VIA MEDICA

ORIGINAL ARTICLE

Int Marit Health
2024; 75, 1: 35–42
10.5603/imh.98770
www.intmarhealth.pl

ISSN 1641-9251
eISSN 2081-3252

Cost-effectiveness analysis of adjunctive hyperbaric oxygenations in diabetic feet ulcer: a systematic review

Ana Khusnul Faizah[1, 2], Tri Murti Andayani[1], Libriansyah[3], Dwi Endarti[1]

[1]Gadjah Mada University, Bulaksumur, Caturtunggal, Kec. Depok, Kabupaten Sleman, Daerah Istimewa Yogyakarta, Sleman, Indonesia
[2]Pharmacy Department, Hang Tuah University, Arif Rahman Hakim, Surabaya, Indonesia
[3]Department of Internal Medicine, Dr. Ramelan Navy Hospital, Surabaya, Indonesia

ABSTRACT

Background: *Hyperbaric oxygen therapy (HBOT) has been reported to be beneficial in enhancing wound healing and preventing amputations in diabetic foot ulcers (DFU), though not many studies are available to demonstrate how cost-effective this treatment is. A comprehensive assessment of cost-effectiveness evaluations about hyperbaric oxygen therapy (HBOT) considering financial viability into account is critical and essential.*

Objective: *To assess the cost-effectiveness of HBOT in DFU patients.*

Materials and methods: *A systematic search (October 2023) was performed in 3 databases: PUBMED, EMBASE, and Cochrane CENTRAL. The study was guided by the PICO research question as detailed (Population: DFU patients; Intervention: HBOT; Comparison: standard care; Outcome: ICER). Cost-effectiveness analyses (CEAs) involving interventions in DFU patients with Wagner III and above were included. The main outcomes of this review were costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratio (ICER). The CHEERS checklist was used to assess the quality of CEAs.*

Results: *Two studies revealed the cost-effectiveness of standard wound care (SWC) plus HBOT, whereas one study showed that HBOT was not cost-effective as adjunctive treatment for DFU. The ICER of HBOT in 12 years were $2,255/QALY and US$2621/QALY.*

Conclusion: *The evidence to support the cost-effectiveness of HBOT is insufficient. However, the majority of HBOT studies have reported this therapy was cost-effective. Instead of model-based evaluations, further studies should combine clinical application of interventions with concomitant economic assessment.*

(Int Marit Health 2024; 75, 1: 35–42)

Keywords: HBOT, cost-effectiveness, DFU, diabetic wound, cost

INTRODUCTION

Diabetes mellitus will continue to rise in prevalence, reaching 578 million patients by 2030 [1]. With 10.7 million diabetic patients, Indonesia ranks seventh in the globe [2]. Diabetes mellitus is a metabolic disorder marked by hyperglycaemia that results in decreased insulin secretion, impaired insulin action, or both [3]. Inadequate diabetes treatment may increase the risk of complications. Diabetes foot ulcers (DFU) are one of the most devastating consequences of type 2 diabetes. Untreated diabetic foot ulcers can lead

Tri Murti Andayani, Gadjah Mada University, Bulaksumur, Caturtunggal, Kec. Depok, Kabupaten Sleman, Daerah Istimewa Yogyakarta 55281, 55281 Sleman, Indonesia, e-mail: trimurtia@ugm.ac.id

Received: 3.01.2024 Accepted: 28.02.2024

to osteomyelitis, gangrene, and amputation. Amputees have a higher chance of death and a higher number of bacterial resistances among survivors [4]. DFU therapy entails wound care, antibiotics, amputations, and other routine care that incurs considerable annual costs [5, 6]. Diabetes care costs USD 740.1 per year, with the direct cost (drugs and hospitalisation) totalling USD 646.7 and indirect costs totalling USD 93.65 [7]. Diabetes-related issues of the lower limbs continue to be extremely onerous, and related expenditures have risen over the previous 20 years [8, 9].

The Wound Healing Intervention Guidelines of the International Working Group on the Diabetic Foot (IWGDF) recommend systemic hyperbaric oxygen therapy (HBOT) as a supplementary treatment for diabetic foot ulcers that are refractory despite the best standards of care [10]. Previous studies revealed that HBOT can expedite wound healing through a variety of pathways, including enhanced ROSs, angiogenesis, fibroblast replication, osteoclast activation, antioxidant plasma status, resolution of inflammation, and the up-regulation of VEGF and platelet-derived growth factor (PDGF) [11–14]. In 2019, a set of two randomised controlled trials revealed that HBOT in diabetic foot ulcers reduced wound area much more than standard therapy [15, 16]. Furthermore, a worldwide meta-analysis of 14 studies found that HBOT was considerably more effective than conventional therapy in treating diabetic foot wounds (OR = 0.29) and reducing major amputation (RR = 0.60) [17]. In addition, a meta-analysis of 11 RCTs (668 patients) on amputation and wound healing revealed that patients who received HBOT had a lower risk of amputation (OR 0.53) and a greater probability of wound recovery (OR 4.00) [18].

Although several studies have shown that HBOT is a promising treatment for ulcers in diabetic feet, the cost of applying HBOT to patients should be considered before its utilised. Numerous economic analyses have been performed, but there has been no systematic review focused on the cost-effectiveness of HBOT in diabetic foot wounds. The aim of this systematic review was to evaluate the cost-effectiveness of HBOT in patients with diabetic foot ulcer compared to standard care.

MATERIALS AND METHODS

SEARCH STRATEGY

A literature search was performed between the establishment of the database and 2023, using the databases Medline, Embase, and Cochrane. As Medical Subject Headings (MeSH) terms such as diabetic foot, economic, and hyperbaric oxygen were employed. Table 1 shows the Medline search approach, which can be applied to different databases. The most recent database search occurred on November 10, 2023.

Table 1. Search terms

	Searches
1	Diabetic foot
2	Diabetes mellitus
3	Ulcer or wound or lesion or lower limb
4	1 AND 2 AND 3
5	Cost or economic or cost analysis or cost-effectiveness or cost-effectivity
6	4 AND 5
7	Oxygen therapy or hyperbaric oxygen therapies or hyperbaric oxygenation
8	6 AND 7

STUDY SELECTION

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards, and Population, Intervention, Comparator, Outcome (PICO) research questions as detailed below [19, 20].

Population: Patients of all ages with diabetic foot ulcers

Intervention: Hyperbaric oxygen therapy

Comparator: Standard wound care

Outcome: Incremental cost effectiveness ratio (ICER)

Manuscript titles and abstracts were assessed, followed by a full-text eligibility assessment. The study investigators (A.K.F. and T.M.A.) separately and in duplicate reviewed the title and abstract. For studies assessing cost-effectiveness [calculating the incremental cost-effectiveness ratio], they proceed on to full-text review.

Articles were excluded if they were only published in abstract form, were not published in peer-reviewed journal, were written in a language other than English, did not include a cost-effectiveness assessment, did not evaluate patients with diabetic ulcers, or did not use HBOT. Disagreements among reviewers were handled through consensus, and agreement was measured (kappa statistics).

DATA EXTRACTION AND ANALYSIS

The main finding of this study was the cost-effectiveness of using HBOT for patients with diabetic foot wound. Study investigators (A.K.F. and T.M.A.) extracted data independently and in duplicate. The following data were extracted in duplicate: author, year, nation, population, model type, perspective, time horizon, discount rate, outcomes assessed, input details (clinical inputs and costs), clinical input sources, currency, main results, uncertainty evaluations, and general conclusions. Disagreements amongst reviewers were settled through consensus and a thorough examination of source texts.

The quality assessment of the studies included in the review was carried out based on the 2022 Consolidated

Health Economic Evaluation Reporting Standards (CHEERS) checklist, which consists of 28 items [21]. Two reviewers independently evaluated the studies against the standard, yielding a grade of 28. Every part was given single point; a half score (0.5) was allocated if the article did not fully meet the criteria, for instance, if the choice of perspective or discount rate was not interpreted. If the requirement was not met, 0 points were given. For all standard that were not applicable (N/A) to a single study, the overall possible grade was deducted by one point. The percentage values were calculated and identified using the previous literature [22, 23]. Excellent (> 80%), very good (70–80%), good (55–69%), and bad (< 55%) are the article classifications.

RESULTS

STUDY SELECTION

A database search retrieved 727 publications (Fig. 1). The same articles were removed, and 675 were evaluated for title or abstract. Following that, 666 items were eliminated since they did not fit into the criteria. A total of eight full-text articles were reviewed; three were included, while the remaining five (3 review articles, 1 protocol and 1 not HBOT) did not fit the requirements. Of all the cost-effectiveness studies, one was from Canada, one from the United States, and one from India. All studies were published between 2003 and 2022 (Table 2). The number of CHEERS Checklist items met by each study and their scores are shown in Table 3. Two articles met the criteria of excellent (Guo et al. [24] and Thiruvoth et al. [25]) and very good (Chuck et al. [26]). All articles do not explain the impact of interventions provided on other populations or approaches related to interventions to engage patients and stakeholders.

POPULATION AND INTERVENTION

In Guo's study [24], 1000 patients with DFU, aged 60 years or older and having a Wagner wound classifica-

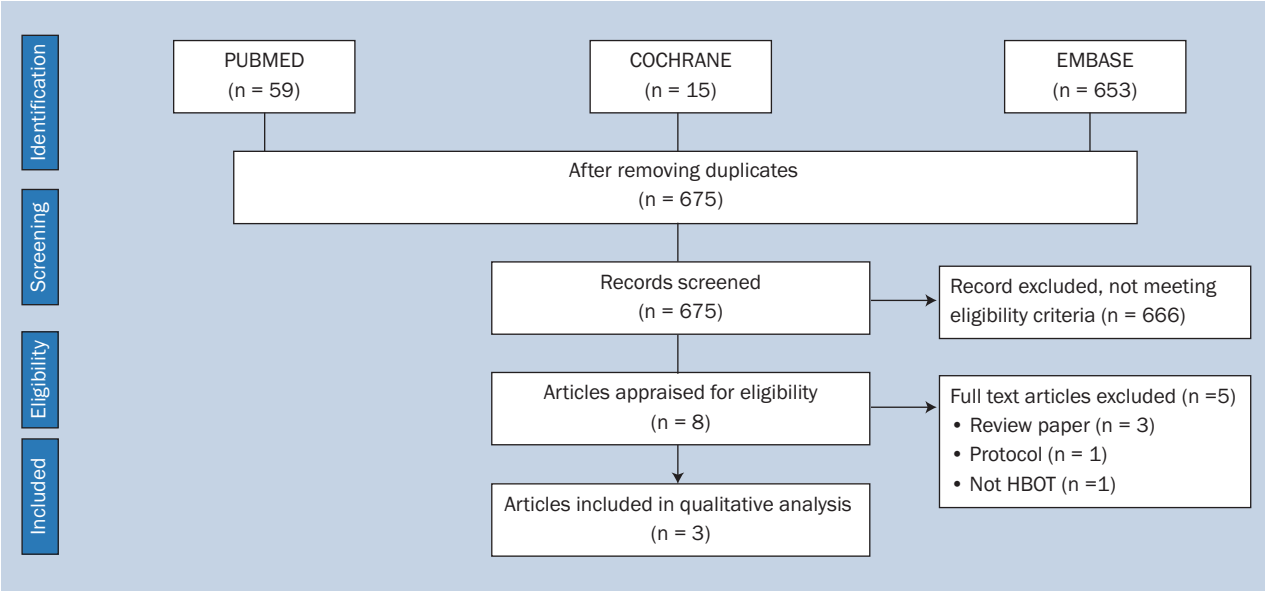

Figure 1. Flowchart of PRISMA study retrieval

Table 2. Study characteristics of article

Authors, country, year	Economic assessment	Population	Intervention and comparator	Perspective, year of costs	Discount rate (%)	Model	Outcome
Guo et al., US, 2003 [24]	CEA	60-year-old and older patients with severe DFU (Wagner Grade III and higher)	SWC combination HBOT versus SWC	Payer's and societal; 2001 USD.	3	Decision tree	LEAs, QALYs
Chuck et al., Canada, 2008 [26]	CEA	65-year-old Canadian patients with DFU	Adjunctive HBOT and SWC versus SWC	Ministry of Health; 2004 CAD	—	Decision tree	LEAs, healed wounds, unhealed
Thiruvoth et al., India, 2022 [25]	CUA	55-year-old patients with DFU (Wagner Grade II and higher)	Adjunctive HBOT plus SWC versus SWC	Societal, –	3	A Markov decision analysis	LEA, QALYs

CEA — cost-effectiveness analysis; CUA — cost-utility analysis; HBOT — hyperbaric oxygen therapy; LEA — low-extremity amputation; SWC — standard wound care; QALYs — quality-adjusted life years

tion > III were included. Patients were divided into groups for the HBOT intervention and control. HBOT group was administered 40 sessions; the type of chamber and pressure were not disclosed. Furthermore, Chuck's study included a sub-group of 65-year-old DFU patients. The HBOT group consisted of 149 patients, while the control group consisted of 156 patients. Each session of HBOT lasted 90 minutes and was administered 30–40 times. The pressure and kind of chamber utilised are not disclosed. Thiruvoth's study included patients with a Wagner wound grade > II DFU. The intervention group received approximately 30 HBOT sessions of 90 minutes each, with a pressure of two or three atmospheres in multiple chambers (Table 4).

METHODOLOGY OF THE COST-EFFECTIVENESS ANALYSES

The three studies used different perspectives, namely the societal perspective (Guo et al. [24], Thiruvoth et al. [25]) and the perspective of the Ministry of Health (Guo et al. [24]; Chuck et al. [26]). The time horizon began to be analysed in the first, fifth, and twelfth year in the remaining studies. The discount rate used in the analysis in two studies was 3% (Guo et al. [24]; Thiruvoth et al. [25]), while no information was provided in the third study. The economic analysis method used in all studies was the decision model. Decision analysis is a systematic, quantitative, and transparent approach to making decision beneath uncertainty. The basic instrument of decision analysis is a decision-analytic model, most frequently a decision tree or a Markov model.

RESULTS OF THE COST-EFFECTIVENESS ANALYSES

The QALY value obtained in the control group was 3.61–9.31, while the QALY in the HBOT group was 3.64–10.26. The ICER obtained in the first, fifth, and twelfth years includes 27,310 (first year); 5,166 (fifth year); –$4800; $2,255; CND$14,430; and INR193,939 (twelfth year). Two studies concluded that HBOT was cost-effective for DFU therapy, while the research performed in India stated that HBOT was not cost-effective.

DISCUSSION

This systematic review only analyses three articles on the cost-effectiveness of hyperbaric oxygen treatment in diabetes mellitus patients with feet wounds. Diabetic foot ulcers are diabetes complications that may contribute to leg amputations in individuals. Several therapies for accelerating ulcer repair and preventing intervention in diabetic patients include debridement, hydrotherapy, antibiotics, dressing, surgery of chronic ulcers, negative pressure wound therapy (NPWT), growth factors, cellular products, skin grafts, oxygen therapy, physical therapy, and other systemic therapies including medical and nutritional therapies [27–31]. Hyperbaric oxygen treatment is an additional therapy for diabetes mellitus that aids patients heal wounds and prevent leg amputation [32].

We identified a range of cost-effectiveness approaches that can influence the cost-effectiveness of HBOT, such as perspectives, models, types of costs included, and length of hyperbaric oxygen therapy. One article uses two perspectives, payers and societal, while the other two represent the Ministry of Health and societal perspectives, respectively. The payer or healthcare sector perspective is only concerned with direct care expenses (e.g. HBOT costs, physician expenditures, hospitalizations, outpatient visits, and medication). The cost-utility of HBOT in DFU patients in India was the only study that addressed indirect expenditures. The expenses of production losses due to illness in patients are used in this study from a society perspective.

We identified two research [24, 25] that prove the cost-effectiveness of expediting wound healing and preventing amputation. Based on a hypothetical cohort in the United States, 155 major lower extremity amputation (LEA) cases may have been averted, and 50.2, 265.3, and 608.7 QALYs gained at 1st, 5th and 12th year, respectively. The additional cost of using HBO2 therapy was estimated as ($5,901,500 HBOT treatment) + ($1,773,780 related to increased total of minor LEAs) + ($6,304,315 related to preventable major LEAs). These calculations resulted in higher expenses per additional QALY gained of about $27,310, $5,166, and $2,255 during the 1, 5, and 12-year time periods, demonstrating that HBOT is more cost-effective in the long term.

One-way sensitivity analysis conducted by Guo et al. revealed that the CE ratio is particularly sensitive to quality weights, the number of HBOT per patient, HBO2 expenses per session, major and minor LEAs treatment expenditures per case. The CE ratio is less affected by mortality and discount rates.

The Canadian study indicated a much lower percentage of serious LEA (11%) in participants undergoing adjuvant HBOT compared to conventional therapy alone (32%). Furthermore, when compared to controls, patients receiving HBOT had a greater prevalence of mild LEA. The cost of HBOT for DFU patients was CND$40,695 over a 12-year period, compared to CND$49,786 for those who received only standard treatment. The outcomes of HBOT group were 3.64 quality-adjusted life years (QALY) and 3.01 QALY for the controls. Because the results are better and the cost of HBOT is lower, adjuvant HBOT used in conjunction with conventional therapy is the being dominant technique. The model was found to be resilient when sensitivity analysis was done to the primary variables.

Only one study [25] found that HBOT was not cost-effective for DFU patients in India. When compared to the stan-

Table 3. Quality assessment of studies using CHEERS checklist

Article	Consolidated Health Economic Evaluation Reporting Standards 2022																											Score (%)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
Guo, 2023	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1	0	0	82
Chuck, 2008	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	0	0	0	75
Thiruvoth, 2022	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	–1	1	1	0	1	0	1	1	1	1	1	1	1	86

Table 4. Summary of outcome values from studies

Study	Time horizon (years)	Sessions, pressures, chambers of HBOT	Cost included	Clinical outcome	Cost	QALYs	CET	ICERs	Sensitivity analysis	Study conclusions
Guo et al., US, 2003	1, 5 and 12	4–38, (N.A.), (N.A.), (N.A.)	HBOT services; physician fees; amputation procedure, inpatient treatment, rehabilitation, outpatient visits over the first year	Healed, minor LEA, major LEA	HBOT $5,901,500	50.2, 265.3, and 608.7	$50,000	$27,310; $5,166; and $2,255/QALY	ICER are most sensitive to the quality weights, particularly for major LEA	In addition HBOT cost-effective. At years 1, 5 and 12, the ICER was $27,310, $5,166, and $2,255 respectively
Chuck et al., Canada, 2008	12	30–40, 90 min, (N.A.), (N.A.)	Annual wound care cost, HBOT costs.	Healed, unhealed, death, minor LEA. major LEA	HBOT C$40,695 SWC C$49,786	HBOT 3.64 SWC –3.01	C$ 50,000	—	HBOT remains to dominate	HBOT with SWC dominant compared to SWC alone CND$14,430
Thiruvoth et al., India, 2022	12	30, 90 min, 2–3 atm, multiple	Indirect medical cost,-Onon-medical0cost, and lost productivity due to illness	Healed ulcer, unhealed, minor LEA, major LEA, death	HBOT 659,790 SWC 500,92	HBOT 9.14 SWC 8.32	99,694–145,679 INR	193,735 INR (US$2621)/QALY	At the one GDP per capita level, only 10.5% of the scenarios are cost--effective	HBOT plus SWC is not cost-effective in the Indian context (INR193,939)

N.A. — not available

dard wound care (SWC) group alone, the HBOT group reduced minor and major LEA by 6.1% and 4.2%, respectively. The ICER per amputation avoided and per QALY gained were INR 125,761 (US$ 1,699) and 193,939 (US$ 2,621), respectively, which are both higher than the one-time Gross Domestic Product (GDP) per capita threshold (INR 99,694–45,679).The results of the one-way sensitivity analysis revealed that HBOT and SWC prices had the greatest impact on ICER. According to the PSA results, the simulated ICER value is higher than the one-time GDP threshold. If the CET value is INR 47,159 (US$ 637), hyperbaric oxygen therapy will be cost-effective.

The differences in costs and ICER values may be caused by variations in economic circumstances and clinical practice. Disparities in the cost-effectiveness of hyperbaric oxygen therapy in the United States, Canada, and India may be attributable to differences in these nations' economic conditions. The cost of hyperbaric oxygen therapy is higher in Canada and the United States than in India. Furthermore, because each author estimates a different session of hyperbaric oxygen therapy procedures, the expenditures incurred to obtain wound repair and avoid amputation vary. Willingness-to-pay (WTP) thresholds represent differences in the opportunity costs of health between countries. According to World Health Organisation (WHO) recommendations, The WTP threshold in India is one-time GDP per capita. When the ICER value of an intervention is less than one-time GDP per capita, it is deemed cost-effective and an adequate investment. Adopting GDP per capita standards, on the other hand, may not correctly represent the underlying health impact of increases in health expenditure, especially in low-resource situations [33–35].

There are numerous limitations to this systemic review. First of all, the number of research was limited, with two [22, 23] presenting data from around 20 years ago. Second, the findings reported in our study are limited region and cannot be generalised. These investigations were conducted in different countries with varied economic situations, making comparisons impossible. Third, the cost data on which the economic model's variables are based is of inferior quality. Utility measurements, for example, are based on research that indicates that the number of observations of people with severe amputations is quite limited. Since the number of amputations has declined dramatically in recent years, getting a large number of participants may be difficult. HBOT cost data is based on a small number of facilities, and reporting is not standardised. Nonetheless, there is high assurance in the fact that adjuvant HBOT for DFU patient is cost-effective.

CONCLUSION

Although HBOT is useful in hastening the healing process and averting amputations, its cost-effectiveness has not been proven in the present study since there is insufficient evidence to support its use in treating patients with diabetic foot wounds. The majority of HBOT studies have reported that HBOT is cost-effective. Currently, there is a limited number of pharmacoeconomic evaluations for the cost-effectiveness of HBOT in DFU. With the increasing prevalence of LEA in DFU, a comprehensive cost-effectiveness evaluation for the topic is fundamental.

ARTICLE INFORMATION AND DECLARATIONS

Author contributions: AAK: designed the analysis, collected data, performed the analysis and wrote the paper; TMA: performed the analysis and wrote the paper; LL: performed the analysis and wrote the paper.

Funding: This research was funded by LPDP (Educational Fund Management Institution) and BPPT (Higher Education Financing Centre) Indonesian Ministry of Education and Culture.

Acknowledgments: This research was funded by LPDP (Educational Fund Management Institution) and BPPT (Higher Education Financing Centre) Indonesian Ministry of Education and Culture.

Conflict of interest: The authors declare no conflict of interest.

Supplementary material: No supplementary material.

The dictionary of acronyms:

- CEA (cost-effectiveness analysis) is a type of economic study that compares the relative costs and outcomes of two or more interventions that perform the same activity.
- CUA (cost-utility analysis) is a type of economic study that compares the incremental cost of a program from a specific perspective and the incremental health improvement measured in quality-adjusted life years (QALYs).
- ICER (incremental cost-effectiveness ratio) is expresses as the difference in expenditures between two interventions divided by the difference in medical gain or quality of life.
- LEA (lower extremity amputation) is defined as the total loss of any lower limb component in the transverse anatomical plane.
- QALYs (quality-adjusted life years) are a unit of assessment for health outcomes which are also used as the denominator of an incremental cost-effectiveness ratio.
- SWC (standard wound care) is the current treatment.

REFERENCES

1. IDF Diabetes Atlas. https://diabetesatlas.org/atlas/ninth-edition/ (02.12.2023).
2. IDF DIABETES ATLAS, 10th edition. https://www.ncbi.nlm.nih.gov/books/NBK581934/ (02.12.2023).
3. DiPiro JT, Yee GC, Posey M. Pharmacotherapy: A Pathophysiologic Approach. 2020.

4. Shaheen MMA, Al Dahab S, Abu Fada M, et al. Isolation and characterization of bacteria from diabetic foot ulcer: amputation, antibiotic resistance and mortality rate. Int J Diabetes Dev Ctries. 2022; 42(3): 529–537, doi: 10.1007/s13410-021-00997-7, indexed in Pubmed: 34522073.
5. Kruse I, Edelman S. Evaluation and treatment of diabetic foot ulcers. Clinical Diabetes. 2006; 24(2): 91–93, doi: 10.2337/diaclin.24.2.91.
6. Raghav A, Khan ZA, Labala RK, et al. Financial burden of diabetic foot ulcers to world: a progressive topic to discuss always. Ther Adv Endocrinol Metab. 2018; 9(1): 29–31, doi: 10.1177/2042018817744513, indexed in Pubmed: 29344337.
7. Butt MD, Ong SC, Wahab MU, et al. Cost of illness analysis of type 2 diabetes mellitus: the findings from a lower-middle income country. Int J Environ Res Public Health. 2022; 19(19), doi: 10.3390/ijerph191912611, indexed in Pubmed: 36231911.
8. Jodheea-Jutton A, Hindocha S, Bhaw-Luximon A. Health economics of diabetic foot ulcer and recent trends to accelerate treatment. Foot (Edinb). 2022; 52: 101909, doi: 10.1016/j.foot.2022.101909, indexed in Pubmed: 36049265.
9. Armstrong DG, Swerdlow MA, Armstrong AA, et al. Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. J Foot Ankle Res. 2020; 13(1): 16, doi: 10.1186/s13047-020-00383-2, indexed in Pubmed: 32209136.
10. IWGDF Guideline on interventions to enhance healing of foot ulcers in persons with diabetes. www.iwgdfguidelines.org (02.12.2023).
11. Capó X, Monserrat-Mesquida M, Quetglas-Llabrés M, et al. Hyperbaric oxygen therapy reduces oxidative stress and inflammation, and increases growth factors favouring the healing process of diabetic wounds. Int J Mol Sci. 2023; 24(8), doi: 10.3390/ijms24087040, indexed in Pubmed: 37108205.
12. Memar MY, Ghotaslou R, Samiei M, et al. Antimicrobial use of reactive oxygen therapy: current insights. Infect Drug Resist. 2018; 11: 567–576, doi: 10.2147/IDR.S142397, indexed in Pubmed: 29731645.
13. Yıldırım AO, Eryılmaz M, Kaldırım U, et al. Effectiveness of hyperbaric oxygen and ozone applications in tissue healing in generated soft tissue trauma model in rats: an experimental study. Ulus Travma Acil Cerrahi Derg. 2014; 20(3): 167–175, doi: 10.5505/tjtes.2014.09465, indexed in Pubmed: 24936837.
14. Sunkari VG, Lind F, Botusan IR, et al. Hyperbaric oxygen therapy activates hypoxia-inducible factor 1 (HIF-1), which contributes to improved wound healing in diabetic mice. Wound Repair Regen. 2015; 23(1): 98–103, doi: 10.1111/wrr.12253, indexed in Pubmed: 25532619.
15. Hisamuddin N, Zahiruddin WN, Yazid BM, et al. Use of hyperbaric oxygen therapy (HBOT) in chronic diabetic wound — a randomised trial. Med J Malaysia. 2019; 74(5): 418–424, indexed in Pubmed: 31649219.
16. Oley MH, Oley MC, Islam AA, et al. Hyperbaric oxygen therapy in managing systemic inflammatory response syndrome caused by ischemia-reperfusion injury following hand replantation and long-term outcomes: A report of two cases. Ann Med Surg (Lond). 2020; 60: 155–161, doi: 10.1016/j.amsu.2020.10.023, indexed in Pubmed: 33145024.
17. Sharma R, Sharma SK, Mudgal SK, et al. Efficacy of hyperbaric oxygen therapy for diabetic foot ulcer, a systematic review and meta-analysis of controlled clinical trials. Sci Rep. 2021; 11(1): 2189, doi: 10.1038/s41598-021-81886-1, indexed in Pubmed: 33500533.
18. Moreira DA Cruz DL, Oliveira-Pinto J, Mansilha A. The role of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers: a systematic review with meta-analysis of randomized controlled trials on limb amputation and ulcer healing. Int Angiol. 2022; 41(1): 63–73, doi: 10.23736/S0392-9590.21.04722-2, indexed in Pubmed: 34236155.
19. "PRISMA". http://www.prisma-statement.org/PRISMAStatement/ (02.12.2023).
20. Aslam S, Emmanuel P. Formulating a researchable question: a critical step for facilitating good clinical research. Indian J Sex Transm Dis AIDS. 2010; 31(1): 47–50, doi: 10.4103/0253-7184.69003, indexed in Pubmed: 21808439.
21. Husereau D, Drummond M, Augustovski F, et al. CHEERS 2022 ISPOR Good Research Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. BMC Med. 2022; 20(1): 23, doi: 10.1186/s12916-021-02204-0, indexed in Pubmed: 35022047.
22. Hope SF, Webster J, Trieu K, et al. A systematic review of economic evaluations of population-based sodium reduction interventions. PLoS One. 2017; 12(3): e0173600, doi: 10.1371/journal.pone.0173600, indexed in Pubmed: 28355231.
23. Langer A. A framework for assessing Health Economic Evaluation (HEE) quality appraisal instruments. BMC Health Serv Res. 2012; 12: 253, doi: 10.1186/1472-6963-12-253, indexed in Pubmed: 22894708.
24. Guo S, Counte MA, Gillespie KN, et al. Cost-effectiveness of adjunctive hyperbaric oxygen in the treatment of diabetic ulcers. Int J Technol Assess Health Care. 2003; 19(4): 731–737, doi: 10.1017/s0266462303000710, indexed in Pubmed: 15095781.
25. Thiruvoth FM, Rajasulochana S, S M, et al. Hyperbaric oxygen therapy as an adjunct to the standard wound care for the treatment of diabetic foot ulcers in Indian patients: a cost utility analysis. Expert Rev Pharmacoecon Outcomes Res. 2022; 22(7): 1087–1094, doi: 10.1080/14737167.2022.2085562, indexed in Pubmed: 35649289.
26. Chuck AW, Hailey D, Jacobs P, et al. Cost-effectiveness and budget impact of adjunctive hyperbaric oxygen therapy for diabetic foot ulcers. Int J Technol Assess Health Care. 2008; 24(2): 178–183, doi: 10.1017/S0266462308080252, indexed in Pubmed: 18400121.
27. Vas P, Rayman G, Dhatariya K, et al. Effectiveness of interventions to enhance healing of chronic foot ulcers in diabetes: a systematic review. Diabetes Metab Res Rev. 2020; 36 Suppl 1: e3284, doi: 10.1002/dmrr.3284, indexed in Pubmed: 32176446.
28. Chen L, Zhang S, Da J, et al. A systematic review and meta-analysis of efficacy and safety of negative pressure wound therapy in the treatment of diabetic foot ulcer. Ann Palliat Med. 2021; 10(10): 10830–10839, doi: 10.21037/apm-21-2476, indexed in Pubmed: 34763444.
29. Lim JZ, Ng NS, Thomas C. Prevention and treatment of diabetic foot ulcers. J R Soc Med. 2017; 110(3): 104–109, doi: 10.1177/0141076816688346, indexed in Pubmed: 28116957.
30. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. Ann N Y Acad Sci. 2018; 1411(1): 153–165, doi: 10.1111/nyas.13569, indexed in Pubmed: 29377202.
31. Core MD, Ahn J, Lewis R, et al. The evaluation and treatment of diabetic foot ulcers and diabetic foot infections. Foot Ankle Orthop. 2018; 3(3): 247301141878886, doi: 10.1177/2473011418788864.
32. Elraiyah T, Tsapas A, Prutsky G, et al. A systematic review and meta-analysis of adjunctive therapies in diabetic foot ulcers. J Vasc Surg. 2016; 63(2 Suppl): 46S–58S.e1, doi: 10.1016/j.jvs.2015.10.007, indexed in Pubmed: 26804368.

33. Tuglo LS, Nyande FK, Agordoh PD, et al. Knowledge and practice of diabetic foot care and the prevalence of diabetic foot ulcers among diabetic patients of selected hospitals in the Volta Region, Ghana. Int Wound J. 2022; 19(3): 601–614, doi: 10.1111/iwj.13656, indexed in Pubmed: 34190402.
34. Home — TreeAge Software. https://www.treeage.com/ (02.12.2023).
35. Woods TJ, Tesfay F, Speck P, et al. Economic evaluations considering costs and outcomes of diabetic foot ulcer infections: a systematic review. PLoS One. 2020; 15(4): e0232395, doi: 10.1371/journal.pone.0232395, indexed in Pubmed: 32353082.