A cost minimization analysis of olive oil vs. hyperoxygenated fatty acid treatment for the prevention of pressure ulcers in primary healthcare: A randomized controlled trial

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ABSTRACT

Pressure ulcers represent a major current health problem and cause an important economic impact on the healthcare system. Most studies on the prevention of pressure ulcers have been carried out in hospital contexts, with respect to the use of hyperoxygenated fatty acids (HOFA), and to date no studies have specifically examined the use of olive oil-based treatments. Aim: To evaluate the cost of using extra virgin olive oil, rather than HOFA, in the prevention of pressure ulcers among persons with impaired mobility and receiving home care. Study Design: Cost minimization analysis of the results obtained from a noninferiority, triple-blind, parallel, multicenter, randomized clinical trial. Population attending primary healthcare centers in Andalusia (Spain). Study sample: 831 immobilized patients at risk of suffering pressure ulcers. These persons were included in the study and randomly assigned as follows: 437 to the olive oil group and 394 to the HOFA group. At the end of the follow-up period, the results obtained by the olive oil group were not inferior to those of the HOFA group, and did not exceed the 10% delta limit. The total treatment cost for 16 weeks was € 19,758 with HOFAs and € 9,566 with olive oil. Overall, the olive oil treatment was € 10,192 less costly. It has been concluded the noninferiority of olive oil makes this product an effective alternative for the prevention of pressure ulcers in patients who are immobilized and in a domestic environment. This treatment enables considerable savings in direct costs.

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Pressure ulcers have a major impact on the family, society, and the economy. First, because they commonly occur in healthcare and social attention. Their prevalence in hospitals in Spain (8.24%)[1] is very similar to corresponding values for neighboring countries such as Italy (8.3%), France (8.9%), Germany (10.2%), and Portugal (12.5%)[2,3] and also to those of more distant countries, such as Jordan (12%)[4]. The highest prevalence values reported correspond to Ireland (18.5%), Wales (26.7%)[5,]Belgium (21.1%), United Kingdom (21.9%), Denmark (22.7%), and Sweden (23.0%)[6] With respect to the occurrence of pressure ulcers in homes for the elderly, perhaps the most important study carried out is that by Park-Lee[7], who analyzed the situation of nursing homes in the United States and recorded a prevalence of 11%. In Spain, nursing homes have reported a crude prevalence of 6.39% with an average prevalence of 7.35% 66.4% (median 5.55)[1]. In primary healthcare, and specifically in patients receiving home care, a crude prevalence rate of 5.89% has been reported[1].

This problem, in addition to the clinical implications and the personal suffering it causes, is a challenge from the point of view of the costs provoked. Studies have analyzed the economic costs associated with ulcers, both from a global perspective (that of the financial repercussions) and concerning the impact on the individual[8].

Compared to other health problems, which at first glance might appear to be of much greater significance to the health system and society in general, pressure ulcers are in fact of major importance. Thus, annual spending on antiretroviral treatment is around € 422 million, while the annual cost of the most economic option related to the treatment of pressure ulcers (moist wound healing) is € 461 million, while that of the most costly approach (traditional healing) is € 602 million[9]. These figures give an idea of the importance of pressure ulcers in health service planning and decisions, taking into account, moreover, that population aging and increasingly common situations of chronic dependence will only increase the probability of this problem occurring.10 Preventive strategies are of special importance[8,11], both for patients and for service providers and decision makers, as such strategies have been shown to reduce incremental costs, reducing the prevalence of ulcers and also the numbers of avoidable deaths, in different care settings[12,13] and under different treatment approaches[14,15].

One type of preventive intervention of pressure ulcers that is widely used in nursing is the application of hyperoxygenated fatty acids (HOFA), although the quality of research evidence is limited because most studies have been conducted vs. a placebo and have suffered considerable imprecision in the results reported, as well as being subject to additional costs[16,17].1 Important results were obtained by Torra i Bou, who reported an incidence of pressure ulcers of 7.32% in the HOFA group vs. 17.37% in the placebo group[18]. Our research group conducted a clinical trial focused on the use of olive oil as a preventive strategy against pressure ulcers, taking into account the high concentration of antioxidants in this substance and its great resistance to oxidation. The resistance of the skin is enhanced by the oleic acids in the oil, which are of key importance in reconstructing the cellular membranes, renewing the epidermal cells and restoring capillary circulation, thus increasing microcirculation[19,21].By means of a multicenter randomized triple-blind controlled noninferiority trial, we evaluated the noninferiority of virgin extra olive oil vs. HOFA. The results obtained show that none of the body areas evaluated presented risk differences for pressure ulcer incidence that exceeded the preestablished 10% delta value[22]. However, despite these promising clinical results, to date no information has been published concerning the cost implications of such an intervention. The aim of the present study is to evaluate the economic impact of the treatment strategy described.

METHODS

Trial design

This analysis is based on the interventions carried out in a non-inferiority triple-blind parallel multicenter randomized clinical trial, performed in a primary health setting with home care patients. The study protocol, the sample characteristics and the clinical outcomes are reported elsewhere[22].The study consisted of two different interventions: usual care, with the application of HOFA to the control group, and usual care with the application of an olive oil composition to the target group. The most important outcome was the appearance of Stage 2 or higher-pressure ulcers at 16 weeks of follow up. A cost minimization analysis comparing olive oil and HOFA was carried out. This form of economic analysis was considered to be the most appropriate for assessing treatment options that are equivalent in terms of efficacy and safety[23].

Recruitment and selection

The study population was composed of patients included in the immobilized patients program and receiving the home nursing service provided by health centers in Andalusia (Spain). Our sample characteristics were similar to those observed in previous HOFA efficacy trials[24-26].

Patients were excluded if their permanent address was external to the catchment area of the corresponding health center, if they were assigned to another area, if they refused to take part in the study during the follow-up period, if hospitalization was required during the sampling period, if they were critically ill or if the screening revealed the current presence of a pressure ulcer. The following inclusion criteria were applied: patients aged over 18 years, who had the support of a family member or paid caregiver for treatment application, who were at risk of impaired skin integrity according to the Braden Scale ≤16, who were examined by a nurse and who presented a nutritional status of ≤10 according to the Mini Nutritional Assessment. Patients included in the study were randomly allocated to a 1: 1 control/target group scheme by a computer system blinded to the professionals and the research team. When a patient met the inclusion criteria, his/her nurse was informed of the group to which they were allocated by means of a telephone call from a centralized randomization unit.

Outcome measures

The general outcome measure applied was the incidence of Stage 2 pressure ulcers during the 16-week follow-up period, according to the International NPUAP/EPUAP pressure ulcer classification system (partial thickness skin loss).27 A baseline assessment was conducted on all patients at the beginning of the trial and repeated each week until the conclusion of the follow-up period, or until the appearance of a pressure ulcer. Sociodemographic and specific patient variables were collected.

Direct costs

In this clinical trial, both products (olive oil and HOFA) were masked with the same presentation. For the cost minimization analysis, we calculated the price of a unit dose of each product, based on the price per application (spray).

The amount of product consumed by each spray was 0.133 ml, and so the cost of spraying with olive oil was € 0.02384 and with HOFA it was € 0.05719. According to the intervention protocol for this clinical trial, every patient received 10 sprays per day in

total, distributed in two daily applications in five zones (2 heels12 trochanters11 sacrum), in each branch of the study. Thus, the daily cost per patient was € 0.2384 with olive oil and € 0.5719 with HOFA. Subsequently, the weekly treatment cost was calculated by computing the weekly compliance for each patient, adjusted by the price per dose of the product.

In its commercial presentation of 100 ml, HOFA costs e43 and, according to the manufacturer, this is sufficient for 750 applications. The commercial presentation of the olive oil preparation contains 100 ml and costs € 18. According to the manufacturer, this is sufficient for 1,000 applications.

The study was carried out from 2012 to 2015.

No structural fixed costs were assigned to either of the products because in all cases this healthcare was provided in the patient's home. Neither was it possible to assess the cost of family care, because this factor is difficult to determine and subject to considerable variability. The presence or otherwise of a salaried caregiver was also excluded from our cost calculation, because this consideration would generate bias in the estimation with respect to patients who did not use such a person. Finally, we were unable to assess intangible costs arising from aspects such as the level of pain suffered during the process.

Ethics statement

This study was approved by the ethics committee of the Malaga Regional Hospital.

Informed consent

Written informed consent was obtained from all participants involved in the study.

Procedure

Both groups were instructed regarding preventive care[28]. The patients in the control group received two applications per day in five zones (10 applications in total) of the HOFA-based product, in the sacral area and on the hips and heels. The HOFA product used offered the CE mark, Class IIb, a higher classification than that of competing products. The olive oil procedure involved applying a magistral formula, in liquid spray form, containing 97% extra-virgin olive oil and 3% Hypericum perforatum and peppermint. This group, too, received two applications per day in five zones (10 applications in total).

Any presence of pressure ulcer was recorded in the weekly follow-up report, stating also whether skin integrity was maintained. Any adverse effects occurring during the follow-up period were reported using a purpose-designed document.

Statistical analysis

Descriptive statistics were obtained, with measures of central tendency and dispersion and the verification of normal distributions. In addition, the difference of the means was calculated for each week of treatment and for the overall period, using nonparametric Wilcoxon tests.

Analyses were performed per protocol, in accordance with the standard indications for noninferiority studies, and included all patients who completed the follow-up period and received the treatment assigned, to maximize the difference between treatments and to strengthen the conditions for rejection of the null hypothesis. However, an analysis by intention to treat was also performed, to compare the two analyses and to assess, in the absence of coincidence, the subgroups of patients who did not fulfil the study protocol, to identify possible causes of treatment dropout, before rejecting or accepting the null hypothesis. In this analysis, missing data were estimated by multiple imputation, a process in which five imputations were made for each variable (the incidence of any pressure ulcer in the sacrum, hips or heels)[29,30].

The following monotonic method was applied if the data presented a monotonic pattern of missing values. A univariate model (with a single dependent variable) was fitted to each variable of the monotonic order, using all previous variables (incidence of pressure ulcers) as predictors, and then imputing the missing values of the variables being fitted. Otherwise, the fully conditional specification was used. The imputation model of each variable included a constant term and the main effects of the predictor variables.

Finally, a sensitivity analysis was conducted to determine possible differences between patients who complied with the protocol and those who did not, to estimate potential bias in this respect. This analysis was performed on the following variables: patient sex and age, sex of the family caregiver, degree of mobility, history of pressure ulcers, cognitive impairment, incontinence, diabetes, other chronic diseases, technical aids, ankle

protectors, and other pressure relief devices, and the prior use of another product for the prevention/relief of pressure ulcers. A longitudinal analysis was performed using the Cox proportional regression model, for the 16-week follow-up period, to estimate the hazard ratio for pressure ulcers with respect to sex, age, nutritional status, pressure ulcer history, cognitive status, type of product, degree of mobility, and risk of pressure ulcer (measured on the Braden scale).

Statistical analyses were performed using SPSS 22 software.

RESULTS

Eight hundred thirty-one persons were included in the study, and randomly assigned as follows: 437 to the olive oil group and 394 to the HOFA group, with no differences in baseline characteristics between the groups. In the between-groups analysis, conducted at the end of the follow-up period, per protocol, none of the body areas evaluated presented risk differences for pressure ulcer incidence that exceeded the pre-established 10% delta value. The intention-to-treat analysis showed that the lower limit of the confidence interval established for noninferiority was not exceeded in any of the areas assessed[22].

Thus, the absolute risk reduction in pressure ulcers with imputed data at week 16 in the sacrum was 20.2 (95%CI: 22.3 to 1.8; p50.282), on the right heel 6.2 (95%CI: 20.1 to 12.5; p50.264), on the left heel 5.9 (95%CI: 20.4 to 12.2; p50.250), on the right trochanter 6.8 (95%CI: 0.5 to 13.1; p50.515), and on the left trochanter 3.2 (95%CI: 21.3 to 7.7; p50.257).

The total treatment cost for 16 weeks was € 19,758 with HOFA and € 9,566 with olive oil. The overall cost difference between the two treatments was € 10,192 in favor of olive oil. Throughout the follow-up period, the total treatment cost for the HOFA group doubled that of the olive oil group (see Figure 1). Thus, in week 1, the treatment cost in the olive oil group was € 729, vs. € 1574 euros for the HOFA group. In week 8, halfway through the followup period, the costs were € 606 and € 1282, respectively. Finally, in week 16, the costs were € 523 and € 1039, respectively. The weekly cost per patient throughout the study is shown in Figure 1 (€ 1.60 for olive oil, and € 4.00 for HOFA).

The total cost comparison, over 4-week periods and overall, confirms the difference illustrated in Figure 1. During the first 4-week period, the treatment costs were € 2,757

for olive oil and € 5,811 for HOFA; in the second, they were € 2,463 and € 5,242, respectively; in the third, they were € 2,244 and € 4,527, respectively; and in the fourth, they were € 2,102 and € 4,179, respectively. The cost of the entire follow-up period with olive oil treatment was € 9,566 compared to € 19,758 in the HOFA group.

DISCUSSION

The results obtained confirm the non-inferiority of the olive oil treatment. There were no differences exceeding the lower limit of the confidence interval. Thus, the olive oil preparation is no less effective than HOFA for preventing pressure ulcers in immobilized patients in a home setting.

This clinical trial highlights the feasibility of preventing pressure ulcers at considerable economic savings amounting to € 10,192 during the study period, by means of the olive oil alternative treatment.

The costs of treating pressure ulcers represent a significant outlay for the healthcare system and for society in general, and for this reason cost-effective prevention is the main focus of this study. Significant reductions in direct and indirect costs could be achieved by reducing the incidence of pressure ulcers; this would lower drug costs, alleviate the workload of healthcare professionals, shorten hospital stays, and even decrease rates of morbidity among carers related to overload and stress. A lower product cost would enable greater accessibility to it, thus providing the health system with cost savings and constituting an alternative treatment to HOFA.

The cost of treating a pressure ulcer increases substantially in direct proportion to the severity of the ulcer, ranging from € 24 euros for Grade I to € 6,802 euros for Grade IV for patients treated in hospitals[31].The total annual cost of treating pressure ulcers in Spain is about € 461 million, which represents 5% of total health spending; of this amount, dressings and other materials account for 15%, nursing time another 19%, and the extra hospital time required by these lesions, another 45%.

There is broad consensus that prevention is the most efficient means of addressing the problem, in view of the substantial cost of treatment[32-35], hence the importance of continuing research into prevention.

In view of the major economic savings reflected in this study, we believe that the results we report, for the different scenarios, are of great importance. For example, in the domestic setting, patients can be offered a treatment alternative providing a financial saving of over 50% compared to the conventional approach. In a context of major socioeconomic inequalities, as is the case of healthcare in the home, and moreover, exacerbated by the current financial crisis, access to high-cost measures that are not funded by the public health system can be an almost insuperable problem for persons with low incomes[36].In future studies in this area, it would be useful to examine the question of accessibility and the use of different treatment options, taking into account the existence of different social profiles.

As regards the management of healthcare services, our results show that there is an interesting alternative which could significantly reduce pharmaceutical expenditure. If, as expected, this achieved a lower incidence of pressure ulcers, it would very likely have a direct impact in reducing the consumption of human resources for the treatment of active pressure ulcers and of materials for treating this condition, with the consequent reduction in costs. However, further studies are needed to specifically assess this potential impact on the costs of human resources.

A decrease in the prevalence of pressure ulcers would shorten the total number of hospital stays and thus reduce costs[11,13], although the full extent of these benefits remains to be established. Finally, although the relationship is indirect, it is also necessary to evaluate the potential impact of this change on reducing the morbidity of overload among caregivers.

However, another factor that must be taken into consideration is that of potential organizational barriers to the development of prevention policies within the public healthcare system. Hospitals and health district administrators may be reluctant to pay more for the prevention of an event such as pressure ulcers, which may or may not appear. Nevertheless, our study shows that prevention with the olive oil treatment is even cheaper than the HOFA alternative and that the apparent increase in initial costs would not be accompanied by a budget increase, because the benefits of the prevention strategy would

offset the additional investment made. These claims need to be experimentally proven in the context of healthcare in Spain, to determine the precise savings that could be achieved.

To the best of our knowledge, to date no specific studies have been conducted into the cost of preventing pressure ulcers in the domestic context, but various cost-effectiveness analyses have been performed in hospitals and nursing homes, and all of them report very significant data on the profitability of preventive measures, although with several limitations. These findings can serve as valuable indications for future research. One such study is that by Shannon[37], who evaluated pressure ulcer prevention strategies in nursing homes and rehabilitation centers and measured a 67% incidence attributable to preventive measures. Similarly, Mathiesen[12] demonstrated that pressure ulcer prevention programs in Danish hospitals can be profitable. Finally, Padula13 concluded that the prevention of nosocomial pressure ulcers was more cost effective than standard care.

Specific research is required, especially in the home environment, into cost effectiveness and cost utility, comparing this new intervention with other possible preventive interventions, together with specific studies into the cost of prevention vs. the cost of treatment of pressure ulcers, addressing the following issues: the impact of a declining incidence of pressure ulcers on treatment costs, comparing methods aimed at prevention with those oriented toward treatment; and determining the threshold at which the cost of preventing pressure ulcers is greater than its cost effectiveness.

Limitations

In the cost analysis performed, indirect costs such as the inputs of formal and informal caregivers were not included in the model because this variable is difficult to obtain and is subject to high variability. Moreover, when a salaried caregiver was present, this circumstance was not included in the cost calculations, because it would generate a bias with respect to patients who did not have this benefit. Finally, the intangible costs related to the suffering of the patient could not be calculated.

We acknowledge that family caregivers could have paid greater attention to pressure ulcers as a result of their participation in this study. Nevertheless, this phenomenon could have occurred in both or either of the groups, and the triple blinded randomized controlled

study design prevented any potential bias in favor of either group. The product was masked for caregivers and nurses, and the conditions for its administration were of routine practice, within the usual care that the family caregivers provided. Moreover, it is unlikely that the study would raise caregivers' attention, as monitoring of the skin in risk areas is a common practice in this type of home healthcare, managed and guided by community nurses.

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Authors' Contributions Statement: ILP took part in the original concept and design of this study and drafted the initial manuscript. JMMA, JCM, SKU, YLP, MCFG FJMS, and JCB took part in the concept and design of the study and critically reviewed the draft manuscript, providing a major intellectual contribution to the final version. All authors have read and approved the final manuscript.

REFERENCES

1. Soldevilla Agreda JJ, Torra i Bou J-E, Verd u Soriano J, López Casanova P. 3.er Estudio Nacional de Prevalencia de Ulceras por Presión en España, 2009: Epidemiología y variables definitorias de las lesiones y pacientes. Gerokomos 2011; 22 (2): 77–90.

2. Kottner J, Lahmann N, Dassen T. [Pressure ulcer prevalence: comparison between nursing homes and hospitals]. Pflege Z 2010; 63 (4): 228–31.

3. Wilborn D, Halfens R, Dassen T, Tannen A. [Pressure ulcer prevalence in German nursing homes and hospitals: what role does the National Nursing Expert Standard Prevention of Pressure Ulcer play?]. Gesundheitswesen 2010; 72 (4): 240–45.

4. Tubaishat A, Anthony D, Saleh M. Pressure ulcers in Jordan: a point prevalence study. J Tissue Viability 2011; 20 (1): 14–9.

5. James J, Evans JA, Young T, Clark M. Pressure ulcer prevalence across Welsh orthopaedic units and community hospitals: surveys based on the European Pressure Ulcer Advisory Panel minimum data set. Int Wound J 2010; 7 (3): 147–52.

6. Defloor T, Schoonhoven L, Katrien V, Weststrate J, Myny D. Reliability of the European Pressure Ulcer Advisory Panel classification system. J Adv Nurs 2006; 54 (2): 189–98.

7. Park-Lee E, Caffrey C. Pressure ulcers among nursing home residents: United States, 2004. NCHS Data Brief 2009; (14): 1–8.

8. Silva AJ, Pereira SM, Rodrigues A, Rocha AP, Varela J, Gomes LM, et al. [Economic cost of treating pressure ulcers: a theoretical approach]. Rev Esc Enferm U P 2013; 47 (4): 971–6.

9. Javier SA, Jos e J-E. T i B, John P, Jos e VS, Lorena SM, M MS J. Una aproximación al impacto del coste económico del tratamiento de las ulceras por presión en España. Gerokomos Rev Soc Esp Enferm Geriatrica Gerontológica 2007; 18 (4): 201–10.

10. Foglia E, Restelli U, Napoletano AM, Coclite D, Porazzi E, Bonfanti M, et al. Pressure ulcer management: an economic evaluation. J Prev Med Hyg 2012; 53 (1): 30–6.

11. Dealey C, Posnett J, Walker A. The cost of pressure ulcers in the United Kingdom. J Wound Care 2012; 21 (6): 261–2, 264, 266.

12. Mathiesen ASM, Nørgaard K, Andersen MFB, Møller KM, Ehlers LH. Are labour intensive efforts to prevent pressure ulcers cost-effective?. J Med Econ 2013; 16 (10): 1238–45.

13. Padula WV, Mishra MK, Makic MBF, Sullivan PW. Improving the quality of pressure ulcer care with prevention: a cost-effectiveness analysis. Med Care 2011; 49 (4): 385–92.
14. Sanada H, Nakagami G, Mizokami Y, Minami Y, Yamamoto A, Oe M, et al. Evaluating the effect of the new incentive system for high-risk pressure ulcer patients on wound healing and cost-effectiveness: a cohort study. Int J Nurs Stud 2010;
47 (3): 279–86.
15. Schuurman J-P, Schoonhoven L, Defloor T, van Engelshoven I, van Ramshorst B, Buskens E. Economic evaluation of pressure ulcer care: a cost minimization analysis of preventive strategies. Nurs Econ 2009; 27 (6): 390–400, 415.
16. National Clinical Guideline Centre (UK). The prevention and management of pressure ulcers in primary and secondary care [internet]. London: National Institute for Health and Care Excellence (UK), 2014. Available at http://www.ncbi.nlm.nih. gov/books/NBK248068. Accessed February 2, 2016.
17. Candela-Zamora MD, Martín-Gómez MA, Solas-Gómez B, Fernández-P erez C, Martín-González M, Manzanedo-Basilio L, et al. Comparative study of the effectiveness two of hyperoxygenated fatty acids in the treatment of grade I ulcers in geriatric hospitalized patients. Enferm Clínica 2010; 20 (1): 10–6.
18. Torra i Bou JE, Segovia Gomez T, Verd u Soriano J, Nolasco Bonmat ı A, Rueda Lopez J, Arboix i Perejamo M. The effectiveness of a hyperoxygenated fatty acid compound in preventing pressure ulcers. J Wound Care 2005; 14 (3): 117–21.
19. Beauchamp GK, Keast RSJ, Morel D, Lin J, Pika J, Han Q,
et al. Phytochemistry: ibuprofen-like activity in extra-virgin olive oil. Nature 2005; 1437 (7055): 45–6.
20. Owen RW, Giacosa A, Hull WE, Haubner R, W€urtele G, Spiegelhalder B, et al. Olive-oil consumption and health: the possible role of antioxidants. Lancet Oncol 2000; 1: 107–12.
21. Carrillo P. Propiedades del aceite de oliva en el mantenimiento de la integridad cut anea. Semin M ed 2009; 61 (2): 61–90.
22. Lupiañez-Perez I, Uttumchandani SK, Morilla-Herrera JC, Martin-Santos FJ, Fernández-Gallego MC, Navarro-Moya FJ, et al. Topical olive oil is not inferior to hyperoxygenated fatty AIDS to prevent pressure ulcers in high-risk immobilized patients in home care. Results of a multicentre randomised triple-blind controlled non-inferiority trial. PLoS One 2015; 10 (4): e0122238.

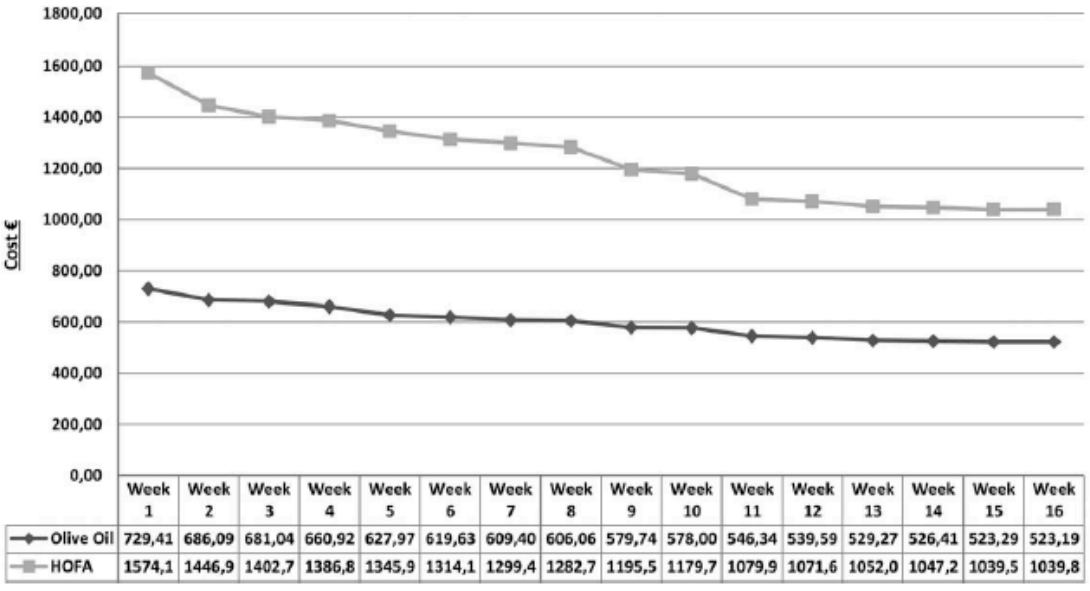
23. Drummond MF. Métodos para la evaluación económica de los programas de asistencia sanitaria. Ediciones Dıaz de Santos, Spain, 2001:382.
24. Segovia Gómez T, Bermejo Martínez M, Molina Silva R, Rueda López J, Torra i Bou JE. [Skin care and pressure ulcer. Hyperoxygenated fatty acids in the prevention of pressure ulcers and treatment of stage I lesions.]. Rev Enferm
Barc Spain 2001; 24 (9): 18–22.
25. Torra i Bou J-E, Rueda Lopez J, Segovia Gomez T, Bermejo Martínez M. [Topical administration of a hyperoxygenated fatty acid compound. Preventive and curative effects on pressure ulcer.]. Rev Enferm Barc Spain 2003; 26 (1): 54–61.
26. Gallart E, Fuentelsaz C, Vivas G, Garnacho I, Font L, Ar an R. Estudio experimental para comprobar la efectividad de los ácidos grasos hiperoxigenados en la prevención de las ulceras por presión en pacientes ingresados. Rev Enferm Clínica
2001; 11 (5): 179–83.
27. National Pressure Ulcer Advisory Panel. European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers: Quick Reference Guide. Available at www.npuap.org/wp-content/ uploads/2014/08/Quick-Reference-GuideDIGITAL-NPUAPEPUAP- PPPIA.pdf. Accessed Feb 2, 2016.
28. Morilla Herrera JC, Martín Santos FJ, Blanco Morgado J, Morales Asensio JM. Guía de práctica clínica para el manejo del deterioro de la integridad cutánea: ulceras por presión. 2004 [cited 2012 Jul 26]. Available at http://www.index-f.
com/lascasas/documentos/lc0281.pdf. Accessed February 2, 2016.
29. Matilde Sanchez M, Chen X. Choosing the analysis population in non-inferiority studies: per protocol or intent-to-treat. Stat Med 2006; 25 (7): 1169–81.
30. Snapinn SM. Noninferiority trials. Curr Control Trials Cardiovasc Med 2000;1 (1): 19–21.
31. Brem H, Maggi J, Nierman D, Rolnitzky L, Bell D, Rennert R, et al. High cost of stage IV pressure ulcers. Am J Surg 2010; 200 (4): 473–7.
32. Delmore B, Lebovits S, Baldock P, Suggs B, Ayello EA. Pressure ulcer prevention program: a journey. J Wound Ostomy Cont Nurs 2011; 38 (5): 505–13.
33. Salcido R, Lee A, Ahn C. Heel pressure ulcers: purple heel and deep tissue injury. Adv Skin Wound Care 2011; 24 (8): 374–80. quiz 381–2.
34. White-Chu EF, Flock P, Struck B, Aronson L. Pressure ulcers in long-term care. Clin Geriatr Med 2011; 27 (2): 241–58.

35. Lee T-T, Lin K-C, Mills ME, Kuo Y-H. Factors related to the prevention and management of pressure ulcers. Comput Inform Nurs CIN 2012; 30 (9): 489–95.

36. Impacto de la Crisis Económica en la Salud y en el Sistema Sanitario en España [Internet]. Escuela Andaluza de Salud Pública. 2015. Available at http://www.easp.es/project/ impacto-de-la-crisis-economica-en-la-salud-y-en-el-sistemasanitario- en-España. Accessed February 2, 2016.

37. Shannon RJ, Brown L, Chakravarthy D. Pressure Ulcer Prevention Program Study: a randomized, controlled prospective comparative value evaluation of 2 pressure ulcer prevention strategies in nursing and rehabilitation centers. Adv Skin Wound Care 2012; 25 (10): 450–64.

Figure 1. Weekly treatment cost for each product, per patient.



	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16
Olive Oil	729,41	686,09	681,04	660,92	627,97	619,63	609,40	606,06	579,74	578,00	546,34	539,59	529,27	526,41	523,29	523,19
HOFA	1574,1	1446,9	1402,7	1386,8	1345,9	1314,1	1299,4	1282,7	1195,5	1179,7	1079,9	1071,6	1052,0	1047,2	1039,5	1039,8