# Evidence Summary:

## Hyperbaric Oxygen Therapy

## May 2015

# NHS England

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# Hyperbaric Oxygen Therapy

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# 1. Introduction

## 1.1 Commissioning HBOT

In allocating the resources available for health care, commissioners must take account of the fact that in all health systems across the world, the demands that could be made on the system outstrip the available resources. So, difficult decisions have to be made as to how the resources are distributed, what health care needs will be met and what will not.

In 2008 the NHS confederation published a series of advisory documents that have formed the basis of NHS commissioning[1,2]. Commissioners cannot simply decide whether it is a good thing or not to provide a particular treatment. Rather a commissioning organisation must aim to find the optimal way to invest across all patient groups and at the same time, try to provide a range of healthcare, prevention, treatment, rehabilitation and palliation.

Central to decisions on the distribution of healthcare resources is the need for fair and equitable access to healthcare based on need. A consequence of demand exceeding the available resource is that some treatments that might be effective, cannot always be provided. Because of this, and to ensure decision making is fair and equitable, decisions on whether to routinely commission a treatment, are commonly based on the following factors:

- nature of the health gain, both for the individual and the population as a whole
- confidence in the clinical evidence, i.e. how certain it is that the benefits in research trials are reproducible and will be found in practice
- number of individuals benefiting and the level of improvement
- cost effectiveness, i.e. whether the treatment represents good value for money compared to other treatments for the same and other conditions
- need to redress inequalities and inequities of access, this not only refers to geographic access but also access to proven treatments over more experimental interventions
- accessibility
- national priorities
- clinical risk
- service risk
- absolute cost of the development
- legislation and directives
- patient choice

So, decisions whether or not to commission a treatment rely on both a consideration of the treatment itself and how it compares not only with other treatments for the same condition but also how it compares to treatment options for other health problems. It is the combination of these factors together, rather than any one alone that informs the decision to commit NHS resources.

## 1.2 Evaluating hyperbaric oxygen therapy

In evaluating the evidence base for the clinical and cost effectiveness of hyperbaric oxygen therapy (HBOT), it is clear that the quantity and quality of evidence is less than is present for many other interventions. A number of factors have contributed to this. Amongst them are:

- **The absence of an industry sponsor**. The resources available to undertake evaluative research are often part of the commercial drive to obtain a market share of clinical management. The absence of a single commercial interest in HBOT means that there has not been an obvious source of funding, nor coordinated commercial drive, to develop the evidence base.
- **The nature of the present service model.** The service is predominantly provided by stand-alone independent sector chambers. Historically, medical support has been supplied by the part time commitment of doctors whose main role often lies elsewhere within the NHS. This is still the case in over half of the current providers. Whilst some chambers have an active research programme, in the past, the service has focussed on generating supportive local clinical opinion as a result of positive patient outcomes. In most areas, this has resulted in local referral practice rather than production of a significant research portfolio or accrual of a UK evidence base.
- **Variation of commissioning approach**. With the exception of the management of decompression illness and gas embolism, there has been no consistent approach to the routine commissioning of HBOT and thus little NHS funded opportunity for co-ordinated evaluation.
- **Variable access to chambers**. The majority of chambers are situated in coastal locations, reflecting the longest established use of HBOT. Consequently, many are distant from the centres of greatest population density. Since many indications require daily treatments, the additional cost of local accommodation has often presented a barrier to wider participation in studies.
- **Variable support in referring specialities**. HBOT is an adjuvant therapy for the majority of indications. In most of the referring specialities, the paucity of research evidence in comparison to that available for pharmaceutical agents, together with the accessibility of chambers, has led to generally low levels of awareness and interest in HBOT research as a potential management option, especially amongst clinicians who do not practice in the vicinity of a hyperbaric facility.

Because of this, it attempting to assess the evidence base that exists for the use of HBOT, a number of sources have been used as triangulation points. These are:

- A review of the published research literature
- A survey of NHS clinicians working in acute sector Trusts in the NHS in England, relevant Clinical Reference Groups advising NHS England and the professional bodies of the most significant referring specialties
- Commissioning data (Hospital episode statistics, (HES)) for admissions to hospital for specified indications
- A brief appraisal of the approach to commissioning HBOT in health systems other than the NHS

## 2. Evaluation of Evidence

### 2.1 Published Research

In 2008, NHS Quality Improvement Scotland was commissioned by the NHS to undertake a systematic review of the evidence base underpinning the inclusion of HBOT in the management of a wide range of indications[3]. The conclusions of this review found that:

- for the majority of indications there was insufficient evidence to support the routine commissioning of HBOT as part of the care package
- in the management of decompression illness (DI) and gas embolism, HBOT should be considered as standard care.
- the evidence was supportive of the inclusion of HBOT in algorithms for the management of carbon monoxide poisoning (CO) and radiation proctitis.
- this was not the case for the management of other forms of soft tissue radionecrosis.
- further large scale trials were necessary to establish the place of HBOT in the routine management of lower extremity ulceration in patients with diabetes.

The CRG agreed that this review had identified all relevant research published at that time. It was also agreed that it was clear from this report and a Cochrane Review that a randomised controlled trial was necessary to establish the place of HBOT in the management of lower limb ulceration associated with diabetes. As a consequence, the commissioned literature review did not address the inclusion of HBOT management of that indication. The requirement for further evaluation of HBOT in the management of diabetic lower extremity ulcers is discussed in the conclusions section of this summary (section 4, table 10, p 31)

The CRG identified three indications in which it was thought that there had been significant development since the completion of the QIS evaluation. New reviews of the published evidence were commissioned to assess the current evidence of clinical and cost effectiveness. These indications related to the management of:

- soft tissue radiation damage,
- malignant otitis externa and
- necrotising soft tissue infections.

In addition, because of the recent change in the National Poisons Information Service advice on the management of carbon monoxide poisoning[4] removing it from the advised management protocol, a fourth review was commissioned for this indication.

NHS England commissioned rapid evidence reviews from an independent service provided by Solutions in Public Health (SPH). These topics were of the series of evidence reviews that SPH was commissioned to provide in support of policy development across a range workstreams within specialised services

### 2.1.1 Research questions for the literature review

The research question for the literature review of each indication is given in the table below

**Table 1 Research questions for published evidence review**

| Indication | Research question |
|---|---|
| Carbon Monoxide poisoning | Is there evidence to support the use of HBOT in enhancing recovery from acute carbon monoxide(CO) poisoning (either speed or completeness) compared to conventional treatments with normobaric oxygen?<br>Is there evidence to support the addition of HBOT into the management pathway for acute CO poisoning resulting in a more rapid or complete resolution of neurological sequelae?<br>Is there evidence to describe the patient group who are likely to derive benefit and the intervention that should be used?<br>Is there evidence for the cost effectiveness of HBOT in the management of CO poisoning? |
| Soft tissue radiation damage | Is HBOT clinically effective in patients with soft tissue radiation damage whose symptoms have proved refractory to other modalities of treatment?<br>Is there evidence to suggest that previous or ongoing treatment with Bleomycin might be a contraindication for HBOT for soft tissue radiation damage? |
| Malignant otitis externa | Is the addition of HBOT to standard best treatment (antibiotic treatment and surgical debridement) clinically effective in patients with malignant otitis externa whose symptoms are refractory to treatment with antibiotics and debridement alone?<br>Is there sufficient evidence to identify the patients who are most likely to benefit and the treatment regimes that will produce best outcomes for translation into service provision? |
| Necrotising soft tissue infections | Is HBOT clinically effective in adult patients with necrotising infection compared to conventional treatment with antibiotics and surgical debridement ?<br>Is HBOT cost effective in adult patients with necrotizing soft tissue infection compared to conventional treatment with antibiotics and surgical debridement? |

### 2.1.2 Methodology

Literature searches were carried out during January 2014 and in July 2014 for CO. Searches were undertaken on Medline, Embase, the Cochrane Library, Trip, DARE and NHS evidence for systematic reviews, clinical trials, comparative studies and economic evaluations of HBOT for the listed indications. PubMed was also searched for the previous three months for any e publications ahead of print publication. The search was limited to English language reports and the last 10 years.

In assessing the evidence the Scottish Intercollegiate Guideline Network (SIGN) levels and grading of evidence was used. These are replicated in tables 2 and 3 below.

**Table2: Scottish Intercollegiate Guideline Network (SIGN) levels of evidence**

| Level of evidence | Type of evidence |
|---|---|
| 1++ | High quality meta-analyses, systematic reviews of RCTs (including cluster RCTs), or RCTs with a very low risk of bias |
| 1+ | Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias |
| 1–* | Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias |
| 2++ | High quality systematic reviews of, or individual high quality non-randomised intervention studies (controlled non-randomised trial, controlled before-and-after, interrupted time series), comparative cohort and correlation studies with a very low risk of confounding, bias or chance |
| 2+ | Well conducted, non-randomised intervention studies (controlled non-randomised trial, controlled before-and-after, interrupted time series), comparative cohort and correlation studies with a low risk of confounding, bias or chance |
| 2–* | Non-randomised intervention studies (controlled non-randomised trial, controlled before-and-after, interrupted time series), comparative cohort and correlation studies with a high risk of confounding, bias or chance |
| 3 | Non-analytical studies (eg case reports, case series) |
| 4 | Expert opinion, formal consensus |
| *Studies with a level of evidence (–) should not be used as basis for making recommendations.<br>*Source*: adapted from SIGN (2001). | |

## Table 3: Scottish Intercollegiate Guideline Network (SIGN) Grades of Evidence

| Grades of recommendations |
|---|
| ***Grade 'A'***<br><br>At least one meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population ***or***<br><br>A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results. |
| ***Grade 'B'***<br><br>A body of evidence including studies rated as 2++ directly applicable to the target |

| |
|---|
| population and demonstrating overall consistency of results ***or***<br><br>Extrapolated evidence from studies rated as 1++ or 1+ |
| ***Grade 'C'***<br><br>A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results ***or***<br><br>Extrapolated evidence from studies rated as 2++ |
| ***Grade 'D'***<br><br>Evidence level 3 or 4 ***or***<br><br>Extrapolated evidence from studies rated as 2+ |

*Source: Adapted from the Scottish Intercollegiate Guidelines Network (SIGN), 2001*

### 2.1.3 Results

The detailed reviews for each indications are contained in appendix 1.This section summarises the review findings. Where systematic reviews and randomized controlled trials exist, their results are considered to be more robust than case series or case reports and were appraised instead of the latter. Table 4 shows the discussions and conclusions from the literature reviews and categorises the evidence using the SIGN level and grade of evidence.

The CRG disagreed with the conclusions of the independent literature reviews. The CRG responses are also summarised in this table. A Public Health England comment is also included. The CRG opinions appear in full, as a commentary to the literature reviews, in appendix 1. The appendix also contains the SPH response to the CRG concerns. .

## Table 4 Summary of published evidence

| Published evidence | | | | |
|---|---|---|---|---|
| **Level of Evidence** | **Indication** | **Studies identified** | **Discussion and conclusions of SPH literature review** | **Commentary** |
| | | | | |
| 1- Not able to be graded because of (-) classification | Soft tissue radiation damage | One systematic review, one health technology appraisal | *Q:Is hyperbaric oxygen therapy (HBOT) clinically effective in patients with soft tissue radiation damage whose symptoms have proven refractory to other modalities of treatment?*<br><br>We found limited evidence for this. A number of small trials included in reviews indicate that HBOT is associated with improved outcomes in patients with soft tissue radiation injury affecting tissues of the head, neck, anus and rectum. However the authors point out that a lot of the trials were of poor quality and there were variations in patient inclusion criteria, measurement and reporting of outcomes.<br>The overall evidence suggests that harms associated with HBOT are generally mild and self-limiting.<br>We did not find any UK based cost-effectiveness analysis of HBOT for the management of soft tissue radiation injuries compared to usual care.<br><br>*Q: Is there evidence to suggest that previous or ongoing treatment with bleomycin might be considered a contraindication for HBOT for soft tissue radiation damage?*<br>There is very little such evidence. We did not find any good quality evidence regarding the use of HBOT with or following bleomycin treatment. However we found a case series of 15 patients that studied the administration of HBOT after bleomycin. The study found no persistent post-HBOT pulmonary complications on follow-up.<br><br>The inherent bias associated with this retrospective, single centre study may mean that the findings reported may not be valid and/or generalisable to a larger population of patients. Therefore well conducted studies are needed to evaluate effect of administering HBOT with or following bleomycin treatment. | **CRG**<br>There appears to be poor understanding of the mechanism of action of HBOT. It is the growth of new small vessels that accounts for the enduring benefit of HBOT beyond the treatment period. Prejudice is likely to arise if the reviewing team doubts the biological plausibility of the intervention because it has been undermined by misunderstandings of this nature.<br>Although the review comments that the studies are small and of poor methodological quality, the Cochrane Review had a different opinion of the methodology of at least one of the studies.<br>We do not interpret the findings on cost-effectiveness within the Medical Services Advisory Committee report in the same way as the authors of the review.<br>It is unclear to us how this level of evidence compares with that currently used to sanction a range of interventions currently employed within the NHS such as grommets, statins, hernia repairs etc.<br><br>**PHE**<br>The review was focussed on the effectiveness of HBOT and found only limited evidence.<br>The conclusions of the review are in keeping with those of other reviews, both systematic and undertaken by commissioning bodies[5].<br>There is a large RCT examining the use of HBOT in the management of radiation proctitis and the outcome of this will be informative<br>There is a clear need for further evaluation and the current evidence base is not adequate for routine commissioning. |

| Published evidence | | | | |
|---|---|---|---|---|
| **Level of Evidence** | **Indication** | **Studies identified** | **Discussion and conclusions of SPH literature review** | **Commentary** |
| | | | | |
| 3 Grade D | Malignant otitis externa | Cochrane review and two retrospective case series of 8 and 17 patients respectively | *Q: Is the addition of HBOT to standard best treatment (antibiotic treatment and surgical debridement) clinically effective in patients with malignant otitis externa whose symptoms are refractory to treatment with antibiotics and surgical debridement alone?*<br>We found no convincing evidence to support the clinical effectiveness of HBOT in MOE. Evidence of the effectiveness of HBOT in the management of MOE is based on low quality data i.e. retrospective case reports and case studies from single centres rather than prospective or comparative studies. Without a control arm, it is impossible to make any comparison of outcomes in patients receiving HBOT compared to those receiving standard treatment alone. The inherent biases associated with the available studies mean that the findings reported may not be valid and/or generalisable to a larger population of patients.<br><br>*Q: Is there sufficient evidence to identify the patients who are most likely to benefit and the treatment regimes that will produce best outcomes for translation into service provision?*<br><br>We did not find any evidence of this. The studies found were small, of poor quality lacking randomisation or control; it therefore was not possible to identify which patients with MOE were most likely to benefit from HBOT. The available evidence is inadequate to demonstrate that HBOT is effective in improving outcomes in any patients with MOE, compared to current standard treatment | **CRG**<br>This indication is rare and so to conclude that the evidence base is flawed because of the absence of large systematic trials would appear perverse. The evidence should be judged in the same way as for a rare condition.<br><br>We would have expected the authors to comment upon the accruing evidence of a positive effect of HBOT in this indication and had expected a more considered and detailed appraisal of case reports and case series.<br>We would conclude that what little evidence there is of the use of HBOT in this indication reports universally positive outcomes.<br><br>HBOT is an adjuvant therapy in this indication but the authors repeatedly compare HBOT with standard treatments rather than as an adjuvant.<br>The evidence has been deemed unconvincing but there is no scoring nor systematic characterisation that takes into account the rarity of the condition and would assist those reading these reviews to put the issue into context.<br><br>**PHE**<br>The evidence base is in line with what would be expected considering the incidence and prevalence of this condition and the availability of HBOT facilities. Whilst the case reports and case series catalogue positive responses to HBOT, nonetheless, it is clear that additional studies are required to confirm both effectiveness of HBOT in this condition and the optimal place in the care pathway |

| Published evidence | | | | |
|---|---|---|---|---|
| **Level of Evidence** | **Indication** | **Studies identified** | **Discussion and conclusions of SPH literature review** | **Commentary** |
| | | | | |
| 2- | Necrotising soft tissue infections | One evidence, six retrospective cohort studies and one health technology assessment | *Q: Is hyperbaric oxygen therapy clinically effective in adult patients with necrotising soft tissue infection compared to conventional treatment with antibiotics and surgical debridement?*<br>The current evidence is inadequate to support HBOT as effective in reducing either mortality or amputation for patients with NSTI. There are no randomised controlled trials investigating the effectiveness of HBOT for NSTI. We found five small and one large retrospective cohort study, all of poor quality with high potential for bias and confounding. Only one small, non-randomised study showed positive results for HBOT in terms of reducing both mortality and amputation rates for patients with NSTI, but systematic differences mean this evidence is insufficient to be able to draw firm, generalisable conclusions about the benefits of HBOT in treating NSTI.<br><br>*Q: Is hyperbaric oxygen therapy cost effective in adult patients with necrotizing soft tissue infection compared to conventional treatment with antibiotics and surgical debridement?*<br>We did not find any UK based cost-effectiveness analysis of HBOT for the management of NSTI compared to usual care | **CRG**<br>Whilst it is clear that the evidence base falls short of that usually expected for treatment options for common disorders the CRG is of the opinion that the evidence is commensurate with the rarity of this condition. What little evidence there is appears to support strongly the clinical impression that the addition of HBOT into the standard management regimes reduces both mortality and amputation rates. There appears to be a dual standard in operation in the review with some case series deemed to give acceptable evidence of risk factors attributable to HBOT whilst the same or similar case series are not considered adequate to demonstrate that differences in outcome can be attributed to HBOT<br><br>**PHE**<br>The absence of an agreed place in the management pathway together with small study numbers and significant heterogeneity in case presentation means that it is impossible to be certain of the value of HBOT in the management of this indication. Additional well designed trails are required. |

| Published evidence | | | | |
|---|---|---|---|---|
| **Level of Evidence** | **Indication** | **Studies identified** | **Discussion and conclusions of SPH literature review** | **Commentary** |
| | | | | |
| 1- | Carbon monoxide poisoning | One Cochrane review, no further RCTs on this topic since the Cochrane review | *Q:Is there evidence to support the use of HBOT enhancing recovery from acute carbon monoxide poisoning (either speed and/or completeness) compared to conventional treatment with normobaric oxygen?*<br>*Q: Is there evidence to support the addition of HBOT into the management pathway for acute carbon monoxide poisoning resulting in a more rapid and/or complete resolution of neurological sequelae?*<br>No. The available evidence does not support either of these conclusions.<br>All the trials suffer from major limitations on their reliability. Only two report benefit from HBOT and none are robust enough to form the basis for policy-making. The Cochrane review concluded that "Based on the results of these trials, HBOT cannot be routinely recommended for the treatment of CO poisoning." We concur.<br>The trials report comparisons of psychological and neurological tests. The evidence indicates that HBOT does not have an effect on activities of daily living and quality of life.<br><br>*Q: Is there evidence to describe the patient group who are likely to derive benefit and the intervention that should be used?*<br>We did not find any evidence which identified a patient group likely to derive benefit from HBOT. Two of the trials that found no benefit appeared to include less severely poisoned patients, but one of the trials which demonstrated benefit included patients with the same level of CO poisoning. It is possible that some patients, particularly those with more severe poisoning, may derive benefit from treatment, but this remains unproven. The Cochrane review noted "Importantly, given the absence of reliable evidence that patients with severe CO poisoning benefit from HBO therapy, exclusion of such patients from future trials is not justified".<br>None of the trials included pregnant women. | **CRG**<br>The evidence review has focussed on the ability of HBOT to reduce the half life of COHb rather than the main value of HBOT in this indication which is the treatment of the inflammatory changes that result from the preceding hypoxia and thus the prevention of persistent or delayed-onset neurological deficit.<br>We disagree with the interpretation that has been placed on the literature. The results of high quality trials in the Cochrane review (Weaver *et al which showed a positive effect*) are not given any greater value than poorly conducted studies (eg Schienkestel which have poor follow-up rates).<br>The review does not distinguish adequately between trials that investigate the administration of doses accepted as standard practice in England and those in which the intervention group has received what CRG clinicians consider to be excessive or sub-therapeutic doses of hyperbaric oxygen.<br>There are multiple reports of the highly toxic effects of CO poisoning on the foetus which have not been reported.<br>The first draft of the review made a point regarding the absence of long term follow up data. This can be attributed to the characteristics of this patient group as many are from vulnerable and disadvantaged groups, commonly lost to follow-up A CRG member pointed out that the Weaver trial overcame this challenge and reported results at 6 and 12 months, yet the final version of the review makes no comment at all on long term outcome.<br><br>**PHE**<br>The review found no reliable evidence that the use of HBOT in CO poisoning enhanced recovery time or completeness. The CRG comments that the review focussed on clearance of COHb, the review was asked to find evaluations of outcome in terms of functional impairment. The review was unable to find studies that included adequate long term follow up or that specifically addressed delayed neurological syndrome. This is important in an assessment of the cost effectiveness of HBOT in the management of CO poisoning. Further evaluation of HBOT in this application is required |

## Table 5 Summary of safety of HBOT taken from published evidence

| Safety | | | | |
|---|---|---|---|---|
| **Level of Evidence** | **Study design & Intervention** | **Outcome measure(s)** | **Results** | **Comments** |
| 3 | Soft tissue radiation damage, carbon monoxide, malignant otitis externa | Complication Rates<br>Side Effects | Evidence from trials of HBOT for a range of indications suggests that harms associated with it are generally mild and self-limiting. The most common adverse events associated with HBOT in the trials were barotraumas and visual changes, particularly myopia, which was reported in five to 10 per cent of all patients. Claustrophobia and anxiety in the treatment chamber was reported in just over one per cent of patients, while seizure or convulsion due to oxygen toxicity of the central nervous system and acute pulmonary toxicity were found to occur in less than one percent of patients. The requirement for patients to undergo multiple treatment sessions, often 20 or more, in a course of HBOT increases the risk of adverse events. | **PHE**<br>Were the evidence to be supportive of a role for HBOT in improving outcome, the complication rates and adverse events are in line in with other routinely available interventions terms of magnitude of risk and severity of complication |

## Table 6 Summary of cost effectiveness from published literature

| Cost-effectiveness | | | | |
|---|---|---|---|---|
| **Level of Evidence** | **Indication** | **Outcome measure(s)** | **Results** | **Comments** |
| | *Cost effective studies were found for soft tissue radiation damage and necrotising soft tissue infections.*<br><br>Soft tissue radiation damage | Cost per wound healed | An Australian cost effectiveness study initially demonstrated that HBOT dominated over usual care. However when the definition of effectiveness was changed to 'significant or complete wound healing' HBOT was no longer dominant | PHE<br>The data from other health systems is not readily transferrable to the UK setting. |
| | Necrotising soft tissue infections | Survival | Systematic review of literature, one Australian study<br>Systematic review concludes that inconsistent and poor quality of studies prevented any conclusion being drawn on cost effectiveness<br>One Australian study reporting statistically significant increase in survival for patients receiving HBOT calculated an ICER per death avoided at trial completion of approximately £7100. It is unclear whether this would translate to the UK situation | |

### 2.1.4 Summary of published evidence

In all of the indications for which research studies were identified, there was a paucity of reliable or robust evidence of the effectiveness of HBOT in the listed indications. In many cases reported benefits were confounded by small study numbers, the heterogeneity of the treatment protocols for both the administration of HBOT and in the clinical management that preceded the use of HBOT. Additionally, few studies included adequate long term follow up.

There are a number of randomised controlled trials in progress and yet to report. These examine the use of HBOT in carbon monoxide poisoning, radiation proctitis, prevention of osteoradionecrosis and the treatment of osteoradionecrosis.

In the UK the following studies are in progress or completed:

- HOPON which is investigating HBO's effectiveness as prophylaxis against osteoradionecrosis [6] and is due to close to recruitment in 2018.
- Hot II investigated the effect of HBOT on radiation proctitis and is due to submit a manuscript for publication in June 15[7].
- DAHANCA-21 which will investigate the effect of HBOT on established osteoradionecrosis. It is planned in the UK and is on the UKCRN portfolio (ID 13565). Ethical approval has been received for UK hyperbaric units to act as participating sites.

In the US:

- One study examines the comparative outcomes of one versus three HBOT treatments for patients with severe carbon monoxide poisoning[8] This trial is planned to complete in May 2018.

The evidence of cost effectiveness is scarce. There are no UK based studies. Those that exist are derived from other health systems (see section 2.4).

Whilst the CRG dispute the interpretation of the data presented in the literature reviews, almost all of the primary source studies, together with the systematic reviews, conclude by calling for further evaluation. For the indications reviewed for this report, reliable estimates of the magnitude of any effect of HBOT and the place of HBOT in the management of the condition under study remain to be established

For a number of indications, there is no agreed standard management preceding HBOT or where it does exist, for example surgical debridement and antibiotic administration, the detail varies, as does the duration. Similarly, where treatment is thought to be appropriate for refractory cases, there is no agreed definition of 'failure to respond' in the standard management protocol.

Overall, the published evidence base is unclear in terms of standard pre HBOT management, optimal HBOT schedules, predictable outcome and degree of enhancement over standard interventions to support a decision for routine commissioning. A number of indications begin to show a trend towards a role for HBOT but further robust evaluation is required in order that the results can be considered reliable and generalisable.

## 2.2 Survey of clinical opinion

In many indications, it is clear that the present published evidence is insufficient clear to justify the commitment of resources for routine commissioning. This is largely due to uncertainty in terms of outcome and position in the overall care pathway. In order to better understand the value placed on HBOT by the wider clinical community, an electronic survey was sent to the medical directors in all acute sector Trusts in England with the exception of Trusts that offer mental health facilities exclusively.

Appendix 2 contains the full survey report. A description of the study together with the key findings and conclusions are presented below.

### 2.2.1 Methodology

Medical directors were asked to distribute the survey to consultant colleagues for completion and onward distribution as desired. Professional bodies of the specialties responsible for the management of the most common indications also received the survey, as did a number of Clinical Reference Groups advising NHS England on specialised services.

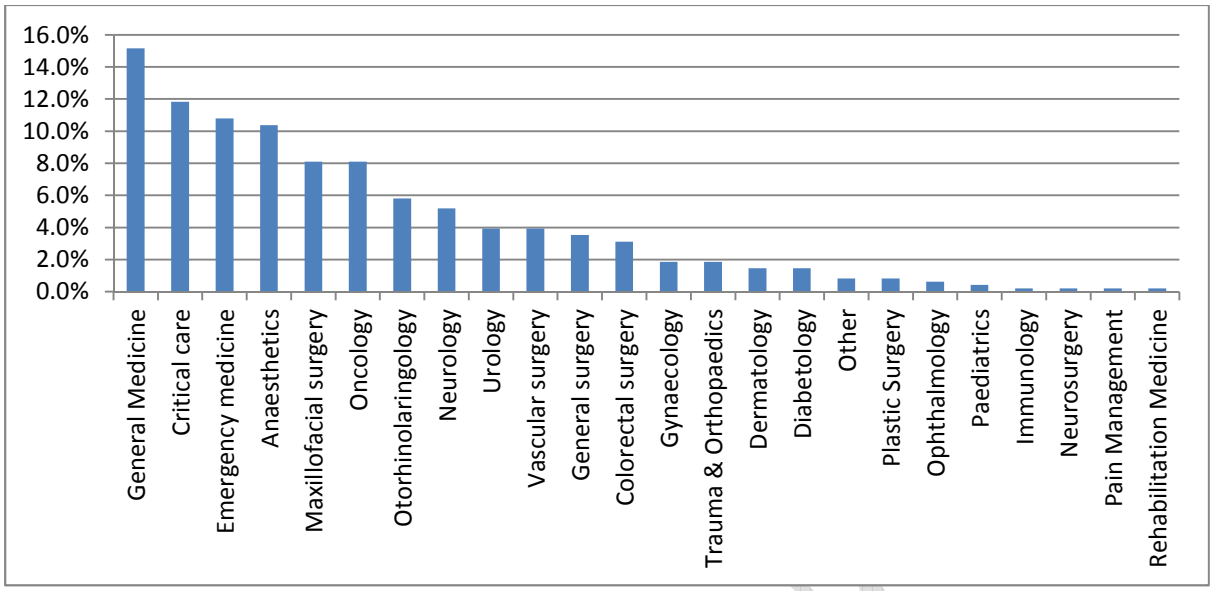
The survey ran from 20th March until 29th April 2015. Respondents were asked to comment upon :

- Their knowledge base in respect of HBOT
- The role of HBOT in the management of their patients
- The basis of their opinion
- The ease with which they were able to access HBOT

### 2.2.2 Results

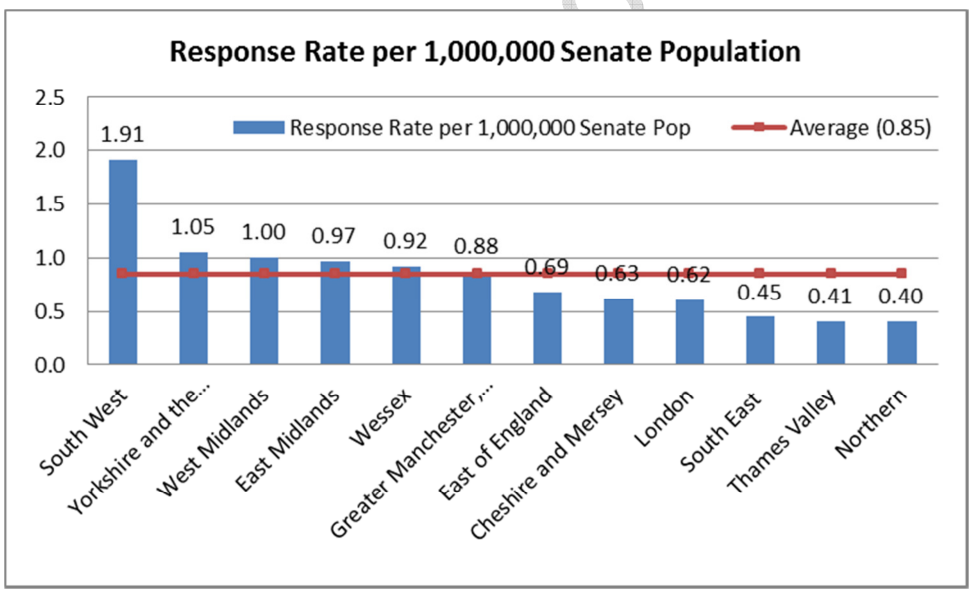
Responses were received from 482 individuals from all regions of the England. The distribution by specialty is shown in Figure 1.

**Figure 1 Response by specialty as % of total responses**




Standardised against the senate population, the South West had the highest per capita response rate from the clinical community (figure 2) and accounted for almost one fifth of all responses.

**Figure 2 Comparison of response rate standardized against senate population.**




It is of note that responses from the South West senate, which covers 8% of the national population contributed 19% (n=92) of all responses, whilst those from the Cheshire and Mersey, Northern and Thames Valley senates, which together cover 23% of the national population, represented 15% of the responses and equate to the opinions of only 16, 13 and 9 clinicians respectively

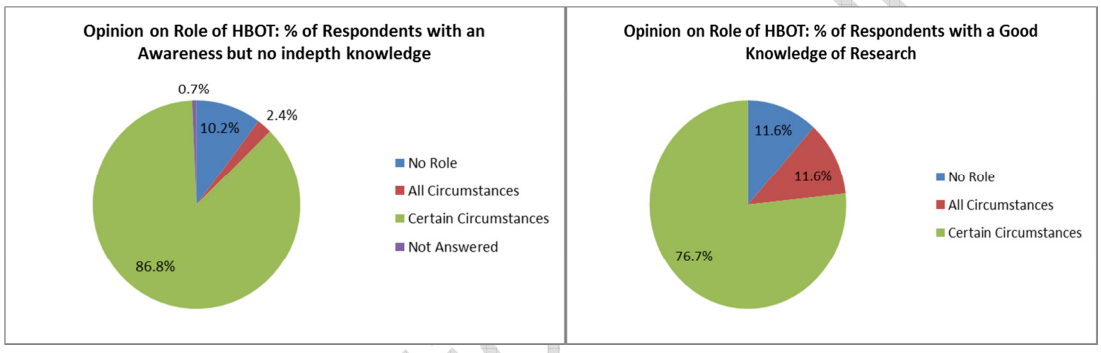
**Availability of HBOT as a management option**

The majority of respondents (79.9%, 385 respondents) were of the opinion that HBOT should be available in certain circumstances. A small minority (5.2%, 25) felt that it should be part of routine care, whilst 13.9% (67 clinicians) felt that there was no role for HBOT in their practice.

## Knowledge of research on HBOT

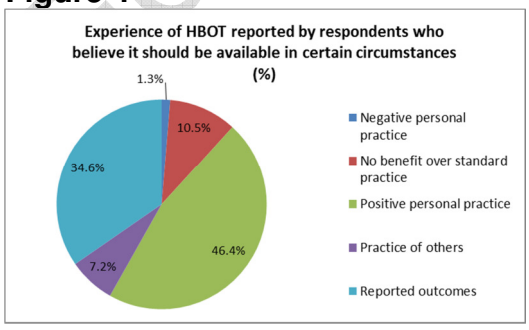
The majority of respondents (61%, 295/482) described their knowledge of the research on HBOT in their specialty as an awareness but lacking an in depth knowledge. Despite this, the majority of the group (85.8 %%) were also of the opinion that HBOT should be available in certain circumstances. This opinion was shared by a slightly smaller proportion (76.6%) of those who described their level of knowledge as being good. Amongst this better informed group, (n=112) equal numbers (n=17, 11.6%) believed that HBOT had no role to play in the management of their patients as believed HBOT should be routinely available.

**Figure 3**




Of the 385 respondents who considered that HBOT should be an option available in certain circumstances, 153 (equivalent to 39.7%) explained the basis for their opinion.
Almost half of this cohort (46.4%) commented that they had positive personal practical experience of the use of HBOT, whilst another third of respondents (34.6%) commented that their opinion was based on reported outcomes (figure 4).

**Figure 4**




Paradoxically, 11.6% of those who said they had had a negative personal experience using HBOT with their patients or who believed that it conferred little

benefit over standard treatments, still believed that HBOT should remain available in certain circumstances. It is not clear whether this opinion referred to the use of HBOT in specialities other than their own or whether they believed their own experience to be uncharacteristic

**Specified indications**

In total 27 different indications for HBOT were identified, however the most frequently cited were carbon monoxide poisoning (n=70), decompression illness (n=38, osteoradionecrosis (n=33), radiation cystitis /proctitis (23), hard to heal wounds (n=19) and necrotizing infections (n=14).

However, across these indications over 50% of respondents who felt HBOT should be available in certain circumstances rated their knowledge of the evidence base as lacking an in-depth knowledge ('aware of the research but without an in depth knowledge) The exception to this was those who cited osteoradionecrosis as the indication for HBOT in their practice. Sixty seven percent of these respondents rated their knowledge of the evidence base as good. This may reflect the presence of an active trial of HBOT as a preventative therapy in osteoradionecrosis. Conversely, only 14% of those who considered HBOT a treatment for carbon monoxide poisoning rated their knowledge as good.

**Assessment of the quality of the evidence base**

Thirty five responses included a comment relating to the quality of evidence supporting a role for HBOT. Almost half (48.6%) were of the opinion that the evidence base needed to be developed whilst only 20% commented that they felt that present quality of evidence was good. Extrapolating from this, 80% of respondents felt that the absence of good evidence of effectiveness was not a barrier to the provision of HBOT in certain circumstances. Amongst those not supporting the use of HBOT, the quality of the evidence of effectiveness was the most frequently cited reason for their opinion

**Access to HBOT**

Accessing HBOT presented problems to most respondents. 34% reported significant barriers. 8.5% respondents no longer tried to refer patients for HBOT as they felt the barriers were impossible to overcome

## 2.2.3 Discussion

It is clear that there is overwhelming support amongst those who responded to the survey for the continued availability of HBOT across a range of specialties. However, with the possible exception of the South West senate, which was well represented, it is not clear how far these findings can be generalised to the larger English consultant population. Nonetheless, with a response rate of almost 500 consultants, the findings are likely to give an indication of the opinions of those who consider HBOT to play a role in the management of their patients.

Although their knowledge of the research underpinning the use of HBOT in their specialty was rated as good by only 30% of respondents, for 70% of respondents, an awareness of the relevant research but no in-depth knowledge, was sufficient for them to conclude that HBOT should be available in certain circumstances.

There appeared to be a relatively small number of indications that were regularly cited as those in which HBOT might have a role to play.

Previous commissioning positions, which are still in place, present significant barriers to the majority of clinicians who wish to use HBOT in their patients. Some found these barriers impossible to overcome and no longer considered HBOT a therapeutic option as a result.

There are a number of weaknesses in the study design that limit the generalisability of the findings. Firstly, the reliance on medical directors to circulate the survey link introduces a significant source of bias into the findings. Numerous factors may affect whether and how quickly the survey links were circulated to consultant colleagues.

The survey respondents can be best described as a sample of convenience, the weakest form of sampling techniques. Further, the absence of a robust denominator prevents an estimation of the proportion of consultants working in English NHS Trusts whose views are represented in this survey.

Respondents were asked for their opinion of the role of HBOT in their specialty without reference to the resources required to incorporate it. Thus, in essence, respondents gave their opinion on whether HBOT was useful component of the care pathway without prioritising it against other existing treatment options. For some indications in which HBOT is not widely available (perhaps due to commissioning positions or the location of HBOT chambers in relation to the distribution of patients with the condition) or in which the potentially population who might benefit is large (for example hard to heal wounds), there would be significant resource implications of expanding the availability of HBOT.

### 2.2.4 Conclusion

In conclusion, the survey respondents were predominantly in favour of HBOT being available for a range of conditions. In the majority of cases, this opinion was moderated by a consideration that access criteria should apply. The study does not provide any information on the relative priority that respondents would ascribe to the incorporation of HBOT into clinical practice.

It is unclear how representative the respondents are of the wider clinical community and so the results cannot be considered generalizable. Consequently, further commissioning decisions of the use of HBOT should not only include a prioritisation of this intervention against other improvements within the specialties but should also employ a systematically constructed, representative, clinical sample.

In terms of the quality of evidence that this survey presents to inform commissioning of HBOT services, this could at best be regarded as SIGN level 4 evidence

### 2.2.5 CRG and professional body commentaries

The Adult Critical Care and Vascular CRGs submitted formal responses. Whilst the Adult Critical Care CRG supported the use of HBOT for decompression illness and in some cases of CO poisoning, neither the vascular CRG nor the Faculty of Intensive Care Medicine supported the use of HBOT within their specialties. The Faculty of Intensive Care Medicine concluded that the evidence for indications other than decompression illness and gas embolism was less than convincing. However, the British Society of Maternal and Foetal Medicine, asked to comment on the use of HBOT in pregnant women with carbon monoxide poisoning, concluded that the increased susceptibility of the foetus to anoxia justified the use of HBOT despite the less than ideal evidence for the management of a very rare situation

## 2.3 Hospital admissions data

The absence of an agreed point at which HBOT might be used in the care pathway together with the historical variation in commissioning practice means it is hard to obtain data on the number of patients who have had access to HBOT as part of their care and for whom this may have resulted in enhanced recovery The best proxy measure that could be obtained was in-patient admission for a specific indication. This was chosen because:

- There is significant variation in the availability of HBOT across the country and it is possible that, for indications in which HBOT is used predominantly outpatient setting, there may be a reduction in hospitalisation for that condition as progression to severe disease is prevented
- In patient admission reflects the severity of the condition and thus, as HBOT is commonly used as an adjunct to standard treatments when there is a suboptimal or failed response to conventional treatment, it may give an indication of the possible size of the potential patient cohort for future evaluative studies.

A report was commissioned using Hospital Episodes Statistics data covering admissions to acute trusts in England during 2013/14 for the following indications when coded as the primary diagnosis on admission:

- A480 Gas gangrene
- A691Other Vincent infections
- M726Necrotising fasciitis
- N304Radiation cystitis
- H602Malignant or necrotizing otitis externa
- L88XPyoderma gangrenosum
- T58XCarbon monoxide poisoning
- K627Radiation proctitis
- K122Cellulitis and abscess of the mouth
- L984Chronic ulcer
- N498Inflammatory disorders of other specified male genital
- L581Radiodermatitis
- N768Other specified inflammation of vagina and vulva

:

The resulting data (shown in full in appendix 3) failed to show any significant difference in hospital admission rates between areas know to have routine access to HBOT for these conditions. Using admissions for the treatment of chronic ulcer (n=999) and radiation proctitis, (n=2,067) admission rates were comparable in both the population covered by Devon Cornwall and Isles of Scilly NHS England Area Team, where there was routine access to HBOT for these conditions and that recorded from the aggregated Area Teams in the North West where the commissioning policies did not include routine access to HBOT as part of the care pathway.

At the time of analysis, no population statistics were available for the Area Team footprint since these had been reconfigured and so admissions were standardised against the nearest corresponding previous PCT geography and triangulated against ONS mid year population estimates. This gave a population for Devon Cornwall and the Isles of Scilly of 1.7 million and for the North West, 7.1 million.

Admissions for management of chronic ulcer were also standardised against an estimate of the diabetic population in the two areas based on a 6% prevalence of type 2 diabetes[9] (Prevalence of Diabetes in QoF register 2013 (published 2014)) The admission rates were as follows:

Table 7 Admissions to hospital for range of indications

| Indication | Rate of admission to hospital | |
|---|---|---|
| | Devon, Cornwall Isles of Scillly Area Team | North West Area Teams |
| *Standardised per million of general population* | | |
| Chronic ulcer | 30 | 22.4 |
| Radiation proctitis | 39 | 28.7 |
| *Standardised per 100,000 diabetic population* | | |
| Chronic ulcer | 50 | 37 |
| | | |

Whilst there are numeric differences in the admission rates for both indications and for admissions for the management of chronic ulceration, it is unclear whether these are of significance in terms of indicators of the effectiveness or otherwise of HBOT in the management of these conditions. This is because:

- There is no information on the quality of out-patient management of these patient groups. Outcomes of management in chronic ulceration in particular are dependent upon the quality of community ulcer care. So, without data on the incidence of chronic ulceration and the diabetic management protocols in the two areas, any conclusions about any effect of inclusion of HBOT in the care pathway would be speculative. The same is true of radiation proctitis. There is limited clinical consensus on the detailed management of out-patient care and so it is not clear whether or not patients admitted for management have failed to respond to the same management options delivered in line with the same pathway.
- The population denominators were not stable during the period of data collection. The aggregated population of the North West is reliably quoted because boundary changes were fewer and occurred within the broader

boundary, however, the smaller geography of this part of the South West has been subject to significant boundary changes during the period that covers these admission data. Therefore, it is possible that the population denominator could be larger or smaller than that quoted and so, whilst these data may be regarded as better than indicative of overall admission rates, it would not be safe to regard these figures as robust.

- The populations are of different sizes and given the relative prevalence of the conditions under consideration it would be unwise to draw any conclusions on the relative impact of HBOT in one area compared to the other
- It is unknown whether those admitted to hospital in the area where HBOT is routinely available had or had not been treated with this modality prior to admission.

In conclusion, it cannot be stated with certainty that the availability of HBOT for the treatment of chronic ulceration and radiation proctitis has an impact on the admission rate and by extrapolation, on the numbers of patients progressing to the severe end of the spectrum of disease. However, the data are valuable in terms of identifying the population of patients who might be available for further evaluative studies across a range of conditions.

## 2.4 Approach to the use of HBOT in other health care systems

Mirroring the variation seen in historical NHS commissioning, the commissioning of HBOT has varied across developed health systems. In many cases national position statements are over 10 years old. A review of commissioning of HBOT in Belgium in 2008[10] concluded that there was insufficient good quality data for an assessment of HBOT as a treatment modality.

Conversely, HBOT is authorised for use in routine management in a number of other health care settings worldwide[11,12]. In some instances there are technology assessments that advise more rigorous assessment of outcomes prior to wide spread use or have restricted the use of HBOT. It would appear that in many health systems the evidence base for the commissioning position rests on expert consensus, the most common is that of the Undersea and Hyperbaric Medical Society (see appendix 4). Some examples are given below.

**Table 8 Comparison of international commissioning positions on HBOT**

| Health Economy | Nature of health provision | Funded indications |
|---|---|---|
| US | Predominantly insurance | *Insured indications*<br>Generally UHMS indications<br><br>Example - Blue Cross/Blue Shield<br>https://www.bcbsms.com/index.php?q=member-medical-policy-search.html&action=viewPolicy&path=/policy/emed/Hyperbaric%20Oxygen%20(HBO)%20Pressurization.html<br><br>*Medicaid indications*<br>UHMS indications with criteria for poorly healing wounds associated with diabetes.<br>http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=12&ncdver=3&NCAId=37&ver=7&NcaName=Hyperbaric+Oxygen+Therapy+for+Hypoxic+Wounds+and+Diabetic+Wounds+of+the+Lower+Extremities&fromdb=true&IsPopup=y&bc=AAAAAAAAEAgA |
| Canada | National health insurance systems | Coverage determined by states and provinces No national policy but selection of HTA reports advising development of guidelines for use of HBOT across a range of indications[1314] |
| Australia | State provision although regional variations. | Decompression illness, gas gangrene, air or gas embolism; diabetic wounds including diabetic gangrene and diabetic foot ulcers; necrotising soft tissue infections including necrotising fasciitis or Fournier's gangrene; or for the prevention and treatment of osteoradionecrosis, |
| Belgium | National insurance system | Reimbursement restricted to first and second day of treatment.. Decompression illness, gas embolism. Supportive of research |
| France* | Mixed State and insurance provision | No restrictive list of indications |
| Netherlands* | National health insurance contributions | UHMS but with criteria in some indications |
| Germany* | Insurance based system | No national approach, Agreements between individual insurers and provider units |
| *Devolved nations* Scotland | NHS | Decompression illness, gas embolism, severe carbon monoxide poisoning commissioned routinely. Will consider elective use for HBOT for diabetic lower extremity ulcers, osteoradionecrosis and deep soft tissue radionecrosis. No other indications. |

*Data taken from 2008 Belgian Healthcare Knowledge Centre Report[10]

It is clear that outside the UK HBOT is used in a wider range of indications than are currently commissioned by NHS England. In many cases these decisions appear to rest upon an evidence base that is less robust that that required by the NHS for service commissioning and is largely represented by consensus expert opinion rather than an extensive published literature. Many of the identified documents are over 5 yrs old and a more extensive search would be required in order to provide a comprehensive picture.

In part, this less rigorous evidence requirement may be sustainable because of the differences that arise from the funding of health care. Elsewhere there is a much greater use of state and patient co-payment than in the UK and this is reflected in the range of options available through a co-payment system (either insurance based or direct co-payment).

Whilst there are a number of national statements relating to the approved use of HBOT for a range of indications, there are no readily available national outcome data for these indications. It is beyond the scope of this report to undertake cross national outcome comparisons between systems in which HBOT is used in routine management and the UK where it is not. As a consequence, it is difficult to translate these national positions into information that would be of value for UK commissioning.

Nonetheless, the inclusion of HBOT for some indications in some state systems may point to a desirability of further systematic evaluation within the UK.



## 3. Discussion

### Evidence base

With the exception of the treatment of decompressions illness and gas embolism, the current evidence base underpinning the use of HBOT in the management of a number of conditions falls below that usually required for routine NHS commissioning of an intervention. Table 9 summarises the findings of this evidence review.

Table 9 Summary of factors for commissioning HBOT for stated indications

| | Quality of published evidence | Magnitude of improvement compared to standard care | Identification of relevant patient population | Clarity of place in care pathway | Comments |
|---|---|---|---|---|---|
| **Soft tissue radiation damage** | Heterogeneity in study design prevent clear conclusions. Current trial of use in radiation proctitis soon to report | Limited evidence from published literature | Used in refractory cases However, standard best practice not established | No published evidence to indicate optimal position<br>CRG protocol identifies optimal place in pathway based on expert opinion | Evidence is most structured for radiation proctitis and cystitis<br><br>Trial due to report June 15 |
| **Malignant otitis externa** | Outcomes derived from retrospective case series and case reports. | Current evidence is inadequate to predict degree of improvement over standard care nor place in pathway. | Inherent biases in reporting make generalisation to wider patient population difficult | Used in refractory cases. No published evidence to indicate optimal position<br>No agreed position on duration or nature of standard treatment<br>CRG protocol identifies optimal place in pathway based on expert opinion | Data limited by low prevalence of this condition.<br>Likely to be years before sufficient cases accrue for meaningful analysis.<br><br>Standardisation of place in pathway and preceding interventions are crucial to further evaluation |
| **Necrotising soft tissue infections** | Most studies have small numbers and have a high potential for bias.<br>Inadequate for drawing generalisable conclusions | Effect on reducing mortality/amputation is unclear compared to standard treatment is antibiotics and debridement. | Studies use heterogeneous subjects and so prevent identification patient group<br><br>Expert opinion is able to identify group | Used in refractory cases. No published evidence to indicate optimal pathway position.<br>No agreed position on duration or nature of standard treatment<br>CRG protocol identifies optimal | Data limited by low prevalence of most presentations and heterogeneity of study subjects.<br>Potential for systematic assessment but requires standardisation of preceding pathway |

| | Quality of published evidence | Magnitude of improvement compared to standard care | Identification of relevant patient population | Clarity of place in care pathway | Comments |
|---|---|---|---|---|---|
| | | | | place in pathway based on expert opinion | |
| **Carbon monoxide poisoning** | | Quality of published evidence does not indicate that HBOT either enhances or results in more complete recovery from acute poisoning<br>There is a significant lack of follow up data | Pregnant women<br><br>Expert opinion is able to identify group characteristics using quantitative measures | Expert opinion places this as treatment for severe poisoning and also in less severe cases in pregnant women | National Poisons Advisory service does not recommend HBOT for this indication<br><br>US trial in progress due to complete in May 2018 |

The nature of the evidence found during the review is more characteristic of a newly emerging technology than an intervention that has been available for many years. This may be attributable to the absence of a single, resourced, commercial driving force to attract academic interest in robust evaluation as is the case with pharmaceutical interventions or surgical devices.

Compounding this, the location of HBOT chambers does not match the distribution of population centres. The majority are situated in coastal locations reflecting the predominance of decompression illness as the least contentious condition for which HBOT is used. Consequently, evaluating HBOT for the treatment of other indications has in the past involved significant resources associated with travel to or accommodation during treatment schedules which can be in the region of 20-40 daily treatments. Whilst this presents less of a barrier to the further evaluation of more common conditions (because it is likely that there will be a sufficient local patient population) it presents a significant challenge to the evaluation of rare presentations.

Across all presentations evaluated in this report, there appears to be little consensus in what constitutes best standard management nor in the place of HBOT in the care pathway. For example, it is rarely clear whether exhausting conventional therapy is an indicator that the response to HBOT will be suboptimal nor whether earlier incorporation of HBOT might prevent deterioration to a refractory stage of disease. There is increasing consensus amongst the hyperbaric community on the pre-treatment schedules that are likely to be associated with successful outcome, These remain to be tested in practice or in some cases, verified by the referring specialty.

**Clinical opinion**

Opinion amongst those responding to the clinical survey was overwhelmingly in support of the continued availability of HBOT in specific circumstances and for defined indications. Overall, awareness of the evidence base underpinning the use of HBOT was described as ‘not in depth’ amongst respondents. Opinion on the value of HBOT was more varied amongst CRG s and Professional bodies.

**In-patient populations**

Hospital episode statistics have proved less informative than was hoped. There does not appear to be any significant differences between the numbers of patients whose condition necessitated admission to hospital between areas where there is little commissioned HBOT treatment and areas in which there is a more liberal use of this intervention. It may be that this is too crude a measure and in-patient data are a poor proxy marker to detect any ‘admission sparing’ effect of HBOT. In order to make this information more valuable, it would be necessary to link admission to outcome data but this would require access to individual patient level data. This was beyond the scope of this report.

Nonetheless, the HES data does give useful information on likely patient populations that could be approached to take part in any future evaluative study

### International comparisons

Whilst there are sufficient source documents to give an indication of the range of commissioning approaches to the provision of HBOT in other health economies, the absence of comparable outcome data and the differences in funding mean that this of limited value in informing a commissioning decision in the UK.

## 4. Conclusions

Across the indications examined there is a need for development of the evidence base to establish the role of HBOT in the management in a range of conditions. The absence of a clear place in the care pathway together with variation in standard treatment options make estimations of clinical and cost effectiveness difficult. Nonetheless, amongst clinicians responding to the survey, there was a clear value attributed to the availability of HBOT. Those who disagreed, either fellow respondents or advisory bodies, did soon the basis of the poor evidence base rather than clear evidence of ineffectiveness.

For the future, NICE guidance has called for further trial to establish the place of HBOT in the management of diabetic lower limb ulceration and there is currently a large multicenter trial of HBOT in the prevention of osteoradionecrosis in progress. It would seem logical that HBOT is available for evaluation in the other indications within a similarly robust framework. Indeed a number of hyperbaric providers have recently participated in a trial of HBOT for radiation proctitis (HOTII) and are preparing for a similar study in the treatment of osteoradionecrosis (DAHANCA-21). NHS England might, therefore, consider encouraging the hyperbaric community to establish links with the referring specialties to formulate such trials through research support networks such as NIHR and MRC. Table 10 describes the possibilities for the indications that have been the subject of the evidence reviews in this report

Table 10 Summary of evidence base and possibility for further evaluation

| Indication | Published evidence | Clinical opinion survey | Hospital admissions | International health systems | Potential for future evaluation |
|---|---|---|---|---|---|
| Soft tissue radiation damage | Limited evidence of effectiveness. SIGN* level 1-**, so not attaining a graded category* | Supported by survey respondents | 2,067 hospital admissions for radiation proctitis annually plus 278 admissions for radiation cystitis. Likely to be larger outpatient population. | Included as part of routine management in state and insurance system based on UHMS approved indications | Patient numbers commensurate with well constructed RCT |
| Malignant otitis externa | Low quality data without control arms. SIGN level 3. Not eligible for graded level. | Supported by those responding to survey | 265 hospital admissions annually. Unknown outpatient population. | Not specifically mentioned in most | Place of HBOT in pathway unclear, No agreed standard care<br>Relatively low patient numbers nationally thus even lower numbers in areas in proximity to HBOT unit.<br><br>Registry data collection possible if agreement on standard care could be reached |
| Necrotising soft tissue infections | Weak evidence from two non randomised, retrospective cohort studies. Weaknesses apparent in study design<br>SIGN level 2- | Supported by survey respondents | In the order of 700 hospital admissions annually. Unlikely to be larger outpatient population but severity unknown and place in pathway unclear | Included in UHMS based systems. Excluded in others | Lack of clarity in place in care pathway. No agreed standard management. Range of conditions fall under this category. Significant work required to construct systematic evaluation. |

| Indication | Published evidence | Clinical opinion survey | Hospital admissions | International health systems | Potential for future evaluation |
|---|---|---|---|---|---|
| Carbon monoxide poisoning | Significant heterogeneity in patient selection criteria, treatment regimes, outcome statements and follow up<br>SIGN level 1-<br><br>Animal studies suggest biological mechanism for resolution of neurological sequelae persisting after exposure.<br><br>No longer recommended by National Poisons Information service (Toxbase) | Supported by respondents | 364 hospital admissions annually. Unknown outpatient population. | Included as part of routine management in state and insurance system | Adequate patient population, however high proportion of patients have psychiatric co morbidity or are otherwise in vulnerable circumstances making follow up difficult. Incidence is highest in densely populated urban areas as opposed to coastal chamber locations. RCT/ case controlled study feasible. Currently little use of HBOT for this indication beyond one or two providers. |
| Hard to heal wounds | Cochrane review and NICE guideline recommend RCT to establish place if any in management of this condition | | Not assessed in view of NICE guidance | Included in some systems many with criteria for earlier part of care pathway | Large population in structured healthcare environment. RCT feasible. |

*See tables 2 and 3 for description of Scottish Intercollegiate Network (SIGN) categorisation of evidence

**Studies with a level of evidence (-) should not be used as the basis of making recommendations

## 5 Options for commissioning

1. Whilst it might appear that HBOT could be commissioned for decompression illness on a case by case from chambers that provide treatment for commercial divers, these chambers are not equipped to accept seriously ill casualties. Currently this category of patient is transferred into a category 1 facility for NHS funded care. There will be a continuing need for this emergency treatment facility. In addition, funding emergency care on a case by case basis would threaten the present service structure which lacks resilience to variation in commissioning levels. Such a move would be likely to lead to a level of destabilisation that would result could jeopardise safe emergency management of decompression illness.

2. HBOT could continue to be routinely commissioned for the treatment of decompression illness and gas embolism from existing providers.

3. Based on the review of a range of evidence sources, all other indications could be commissioned as part of a systematic evaluative framework. To do otherwise would perpetuate the significant opportunity costs associated with continued allocation of resources to treatment protocols that have variable pathway components and unclear outcomes.

4. The methodologies for such evaluations would be determined by the nature of the condition but should adhere to standard techniques for studying similar conditions. Because there is the potential for significant expansion of HBOT if studies demonstrate clinical and cost effectiveness, methodological rigor is paramount in continued assessment of HBOT.

5. Part of any evaluative methodology should include the identification of the necessary duration of the data collection. Thereafter, following analysis of the results, NHS England would be in a position to take a definitive commissioning decision in relation to each indication.

6. Given the clinical opinion in support of continued availability of HBOT, a pragmatic solution may appear to be to continue to resource HBOT in these indications using systematic data collection tools. Compared to the use of properly constructed research studies, a simple data collection exercise is unlikely to produce either the rigor or the detail necessary to inform future decision making since it will not include any requirement for standardisation of the pathway leading up to referral for HBOT, HBOT treatment protocols themselves nor outcome focused follow-up within the referring specialties.

## Search strategy

**Question(s)**

*Identify all aspects of the topic that need to be explored in order to develop a policy*

- Is the intervention in tariff?
- Is it, or can it be, adequately covered by the appropriate detail in the service specification?
- Is it very low volume or does it have a low number of requests, such as less than 10 per year? If it is low volume then it may not merit a clinical commissioning policy or may be deferred to the next round of policy reviews.
- Does it appear too difficult to establish an evidence base or find suitable evidence to support a new clinical commissioning policy? If there is such limited evidence that it will not be possible to answer the review question then it will not be possible to generate a clinical commissioning policy.
- Is it a clinical area included within the scope? If not, then a clinical commissioning policy may not be suitable for this

**Search strategy** *Indicate all terms used in the search*

| | |
|---|---|
| P – Patients / Population<br><br>Which patients or populations of patients are we interested in? How can they be best described? Are there subgroups that need to be considered? | |
| I – Intervention<br><br>Which intervention, treatment or approach should be used? | |
| C – Comparison<br><br>What is/are the main alternative/s to compare with the intervention being considered? | |
| O – Outcomes<br><br>What is really important for the patient? Which outcomes should be considered? Examples include intermediate or short-term outcomes; mortality; morbidity and quality of life; treatment complications; adverse effects; rates of relapse; late morbidity and re-admission; return to work, physical and social functioning, resource use. | *Critical to decision-making:*<br><br>*Important to decision-making:* |

**Assumptions / limits applied to search**

*e.g. date limits, inclusion and exclusion criteria (study type or aspect of topic)*

## Version Control Sheet

| Version | Section/Para/Appendix | Version/Description of Amendments | Date | Author/Amended by |
|---|---|---|---|---|
| 1 | | | | |
| 2 | | Sent to PHE Specialised Services Public Health Network for QA. | 18/5 | COD |
| 3 | 2.1.1<br><br>Table 4 malignant otitis externa<br><br>2.2.4<br><br>5 | QA 1&2 - Clarification of authors of rapid evidence review<br>Additional comment into PHE view of CRG comment<br>Rating of survey evidence<br>Addition of capped activity to options | 29/5 | COD |
| 4 | | | | |
| 5 | | | | |
| 6 | | | | |
| 7 | | | | |
| 8 | | | | |
| 9 | | | | |
| 10 | | | | |



## References

[1]NHS Confederation Priority setting - an overview available to download at http://nhsconfed.org/resources/2008/12/priority-setting-an-overview

[2] NHS Confederation Priority setting – managing new treatments available to down load at http://nhsconfed.org/resources/2008/02/priority-setting-managing-new-treatments

[3] Quality Improvement Scotland.HTA Systematic Review 2 The clinical and cost effectiveness of hyperbaric oxygen therapy 2008 Available to download at http://www.healthcareimprovementscotland.org/previous_resources/hta_report/hta_systematic_review_2.aspx

TOXBASECarbonmonoxide.doc

[4]

[5] NHS National Services Scotland 2011 Review of national hyperbaric and national registration service NSSC 2013/44B National Services Scotland.

[6] Details of the HOPON trial are available at http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=4550

[7] Details of HOT II available at https://clinicaltrials.gov/ct2/show/NCT01087268?term=NCT01087268&rank=1.

[8] The details of the carbon monoxide trial can be found at http://clinicaltrials.gov/ct2/show/NCT00465855?term=hyperbaric+oxygen&rank=2.

[9] QoF Available to down load athttp://www.diabetes.org.uk/About_us/What-we-say/Statistics/Diabetes-prevalence-2013/

[10] Belgian Healthcare Knowledge Centre 2008 Hyperbaric Oxygen Therapy: a Rapid Assessment available to down load at https://kce.fgov.be/sites/default/files/page.../d20081027315.pdf

[11] Australia – Medicare Benefits Schedule Item 13020 available to down load at http://www9.health.gov.au/mbs/search.cfm?q=13020%2C13025%2C13030&sopt=I

[12]Ontario Health Technology Assessment Series 2005; Vol. 5, No. 11 Hyperbaric oxygen therapy for non healing ulcers in diabetes mellitus. Available to download at http://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&frm=1&source=web&cd=2&ved=0CDUQFjAB&url=http%3A%2F%2Fwww.health.gov.on.ca%2Fenglish%2Fproviders%2Fprogram%2Fmas%2Ftech%2Freviews%2Fpdf%2Frev_hypox_081105.pdf&ei=5C0AVdXuIM7taqGsgsgE&usg=AFQjCNFStE6qngbtN1bSVVcMI6r3HjGcwA

20070300 Canadian economic analysis of

[13]

[14] CADTH Hyperbaric Oxygen for difficult wound healing available to down load at *https://www.cadth.ca/media/pdf/M0016_**HBOT**_L3_e.pdf*