randomised and conflict: some found gains with HBO2 [9, 12, 13]; others found no clear benefit in central occlusion or no significant difference [6, 8, 11, 14]. Pooled analyses point both ways: in 7 oxygen-therapy studies (251 patients, 6 hyperbaric) the hyperbaric subgroup did better than the normobaric study [1]; 9 comparative studies (499 patients) showed better best-corrected acuity only after sensitivity analysis [4]; and a meta-analysis of 3 comparative studies (207 vs 89 patients) found no improvement in final vision [2]; all are rated critically low quality or are abstracts. A randomised trial of alteplase against aspirin (70 patients) found no significant benefit and was underpowered, and two earlier thrombolysis trials were stopped early [20]. Reported gains were more consistent when HBO2 started within about 12 hours, but that comes from non-randomised data [5, 18].

OCEBM 3 (non-randomised cohorts) **GRADE** Very low (our assessment: visual acuity) **Published** ECHM Type 2, Level C · SAUHMA Level C · UHMS AHA IIb

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **When:** as early as possible: gains were more consistent within 12 hours than later in non-randomised comparisons [5, 18]; the UHMS chapter advises within 24 hours [21]; one adjusted analysis within 24 hours found no timing effect [13].
- **Pressure:** an initial 2.8 ATA session gave a greater 24-hour gain than 2.0 ATA in 139 eyes (retrospective) [19]; a protocol of 2.8 ATA for 90 min, then 2.4 ATA twice daily for 5 days, 10 treatments, was used in 39 patients [15]; a protocol of 2.5 ATA twice daily (delivered twice daily in 20 of 28) [16]. UHMS gives 2.0-2.8 ATA and advises not stopping after one non-responding session [21].
- **Practice varies:** 84 US centres had no common protocol; 42% started at 2.4 ATA [22].
- **Alongside:** a retinal artery occlusion is an eye stroke: 14% of 190 patients had a stroke or myocardial infarction over about two years, linked to high blood fats [14]; arrange vascular work-up.

Synthesised from the studies below; no trial has tested this protocol. Treat as an emergency alongside stroke work-up.

POOLED ANALYSES AND REVIEWS

Ref	Analysis	Scope	Finding	Appraisal
1	**Wu 2018**	7 studies, 251 patients (design classification doubtful)	Hyperbaric oxygen subgroup did better than normobaric; treatment within 3 months and over 9 h in total did better (subgroup analyses)	AMSTAR-2: critically low
2	**Rosignoli 2021**	3 non-randomised comparative studies (207 HBO2 vs 89 control) plus the authors' own 48 patients	No significant improvement in final vision (p=0.83)	AMSTAR-2: critically low
3	**Yu 2024**	review of six HBO2 reports (includes Rosignoli)	Mixed: 3 of 5 small retrospective studies reported significant improvement; no gold standard treatment	AMSTAR-2: see appraisal
4	**Elfil 2025** (abstract)	9 comparative studies, 499 patients (Newcastle-Ottawa)	Best-corrected acuity improved only after sensitivity analysis (MD -0.63 logMAR, CI -1.14 to -0.12); no difference in uncorrected acuity or lines gained	AMSTAR-2: critically low
5	**Albalawi 2026**	12 mostly observational studies	Better vision recovery with HBO2, best within 12 hours	AMSTAR-2: critically low

COMPARATIVE COHORTS (HBO2 VS STANDARD CARE WITHOUT HBO2; NON-RANDOMISED)

Ref	Study	n	Result	Quality
6	**Aisenbrey 2000**	CRAO 8 vs 8; BRAO 10 vs 6	CRAO: no clear difference in mean gain (6/8 vs 2/8 reached 0.04 or better); branch: larger gain (8 vs 4 lines), untested; prospective pilot, controls declined or contraindicated	ROBINS-I: serious
7	**Beiran 2001**	35 vs 37	HBO2 within 8 h did better at discharge than patients from another centre, but only in those with high blood pressure; HBO2 group older and more hypertensive	ROBINS-I: serious
8	**Menzel-Severing 2012**	51 vs 29, within 12 h	HBO2 + haemodilution vs haemodilution alone: gain about 3 vs 1 lines, not significant	ROBINS-I: serious
9	**Rozenberg 2022**	121 vs 23	Final acuity better with HBO2 after adjustment (p=0.023); similar shares reached 20/200 or better (HBO2 20% vs standard care 17%, p=0.52)	ROBINS-I: serious
10	**Schmidt 2020**	14 vs 14, branch occlusion	Matched pairs: better vision at discharge with HBO2 (0.69 vs 0.32 decimal); unmatched cohort 17 vs 160: 0.60 vs 0.58; HBO2 given selectively	ROBINS-I: serious
11	**Kalaw 2024**	75, 27 given HBO2	No significant improvement in vision and no reduction in later stroke or glaucoma	ROBINS-I: serious
12	**Lee 2024**	29 vs 21	HBO2 as rescue therapy; controls contraindicated, declined or no chamber; similar at baseline; HBO2 gained vision over 6 months, controls did not; started 3.6 days after onset	ROBINS-I: serious
13	**Thoongsuwan 2025**	17 vs 32, within 24 h	More gained vision with a five-day HBO2 course; no adjusted timing effect within 24 h	ROBINS-I: serious
14	**Hayat 2026** (abstract)	190, over 2 years	HBO2-treated eyes improved but ended no better than untreated eyes	ROBINS-I: serious

UNCONTROLLED SERIES WITH HBO2

Ref	Series	n	Outcome
15	**Masters 2021**	39	72% improved after 10 treatments (first 2.8 ATA, then 2.4 ATA twice daily); ear barotrauma about a quarter; no untreated comparison
16	**Di Vincenzo 2022**	28 (15 central, 13 branch)	Protocol 2.5 ATA twice daily (given twice daily in 20); 14 of 28 gained 0.3 logMAR or more at 1 month (10 of 15 central)
17	**Hadanny 2017**	128	Vision improved after HBO2; the authors propose the cherry-red spot rather than elapsed time as the marker, though delay was a smaller significant predictor of gain

TIMING, DOSE AND THE ONE RANDOMISED TRIAL OF ANOTHER TREATMENT

Ref	Study	n	Result
18	**Cevik 2026** (abstract)	101 eyes	Vision gain greatest when HBO2 began within 12 hours
19	**Gur 2026**	139 eyes	An initial 2.8 ATA session (then two at 2.0 ATA) gave a greater 24-hour gain than 2.0 ATA throughout; earlier treatment did better (retrospective)
20	**Préterre 2025** RCT	70	Alteplase 0.9 mg/kg vs aspirin within 4.5 h: improved 66% vs 48% (not significant, underpowered); two earlier thrombolysis trials were stopped early

WHY GAINS ARE HARD TO ATTRIBUTE

- **Natural recovery and selection:** controls were contraindicated, declined or had no chamber [12], declined or were contraindicated [6] or came from another centre [7]; HBO2 was sometimes a rescue therapy [12, 10].
- **Irreversible damage:** in 128 patients the authors propose the cherry-red spot, not elapsed time, as the marker of irreversibility [17]; early inner-retinal disorganisation on OCT predicted poor vision [23], and in 35 non-reperfused eyes (25 HBO2, 10 not) inner-retinal thinning progressed in both groups; reperfused eyes were excluded, so the study cannot test HBO2 [24].

GAPS IN THE EVIDENCE

- No randomised trial of HBO2; no dose-finding; controls differ; most studies single-centre.

MECHANISM

- **Rationale (hypothesis):** HBO2 raises choroidal oxygen delivery while the retinal circulation is blocked. Fluorescein angiography in 31 patients (19 central, 12 branch) showed blood flow returned in 87% by three weeks, without a control group [25].

Complex and problem wounds

Hyperbaric oxygen (HBO2) added to standard wound care: evidence overview, mainly diabetic foot ulcers

SA ICD-10: I70.20, I70.21; E10.5, E11.5, E14.5; each with L97; T87.5
UHMS accepted indication · NRPL 2006 recognised (SA §4.8f) · PMB only for gangrene (DTP 915E)

Evidence developing **Benefit of HBO2 for problem wounds is unproven: possible in ischaemic diabetic ulcers that fail standard care**

The randomised trials of diabetic foot ulcers conflict. Small trials report fewer amputations [2, 5, 9, 1] or more healing [6, 3], but the two largest, one sham-controlled and one without sham, found no benefit for healing or amputation [7, 8]. The Cochrane review found faster healing at six weeks (RR 2.35, 1.19-4.62) but no significant effect on amputation or on long-term healing [13]; later pooled analyses disagree [16, 15], and the positive amputation result in one depends on a single trial [16]. Benefit is more plausible in ischaemic ulcers [14, 17] and not shown in non-ischaemic ones [18]. UHMS, IWGDF and vascular surgeons recommend it only conditionally, after standard care has failed [20, 22, 21]; for venous ulcers a placebo-controlled trial was null for complete healing [25], and pooled venous data are inconsistent [23, 24].

OCEBM 1 (Kranke 2015 Cochrane, 12 trials) **GRADE** Moderate (published: diabetic foot amputation, RR 0.36, 0.11-1.18)
Published ECHM Type 2, Level B (diabetic foot), Level C (ischaemic ulcers) · SAUHMA Level B (diabetic foot ulcer), C (other problem wounds) · UHMS guideline: conditional, moderate

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** diabetic foot ulcer of Wagner grade 3 or higher that has not improved after 30 days of standard care, or just after debridement of an infected foot; not Wagner 2 or lower; not venous ulcers [20]. IWGDF limits it to neuro-ischaemic or ischaemic ulcers where standard care has failed [22]. Arterial ulcers: those failing despite revascularisation, or not candidates for it [20].
- **Dose:** 2.0-2.5 ATA for 90-120 min, usually 30 sessions and up to 40 [20]. In-chamber skin oxygen above 200 mmHg predicts response; if it is poor and amputation is the only alternative, try 10-15 sessions and stop if there is no response [20]. Used: 40 sessions, 5 days a week [6].
- **Review:** utilisation review after the first 30 days or treatments [20]. Completion matters: 35% of the treated arm in the largest ischaemic-ulcer trial did not complete the planned course (at least 30 sessions or wound closure) [8].

UHMS selection and dose; no trial has compared protocols. Offloading, revascularisation, debridement and infection control come first.

RANDOMISED TRIALS IN DIABETIC FOOT ULCERS

Ref	Study	n / design	Result	Quality
1	**Doctor 1992**	30; only 4 HBO2 sessions	Major amputations 2 vs 7	RoB 2: some concerns
2	**Faglia 1996**	68; no sham, amputation decided by a surgeon unaware of allocation	Major amputation 8.6% vs 33.3%	RoB 2: some concerns
3	**Abidia 2001** (abstract)	18, 33 ulcers; double-blind vs hyperbaric air	Healed at 12 weeks 13/19 vs 4/14 ulcers; no difference in amputation	RoB 2: provisional
4	**Kessler 2003**	28; non-ischaemic ulcers	Area fell 42% vs 22% at day 15; no difference at day 30	RoB 2: some concerns
5	**Duzgun 2008**	100; no sham; odd/even allocation	Amputation proximal to the metatarsophalangeal joint 0% vs 34%	RoB 2: some concerns
6	**Londahl 2010**	94; sham-controlled, 40 sessions	Healed at 1 year 52% vs 29%; major amputations 3 vs 1	RoB 2: some concerns
7	**Fedorko 2016**	107; sham-controlled	Healed 20% vs 22%; major amputation criteria 11/49 vs 13/54	RoB 2: some concerns
8	**Santema 2018** (DAMOCLES)	120; ischaemic ulcers, multicentre	Limb salvage 88% vs 78% (not significant); 35% did not complete	RoB 2: some concerns
9	**Kumar 2020**	60 randomised, 54 analysed; double-blind	Amputation of any level 2/28 vs 15/26	RoB 2: some concerns
10	**Chen 2017**	38; poor candidates for vascular surgery	Closure 25% vs 5.6%; reported P=.001 does not recompute (Fisher about 0.17)	RoB 2: some concerns
11	**Myrthong 2024**	60 inpatients; 3.0 ATA, 24 sessions; no blinding described	Any amputation 4/30 vs 26/30; complete healing not reported	RoB 2: see appraisal
12	**Salama 2019**	30; non-ischaemic ulcers	Complete closure 5/15 vs 0/15	RoB 2: some concerns

POOLED ANALYSES, GUIDELINES AND VENOUS ULCERS

Ref	Study	Scope	Result	Quality
13	**Kranke 2015** (Cochrane)	12 trials, 577 patients	DFU healing at 6 weeks RR 2.35 (1.19-4.62); major amputation RR 0.36 (0.11-1.18), not significant	AMSTAR-2: low
14	**Stoekenbroek 2014**	RCTs only	Some evidence for healing in ischaemic ulcers; no consistent effect on amputation; no pooling	AMSTAR-2: moderate
15	**Zhao 2017**	9 RCTs	Healing RR 2.22 (0.87-5.62); major amputation RR 0.47 (0.17-1.28); neither significant	AMSTAR-2: critically low
16	**Golledge 2019**	9 RCTs, 585 patients	Healing RR 1.95 (1.51-2.52); major amputation RR 0.54 (0.36-0.81); without Duzgun healing is 1.44 (1.11-1.86), still significant, but amputation 0.78 (0.50-1.20) is not	AMSTAR-2: see appraisal
17	**Brouwer 2020**	11 diabetic foot ulcer studies, 729 patients; 4 ischaemic-only studies pooled	Major amputation 10.7% vs 26.0%, NNT 7; 3 of the 4 pooled were randomised	AMSTAR-2: low
18	**Lalieu 2019**	non-ischaemic ulcers	No faster healing or fewer amputations	AMSTAR-2: high risk of bias
19	**Perez-Gonzalez 2025**	17 studies, 7 RCTs	Healing low-certainty, amputation very low; the two largest trials null	AMSTAR-2: see appraisal
20	**UHMS 15th ed, ch 2B**	guideline	Suggests HBO2 for Wagner 3+ after 30 days or after debridement; against Wagner 2 or lower; venous: insufficient evidence	AGREE II: see appraisal
21	**SVS 2016** (Hingorani)	vascular surgery guideline	Suggests HBO2 for adequately perfused diabetic feet that fail 4-6 weeks of standard care	AGREE II: see appraisal
22	**IWGDF 2023**	guideline	Consider as adjunct in neuro-ischaemic or ischaemic ulcers where standard care failed (conditional, low)	AGREE II: 6 of 7
23	**Bai 2023**	11 studies, venous ulcers	Smaller area, faster healing, less pain mainly with venous surgery; complete healing not shown	AMSTAR-2: critically low
24	**Keohane 2023**	venous ulcers	No benefit for complete healing; ulcers smaller	AMSTAR-2: critically low
25	**Thistlethwaite 2018**	venous ulcers; placebo-controlled	Healing at 12 weeks 40% placebo vs 39% HBO2; underpowered	RoB 2: low
26	**Elsharnoby 2022**	resistant venous ulcers	Added to vein treatment, healing at 12 months 83% vs 54%; none at 3 months; non-randomised	ROBINS-I: serious
27	**Ontario HTA 2017**	economic model	Cost -$3,700 per patient and 0.02 QALY gain; 45-50% chance of being cost-effective	AMSTAR-2: critically low

WHY THE EVIDENCE IS WEAK

- **Heterogeneity:** trials differ in ischaemia, Wagner grade, dose (4 to 40 sessions) and endpoint, and the amputation signal comes from trials without sham [5, 1, 2].
- **Fragility:** the pooled amputation benefit disappears without one trial [16]; the two largest trials are null [7, 8].
- **Adherence:** only 57% of Londahl's patients completed 40 sessions, and 35% of DAMOCLES' treated arm did not finish [6, 8].

GAPS IN THE EVIDENCE

- No adequately powered trial in ulcers selected by in-chamber skin oxygen; Cochrane found no trial in arterial or pressure ulcers [13].

MECHANISM

- **Tissue oxygen:** chronic wound tissue is hypoxic; in-chamber skin oxygen above 200 mmHg predicts response, UHMS considers it reasonable to measure in-chamber skin oxygen, especially when amputation is the only alternative [20].

Evidence labels, OCEBM level and GRADE are defined on the reference sheet. Evidence base held for this indication: 421 appraised records (10 randomised trials; 15 systematic reviews; 79 non-randomised studies; 134 case reports and series; 99 narrative reviews; 40 animal and laboratory). Shown: the highest-certainty studies. Full references, PMIDs and DOIs: https://www.hbo.co.za/cards/refs/complex-wounds.html

Compromised grafts and flaps

Hyperbaric oxygen (HBO2) for threatened skin grafts and flaps: evidence overview

SA ICD-10: T86.8, T87.0, T87.1
UHMS accepted indication · NRPL 2006 recognised (SA §4.8j) · no PMB code

Evidence developing **Small randomised trials lean towards benefit for graft take and flap survival; certainty is low and benefit in threatened tissue is unproven**

Randomised evidence is small, mostly open and low certainty, and leans towards benefit. Split-skin graft take was higher with HBO2 in two small trials (complete take 64% vs 17% in 48 patients, after excluding two failed treated grafts [2]; day-7 uptake 91.7% vs 83.1% in 64 patients [3]), and four small flap trials pooled to OR 2.84 (1.55-5.22) [5]; Cochrane found 4 trials (229 patients), not pooled, all at unclear or high risk of bias, and called the evidence insufficient for routine use [6]. Prophylactic HBO2 in free flaps (10 patients, no failures among the 8 analysed) and hair transplantation (34, early shedding and folliculitis reduced but no difference in final follicle survival) did not improve final survival [1, 4]. A 13-trial meta-analysis reported OR 8.6 but is rated critically low [7]; others found no significant effect on complications [8, 9]. Small confounded cohorts point different ways: in breast surgery nipple necrosis healed faster with HBO2 in a matched cohort [12], not significantly in a small one [10]; skin-flap ischaemia was not prevented [11]; complications were similar [13]; in hypospadias and fingertip repairs differences favoured HBO2 but were mostly not significant [15, 16, 14]. Rat experiments are mostly positive [18, 19, 22, 21]. Use rests on rationale, small trials and case series; UHMS limits it to already compromised flaps and grafts [23].

OCEBM 1 (Carter 2026 systematic review, 13 RCTs) **GRADE** Low to very low (our assessment: flap and graft survival)
Published ECHM Type 2, Level C · SAUHMA no protocol · UHMS Class IB

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** only grafts or flaps that are already compromised (failing perfusion, venous congestion, irradiated bed); routine use in uncomplicated surgery did not improve final graft or follicle survival [1, 4, 23]. Correct mechanical causes first [24]; irradiated head and neck flaps: success 18/23 with pre- and post-operative HBO2, 5/19 post-operative only, 0/6 none (abstract) [25].
- **When:** as soon as compromise appears: HBO2 within 24 hours of surgery, 20 of 27 compromised flaps took [17]; breast cohort: on diagnosis, 2-5 days after surgery [12].
- **Dose:** 2.0-2.5 ATA, 90-120 min, twice daily then daily, reviewed at about 20 sessions [23]. Used: 2.0 ATA 60 min daily for 7 days [4]; 2.4 ATA 90 min, 2-4 sessions [12]; 2.0 ATA, 20 then 10 sessions [15]; 2.8 ATA 45 min then 2.0 ATA [14].
- **Monitor:** skin oxygen below 40 mmHg is the usual trigger to continue [24]; daily once the flap is stable; if it fails, daily HBO2 may continue to prepare the bed for salvage [23].

Synthesised from the studies below; no trial has tested this protocol. Correct mechanical causes of compromise first.

RANDOMISED TRIALS AND POOLED ANALYSES

Ref	Study	n / scope	Result	Quality
1	**Vishwanath 2011** RCT	10 (5 vs 5), free-flap surgery	Prophylactic HBO2 after free-flap surgery: no flap failure among the 8 analysed, so uninformative	RoB 2: high
2	**Perrins 1967** RCT	48, split-skin grafts in burns-unit patients; 2 ATA, 120 min, about 7 sessions	Complete take 64% (of 22 analysed) vs 17% (4/24); Cochrane intention-to-treat 14/24 vs 4/24, RR 3.50 (1.35-9.11); randomisation not described, unblinded	RoB 2: some concerns
3	**Uniyal 2025** RCT	64, post-traumatic split-thickness grafts; 1.5-2 ATA, 90 min daily	Graft uptake at day 7 91.7% vs 83.1% (P=0.026); donor site healed in 15.2 vs 18.0 days; no sham; uptake assessed to day 7	RoB 2: some concerns
4	**Fan 2021** RCT	34, hair transplant; HBO2 2.0 ATA 60 min daily x7	Early shedding 28% vs 69%; survival at 9 months 97% vs 94%, no difference	RoB 2: see appraisal
5	**Carter 2026**	24 studies (13 RCTs, 1,018 patients); 4 RCTs of flap survival pooled	Pooled OR 2.84 (1.55-5.22); two of the four trials individually not significant; its own GRADE very low to moderate; funded by UHMS	AMSTAR-2: see appraisal
6	**Eskes 2013** (Cochrane)	4 RCTs, 229 patients, not pooled (Perrins, Bouachour, Xie, Vishwanath)	All at unclear or high risk of bias; evidence insufficient for routine use	AMSTAR-2: see appraisal
7	**He 2026**	13 RCTs, 1,226 patients, searched Chinese databases	Skin-flap survival much better with HBO2, OR 8.6	AMSTAR-2: critically low
8	**Molina-Vega 2026**	18 plastic-surgery studies, 7 on flaps or grafts	Complications OR 0.48 (0.09-2.66), I2 82%; not flap survival	AMSTAR-2: low
9	**Machado 2026** (abstract)	7 non-randomised breast-reconstruction studies	No significant reduction in haematoma, skin death, reoperation	AMSTAR-2: cannot be rated

COMPARATIVE COHORTS (NON-RANDOMISED)

Ref	Study	n	Result	Quality
10	**Shuck 2017**	13, nipple ischaemia	Healing 36 vs 65 days (8 HBO2 vs 5), not significant	ROBINS-I: serious
11	**Sosin 2018** (abstract)	99 breasts	Skin-flap ischaemia progressed more (75% vs 15%, 12 treated); nipple similar (25% vs 18%)	ROBINS-I: serious
12	**Yi 2026**	213, matched 57 per arm	Nipple necrosis healed in 36 vs 45 days; topical oxygen (distributor-funded) 30	ROBINS-I: serious
13	**Meier 2021**	45 (15 HBO2)	HBO2 group had worse radiation damage at baseline and no more complications	ROBINS-I: serious
14	**Lee 2020**	55 fingertips	Graft survival 57% vs 47% (p=0.47); guillotine injuries 10/10 vs 15/24 (unadjusted subgroup; crush 1/8 vs 1/10); healing 3 vs 4 weeks; historical controls	ROBINS-I: serious
15	**Neheman 2020**	21 boys, hypospadias	Good graft take 7/7 with HBO2 vs 8/14 (our Fisher p=0.061); parents chose HBO2	ROBINS-I: serious
16	**Alvarez-Vega 2026**	47, redo hypospadias	Complications 2/31 with HBO2 vs 4/16 with nitroglycerin (p=0.179); allocated by insurance	ROBINS-I: serious

UNCONTROLLED SERIES

Ref	Series	n	Outcome
17	**Eltorai 1981**	27 compromised of 521 flaps	20 took (completely or slight necrosis), 6 partly, 1 failed; no comparator

ANIMAL EXPERIMENTS (RATS, SKIN FLAPS)

Ref	Study	Model	Result
18	**Tan 1984**	35 rats, island flaps	Survival 60-64% of area with HBO2 or hyperbaric air vs 35%; 8% oxygen did nothing
19	**Kaelin 1990**	rats, free and island flaps, 2 ATA x14	Stored free flaps 0-20% to 40-67%; island-flap viable area 35% to 53-66%
20	**Stevens 1996**	133 rats, secondary ischaemia	Tolerated ischaemia rose from about 6 to 10 h; normobaric oxygen did nothing
21	**Gampper 2002**	32 rats, two ischaemic insults	All treated flaps survived at least in part (6 of 23 fully); all 9 untreated died

WHY THE EVIDENCE IS WEAK

- **Selection:** in breast cohorts selection bias was suspected [11] and the HBO2 group had more radiation damage [13]; hypospadias allocation followed parental choice (higher-risk boys chose HBO2) [15] or insurance [16].
- **Surrogates:** the fingertip gain rests on an unadjusted subgroup and historical controls [14]; hair-transplant HBO2 reduced shedding, not survival [4].
- **Randomised trials:** all small, mostly open-label, at unclear or high risk of bias [6]; the OR 8.6 meta-analysis is rated critically low [7].

GAPS IN THE EVIDENCE

- No adequately powered randomised trial in a compromised flap or graft; no dose or timing study.

MECHANISM

- **Rats:** oxygen beneath flaps, grafts and burns was 30-50% of normal skin and rose at pressure [26]; flap survival improved with HBO2 but not with 8% oxygen at pressure or normobaric oxygen [18, 20].

Evidence labels, OCEBM level and GRADE are defined on the reference sheet. Evidence base held for this indication: 200 appraised records (2 randomised trials; 14 systematic reviews; 13 non-randomised studies; 89 case reports and series; 13 narrative reviews; 52 animal and laboratory). Shown: the highest-certainty studies. Full references, PMIDs and DOIs: https://www.hbo.co.za/cards/refs/compromised-grafts-flaps.html

Decompression sickness

Hyperbaric oxygen (HBO2) recompression: evidence overview

SA ICD-10: T70.3, T70.8, T70.9
UHMS accepted indication · NRPL 2006 recognised (SA §4.8b) · PMB DTP 908S

Accepted standard of care **Benefit of recompression is unproven by controlled data, but it is the accepted treatment and a trial is not ethical**

No randomised trial of recompression against none exists, and Cochrane found none [16]. The only randomised trials test an adjunct or a table: tenoxicam cut the number of recompressions without improving recovery [2], and a shorter monoplace table needed fewer treatments in mild cases [1]. Uncontrolled series report most divers recovering, for example 21 of 63 with spinal cord DCS (33%) incompletely recovered at one month despite recompression [4], but nothing compares them with untreated divers. Evidence on delay conflicts: three cohorts found small or no effect of a shorter delay on recovery [4–6], while a review reports more incomplete recovery in serious DCS after 6 hours [18]. UHMS rates it Class I, level of evidence C [19], and ECHM recommends it (Type 1, Level C) [20].

OCEBM 4 (case series and cohorts) **GRADE** Not rated (no controlled data) **Published** ECHM Type 1, Level C · SAUHMA Level C · UHMS Class I, level C

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **First aid:** highest available oxygen fraction, lying flat, isotonic non-glucose fluids and an NSAID [19, 23]. Oxygen given first was linked to more complete relief after the first recompression (67% vs 58%, confounded by severity) [7].
- **Who:** HBO2 for all DCS where feasible; diagnosis is clinical and imaging should not decide treatment; mild cases stable for 24 hours or more with a normal neurological examination may be managed without recompression when access is hazardous [19]. Late presenters are still treated [6].
- **First treatment:** oxygen at 2.8 ATA, US Navy Table 6; Table 5 only for asymptomatic or omitted-decompression cases, or pain-only DCS completely relieved within 10 minutes at 2.8 ATA [24]. Tables peaking below 2.8 ATA are not recommended, and no gain is shown above 2.82 ATA or with heliox [19]. For mild DCS a shorter monoplace table needed fewer treatments in one small trial [1].
- **Repeat:** while improving stepwise; stop at full resolution or no gain over two sessions, usually 1-2, review after 10 [19]. Monoplace: 94% of 118 Table 6 schedules were completed with air breaks, though less often than in multiplace chambers [14]; no oxygen seizure in 331 monoplace sessions [15].

UHMS, SAUHMA and the guidelines below; no trial has tested this whole protocol. Do not delay referral for imaging.

RANDOMISED TRIALS (ADJUNCT OR TABLE COMPARISONS; NONE OF RECOMPRESSION ITSELF)

Ref	Study	n / design	Result	Quality
1	**Banham 2022**	41 mild DCS, single-blind, monoplace	Short table vs modified Table 6: median treatments 1 vs 2 (P=0.01); resolved after first treatment 17/20 vs 8/21 (P=0.003); final asymptomatic 19/20 vs 20/21	RoB 2: some concerns
2	**Bennett 2003**	180 DCI, all recompressed, double-blind	Tenoxicam vs placebo: residual symptoms at discharge 37% vs 30% (P=0.41); median recompressions 2 vs 3 (P=0.01)	RoB 2: some concerns
3	**Drewry 1994** (interim abstract)	88 entered, 56 analysed	Oxygen-helium vs oxygen: not durably recovered after first treatment 9 of 25 vs 20 of 31	RoB 2: some concerns

HUMAN OUTCOME STUDIES (OBSERVATIONAL)

Ref	Study	n / design	Result	Quality
4	**Gempp 2010**	63 spinal cord DCS, all recompressed	21 (33%) incomplete at 1 month; time to treatment did not predict outcome (P=.15); shortest delay 2 h, median 3 h	ROBINS-I: moderate
5	**Blatteau 2011**	59 military neurological DCS	Within 6 hours recovery not dramatically better with shorter delay; adjusted OR per minute 1.01 (1.00-1.02), P=0.03, judged small	ROBINS-I: moderate
6	**Sokolowski 2022**	546 DCI, Finland	Delay 24 h (recovered) vs 28 h (residual), not significant; similar outcomes over and under 48 hours; shorter delay, fewer treatments (P=0.002)	ROBINS-I: high
7	**Longphre 2007**	2,231 recompressed divers	First-aid oxygen: complete relief after first recompression 67% vs 58%; within 4 hours repeat treatment 33% vs 50%	ROBINS-I: serious
8	**Sayer 2009**	536 and 300 Scottish divers, 150 shared	Complete response 55% after unmodified Royal Navy 62 or US Navy 6 vs 15% after shorter or shallower tables (n=33), unadjusted	ROBINS-I: serious
9	**Simonnet 2023**	102 spinal cord DCS	Fewer sequelae on 2.8 ATA tables than 4 ATA tables; table not randomly chosen	ROBINS-I: serious
10	**Bond 1990** (abstract)	327 sport divers, DCS or AGE	Enhanced tables 54 of 113 successes vs regular 135 of 214; regular tables better after adjustment, OR 0.47 (0.28-0.78)	ROBINS-I: serious
11	**Dunford 2001**	302 delayed Miskito divers	Failing at least one neurological test 69.2% before recompression vs 35.1% after; no comparison group	JBI: 7 of 10

ANIMAL EXPERIMENT, ADJUNCT AND DELIVERY

Ref	Study	n / design	Result
12	**Smith 1994** (abstract)	pigs with CNS DCS	Nerve injury 78% untreated vs 33% and 22% after recompression at 10 and 30 minutes
13	**Weenink 2014**	35 patients, historical controls	Lidocaine added to HBO2 for neurological DCI; retrospective, so lidocaine remains unproven
14	**Weaver 2006**	90 patients, 118 monoplace Table 6	94% of schedules completed; 7 not completed (4 oxygen toxicity, 3 claustrophobia); no outcomes collected
15	**Bonnington 2021**	1,000 Table 6 treatments	4 oxygen seizures, all in multiplace chambers, none in monoplace

REVIEWS, CONSENSUS AND GUIDANCE

Ref	Source	Scope	Position	Quality
16	**Bennett 2012** (Cochrane)	DCI	Recompression is standard care; no randomised trial of it; two trials (268 patients): tenoxicam, and heliox vs oxygen	AMSTAR-2: see appraisal
17	**Vann 2011** (Lancet)	DCI overview	Recompression as soon as feasible; narrative seminar, not a systematic review	narrative review
18	**Mitchell 2024**	comprehensive overview	Incomplete recovery in serious DCS about 40% vs 60% beyond 6 hours	narrative review
19	**UHMS 15th ed, ch 7**	indications manual	Class I, level C; first treatment 2.82 ATA; review after 10	AGREE II: 4 of 7
20	**ECHM 2016** (Mathieu 2017)	consensus conference	DCI recommended (Type 1, Level C)	AGREE II: 4 of 7
21	**GTUeM 2008** (Muller)	German consensus	Table 6 at 280 kPa first; no in-water recompression	consensus
22	**Juttner 2023**	S2k guideline	HBO2 at 280 kPa for severe injury and unresolved mild symptoms	AGREE II: 5 of 7
23	**Mitchell 2018**	pre-hospital consensus	Oxygen, fluids, transport; defines mild disease	AGREE II: see appraisal

WHY THE EVIDENCE IS WEAK

- **No controlled trial:** recompression has never been compared with none [16, 19].
- **Confounding by severity:** the sickest divers reach a chamber fastest, so delay studies may be biased against finding a benefit of speed; in the Finnish cohort severe cases had shorter delays [6].
- **Surrogate and uncontrolled data:** most series report recovery after treatment with no untreated group [11, 4], and two key comparisons were checked against abstracts only [10, 3].

GAPS IN THE EVIDENCE

- No registry comparison of treated and untreated divers, no randomised comparison of first-treatment tables in serious DCS, and no trial of heliox beyond an interim abstract [3].

MECHANISM

- **Bubble and tissue:** pressure shrinks the inert-gas bubble (Boyle's law: about 36% of its volume at 2.8 ATA, calculated) and oxygen promotes inert-gas washout and tissue oxygenation [17, 19].

Evidence labels, OCEBM level and GRADE are defined on the reference sheet. Evidence base held for this indication: 664 appraised records (7 randomised trials; 12 systematic reviews; 76 non-randomised studies; 356 case reports and series; 50 narrative reviews; 75 animal and laboratory). Shown: the highest-certainty studies. Full references, PMIDs and DOIs: https://www.hbo.co.za/cards/refs/decompression-sickness.html

Gas gangrene (clostridial myonecrosis)

Hyperbaric oxygen (HBO2) added to surgery and antibiotics: evidence overview

SA ICD-10: A48.0 (gas gangrene); B96.7 secondary code only
UHMS accepted indication · PMB DTP 277S names hyperbaric oxygen in its treatment component

Clinical consensus **Benefit of adding HBO2 to surgery and antibiotics is unproven**

No randomised trial of HBO2 against no HBO2 exists: the Cochrane review found two small trials (90 patients), neither comparing HBO2 with none, GRADE very low [1]. The only human comparisons are small historical series: the authors of one claimed a significant fall in deaths without a test (5/9 vs 4/15; Fisher exact p=0.21 on recalculation) [2], and the other found no clear advantage (50% vs 38%) [3]. Animal studies conflict: HBO2 improved healing and morbidity in rats, and deaths in one of two rat models [20, 21]; it helped mice given clostridia with Adrenalin but not with calcium chloride [19]; and alone it did not improve survival in two further mouse models [22, 23]. Uncontrolled series report mortality between 5% and 38% with HBO2 [5–16]. Surgery and antibiotics are the established backbone of treatment; the contribution of HBO2 cannot be separated from them.

OCEBM 4 (historically controlled series) **GRADE** Very low (our assessment: mortality) **Published** ECHM Type 1, Level C · SAUHMA Level C · UHMS no class stated

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Order:** debridement and antibiotics alongside HBO2, not instead of it. In rats HBO2 helped only when added to very early debridement (45 min); alone it saved no rat (12 of 12 died) and it added nothing when debridement was delayed 75 min or more [20]. Brummelkamp's 1963 authors operated before HBO2 in only 5 of 26 (local incision; 6 more had failed surgery elsewhere) and never in 12 [5].
- **Timing:** start as early as possible. Rabbits were protected when oxygen began within 2 h, not at 6 h [17]; at once gave limited protection, at 5 h none [18]. A longer estimated diagnosis-to-HBO2 interval went with death in one series, confounded by severity [12].
- **Regimens used:** 2.5 ATA for 90 min about every 8 h for the first 24 h, then twice daily [8]; 2.8 ATA twice daily while gas was visible on X-ray, then 2.0 ATA daily [16]; about 3 ATA in the earliest series [5, 6]. SAUHMA 2023 gives 3.0 ATA for 90 min, q8h for 24 h then q12h for 48 h [24].
- **Antibiotics:** clindamycin or metronidazole beat penicillin alone in mice [22, 23]; HBO2 added nothing to any antibiotic in one model [23], and in another only to penicillin or metronidazole at high inocula when started early [22].

Synthesised from the studies below; no study has tested this protocol against surgery and antibiotics alone. Surgery must not be delayed.

HUMAN COMPARATIVE DATA AND THE COCHRANE REVIEW

Ref	Study	n	Comparison	Result	Quality
1	**Yang 2015** Cochrane	2 RCTs, 90	Two trials: Chinese herbs vs standard care; topical vs systemic HBO2. None compared HBO2 with none	Topical vs systemic HBO2: RR 1.10 (0.25-4.84), 3/21 vs 3/23 on cure only; 19/21 vs 11/23 on cure or improved	GRADE very low
2	**Jackson 1973** historical control	24	Surgery + antibiotics (9) vs the same + HBO2 3 ATA (15); three Toronto hospitals 1960-70	Died 5/9 vs 4/15. Authors claimed a significant fall without a test; Fisher exact p=0.21 (recalculated)	ROBINS-I: serious risk
3	**Nier 1978** historical control	100	1950-67 without HBO2 (34) vs after 1967 with HBO2 in a monoplace (66)	Died 50% vs 38%; authors found no clear advantage (37% vs 38% after removing the 7 fatal criminal-abortion cases, all in the non-HBO2 group)	ROBINS-I: critical risk
4	**Hitchcock 1976** series, bowel origin	33	Among 21 with spreading disease: oxygen therapy vs none	Died 6/16 vs 3/5; too few to tell	Retrospective

UNCONTROLLED HUMAN SERIES (HBO2 GIVEN TO ALL OR MOST)

Ref	Series	n	HBO2 regimen	Outcome
5	**Brummelkamp 1963**	26	3 ATA; surgery deferred or omitted	25 recorded as cured of the infection, 5 died, 1 death clearly from gas gangrene
6	**Trippel 1967**	23	about 3 ATA	17 (74%) survived; all 5 with upper-limb disease kept at least the arm above the elbow
7	**Slack 1969**	40	monoplace chamber	9 of 32 clostridial patients died, none attributed to the clostridial infection; 13 of 40 died in all
8	**Hart 1974**	44	2.5 ATA, monoplace	34 improved, 10 died (23%); deaths commoner with spontaneous infection and age over 30
9	**Caplan 1976**	34	29 had HBO2	11 died (32%), 6 with abdominal-wall disease; authors could not assess the value of HBO2
10	**Darke 1977**	88	2.5 ATA, all patients	83% of 66 clostridial cases improved (44% after one session); none of 12 non-clostridial cases with an isolated organism improved at once (4 improved steadily)
11	**Lamy 1977**	48	monoplace, minimal surgery	33% died: 65% with trunk or abdominal-wall disease vs 7% for limbs; 15 lost a limb
12	**Hart 1983**	139	HBO2	81% survived; estimated diagnosis-to-first-HBO2 interval ('incubation period') 32 h in deaths vs 12 h in survivors (retrospective)
13	**Unsworth 1984**	73	HBO2 + conservative surgery	15 died (22%), 7 directly from the infection, mostly after only 1-2 sessions
14	**Korhonen 1999**	53	2.5 ATA	12 died (22.6%)
15	**Clark 1999** (abstract)	217	HBO2, necrotising infections	22% died: C. septicum 69% (n=13, 62% cancer) vs C. perfringens 17% (n=30, 17% cancer)
16	**Kawashima 2020** (abstract)	65	2.8 ATA twice daily, then 2.0 ATA daily	3 died (4.6%); 33 recovered without amputation; only 7 of the 65 were clostridial, 58 non-clostridial

ANIMAL EXPERIMENTS (CLOSTRIDIAL INFECTION)

Ref	Study	Model	Result
17	**Klopper 1964**	rabbits, hepatic artery tied, 3 ATA	Within 2 h prevented infection about as well as antibiotics; at 6 h did not
18	**Glover 1964**	rabbits, C. perfringens, 2 ATA	At once: infected by day 3 8/15 vs 15/15 (10/15 by the end), deaths not reduced; at 5 h no help, possible harm at high inocula
19	**Hill 1972**	mice, clostridia + Adrenalin, 3 or 4 ATA repeated	Deaths from about 60-80% to under 20%; no benefit in the clostridia + calcium chloride model at 4 ATA
20	**Hirn 1992**	rats, surgery +/- HBO2 2 ATA x5	Deaths 37.5% to 12.5%; full healing 12.5% to 82.5%; all untreated rats died
21	**Hirn 1993**	rats, mixed bacteria	Deaths 20% (surgery + HBO2) vs 35% (surgery alone), not significant; poor outcome 32.5% vs 90% (p<0.001)
22	**Stevens 1993**	mice, C. perfringens myositis	HBO2 alone: no survival benefit at any inoculum; added to penicillin or metronidazole only at the highest inocula (about 10^9-10^10 cfu) and only when started early; clindamycin best
23	**Muhvich 1994**	mice, lethal infection, 303 kPa	HBO2 did not improve survival alone or with penicillin, imipenem, clindamycin or metronidazole

DIAGNOSIS, PROGNOSIS AND LIMITS

- **Prognosis depends on site and organism:** trunk or abdominal wall 65% vs limb 7% mortality [11]; C. septicum 69% vs C. perfringens 17%, with far more cancer in the C. septicum group [15]; spontaneous onset and age over 30 raised mortality [8].
- **Many suspected cases are not proven clostridial:** 54 of 132 patients admitted as gas gangrene had no bacteriological evidence of C. perfringens [25]; only 10 of 409 necrotising infections in a Scandinavian cohort were purely clostridial [26].
- **Limbs are still lost:** 15 of 48 lost a limb despite HBO2 [11]; amputation followed limb injury in 55% of 78 proven cases [25]; half of 20 patients cured needed an amputation at a higher level [27].

GAPS IN THE EVIDENCE

- No randomised or adequately controlled human study of HBO2 against surgery and antibiotics alone; historical comparisons are confounded by era, case mix and surgery [2, 3]. No human dose-finding: 2.0 to 3.0 ATA and differing schedules.

MECHANISM

- **Toxin:** in broth, 3 ATA oxygen stopped Clostridium perfringens making alpha toxin while 2 ATA did not; the bacteria survived and resumed toxin production once oxygen was removed [28].

Intracranial abscess

Hyperbaric oxygen (HBO2) added to drainage and antibiotics: evidence overview

SA ICD-10: G06.0, G06.2, G08
UHMS accepted indication · NRPL 2006 recognised (SA §4.8m)

Clinical consensus **Benefit of adding HBO2 to drainage and antibiotics is unproven**

There is no randomised trial. Two retrospective comparisons (40 and 55 patients) favour HBO2 on some endpoints, but their headline results do not survive scrutiny: in the 40-patient cohort the reoperation gap (10% vs 45%) counted reoperations over unequal windows and was 7/20 vs 9/20 (p=0.75) counted from first surgery, and the HBO2 group had better baseline consciousness [1]; in the 55-patient cohort residual abscess at 6 months favoured HBO2 (20/25 vs 14/30 without residual abscess) but the 12-month difference was not significant [2]. Uncontrolled HBO2 series report 0-1 deaths in 5-21 patients [6–10], but a meta-analysis of 123 series gives about 10% mortality since 2000 and 3% in stereotactic series [14]. Drainage and culture-directed antibiotics are the established treatment; the contribution of HBO2 cannot be separated from them.

OCEBM 3 (non-randomised cohorts) **GRADE** Very low (our assessment: functional outcome) **Published** ECHM Type 1, Level C · SAUHMA no protocol · UHMS no class stated

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** as an adjunct, considered for multiple or deep abscesses, a compromised host (especially fungal infection), poor surgical risk, or failure or deterioration despite drainage and antibiotics [17, 10]; the UHMS chapter also lists a low Glasgow Coma Score [18]. No study has tested whether this selection improves outcome (the card's own appraisal).
- **Pressure and time:** 2.0-2.8 ATA, 60-90 min, once or twice daily (twice daily early or when life-threatening) [18]. In the series: 2.5 ATA, 60-120 min, 4-27 sessions [6]; 2.5 ATA, 60 min twice daily for 5 days then daily, 35 sessions in all [8]; 2.2 ATA, 26-45 sessions in children [9].
- **Course:** individualised to response and repeat MRI or CT; the UHMS chapter suggests review after about 20 treatments and more than 40 sessions where skull osteomyelitis is present [18].
- **Order:** every series gave HBO2 with surgical drainage or aspiration and antibiotics; none supports delaying surgery or using HBO2 alone.

Synthesised from the studies below; no trial has tested this protocol. Drainage and culture-directed antibiotics come first.

COMPARATIVE COHORTS AND FUNGAL COMPARISONS (ALL NON-RANDOMISED)

Ref	Study	n	Comparison	Result	Quality
1	**Bartek 2016** Karolinska	40	HBO2 (20) vs none (20); allocation by calendar time; blinded Glasgow Outcome Score	Reoperation 10% vs 45% (p=0.03) but windows unequal: 7/20 vs 9/20 from first surgery (p=0.75, recalculated); recurrence 14% vs 58% conditioned on outcome; the Glasgow Outcome Score gap lost significance after excluding 3 sicker controls (p=0.08) while return to pre-morbid state persisted (p=0.05)	ROBINS-I: serious
2	**Brunner 2025** Graz	55	HBO2 (25) vs none (30); all had surgery	No residual abscess at 6 months 20/25 vs 14/30, counting 5 and 10 missing scans as not resolved (20/20 vs 14/20 among recorded; p=0.009 printed; Fisher 0.014); at 12 months 20/25 vs 17/30 (printed p=0.477 tests volume categories; binary Fisher 0.087; 11 of 30 control scans missing); mRS 0 at 12 months 15/25 vs 9/30	ROBINS-I: serious
3	**Ferguson 1988** rhinocerebral mucormycosis	13 episodes	HBO2 2 ATA vs earlier episodes treated without	Died 2/6 with HBO2 vs 4/7 without (p=0.59, recalculated); historical controls	ROBINS-I: critical
4	**Gamba 1986** craniofacial mucormycosis	10	HBO2 2 atm (5) vs none (5); CT series	Survived 4/5 vs 1/5; the authors said no statistical conclusion could be drawn	JBI case series
5	**Roden 2005** zygomycosis review	929 cases	Published cases; 44 given HBO2	28 of 44 (64%) given HBO2 survived; overall mortality 54%; HBO2 was never adjusted for	AMSTAR-2: critically low

UNCONTROLLED SERIES WITH HBO2 (GIVEN TO ALL)

Ref	Series	n	HBO2 regimen	Outcome
6	**Lampl 2000**	20	2.5 ATA, 60-120 min, 4-27 sessions	All survived; about 14 recovered fully
7	**Lampl 2006**	21	2.5 ATA, 60-90 min, 4-27 sessions	No deaths, 16 recovered fully (the author's own series, reported as Lampl 2003); the authors compare with about 19% mortality in older published series
8	**Kutlay 2005**	13	2.5 ATA, 35 sessions, with stereotactic aspiration	All healed, no deaths; 9 (69%) no lasting deficit; 2 abscesses re-aspirated early
9	**Kurschel 2006**	5 children	2.2 ATA, 26-45 sessions	All improved, none died, no recurrence over a mean 21 months; all 5 had drainage surgery, 4 also sinus or source surgery
10	**Mathieu 1999** (abstract)	8, failing standard care	mean 23.5 sessions	7 of 8 survived
11	**Lackner 2009**	4 children, leukaemia	HBO2 + antibiotics + liposomal amphotericin	All survived; 2 complete resolution, 2 residual lesions
12	**Keogh 1973**	1 child, clostridial abscess	20 h over 5 days	No change on HBO2; an abscess formed anyway; recovered almost fully after re-operation
13	**Woodard 2023** (abstract)	1	5 sessions after a second operation	Abscess shrank from 3.4 x 3.9 cm to 1.4 x 0.6 cm in a month; surgery and antibiotics were also given

BENCHMARKS: BRAIN ABSCESS OUTCOMES IN GENERAL SERIES, AND ANIMAL WORK

Ref	Study	n / model	Outcome
14	**Brouwer 2014** meta-analysis	123 series, 9,699 patients	Mortality fell from 40% to about 10% across decades; 20% overall (1,823/9,011); 3% in stereotactic series
15	**Tekkok 1992**	130 children, no HBO2	Surgical mortality 15.5%, 30% before CT (20 cases) and none in the last 3 years (21 cases) as aspiration became the main technique; the fall was not significant and mortality did not differ by technique
16	**Bilic 2012**	rats, staphylococcal abscess	HBO2 alone or with antibiotic increased new vessels in the abscess wall, mainly at early time points

LIMITS OF THE EVIDENCE

- **Selection:** in Bartek, HBO2 was given by calendar-time policy, more of the HBO2 group had normal consciousness (Glasgow Coma Score 15: 75% vs 50%), and all three patients with a score under 13 were controls [1].
- **Counting:** Brunner's printed 12-month p (0.477) tests volume categories; the binary Fisher is 0.087 [2]; quote the counts.
- **Case mix:** 0-1 deaths in 5-21 patients per HBO2 series cannot be read against a historical 19%: Lampl gives 13% for recent series and 19% overall [7] and a meta-analysis gives about 10% since 2000 and 3% in stereotactic series [14].

GAPS IN THE EVIDENCE

- No randomised trial; no study of dose, timing, session number, or which abscesses benefit.

MECHANISM

- **Proposed:** UHMS chapter attributes the effect to inhibition of anaerobes, less perifocal oedema, better neutrophil killing and better antibiotic transport in the hypoxic abscess [18]; direct human evidence is not available.
- **Rats:** more new vessels in a staphylococcal abscess at some early time points [16].

Delayed radiation injury of soft tissue

Hyperbaric oxygen (HBO2) for late radiation cystitis, proctitis and other soft-tissue injury: evidence overview

SA ICD-10: N30.4, K62.7, K52.0, L59.8, L58.1, J70.1 (also SAUHMA-listed L59.9, J37.0, K13.5)
UHMS accepted indication · NRPL 2006 recognised (SA §4.8i) · PMB only for radiation colitis with life-threatening bleeding or dehydration (K52.0, DTP 901F)

Evidence developing **Benefit differs by site: probable for radiation cystitis, unproven for proctitis and head and neck, doubtful for nerve injury and arm lymphoedema**

Cystitis: the one controlled trial of HBO2 against standard care improved the urinary symptom score by 10.1 points more (95% CI 2.2-18.1) [1], but it was unmasked and benefit beyond 6 months rests on uncontrolled follow-up [14]. Proctitis: one trial favoured HBO2 (responders 89% vs 63%) [4] and a later sham-controlled trial in chronic bowel dysfunction (84 patients) found no benefit [5]. Head and neck and breast: small positive trials [6, 7] against a pragmatic breast trial that was null for pain, with less fibrosis [8]. Brachial plexus injury [9] and arm lymphoedema [10] were null in randomised trials. Pooled across sites the Cochrane review found low-certainty benefit (resolution RR 1.39, 1.02-1.89) with a high-certainty increase in visual change and, against uncompressed controls, ear barotrauma [11].

OCEBM 1 (Lin 2023 Cochrane, 18 RCTs) **GRADE** Low (published: resolution, Cochrane 2023)
Published ECHM Type 1, Level B (cystitis, proctitis); Type 2, Level C (other) · SAUHMA Level B · UHMS no class stated

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** injury typically appears 6 months or more after radiotherapy [19]; SAUHMA requires failed conservative or surgical management and biopsy of non-healing tissue when indicated [20]. Clarke required the diagnosis for at least 3 months and refractoriness [4]; RICH-ART required a urologist-confirmed diagnosis [1].
- **Course:** daily, 2.0-2.5 ATA, 2.4 ATA preferred (at 2.0 ATA extend to 120 minutes); typically 40-60 treatments, review after 60; cystitis may need more than 60 or a second course, with cystoscopy at 30-40 to guide [19]. Trials gave 30-40 sessions [1] and 40 [5].
- **SAUHMA 2023:** 2.0-2.5 ATA for 90 minutes, 20 sessions then reassess, add 10 if improving but significant, threshold 20-40 and maximum 60 [20]. This card follows UHMS where the two differ.
- **Safety:** expect temporary visual change and ear barotrauma [11]. A bladder ruptured when alum was pumped in by mistake on the ward, and the authors retracted their in-chamber pump irrigation: use gravity irrigation [23].

UHMS 15th ed governs where it differs from SAUHMA; no trial has tested these exact courses. HBO2 is added to standard urological, bowel or surgical care.

RANDOMISED TRIALS

Ref	Study	n / design	Result	Quality
1	**Oscarsson 2019 (RICH-ART)**	79 analysed, cystitis, HBO2 vs standard care, unmasked	EPIC urinary score 10.1 points more with HBO2 (2.2-18.1), P=0.013; 7 of 45 controls withdrew after randomisation vs 1 of 42	RoB 2: some concerns
2	**Shao 2011**	36, cystitis, HBO2 vs intravesical hyaluronic acid	No difference in improvement at 6, 12 and 18 months; active comparator, not an untreated control	RoB 2: some concerns
3	**Lewis 2005** (abstract)	26 enrolled, 7 withdrew, cystitis, crossover	Haematuria resolved in 14/16 after HBO2 vs 3/19 before; not a randomised comparison	abstract only
4	**Clarke 2008**	150 randomised, 120 evaluable, proctitis, sham-controlled crossover	Responders 88.9% vs 62.5% (P=0.0009); 20% excluded after randomisation; sham arm later crossed over	RoB 2: some concerns
5	**Glover 2016 (HOT2)**	84, chronic bowel dysfunction, sham-controlled	IBDQ bowel score change P=0.50 and bleeding P=0.092; few had transfusion-dependent bleeding	RoB 2: low
6	**Teguh 2009**	19, head and neck, HBO2 early after radiotherapy	Better late swallowing (P=0.011), dry mouth (P=0.009) and mouth pain; prophylactic HBO2 after radiotherapy, patient-reported, stopped early	RoB 2: high
7	**Otón-Sánchez 2013** (abstract)	37 randomised, 26 completers, cervical fibrosis, HBO2 plus drugs vs drugs	Fibrosis improved in 10/13 vs 4/13 at 6 months (P=0.047); the 3-month P value does not reproduce	abstract only
8	**Mink 2024 (HONEY)**	189 randomised, breast, 30-40 sessions	Pain 50% vs 62%, OR 0.63 (0.32-1.23); fibrosis 33% vs 51%, OR 0.36, P=0.02 (secondary); 25% took up HBO2	RoB 2: high
9	**Pritchard 2001**	34, brachial plexopathy, sham-controlled	No difference in sensory threshold or nerve conduction to 12 months	RoB 2: low
10	**Gothard 2010**	58, arm lymphoedema after breast radiotherapy	No difference in arm volume at 12 months	RoB 2: some concerns

REVIEWS, COHORTS AND MECHANISM

Ref	Study	Scope	Result	Quality
11	**Lin 2023** (Cochrane)	18 RCTs, 1,071 participants, all sites	Resolution RR 1.39 (1.02-1.89), low certainty; wound dehiscence RR 0.24; visual change RR 4.03, high certainty; ear barotrauma RR 9.08 against uncompressed controls only; no clear effect on 1-year death	AMSTAR-2: low
12	**El Hadji 2025**	17 studies, head and neck	HBO2 may be effective and safe; evidence mainly low quality with inconsistent outcomes	AMSTAR-2: see appraisal
13	**Zumstein 2023**	4 studies, postradiation pelvic pain	Evidence too weak to recommend; pain results mixed: Clarke favoured HBO2 at 6 weeks, HOT2 was null at 12 months, Shao used an active comparator	AMSTAR-2: see appraisal
14	**Oscarsson 2025**	RICH-ART follow-up to 5 years	EPIC +19.1 at 5 years (13.3-24.9), single-group after 6 months; 44% missing at year 5	ROBINS-I: serious
15	**Thomas 2026**	707 users vs matched non-users, Ontario	Fewer emergency visits and procedures after HBO2; users started with higher use; transfusions no different at 3 years	ROBINS-I: serious
16	**Andren 2020**	52 pelvic injury, before and after	LENT-SOMA fell 3.7 points (2.6-4.8); no comparison group	ROBINS-I: serious
17	**Svalestad 2014**	irradiated head and neck skin, with controls	Tissue oxygen rose in the irradiated cheek and stayed raised at 6 months; no change in controls	surrogate outcome

GUIDANCE

Ref	Source	Scope	Position	Quality
18	**ECHM 2016** (Mathieu 2017)	consensus conference	Cystitis and proctitis Type 1, Level B (corrected table); other soft-tissue lesions Type 2, Level C	AGREE II: 4 of 7
19	**UHMS 15th ed, ch 8**	indications manual	Recommends HBO2 at all sites; 2.4 ATA, 40-60 treatments; no AHA class given	AGREE II: 3 of 7
20	**SAUHMA 2023**	protocols	Pelvic and other soft-tissue radionecrosis, Level B	protocol
21	**ASCRS 2018** (Paquette 2019)	colorectal guideline	Strong recommendation, moderate-quality evidence (1B), to reduce bleeding in chronic radiation proctitis	AGREE II: see appraisal
22	**Alberta 2011** (Craighead)	gynaecological guideline	HBO2 effective, particularly head, neck, anus, rectum; consider when conservative care fails; modest evidence	AGREE II: see appraisal

WHY THE EVIDENCE IS WEAK

- **Conflicting trials:** proctitis positive [4] but null for chronic bowel dysfunction [5]; breast pain null with fibrosis better [8].
- **Design limits:** RICH-ART was unmasked with unequal early withdrawal [1]; the head and neck trials are small and open [6, 7]; Cochrane's pooled benefit is sensitive to missing data and includes an active-comparator trial [11, 2].

GAPS IN THE EVIDENCE

- RICH-ART's control was standard care, and the wiki corpus holds no sham-controlled cystitis trial; no randomised evidence for brain or spinal injury; durability beyond 6 months is uncontrolled [14].

MECHANISM

- **Tissue:** irradiated tissue is hypoxic and poorly vascularised, and HBO2 raised tissue oxygen in the irradiated field for 6 months [17]; this is a surrogate outcome. The lymphoedema trial did not measure tissue oxygen and was null [10].

Evidence labels, OCEBM level and GRADE are defined on the reference sheet. Evidence base held for this indication: 151 appraised records (14 randomised trials; 25 systematic reviews; 20 non-randomised studies; 45 case reports and series; 3 narrative reviews; 7 animal and laboratory). Shown: the highest-certainty studies. Full references, PMIDs and DOIs: https://www.hbo.co.za/cards/refs/late-radiation-soft-tissue-injury.html

Necrotising soft-tissue infections

Hyperbaric oxygen (HBO2) added to surgery and antibiotics: evidence overview

SA ICD-10: M72.65, M72.66, M72.67, N49.8, N76.8
UHMS accepted indication · PMB DTP 349J

Clinical consensus **Benefit of adding HBO2 to surgery and antibiotics is unproven**

There is no randomised trial: the Cochrane review found none [1]. The observational data point both ways. Pooled analyses of retrospective cohorts find lower mortality with HBO2 (OR 0.44 [3]; RR 0.52 in 49,152 patients [4]) but rate the evidence low quality, and the large cohorts that favour HBO2 compare patients chosen for treatment, who were less ill [15, 19] and in one cohort may have had to survive long enough to be treated (the authors' suggestion) [15]; adjustment for predicted mortality removed one apparent benefit (p=0.01 to p=0.11) [16]. Small and ICU cohorts did not show a significant mortality difference [9, 13, 17]. Surgery and antibiotics are the established treatment and surgery must not be delayed.

OCEBM 3 (controlled cohorts, meta-analysis) **GRADE** Very low (our assessment: mortality) **Published** ECHM Type 1, Level C · SAUHMA Level C · UHMS no class stated

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Order:** early surgical debridement, antibiotics and intensive care first. HBO2 was given as an addition in every cohort below; none shows that it replaces or justifies delaying them.
- **Timing and sessions:** as early as practicable; no study tested timing. One unit's protocol was three sessions in the first 24 h, two in the second, then daily, but the median first session came 38.8 h after presentation [15]; the Danish register cohort gave a median of three 90-min sessions [18].
- **Pressure:** about 2.5-2.8 ATA, 90 min (2.5 ATA, 90 min [8]; 2.8 ATA [15]; 284 kPa, 90 min [18]). UHMS 2023 gives 2.0-2.5 ATA twice daily until necrosis stops extending, then daily to about 30 treatments, and 2.8-3.0 ATA if clostridial infection is possible or the diagnosis is unclear [25].
- **Selection in the ICU:** ventilated or vasopressor-dependent patients can be treated, but 23 of the 128 treated ICU patients (18%) in one cohort had severe complications [17].

Synthesised from the studies below; no trial has tested this protocol. Surgery (early, repeated debridement) and antibiotics come first.

COCHRANE REVIEW AND POOLED ANALYSES

Ref	Analysis	Scope	Finding	Appraisal
1	**Levett 2015** Cochrane	necrotising fasciitis	No randomised trials found (empty review)	AMSTAR-2: high
2	**Faunø Thrane 2019**	systematic review, narrative	Found little efficacy evidence for HBO2	AMSTAR-2: low
3	**Hedetoft 2021**	observational studies	Mortality OR 0.44 with HBO2; amputation not significantly different; low-quality observational evidence	AMSTAR-2: low
4	**Huang 2023**	observational, 49,152 patients	Lower risk of death with HBO2, RR 0.52	AMSTAR-2: critically low
5	**Raizandha 2022**	Fournier's gangrene, 10 observational studies	About 70% lower odds of death with HBO2, OR 0.29	AMSTAR-2: low
6	**Patel 2026**	Fournier's gangrene, 13 retrospective studies (322 HBO2, 366 controls)	Mortality RR 0.43 (0.21-0.86), pooled from 9 of the 13 studies; unadjusted comparisons with possible selection bias	AMSTAR-2: see appraisal

COMPARATIVE COHORTS (HBO2 VS NO HBO2; ALL NON-RANDOMISED)

Ref	Study	n	Result	Quality
7	**Riseman 1990** (abstract)	29	Mortality 23% vs 66%; debridements 1.2 vs 3.3 per patient	ROBINS-I: cannot be rated
8	**Oberg 1993** (abstract)	60	Mortality 15% vs 66% (HBO2 90 min at 2.5 ATA, average 11.5 treatments; 15 controls)	ROBINS-I: serious risk
9	**Brown 1994**	54, trunk	Mortality 30% vs 42%, not significant; clinician preference	ROBINS-I: serious
10	**Shupak 1995**	37	Mortality 36% with HBO2 vs 25% without; more operations in the HBO2 group	ROBINS-I: serious risk
11	**Mindrup 2005**	42, Fournier	Mortality 27% with HBO2 vs 12.5% without; cost more per day	ROBINS-I: serious risk
12	**George 2009**	78, two centres	Not linked to fewer deaths or hospital days; more debridements with HBO2 (median 3.0 vs 2.0, p=0.03); 8 deaths in all	ROBINS-I: serious risk
13	**Massey 2012**	80	No difference in death or amputation	ROBINS-I: critical risk
14	**Soh 2012**	about 45,900, US database	Lower risk of death with HBO2, OR 0.49; higher cost	ROBINS-I: serious
15	**Devaney 2015**	341, one hospital	Mortality 12% vs 24%; treated were less ill and may have had to survive to be treated	ROBINS-I: serious risk
16	**Rosen 2015**	NSTI cohort	One-month mortality 6.7% vs 27.8% (p=0.01); p=0.11 after adjusting for predicted mortality	ROBINS-I: serious risk
17	**Bouges 2019** (abstract)	172, ICU	HBO2 not linked to lower 90-day mortality (30.8%); 23 of 128 treated had severe complications	ROBINS-I: serious risk
18	**Hedetoft 2023**	671, Danish register	30-day mortality lower with HBO2 after adjustment (266 treated vs 405); treated were clinician-chosen; severity missing in many; death counts inconsistent	ROBINS-I: serious risk
19	**Hyldegaard 2025**	405, Scandinavian	30-day death 7% with HBO2 vs 43% without; the treated were less ill	ROBINS-I: moderate
20	**Toppen 2024**	60,481, US database	Mortality under 2% with HBO2 vs 5.9% without	ROBINS-I: serious

UNCONTROLLED SERIES (HBO2 GIVEN TO ALL PATIENTS)

Ref	Series	n	Outcome
21	**Escobar 1999**	42	11.9% died, against 34% in published reports
22	**Korhonen 1998**	33, perineal	3 died (9%); uncontrolled retrospective series, so not attributable to HBO2 (the authors conclude it is life saving)
23	**Brunet 2000**	81, perineal	25% died; twice-daily HBO2; no patients without oxygen
24	**Elander 2016**	59, cervical	10% died (6 of 59); no concurrent non-HBO2 group (1 of the 6 deaths did not receive HBO2)

WHY THE COHORT RESULTS CANNOT BE TAKEN AT FACE VALUE

- **Selection:** treated patients were less ill [15, 19] and, in one cohort, may have had to survive long enough to be treated (first HBO2 at a median 38.8 h; the authors' suggestion) [15]; unadjusted mortality gaps shrank or vanished after adjustment [16]; the earliest large gaps (23% vs 66%, 15% vs 66%) came from small single-centre comparisons [7, 8].
- **Centre effect:** among 984 Danish patients at two high-volume hospitals, 30-day mortality (OR 0.54) and 90-day mortality (OR 0.61) favoured the HBO2 hospital (859 patients) over one without (125), but the hospitals differ in other ways [26].
- **Harms:** 23 of 128 treated ICU patients had severe complications, associated with norepinephrine and mechanical ventilation [17].
- **Tissue oxygen may matter:** in 52 patients given HBO2 at 300 kPa, mortality was 35% overall, 100% when chamber transcutaneous PO2 stayed below 1,200 mmHg and 18% above 1,800 mmHg [27].

GAPS IN THE EVIDENCE

- No randomised trial, and no trial of HBO2 dose, timing or number of sessions.
- No adjusted analysis can remove selection of the sicker or the healthier patient for the chamber.

MECHANISM

- **Neutrophils:** in three patients with necrotising fasciitis neutrophil adhesion in vitro fell from 77.6% to 41% after the first HBO2 session [28].
- **Cytokines:** in 209 treated patients IL-6 rose slightly after the first session but fell after the second and in group A streptococcal infection; G-CSF fell; no non-HBO2 comparison group [29].

Osteoradionecrosis of the jaw

Hyperbaric oxygen (HBO2) for treatment and prevention: evidence overview

SA ICD-10: K10.8, K10.2, M87.38, K02.8, K04.2, K13.5, L59.8
UHMS accepted indication · NRPL 2006 recognised (SA §4.8i) · no direct PMB code

Evidence developing **Randomised trials conflict, and pooled analyses are low certainty, so benefit is unproven**

For established ORN the only sham-controlled trial found no benefit and stopped early for possible harm: 1-year recovery 19% with HBO2 vs 32% with sham [1]. Two later trials of surgery with or without HBO2 pooled to 70% vs 51% healing, not significant and underpowered [2]. The current Cochrane review found little or no difference in healing (RR 1.26, 0.87-1.82, low certainty), but less ORN pain at 12 months and less wound breakdown after surgery [6]. For prevention before extraction, the first trial favoured HBO2 over penicillin [3] and the HOPON trial found no difference [4]. ECHM recommends it for mandibular ORN and prevention (Type 1, Level B) [19], SAUHMA grades it Level B [21], while the ISOO-MASCC-ASCO guideline calls its use largely unjustified, allowing it with surgery [18].

OCEBM 1 (Lin 2023 Cochrane, 2-3 RCTs per jaw outcome) **GRADE** Low (published: ORN healing, Cochrane 2023)
Published ECHM Type 1, Level B (mandible, prevention after extraction); Type 2, Level C (other bones) · SAUHMA Level B · UHMS no class stated

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** confirmed ORN with referral by a surgical specialty, radiation dose above 30-50 Gy to the area, and cancer-free (or risk and benefit weighed) [21]; guideline use is limited to cancer-free patients [18].
- **Treatment (30/10):** oxygen at 2.0-2.5 ATA for 90 minutes daily (UHMS recommends 2.4 ATA) [21, 20]. Stage I: 30 sessions then examine; 10 more if healing toward mucosal cover; non-responders advance to stage II [21].
- **With surgery:** stage II, remove exposed bone then 10 sessions; stage III, resection and reconstruction then 10, with a possible further 10 after bone grafting; 30-50 sessions in all [21].
- **Prevention (20 + 10):** 20 sessions, the extraction or surgery, then 10, in a field that received more than 30-50 Gy, radiotherapy finished at least 2 months earlier [21]. Routine use is not recommended, and it may be offered to patients at elevated risk [18].

SAUHMA 2023 and UHMS; no trial has tested these exact protocols. HBO2 is an adjunct to surgical and dental care, not a substitute.

RANDOMISED TRIALS

Ref	Study	n / design	Result	Quality
1	**Annane 2004**	68 established ORN, double-blind, sham-controlled	1-year recovery 6/31 (19%) vs 12/37 (32%), RR 0.60 (0.25-1.41); stopped early for possible harm	RoB 2: some concerns
2	**Forner 2022**	two RCTs, 97 randomised, 65 analysed	Surgery plus HBO2 vs surgery alone: healing at 1 year 21/30 (70%) vs 18/35 (51%), not significant; underpowered	RoB 2: high
3	**Marx 1985**	74 irradiated, needing extraction, unblinded	ORN 2/37 (5.4%) with HBO2 vs 11/37 (about 30%) with penicillin, P=0.005	RoB 2: high
4	**Shaw 2019 (HOPON)**	144 randomised, 100 analysed	ORN at 6 months 6.4% vs 5.7%, OR 1.13 (0.14-8.92); closed early, event rate far lower than planned	RoB 2: some concerns
5	**Schoen 2007**	about 13 per arm, implants in irradiated jaw	No significant benefit for implant health or function; implant survival 85.2% with HBO2 vs 93.9% without	RoB 2: some concerns

SYSTEMATIC REVIEWS AND POOLED ANALYSES

Ref	Study	Scope	Result	Quality
6	**Lin 2023** (Cochrane)	18 RCTs, 1,071 participants, late radiation injury	ORN healing or substantial improvement RR 1.26 (0.87-1.82), low certainty; ORN pain at 12 months MD -10.72 (-18.97 to -2.47); wound dehiscence after head and neck surgery RR 0.24 (0.06-0.94)	AMSTAR-2: low
7	**Geckil 2025**	13 studies	Success 69% HBO2 plus surgery, 38% HBO2 alone, 36% surgery alone	AMSTAR-2: critically low
8	**Yin 2021**	RCTs and cohorts, jaw ORN	No significant difference: HBO2 plus antibiotics plus surgery vs surgery plus antibiotics RR 1.16 (0.86-1.58)	AMSTAR-2: low
9	**Quah 2024**	29 studies, prevention at extraction	HBO2 vs antibiotics pooled OR 0.57 (0.10-3.28)	AMSTAR-2: critically low
10	**El-Rabbany 2019** (Cochrane)	4 trials, 342 adults, prevention	Extraction: HBO2 alone vs penicillin RR 0.18; before implants (one trial, 26) HBO2 plus antibiotics vs antibiotics RR 3.00, CI 0.14-65.16; very low certainty	RoB: high

OBSERVATIONAL STUDIES AND MECHANISM

Ref	Study	n / design	Result	Quality
11	**Marx 1983** (protocol)	58 refractory mandibular ORN, no control	Staged protocol at 2.4 ATA, reassessed from 30 dives: all 58 resolved (9, 8 and 41 at stages I, II, III)	JBI: 3 of 10
12	**Jenwitheesuk 2018**	84 ORN, all given HBO2 around surgery	No healing rate and no comparison group reported	ROBINS-I: critical
13	**Rao 2025**	60 jaw ORN, non-randomised	Conservative package with HBO2 healed half; surgery healed 83%; allocation not described, stage mix similar	ROBINS-I: serious
14	**Bertalan 2022** (abstract)	34 with exposed mandible	76% had over half the bone covered after about 34 sessions vs 15% in historical controls	ROBINS-I: critical
15	**Marx 1983** (pathology)	26 ORN, 12 resections cultured	No organisms in deep bone in any specimen; model of hypoxic, hypocellular, hypovascular tissue	moderate
16	**Marx 1990**	35 irradiated rabbits	Vessel density 93 with HBO2 vs 13 with normobaric oxygen and 13 with air	RoB: high
17	**Thorn 1997**	10 ORN patients, 30 sessions	Gingival oxygen tension rose from about 50% to about 86% of healthy values	no untreated group

GUIDANCE AND REVIEWS

Ref	Source	Scope	Position	Quality
18	**ISOO-MASCC-ASCO 2024**	ORN guideline	HBO2 largely unjustified; routine prophylaxis not recommended; with surgery may be used (low, weak)	AGREE II: see appraisal
19	**ECHM 2016** (Mathieu 2017)	consensus conference	Mandibular ORN and extraction prevention Type 1, Level B; other bones, implants Type 2, Level C	AGREE II: 4 of 7
20	**UHMS 15th ed, ch 8**	indications manual	2.4 ATA; reviews trials; no AHA class given	AGREE II: 3 of 7
21	**SAUHMA 2023**	protocols	30/10 for treatment and 20+10 for prevention, Level B	protocol
22	**Shaw 2011**	narrative review	Evidence for HBO2 in established ORN remarkably weak	narrative review
23	**Fritz 2025**	narrative review	Shift away from HBO2 towards drugs and rescue flap	narrative review

WHY THE EVIDENCE IS WEAK

- **Conflicting trials:** sham-controlled treatment trial negative [1], surgery trials favourable but underpowered [2], prevention trials split [3, 4].
- **Design limits:** Marx 1985 was unblinded against penicillin [3], and the Cochrane dehiscence result comes from trials first reported in a textbook chapter [6].

GAPS IN THE EVIDENCE

- No adequately powered sham-controlled trial of HBO2 plus surgery for established ORN; the first treatment trial excluded severe ORN and stopped early [1, 2].

MECHANISM

- **Tissue:** irradiated bone is hypoxic, hypocellular and hypovascular, not infected [15]; HBO2 raised vessel density in irradiated rabbits and tissue oxygen in ORN patients [16, 17].

Chronic refractory osteomyelitis

Hyperbaric oxygen (HBO2) added to debridement and antibiotics: evidence overview

SA ICD-10: M86.47, M86.46, M86.45, M86.49 (also M86.6x)
UHMS accepted indication · NRPL 2006 recognised (SA §4.8h) · PMB DTP 206H (treatment component: incision and drainage)

Clinical consensus **Benefit of adding HBO2 to surgery and antibiotics is unproven**

No randomised trial exists [2, 1]. A systematic review of mostly uncontrolled series reports success in about 73% of patients, only one study having a control group [1]. The few comparisons are small and non-randomised, and mostly show no significant benefit in bone infection [5, 7, 8] or jaw infection [6]; in sternal infection HBO2 patients relapsed less [10] and had shorter ICU stays [11], but allocation followed consent, cover or perceived risk. One hospital's summary from Japan printed P<0.01 for recurrence of 5.8% vs 9.0%, but it recalculates to p=0.12 [9]. In animals HBO2 raised bone oxygen [21] and lowered bacterial counts [22]. UHMS supports it as an adjunct to debridement and antibiotics, never alone, and rates the evidence as mostly case series (29 of 37 reports), with no conclusive randomised trial [23].

OCEBM 4 (Savvidou 2018 review of cohorts and case series) **GRADE** Very low (our assessment: remission)
Published ECHM Type 2, Level C · SAUHMA Level C · UHMS Class IIa with debridement and antibiotics

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** chronic osteomyelitis that has failed adequate debridement and antibiotics [23]; not as sole therapy [23].
- **Dose:** 2.4-2.5 ATA preferred, 20-40 sessions over 4-6 weeks, with review after 30-40 [23]. The European consensus advises at least 11-12 weeks, about 60 sessions, before an effect should be expected [4]; the two overlap, and UHMS governs.
- **Order:** debridement and culture-directed antibiotics alongside HBO2 [23].

UHMS parameters; no trial has tested this protocol. Surgery and antibiotics remain the treatment; HBO2 is the adjunct for disease that has failed them.

REVIEWS AND CONSENSUS

Ref	Study	Scope	Result	Quality
1	**Savvidou 2018**	45 studies, mostly case series	Success 308/419 (73.5%), no relapse reported in the abstract; one study had controls	AMSTAR-2: critically low
2	**Hart 2013** (UHMS review)	34 studies (26 human), none randomised	Supports HBO2 as adjunct: Class IIa with debridement and antibiotics, IIb with antibiotics alone, III as sole therapy; human data mostly case series	AMSTAR-2: critically low
3	**Byun 2021**	16 studies, 58 patients, malignant otitis externa	Cure 91.4%, mortality 8.6%; all received antibiotics; efficacy called unproven	AMSTAR-2: see appraisal
4	**ECHM 2016** (Mathieu)	consensus conference	Suggested (Type 2, Level C); course of 11-12 weeks	AGREE II: 4 of 7

COMPARATIVE STUDIES (NON-RANDOMISED)

Ref	Study	n / design	Result	Quality
5	**Esterhai 1987**	28; 14 with HBO2	No difference in stay, wound repair or recurrence; 13 of 14 controls healed	ROBINS-I: serious
6	**Calhoun 1988**	60 jaw infections; 49 with HBO2	Cure 80% (28/35) with HBO2 vs 5/6 without; no significant difference	ROBINS-I: critical
7	**Fosco 2014**	154 on immunotherapy; 104 chose HBO2	Non-response 52% without vs 41% with HBO2, p=0.17, not significant	ROBINS-I: moderate
8	**Walter 2014**	61 anaerobic bone and joint infections; 17 with HBO2	Remission 8/12 vs 28/35, p=0.35; unadjusted	ROBINS-I: moderate
9	**Kawashima 2003**	689 (header says 668); one hospital's own series, surgery with irrigation vs HBO2	Recurrence 9.0% vs 5.8%; printed P<0.01, recalculated p=0.12	high risk of bias
10	**Barili 2007**	32 sternal infections; 14 had HBO2	Relapse 0% vs 33% (p=0.024); allocated by consent	ROBINS-I: serious
11	**Yu 2011**	12 sternal infections; 6 with HBO2	ICU stay 8.7 vs 48.8 days; deaths 0 vs 3, printed p=0.046 recalculates to 0.18	ROBINS-I: serious

UNCONTROLLED SERIES AND EXPERIMENTS

Ref	Study	n / model	Outcome
12	**Davis 1986** (abstract)	38 chronic cases, mean 48 sessions	89% infection-free at a mean of 34 months; no comparator
13	**Lopez 2005**	39, about 31 sessions	79.5% had no recurrence; no comparator
14	**Maynor 1992**	34 tibial cases, HBO2 and surgery	Drainage-free at 5 years in 6/7 without and 5/6 with muscle flaps; no comparator
15	**Handschel 2007**	27 chronic jaw cases, about 40 sessions	Surgery avoided in 16 (59%); no comparator
16	**Baltensperger 2004**	30 primary chronic jaw osteomyelitis; 12 had HBO2	Outcome by HBO2 not reported
17	**Yeheskeli 2016**	23 refractory necrotising otitis externa, all HBO2	90-day deaths: none among 3 known jaw-joint cases, 4 among 19 others; no comparator for the oxygen
18	**Kawashima 2020**	269 long-bone cases	92.1% reported successful; no comparator
19	**Sarigul 2026**	13 spinal infections after failed operations	Pain and function improved after radical surgery plus 21 sessions; all treated, so HBO2's share cannot be isolated
20	**Tofuku 2014**	23 spinal infections with abscess	No recurrence; CRP normalised in 28 days, similar to 30 in the authors' earlier series without HBO2
21	**Mader 1980**	rabbits, Staphylococcus aureus	Bone oxygen rose from 21 to 104 mmHg at 2 ATA; white cells kill poorly at low oxygen
22	**Mendel 1999**	104 rats	HBO2 and cefazolin each lowered bone bacterial counts; lowest with both

WHY THE EVIDENCE IS WEAK

- **No control group:** the success figures come from series in which every patient had HBO2 and antibiotics, and some had surgery [1, 12, 18].
- **Selection:** allocation followed consent, cover or perceived risk in the comparisons [10, 7, 11], and the largest comparison's P value does not reproduce [9].
- **Definition:** studies differ on what failed treatment means, and several are abstracts or very small [12, 11]; one jaw series does not report outcome by HBO2 [16].

GAPS IN THE EVIDENCE

- No randomised trial of HBO2 added to debridement and antibiotics in refractory osteomyelitis [2]; UHMS notes a specific pressure is not supported by data [23].

MECHANISM

- **Infected bone:** bone oxygen rose from 21 to 104 mmHg at 2 ATA in rabbits; in vitro, white-cell killing of bacteria improved when oxygen tension rose from 23 to 45 mmHg [21].

Severe anaemia (exceptional blood loss)

Hyperbaric oxygen (HBO2) as a bridge when transfusion cannot be given: evidence overview

SA ICD-10: D62 (also D64.8, D64.9); code the cause of the blood loss as well
UHMS accepted indication · NRPL 2006 recognised (SA §4.8l)

Clinical consensus **Benefit of HBO2 as a bridge in severe anaemia is unproven**

There is no controlled human study in patients who cannot be transfused. The one randomised trial (45 patients with low haemoglobin after liver surgery) found no reduction in transfusion (13 of 20 vs 13 of 21) [1]. The human evidence is case reports and small series, mostly Jehovah's Witnesses who also received iron, erythropoietin, fluids and intensive care, so the contribution of HBO2 cannot be separated [2, 4, 8]; deaths are reported [9, 10]. A review of 35 publications found 26 were animal experiments [2]. In dogs bled into shock HBO2 improved survival in one laboratory's experiments and in another's [17, 18], but not in others [14, 19, 20]; in rats it helped in haemolysis, not in histamine shock [16]. The physiological case is strongest at near-zero haemoglobin [15, 22]; against it, HBO2 lowered erythropoietin in healthy volunteers [23].

OCEBM 2 (one small, indirect RCT) **GRADE** Not rated (no controlled data in patients who cannot be transfused)
Published ECHM not addressed · SAUHMA no protocol · UHMS Class IIb

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **When:** only when transfusion is refused or impossible and there are signs of tissue hypoxia (altered mental status, ischaemic ECG changes, haemodynamic instability, raised lactate, multi-organ failure), as in the reports [6, 24].
- **Pressure and frequency:** 2.0-2.5 ATA in the cases: 2.4 ATA, 90 min, daily or twice daily, 10-11 days [11, 10]; 2.5 ATA, 2 h twice daily for 3 days then daily [12]; 22 pulsed sessions at 2 ATA over 16 days [8]; 17 cycles in about 4 days [3]. UHMS 2023 gives 2-3 ATA for 3-4 h, three to four times daily [25].
- **Alongside:** restore haemoglobin by other means. Effect on erythropoiesis is disputed: erythropoietin fell in volunteers and anaemic rats [23, 26]; one report found it unimpaired [7]. Erythropoietin was given in [7, 13], iron in [13].
- **Stop and limits:** HBO2 was stopped in survivors when ischaemic signs resolved (average haematocrit then 24%) [4]; one patient was transferred for HBO2 only after brain injury and died [9]; another was stable for 7 days on HBO2 plus intensive care, then died of septic shock [10].

Synthesised from the cases and animal work below; no trial has tested this protocol. Treat as a bridge while the cause is controlled and haemoglobin is restored by other means.

RANDOMISED TRIAL, SYSTEMATIC REVIEW AND REVIEWS

Ref	Study	n	Design and regimen	Result	Quality
1	**Ueno 2011** RCT	45 randomised, 41 analysed	Haemoglobin under 9 g/dL after liver-cancer surgery: HBO2 2.0 ATA, 60 min, at 3 h and 24 h (48 h if needed) vs none	Red-cell transfusion 13/20 (65%) vs 13/21 (62%); RR 1.05, ARR -3.1% (95% CI -32.6 to 26.4)	RoB 2: some concerns; GRADE low; not a transfusion-refusing population
2	**Van Meter 2005** review	35 publications	26 animal haemorrhagic-shock experiments, 8 human case reports and series and 1 in vitro red-cell study	Narrative evidence-graded review; authors report all 35 as positive; human data are the 8 clinical reports	AMSTAR-2: critically low; GRADE very low

HUMAN CASES AND SERIES (ALL UNCONTROLLED; MOST ALSO RECEIVED OTHER TREATMENT)

Ref	Report	n	Regimen	Outcome
3	**Amonic 1969**	1	17 cycles over about 4 days	Haemoglobin 2.2 g/100 mL; survived; a convulsion on the first switch from oxygen to air (stopped by resuming oxygen)
4	**Hart 1985** (abstract)	18	HBO2, stopped when ischaemic signs resolved	5 died (all women); survivors' admission haematocrit averaged 14.4%, and 24% when HBO2 stopped
5	**Hart 1987**	26	HBO2	Known only through secondary sources: survivors' admission haematocrit 13.6%, deaths 10.5%; 6 of 26 died (about 77% survived)
6	**Dalton 1991** (abstract)	2	emergency HBO2	Haemoglobin 3.5 and 2.9 g/dL after hysterectomy; both alive at day 24 (7.1 and 7.6 g/dL)
7	**Lepawsky 1991** (abstract)	1	HBO2 + erythropoietin	Haemoglobin rose from 36 to 107 g/L; authors report erythropoiesis not impaired by HBO2
8	**McLoughlin 1999**	1	22 pulsed sessions, 2 ATA	Haemoglobin 2.0 g/dL after obstetric haemorrhage; discharged at 11.3 g/dL
9	**Shaw 2000**	1	transferred for HBO2 after encephalopathy; regimen not reported	Haemoglobin 2.8 g/dL; declared brain-dead on day 3; whether HBO2 was given is not reported
10	**Perdrizet 2007** (abstract)	1	2.4 ATA, 90 min daily x10	Haemoglobin 9 to 3 g/dL; stable for 7 days with HBO2 and intensive care; died of septic shock on day 10
11	**Miller 2008** (abstract)	2	2.4 ATA, 90 min, twice daily then daily, 10-11 treatments	Haemoglobin 3.3 and 5.0 g/dL on presentation (nadirs 2.6 and 4); both recovering at last report
12	**Weiland 2008** (abstract)	1	2.5 ATA, 2 h twice daily for 3 days, then daily	Trauma; haemoglobin/haematocrit 2.8/9.4 on day 4, 9.3/30.9 by day 20; home on day 35 without deficit
13	**Salmen 2017**	1	11 sessions + blood substitute, erythropoietin, iron	Postpartum bleeding, haemoglobin about 2.3 g/dL; survived

ANIMAL EXPERIMENTS (SHOCK AND BLOOD WASHOUT)

Ref	Study	Model	Result
14	**Frank 1943**	dogs bled into shock, 3 ATA	All 5 given oxygen after shock died; 9 of 10 given it from before the bleed died
15	**Boerema 1959**	piglets, exchange transfusion, 3 ATA	Haemoglobin lowered to 0.4-0.6% (Sahli); all animals in the final series survived about 45 min; 3 normobaric pigs did not tolerate haemoglobin below 10%; no statistics
16	**Burnett 1959**	rats, 2 ATA, non-haemorrhagic shock models	No benefit in drum trauma (22/41 vs 20/41) or histamine shock; haemolysis 24/25 alive at 2 h vs 5/25 in air
17	**Attar 1962**	dogs bled to 30 mmHg, 3 ATA	25 of 30 controls died vs 7 of 19 given oxygen; not randomised (same laboratory as Esmond 1962 and Cowley 1963)
18	**Blair 1964**	rats in drum (traumatic) shock; dogs bled; 3 ATA	Survival 17/21 vs 6/15 (rats) and 14/18 vs 3/20 (bled dogs); no dog survived faecal peritonitis
19	**Clark 1965**	dogs bled to low pressure, 2 ATA	All 5 given oxygen died within 18 h vs 6 of 8 on air
20	**Jacobson 1966**	rabbits in shock, 2 ATA	Mean survival 15.2 h at 2 ATA vs 11.6 and 11.3 h ($p<0.05$); 9 of 10 died in each oxygen group, all on air
21	**Ruiz 1972**	dogs, coronary ligation + haemodilution (Hb about 8 g/dL), 2 ATA	6 of 7 survived vs 3 of 8 controls (authors $P<0.10$; Fisher $p=0.12$ recalculated); non-random allocation
22	**Norman 1975**	30 dogs, total blood washout with dextran; consecutive groups	Deaths 4/10 at 2 ATA, 2/10 at 2.5 ATA, 0/10 at 3 ATA (higher pressures applied during the washout only)

HARMS AND LIMITS

- **Convulsions and arrhythmia:** one patient convulsed when switched from oxygen to air (stopped by resuming oxygen; the paper does not call it oxygen toxicity) [3]; in dogs at 3 ATA one convulsed and died and one had hind-leg paralysis [27], and 3 of 25 dogs in shock died of ventricular fibrillation in the chamber [28].
- **Haemolysis:** after one 26-min session at 2 ATA a man with a recent stroke fell from haematocrit 48% to 35% by day 6; 20 other subjects did not show his red-cell abnormalities [29].
- **Erythropoiesis:** one session at 2.5 ATA for 90 min lowered erythropoietin by 53% at 24 h in 15 healthy volunteers [23]; anaemic rats in 2-3 ATA oxygen had no detectable erythropoietin [26].

MECHANISM AND GAPS

- **Dissolved oxygen:** piglets at haemoglobin 0.4-0.6% survived about 45 min at 3 ATA [15]; dogs washed free of haemoglobin did better at higher pressure (0/10 deaths at 3 ATA) [22].
- **Gaps:** no controlled study in transfusion-refusing patients; no dose or timing study; human reports are a rare, selected situation.

Idiopathic sudden sensorineural hearing loss

Hyperbaric oxygen (HBO2) added to corticosteroids: evidence overview

SA ICD-10: H91.2 (also H90.3, H90.4, H90.5, H91.9)
UHMS accepted indication · not on the NRPL 2006 §4.8 recognised list · no PMB code

Supported by trials **HBO2 added to steroids probably improves recovery in acute hearing loss**

Most randomised trials favour adding HBO2 to steroids or other drugs [3, 1, 9, 8, 6], and one favoured it over vasodilators [2]; two small ones found no significant difference [4, 11]. Trials that gave HBO2 in both arms cannot show an HBO2 effect [28, 29]. The Cochrane update pooled seven trials: improvement RR 1.5 (1.2-1.7), NNT 4, about 15 dB more gain; but one of the seven was pseudo-randomised, none concealed allocation adequately, and the review is rated critically low [14]. Other pooled analyses agree [13, 16, 17]. Untreated recovery is itself about 60% [19], and large cohorts conflict, probably because sicker patients received HBO2 [20, 21]; one found HBO2 worse in total deafness [22]. Benefit falls with delay [24, 23], and none was shown for chronic loss [13] or isolated tinnitus [27]. No adequately powered low-risk-of-bias trial exists; one is under way [30].

OCEBM 1 (Newth 2025, 7 trials) **GRADE** Moderate (published: hearing gain, Cochrane 2012) **Published** ECHM Type 1, Level B · SAUHMA Level B · UHMS no class stated

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** loss over 40 dB, first treated within 14 days of onset [31]. The otolaryngology guideline offers HBO2 with steroids within 2 weeks, and as salvage up to 1 month [32].
- **When:** as early as possible. In one cohort each day of delay cut the odds of complete recovery by about 12% [24]; mean gain was 19.9 dB within 12 days, 9.8 dB at 13-27 days and 3.2 dB (-0.7 to 7.1) after 27 days [23].
- **Dose:** 100% oxygen at 2.0-2.5 ATA for 90 min daily, 10-20 sessions, with steroids [31]. Pooled data favour at least 1,200 min in total [15]. Used: 2.5 ATA 90 min, 25 sessions [3]; 2.2 ATA, 15 sessions [11]; 2.5 ATA, 14 days [9]; 20 sessions, once or twice daily, equivalent [8]; pressure choice is unsettled [25, 26].
- **Stop:** not for chronic loss [13]; benefit in tinnitus alone is unproven [27]; no review point is set by UHMS, so reassess with audiometry and continue only if hearing is improving.

UHMS parameters, with timing from the cohorts; no trial has compared protocols. Give steroids as well and co-manage with ENT.

RANDOMISED AND QUASI-RANDOMISED TRIALS

Ref	Study	n / design	Result	Quality
1	**Pilgramm 1985**	37 fresh (88 in two studies); 10 sessions added	Fresh cases (14 days or less): gain 29.1 vs 20.2 dB; old or pre-treated cases no benefit	RoB 2: some concerns
2	**Fattori 2001**	50; HBO2 vs vasodilators (not steroids); allocation method unclear	Relative gain 61% vs 24% (p=0.005)	RoB 2: some concerns
3	**Topuz 2004**	51; 30 vs 21, steroids in both, 25 sessions	Mean gain 33.3 vs 17.4 dB, confined to loss over 60 dB	RoB 2: some concerns
4	**Cekin 2009**	57; steroids with or without HBO2	Success 79% (ears) vs 71%, not significant; control arm sicker at baseline	RoB 2: high
5	**Cvorovic 2013**	50; salvage, HBO2 vs intratympanic steroid	No difference at 4 of 5 frequencies; better at 2 kHz; arms unmatched	RoB 2: some concerns
6	**Chi 2018**	60 soldiers, alternate allocation	Day 180 partial or complete recovery 80% vs 47%; early timepoints no difference	RoB 2: high
7	**Cho 2018**	60, severe to profound; allocated by visit order	No gain in average threshold; word discrimination 66% vs 57%	RoB 2: high
8	**Hu 2020**	107; drugs with HBO2 once or twice daily vs drugs alone	Effective response 80% vs 62%; +9.5 dB	RoB 2: some concerns
9	**Tong 2020**	136; HBO2 plus drugs vs drugs	Success 60.6% vs 42.9% (p=0.038)	RoB 2: high
10	**Cavaliere 2022**	171; HBO2 vs oral steroids vs both	HBO2 best within 7 days; no arm improved significantly after 14; arms differed in age	RoB 2: high
11	**Dova 2022**	50; steroids with or without HBO2	Success 64% vs 56% (p=0.37); no significant difference	RoB 2: high
12	**Feng 2022**	104; alprostadil with or without HBO2	Tinnitus, fullness and vertigo recovered better; no steroid arm	RoB 2: high

POOLED ANALYSES AND NATURAL HISTORY

Ref	Study	Scope	Result	Quality
13	**Bennett 2012** (Cochrane)	7 RCTs, 392 patients	25% threshold gain RR 1.39 (1.05-1.84), NNT 5, from 2 trials; 50% threshold not significant; none in chronic loss	AMSTAR-2: low
14	**Newth 2025** (update of the Cochrane review)	7 trials, 562 patients	Improvement RR 1.5 (1.2-1.7), NNT 4; +15.1 dB (8.2-22.0); effect to 30 days; GRADE moderate (authors)	AMSTAR-2: critically low
15	**Rhee 2018**	3 RCTs and 16 non-randomised studies, 2,401 patients	Complete recovery OR 1.61 (1.05-2.44); larger with 1,200 min or more in total and in salvage (unadjusted subgroups)	AMSTAR-2: critically low
16	**Alter 2026**	20 studies (16 RCTs), 1,687 patients	Recovery OR 2.61 (1.86-3.68), from 10 of the 20 studies	AMSTAR-2: moderate
17	**Joshua 2022**	3 RCTs, 150 patients	+10.3 dB (6.5-14.1); recovery OR 4.3 (1.6-11.7)	AMSTAR-2: critically low
18	**Kuo 2022**	4 studies, 314 patients, salvage	HBO2 vs intratympanic steroid: 2.70 dB (-0.63 to 6.02) favouring steroid; no significant difference	AMSTAR-2: critically low
19	**Chaushu 2023**	untreated and placebo arms	Spontaneous recovery 60.3% (38.9-79.9), I2 86%	AMSTAR-2: critically low

COHORTS AND OTHER STUDIES

Ref	Study	n / design	Result	Quality
20	**Chen 2025**	505; 102 with HBO2 plus steroid	Gain 22.7 vs 16.2 dB (p=0.007); HBO2 group started at 53.5 vs 34.9 dB, unadjusted	ROBINS-I: serious
21	**Xie 2026**	413; matched 135 pairs	Recovery 44% vs 56% before matching (p=0.02); 47% vs 56% after (p=0.18)	ROBINS-I: moderate
22	**Zhi 2025**	248; 212 with HBO2	Total deafness gain 19.9 dB with HBO2 vs 43.1 dB without; not adjusted	ROBINS-I: critical
23	**Chin 2026**	255, all treated, no comparator	Gain by delay: 19.9, 9.8, 3.2 dB (see protocol)	ROBINS-I: critical
24	**Bagli 2020**	96, all treated	Delay the only independent predictor: OR 0.88 per day (0.82-0.95)	ROBINS-E: serious
25	**Chen 2021**	160, 2.0 vs 2.2 ATA vs none	250-500 Hz gain 21 and 20 vs 12 dB; overall gain not significant	ROBINS-I: serious
26	**Krajcovicova 2019**	115; standard care vs 2.0 ATA (49) vs 2.5 ATA (31)	Both HBO2 groups beat standard care at 250-500 Hz; no significant 2.0 vs 2.5 ATA difference; not randomised	ROBINS-I: serious
27	**Porubsky 2007**	360, tinnitus	Response tracked patient expectation, not the HBO2 protocol	RoB 2: high

WHY THE EVIDENCE IS WEAK

- **Design:** the trials are small and open, and two used alternate or sequential allocation [6, 7] and allocation in another is unclear [8]; the two arms-both-HBO2 steroid trials say nothing about HBO2 itself [28, 29].
- **High baseline recovery:** with about 60% recovering untreated [19], absolute gains are modest and a small bias can create an apparent benefit.
- **Confounding:** in the cohorts the HBO2 arm started with worse hearing [20]; matching turned a deficit into a null [21].

GAPS IN THE EVIDENCE

- No adequately powered low-risk-of-bias trial of HBO2 added to steroids; SuDHO (assessor-blinded, 15 sessions at 2.4 ATA) completes recruitment about 2028 [30].

MECHANISM

- **Cochlea:** high metabolic demand and poor collateral supply; HBO2 is thought to raise perilymph oxygen tension; earlier treatment is associated with better outcomes [31].

Thermal burns

Hyperbaric oxygen (HBO2) added to burn-unit care: evidence overview

SA ICD-10: by site and depth (T20-T25 .2/.3, T29.2, T29.3) plus T31.x for extent
UHMS accepted indication · NRPL 2006 recognised (SA §4.8k) · PMB DTP 900J (burns over 10% or full-thickness)

Evidence developing **Benefit of HBO2 for burns is unproven**

The largest randomised trial found no effect: 125 patients, mortality 7/63 vs 7/62, no difference in operations or stay, but unblinded [2]. A 1974 trial is reported by Cochrane to show healing in 19.7 vs 43.8 days, but only a digest of it is held [1, 5]; a 17-patient pilot found no effect on burn depth [3]; a 20-patient trial favoured HBO2 but did not describe its randomisation [4]. Cochrane found the evidence insufficient either way [5], and a 2026 review found it inconsistent [6]. Small non-randomised series report shorter stays [9, 10] or lower mortality against historical controls [15], while a matched comparison found no mortality difference [11], a cohort no deaths and faster procalcitonin fall [16], and a registry higher mortality with probable confounding [17]. Animal experiments are mostly positive, with exceptions [19–21, 24]. UHMS supports it as an adjunct but concedes that no adequately powered multicentre trial exists [25].

OCEBM 1 (Villanueva 2004 Cochrane, 2 RCTs) **GRADE** Very low (our assessment: mortality, stay, healing)
Published ECHM Type 2, Level C (burns over 20% BSA) · SAUHMA no protocol · UHMS no class stated

RECOMMENDED PROTOCOL (MERIT-BASED SYNTHESIS)

- **Who:** deep partial- or full-thickness burns over 20% of body surface and/or involving the hands, face, feet or perineum, others at the surgeon's discretion; not where survival is not expected [25].
- **When:** early; in the null trial the first session was a mean of 11.5 hours after admission [2].
- **Dose:** 2.0-2.4 ATA for 90 min, several sessions in the first 24 hours then twice daily, 10-14 days in burns of 40% or more [25]. Used: 2.0 ATA 90 min twice daily, at least 10 sessions [2]. Across animal studies pressure below 3 ATA did better than 3 ATA or more [8].
- **Safety:** some centres remove mafenide (Sulfamylon) before treatment, control fever, and watch fluid balance and post-chamber hypotension [25]; seizures and deaths followed three 2-hour sessions in burned mice [22].

UHMS parameters; no trial has compared protocols. HBO2 is an adjunct and must not delay burn-unit resuscitation, surgery or critical care.

RANDOMISED TRIALS

Ref	Study	n / design	Result	Quality
1	**Hart 1974** (digest only)	16 (per Cochrane), HBO2 vs control	Healing 19.7 vs 43.8 days per Cochrane; digest says early HBO2 cut healing time, morbidity, mortality	not assessed
2	**Brannen 1997** (abstract)	125; 2 ATA 90 min twice daily	Mortality 7/63 vs 7/62; operations and stay no different; allocation depended on chamber availability	RoB 2: high
3	**Chong 2013**	17 (8 vs 9), burns under 40%	No effect on burn depth or inflammatory cytokines; underpowered	RoB 2: high
4	**Oley 2021**	20, large burns	Severe complications 0 vs 6; stay 17.5 vs 26.3 days; randomisation not described	RoB 2: see appraisal

POOLED ANALYSES AND REVIEWS

Ref	Study	Scope	Result	Quality
5	**Villanueva 2004** (Cochrane)	2 RCTs, 141 patients	Insufficient evidence either way; trials not pooled	AMSTAR-2: see appraisal
6	**Molina-Vega 2026**	13 studies (5 RCTs); 566 HBO2 patients, 13,481 controls	Evidence inconsistent; no pooling	AMSTAR-2: critically low
7	**Daneshi 2026** (abstract)	12 studies, 445 given HBO2	Mortality OR 1.54 (0.59-4.07); infection and stay no significant effect, very imprecise	AMSTAR-2: critically low
8	**Smolle 2024**	47 papers, 94 experiments, mostly animal	67% of experiments positive; pressure below 3 ATA better (p=0.0005)	AMSTAR-2: critically low

NON-RANDOMISED COMPARISONS AND SERIES

Ref	Study	n / design	Result	Quality
9	**Cianci 1989**	20; 8 HBO2 vs 12 without access	Stay 20.8 vs 33.0 days; operations and cost no different	ROBINS-I: serious
10	**Cianci 1990**	21; 10 HBO2 vs 11 matched	Stay 28.4 vs 43.2 days; operations and cost not significant	ROBINS-I: serious
11	**Waisbren 1982**	72, 36 matched pairs	Deaths 22 vs 21; positive blood cultures 17/27 vs 2/19; less autograft	ROBINS-I: serious
12	**Grossman 1978**	49 with burns of 50% or more; non-randomised comparison	Deaths 10/24 vs 17/25 (our Fisher p=0.088)	critical risk of bias
13	**Cianci 1991** (abstract)	survivors of 40-80% burns; 11 HBO2 vs 1982-85 controls	Operations 2.1 vs 7.8; stay 51.8 vs 108 days	ROBINS-I: serious
14	**Ray 1991** (abstract)	28; 20 HBO2 vs 8	Stay 30.5 vs 75.6 days; ventilator days 5.3 vs 26; allocation not reported	ROBINS-I: critical
15	**Gorman 1988**	67 vs 113 historical	Mortality 4.4% vs 21.3%; better nursing could explain the fall	pilot; not scored
16	**Chiang 2017**	53; 38 HBO2 by surgeon preference, unmatched	Grafted area, operations and stay no different; procalcitonin fell faster; no deaths	ROBINS-I: serious
17	**Nygaard 2021** (abstract)	13,044 with inhalation injury; 67 HBO2	Mortality 29.9% vs 17.5%, also after adjustment; HBO2 patients older, burns smaller	ROBINS-I: serious
18	**Pham 2025**	82, all treated	84% pain-free by day 14; stay 8.9 days against a formula 13.2; no controls	JBI: 5 of 10

ANIMAL EXPERIMENTS

Ref	Study	Model	Result
19	**Korn 1977**	117 guinea pigs, scald	Re-epithelialised at day 4: 12/23 with HBO2 vs 1/19 untreated
20	**Stewart 1992**	rats, 15% partial-thickness burn	Abstract only: wound ATP, phosphocreatine and collagen synthesis fell after the burn, then returned to or above normal with oxygen
21	**Bilic 2005**	70 rats, deep partial-thickness	Less swelling on day 5 only; earlier signs of regrowth (9/10 vs 1/10); no difference in tissue death
22	**Tenenhaus 1994**	burned mice	Two sessions: mesenteric bacteria 1/25 vs 9/24; three 2-hour sessions caused seizures and deaths
23	**Hatibie 2019**	36 rabbits, second-degree	More skin regrowth with HBO2; randomisation method not described
24	**Shoshani 1998**	54 guinea pigs, deep second-degree	Slower epithelialisation than normobaric oxygen at day 10 (p=0.02); no gain in contraction or blood flow

WHY THE EVIDENCE IS WEAK

- **Design:** the only randomised trials are small or unblinded, and the 1974 trial is known only through Cochrane [1, 2, 4].
- **Selection:** in the comparisons HBO2 patients were chosen by surgeon preference or chamber access [16, 9], and in the registry the treated patients were older and confounding is probable [17].
- **Surrogates:** hospital stay carries most of the positive claims; cost and operation savings were not significant [9, 10].

GAPS IN THE EVIDENCE

- No adequately powered, blinded multicentre randomised trial of HBO2 added to modern burn care; the Cochrane trials date from 1974 and 1997 [5].

MECHANISM

- **Burn wound:** HBO2 is thought to preserve the ischaemic zone of stasis, reduce oedema and support neutrophil killing and angiogenesis [25]; in animals wound energy stores recovered [20] but did not always speed healing [24].