MANAGEMENT IN CONFIDENCE

CLINICAL PRIORITIES ADVISORY GROUP
05 March 2019

Agenda Item No	04.2
National Programme	Trauma
Clinical Reference Group	Hyperbaric Oxygen Therapy (HBOT) Clinical Advisory Group
URN	1779

Title
Hyperbaric Oxygen Therapy for Diabetic Lower Limb Ulceration (Diabetic Foot Ulcer)

Actions Requested	1. Support the adoption of the policy proposition
	2. Recommend its approval as an IYSD

Proposition
Not for routine commissioning. The policy position for this indication does not represent a change from the current published policy, however this policy will replace the current published version if accepted for publication.

Clinical Panel recommendation
The Clinical Panel recommended that the policy progress as a not for routine commissioning policy.

The committee is asked to receive the following assurance:	
1.	The Head of Clinical Effectiveness confirms the proposal has completed the appropriate sequence of governance steps and includes an: Evidence Review; Clinical Panel Report.
2.	The Head of Acute Programmes confirms the proposal is supported by an: Impact Assessment; Stakeholder Engagement Report; Consultation Report; Equality Impact and Assessment Report; Clinical Policy Proposition. The relevant National Programme of Care Board has approved these reports.
3.	The Director of Finance (Specialised Commissioning) confirms that the impact assessment has reasonably estimated a) the incremental cost and b) the budget impact of the proposal.

4.	The Clinical Programmes Director (Specialised Commissioning) confirms that the service and operational impacts have been completed.

The following documents are included (others available on request):	
1.	Clinical Policy Proposition
2.	Consultation Report
3.	Evidence Summary
4.	Clinical Panel Report
5.	Equality Impact and Assessment Report

No	*Metric*	*Summary from evidence review*
1.	Survival	
2.	Progression free survival	
3.	Mobility	
4.	Self-care	
5.	Usual activities	
6.	Pain	
7.	Anxiety / Depression	
8.	Replacement of more toxic treatment	
9.	Dependency on care giver / supporting independence	
10.	Safety	This is an assessment of the incidence of adverse effects resulting from HBOT. Fedorko et al (2016): Participants reported the incidence of solicited adverse effects such as acute respiratory distress, pneumothorax, barotrauma, dizziness, convulsions or seizures, and visual changes. They also recorded other adverse events as unsolicited. These included - inability to equalise middle ear pressures, anxiety, chest pain, nausea, hypo- and hyperglycaemia, wound infection, pain after tympanic membrane rupture and congestive heart failure. Fedorko et al. (2016) reported solicited adverse events in 9 HBOT and 6 controls (p=0.44), and unsolicited adverse events in 24 HBOT and 5 controls (p=0.02).

		This result indicates that HBOT causes a significant number of adverse effects. Safety of HBOT is important to patients.
11.	Delivery of intervention	

Other health metrics determined by the evidence review		
No	Metric	Summary from evidence review
1.	Freedom from major amputation or meeting the criteria for major amputation	Freedom from major amputation or meeting the criteria for major amputation (defined as below-knee or metatarsal level amputation) at 12 weeks, was based on not having any of the following criteria for amputation: 1. Lack of significant progress in wound healing over the follow-up period, which indicated a risk of severe systemic infection related to the wound 2. Persistent deep infection involving bone and tendons (antibiotics and hospitalisation required, pathogen involved) 3. Inability to bear weight on the affected limb 4. Pain causing significant disability. This is a subjective judgement of the presence of indications for amputation, made by a single surgeon, blinded to the participant's treatment allocation. Only Fedorko et al. (2016) reported this outcome measure. They reported no effect of HBOT on this outcome in a high quality double-blind trial with 103 participants. They reported that 23% of HBOT and 24% of controls met criteria for major amputation over the 12 weeks of the study. This result suggests that HBOT had no effect on this outcome. The result provides an indication of whether HBOT reduces the risk of a below-knee or metatarsal-level amputation. This would be of major benefit, but the results provide no reason to believe HBOT has this effect.
2.	Recommendation in favour of major or minor amputation	This is a subjective judgement of the presence of indications for amputation, made by a single surgeon, blinded to the participant's treatment allocation. Only Fedorko et al. (2016) reported this outcome measure. They reported that 51% of HBOT and 48% of controls were judged to need major or minor amputation over the 12 weeks of the study.

		The result provides an indication of whether HBOT reduces the risk of a below-knee or metatarsal-level amputation, or a minor amputation of one or more toes. This would be of major benefit, but the results provide no reason to believe HBOT has this effect.
3.	Progress of ulcer healing over 12 weeks	Wound size was measured weekly manually and by computerised analysis of wound surface area and perimeter from high-resolution calibrated digital photographs. The authors also calculated the linear advancement of the wound edge. All measurements were made at 12 weeks. This is an assessment of the progress and extent of wound healing, made blind to the participant's treatment allocation. Only Fedorko et al. (2016) reported this outcome measure. They reported a difference in mean width reduction of -0.12cm, 95% CI -0.46 to 0.22, p = 0.491. This result suggests that HBOT had no effect on this outcome. Faster wound healing would be of major benefit, but the results do not indicate that HBOT hastens this outcome.
4.	Progress of ulcer healing by day 14	Average reduction in ulcer area by day 14 was assessed. Ulcer area was assessed by computerised examination of clinical photographs. Only Ma et al.'s (2013) unblinded randomised trial with 36 participants reported this outcome measure. In the HBOT arm, the average reduction in ulcer area was 42%, compared with 20% in the control arm ($p<0.05$). Faster wound healing would be of major benefit; the results suggest that HBOT may hasten this outcome. The assessment was made without blinding to the participant's treatment allocation, increasing the risk of bias.
5.	Progress of ulcer healing as measured by the Bates-Jensen would assessment tool	The Bates-Jensen wound assessment tool was used weekly to measure progress of ulcer healing. This is an assessment of the progress and extent of wound healing, made blind to the participant's treatment allocation. This tool assesses 13 wound characteristics, with each item scored on a 1 to 5 scale (maximum score 65). The individual scores are summated for a total score. The higher the total score, the more severe the wound status.

		Only Fedorko et al. (2016) reported this outcome measure. They reported a difference in mean change in score of 0.53, 95% CI -2.58 to 3.64, p = 0.735. This result suggests that HBOT had no effect on this outcome. Faster wound healing would be of major benefit, but the results do not indicate that HBOT hastens this outcome.
6.	Proportion of ulcers healed at 12 weeks	The proportion of ulcers healed (i.e. Wagner grade 0 or 1) was measured at 12 weeks. This is an assessment of the progress and extent of wound healing, made blind to the participant's treatment allocation. (The Wagner classification of diabetic foot ulceration is as follows: Grade 0 No open ulcer, high risk; Grade 1 Superficial ulcer with subcutaneous involvement; Grade 2 Deep ulcer with tendon or joint involvement; Grade 3 Deep ulcer with bone involvement; Grade 4 Wet or dry gangrene (forefoot), without cellulitis; Grade 5 Generalized (whole foot) gangrene.) Only Fedorko et al. (2016) reported this outcome measure. They reported that 20% of HBOT and 22% of controls had healed at 12 weeks. This result suggests that HBOT had no effect on this outcome. A higher likelihood of ulcer healing would be of major benefit, but the results do not indicate that HBOT hastens this outcome.
7.	Proportion of ulcers healed by day 14	This assessment of the completion of wound healing was made by examination of clinical photographs, without blinding to the participant's treatment allocation. Only Ma et al. (2013) reported this outcome measure. They reported no effect of HBOT on this outcome in an unblinded trial with 36 participants. Faster wound healing would be of major benefit, but the results do not indicate that HBOT hastens this outcome.
8.	Clinical outcome	This outcome measure enumerated how many participants were in each of six clinical categories at the completion of the trial. The categories were: healed (complete closure without debridement in the operating room), graft or flap (graft or flap closure required), distal amputation (amputation distal to metatarsophalangeal joints), proximal amputation (amputation proximal to the metatarsophalangeal joints), debridement (standard

		therapy wound or operative debridement), no change (failure to heal during the course of treatment). Only Duzgun et al. (2008) reported this outcome measure, in an unblinded trial with 100 participants. Faster wound healing would be of major benefit. The study suggests it may be more likely after HBOT, but was unblinded, so the results may be attributable to observer bias. It is surprising that none of 50 control participants' ulcers were healed after 92 weeks, indicating that the control intervention was ineffective. Since treatment without HBOT usually leads to ulcer healing, this result suggests the control treatment was not representative of normal care, reducing the generalisability of the trial's result.
9.	Cost utility	This is a measure of costs, outcomes (major amputation, healed with or without a minor amputation, unhealed) and the utility of these outcomes. This result is intended to indicate the cost utility, or health value for money, of HBOT for diabetic foot ulcers. Only Chuck et al. (2008) reported this outcome. They used modelling based on a 2003 study of the effectiveness of HBOT (Guo et al. 2003) and Canadian healthcare cost data. Their modelling indicated that HBOT was more effective and less expensive than standard care. The unreliable assumptions used in this study's model undermine its usefulness to NHS policymakers. The estimates of the effectiveness of HBOT were based on unreliable and potentially obsolete studies, and not compatible with Fedorko et al's (2016) high-quality randomised trial. Also, the costs are based on the Canadian health care system in 2008, and may be materially different from those in the NHS.

Considerations from review by Rare Disease Advisory Group
Not applicable.

Pharmaceutical considerations
Not applicable.

Considerations from review by National Programme of Care
2) The proposal received the support of the Trauma PoC Board on 29 January 2019, subject to the following comments: CPAG is asked to note the consultation

report which outlines the concerns of clinicians regarding the evidence review and actions taken in relation to the feedback received during public consultation.