UNIVERSITY OF BIRMINGHAM

West Midlands
Commissioning Support Unit

Hyperbaric oxygen therapy
Guidance to commissioners

March 2012

This document accompanies the West Midlands Commissioning Support Unit's report entitled
Hyperbaric oxygen therapy: Technical Report (08.02.12)

The original target audience for these two documents was the PCT clusters and clinical commissioning groups of the West Midlands region.

The WMCSU understands that the decision to remove hyperbaric oxygen (HBO) therapy from the list of specialised services has been reversed and the intention is for this treatment to come under the auspices of the NHS Commissioning Board. This change has made no material difference to the policy recommendations, except that additional recommendations have been included which will be relevant to the future commissioning of this intervention at national level.

Individuals involved in commissioning over the past 15-20 years will identify the commissioning of HBO as an ongoing problem area. This commissioning guidance addresses three critical issues: the evidence base, strategic risks and variation in approaches to funding decisions.

1. The evidence base

The evidence landscape for HBO is unusually striking in that the quality of the medical research is poor, given the length of time this intervention has been investigated and the large number of trials that have been undertaken.

The primary research studies investigating the efficacy of HBO are remarkable for the consistent poor quality of the published clinical trials as well as the lack of evidence demonstrating significant health benefits. There is a lack of adequate clinical evidence to support the view that HBO therapy is efficacious for any of the indications for which it is being used. The nature of the treatment would suggest that the potential for significant placebo effects is high and because the evidence base consists mostly of uncontrolled case studies, significant overestimation of any observed effect size is highly likely. Published controlled clinical trials are small in number, generally poorly designed or reported, and their results do not justify the recommendations made for the use of HBO, as judged by current standards of robust evidence-based practice.

For most indications, justification for the use of HBO is based solely on clinical experience and expert opinion. Much of the case for using HBO is based on arguments of biological plausibility. Support for its use based on biological plausibility might, on the face of it, appear valid. However the complex role of oxygen in tissue healing, and an incomplete understanding of the effects of raising oxygen pressure on complex tissue processes in different conditions may mean that the potential of this treatment might not be realised in reality. In clinical practice HBO may simply not work or be sufficiently effective.

In 2012 NHS commissioners find themselves in the unfortunate situation that despite HBO having been used for many years as a therapeutic intervention for a variety of indications, the evidence for its use remains poor and uncertain, and we are no closer to establishing its efficacy, let alone comparative effectiveness or cost-effectiveness. The large number of on-going uncontrolled trials (listed on page 12 of the technical report) suggests that this situation is unlikely to change without some intervention from outside the clinical community.

Another concerning aspect is the lack of clarity around treatment protocols, unsurprising given the inability for clinicians to develop evidence based guidelines when the evidence is so poor. Establishing the optimum treatment regimen is essential for such an expensive treatment.

2. Strategic risks

The potential for clinical creep and extension of treatment packages in the absence of good evidence has already been identified as a risk. There are a number of issues which represent strategic risks to a commissioner.

HBO presents a provider trust with an infrastructure problem – both in terms of capital and running costs. There will always be pressure in the system to utilise HBO facilities beyond the original reason, for establishing these units, namely the support of deep water diving. While it has not been the purpose of this report to consider capacity in the supply of HBO to meet the needs of commercial and recreational diving communities – it is clear that, in total, there is considerable spare capacity. More concerning is the expansion of units where provision of facilities for divers is not the main reason for their establishment.

There are a growing number of clinicians with a special interest in this area of clinical practice wishing to have this treatment funded. Private practice is also expanding, with use of HBO to treat sports injuries being a particular area of growth.

Although it is outside the remit of the NHS, it should be noted that there are a number of non-certified chambers in use at multiple sclerosis centres; these services may not necessarily follow a Code of Practice, and may be being used to treat serious medical conditions.

3. Variable commissioning approaches to HBO

Variation in commissioning positions taken by commissioning bodies is not necessarily inappropriate and may reflect differing population needs and priorities. Statutory organisations are at liberty to take different positions on a treatment. However, ongoing management of this service through the individual funding request process by some organisations is a problem. The serious nature of many of the conditions being treated and arguments of biological plausibility can put considerable pressure on decision makers and risks them resorting to 'rule of rescue' in their decision-making.

Recommendations

1. A policy approach to commissioning HBO is essential. A national policy should be swiftly put in place – preferably prior to bringing the service into national commissioning arrangements.

2. Case-by-case decision making should be stopped by existing commissioners and should not be initiated by the NHS Commissioning Board, once this body assumes commissioning responsibility. The collective experience over the last decade is that most, if not all, individual funding requests being considered by commissioners represent groups of patients and as such policies should be agreed and requests kept out of the IFR process.

3. The policy recommendation is that HBO is only funded for decompression sickness & gas embolism. It is essential that consistent standards for the evidence for effectiveness and safety are adopted for agreeing additional indications.

4. Outside of decompression sickness and gas embolism, it can be expected that individual funding requests that are forwarded to the individual funding request panel are likely to be rare events. This is because experience of individual funding requests across the country indicates that IFR requests represent cohort of patients.

5. Collectively commissioners do not have sufficient information about how this treatment is used in practice to sufficiently understand the risks. The benefit of national commissioning in this context is to gather better information about current clinical practice. The policy should therefore also require providers of HBO services to supply information as a condition of funding. Useful information includes: numbers treated, the severity of injury/condition, number of treatments and

pressures given, and appropriate patient/clinical outcomes. It is essential that commissioners build up a better picture of what is currently happening in this service.

6. Another advantage of national commissioning is that it is possible to address the quality of research. A major recommendation is that there are moves to create more coherent and better quality research in this area. External methodological support is required.

7. When considering funding patients in the context of an existing clinical trial, the NHS Commissioning Board should assess the quality of the trial before agreeing to support it. In particular whether or not the design of the trial is robust, whether it will generate the evidence sought and the availability of the trial data to the public sector once the trial has been completed.

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8. Commissioners should contribute to setting priorities for research. Of the indications reviewed, the potential for this treatment to heal diabetic ulcers is the most promising and potentially of most importance taking the population medicine perspective.

9. Finally, specialised commissioning organisations have the power of designating services. We suggest that designation follows policy – namely the services are designated in line with the requirements of the indications that are funded.

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Hyperbaric oxygen therapy
Technical Report

Date completed: 08/02/2012

History

Hyperbaric oxygen (HBO) therapy is the provision of 100% oxygen at pressures greater than normal atmospheric pressure (generally 2 to 3 times, i.e. 2.0 to 3.0 *atmospheres absolute* or ATA), in a special chamber. It has been recommended for the treatment of many conditions over several centuries, although for many of these conditions the theoretical basis is unclear, and the evidence for efficacy and cost-effectiveness is unconvincing.

The Department of Health included HBO in the Specialised Services National Definitions Set (SSNDS) until 2010, when HBO Treatment (definition set number 28) was removed. There has never been a national policy for this therapy. PCTs have, for the most part, not taken a policy approach to the use of HBO but instead have treated requests for its use on a case-by-case basis, as Individual Funding Requests.

In 2007, a systematic review was commissioned from NHS Quality Improvement Scotland (QIS) through the Health Technology Assessment programme (part of the NIHR programme), by the Specialised Services Public Health network in an attempt to classify for which conditions, based on the quality of the evidence, HBO was of proven benefit and cost effective, and therefore for which conditions it should be used in the NHS. The review attempted to identify all the indications for which HBO had been suggested as appropriate therapy. The report from QIS was published in 2008.[1]

Subsequently, a draft commissioning policy for the funding of HBO therapy was developed for primary care trusts and specialised commissioning groups in England through an informal network of public health specialist across the UK. However, the attempt to produce nation-wide policy was unsuccessful. Some regions and individual PCTs have developed their own policies, in some cases for specific indications (for examples, see Table 1 on page 15). The East Midlands Specialised Commissioning Group (in 2011) and South Central Priorities Committee (Portsmouth PCT, 2009) considered all indications. These bodies decided to routinely fund decompression illness and gas embolism, with the East Midlands Specialised Commissioning Group adding acute CO poisoning after the Department of Health issued a statement in November 2010 about use of HBO therapy for patients with CO poisoning who met specific criteria.[2] Other conditions are not funded by these two bodies. (This position is in line with that of the SSNDS.)

The British Hyperbaric Association (BHA, an independent body that aims to promote the understanding and safe practice of hyperbaric medicine in the UK, and to self-regulate member chambers) lists additional conditions for which it considers HBO therapy to be suitable <http://www.hyperbaric.org.uk/>. The Undersea and Hyperbaric Medical Society (UHMS, an international organisation based in the USA to support practitioners of hyperbaric medicine <http://www.echm.org/>) and the European Committee for Hyperbaric Medicine (ECHM <http://www.echm.org/>) have listed a number of indications for which they recommend the use of HBO. For the 13 indications listed by the UHMS, "research data and extensive positive clinical experience have become convincing" according to their report of 1999.[3]

HBO has never been commissioned at regional level within the West Midlands. However the removal of HBO from the national definition set, the establishment of a new facility at Rugby and a potential development at Dudley Hospital stimulated a request to the WMCSU, by the West Midlands Specialised Commissioning Team, to update the evidence review and provide guidance to local PCTs.

This report consists of a pragmatic review of the clinical evidence (Section 1) and supplementary supporting information (Section 2).

Contents

Glossary

ATA	atmospheres absolute
BHA	British Hyperbaric Association
BMJ	British Medical Journal
CI	confidence interval
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease
DB	double-blind
DDRC	Diving Diseases Research Centre
DH	Department of Health
DMSO	dimethyl sulfoxide
DTB	Drug & Therapeutics Bulletin
ECG	electro-encephalogram
ECHM	European Committee for Hyperbaric Medicine
HBO	hyperbaric oxygen
HSE	Health & Safety Executive
HTA	Health Technology Assessment
IFR	individual funding request
ISRCTN	International Standard Randomised Controlled Trial Number
ITT	intention-to-treat
MS	multiple sclerosis
NBO	normobaric oxygen
NIHR	National Institute for Health Research
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NPIS	National Poisons Information Service
NSAID	nonsteroidal anti-inflammatory drug
QIS	Quality Improvement Scotland
RCT	randomised controlled trial
SSNDS	Specialised Services National Definitions Set
$TcPO_2$	transcutaneous oxygen tension
UHMS	Undersea & Hyperbaric Medical Society
US	United States
WHO	World Health Organisation

Section 1: Pragmatic review of evidence for efficacy and safety

Summary

- The purpose of this review was to assess the evidence for efficacy of HBO therapy to allow identification of the conditions for which its use could be justified.
- The review was based on the Health Technology Assessment produced by NHS Quality Improvement Scotland in 2008, relevant Cochrane reviews, and the results of a search for controlled trials and systematic reviews published since 2007. Where necessary, the primary evidence was examined in detail. The conditions for which HBO has been used were grouped into several categories based on the evidence.
- HBO was considered to be accepted standard therapy for decompression sickness and gas embolism associated with decompression sickness or trauma, based on the theoretical rationale for such treatment and clinical experience, although there was no robust evidence for efficacy.
- No robust evidence was found for the treatment of carbon monoxide poisoning with HBO either soon after acute poisoning, or for delayed effects of acute poisoning. HBO treatment for acute carbon monoxide poisoning is not currently recommended by the UK National Poisons Information Service (on Toxbase) or NHS Direct; these bodies recommend the use of normobaric 100% oxygen. However, the national position was confused by a statement issued by the Department of Health in November 2010 that the use of HBO therapy should be considered for patients with CO poisoning who met specific criteria, but that advice from Toxbase should be considered.
- Reasonable evidence indicated that HBO was not efficacious for the treatment of multiple sclerosis, and its use for this indication is not recommended by NICE Clinical Guideline 8.
- Several controlled trials, including those with adequate randomisation, suggested possible efficacy for the use of HBO for the treatment of chronic diabetic foot ulcer, and one for chronic refractory radiation-induced proctitis. However, no clear conclusions could be drawn because of serious weaknesses in the design and reporting of most of the trials and inconsistency in the results between trials. The current body of evidence does not support the routine treatment of these indications with HBO, but does justify further research (as also reflected by NICE Clinical Guideline 119). Large and robustly designed double-blind randomised controlled trials, with meaningful outcomes and appropriate comparator therapy, are needed to establish whether HBO therapy is effective for the treatment of diabetic foot ulcer and radiation-induced soft-tissue injury.
- For nearly 40 other indications for which HBO is used or has been suggested, the current evidence is clearly inadequate in quality or quantity to support the use of HBO therapy.
- For most of the indications, justification of the use of HBO is based on expert opinion rather than robust evidence.

Objective of review

The objective of this review was to assess the evidence for efficacy of HBO therapy to enable categorisation of the indications for which it has been considered or used (as listed in a Health Technology Assessment published by NHS Quality Improvement Scotland, the QIS report[1]) into those for which there was robust evidence for efficacy, those for which there was robust evidence for no efficacy, and those for which the evidence was suggestive and further research was justified. Where use of HBO seemed justified by the evidence, and for those indications for which HBO was considered to be standard therapy, the objective was to try to define the patient populations and inclusion criteria for appropriate HBO use, as well as the treatment conditions.

Procedure used

1. The comprehensive QIS report[1] and any relevant Cochrane reviews published since the QIS report were used as a starting point. Their description of the trials was used to categorise each indication listed. For those indications where the evidence was suggestive of efficacy, and where the conclusion drawn for this review did not match that of the QIS report or Cochrane review, the trial evidence was examined more closely.

2. A search was carried out for any controlled trials or systematic reviews of HBO for any indication published from 2008 onwards in Medline (see Literature Search Protocol on p. 21 for limits and inclusion criteria). If any trials found were not included in the QIS report or relevant Cochrane review, they were examined in detail for this report. (Thirty-one additional controlled trials or reviews were found.)

3. Websites of UK bodies providing national guidance, major health insurance companies worldwide, and websites listing registered on-going trials were searched (see Literature Search Protocol).

4. The findings were listed in Tables as follows:

    Table 1, the indications for which HBO use is accepted standard practice
    Table 2, the indications for which reasonable evidence indicated no efficacy for HBO
    Table 3, the indications for which the evidence was suggestive and further research was warranted
    Tables 3a and 3b, summaries of the randomised controlled trials for indications in Table 3
    Table 4, the indications for which there was clearly inadequate evidence (in quantity or quality) to support use of HBO

The findings of this review are described under the various categories of indications (A to E below).

Note: efficacy and effectiveness
The term efficacy, when used in connection with medicine, measures how well a treatment works in clinical trials (or laboratory studies), as opposed to effectiveness, which relates to how well a treatment works in practice. Thus, when discussing clinical trial evidence, the term efficacy is generally used.

A. Indications for which there was robust evidence that HBO therapy was beneficial

None were found.

B. Indications for which HBO use was accepted standard practice (Table 1, p. 15)

B.1. Decompression sickness and gas embolism

Spending time at a raised environmental pressure (e.g. during SCUBA diving) results in additional nitrogen dissolving in the blood and other tissues. If decompression to normal atmospheric pressure occurs too quickly to allow the dissolved gas to be eliminated by the lungs, gas bubbles may form in the blood or tissues (this is called decompression sickness or "the bends"), which may cause a variety of symptoms such as skin itching, joint pain, and fatigue. If these bubbles enter the arterial circulation through the lungs (gas embolism), they may cause serious neurological injury ranging from visual disturbance to quadriplegia. The term decompression illness may or may not include gas embolism, which may also be caused by trauma, including that caused by surgery, mechanical ventilation and haemodialysis.[3]

Postulated mechanism of action of HBO
Both decompression sickness and gas embolism can be treated by recompression followed by slower decompression. Hyperoxia additionally increases the diffusion gradient with the embolised gas, enhancing the movement of the gas into solution.

Treatment methods
Tables have been developed using mathematical models of the ascent process depending on the depth and duration of descent. However, since individuals can undergo physiological adaptation to work at high pressure, there is debate about the application of the tables in practice. Recompression with air was standard practice until 2001, when the Health & Safety Executive approved oxygen recompression (i.e. HBO) as a result of their work on rates of bubble formation during air and oxygen recompression.[1] The UHMS recommends treatment with HBO at 2.8 ATA, repeated up to 10 times if symptoms persists in the case of decompression sickness, or until no further improvement is seen, usually after 5 to 10 treatments (no further details available).[3]

Evidence
The highest level of relevant evidence for decompression sickness comprised 15 reports of case series; there were no controlled studies.[1] A Cochrane review found two RCTs but these did not use appropriate control groups to assess the efficacy of HBO treatment (one assessed the effect of adding an NSAID to HBO and the other assessed the effect of helium plus oxygen compared with oxygen alone). The reports on the case series suggested that many cases were effectively treated by HBO, with 30 to 98% of patients experiencing full recovery, although the limitations of such studies were recognised (absence of control group, selection bias, poor reporting).[1]

Three case series were identified that studied the effect of HBO on gas embolism specifically. These provided conflicting evidence, but were limited by the relatively small size of the studies, the use of different treatment schedules and insufficient detail in the reporting.

Comments
In spite of the lack of robust evidence for these two indications, treatment with HBO is considered to be standard, based on theoretical plausibility, clinical consensus and absence of alternative treatments.

B.2. Acute CO poisoning

This indication is discussed here because of the perception that HBO treatment is standard care for patients with acute CO poisoning. However, such treatment is not generally recommended in the UK (see National guidance below).

Carbon monoxide binds to haemoglobin (forming carboxyhaemoglobin), with an affinity about 200-fold greater than oxygen, and also increases the affinity of the unoccupied sites for oxygen, thereby reducing the capacity of the blood to carry oxygen as well as to deliver it.[4] This leads to oxidative stress, cell apoptosis,

inflammation and necrosis, neurological and cardiac damage and potentially, death. Neurological and psychological sequelae may persist or develop days or weeks after acute CO poisoning, in up to 50% of poisoned patients.[5] These effects are thought to involve mitochondrial dysfunction and lipid peroxidation in the brain. They may include cognitive, affective and motor disturbances, peripheral neuropathy, hearing loss, and dementia and psychosis.[5]

Postulated mechanism of action of HBO

The elimination half-life of carboxyhaemoglobin is 4 to 6 hours in room air, and 80 to 100 minutes with administration of 100% oxygen at atmospheric pressure (normobaric oxygen, NBO). HBO at 3 ATA decreases the half-life to about 20 minutes[4] (no primary references provided in article). Furthermore, HBO at 3 ATA increases the oxygen dissolved in the plasma from about 3 ml/L at normal pressure to about 60 ml/L, which is almost sufficient to supply the requirement of many tissues independent of oxygen bound to haemoglobin.[4] Whether HBO improves survival or long-term outcomes compared with 100% oxygen at normal pressure is recognised to be unclear from the evidence (see below).

National and international guidance

In the UK, the National Poisons Information Service (NPIS), on the website Toxbase, stated in 2008 that: "Treatment with hyperbaric oxygen is not currently recommended, because there is insufficient evidence that hyperbaric oxygen therapy improves long-term outcomes of people with severe monoxide poisoning, compared with standard oxygen therapy."[6]

NHS Direct, in NHS Choices, states: "There is currently insufficient evidence regarding the long-term effectiveness of HBO for treating severe cases of CO poisoning. Therefore, standard oxygen therapy [100% oxygen given through a mask] is usually the recommended treatment option." <accessed 05/09/2011>

A NICE topic selection panel rejected the treatment of CO poisoning with HBO as a topic for a potential technology appraisal in 2008.

The national position in the UK is confused by a letter issued by the DH on CO poisoning in November 2010 which states:[2]

> ***"Indications for hyperbaric oxygen therapy (HBOT)***
> *There is debate about the added value provided by hyperbaric oxygen. A COHb concentration of >20% should be an indication to consider hyperbaric oxygen and the decision should be taken on the basis of the indicators listed below:*
> - *Loss of consciousness at any stage;*
> - *Neurological signs other than headache;*
> - *Myocardial ischaemia /arrhythmia diagnosed by ECG; or*
> - *The patient is pregnant.*
>
> *HBOT is also thought to be of use for extensive exposure to CO and if neurological damage is suspected, its use should be on a case by case basis."*
> Under Management:
> *"Consider referring for hyperbaric oxygen treatment."*
>
> However, the DH Letter also states that advice from Toxbase should be followed, which specifically does not recommend the use of HBO.

Recommendations (by three specialists in an "ABC" article in the BMJ in 1998) following acute CO poisoning were that patients who were unconscious, or had convulsions, neurological impairment (including abnormal gait or mental state test results) or severe metabolic acidosis, should be discussed with the nearest regional centre with HBO facilities (no references provided in article).[4] Patients with less severe poisoning should be treated with normobaric 100% oxygen.[4]

A US Department of Health and Human Services policy paper published in the Annals of Emergency in 2008 (based on a report from the American College of Emergency Physicians) stated that: "*HBO_2 is a therapeutic option for CO-poisoned patients; however, its use cannot be mandated. No clinical variables, including carboxyhaemoglobin levels, identify a subgroup of CO-poisoned patients for whom HBO_2 is most likely to provide benefit or cause harm.*"[7] This was a Level C recommendation, the lowest level of strength of evidence relating to the degree of clinical certainty, which was defined as "*representing other patient management strategies that are based on preliminary, inconclusive, or conflicting evidence, or based on committee*

consensus." The policy was not intended for application to patients with delayed presentations (longer than 24 hours after cessation of exposure) of CO poisoning.[7]

The UHMS recommends HBO for cases where coma, unconsciousness, seizures, focal neurological deficits or cardiac effects are present.[3] HBO treatment is recommended at 2.4 to 3.0 ATA for up to 120 minutes, repeated within 6 to 8 hours if neurological dysfunction persists, until there is no further improvement.[3]

Evidence

A Cochrane review found six RCTs that used clinical outcomes measuring the effect of HBO following acute CO poisoning compared with NBO.[8] The trials were of varying quality, with a total of 1,361 patients (one of the trials was available only as an abstract of an interim analysis). Included patients had CO poisoning of varying severity, and different regimens of HBO and NBO were used. Two trials used "sham" dives for the control group, exposing patients to NBO in a hyperbaric chamber, and these trials were stated to be double-blind. Virtually all patients received supplemental oxygen prior to randomisation, but the exact time point after CO exposure at which patients were treated with HBO or NBO is not clear from the review. Extent of follow-up was considered to be poor and the risk of bias high, according to the authors of the review.[8] Most of the RCTs focussed on outcomes determined by non-specific self-reported symptoms. Several of the trials were terminated prematurely and at least in one, this resulted in lack of power to detect differences between treated groups.[9] (This trial had two parts: one compared HBO with NBO and the other compared one or two sessions of HBO added to NBO. At the interim analysis, recovery rates were significantly lower with two sessions of HBO compared with one session, and the trial was halted. The other part of the trial comparing HBO with NBO was also halted because no difference was seen between the groups and it was felt to be "futile" to continue. However, at that point, only 179 patients had been randomised into this part of the trial as opposed to the 490 that had been calculated would be required to show a significant difference. Therefore, the trial was significantly underpowered.)

Of the six trials, two found a beneficial effect of HBO for the reduction of neurological sequelae at four to six weeks after randomisation, while the other four trials found no benefit. A meta-analysis combining results of all six trials found no evidence of benefit, with an odds ratio for neurological deficits for HBO compared with NBO of 0.78, 95% CI 0.54 to 1.12. [8] However, significant methodological and statistical heterogeneity was found among the trials, which made the result of the meta-analysis less certain. Only one of the two trials including a "sham" control group found a positive benefit. The authors concluded that additional clinical trials comparing HBO with NBO are "ethical, warranted and necessary" because of the many limitations of the currently published trials. [8]

A randomised, double-blind, clinical trial is underway to compare the effect of one versus three HBO sessions on the incidence of cognitive sequelae at six weeks after acute CO poisoning. The study was begun in 2007 and the estimated completion date is May 2013 (ClinicalTrials.gov number NCT00465855).

Comments

The available evidence provides no clear indication of any additional benefit with the use of HBO compared with NBO, for the incidence of neurological or neuropsychological symptoms caused by acute CO poisoning at about four to six weeks after randomisation for treatment. Theoretically, HBO when given soon after exposure to CO would lead to a more rapid elimination of CO from the body and potentially a shorter hospital stay; however, none of the studies reported results for this outcome. No trials were found that studied the effect of HBO treatment given after the acute phase of CO poisoning.

C. Indications for which reasonable evidence indicated no efficacy for HBO (Table 2, p. 15)

C.1. Multiple sclerosis

One systematic review and meta-analysis (an update of an earlier Cochrane review by the same authors) found 12 RCTs conducted between 1983 and 1987.[10] The meta-analysis concluded that there was no clinically significant benefit from the administration of HBO. Most of the trials tested HBO against placebo, at pressures between 1.75 and 2.5 ATA daily, in 20 treatments over four weeks.

In March 2003, NICE stated that HBO "should not be used in patients with multiple sclerosis because research evidence did not show beneficial effects on the course of the condition." (NICE CG 8, 2003).

D. Indications for which the evidence is suggestive and further research is warranted (Table 3, p. 15)

D.1. Diabetic foot ulcer (Table 3a, p. 16)

Chronic wounds are defined as lesions that take a long time to heal, fail to heal or recur. The most common chronic wounds in western countries are diabetic foot ulcers. It has been estimated that 15% of patients with diabetes mellitus suffer foot ulceration (caused by neuropathic and vascular complications), and in these patients the amputation rate is 15-70 times higher than in the general population.[11] Other common chronic wounds are venous leg ulcers (caused by sustained high venous pressures), arterial leg ulcers (caused by arterial insufficiency), and pressure ulcers (caused by unrelieved pressure or friction). Treatment of chronic wounds involves multidisciplinary approaches including treating underlying pathology, systemic treatment such as nutritional supplements, and local treatment to improve the wound environment, such as dressings and pressure-relieving mattresses. However, chronic wounds are resistant to treatment and may slowly progress despite treatment.

In 2011, the Drug and Therapeutics Bulletin (DTB) commented on the incidence of major amputations (at the ankle or above) related to type 2 diabetes in the UK.[12] This incidence rose from 2.0 to 2.7 per 100,000 population between 1996/7 and 2005/6. NICE has advised that in-patients with a diabetic foot problem should be referred to a multidisciplinary specialist foot team,[13] but audit data showed that 20% of hospitals did not have such a team and only 28% of inpatients with diabetes had their feet checked while in hospital. The DTB report further cites evidence that showed a two-fold variation between strategic health authorities in England in major amputation rates in people with type 2 diabetes, and an eight-fold variation between primary care trusts in major amputation rates related to diabetes.[12]

Postulated mechanism of action of HBO

HBO therapy is thought to decrease hypoxia of wound tissue, enhancing perfusion, reducing oedema, promoting collagen production, and angiogenesis.[3] However, the role of oxygen in wound healing is complex[11] and is based largely on *in vitro* studies. Angiogenesis appears to be stimulated by hypoxia, while other phases of tissue repair are oxygen-dependent, e.g. fibroblast proliferation and bacterial killing by macrophages. Therefore, a correct balance between hypoxia in the wound and oxygenation around the wound appears to be associated with successful healing.[11] This makes prediction of the effect of raising tissue oxygen pressure on wound healing difficult.

Evidence

The primary source evidence, which consists of six published RCTs,[14-19] several non-randomised controlled studies, and a number of case series, has been assessed in various combinations in many systematic reviews. Subsequent systematic reviews and HTAs have assessed or summarised older reviews, thereby creating a large body of reports that is based on a small group of primary studies. None of the systematic reviews analysed all six RCTs. The RCTs are summarised in Table 3a and described below.

The RCTs were published between 1992 and 2010, and varied considerably in quality of design, patient inclusion criteria, details of treatment regimen, follow-up periods and completeness of reporting. The number of patients in individual studies ranged from 18 to 100. Included patients had diabetes with foot or lower extremity ulcers that were described as “chronic” or had failed to heal with standard therapy over specific periods ranging 4 weeks to 6 months across the studies. One study restricted inclusion to patients with wounds of Wagner grade 1 to 3, another used Wagner grade 2 to 4.

In all studies, HBO was adjunctive to standard therapy, which was given to all patients. Standard therapy was described in detail in three studies,[14,17,19] as “regular surgical treatment” with a brief description also mentioning antibiotics in one trial,[15] as “conventional medical treatment” with a brief description,[18] and as “daily wound care” with a brief description.[16] HBO was compared with either hyperbaric air therapy in a double-blind design (in two trials[14,19]) or no adjunctive therapy in an open design (four trials).

HBO pressure varied from 2.2 ATA to 3.0 ATA, the treatment duration of each session from 30 to 90 minutes, and the number of sessions from 4 sessions over 2 weeks, to 40 sessions over 8 weeks. The main outcomes measured included:

- reduction in wound size
- number of patients with ulcer healing
- number of major (or proximal) amputations
- number of minor (or distal) amputations

- changes in transcutaneous oxygen tension ($TcPO_2$)

The time points at which these outcomes were measured were not stated in two studies.[15,17] One study did not prespecify a duration of follow-up but reported a mean follow-up period of 92 weeks.[16] One study measured wound size at the end of treatment and after a further four weeks.[18] The two double-blind sham-controlled studies assessed outcomes for up to one year.[14,19] (Omission of the time point of assessment introduces the potential for considerable bias if the treated patients and the control patients have different follow-up periods.)

Methodological quality of the trials varied, with Jadad scores ranging from 1 to 4, with three trials scoring 2. (Jadad scores reflect randomisation, blinding and adequate description of trials; 5 is the maximum score.) A power calculation was reported in one of the trials and intention-to-treat analysis in one other.

Wound size reduction. This was measured in two trials including one of the double-blind sham-controlled trials.[14] In one trial[18] (n = 28), the wound size decreased significantly more (by about 20%) during the two-week treatment period with HBO compared with no treatment, but there was no significant difference at final follow-up four weeks later. The second trial[14] (n = 18) also found a difference in the reduction in wound size at the end of treatment (compared with sham treatment) but not at final follow-up assessment at 6 months. In both these trials, wound size decreased more rapidly in the control groups compared with the treated group, resulting in no difference between the groups at the final assessment.

Proportion of ulcers healed. This outcome was measured in three trials. Significant differences were reported between the HBO and control groups in all three trials:

5/8 *vs.* 0/8 at final follow-up at one year ($p < 0.05$)[14]

52% *vs.* 29% of patients after one year ($p < 0.05$, n = 94)[19]

66% *vs.* 0% of patients ($p < 0.05$, n = 100)[16] (in this study no prospectively specified duration of follow-up was reported)

Major amputation. The incidence of major amputation was reported in five studies.[14-17,19] It was measured at variable times after HBO treatment. In the five individual studies, the numbers of amputations in the HBO- and control groups respectively were:

3 *vs.* 1 at one year (total n in trial = 94; p = not significant)[19]

1 *vs.* 1 at one year (n = 18; p = not significant)[14]

2 *vs.* 7 at unspecified times (n = 30; $p < 0.05$)[15]

3 *vs.* 11 at a mean of 57 ± 24 days *vs.* 73 ± 59 days respectively (not pre-specified according to the article (n = 70; $p = 0.016$)[17]

4 *vs.* 24 at unspecified times (n = 100; $p < 0.05$)[16]

If the results are restricted to those from the two double-blind trials with clearly specified follow-up times (at one year, the first two trials listed), then it is clear that there were too few amputations to show any difference in the incidence of major amputation. The authors of the first trial (involving 94 patients) suggested that there may be differences in criteria used for amputation in the different studies, accounting for the large differences in overall rates (e.g. note the incidences in the first trial, conducted in Sweden,[19] and the last trial, conducted in Turkey[16]). Furthermore, if a trial investigator is involved in the decision to amputate, there may be bias in the trials that are not double-blind in design. The quality of standard treatment to treat the ulcer can also be a confounding factor if it is different among the groups. Sufficient information was provided to deduce that such treatment was optimal in three trials[14,17,19] but not in the other three trials.[15,16,18]

Minor amputation. The incidence of minor amputation was reported in four trials but no indication of the time from treatment was given. The differences were reported to be significantly different between the groups in one trial (0 *vs.* 17)[16] but not in the others.[14,15,17]

Comments

Of the three most relevant clinical outcomes measured in the six trials (reduction in wound size, proportion of ulcers healed, and incidence of major and minor amputations), HBO was associated with significant benefit for one, the proportion of ulcers healed, based most reliably on the two double-blind trials with specified follow-up periods. Wound size appeared to be decreased more by HBO than no treatment or sham treatment in two trials, but over time this difference became not significant because of faster healing in the control groups. This raises the question of the durability of effect of HBO, and the possibility that if there is a beneficial effect, treatment would need to be continued chronically.

Because of the small numbers of patients in the trials, variations in the design of the trials (entry criteria, outcomes, follow-up periods, lack of blinding in four trials), and poor reporting of methods (e.g. only three trials providing sufficient information about standard care), no conclusions could be drawn about the possible benefits or lack of benefits on the other relevant outcomes. There is a need for large, adequately powered, double-blind randomised controlled trials, using healing as an outcome at clinically meaningful and pre-specified assessment and follow-up time-points, with explicit entry criteria, allocation concealment, and appropriate comparator therapy.

In March 2011, NICE stated that there was little evidence for the use of HBO for diabetic foot ulcer and that further evaluation of its clinical effectiveness was required before it could be recommended (NICE CG 119, 2011).[13]

A study protocol has been published describing a prospective, double-blind, randomised, controlled clinical trial comparing standard wound care plus adjunctive HBO therapy, with standard wound care only, for the treatment of chronic, non-healing ulcers of foot in patients with diabetes.[20] One hundred and eighteen adult patients with a Wagner grade of 2, 3 or 4 are being recruited. Patients will be treated with HBO daily for six weeks during the treatment phase and then followed up for a further six weeks, with weekly assessment. The primary outcome is freedom from having, or meeting the criteria for, a major amputation up to 12 weeks after randomisation. The study was begun in 2008 and the estimated completion date is November 2012 (ClinicalTrials.gov number NCT00621608).

[Four of the trials described here[14,15,17,18] were included in a Cochrane review published in 2003[21] (and subsequently published in the British Journal of Surgery in 2005[11]). (The review was updated in 2009, but the two additional trials described here were not included.) A fifth trial had been published as an abstract only and has therefore not been included in the current review. The Cochrane review found that, based on pooled data from three of the trials[14,15,17] (total n = 118), the risk of major amputation was significantly lower with HBO compared with control therapy, but added that "in view of the modest number of patients, methodological shortcomings and poor reporting, this result should be interpreted cautiously, and that an appropriately powered trial of high methodological rigour is justified".[21]]

D.2. Chronic refractory radiation-induced proctitis (Table 3b, p. 18)

Postulated mechanism of action
This was not clear from the article.

Evidence
One multicentre, double-blind, RCT randomised 150 patients with refractory "late" radiation-induced proctitis to receive 30 sessions of either HBO at 2.0 ATA or normobaric air at 1.1 ATA, for 90 minutes per session, over a period of 6 weeks.[22] (The time from radiation to the diagnosis of late radiation-induced injury ranged from 2.5 to 155 months in the patients included in the trial.) Measures were taken to preserve blinding of the control group by a brief compression to 1.34 ATA followed by decompression to 1.1 ATA. After 30 sessions, 10 further sessions were provided to selected patients at the discretion of the referring physician, who remained unaware of the allocation. Subsequently, unblinding took place, and the HBO group entered the follow-up phase, with assessment occurring at 3 and 6 months, then at 1, 2, 3, 4, and 5 years. At the time of unblinding, the patients in the control group were crossed over to the active treatment arm, but it is not clear from the article for how long these patients were then treated; this time period would have extended into the follow-up phase.

The SOMA-LENT score (a measure of the severity of radiation-induced complications with a maximum score of 56) was 12.55 and 12.84 in the HBO and sham groups respectively, at the start of treatment. In both groups, the score decreased (indicating improvement) over the six-week double-blind treatment phase, with a significantly greater decrease in the HBO group compared with the sham group (decrease = 5.00 *vs.* 2.61 points, p = 0.015). After the sham group crossed over to active treatment, the difference between the two groups became not significant, but it is not clear for how long treatment with HBO was continued or at what time point this was measured. During follow up, improvement continued, with no significant differences being reported for the scores in the two groups. At one year, when 105 patients remained in the study, the scores were 5.29 and 6.72 respectively, and at two years (n = 61) they were 3.61 and 6.20 respectively (p values were not reported for times after "completion of crossover"). For the secondary outcome involving a standardised clinical assessment, the percentage of patients considered to be healed or improved was

significantly higher with HBO than with sham treatment (88.9% *vs.* 62.5% respectively) at the end of the double-blind phase. The other secondary outcomes were related to quality of life issues; no statistically significant differences were reported between the groups.

Comments
This trial appeared to be well designed, but was poorly reported. The time points at which the results were obtained were not clear from the article, and the duration of treatment of the control group after cross-over was not stated. What appears to be the time-point at which the double-blind treatment phase was completed was variously referred to as "completion of randomisation" or "post-randomisation" or "completion of initial allocation". The time axis on the graph showing the changes in the SOMA-LENT score is not drawn to scale, and does not clarify the timing of measurements. No statistical comparisons between groups for the primary outcome beyond the first phase were reported. Furthermore, the numbers of patients at the various time points are inconsistent between the trial profile figure and the text.
Potentially, this trial produced valuable information because of the care taken over randomisation and blinding, but the lack of a clear explanation of the methods and results means that the reported results are not convincing. A re-analysis of the primary data, if available, might yield more reliable results, providing the methods were robust. Further research appears to be warranted.

E. Indications for which there was clearly inadequate evidence (in quantity or quality) to support use of HBO (Table 4, p. 19)

The published trials relating to these indications, as described in the QIS Report and relevant Cochrane reviews, was considered to be inadequate to support use of HBO because of absence of controlled trials, conflicting results, poor quality in design (e.g. underpowered because of too few patients, non-clinical surrogate outcomes, high risk of bias), or inadequate reporting (e.g. of randomisation procedure, duration of follow-up, patient population not described adequately, insufficient details of methods used). These limitations made it impossible to draw any conclusions regarding the efficacy of HBO.

On-going studies

Two on-going studies have been mentioned under CO poisoning and diabetic foot ulcer above. Other on-going trials throughout the world that have clinical outcomes and are registered with ClinTrials.gov, the ISRCTN Register and the NIHR, include the following:

Controlled trials
HBO therapy:

- as post-operative therapy to reduce complications in diabetic patients undergoing vascular surgery (double-blind RCT, sham control)
- in calcaneal intra-articular fractures (open-label RCT, sham control)
- to prevent osteonecrosis in patients who have taken bisphosphonates (open-label RCT, untreated control)
- for interstitial cystitis (open-label RCT, interstitial instillation of DMSO as control)
- for trigeminal neuralgia (double-blind RCT, sham control)
- to improve erectile function following surgery for prostate cancer (double-blind RCT, sham control)
- to treat mandibular osteoradionecrosis
- for prevention of osteoradionecrosis in patients requiring surgery to the mandible who have previously undergone radiotherapy

Uncontrolled trials
HBO therapy:

- as adjuvant treatment for frost injury
- for persistent post-concussive symptoms after mild traumatic brain injury
- for mandibular osteoradionecrosis
- in patients with white matter hyperintensities
- for treatment of traumatic brain injury
- for post-concussive symptoms

- for the treatment of osteoradionecrosis
- as preconditioning in cardiovascular surgery
- for insulin resistance
- In children with autism (5 uncontrolled studies)
- for lower leg trauma
- for retinitis pigmentosa
- for trigeminal neuralgia
- in chronic traumatic brain injury or post-traumatic stress disorder
- with radiotherapy and temozolomide in adults with newly diagnosed glioblastoma
- to treat long-term gastro-intestinal adverse effects caused by radiation therapy in patients with pelvic cancer

One study of acute CO poisoning in comatose patients was halted after the first interim analysis as there were significantly more patients who recovered at one month in the control arm than in the HBO arm. Another study of acute domestic CO poisoning was terminated "for futility" (no further details provided).

A number of controlled trials are listed as having been completed but no publications have been reported.

On-going studies in the UK

On-going studies in the UK include the last controlled trial in the list on the previous page, which will assess HBO for the prevention of osteoradionecrosis (the HOPON trial http://controlled-trials.com/ISRCTN39634732/hopon). The trial is being run by the University of Liverpool and aims to recruit 200 patients at multiple centres in the UK. Using a randomised, controlled design, HBO therapy plus standard management will be compared with standard management alone (chlorhexidine 0.2% mouthwash and amoxicillin pre-operatively and for five days postoperatively) in patients requiring surgery to the mandible who have previously undergone radiotherapy. The HBO therapy will comprise 20 treatments before surgery followed by a further 10 treatments, using 100% oxygen at a pressure of 2.4 ATA lasting 90 minutes, in a hyperbaric chamber recognised by the BHA. The primary outcome will be the prevention of osteoradionecrosis subsequent to a surgical procedure in the irradiated mandible, assessed as mucosal healing and/or the presence of necrotic bone at six months following surgery. The assessment will be blinded. The study is expected to run until 2014. This appears to be an appropriately designed trial to assess HBO therapy.

Two other studies in the UK are the last uncontrolled trial in the list above, and another study listed with ClinTrials.gov as having unknown recruitment status because the information on the register could not be verified recently (on HBO therapy compared with standard therapy in treating chronic arm lymphedema in patients who have undergone radiation therapy for cancer).

Adverse effects

Barotrauma, pulmonary symptoms and reversible optic symptoms are the most commonly reported adverse effects of HBO, said to occur in up to 20% of patients.[4] A review on the use of HBO for treating diabetic foot ulcer reported that about 20% of patients experienced some degree of middle ear barotrauma, and 60 to 70% a measurable reversible worsening of myopia.[11] The myopia is thought to be an effect of oxygen toxicity, causing deformity of the lens. These effects have also been reported in other studies of HBO.[23,24] As an example, in the study on proctitis, ear pain or ear discomfort (ear barotrauma) occurred in 15.8% patients.[22] Of these, seven had changes in the tympanic membrane and one had tympanic membrane injury and middle ear effusion. Fifteen patients were treated with either decongestants or ventilation tube placement. In this study, four patients had transient myopia and two had confinement anxiety.

Claustrophobia and decompression illness during HBO therapy have also been reported.[9,25,26] Oxygen-induced seizures have been reported rarely.[3,27]

Untreated tension pneumothorax is an absolute contraindication to therapy with HBO; relative contraindications are impaired pressure equalization and cardiac disease.[3]

Comments

This topic is remarkable for the very small number of primary studies of efficacy of HBO that are robust, and the large number of reviews of the data, both narrative and systematic. Some reviews, especially those reported by national advisory bodies, are based on other secondary reviews. However, when examined closely, these are all based ultimately on primary evidence that is severely flawed by current standards of robust evidence and does not justify many of the different recommendations made. The example given in the QIS report is of osteoradionecrosis, where five health technology assessments and seven systematic reviews have been published, but each of these identified only two published controlled trials on prevention and one on treatment.[1] This can be misleading, as the existence of many systematic reviews suggests that there is more evidence than is actually the case. Many authors have commented on the scarcity of robust evidence for HBO (e.g. QIS report,[1] ECHM,[28] AETMIS,[29] MSAC,[25] Gill and Bell, 2004[3]). For most of the indications, justification of the use of HBO is based solely on clinical experience and a consensus of experts as expressed by the UHMS and the ECHM,[28] and on the fact that this treatment has been used historically and therefore it is difficult to withdraw it in spite of the absence of evidence. In the 7th ECHM Consensus Conference held in 2004, nearly all the recommended indications for HBO therapy were supported by "level 3" evidence, which was defined as "weak evidence of beneficial action based only on expert consensus or uncontrolled studies".[28]

Much evidence consists of case reports or case series, with no control group. These often show positive effects, but as a result of design flaws, the effect cannot be attributed to HBO therapy. A major problem with case reports is the likelihood of selection bias, i.e. the reporting of cases only where the outcome was positive. As has been pointed out by others,[1,3,30,31] robust controlled trials, preferably randomised, are needed if treatment is to be based on evidence. Although clearly it is difficult to conduct a randomised controlled trial for this type of treatment, the number of on-going uncontrolled trials, as listed above, is noteworthy, as this suggests that the need for robust evidence is not well understood by practitioners of HBO therapy.

[Completed October 2011, amended 25 November 2011 and 31 January 2012]

Table 1. Indications for which HBO is accepted standard practice, although robust evidence was not found

Indication	Number & type of studies	Results	Justifications for use
Decompression sickness	No controlled trials 15 case series	Suggestive of efficacy; evidence not robust	Theoretical plausibility for recompression treatment with air or oxygen, clinical consensus Addition of oxygen approved by HSE in 2001, now considered standard (cost implications negligible according to the QIS Report)
Gas embolism associated with decompression sickness or surgery	3 case series (with > 5 patients)	Inconclusive; evidence not robust	Theoretical basis, clinical consensus

Table 2. Indication for which reasonable evidence indicated no efficacy for HBO

Indication	Number & type of studies (n)	Comments
Multiple sclerosis	Cochrane review of 12 RCTs[10]	No plausible benefit identified by meta-analysis

Table 3. Indications for which for which the evidence was suggestive (for details see Tables 3a and 3b)

Indication	Number & type of studies (n)	Comments
Diabetic foot ulcer	6 RCTs (340)	Results suggestive but inconclusive because of poor quality of trials and reporting; robust research required (also recommended by NICE CG119, 2011)
Refractory radiation-induced proctitis	1 RCT (150)	Well designed but poorly reported trial; results suggestive of benefit with HBO; robust research required

Table 3a. Diabetic foot ulcer: Summary of randomised controlled trials

Study (n randomised)	**Patient criteria**	**Methods**	**Treatment arms (n)**	**Main outcome measures** Primary *Secondary*	**Results** HBO *vs.* control
Abidia *et al*., 2003[14] Single-centre DB RCT (n = 18) Jadad: 4 Power calculation provided No ITT analysis	**Inclusion criteria**: Patients with diabetes and lower extremity ulcer 1 to 10 cm in diameter, which had not shown any signs of healing for > 6 weeks since presenting. Patients for whom vascular surgery, angioplasty or thrombolysis was planned were excluded.	1 session daily for 5 days per week for 6 weeks (= 30). Session involved 90 min at 2.4 ATA. Assessment at 6 weeks, 6 months, 1 year.	Hyperbaric oxygen (9) Hyperbaric air (9) All patients had standard treatment involving multidisciplinary wound care.	• Mean reduction in ulcer size at 6 weeks • *Mean reduction in ulcer size at 6 months* • *Number of ulcers completely healed at 6 weeks* • *Number of ulcers completely healed at 1 year* • *Major amputation* • *Minor amputation*	• 100% *vs.* 52% * • *100% vs. 95% ns* • *5/8 ulcers vs. 1/8 ns* • *5/8 vs. 0/8 ** • *1 vs. 1 ns* • *1 vs. 0 ns*
Londahl *et al*., 2010[19] Single-centre DB placebo-controlled RCT (n = 94) Jadad: 3 No power calculation provided ITT analysis	**Inclusion criteria**: Patients with diabetes and at least one full-thickness wound below the ankle for > 3 months. Previously treated at a diabetes foot clinic for ≥ 2 months. Patients had adequate distal perfusion or non-reconstructable peripheral vascular disease. If patients had an acute foot infection, they were included only when the acute phase was resolved. **Exclusion criteria**: Contraindications for hyperbaric treatment (severe COPD, malignancy, untreated thyrotoxicosis), current drug or alcohol misuse, vascular surgery in lower limbs within last 2 months.	Treatment given 5 days per week for 8 weeks[a] (= 40). Session involved 5 min compression in air, treatment period at 2.5 ATA for 85 min, decompression for 5 min. Assessment: weekly during treatment, then 3-monthly up to 1 year.	Hyperbaric oxygen (49) Hyperbaric air (45) All patients had multidisciplinary standard treatment including treatment of infection, revascularization, debridement, off-loading.	• Healing of index ulcer (definition provided) at 1 year • *Major amputations after 1 year* • *Death*	No. patients completing > 35 sessions: 38 (HBO), 37 (air) • 52% *vs.* 29%* • *3 vs. 1* • *1 vs. 3*
Doctor *et al*., 1992[15]	**Inclusion criteria**: Patients with diabetes and chronic foot	4 sessions over 2 weeks.	Hyperbaric oxygen (n not stated)	• Major amputations (period not stated)	• 2 *vs.* 7*

Single-centre RCT (n = 30) Jadad: 2 No power calculation provided No ITT analysis	lesions.	Session involved 45 min at 3.0 ATA.	Standard treatment only (n not stated) All patients had "regular surgical treatment" with a brief description provided, also mentioning antibiotics.	• Minor amputations (period not stated) • Hospital stay	• 4 *vs.* 2 ns • 41 *vs.* 47 days
Faglia *et al*., 1996[17] Single-centre RCT (n = 70) Jadad: 2 Power calculation provided No ITT analysis	**Inclusion criteria**: Patients with diabetes and foot ulcer Wagner grade 2 to 4.	Average number of sessions given = 38 ± 8. Session involved 90 min at 2.2 to 2.5 ATA.	Hyperbaric oxygen (35) Standard treatment only (30) All patients had standard treatment involving multidisciplinary wound care.	• Major amputations (performed at 57 ± 24 days *vs.* 73 ± 59 days) • Minor amputations (period not stated) • Increase in TcPO2 during hospital stay	• 3 *vs.* 11* • 21 *vs.* 12 ns • 14.0 ± 11.8 *vs.* 5.0 ± 5.4 ***
Kessler *et al*., 2003[18] Single-centre RCT (n = 28) Jadad: 2 No power calculation provided No ITT analysis	**Inclusion criteria**: Patients with diabetes and foot ulcer Wagner grade 1 to 3, not improved over 3 months.	2 sessions daily for 5 days per week for 2 weeks (= 20). Session involved compression in air for 15 min, 3 x 30-min sessions at 2.5 ATA separated by 5-min periods on air, decompression for 15 min.	Hyperbaric oxygen (14) Standard treatment only (13) All patients had "conventional medical treatment" with a brief description provided.	• Reduction in wound size at end of treatment • Reduction in wound size 4 weeks later • Increase in TcPO2 during hospital stay	• 41.8 ± 25.5 cm^2 *vs.* 21.7 ± 16.9* • 61.9 ± 23.3 cm^2 *vs.* 55.1 ± 21.5 ns • ns
Duzgun *et al*., 2008[16] Single-centre RCT (n = 100) Jadad: 1 No power calculation No ITT analysis	**Inclusion criteria**: Patients over 18 years with diabetes and foot wound present for ≥ 4 weeks despite appropriate care. **Exclusion criteria**: Untreated pneumothorax, COPD, history of otic surgery, upper respiratory tract infection, febrile state, history of idiopathic convulsion, hypoglycaemia, current use of corticosteroid, amphetamine, catecholamine, or thyroid hormone. **At baseline**, the HBO group had significantly more males, smokers, and obese patients.	2 sessions on odd days and 1 session on even days for 20 to 30 days (max = 45). Session involved 90 min at 2 to 3 ATA. Mean duration of follow-up = 92 ± 12 weeks.	Hyperbaric oxygen (9) Standard treatment only (9) All patients had "daily wound care" with a brief description provided.	Number of patients with: • Total healing • Distal amputation • Proximal amputation • No change	• 33 *vs.* 0 * • 4 *vs.* 24 * • 0 *vs.* 17 * • 9 *vs.* 0 *

RCT, randomised controlled trial; DB, double-blind; ITT, intention to treat; COPD, chronic obstructive pulmonary disease; ATA, atmosphere absolute; min, minutes; $TcPO_2$, transcutaneous oxygen tension before and after a HBO therapy course
*, $p < 0.05$;***, $p < 0.001$
[a], Used multi-place chambers so patients from both groups could be treated simultaneously (100% O_2 or air, supplied in double-blind pipes).

Table 3b. Chronic refractory radiation-induced proctitis: Summary of randomised controlled trial

Study (n randomised)	**Patient criteria**	**Methods**	**Treatment arms (n)**	**Main outcome measures** Primary *Secondary*	**Results** HBO *vs.* control
Clarke *et al*., 2008[22] Multi-centre DB placebo-controlled cross-over RCT (n = 150) Jadad: 3 No power calculation provided Not ITT analysis	**Inclusion criteria**: Patients with "late" radiation proctitis after pelvic radiotherapy, refractory to other treatment for ≥ 3 months.	Treatment given once daily for 5 days per week for 6 weeks (= 30) + potentially 10 further sessions. Session involved HBO at 2.0 ATA or normobaric air at 1.1 ATA for 90 min. Trial unblinded after 6 weeks & control patients crossed over to HBO. Treatment duration not stated. Assessment: at 3 and 6 months, and years 1 to 5.	Hyperbaric oxygen (75) Normobaric air (75)	• Changes in the (SOMA-LENT) score after DB phase • *Standardised clinical assessment: % healed or improved* • *Bowel Function and Bowel Bother subscales of the Bowel domain of a QoL survey* • *Change in quality of life using the physical and mental results from the SF-12 General Health Function Survey*	• -5.00 *vs.* -2.61 ** • 88.9% *vs.* 62.5%** • *Comparisons between groups not reported* • *No differences observed*

RCT, randomised controlled trial; DB, double-blind; ITT, intention to treat; ATA, atmosphere absolute; min, minutes; SOMA-LENT score, score on the Late Effects Normal Tissue – Subjective, Objective, Management, Analytic scale (provides an ascending order of severity of radiation-induced complications, maximum score = 56)
**, $p < 0.01$

Table 4. Indications for which inadequate evidence for efficacy exists

Indication	Source of conclusion	Number, type of studies (total n)	Results; reasons why treatment not considered justified
Chronic wounds			
Venous ulcers	Cochrane review (Kranke, 2009[21])	1 RCT (16)	Poor quality trials
Arterial & pressure ulcers	Cochrane review (Kranke, 2009[21])	No trials	No adequate evidence
Acute injury			
Thermal burns	Cochrane review (Villanueva, 2009[32])	2 RCTs (141)	Poor quality trials
Traumatic brain injury	Cochrane review (Bennett, 2009[33])	5 RCTs (442)	Poor quality trials
Acute soft-tissue injury	QIS report 2008[1]	1 RCT (36)	Poor quality trial
Blunt chest injury	QIS report 2008[1]		
Delayed-onset muscle soreness and closed soft tissue injury (including ankle sprain & knee ligament injury)	Cochrane review (Bennett, 2010[34])	9 RCTs (219)	Small trials, no evidence for benefit (pain worsened)
Surgery			
Grafts and flaps	QIS report 2008[1]	1 RCT (48)	Old study (1967) of poor quality
Orthopaedics, fracture healing	Cochrane review (Bennett, 2008[35])	No RCTs	No adequate evidence
Surgery	QIS report 2008[1]	1 RCTs (24)	Poor quality trials, surrogate outcomes
Surgical & traumatic wounds	Cochrane review (Eskes, 2010[36])	3 RCTs (219)	Trials at high risk of bias
Infections			
Necrotising soft-tissue infections	QIS report 2008[1]	No RCTs	No adequate evidence
Surgical site infections	QIS report 2008[1]	1 non-randomised trial (32)	Small trial, poorly reported
Livedoid vasculopathy	QIS report 2008[1]	No controlled trials	No adequate evidence
Periodontitis	QIS report 2008[1]	1 RCT (24)	Poor quality trial
Malignant otitis externa	Cochrane review (Phillips, 2011[37])	No RCTs	No adequate evidence
Cardiovascular			
Acute coronary syndrome	Cochrane review (Bennett, 2009[38])	5 RCTs (536)	Poor quality trials
Stroke	Cochrane review (Bennett, 2009[39])	6 RCTs (283)	Inconsistent results, impossible to draw conclusion
Cardiopulmonary bypass	QIS report 2008[1]	1 RCT (64)	Outcomes not clinical
Cancer & radiation-induced			
Tumour sensitisation to radiotherapy	QIS report 2008[1]	Unclear from reviews	Inconsistent findings, poor quality trials
Soft-tissue radionecrosis other than proctitis	Cochrane review (Bennett, 2010[40]) Systematic review (Spiegelberg, 2010[41])	8 RCTs (566) 1 RCT (26), 7 other controlled	Evidence suggestive only, no conclusions possible RCT found no benefit, 2 other trials found

		trials (277) (3 prospective)	benefit, results inconclusive
Teeth implantation in irradiated patients	Cochrane review (Esposito, 2008[42])	1 RCT (26)	No differences found
Osteoradionecrosis post tooth extraction in irradiated patients	Systematic review (Fritz, 2010[43])	1 RCT (37) & 8 case-control trials (569)	Poor quality trials, inconclusive results
Neurological & pain			
Headache & migraine	QIS report 2008[1] Cochrane review (Bennett, 2009[44])	4 RCTs (8 - 40) 9 RCTs (201)	Results inconclusive Small trials, no evidence for prevention, weak evidence for relieving
Idiopathic sudden hearing loss, tinnitus	Cochrane review (Bennett,2010[45]) Controlled trial (Cekin, 2009[46]) Controlled trial (Ohno, 2010[47])	7 RCTs (392) 1 controlled trial (57) 1 controlled trial (92)	Evidence suggestive only No difference found No difference found
Pain syndromes	QIS report 2008[1]	2 controlled trials (121)	Poorly reported , no conclusions possible
Miscellaneous			
Urology	QIS report 2008[1]	1 RCT (21)	Small study, no benefit in 1° outcome
Chronic hepatitis	QIS report 2008[1]	1 RCT (60)	Poorly reported, laboratory outcomes
Crohn's disease	QIS report 2008[1]	No controlled trials	No adequate evidence
Bell's palsy	QIS report 2008[1]	1 RCT (79)	Poorly reported , no conclusions possible
Eye disorders	QIS report 2008[1]	3 RCTs (111)	Poorly reported , no conclusions possible
Infertility	QIS report 2008[1]	1 controlled trial (32)	Poorly reported, outcomes not clinical
Severe anaemia	QIS report 2008[1]	No RCTs	No adequate evidence
Calciphylaxis	QIS report 2008[1]	No RCTs	No adequate evidence
Cardiac neural dysfunction in diabetic patients with foot ulcers	QIS report 2008[1]	1 RCT (38)	Poor quality trial, outcomes not clinical
Autism	QIS report 2008[1]	No RCTs	No adequate evidence
Cognitive impairment	QIS report 2008[1]	No RCTs	No adequate evidence
Cerebral palsy	QIS report 2008[1]	3 RCTs (n unclear)	Trials considered experimental
CO poisoning	Cochrane review (Buckley, 2011[8])	6 RCTs (1,361)	Poor quality trials, inconclusive results

Literature Search Protocol

Subject: Hyperbaric oxygen **Date of searches: August/October 2011**

Review question		What is the efficacy and safety of hyperbaric oxygen therapy for any indication?
Search strategy	*Sources*	See table below
	Search terms	hyperbaric oxygen, HBO, HBOT (in title only)
	Publication period	2008-2011
	Restrictions	Humans, English
Inclusion criteria	*Study design*	Efficacy: any controlled trials (n > 10 patients), systematic reviews Safety: any study
	Population	Patients with a defined condition
	Intervention	Hyperbaric oxygen added to standard treatment
	Comparator	Any, including standard treatment alone
	Outcomes	Any clinically meaningful outcome relevant to the indication being assessed
	Publication	Peer-reviewed journal
Exclusion Criteria	*Study design*	Uncontrolled trials, unpublished trials, conference proceedings, abstracts only, preliminary reports, narrative reviews
	Outcomes	Not clinically meaningful

Sources searched

Source	**Date searched (2011)**
Medline 2008-2011	04/08
Cochrane Library 2008-2011	05/08
NHS Direct	05/09
ClinicalTrials.gov	19/08
DH website	19/09
Toxbase (NPIS)	05/09
NICE website	22/08
NHS Choices	05/09
SIGN	19/09
Clinical Evidence	05/09
CKS	05/09
British Hyperbaric Association (http://www.hyperbaric.org.uk/)	22/08
Hyperbaric Medicine Unit (Scotland) (http://www.hyperchamber.com/)	22/08
Undersea and Hyperbaric Medical Society (http://membership.uhms.org/)	22/08
European Committee for Hyperbaric Medicine (ECHM) Consensus Conference, 2004	19/09
AETMIS, Quebec; AETNA Insurance	19/09
Blue Cross Blue Shield	19/09
ClinTrials.com	13/10
NIHR National Research Archive; ISRCTN Register	13/10

Section 2: Supporting information

Regional policies for HBO therapy in England

Some regional policies exist, for example, for the East Midlands and a group in the South of England covering all indications, and a Consortium in Derbyshire, South Yorkshire and Bassetlaw for some indications. A local policy has been developed for South Staffordshire PCT for one indication. These are summarised in Table 5 on p. 26.

HBO therapy facilities available

HBO therapy chambers are classified into four categories depending on the suitability for different types of patients, the availability of medical staff and facilities, and whether one or more patients can be accommodated at the same time.

The Code of Practice of the BHA defined the categories of chambers as follows:

> **Category 1** (Multi-place chambers)
> Comprehensive hyperbaric facilities capable of supporting the treatment of patients who are critically ill, from any cause, and who may require hyperbaric intensive care.
>
> **Category 2** (Multi-place chambers)
> Facilities capable of receiving elective or emergency referrals for any accepted application of HBO therapy, but excluding patients who are critically ill at the time of referral or are considered likely to become so.
>
> **Category 3** (Multi-place chambers)
> Facilities without some of the capabilities of Categories 1 or 2, which are sited specifically to support diving projects (either commercial or recreational) and work in compressed air. These facilities should also be capable of providing elective treatment of residual symptoms of decompression illness.
>
> **Category 4** (Mono-place chambers)
> Facilities operating at relatively low pressure and without an air-lock capability. The expectation is that such chambers providing a treatment on behalf of the NHS or the private health care sector would normally be sited within the boundaries of, or in very close proximity to, a hospital. These facilities should be capable of receiving elective and emergency referrals of patients in any diagnostic category where the Medical Director or Hyperbaric Duty Doctor supervising the treatment judges that a requirement to have access to the patient during hyperbaric treatment is unlikely. Normally mono-place chambers are not suitable for the immediate treatment of acute decompression illness.

(The BHA also uses slightly different definitions on its website, which were used by the DH Specialised Services National Definition Set: 28 Hyperbaric treatment services. These alternative definitions are listed in Appendix 1 on p. 29.)

HBO units in mainland England (see Table 6 on p. 27)
HBO facilities in the UK may be independent charities or privately owned. The latter may be based in NHS or private hospital grounds or based outside hospital grounds.

The BHA lists nine centres in mainline England (with additional facilities in Scotland, Wales and on islands within the UK). One of these centres, the Diving Diseases Research Centre (DDRC) in Plymouth uses four units in Plymouth and two in Wales; the other centres listed in Table 6 involve one unit. All the units listed are multi-place chambers, mostly Category 1 with two being Category 2. (Two mono-place chambers, one at Manchester, and one at Peterborough, which are both Category 4 chambers, were not included in Table 6.) The websites of most centres stated that the conditions treated were recompression as well as other conditions; several referred to the list of conditions produced by the UHMS. Several centres, e.g. the Midlands Diving Chamber, have a clear focus on diving, and provide courses, dive “medicals”, and “dry dives”.

As members of the BHA, these centres would be expected to follow the Code of Practice for Health and Safety for Therapeutic Hyperbaric Facilities, and the guideline for Training and Education of Hyperbaric Unit Personnel, both published by the BHA on their website. The Code of Practice does not specify criteria for the

hyperbaric chamber or the procedures used for any treatment. The list of applicable legislation included in the Code does not include any documents that are specific for hyperbaric units or their use, except those related to offshore diving, e.g. The Diving at Work Regulations 1998 and guidance notes from the Diving Medical Advisory Committee and the Association of Offshore Diving Contractors.

The BHA Code of Practice refers to the UHMS and the ECHM 1st European Consensus Conference on Hyperbaric Medicine Report of 1994.

Local facilities
One of the listed centres is in the West Midlands, the Midlands Diving Chamber, at Rugby, which is a Category 2 unit. <http://midlandsdivingchamber.co.uk/index.php>

Other facilities
The Multiple Sclerosis Trust lists MS Therapy Centres that are stated to have HBO treatment available. Their website states: "Research into HBO therapy in multiple sclerosis has failed to find scientific evidence that it is effective. However, anecdotal reports suggest the treatment can be helpful for some people, particularly with fatigue and bladder problems." <http://www.mstrust.org.uk/atoz/HBOT.jsp>

MS Therapy Centres that list HBO therapy available (in England) are at Reading, Milton Keynes, Huntington, St Austell in Cornwall, Exeter, Chelmsford in Essex, Gloucester, Portsmouth, Canterbury, Swanley in Kent, Leicester, Walthamstow in London, Manchester, Norwich, Nottingham, Abingdon, Guildford, Wolverhampton, Leeds, and Warminster. Other Centres list "oxygen therapy" but it is not clear whether this refers to hyperbaric oxygen. <http://www.msrc.co.uk/index.cfm/fuseaction/show/pageid/258>. A survey conducted in 2009 reported that there were 56 MS HBO units.[48]

Standards of HBO therapy facilities
Hyperbaric treatment chambers that are intended for use in Europe should be built and certified according to the European Directives 93/42/EEC "Medical Devices" and 97/23/EC "Pressure Equipment" to ensure that they comply with the relevant European health and safety requirements. The ECHM recommended at the 7th European Consensus Conference on Hyperbaric Medicine (2004) that the performance, testing and safety requirements of new multi-place chamber systems shall conform with the new European norm prEN 14931 CEN TF 127, and that all new chambers shall be CE marked.[28]

In the UK, according to a verbal communication from the MHRA (personal communication with Doug McIver, 01/12/2011), all private and hospital-associated HBO therapy facilities (i.e. all those listed by the BHA) should be CE marked, except those that were in use before 2000 and which pre-date CE marking. These facilities are inspected by the Care Quality Commission for safety using the 2009/105/EC Pressure Vessel Directive and the 97/23/EC Pressure Equipment Directive. According to the communication, these comments do not apply to HBO chambers not being used for "accepted medical treatment" such as those at multiple sclerosis centres.

Staffing at HBO therapy facilities
According to the BHA Code of Practice, each therapeutic hyperbaric chamber shall have one person nominated as the **Hyperbaric Therapy Provider**, who is in overall administrative control of the facility and either employs the medical and technical personnel or provides medical or technical support personally. This person shall ensure that the operation of the facility is conducted in a manner that protects the health and safety of all persons involved (although the professional medical responsibility may be delegated to the Medical Director or the hospital consultant in clinical charge of the case).

Each unit also has a **Medical Director** (who may also be the **Hyperbaric Duty Doctor**) who should be a registered medical practitioner; a postgraduate qualification in a relevant speciality is an advantage. This person should have practical experience and be competent in all medical aspects of therapeutic hyperbaric facility activities, consistent with the types of patients accepted for treatment by the facility in which he or she works.

According to the BHA Code of Practice, the staffing will differ at different facilities, but the minimum team size normally required to be present on site to conduct a safe hyperbaric treatment is three for a multi-place chamber (**Hyperbaric Duty Doctor**, **Supervising Chamber Operator**, and **Chamber Attendant**). The Hyperbaric Duty Doctor should only be allowed to work unsupervised by the Medical Director once he or she has demonstrated his or her competence in a range of standard treatments, and should have access to advice from a more senior colleague when working unsupervised. The Supervising Chamber Operator should be

appointed by the Hyperbaric Therapy Provider in writing; no formal qualification currently exists for this position.

Use of facilities

An example of what kinds of facilities are being used in the UK was provided by a telephone survey of 76 HBO chambers.[48] The treatment of patients for osteoradionecrosis during 2006 to 2007 was surveyed. Twenty-five chambers treated 273 patients during this period, 10 were listed by the BHA and 15 were at MS centres, where 23 (8%) of the patients were treated. Most BHA centres treated patients at 2.2 ATA for 90 minutes per session, for 30 preoperative and 10 postoperative sessions per patient. The MS centres used a variable number of sessions of shorter duration (generally 60 minutes) and lower pressures, typically 2.0 ATA with some using 1.7 ATA.

Funding and costs

According to the Midlands Diving Chamber at Rugby, the NHS funds treatment for decompression illness provided the diver is a UK citizen or resident. The NHS also funds HBO treatment for non-diving medical problems, provided a consultant refers the patient to the chamber doctor, the doctor deems the patient "fit for HBO treatment" after examination, and the patient's PCT agrees to fund the treatment. There is also a charity that may fund treatment, the Diving Chamber Treatment Trust.

The East Midlands policy listed direct costs (using information from IFRs across the East Midlands PCTs). In 2010/11, costs charged to PCTs for treatment of decompression sickness ranged from £22,000 to £42,000, plus a possible "standby cost" for preparing the facilities of £2,900. A case of emergency treatment of CO poisoning was charged at £8,200 in 2008/09.

The NORCOM policy stated that treatment for osteonecrosis cost £4,000 per course per patient, assuming two or more patients being treated in the chamber at the same time, using the facilities at Hull.

Use of HBO in the West Midlands
(information current on 27/01/2012)

IFR manager	Date	Indication	Decision re funding
NHS Coventry	06/2010 to 02/2011	Ulcer (5 requests)	Refused
NHS Warwickshire	09/2009 11/2009 05/2010 09/2010 03/2011	Cancer Osteonecrosis of jaw Radiation tissue damage Wound healing following amputation Pressure sores	Refused Refused Funded Funded Refused
NHS Worcestershire	02/2008 05/2008 05/2008 08/2008 06/2009 09/2009 09/2009 06/2011	Prevention of osteoradionecrosis prior to tooth extraction Pain in arm Suspected decompression illness Diving accident Prevention of osteoradionecrosis prior to tooth extraction Radiation tissue damage Osteoradionecrosis of jaw Large leg wound after surgery & radiotherapy	Refused Refused Funded Funded Refused Refused Refused Pending
Shropshire PCT	2011-2012	Osteoradionecrosis of jaw in cancer patient	Funded (usually fund 2-3 per year)
Birmingham East & North PCT	2010-2011 2011-2012	1 (not specified) 2 (not specified)	Funded Refused

NHS Wallsall	2009-2010 2011-2012	Radiation tissue damage (2 cases) Malignant otitis externa	Funded Funded
South Staffordshire PCT		None (policy in place)	
Heart of Birmingham PCT		None	
South Birmingham PCT		None	
Wolverhampton City PCT		None	
Dudley PCT		None	
North Staffordshire PCT		(did not respond)	
NHS Stoke		(did not respond)	
NHS Herefordshire		(did not respond)	
Telford & Wrekin PCT		(did not respond)	
NHS Solihull		(did not respond)	
Sandwell PCT		(did not respond)	

Table 5. Local policies for HBO therapy in England (selected)

Source	Indications for HBO considered	Decision: Routinely funded/commissioned (*reason given*)	Decision: Not routinely funded/commissioned (*reason given*)	Other comments	Costs according to IFR leads (K = thousand)
East Midlands Specialised Commissioning Group 2011	All as in QIS report	• Decompression illness • Gas embolism • Acute CO poisoning (*Use not supported by RCT level data but given good theoretical basis, long-standing use and clinical consensus, it would be hard to justify further trials*)	• All other indications (*evidence did not support routine use*)	IFR policy to be followed for non-funded indications Exceptional circumstances not anticipated	Decompression illness (2010-11): £22K to £42K per case CO poisoning (2008-9: £8,200 per case
South Central Priorities Committee (Hampshire, Isle of Wight) (Portsmouth PCT) 2009	All indications	• Acute decompression illness • Gas embolism in severe cases (*Limited evidence but QIS report found that for acute decompression illness, there was sufficient empirical evidence, theoretical basis and clinical consensus to support use. For gas embolism the evidence was less robust with a lack of empirical evidence*.)	• All other indications: low priority (*lack of evidence of clinical and cost effectiveness*)		
NORCOM (North Derbyshire, South Yorkshire, & Bassetlaw Commissioning Consortium) 2006	Oral cancer: prevention & treatment of ORN, promoting osseointegration for dental implants, wound healing		• For the indications considered: As the evidence for use of HBO is inconclusive, requests for treatment should be assessed on a case-by-case basis in conjunction with specialist advice from all 3 Directors of Dental Public Health. Patients must meet specific criteria.	Approximately 5 patients per year may be considered	£4K per course per patient (assuming 2 or more patients in chamber at one time) (treatment in the Hull facility)
South Staffordshire PCT 2010	Prevention & treatment of ORN		• For the indication considered: low priority (*lack of clinical and cost effectiveness*)	Exceptional circumstances may be considered	

Table 6. Hyperbaric oxygen chamber facilities in mainland England
(information from BHA, Midlands Diving Chamber websites, individual websites of units)

Facility & location	Multi- or mono-place	Category	Principal Medical Director	Treatment available	Funding	Responsible Health Authority or supporting hospital
London Diving Chamber, St John's Wood http://londondivingchamber.co.uk/index.php?id=hbot	Multi (up to 10)	2	Dr O Firth	Recompression, CO poisoning, others	NHS	Hospital of St John & St Elizabeth
Midlands Diving Chamber, Rugby http://midlandsdivingchamber.co.uk/index.php	Multi	2	Dr T Oxley	Recompression, CO poisoning, others	Not stated	Hospital of St Cross
North of England Medical Hyperbaric Unit, Hull http://www.subaqua.co.uk/North_of_England_Medical_Hyperbaric_Unit	Multi	1	Dr G Purdy, MB BCH BAO FFARCSI MRCP	Not stated	Not stated	E Riding HA (BUPA Hospital)
North West Emergency Recompression Unit, Wirral http://www.oxynet.org/03HBOCenters/centres.php?id=179	Multi	1	Dr J Harrison	Not stated	Not stated	Murrayfield Hospital
DDRC, Plymouth (listed as Charity) http://www.ddrc.org/index.html	Multi (use 4 facilities in England)	1, 4	Dr C Cridge	Recompression, CO poisoning, others (referred by Consultants)	Varies	Plymouth NHS Trust
Poole Hyperbaric Centre, Poole & Reading http://www.thediverclinic.com/	Multi	1	Dr D McCann	@ UHMS list	Not stated	Dorset HA
Whipps Cross University Hospital, London http://www.londonhyperbaric.com/london-hyperbaric-chamber	Multi (system at Great Yarmouth described)	1, 4	Dr P Bothma, Hyperbaric Physician and Consultant in Anaesthesia and Intensive Care	Recompression, CO poisoning, others	Not stated	Whipps Cross University Hospital NHS Trust
East of England Hyperbaric Unit, Great Yarmouth http://www.yarmouthhyperbaric.com/contact.shtml http://www.londonhyperbaric.com/london-hyperbaric-chamber	Multi (also described on Whipps Cross website)	1	Same as on Whipps Cross website	Recompression, CO poisoning, others	Not stated	E Norfolk HA
Hyperbaric Medicine Unit, Chichester	Multi	1	Dr M Glover	@ UHMS list	Not stated	St Richards Hospital

Appendix 1

Alternative definitions of chamber categories (from BHA; these are also quoted by DH Specialised Services National Definition Set: 28 Hyperbaric treatment services)

Category 1

Facilities should be capable of receiving patients in any diagnostic category who may require Advanced Life Support either immediately or during hyperbaric treatment.

Category 2

Facilities should be capable of receiving patients in any diagnostic category who are judged by the referring medical officer not to be likely to require Advanced Life Support during hyperbaric treatment.

Category 3

Facilities should be capable of receiving emergency referrals of divers and compressed air tunnel workers. These facilities should also be capable of providing elective treatment of residual symptoms of decompression illness. Patients may be accepted, in the name of the Medical Director, even when no Hyperbaric Duty Doctor is available at the time of referral provided, when in the view of the referring clinician, the patient's condition demands immediate action. This does not obviate the need for discussion with the Hyperbaric Duty Doctor who should attend the patient as soon as is practicable.

Category 4

Facilities should be capable of receiving elective and emergency referrals of patients in any diagnostic category who are judged by the referring medical officer, on the advice of the Hyperbaric Duty Doctor, not to be likely to require access during hyperbaric treatment. Normally mono-place chambers are not suitable for the immediate treatment of acute decompression illness.

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