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EFFICIENCY IN SPINE CARE

ASSESSING OUTCOMES AND COSTS TO INFORM HEALTHCARE IMPROVEMENT

DANIELA LINHARES

TESE DE DOUTORAMENTO APRESENTADA

À FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO EM

INVESTIGAÇÃO CLÍNICA E EM SERVIÇOS DE SAÚDE

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Efficiency in Spine Care

Assessing Outcomes and Costs to Inform Healthcare Improvement

Doctoral thesis in Clinical and Health Services Research submitted to the Faculty of
Medicine of the University of Porto

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Co-supervisor – Bernardo Manuel de Sousa Pinto, MD PhD

LIST OF PUBLICATIONS

In accordance with the Doctoral studies regulation of Portuguese Universities, this Dissertation comprises the following publications:

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*equal contributions as last author

ABBREVIATIONS

ANOVA: Analysis of Variance

AO: Arbeitsgemeinschaft für

Osteosynthesefragen

AUC: Area Under the Curve

BC: before Christ

BP: Back Pain

CEA: Cost-effectiveness Analysis

CfB: Change from Baseline

CI: Confidence Interval

CUA: Cost-utility Analysis

GDP: Gross Domestic Product

HTA: Health Technologies Assessment

ICER: Incremental Cost-Effectiveness Ratio

IF: Impact Factor

L1-5: Lumbar vertebrae 1 to 5

LOS: Length of stay

LP: Leg Pain

mD: mean Differences

MD: Microdiscectomy

NASS: North America Spine Society

NHS: National Health Service

ODI: Oswestry Disability Index

OR: Operatory Room

PRISMA: Preferred Reporting Items for

Systematic Reviews and Meta-Analyses

PROMs: Patient Reported Outcome

Measurements

PROSPERO: International prospective

register of systematic reviews

QALYs: Quality-Adjusted Life Years

RCT: Randomized Controlled Trials

RMDQ: Roland-Morris Disability

Questionnai

SD: Standard Deviation

SF-36: 36-Item Short Form Survey

SMD: Standardized mean Differences

T1-T12: Thoracic vertebrae 1 to 12

TL: Thoracolumbar

TLSO: Thoracolumbosacral Orthosis

UN: United Nations

US: United States of America

VAS: Visual Analogue Scale

WHO: World Health Organization

WoS: Web of Science

WTP: Willingness to pay

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ABSTRACT

Spine conditions are among the worldwide leading causes of disability, being responsible for a substantial burden to societies and healthcare systems. The ongoing growing healthcare pressure posed by these conditions highlights the importance of an adequate assessment of health technologies used in spine care, in order to select those that combine the lowest costs with the best clinical outcomes. From diagnosis and prevention to treatment and prognosis, spine care is populated by several paradigms and interventions that need further assessment and potential revision.

In this doctoral thesis, we aim to identify interventions and practices in spine care, that may be eliminated or modified, resulting in a positive economic and clinical impact, thus improving spine care efficiency. To do so two models were developed focusing health technologies assessment.

In the first model, we assessed the conservative treatment of thoracolumbar fractures with orthosis. These devices are used almost ubiquitously in the treatment of thoracolumbar fractures but this practice is not supported by adequate scientific background and recent studies suggest no benefit and even a possible negative impact in recovery. Two studies were conducted in this model. In the first, we aimed to evaluate the effect of orthosis in skeletally mature patients with acute traumatic thoracolumbar spine fractures. To do so we performed a systematic review and meta-analysis of randomized controlled trials comparing adult patients with acute thoracolumbar fractures treated with and without orthotic devices. Five

studies (eight articles) were included, reporting no significant differences in pain, kyphosis progression, and loss of anterior height. The meta-analysis computed showed a significant increase of 3.47 days in mean admission time in orthosis group. This review showed no advantage from orthosis use in the conservative treatment of these patients.

The results of this study led to the second study question, which aimed to assess the costs of orthosis in European and North American countries and evaluate the current practice and opinion of spine specialists from these world regions regarding the use of orthotic devices in adult patients with acute thoracolumbar fractures. A survey study was performed, and 130 spine specialists, from 28 European and five North American countries answered the questionnaire. Of those, 90% still use these devices but only 11.5% brace all patients with acute thoracolumbar fractures. Orthosis's overall mean cost was around €546 and increased cost was associated with higher gross domestic product per capita and higher health expenditure. Both cost and use were significantly higher in North America when compared to Europe. These studies showed a tendency towards an orthosis-free treatment, with only a small percentage of respondents still using this device in all patients.

This first model showed that, on one hand, orthosis seems to add no advantage in the treatment of patients with acute thoracolumbar fractures and, on the other hand, these devices are associated with a non-negligible cost.

The second model aimed to assess the cost-effectiveness of outpatient lumbar microdiscectomy when compared with the inpatient procedure. Lumbar microdiscectomy is considered the gold standard in the surgical treatment of patients with lumbar disc herniation. It was the first spine procedure to transition to the outpatient setting, but this transition was

never the target of a full economic assessment. In this model, we performed a study on the cost-utility of outpatient versus inpatient lumbar microdiscectomy in adult patients with lumbar disc herniation and sciatica. A prospective assessment of costs and utilities was performed in 20 patients submitted to outpatient microdiscectomy. Twenty inpatients costs were retrospectively assessed and inpatient utilities were obtained from a literature review. Quality-adjusted life-years (QALY) were calculated from Oswestry Disability Index values and both probabilistic and deterministic sensitivity analyses were conducted.

Microdiscectomy in outpatient basis was cost-effective at 3- and 6-months, with average savings of €847, when compared with the inpatient procedure. The Incremental Cost-Effectiveness Ratio associated with the inpatient microdiscectomy at 3 months was €135,753 or €345,755/QALY, much higher than the defined willingness to pay threshold of €60,000/QALY. At the 6-month assessment outpatient procedures associated both with less cost and higher utilities, with inpatient procedure being the dominated strategy. Outpatient procedure was the better option in 65% to 73% of simulations, representing savings of about 55%. Being the first of its kind on this subject this study showed a significant reduction in costs with outpatient microdiscectomy, with a similar clinical outcome, proving this option as cost-effective.

With these two models of health technology assessment, this thesis shows how changes in current practices can obtain substantial cost reductions with no negative, or even positive, impacts on clinical outcomes. These approaches illustrate the foundation for a value-based spine care, with proper outcome and economic assessment sustaining the improvement of spine care efficiency.

RESUMO

As patologias da coluna vertebral estão entre as principais causas de incapacidade em todo mundo, representando uma sobrecarga importante para a sociedade e para os serviços de saúde. O aumento crescente desta pressão reforça a importância de uma adequada avaliação das tecnologias de saúde utilizadas em patologia da coluna vertebral, de forma a que seja efetuada uma seleção daquelas que combinam os custos mais baixos com os melhores resultados clínicos. Do diagnóstico e prevenção ao tratamento e prognóstico, são vários os paradigmas e intervenções que carecem de avaliações mais profundas e de uma potencial revisão.

O objetivo desta tese de doutoramento é identificar intervenções e práticas, dentro da prestação de cuidados em patologia da coluna vertebral, cuja eliminação ou modificação resulta num impacto positivo do ponto de vista clínico e económico e, subsequentemente, numa melhoria da eficiência na prestação destes cuidados. Para isso, foram desenvolvidos dois modelos de avaliação de tecnologias de saúde.

No primeiro modelo foi avaliada a utilização de ortóteses no tratamento conservador de fraturas toracolombares. Embora estes dispositivos sejam usados quase ubiquamente no tratamento das fraturas toracolombares, esta utilização não é suportada por evidência científica adequada e os estudos científicos mais recentes têm sugerido uma ausência de benefício com a sua utilização e até a possibilidade de estes dispositivos terem um impacto negativo na recuperação dos doentes. Foram efetuados dois estudos neste modelo.

No primeiro, o objetivo foi avaliar o efeito da utilização de ortóteses em doentes com maturidade esquelética que apresentam fraturas agudas da coluna vertebral toracolombar. Para tal, foi efetuada uma revisão sistemática e meta-análise de estudos randomizados controlados, comparando doentes adultos com fraturas toracolombares agudas, tratados com e sem ortóteses. Cinco estudos (oito artigos) foram incluídos. Não foram encontradas diferenças significativas na dor, progressão da cifose, e perda de altura vertebral anterior entre os dois grupos. As meta-análises realizadas mostraram um aumento significativo no tempo médio de admissão de 3.47 dias no grupo tratado com ortóteses. Esta revisão não encontrou qualquer vantagem da utilização das ortóteses no tratamento conservador destes doentes.

Os resultados deste estudo conduziram à questão do segundo estudo, que pretendia aferir os custos das ortóteses em países europeus e norte americanos, e avaliar a opinião e a prática habitual dos especialistas em patologia da coluna vertebral destas zonas do mundo, no que toca à utilização destes dispositivos em doentes adultos com fraturas da coluna toracolombar. Foi realizado um estudo por questionário, com respostas de 130 especialistas em patologia da coluna vertebral, de 28 países europeus e cinco norte-americanos. Destes, 90% reportaram ainda utilizar ortóteses, mas apenas 11.5% as prescrevem a todos os doentes com fraturas agudas da coluna toracolombar. O custo médio do dispositivo rondou os €546. Encontrou-se uma associação entre um aumento deste custo e, ambos, um maior produto interno bruto per capita e uma maior despesa pública associada à saúde. Verificou-se que, quer o custo, quer a utilização das ortóteses, são significativamente superiores na América do Norte quando comparados com a Europa. Este estudo mostra então, uma tendência para um tratamento das

fraturas agudas da coluna toracolombar sem ortótese, com apenas uma pequena percentagem dos inquiridos a reportar o uso deste dispositivo em todos os doentes.

Este primeiro modelo mostrou que, por um lado, as ortóteses não parecem adicionar qualquer benefício no tratamento conservador dos doentes com fraturas agudas da coluna toracolombar e que, por outro lado, estes dispositivos se associam a um custo não negligenciável.

O segundo modelo tinha como objetivo avaliar o custo-efetividade da microdiscectomia lombar efetuada em ambulatório, quando comparada com o procedimento em regime de internamento. A microdiscectomia lombar é considerada o *gold standard* no tratamento cirúrgico de doentes com hérnias discais lombares. Embora tenha sido o primeiro procedimento na coluna vertebral a transitar para ambulatório, esta transição nunca foi alvo de uma avaliação económica completa. Neste modelo, foi realizado um estudo de custo-utilidade que avalia a microdiscectomia lombar em doentes adultos com hérnia discal lombar e ciatalgia, comparando o procedimento em ambulatório com o realizado em regime de internamento. Foram colhidos dados prospetivos sobre os custos e utilidades de 20 doentes submetidos a microdiscectomia em ambulatório. Adicionalmente, foram retrospectivamente avaliados os custos de 20 doentes intervencionados em regime de internamento e as suas utilidades foram obtidas através de uma revisão da literatura. Os anos de vida ajustados pela qualidade (QALY) foram calculados a partir do Índice de Incapacidade de Oswestry e foram realizadas análises de sensibilidade determinística e probabilística.

Observou-se que microdiscectomia em ambulatório foi custo-efetiva a 3 e 6 meses, com uma poupança média de €846, quando comparada com o procedimento em regime de

internamento. A razão de custo-efetividade incremental associada ao procedimento realizado em regime de internamento foi de €135,753 ou €345,755/QALY aos 3 meses, tendo sido muito superior ao valor que estaríamos dispostos a pagar, de €60,000/QALY. Já na avaliação de 6 meses, o procedimento em ambulatório associou-se a menores custos e a maiores utilidades, com o regime de internamento a ser a estratégia dominada. O procedimento ambulatório foi a melhor opção em 65% a 73% das simulações, representando uma poupança de cerca de 55%. Este estudo, o primeiro a debruçar-se sobre o tópico, mostrou uma redução significativa de custos com a microdiscectomia lombar em ambulatório, com os doentes a apresentarem resultados clínicos similares aos tratados em regime de internamento, provando que esta opção é custo-efetiva.

Com estes dois modelos de avaliação de tecnologias de saúde, esta tese mostra que alterações de práticas correntes podem resultar em reduções substanciais de custos sem impactos negativos, ou mesmo com impactos positivos, nos resultados clínicos. Estas abordagens, com avaliações económicas e de resultado adequadas, ilustram a base de uma prestação de cuidados de saúde em patologia da coluna vertebral e sustentam assim uma melhoria da eficiência desta prestação de cuidados.

CHAPTER I

Introduction

Aims of the thesis

INTRODUCTION

BURDEN OF SPINE CARE

According to the World Health Organization (WHO), economic considerations assume an increasingly prominent role in the planning, management, and evaluation of health systems, with an increased focus on issues of cost and efficiency¹. The WHO emphasizes that ensuring that scarce resources are used efficiently is key to lower overall costs for both individuals and countries¹. This is all the more relevant when considering conditions with high clinical and economic burden, such as low back and neck pain.

In fact, low back and neck pain are globally the fourth leading cause of disability-adjusted life years, after ischemic heart disease, cerebrovascular disease, and lower respiratory infection, according to The Global Spine Care Initiative on the burden of spine diseases².

Additionally, low back and neck pain are the leading cause of years lived with disability in most world countries and age groups². The economic burden related to the management of spinal conditions is increasing worldwide. In the United States (US), from 1999 to 2008, spine-related expenditures increased by 95% for adults with a primary diagnosis of a spine condition³. Only in 2008, 6% of adults in US reported an ambulatory visit due to back or neck pain⁴.

There is considerable agreement among spine surgeons that devotion to patients' best interests should not solely rely on associated costs. Nevertheless, and although professionals recognize their role in reducing the costs of healthcare, they also agree that the focus should be on reducing wasteful spending, and not on limiting access to expensive treatments when needed⁵. This explains the recently observed shift towards a value-based system, that focuses

on maximization of quality with minimization of costs⁶. Therefore, the development of policies based on evidence is of utmost importance. These should be built by health technologies assessment methods, regarding the use of practices and devices and identifying how to achieve cost reduction with minimal impact on clinical outcomes.

Health Technologies Assessment

The ongoing growing pressure on healthcare budgets is increasing the scrutiny on new products and activities used to promote health in any way, the so-called health technologies⁷. The seek for the best decisions with the existing resources constraints reinforces the importance of health technologies assessment (HTA), “a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle, with the purpose to inform decision-making in order to promote an equitable, efficient, and high-quality health system”⁸.

Multiple methodological strategies are used in the context of HTA, based on the premise that information should be enriched by multiple sources and include the perspective of multiple stakeholders⁹. In fact, these methodologies can rely on primary data, integrative methods, or economic analysis^{9,10}. While primary data methods include the collection of original data, integrative methods combine data from existing sources⁹.

Primary data methods encompass a huge variety of study designs, enabling the assessment of the direct effectiveness or impact of a health technology in the multiple intervenients of the system. Several examples thrive in the literature, from trials directly studying the efficacy or effectiveness of interventions in patients, to surveys trying to understand the impact on the practice and the receptivity of a technology¹⁰.

Many HTA questions, however, cannot be answered by any single definitive primary study, prompting the need for secondary data. Secondary data can be gathered from multiple existing sources, including clinical registries, epidemiologic surveys, administrative records, governmental or non-governmental technical reports, and scientific literature. Data retrieved from the existing scientific literature is usually presented in the structured and formal construct of a systematic review, one of the most methodologically adequate choices^{11,12}. Accordingly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement, “a systematic review is a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review”¹³. Such review can be complemented with a quantitative synthesis and analysis of data, under a meta-analysis^{12,13}.

Within the context of HTA, retrieved primary and secondary data can be used to support subsequent decision analysis models and economic evaluation studies⁹. The latter encompass several different approaches, with different purposes and require different types of data⁹.

As in many other medical fields, there is increasing attention for HTA in spine care. In fact, not only healthcare professionals but also caregivers are recognizing the scarcity of high-quality evidence supporting many interventions used in spine patients on a day-to-day basis¹⁴. Therefore, there is an increased awareness towards the need for an adequate evaluation of new health technologies, not only prior to their dissemination, but also for those already existent that have been understudied on their safety, effectiveness, and cost-effectiveness¹⁴.

Economic Assessment

The economic interest in health issues began in the 20th century, as a consequence of the II World War. This interest led to the development of the health economics discipline in the second half of the century, with a focus on the medical-care industry¹⁵. This discipline was highly expanded in the following decades and nowadays a multitude of research areas populate this scientific field¹⁵.

Economic assessment studies encompass a set of analytical principles and techniques useful in the comparison among different healthcare strategies¹. Three main components are part of the value equation, as quality and cost over time are considered. Accordingly, it includes (1) measurements of the quality of the care, using an appropriate outcome measurement tool; (2) measurements of the costs; and (3) a time period that enables future events that may affect the value of the studied technology⁶.

Economic evaluation studies can generally be classified as partial or full assessments. A partial economic evaluation is the first step in any full economic evaluation. It is conducted when outcomes are not considered in the analysis and only cost data are gathered¹⁶. Costs calculation is often challenging and thorough assessments should include both direct – including physician time/expertise, facility and material costs – and indirect costs – related, among others, to loss of productivity or associated with patient's inability to function¹⁷.

On the other hand, a full economic evaluation considers both costs and consequences of the technologies being compared. Four main types of such methods are usually described – differing on the methods for measuring consequences –, namely, cost-minimization, cost-benefit, cost-effectiveness, and cost-utility analysis¹⁶. In cost-effectiveness analysis (CEA) costs are considered as monetary units, and consequences are measured as disease-specific

clinical outcomes^{6,16}. However, these specific clinical outcomes are natural units (e.g. life-years gained), that only focus a specific pathway of care, without considering patient preferences, which limits the use of CEA among health programs^{7,16}. To overcome this problem with effectiveness measurement, the cost-utility analysis (CUA) appeared as a subtype of CEA¹⁶. While costs remained monetary units, consequences are measured as units of effectiveness adjusted for patients' preferences, typically quantified in utilities^{16,18}. Utilities are a preference-based measure of health-related quality-of-life, as they quantify the individual or societal preference for a particular health outcome, in a score from 0, that represents the worst possible outcome (usually death), to 1, the perfect health status^{16,18}. Utilities are usually measured with validated preference-based measurement systems and are used to calculate one of the most frequently used measures combining quantity and quality-of-life, the quality-adjusted life years (QALYs)^{16,18}.

Considering utilities and costs, CUA commonly results in a relative measure of costs per QALY gained by choosing one intervention or clinical alternative over another – the incremental cost-effectiveness ratio (ICER)^{7,16}. Obtained ICER is usually compared with a willingness-to-pay (WTP) threshold value below which a technology is deemed cost-effective (i.e., the society is willing to allocate the required resources to obtain the gains underlying the use of the alternative)^{7,16}. This willingness-to-pay threshold is the value per QALY that is considered reasonable for a particular scenario^{7,16}.

Interest in economic analysis under spine care is increasing, with the realization that it is likely to be used to guide payers and policy makers⁶. However, studies based on valid cost-utility analyses are scarce and evidence is still insufficient or inexistent in many spine fields¹⁷.

Outcome Measurements

Traditionally, spine physicians have mostly relied on radiographic measurements to define the success of an intervention. However, while adverse radiographic parameters may correlate with poorer clinical outcomes, flawless images do not warrant a satisfied patient¹⁹. This has prompted a seek for adequate outcome measurements, complemented by a shift from a practitioner-based medicine toward a patient-centred and value-based care¹⁹.

The growth of clinical outcomes research in spine care resulted in an abundance of outcome measurement tools that have been designed to address spine-related disorders¹⁹. Grouped in six categories of outcome measurements, these tools were developed not only to address localized pathologic manifestations but also to include patient-specific factors that can affect both health status and treatment outcomes^{19,20}.

Among outcome measurement tools, patient-reported outcome measurements (PROMs) have been given special attention²⁰. These instruments measure how a patient feels or functions concerning his health or condition, allowing the understanding of the impact of a condition, treatment, or intervention²¹. PROMs include a multitude of measures concepts, that can be of quantitative or qualitative nature²¹. They provide a unique patient's perspective and contribute to narrow the traditional gap between the physician and the diseased, helping to tailor treatment plans according to the needs and objectives of a particular individual^{18,20}.

Although their importance and relevance are recognized worldwide, more than 30% of spine surgeons do not use PROMs in their daily practice, mostly due to financial and implementation issues¹⁸. Nevertheless, it is widely accepted that PROMs not only inform the physician about the severity and changes in patients' complaints, but also allow to measure the value of an intervention and effectiveness of a procedure or surgeon performance¹⁸.

Properly conducted outcome analysis is an invaluable source of valid and reliable estimates of clinical impact that can be put into relation with the incurred costs, and used in the economic analysis, the basis of HTA^{9,19}.

SPINE DISEASES: ECONOMIC INTERVENTIONAL AREAS

Due to their significant burden, spine disorders and spine-related interventions are under the spotlight of HTA, with multiple studies focusing on their impact on the healthcare systems¹⁷. As a multidisciplinary discipline, spine care provides a multitude of fields of intervention, with diagnosis, imaging, treatment, and prognosis being particular targets of economic evaluation studies¹⁷.

Although direct costs are distributed among different healthcare sectors, it is safe to state that the biggest expenditure with spine care is associated with treatment. Actually, multiple options are available for the treatment of spine patients, from conservative approaches to interventional ones, either in emergency or elective settings¹⁷. Moreover, while if drugs are only approved upon given proofs of efficacy, such is not necessarily true for other types of interventions – many therapies, devices, and surgical techniques were never fully scrutinized, neither under outcome research nor in any type of economic analysis¹⁴. In fact, only a few treatments in spine care have been fully evaluated in what comes to their cost-effectiveness and net benefits^{17,22}, with available CUA focusing solely the most commonly performed procedures and many presenting important methodological problems^{6,17,23}.

This lack of economic assessment is particularly true for conservative spine treatments, of whom only few were studied for their cost-utility, and even fewer have any reliable conclusion^{6,17}. Of note, according to the 2020 Evidence-Based Clinical Guideline of the North American Spine Society, conservative treatment “encompass[es] pharmacological treatment, physical therapy, exercise therapy, manipulative therapy, modalities, various types of external stimulators and injections”²¹.

Although traditionally divided between conservative and surgical approaches, spine treatment goes well behind this division. Due to the complex nature of the spine, treatment can range from elective and programmed interventions to urgent and emergent ones, with HTA studies being required in all scenarios. The awareness towards the importance of an adequate HTA in spine care is increasing. So, and although authors identify possible bias in many economic assessments under spine care, they recognize the need for appropriate identification of dispensable interventions and practices, and of an adequate revision of obsolete paradigms^{24,25}. This revision may lead to a substantial reduction of the spine burden and, possibly, to a positive impact on patient's management and clinical outcomes^{24,25}.

Emergency Spinal Care – Spine Trauma

Traumatic spinal injuries are an important cause of morbidity and mortality around the world. The estimated worldwide incidence of these lesions is around 10.5 cases per 100,000 persons²⁶. Vertebral fractures are some of the most common traumatic spinal injuries, being associated with different types of trauma, as falls from height and motor vehicle accidents²⁷. Additionally, they are believed to be important predictors for future vertebral and other fractures, associating with an at least 4- to 5-fold increase in the risk of those lesions²⁷.

Vertebral trauma is associated with an important expenditure. Lindsay et al, in a study with a one-year follow-up after a vertebral fracture, found an average cost per patient of \$1,541 in the US and of €958 in Sweden²⁷. These authors suggested that therapies with proven and rapid efficacy are needed, since they may offer important economic value to healthcare payers, providers, and patients²⁷.

From all vertebral fractures, thoracolumbar (TL) are the most common²⁸. The thoracic section of the spine is composed of twelve vertebrae (T1–T12) and twelve intervertebral discs. It extends from the cervical region to the lumbar spine, which is composed of five vertebrae (L1–L5) and five intervertebral discs²⁸. While the thoracic region of the spine is the least mobile segment, lumbar spine allows movements from bending over to standing straight in an average range of 50 degrees²⁸. This transition from a less mobile thoracic segment to a more dynamic lumbar spine turns the TL junction into an area of great biomechanical stress, explaining why fractures are particularly common in this area²⁹.

The treatment of TL fractures is based, among other factors, on the pattern and morphology of injury and on the presence of associated lesions³⁰. In general, surgical treatment is indicated when the biomechanical stability of the spine is severely compromised and/or a neurologic deficit is imminent or present³¹. A plethora of surgical techniques have been described, but none is yet consensual, mostly due to the lack of adequate comparisons on the performance of the different options^{29,31}. Nevertheless, surgical treatment of traumatic TL fractures is usually safe and effective³¹. In fact, while no technique was proven capable of restoring the normal spinal alignment and many patients do not fully recover from neurologic deficits, the outcomes in terms of pain and re-employment are usually favourable³¹.

Fortunately, most TL fractures are stable lesions and do not require surgical treatment²⁹. As observed for interventional approaches, the best option for conservatively treated patients is yet to be defined²⁹. Nevertheless, treatment usually encompasses the prescription of a TL orthosis, a practice that has been almost consensual for many years^{29,32}. These devices keep patients in a position of relative spinal extension, limiting their forward flexion, and subsequently immobilizing and unloading a motion segment of the spine^{32,33}. While many

authors suggested that this movement restriction diminishes the load transferred via the anterior column, preventing further collapse of the fractured vertebra, others stated that it is mainly a psychological reminder to the patient³²⁻³⁴. Since skin and soft tissues lie between the orthosis and the skeleton of the spine, none of these devices is capable of a full immobilization³⁴. Rubery et al, in a motion analysis on a cadaver model, showed that no orthosis is effective in reducing anterior-posterior, medial-lateral, or axial translation at the fracture site³⁵.

Additionally, orthoses immobilize a spine segment through a three-point pressure over bony prominences³⁴. This localized excessive compression in a small area can lead to skin breakage and ulcerations³⁴. This, along with reports of diminished pulmonary capacity and atrophy of the paraspinal musculature suggests that bracing is not without risks, and, although used almost ubiquitously in conservative treatment of TL fractures, orthoses may even impact patient recovery^{33,36}. In fact, recent studies showed no benefit in pain and radiological or functional outcomes between patients treated with or without brace^{24,37}. The risk of overuse of these devices is being pointed out, with increases in associated healthcare-related costs²⁴.

Elective Spine Surgery – Outpatient Lumbar Discectomy

While spine trauma is usually managed on an emergency department basis, spine-related procedures also encompass elective interventions. Elective spine surgery has been increasing all over the world in the last decades⁵, with some authors reporting that the number of procedures duplicates each 10-years⁵. However, this increase in the number of procedures is being followed by a rise in their average cost in the same time frame³⁸.

With growing concern on the great expenditure posed by these traditional inpatient interventions, the possibility of performing spine procedures on an ambulatory basis appeared as a suitable answer. Many countries observed a transition of inpatient surgeries to the ambulatory setting, which led to cost reductions of more than 80% in some interventions, such as in cervical disc arthroplasty, with positive impacts on both healthcare policies and patient satisfaction³⁹.

According to the WHO, a day-surgery patient is the one “who is admitted for an operation on a planned non-resident basis and who nonetheless requires facilities for recovery”, with “a whole procedure that should not require an overnight stay in a hospital bed”⁴⁰. Although outpatient surgery is considered a relatively recent phenomenon, the very earliest procedures, dating from 3500 BC were, in fact, performed on an outpatient basis⁴¹. More recently, the foundations of modern day-surgery were laid by James Nicoll at the turn of the 20th century⁴⁰, with the subsequent emerging economic advantages along with the scarcity of hospital beds leading to the appearance of the first ambulatory programs⁴¹.

Nowadays, there is a wide variation in the proportion of day-surgeries performed in different countries, with an overall agreement on their advantages⁴⁰. The WHO states – in its “Day Surgery” policy brief – that outpatient procedures have no significant differences in medical

outcomes, patients report high levels of satisfaction, and hospital costs are reduced from 25% to 68% when compared with the same procedures on an inpatient basis⁴⁰. Shorter hospital stays enable a rise in the number of patients treated and a reduction in waiting lists⁴⁰. Also, the release of inpatient facilities for more complex cases, the reduced disruption of patient daily routines, and the decrease of staff overnight stays were pointed as advantages of outpatient surgery care⁴⁰. Although concern has been raised about day surgery transferring extra costs to patients or caregivers, the WHO points that the lower risk of cancellation and the earlier return to work may actually reduce costs for the patient, and the reduction in the number of visits to the hospital may reduce the expenses for the caregiver⁴⁰.

Particularly, for spine surgery, there has been a remarkable transition to the outpatient setting. In their systematic review, Bair et al suggested that anterior cervical discectomy and fusion, lumbar decompression, single-level lumbar fusions, minimally invasive surgery transforaminal lumbar interbody fusion, and lateral lumbar interbody fusion can all be safely performed in an ambulatory setting with patients discharged the same day with a small reported risk of complication⁴². In fact, between 1994 and 2006, outpatient surgery for spinal stenosis increased by more than 2000% and for intervertebral disc disorders by 340%⁴³. Also, between 1994 and 2000, while inpatient rates of lumbar procedures remained relatively stable, the number of outpatient surgeries increased over time⁴⁴.

Although outpatient care of spine patients is growing worldwide, not all patients or procedures are suitable for same-day discharge⁴⁵. Actually, outpatient orthopedic surgery is associated with rates of complications ranging from 0.05 to 20% and with readmissions slightly higher than 2%⁴⁵. These negative outcomes carry increasing costs, lessening the

economic benefits of outpatient choices and reinforcing the importance of an appropriate selection of procedures suitable for outpatient transition.

One example of a successful transition was that of lumbar microdiscectomy (MD), the first major spine surgery performed on an outpatient basis, with outpatient procedures now accounting for 40% of all MD in US⁵.

Microdiscectomy is indicated in patients with herniation of intervertebral disc, upon failure of conservative approaches. The intervertebral disc is a complex structure with three main components, an outer ring of fibrous cartilage – annulus fibrosus –, a gelatinous core – nucleus pulposus –, and the cartilage of adjacent vertebral endplates^{38,46}. Due to multiple factors, from mechanical to genetic, the disc can suffer a process of degeneration that usually begins in early adulthood⁴⁶⁻⁴⁸. The associated weakening can facilitate the displacement of disc material, usually nucleus pulposus, beyond the normal margins of the disc space, leading to a herniation⁴⁶⁻⁴⁸. Disc herniations are commonly found in asymptomatic patients, with a prevalence that increases with age, rising to over 75% in patients older than 70 years old⁴⁹.

When symptomatic, patients usually complain of radicular pain, sensory abnormalities, and weakness in the distribution of one or more lumbosacral nerve roots, as a result of mechanical and inflammatory aggressions to local structures^{47,48}. Nevertheless, herniated lumbar discs have a favorable natural history, with many individuals improving within a 6-week period⁴⁶. Surgical treatment, with lumbar discectomy, is then reserved for patients with congruent clinical and radiological findings presenting severe or progressive neurologic deficits, or for those that do not improve within 6 weeks⁴⁶. Lumbar discectomy is a safe procedure, with low complication rates, and is usually associated with a successful outcome and a fast relief of pain⁴⁸.

Several discectomy techniques were already described and a tendency for less invasive approaches is being observed. Among those, MD is still considered the gold standard for surgical treatment of lumbar disc herniation, being pointed out as the safest, simplest, and most effective of all discectomy techniques^{50,51}. As a less invasive intervention, MD uses a smaller incision than the traditional open lumbar discectomy and is associated with a low rate of complications and a fast recovery^{44,51}.

Discectomies were already proven cost-effective when compared with non-surgical approaches⁵², and it is easily understandable why, in some countries, these are 70% to 90% of all spine procedures performed in an outpatient basis³⁶.

Although MD seems the ideal procedure to perform in a one-day surgery, due to its simplicity and low risk, it is critical to note, however, that patient selection is paramount in order to optimize outcomes and safe delivery of care⁴². In fact, the safety of this perioperative experience relies on proper planning and anticipation of complications⁵². This applies not only to MD but also to other spine surgery interventions – if adequate protocols are not implemented, the occurrence of severe complications that could have been potentially avoided in an inpatient setting raises medicolegal questions that cannot be balanced from isolated cost or clinical perspectives³⁹. This is particularly true for spine surgery, with the pendant of potentially devastating sequelae delaying its outpatient expansion in some settings and reinforcing the need for an adequate analysis that will reassure physicians and patients. Although all procedures should undergo this scrutiny under their process of ambulatorization, MD outpatient transition still lacks a complete economic assessment. Essentially, it is important to realize if its massive outpatient transition is economically and clinically advantageous.

AIMS OF THE THESIS

In order to inform a value-based healthcare improvement and increase efficiency of spine care delivery, this thesis goal is to identify interventions that may be eliminated or modified, resulting in a positive impact in costs and outcomes.

Since spine care comprises many domains that can be studied under health technology assessment, two interventions were selected, hereinafter identified as models, each representing interventions in spine care that were identified and studied. Three underlying specific objectives were then defined:

Model 1 – Orthosis in thoracolumbar fractures

Objective I

To evaluate the effectiveness of orthosis in skeletally mature patients with acute traumatic thoracolumbar spine fractures.

Objective II

To assess – by means of a survey – the direct costs of orthosis in European and North American countries and to evaluate the current practice and opinion of spine specialists from Europe and North America regarding the use of these devices in adult patients with acute thoracolumbar fractures.

Model 2 – Outpatient transition of lumbar microdiscectomy

Objective III

Compare outpatient with inpatient lumbar microdiscectomy performed in adult patients with lumbar disc herniation and sciatica, regarding both its costs and effectiveness.

Studies Overview

To answer the above-mentioned aims three studies were conducted.

For Model 1, Objective I, a systematic review and meta-analysis of randomized controlled trials was performed to evaluate the radiological and clinical effect of orthosis in skeletally mature patients with acute traumatic thoracolumbar spine fractures. Data showed that orthosis seems to add no benefit in conservative treatment of acute thoracolumbar fractures.

These results are presented in Chapter II.

To answer Objective II of Model 1, a survey study was conducted, questioning spine specialists from Europe and North America on the direct costs of orthosis in their practice. Also, specialists were questioned on their preference on the use of the device in skeletally mature patients with acute traumatic thoracolumbar spine fractures. Important geographic variation of costs and use of these devices was observed. *These results are presented in Chapter III.*

On Model 2, the specific Objective III was approached with a cost-utility analysis, performed to assess whether outpatient lumbar microdiscectomy was cost-effective when compared with the inpatient procedure. Both primary data from a prospective assessment and secondary data from literature were used. Uncertainty was explored via a one-way deterministic sensitivity analysis and probability sensitivity analysis. A significant reduction in costs, with a similar clinical outcome, proved the inpatient procedure as cost-effective. *These results are presented in Chapter IV.*

CHAPTER II

Orthosis in thoracolumbar fractures

A systematic review and meta-analysis of randomized controlled trials

Article 1

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Orthosis in Thoracolumbar Fractures – A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

Study design: Systematic review and meta-analysis of RCT

Objective: Evaluate radiological and clinical outcomes of acute traumatic thoracolumbar fractures in skeletally mature patients treated with orthosis, versus no immobilization.

Summary of Background Data: Orthosis are traditionally used in conservative treatment of thoracolumbar fractures. However, recent studies suggest no benefit, and a possible negative impact in recovery.

Methods: Databases were searched from inception to June 2019. Studies were selected in two phases by two blinded reviewers; disagreements were solved by consensus. Inclusion criteria were: RCT; only patients with acute traumatic thoracolumbar fractures; primary conservative treatment; comparison between orthosis and no orthosis. Exclusion criteria were inclusion of non-acute fractures, patients with other significant known diseases and comparison of groups different than use of an orthosis. Two independent reviewers performed data extraction and quality assessment. Fixed effects models were used upon no heterogeneity, and random-effects model in the remaining cases. A previous plan for extraction of radiological (kyphosis progression; loss of anterior height) and clinical (pain; disability; length of stay) outcomes was applied. PRISMA guidelines were followed.

Results: Eight articles/5 studies were included (267 participants). None reported significant differences in pain, kyphosis progression and loss of anterior height. One reported a better ODI with orthosis at 12 but not at 24 weeks. No other study reported differences in disability. All authors concluded an equivalence between treatments.

Meta-analysis showed a significant increase of 3.47days (95%CI 1.35; 5.60) in mean admission time in orthosis group. No differences were found in kyphosis at 6 and 12 months;

kyphosis progression between 0-6 or 0-12 months; loss of anterior height 0-6 months; VAS for pain at 6 months; VAS change 0-6 months.

Conclusions: Orthosis seems to add no benefit in conservative treatment of acute thoracolumbar fractures. This should be considered in guidelines and reviews of healthcare policies.

Keywords: Spine, Spinal fractures, Thoracic region, Lumbar region, Conservative treatment, Orthotic devices, Emergency Department, Meta-analysis, Systematic review, Randomized controlled trial

Introduction

The thoracolumbar (TL) spine is the most commonly injured segment of the vertebral column¹. Consequences of TL traumatic fractures range from mild back pain to devastating sequelae such as paralysis, deformity, and loss of function^{1,3}. The choice between surgery or conservative approach is driven by a group of criteria, including the morphology of injured vertebrae and existence of associated lesions, along with clinical judgement and patient characteristics⁴. Nevertheless, in patients with no neurological deficit, it is difficult to choose the best treatment modality, as the existing evidence is both sparse and contradictory.

When conservative treatment is chosen, the use of a thoracolumbosacral orthosis (TLSO) is almost consensual^{2,3,5}. TLSO are devices with a relative extension locked position, and many authors suggest they may have a role in the healing process, diminishing the load transferred via the anterior column, limiting segmental motion, and helping in pain control^{3,5,6}. However, bracing is not without risks, and its overuse may lead to pressure-related skin breakdown, diminished pulmonary capacity, and weakness of the paraspinal musculature. Accordingly, although used almost ubiquitously in conservative treatment of TL fractures, TLSO may even impact patient recovery^{7,8}. In fact, several studies comparing patients managed with and without TLSO not only showed no difference in pain and functional outcomes⁹⁻¹⁵, but also identified risks associated with overuse of these devices, in addition to an increase in healthcare-related costs⁸.

On account of such contradictory information, there is a need for systematically assessing the existing evidence on the efficacy and safety of TLSO. The existent systematic reviews are either limited to patients with osteoporotic lesions¹⁶ or lacking evidence for patients with

traumatic fractures (with the last review being published in 2014 and including only 2 primary studies¹⁷).

Therefore, the aim of this systematic review and meta-analysis of randomized controlled trials (RCT) is to evaluate the effect of orthosis in skeletally mature patients with acute traumatic TL spine fractures.

Methods

Search Strategy

This systematic review follows the recommendations of the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA, eTable 1, at Supplementary File)¹⁸. A systematic search was performed in Web of Knowledge, PubMed, Scopus and in Cochrane Central, using a search strategy combining the keywords “dorsal”, “thoracic”, “lumbar”, “spine”, “vertebra”, “fracture”, “orthosis”, “brace” and “bracing”, from inception to June 2019. The full query used in each database is available at the eTable 2, at Supplementary File. A restriction to RCT was performed, using previously reported strategies to maximize sensitivity in the search for RCT in those databases¹⁹. No filters based on publication date or language were applied to the search. Additional papers were selected by screening of references in previous reviews on TLSO (Figure 1).

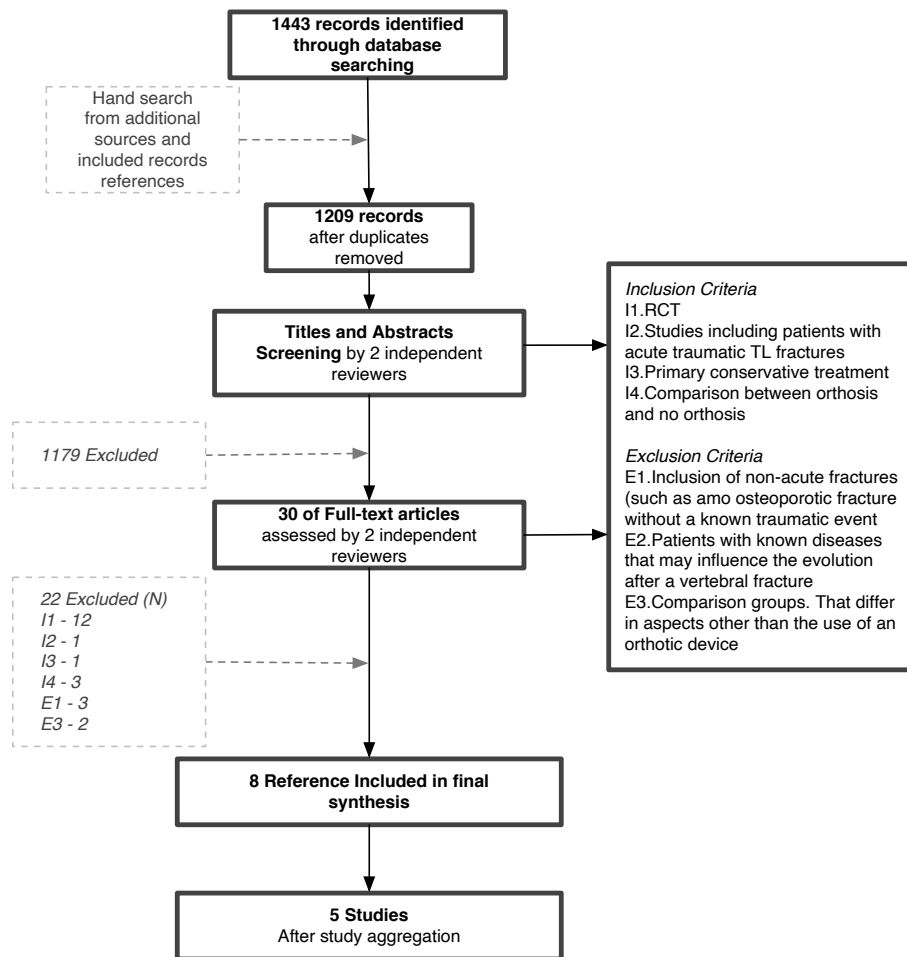


Figure 1. Articles selection process. Based on PRISMA flowchart¹⁸.

Study Selection and Quality Assessment

Primary studies were selected according to predefined eligibility criteria. Studies were included if they consisted of RCT including patients with acute traumatic TL fractures that underwent primary conservative treatment, and in which the use of orthosis was compared with no orthotic devices. Studies were excluded if they (i) assessed patients with non-acute fractures (such as osteoporotic fractures without a known traumatic event), (ii) assessed participants with known diseases that may influence their evolution after a vertebral fracture,

or (iii) had comparison groups with interventions different in aspects other than the use of an orthotic device. Study selection occurred in two phases – titles and abstracts of all references were firstly assessed, and the full texts of manuscripts that were not excluded in the screening phase were then fully read. In both phases, two reviewers independently evaluated each study; any disagreement was solved by consensus. We were able to retrieve all full-texts for analysis.

Data was extracted by two authors independently, using a purposely-built electronic form. For each included primary study, we retrieved data on the setting, participants' age and gender distributions, characteristics of fracture (AO classification and radiological criteria for inclusion), and protocols for clinical evaluations. Results from the individual studies were grouped together based on clinical (pain and functional) and radiological outcomes available. The quality of primary studies was assessed by two independent authors using Cochrane risk of bias tool for RCT²⁰.

Quantitative synthesis of information

We performed meta-analyses for all outcome variables assessed by more than one study and for which we had sufficient data (authors were contacted to provide unreported data) – such variables consisted on the kyphosis degree and progression at 6 and 12 months, loss of height modification at 6 months, visual analogue scale (VAS) of pain at 6 months, VAS of pain modification at 6 months, and length of stay. When data was only available on graphics, numeric values were extracted. Pooled mean differences (mD) or standardized mean differences (SMD) were calculated, except for those variables for which we had access to baseline and subsequent follow-up data – for the later variables, pooled mean changes or

standardized mean changes were calculated instead. Of note, pooled standardized measures were calculated whenever different scales were used across different studies.

Fixed effects models were adopted in cases in which no heterogeneity was detected. In the remaining cases, the random-effects model was adopted, with heterogeneity estimation by the restricted maximum likelihood method.

Heterogeneity was assessed by the Q-Cochrane p value and by the I^2 statistics – a p -value < 0.10 and an I^2 > 40% were considered to represent substantial heterogeneity. Upon detection of substantial heterogeneity, we were not able to perform meta-regression or subgroup analyses on account of the low number of studies in each meta-analysis. All analyses were performed using software R (version 3.5.0), using metafor package.

This review was registered in PROSPERO database, ID 143129.

Results

In the search process a total of 1443 records were obtained, and after removing duplicates, a total of 1209 references were retrieved. After title and abstract screening, 1179 references were excluded (Figure 1). After full text reading, 8 references were included in the final review; three were conference papers²¹⁻²³. The main author of four records (two full articles and two conference papers) was contacted and confirmed that those records concerned the same multicentre setting^{9,12,22,23}. These references were all included as a single entrance and, when data from the same evaluation period was available, we considered the article including the highest number of individuals. Another article from the same study group was an extended follow-up from one of the originally included centres¹⁵. In the primary multicentric RCT, the randomization process was site-specific. Accordingly, we included this study as a separate entry for synthesis purposes, but we only considered data from evaluation periods not available in the other papers from the same setting.

Therefore, in this systematic review, a total of five different primary studies were included. All consisted of hospital-based RCT including skeletally mature patients (defined by the authors as more than 16 years old of age^{9,12,15}) and comparing at least a brace-treated group with a control one. Overall, a total of 267 participants were assessed, with sample sizes ranging from 17 to 108, and participants' mean age ranging from 39 to 47 years old. Four out of five studies included only subjects with fractures at or below T10 level^{9,12,13,15,21}. Fracture inclusion was based in the AO classification²⁴ in all but one study, in which no information on specific fracture classification was available. In four studies, only A3 fractures (or equivalent burst fractures) were included^{9,12,13,15,21}. The other one included patients with A1, A2 and A3 fractures, but comparison between brace and control was only performed for A1/A2

group¹¹. Only one study included patients with neurologic impairment, upon presence of a maximum of a single root deficit⁹. A thermoplastic removable brace was used in one study¹¹, and TLSO was used in three studies²⁵⁻²⁸. Wai et al did not specify the type of brace used²¹. Orthosis was worn over a period of time ranging from 6 weeks to 3 months. In all but two studies^{28,29}, patients were enrolled in a rehabilitation programme^{9,11,12,27}. Follow-up periods ranged from 6 months to 10 years.

All studies performed a radiologic evaluation, with kyphosis progression being studied in the five settings^{9,11,12,27,29} and loss of anterior height in two^{11,29}. All studies reported on pain^{9,11,12,27,29} and four on disability^{9,11,12,27,28}, but different measurement tools were used to assess the latter. One study assessed tolerance of treatment, and found that physical therapy alone was best tolerated than the brace¹¹.

	Favors Orthosis	Similar	Favors Control
2w		Pain (1), SF-36 (1), RMDQ (1), Kyph (1)	
6w		Pain (1), SF-36 (1), RMDQ (1), Kyph (1)	
12w		Pain (2), SF-36 (1), RMDQ (1), Kyph (1)	
24w		Pain (3), SF-36 (2), RMDQ (1), Kyph (3), Height (2), ODI (1)	
1y		Pain (1), SF-36 (1), RMDQ (1), Kyph (2)	
2y		Pain (1), SF-36 (1), Kyph (1)	
5-10y	ODI (1)	Pain (1), SF-12 (1), RMDQ (1), Kyph (1)	
Other		LOS (1)	LOS (1)

Figure 2. Radiological and clinical results from individual studies at different study endpoints

Decision on the category was made based in the significance of the differences presented. SF-36 (36-Item Short Form Survey), RMDQ (Roland-Morris Disability Questionnaire), Kyph (Kyphosis degree), Height (Loss of anterior height), LOS (Length of stay), w (weeks), y(year/s).

Loss of height and Kyphosis progression

All studies performed radiologic evaluations, with kyphosis progression being assessed in the five studies and loss of anterior height in two. No significant differences were found in each primary study regarding radiologic evaluation (Figure 2).

Meta-analyses did not show significant differences on the degree of kyphosis at 6 months (SMD=0.18 degrees; 95%CI=[-0.18; 0.54]; $p=0.317$; $I^2=0\%$, Q-Cochran p -value=0.739) (Figure 3A), or at 12 months (SMD=0.20; 95%CI=[-0.11; 0.52], $p=0.547$; $I^2=0\%$, Q-Cochran p -value=0.547) (Figure 3B).

Kyphosis progression at 6 and 12 months was also not significantly different between patients treated with TLSO and controls. At 6 months, meta-analysis showed a SMD of -0.13 (95%CI=[-0.66; 0.40]; $p=0.612$) (Figure 3C), although substantial heterogeneity was observed ($I^2=42.1\%$, $p=0.162$); at 12 months the standardized mean change was of 0.34 degrees (95%CI =[-0.01; 0.69]; $p=0.612$) Figure 3D), with no heterogeneity observed ($I^2=0\%$; $p=0.781$). Of note, pooled results were estimated assuming a correlation coefficient of 0.5 (as the true value was unknown); if a correlation coefficient of 0.75 had been observed, the pooled results would be estimated as 0.33 (95%CI=[0.06;0.60]; $p=0.016$; $I^2=0\%$, Q-Cochran p -value=0.715), corresponding to a significantly less progression at the TLSO group.

Meta-analysis on loss of height progression between 0 and 6 months after the fracture did not show significant differences between the two groups (mD=0.01; 95%CI=[-3.75; 3.78]; $p=0.995$; $I^2=0\%$, Q-Cochran p -value=0.964) (Figure 3E).

Pain

No study found significant differences between TLSO and control groups regarding reported pain in any studied follow-up time (Figure 2).

Meta-analysis for VAS for pain at 6 months included two studies, and found a pooled mD of -0.20 (95%CI=[-0.88; 0.48]; $p=0.447$) between groups, with no heterogeneity observed ($I^2=0\%$, $p=0.568$) (Figure 3G)). From 0 to 6 months after fracture, the pooled mean change in pain VAS was of 0.12 (95%CI=[-1.76; 2.00], $p=0.903$), although severe heterogeneity was found ($I^2=71.7\%$, $p=0.060$) (Figure 3H). Of note, pooled results were estimated assuming a correlation coefficient of 0.5 (as the true value was unknown); if a correlation coefficient of 0.75 had been observed, similar pooled results would have been observed (mean change of 0.07; 95% CI=[-1.83;1.96]; $p=0.946$; $I^2=83.1\%$; Q-Cochran p -value=0.015).

Disability

No study found significant differences between TLSO and control groups in RMDQ and SF-36 in any studied follow-up time. Two studies assessed disability with the Oswestry Disability Index (ODI) – one of those reported a significant improvement in the TLSO group when compared to controls at a mean of 7-year assessment¹³. In this study ODI scores presented are a combination of two evaluations and the true results from individual assessments are unknown¹³. Other study found no significant difference at a 24-weeks assessment (Figure 2).

Time to discharge

One out of two studies assessing time to discharge found that patients in the control group had a significantly lower length of stay when compared to those using TLSO¹³. In the other study, no significant differences were found^{9,12}.

The meta-analysis showed that TLSO associated with a significantly higher length of stay, with a mean difference of 3.47 days (95%CI=[1.35; 5.60]; $p=0.001$), with no heterogeneity detected ($I^2=0\%$, $p=0.780$) (Figure 3F).

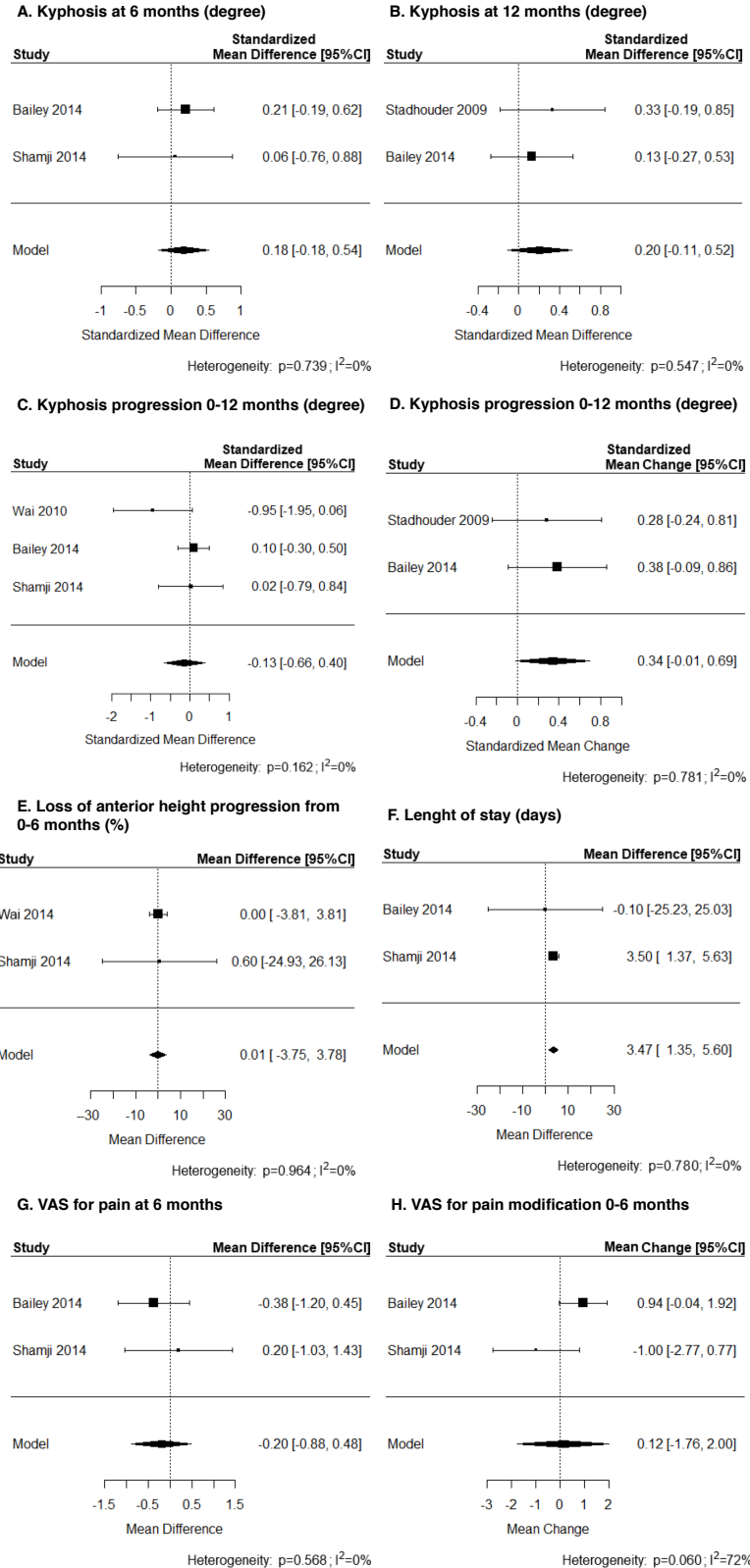


Figure 3. Forest plots

3A-D: Forest plots of kyphosis analysis. A. The standardized mean difference (95%CI) at 6 months was 0.18 (-0.18; 0.54) degrees, $p = 0.317$. $I^2=0\%$, Q-Cochran p -value=0.739; B. The standardized mean difference (95%CI) at 12 months was 0.20 (-0.11; 0.52) degrees, $p=0.547$. $I^2=0\%$, Q-Cochran p -value=0.547; C. The standardized mean change (95%CI) from 0 to 6 months was -0.13 (-0.66; 0.40) degrees, $p=0.621$. $I^2=42.1\%$, Q-Cochran p -value =0.162; D. The standardized mean change (95%CI) from 0 to 6 months was 0.34 (-0.01; 0.69) degrees, $p=0.060$. $I^2=0\%$, Q-Cochran p -value =0.781. In this analysis (D) the correlation values were unknown, so that a value of 0.5 was adopted, if a correlation of 0.75 was observed, the results of the meta-analysis would be a standardized mean difference (95%CI) of 0.33 (0.06;0.60) degrees, $p=0.016$. $I^2=0\%$, Q-Cochran p -value=0.715.

3E: Forest plot on loss of anterior height. The mean difference (95%CI) from 0 to 6 months was 0.01% (-3.75; 3.78), $p=0.995$. $I^2=0\%$, Q-Cochran p -value=0.964.

3F: Forest plots on length of stay. The mean difference was of 3.47 (1.35; 5.60) days, $p=0.001$. $I^2=0\%$, Q-Cochran p -value=0.780.

3G-H: Forest plots on Visual Analog Scale (VAS) for pain. G. The mean difference (95%CI) at 6 months was -0.20 (-0.88; 0.48), $p=0.447$. $I^2=0\%$, Q-Cochran p -value=0.568; H The mean change (95%CI) from 0 to 6 months was 0.12 (-1.76; 2.00), $p=0.903$. $I^2=71.7\%$, Q-Cochran p -value=0.060. The correlation values was unknown, so that a value of 0.5 was adopted; if a correlation of 0.75 was observed, the results of the meta-analysis would be a mean change of 0.07 (-1.83; 1.96), $p=0.904$, $I^2=83.1\%$, Q-Cochran p -value=0.015. In both forest plots (G and H), for the study of Bailey 2014³, values were obtained by graphical methods.

Risk of bias assessment

The results of quality assessment for the included studies are shown in Figure 4 and eFigure 1, at Supplementary File. One reference had high risk of bias in three categories. Since Urquhart study was an extended follow-up of a previous RCT, the risk of bias on incomplete data was also high¹⁵. No other study showed high risk of bias. Nevertheless, information for bias assessment was limited in most articles, with unclear risk of bias in all studies.

Particularly, both the risk of reporting and of selection bias was unclear or high in all but one study.

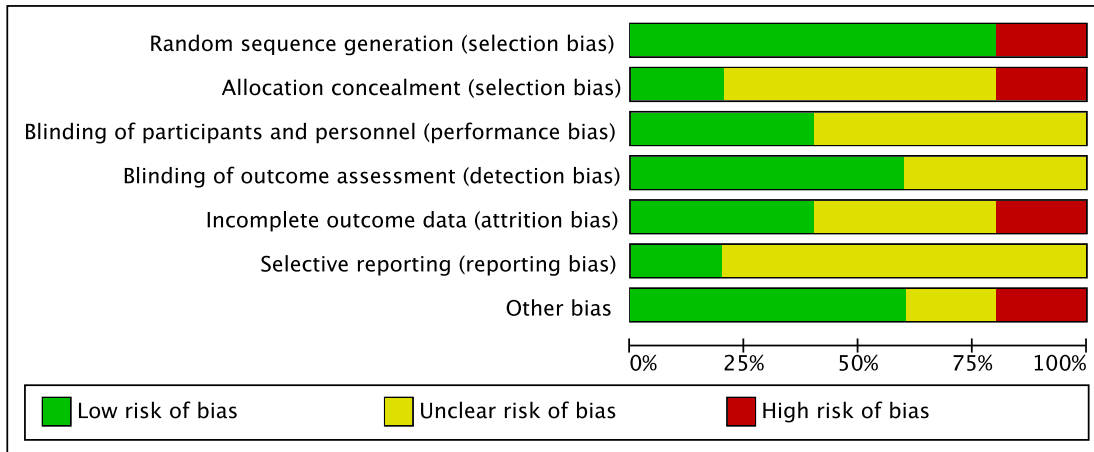


Figure 4. Risk of bias assessment graphic

Discussion

Historically, advocates of brace proposed a role in stabilizing the spine, limiting mobility, improving union, and reducing pain^{2,5,6}. However, this is not without risks, and potentially severe complications have been reported^{5,7,8}.

This systematic review assessed the effect of bracing in patients with TL fractures, and showed that TLSO did not associate with benefits in pain and functional or radiological outcomes, but was associated with a significant increase in admission time. Only five studies were available, most with unclear or high risks of bias and assessing small samples.

Nevertheless, authors agreed in an equivalence between patients treated with or without orthotic devices. This result is in accordance with the previous reviews conducted on bracing after spine surgery³⁰.

Only two previous reviews on orthosis use in TL fractures are available. In 2009, Gielle et al performed a review that included only retrospective studies and allowed inclusion of settings with patients treated either surgically or conservatively, finding no evidence for the effectiveness of bracing in patients with traumatic thoracolumbar fractures³¹. In 2014, a systematic review of RCT was published, including only two papers, and presenting scarce results with no-meta-analytical data for most outcomes, leading the authors to conclude that no recommendation could be drawn. To the best of our knowledge, no other systematic review on the subject has since been published. In the current study, five studies in a total of eight references were included, allowing meta-analysis of more study endpoints, improved data analysis and data synthesis. Also, only RCT were included, with patients initially referred for conservative approaches, in order to simulate the daily clinical practice. The

restriction to RCT is expected to improve the quality of the included data, reducing bias and controlling for confounding factors.

Pain

Pain relief is currently one of the main reasons pointed out for bracing patients after TL fractures⁵. However, improvement in pain in patients with TL fractures is expected to occur irrespectively of treatment modality³². In this systematic review, all five included studies showed similar improvement on pain in patients treated with or without a spinal brace, even in early follow-up assessments. A recent systematic review reported similar results for bracing after spine surgery³⁰.

Disability

Four studies assessed disability, but only one showed a significant benefit from TLSO. This study, that showed the highest risk of bias (eFigure 1, at Supplementary File), assessed ODI in two study points and combined the data from both, achieving a final value in a “long term follow-up”. No information is provided on differences from the individual evaluations performed, and time from initial fracture ranges from one to 10 years. Another study on ODI found no significant differences at the 24-week assessment (Figure 2).

The importance of spine musculature as a natural long-term brace was already recognized³³. Accordingly, previous reports on osteoporotic fractures hypothesized that bracing may decrease the fatigue of the paraspinal musculature, acting in muscle spasm release³⁴. However, electromyography studies showed that spinal muscular activity may even increase when bracing is used³⁵. Additionally, with prolonged periods of bracing, there is potential for

deconditioning and atrophy of the trunk and paraspinal muscles, impairing functional recovery³⁶.

Loss of height and Kyphosis progression

All studies performed radiologic evaluation. Kyphosis progression was assessed in the five, and loss of anterior height in two, with no significant differences found.

Loss of vertebral height after a spine fracture is associated with shortening of the total spinal length and development of neurologic symptoms, including muscular weakness and functional impairment³⁷. A systematic review on the treatment of TL fractures failed to show a relationship between posttraumatic kyphosis and clinical outcomes, showing that kyphosis usually progresses irrespectively of the treatment³². Nevertheless, radiological assessment is important in the follow-up of conservative treatment of TL fractures and, in patients with excessive kyphosis deformity, late surgical treatment may be warranted^{38,39}. Previous reports attributed a role for orthosis on stabilization of the injured spinal segment, diminishing the load on the anterior column and vertebral body⁵. However, as observed in this systematic review, progression of vertebral collapse (as measured by anterior vertebral height) or kyphosis deformity did not differ between patients with or without bracing. In fact, our several meta-analyses on kyphosis assessment did not show any benefit from TLSO use. Although previous biomechanical studies showed that brace can decrease angular motion, no effect was found on the fracture translation and motion at the fracture site remaining irrespectively of the brace used^{40,41}. This residual movement may explain why orthosis fails to prevent vertebral collapse and kyphosis progression.

Time to discharge

Time to discharge after fracture was significantly higher among patients in the orthosis group, with a mean difference of 3.47 days (Figure 3F). Although this may be due to constraints related with the availability of the brace, it reflects the daily clinical practice, with patients remaining in strict bed rest until put on the brace. Prolonged bed rest periods are associated with higher incidence of complications, and longer stays associate with increased healthcare-related costs^{42,43}.

Limitations and strengths

This study has some limitations, mostly related to the included primary studies. Only eight articles (in a total of 5 different primary studies) fulfilled the selection criteria, all having small sample sizes. Although displaying similar outcomes, some studies did not provide adequate numerical results in order to be included in meta-analysis. Also, different measurement scales and follow-up assessment moments were used. Accordingly, we were only able to perform meta-analysis for four main outcome measurements. The methodological quality of included studies tended to be poor – the risk of bias assessment showed that available information was frequently insufficient to a proper bias evaluation, with items being commonly classified as “unclear bias”. In addition, one study had an evident high bias risk. Future studies should have their methodology more carefully described, especially in what comes to issues on randomization, allocation concealment and control for selective reporting.

Additionally, different protocols were used in the included studies. Two did not convey any information on rehabilitation programs; the other three had pre-defined protocols with

physical therapy. Nevertheless, in all included studies, the follow-up was similar for both comparison groups, and these differences in management may reflect the reality of current clinical practice, with some centers having problems in the availability of concurrent therapies. Also, although we included only studies on patients with acute traumatic vertebral fractures, some patients with osteoporotic fractures may have been included.

This systematic review has also several strong points, particularly related to the relevance of the research question and to its methodology. Multiple bibliographic databases were searched, along with reference assessment of included studies. A protocol based on Cochrane recommendations was followed for article selection (with no language or date filters applied), data extraction and quality assessment¹⁸. Authors were contacted to provide missing information, and data was synthesized both qualitatively and quantitatively. This increase the robustness of the results achieved, and this study may be an important tool for future policy making.

Selected studies included patients with TL fractures deemed for conservative treatment. However, the AO classification used for fracture assessment was the one originally described by Magerl et al²⁴. In a recent update, complete burst fractures, potentially more unstable, that were previously considered as A3 (A3.3) are now assigned in a new A4 subtype²⁴. In this systematic review three studies included A3 fractures, possibly including some lesions that would now be considered A4²⁵⁻²⁸. Future works should consider this subclassification of A type fractures.

Recommendations on conservative management of patients with TL fractures are almost inexistent, with no guidelines whatsoever. Although multiple publications from international spine societies are available on fracture assessment and decision between conservative and

surgical treatment^{4,45-47}, the only information available on the conservative management of these patients is outdated and based in empirical knowledge. In this systematic review, all authors from the included studies agreed that TLSO adds no benefit in the conservative treatment of patients with TL acute traumatic fractures. Stadhouder et al, recommended the use of a brace in moderate compression fractures; however, they recognized that physical therapy alone was more tolerated and no significant differences were found in the overall studied outcomes¹¹. In fact, some studies even state that patients may benefit from treatment with no orthosis, reinforcing the economic benefits expected from the subtraction of an unnecessary intervention and reassuring health-care professionals^{9,12}. This study adds a new dimension to this perspective, showing a significant increase in admission time of patients assigned to orthosis, which is expected to result in higher costs. Accordingly, economic studies on orthosis impact in healthcare associated costs and the effect of their elimination are needed.

Clinical Impact

This systematic review and meta-analysis on patients with acute traumatic TL fractures showed that use of orthosis seems not to be beneficial, with no impact in clinical and radiological outcomes and increased length of stay. Since most patients with TL fractures are conservatively treated, guidelines on their management are of utmost importance, and the results of this systematic review should be considered in the development of these recommendations and in the assembly of future healthcare directives.

Although orthoses are used almost ubiquitously in patients with TL fracture, we reinforce the importance of rethinking this practice. New primary studies, with larger samples and better methodological quality are needed, along with economic assessments on the costs and consequences of using TLSO.

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Supplementary File

Online only material

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	9
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7 eTable 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7, 8, 9 eTable 1
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	eTable 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-9
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8, 9, 10

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8, 9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	8, 9
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, 10 Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9, 10 eTable 3
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	13 eFigure 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10,11,12 Figure 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10,11,12
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	13 Figure 4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	14, 15, 16, 17

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17, 18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	21

eTable 1. PRISMA 2009 Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097.

NA: Non applicable

Search queries for different databases

- From inception to 05-06-2019
- No limits

Database	Search Query
Pubmed ¹	(((((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] NOT (animals [mh] NOT humans [mh])))) AND (dorsal or thoracic or lumbar or thoracolumbar or spine OR spinal or vetabr*)) AND fracture) AND (orthosis OR brace OR bracing)
Scopus ²	(TITLE-ABS-KEY ((clinic* W/1 trial*) OR (randomi* W/1 control*) OR (randomi* W/2 trial*) OR (random* W/1 assign*) OR (random* W/1 allocat*) OR (control* W/1 clinic*) OR (control* W/1 trial) OR placebo* OR (quantitat* W/1 stud*) OR (control* W/1 stud*) OR (randomi* W/1 stud*) OR (singl* W/1 blind*) OR (singl* W/1 mask*) OR (doubl* W/1 blind*) OR (doubl* W/1 mask*) OR (tripl* W/1 blind*) OR (tripl* W/1 mask*) OR (trebl* W/1 blind*) OR (trebl* W/1 mask*)) AND NOT (SRCTYPE (b) OR SRCTYPE (k) OR SRCTYPE (p) OR SRCTYPE (r) OR SRCTYPE (d) OR DOCTYPE (ab) OR DOCTYPE (bk) OR DOCTYPE (ch) OR DOCTYPE (bz) OR DOCTYPE (cr) OR DOCTYPE (ed) OR DOCTYPE (er) OR DOCTYPE (le) OR DOCTYPE (no) OR DOCTYPE (pr) OR DOCTYPE (rp) OR DOCTYPE (re) OR DOCTYPE (sh))) AND (dorsal OR thoracic OR lumbar OR thoracolumbar OR spine OR spinal OR vetabr*) AND (fracture) AND (orthosis OR brace OR bracing))
Web of Knowledge ³	(TS= clinical trial* OR TS=research design OR TS=comparative stud* OR TS=evaluation stud* OR TS=controlled trial* OR TS=follow-up stud* OR TS=prospective stud* OR TS=random* OR TS=placebo* OR TS=(single blind*) OR TS=(double blind*)) AND ((dorsal OR thoracic OR lumbar OR thoracolumbar OR spine OR spinal OR vetabr*) AND (fracture) AND (orthosis OR brace OR bracing))
Cochrane	(dorsal or thoracic or lumbar or thoracolumbar or spine OR spinal or vetabr*) AND fracture AND (orthosis OR brace OR bracing) in Title Abstract Keyword - (Word variations have been searched)

eTable 2. Search queries

¹Using Cochrane highly sensitive search strategies for identifying randomized trials in PubMed – Sensitivity-maximizing version (2008 revision); PubMed format. Available from: Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org

²Using SCOPUS filter for randomized trials from Children's Mercy Kansas City. Available from: <http://aub.edu.lb/libguides.com/c.php?g=329862&p=3023731>

³Using Web of Science filter for randomized trials from University of Alberta. Available from: <http://aub.edu.lb/libguides.com/c.php?g=329862&p=3023731>

	Sample characteristics			Inclusion Criteria					Comparisons				General Conclusion
	Sample Size	Mean Age	N of male	Level	Fracture inclusion	Neurologic Deficit	Radiologic criteria	Age	Orthosis (N)		Control (N)	Physical Therapy (Time)	
Bailey, 2009 ^{a,*}	72	39	67	T10-L3	AO type A3, burst, isolated, within 3 days	None or a single nerve root motor and/or sensory deficit	Kyphotic deformity <35°	16 to 60 yo	TLSO –Aspen Medical Products (N=36)	For 8 weeks if out of bed; weaning during 2 weeks	Ambulate immediately; restrictions to trunk bending or twisting and 90° hip extension for 8 weeks (N=36)	O and C (3 mths)	“Equivalence between treatment with a TLSO and no orthosis for thoracolumbar AO Type A3 burst fractures.”
Bailey, 2014 ^{a,*}	96	40	67	T11-L3	AO type A3, burst, within 72 hours	None	Kyphotic deformity <35°	Skeletally mature to 60yo	TLSO –Aspen Medical Products (N=47)	For 8 weeks if out of bed	Mobilized immediately; restrictions to bending and rotations for 8 weeks (N=49)	O and C (3 mths)	For AO-A3 burst fractures between T11 and L3, this multi-center randomized trial demonstrated equivalence between brace and no brace groups using validated disability and pain measures.
Shamji, 2014 ^a	23	O: 37 C: 43	14	T10-L4	AO type A3, acute, isolated	None	AO classification	<80yo	TLSO (N=12)	For 3 months if out of bed	Ambulation encouraged after 24 hours (N=11)	None/NI	“Neurologically intact patients with stable thoracolumbar burst fractures treated with or without bracing had similar radiographic and clinical outcomes at 6 months follow- up. The no-brace group had shorter in-hospital lengths of stay. Conservative therapy involving early mobilization without brace immobilization may be warranted. ”
Stadhouder, 2009 ^a	108	47	43	Thoracic or lumbar	AO type A1/A2, traumatic fracture (A3 and B1 were also included but no control group is available)	None	<50% loss of anterior height, <30% reduction of the spinal canal, no signs of posterior element involvement	>18yo	Thermoplastic removable brace (N=29)	For 6 weeks if out of bed	Physical therapy for 8 weeks (N=29)	O and C (NI in O, 8 weeks in C)	“None of our nonoperative treatments had an effect on the post-traumatic kyphosis measurements. After a compression fracture, physical therapy alone is the most easily tolerated treatment. Brace treatment, however, results in the least residual pain and the least disability on the long term. Despite the fact that our study has some drawbacks, we tentatively recommend brace treatment as the treatment of choice for patients with moderate compression fractures of the thoracic and lumbar spine. For burst fractures, neither treatment had a clear advantage.”
Urquhart, 2017 ^a	36	40.8	22	T10-L3	AO type A3, burst, isolated, within 3 days	None	Kyphotic deformity <35°	16-60yo	TLSO –Aspen Medical Products (N=11)	For 10 weeks if out of bed; weaning at 8 weeks	Mobilized immediately; Restrictions to trunk bending and rotations for 8 weeks (N=12)	O and C (NI)	“This study reassures health care professionals that treating a thoracolumbar burst fracture patient with early ambulation is both safe and effective with or without a TLSO through 5–10 years postinjury”
Wai, 2010 ^a	17	NI	NI	T12-L2	Burst fracture, isolated	None	NI	NI	Brace (N=9)	NI	No brace (N=8)	None/NI	“Patients with stable thoracolumbar burst fractures treated with or without bracing had similar outcomes at 6 months. Radiographic outcomes of fracture geometry and clinical outcomes of pain and disability scores were no different by treatment type. These patients may benefit from conservative therapy simply involving sequential imaging without brace immobilization ”

eTable 3. Summary of included studies

*These two articles were considered as a single study, since they came from the same setting. #Median. O: Orthosis Group; C: Control Group; AO:

Arbeitsgemeinschaft für Osteosynthesefragen; N: Number; T: Thoracic; L: Lumbar; NI: No Information; TLSO: Thoracolumbarsacral orthosis; yo: years old;

mnths: months.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bailey 2009/2014	+	?	+	+	+	?	+
Shamji 2014	+	+	?	+	+	?	?
Stadhouder 2009	-	-	?	?	?	?	-
Urquhart 2017	+	?	+	+	-	+	+
Wai 2010	+	?	?	?	?	?	+

eFigure 1

Risk of bias assessment figure for the included studies

CHAPTER III

Use and cost of orthosis in conservative treatment of acute thoracolumbar fractures

Article 2

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Use and cost of orthosis in conservative treatment of acute thoracolumbar fractures

A Survey of European and North American experts

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Abstract

Study design: Survey study

Objective: Assess practices and opinions of spine specialists from Europe and North America on orthosis use in adult patients with acute TL fractures. Evaluate cost of the devices.

Summary of Background Data: Although orthoses are traditionally used in conservative treatment of thoracolumbar fractures, recent systematic reviews showed no benefit in patient's outcomes.

Methods: A search for contact authors with publications on spine fractures from all European and North American countries was performed. An online questionnaire was sent on demographic data, practice setting, mean number of fractures treated, use of orthosis upon choice for conservative treatment and average orthosis cost. Data was analyzed based in world regions, economic rank of the country and health expenditure.

Results: We received 130 answers, from 28 European and 5 North American countries. Most responders had more than 9 years of practice and worked at a public hospital. 6.2% did not prescribe a brace in any patient with acute thoracolumbar fractures conservatively treated and 11.5% brace all patients. In a scale from 1 to 5, 21 considered that there is no/low benefit (1) and 14 that bracing is essential (5), with a mean of 3.18. Europeans use orthosis less commonly than North Americans ($p<0.05$). Orthosis mean cost was $\$611.4\pm 716.0$, significantly higher in North America compared to Europe and in high income, when compared with upper middle income countries (both $p<0.05$). Although hospital costs were not evaluated, orthosis is costlier when it involves admission of the patient ($p<0.05$). An

increase in orthosis cost associated with higher GDP per capita and higher health expenditure was found.

Conclusions: More than 90% of spine specialists still use orthosis in conservative treatment of adult patients with acute thoracolumbar fractures. Orthosis cost vary significantly between continents, and it is influenced by the country's economy.

Key-words: Spine, Spinal fractures, Thoracic region, Lumbar region, Conservative treatment, Orthotic devices, Emergency Department, Europe, North America, Surveys and Questionnaires

Introduction

Thoracolumbar spine (TL) is the most commonly fractured segment in the vertebral column¹. The final outcome of patients with TL fractures can range from full recovery to death², with a significant amount of individuals showing some type of long-term disability¹². This, along with the fact that traumatic TL fractures occur in relatively young ages, increases the economic and social burden of these lesions¹³.

Although no consensus is available when it comes to decision between surgical and conservative treatment of TL fractures, authors agree that a significant number can be non-operatively managed¹⁴. Nevertheless, the specific treatment of choice is also a matter of debate. In fact, regarding conservative treatment, the classical paradigm of external immobilization with orthosis and braces¹⁵ is being questioned, with recent systematic reviews⁶ of randomized controlled trials showing no benefit of orthosis for both clinical and radiological outcomes.

This is all more relevant as previous authors pointed out that conservative treatment of TL fractures represents a high economic burden for health services, with high direct and even higher indirect costs^{7,8}, of which orthosis and braces play a substantial role. However, although available literature shows relevant costs from orthosis without necessarily bringing measurable benefits, only specific populations were assessed, and no worldwide study was ever conducted. Additionally, no data is available on the decision of when to brace a patient and on the specialist's opinion on the importance of that practice.

Therefore, this study aims to assess the current practice and opinion of spine specialists from Europe and North America regarding the use of orthosis in adult patients with acute TL

fractures. Secondly, we aim to evaluate the direct costs of these devices in European and North American countries.

Methods

We developed an online questionnaire to assess current practices and costs associated with conservative management of acute TL fractures with the use of orthosis.

Responders were asked on their age, gender, years of practice, country and state (in the United States of America - USA), average number of TL fractures treated per week, frequency of orthosis use, current practice in their departments, setting of orthosis prescription (i.e. outpatient or inpatient), and confidence on its necessity (on a Likert scale). Cost estimates associated with the device and information on the payment regimens (i.e. paid by hospital insurance or patient) were also requested. Respondents provided a level of confidence (low, medium, or high) for both the number of weekly treated spine fractures and orthosis costs. The questionnaire included all closed-ended questions, except those on the average number of TL acute fractures managed per week and orthosis cost. All questions had mandatory answers.

The questionnaire was sent by e-mail to a list of European and North American authors of spine trauma papers who had been identified following a comprehensive search on Scopus, targeting specialists in spine trauma who usually decide on and manage adult patients with acute TL fractures. A goal of contacting 10 authors per country (or state, in case of USA) was set. When we were not able to identify 10 corresponding authors per country, the search was broadened for publications on other spine fields.

Data analysis

Orthosis cost and mean number of TL fractures treated per week were defined based in the value provided by the responders. When responders provided a range of values in open

questions an average was used for analysis purposes. All reported costs were converted in United State Dollars (\$). Since inflation was negligible, conversion was based on average value from the first trimester of 2020, the time period closest to data collection^o.

Mean number of TL fractures braced per month was calculated by the average percentage of fractures braced by the responder multiplied by the average number of TL fractures treated per month. Mean cost of orthosis per responder per month was calculated multiplying the last value by mean orthosis cost.

Gross Domestic Product (GDP) per capita in American dollars from World Bank database in 2018 was used to rank the countries according to purchasing power. Current health expenditure as a percentage of GDP in 2018 (% GDP health) from World Health Organization was used to rank the countries according to health-related expenditure. Geographic regions were divided based in United Nations (UN) geoscheme of UN Stats.

Descriptive analysis was performed, using absolute and relative frequencies for categorical and mean and standard deviation (SD) for continuous variables. Comparisons were made using Qui² test, T-student and ANOVA and their non-parametric counterparts, along with univariate linear regression.

Percentage of missing data on open-ended questions was calculated and questions were excluded if >10% of missing data.

Results

Our search retrieved at least one contact from 43 European and 14 North American countries (including 46 states in the USA). We contacted a total of 635 individuals, receiving a total of 130 responses (response rate of 20.5%). Eighty-nine responders were European (68.5%), and the remaining 41 (31.5%) North American; we received answers from 28 European and 5 North American countries (including from experts from 25 USA states) (Table 1).

Continent	Region	Countries
Europe	Eastern Europe	Belarus
		Bulgaria
		Czech Republic
		Hungary
		Poland
		Romania
		Russia
		Slovakia
	Northern Europe	Denmark
		Finland
		Norway
		Sweden
		United Kingdom
	Southern Europe	Albania
		Croatia
		Greece
		Italy
		Kosovo
		Macedonia
		Portugal
		Spain
	Western Europe	Austria
		Belgium
		France
		Germany
		Netherlands
		Switzerland
	Western Asia	Turkey
North America	North America	Canada
		United States
	Latin America Caribbean	Costa Rica
		Cuba
		El Salvador

Table 1. Continents, regions and countries with answers

Ten responders were female (7.7%); 85 Orthopaedic Surgeons (65.4%), and 34 Neurosurgeons (26.2%) (Table 2). Participants had a mean($\pm$ SD) age of 45.9 years old ($\pm$ 10.4), and most responders had more than 9 years of practice in spine surgery (n=84, 64.6%). Most respondents worked at a public hospital (n=84, 64.6%).

The mean($\pm$ SD) number of TL fractures treated per week was 3.5 ± 2.9 , ranging from 0 to 15. The estimates of this number were medium or high confidence in 94.6% of answers (n=123). Apart from one, all responders were from upper middle (13.8%) or high income (85.4%) countries.

Orthosis Use

In a dichotomous question, 10.8% (n=14) of responders stated that when conservative treatment is decided for a patient with a TL fracture they never put the patient on a brace. However, when asked in a categorical question with a scale from 0 to 100%, only 6.2% said that 0% of patients assisted by them with a conservative TL fracture leave without an orthosis. Fifteen individuals (11.5%) reported to brace all patients. Bracing was reported to be a regular practice in the workplace of 107 (82.3%) experts. Among those who never use an orthosis, 42.9% stated that this is not the regular practice in their workplace, versus 13.9% of those who use a brace (p=0.007). Forty-seven responders (36.2%) answered that the brace deliver by the hospital involves the admission of the patient.

In a Likert scale from 1 to 5 (1 is low/no benefit and 5 is essential), upon personal consideration on the benefit of orthosis use, an average value of 3.18 ± 1.2 was verified, with 101 responders (77.6%) rating orthosis need in 3 or more. Twenty-one (16.2%) experts

considered that there is no or low benefit from an orthosis use, while 14 (10.9%) considered that bracing is essential.

The percentage of patients in which the responders usually use an orthosis did not differ significantly in relation to the number of years of practice ($p=0.471$), spine surgery field ($p=0.479$), and practice setting ($p=0.609$). However, it was significantly different when comparing European versus North American experts ($p=0.021$) – in fact, all responders that stated never using an orthosis were from Europe. On the other hand, 43.2% of European responders used an orthosis in 25% or less of patients, versus 19.5% of North American ones (Figure 1).

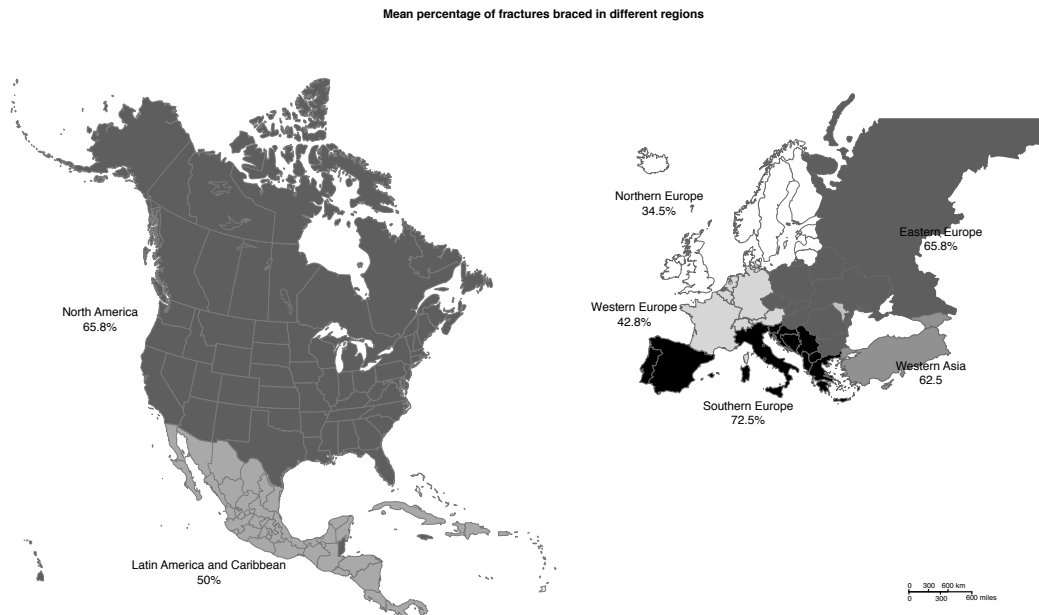


Figure 1. Mean percentage of patients braced in each region. Raising values are correspondent to darker colours. For calculation the range percentage was converted in a scale and mean value was calculated.

Considering the percentage of fractures in which an orthosis is used and the mean number of fractures braced, we estimated a monthly average of 6.5 ± 8.3 orthosis (ranging from 0 to 48) used by our responders. This number is not significantly different when comparing the two continents ($p=0.075$) or world regions ($p=0.135$).

Orthosis Costs

Thirty-two (26.4%) experts answered the brace is bought by the patient outside of the hospital and 47 (36.2%) stated the hospital has a system to deliver it that involves admission of the patient. Regarding payment method, in most cases, braces are either payed by an insurance (20%) or partially paid by the system/insurance and partially by the patient (39.2%) (Table 2).

Continent	North America			Europe					Total	
Region	North	Latin and Caribbean	Total	Eastern	Northern	Southern	Western	Western Asia	Total	
N of countries	2	3	5	8	5	8	6	1	28	33
N responders	38	3	41	19	8	30	28	4	89	130
Mean Age (SD)	50.6±10.7	53.3±7.2	50.8±10.5	46.9±11.6	44.8±8.5	44.1±9.4	41.2±8.8	40.8±8.6	43.7±9.7	45.9±10.4
Male	38 (100)	2 (66.7)	40 (97.6)	16 (84.2)	5 (62.5)	30 (100)	26 (92.7)	3 (75.0)	80 (89.9)	120 (92.3)
Field										
Orthopedics ± Traumatology	24 (63.2)	1 (33.3)	25 (61.0)	9 (47.4)	6 (75.0)	21 (70.0)	23 (82.1)	1 (25.0)	60 (67.4)	85 (65.4)
Neurosurgery	12 (31.6)	1 (33.3)	13 (31.7)	8 (42.1)	2 (25.0)	6 (20.0)	2 (7.1)	3 (75.0)	21 (23.6)	34 (26.2)
Trauma surgery	0 (0)	0 (0)	0 (0)	1 (5.3)	0 (0)	2 (6.7)	2 (7.1)	0 (0)	5 (5.6)	5 (3.8)
Other	2 (5.3)	1 (33.3)	3 (7.3)	1 (5.3)	0 (0)	1 (3.3)	1 (3.6)	0 (0)	3 (3.4)	6 (4.6)
Years of practice										
1-3	3 (7.9)	0 (0)	3 (7.3)	1 (5.3)	1 (12.5)	5 (16.7)	6 (21.4)	0 (0)	13 (14.6)	16 (12.3)
3-6	3 (7.9)	0 (0)	3 (7.3)	2 (10.5)	1 (12.5)	4 (13.3)	4 (14.3)	1 (25.0)	12 (13.5)	15 (11.5)
6-9	4 (10.5)	1 (33.3)	5 (12.2)	2 (10.5)	1 (12.5)	2 (6.7)	4 (14.3)	1 (25.0)	10 (11.2)	15 (11.5)
>9	28 (73.7)	2 (66.7)	30 (73.2)	14 (73.7)	5 (62.5)	19 (63.3)	14 (50.0)	2 (50)	54 (60.7)	84 (64.6)
Setting										
Public	17 (44.7)	1 (33.3)	18 (43.9)	15 (78.9)	8 (100)	22 (73.3)	17 (60.7)	4 (100)	66 (74.2)	84 (64.6)
Private	8 (21.1)	1 (33.3)	9 (22.0)	0 (0)	0 (0)	1 (3.3)	2 (7.1)	0 (0)	3 (3.4)	12 (9.2)
Public and Private in same institution	11 (28.9)	0 (0)	11 (26.8)	3 (15.8)	0 (0)	6 (20.0)	9 (32.1)	0 (0)	18 (20.2)	29 (22.3)
Other	2 (5.3)	1 (33.3)	3 (7.3)	1 (5.3)	0 (0)	1 (3.3)	0 (0)	0 (0)	2 (2.2)	5 (3.8)
Use of brace										
Sometimes or always	36 (94.7)	3 (100%)	39 (95.1)	18 (94.7)	5 (62.5)	29 (96.7)	21 (75.0)	4 (100)	77 (86.5)	116 (89.2)
Never	2 (5.3)	0 (0)	2 (4.9)	1 (5.3)	3 (37.5)	1 (3.3)	7 (25.0)	0 (0)	12 (13.5)	14 (10.8)
Percentage of patients braced										
0%	0 (0)	0 (0)	0 (0)	0 (0)	2 (25.0)	1 (3.3)	5 (17.9)	0 (0)	8 (9.0)	8 (6.2)
0-25%	6 (15.8)	2 (66.7)	8 (19.5)	7 (36.8)	4 (50)	6 (20)	12 (42.9)	1 (25.0)	30 (33.7)	38 (29.2)
25-50%	14 (36.8)	0 (0)	14 (34.1)	2 (10.5)	1 (12.5)	4 (13.3)	6 (21.4)	1 (25.0)	14 (15.7)	28 (21.5)
50-75%	6 (15.8)	0 (0)	6 (14.6)	1 (5.3)	1 (12.5)	4 (13.3)	1 (3.6)	1 (25.0)	8 (9.0)	14 (10.8)
75-100%	6 (15.8)	0 (0)	6 (14.6)	7 (36.8)	0 (0)	10 (33.3)	3 (10.7)	1 (25.0)	21 (23.6)	27 (10.8)
All (~100%)	6 (15.8)	1 (33.3)	7 (17.1)	2 (10.5)	0 (0)	5 (16.7)	1 (3.6)	0 (0)	8 (9.0)	15 (11.5)

Continent	North America			Europe					Total	
Region	North	Latin and Caribbean	Total	Eastern	Northern	Southern	Western	Western Asia	Total	
Brace deliver										
Patient buys outside the hospital	0 (0)	1 (33.3)	1 (2.4)	10 (52.6)	3 (50.0)	16 (55.2)	2 (8.7)	3 (75.0)	21 (38.3)	32 (26.2)
Hospital delivers in outpatient	11 (28.9)	0 (0)	11 (26.8)	2 (10.5)	0 (0)	2 (6.9)	6 (26.1)	1 (25.0)	14 /17.3)	25 (38.5)
Hospital delivers after admission	23 (60.5)	1 (33.3)	24 (58.5)	4 (21.1)	2 (33.3)	2 (6.9)	15 (65.2)	0 (0)	23 (28.4)	47 (20.5)
Some patients buy outside and the hospital delivers to others	1 (2.6)	1 (33.3)	2 (4.9)	3 (15.8)	0 (0)	7 (24.1)	0 (0)	0 (0)	10 (12.3)	12 (9.8)
Other	3 (7.9)	0 (0)	3 (7.3)	0 (0)	1 (16.7))	2 (6.9)	0 (0)	0 (0)	3 (3.7)	6 (4.9)
Payment										
Fully by patient	0 (0)	0 (0)	0 (0)	4 (21.1)	0 (0)	9 (31.0)	0 (0)	0 (0)	13 (16.0)	13 (10.0)
Fully by insurance	8 (22.2)	0 (0)	8 (20.5)	4 (21.1)	0 (0)	2 (6.9)	12 (52.2)	0 (0)	18 (22.2)	26 (21.7)
Fully paid by the public system	4 (11.1)	0 (0)	4 (10.3)	1 (5.3)	6 (75.0)	0 (0)	5 (21.7)	0 (0)	12 (14.8)	16 (13.3)
Partially by patient and partially by insurance	17 (44.7)	1 (33.3)	18 (46.2)	10 (52.6)	0 (0)	14 (48.3)	5 (21.7)	4 (100)	33 (40.7)	51 (42.5)
Other/Combinations	7 (19.4)	2 (66.6)	9 (23.1)	0 (0)	0 (0)	4 (13.8)	1 (4.3)	0 (0)	5 (6.2)	14 (11.7)
Benefit of orthosis use – Opinion										
1 – Low/None	5 (13.2)	0 (0)	5 (12.2)	0 (0)	3 (37.5)	2 (6.7)	11 (39.3)	0 (0)	16 (18.0)	21 (16.2)
2	4 (31.6)	0 (0)	4 (9.8)	1 (5.3)	1 (12.5)	0 (0)	2 (7.1)	0 (0)	4 (4.5)	8 (6.2)
3	16 (42.1)	0 (0)	16 (39.0)	6 (31.6)	3 (37.5)	11 (36.7)	6 (21.4)	0 (0)	26 (29.2)	42 (32.3)
4	12 (31.6)	1 (33.3)	13 (31.7)	7 (36.8)	1 (12.5)	11 (36.7)	8 (28.6)	4 (100)	31 (34.8)	44 (33.8)
5 - Essential	1 (2.6)	2 (66.6)	3 (7.3)	5 (26.3)	0 (0)	6 (20.0)	1 (3.6)	0 (0)	12 (13.5)	15 (11.5)

Table 2. Collected data. Data is presented as N (percentage of category), otherwise indicated.

The mean ($\pm$ SD) reported cost of the orthosis was \$611.4 ($\pm$ 716.0), ranging from 1 to 5000 dollars (median of \$384.3). Eight responders stated not knowing the orthosis cost. The cost estimates were medium or high confidence in 78.5% of answers (n=94).

Average cost estimates were significantly higher in North America when compared to Europe (n=36, \$1002.0 $\pm$ 943.2 versus \$421.4 $\pm$ 476.6, p<0.001), but no significant differences were observed when comparing the different world regions (Figure 2). Significantly higher costs were reported in high income, when compared with upper middle income countries (n=18, \$165.9 $\pm$ 135.0 versus n=91, \$702.4 $\pm$ 754.1, p<0.001).

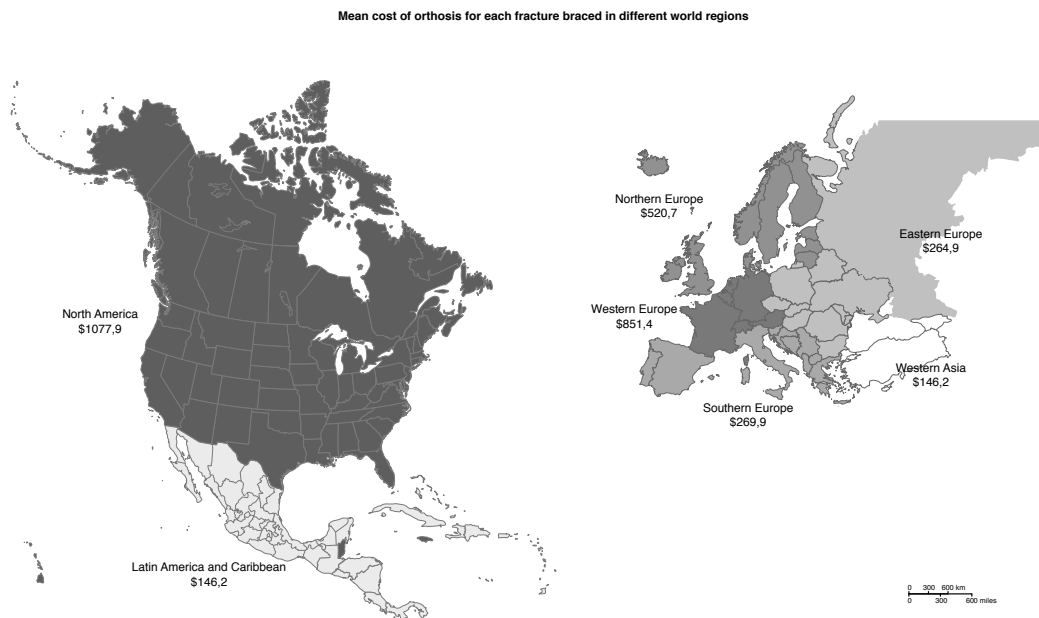


Figure 2. Mean cost of orthosis in different regions defined by UN. Raising values are correspondent to darker colours.

Estimates of costs were significantly higher when the hospital had a delivery system that involves admission of the patient ($n=41$, $\$985.4 \pm 1001.2$) than when the patient buys the orthosis outside of the hospital ($n=32$, $\$282.2 \pm 281.0$, $p < 0.001$). Orthosis cost in hospitals that admit the patients were also significantly higher than in mixed systems when orthosis is sometimes delivered by the hospital and sometimes directly bought by the patient ($n=12$, $\$223.9 \pm 133.7$, $p = 0.006$). However, costs were not different whether is the hospital that delivers the orthosis, either after admission or in an outpatient system ($n=20$, $\$620.7 \pm 305.5$, $p = 0.442$).

Orthosis cost did not differ significantly among payment method ($p = 0.058$). Univariable linear regression analyses showed an increase in orthosis costs associated with higher GDP per capita and with higher %GDP health (Figure 3), but no significant association was found with the weekly average number of treated TL fractures.

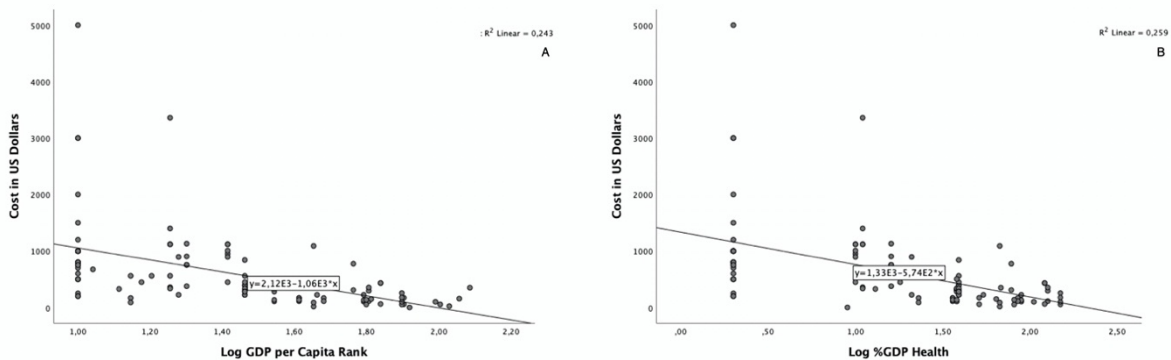


Figure 3. Regression line between orthosis cost and A. Logarithmic transformation of GDP per capita; B. Logarithmic transformation of health expenditure as a percentage of GDP

Considering the average number of braced fractures and the average cost of the device, in each responder monthly practice there is an average expenditure of \$4824.6±12379.6 (median of \$1343.4/month) (Table 3). The amount spent is different among continents and world regions (p=0.018), being significantly higher in North America when compared to Europe (10759.5±20165.9/month, versus \$2260.1±5040.3, p=0.001). Particularly, the North America region (\$11761,5±20830.9/month) spends significantly more with braces when compared with Southern Europe (\$1590.5±1749.9, p=0.022).

Continent (n responders)	Region by UN (n responders)	Mean number TL fractures/ week	Orthosis cost (\$)	Orthosis overall cost/ responder/ month (\$/month)
Europe (89)	All	3,5±2.7	421,4±476.7	2260,1±5040.3
	Eastern Europe (18)	3,2±3.5	264,9±271.0	1162,4±1603.6
	Northern Europe (8)	4,8±3.6	520,7±176.7	4209,2±7209.3
	Southern Europe (30)	2,9±2.4	269,9±173.5	1590,5±1749.9
	Western Europe (28)	3,8±2.3	851,4±721.0	3832,3±8245.7
	Western Asia (4)	1,8±1.5	146,2±88.9	352,5±248.1
North America (41)	All	3,7±3.2	1002,0±943.2	10759,5±20165.9
	North America (38)	4,0±3.2	1077,9±948.6	11761,5±10830.9
	Latin America and Caribbean (3)	0,8±0.3	167,0±175.1	72,2±90.6

Table 3. Number of TL fractures by UN region and associated costs.

The expected cost for each 100 acute TL treated conservatively in the different considered regions, and its variation accordingly to the relative percentage of patients braced is depicted in Table 4.

Continent (n responders)	Region by UN (n responders)	Cost/Fracture braced (\$)	Cost/100 fractures if braced:			
			25%	50%	75%	100%
Europe (89)	All	421.4±476.7	10535.5±11916.3	21071.1±23832.6	31606.6±35748.9	42142.2±47665.2
	Eastern Europe (19)	264.9±271.0	6623.4±6775.5	13246.7±13551.1	19870.1±20326.6	26493.5±27102.1
	Northern Europe (8)	520.7±176.7	13018.4±4418.5	26036.8±8837.0	39055.2±13255.5	52073.6±17674.0
	Southern Europe (30)	269.9±173.5	6748.4±4339.6	13496.8±8679.1	20245.2±13018.7	26993.6±17358.3
	Western Europe (28)	851.4±721.0	21284.7±18025.3	42569.5±36050.8	63854.2±54075.9	85139.0±72101.1
	Western Asia (4)	146.2±88.9	3654.3±2222.4	7308.5±4444.7	10962.8±6667.1	14617.1±8889.4
North America (41)	All	1002.0±943.2	25048.8±23579.7	50097.5±47159.4	75146.3±70739.2	100195.1±94318.9
	North America (38)	1077.9±948.6	26946.4±23714.3	53892.8±47428.6	80839.1±71143.0	107785.5±94857.3
	Latin America and Caribbean (3)	167.0±175.1	4175.0±4378.0	8359.0±8756.0	12525.0±13134.0	16700.0±17512.0

Table 4. Costs of fractures braced by UN region and variation of costs associated with relative percentage of fractures braced

Discussion

To the best of our knowledge, this is the first survey on the use and costs of orthosis in adults with acute TL fractures in Europe and North America. More than 90% of spine specialists reported using these devices in some of their patients, with cost estimates averaging \$611.

Orthosis use

About 90% of responders reported to use an orthosis in adult patients with acute TL fractures. In fact, the idea that these devices are needed for an adequate conservative treatment of TL fractures is commonplace and referred in previous literature⁴⁵. This may also explain why more than half of responders rated the need for a brace as ≥ 3 on a scale from 1 to 5.

While some authors proposed that braces may cause pressure-related skin breakdown, diminish pulmonary capacity, and weaken the paraspinal musculature, their malicious effect is yet to be proven^{10,11}. However, although recent trials and systematic reviews showed no benefit in clinical and radiological outcomes⁶, physicians are still using orthosis, what might be explained by the expected science lag, that may take up to 17 years¹². Nevertheless, only 15 responders (11.8%) brace all patients, showing a tendency in leaving some patients with no immobilization device.

Brace use was lower in Europe when compared with North America. Although we found no explanation for that in the literature, it may be related with the higher litigation costs found in North America, that may render the physicians more cautious when abandoning long established practices and implementing the results of newer scientific reports¹³.

Orthosis costs

Our responders reported orthosis costs ranging from \$1 to \$5000. This wide variation can be due to multiple factors. In fact, and although 78% responders reported medium to high confidence in their reported value, it is known that many physicians do not know the real cost of the devices¹⁴. Also, some responders may have reported partial values (i.e. those covered by the insurance or paid by the patient), leading to an underreport of the direct orthosis cost. Additionally, our sample of countries included different economies, with significant differences between upper-middle and high-income countries.

This difference in costs between different economies, along with the relationship found between orthosis cost and GDP per capita and % GDP health ranks can be explained by the fact that income is the most important determinant of health care spending¹⁵. In fact, health is considered a luxury, and GDP is one of the most important predictor of health expenditure¹⁶. The lower cost of devices in lower ranked countries may be explained by the use of different devices, namely low cost alternatives that are developed to fit those markets^{17,18}. Additionally, the higher costs reported by experts in more developed countries can result from overpricing, that companies use to improve upon an already existing product, with only marginal value to the end customer¹⁸.

Our cost report does not include other direct costs associated with hospitalizations (reported by 36.2%) and indirect costs associated with the burden of this device. However, as estimated by World Health Organization (in 2010, in international dollars (int\$)) the cost per inpatient bed day may range from 234.7-757.5 int\$ in European countries to 646.5-1093.5 int\$ in USA and Canada¹⁹. A previous study on a sample from an USA hospital found costs associated

with orthosis that ranged from about \$7000-13000, including hospitalization until the orthosis was fitted²⁰.

Apart from the costs associated with hospitalization, the cost of the device itself was also significantly higher in inpatients compared with outpatients. This may be associated with the fact that inpatients receive custom-made orthosis, significantly more expensive than pre-fabricated ones.

Trying to understand the burden of orthosis, Table 4 shows the cost for each 100 TL fracture treated conservatively, with different percentage of patients braced. Even this analysis does not include costs related with orthosis use and appliance, and, a severe underreport of the whole cost is expected. Nevertheless, there is an important variation of values, reinforcing the need for adequate criteria on orthosis use.

Strengths and Limitations

This study has some limitations. Firstly, we observed a relatively low response rate (20.5%), which may be explained by the fact that (i) the questions demand some specific knowledge on the cost of devices (which is sometimes unknown by physicians²¹), (ii) corresponding authors may change their contacts, and (iii) the absence of a monetary incentive given to our responders²¹. Sample bias is expected, since responders were selected from those who have co-authored a study on acute TL fractures, and many spine and trauma specialists were not considered. Answers double checking was not performed, and some inaccuracies are expected. Also, cost estimates were based in individual reports, that might be influenced by responders' knowledge on devices price and delivery systems. Nevertheless, almost 95% of responders reported medium to high confidence on their cost estimation. A wide range of

spine experts answered our questionnaire, from different backgrounds and practice realities, what may render our responses quite heterogeneous.

Nevertheless, this is the first study including such a wide array of responders, with data from 33 different countries from Europe and North America, enabling a representation of the practice reality on these continents. This study showed a wide variation in orthosis use and for the first-time displayed orthosis costs from different places and practice settings. With a significant number of countries included and a wide reach, if cautiously interpreted, our results may guide worldwide healthcare related policies.

Conclusion and Future

This is the first study providing data in use of orthosis and its costs in Europe and North America. It included 130 spine specialists from both continents and aggregated data on their daily practice. We found that orthoses are still widely used, but some practitioners already choose to treat their patients with no devices. A substantial cost is associated with their use, sometimes added to the need of admission of the patient. Given the high prevalence of acute TL fractures in adults and the fact that recent systematic reviews did not identify any benefit associated with orthosis, a parsimonious use of this devices is needed, since their cost is not negligible and may represent a significant burden to healthcare systems. In fact, future cost-benefit analyses are needed, along with studies on orthosis use in different subtypes of TL fractures deemed for conservative treatment, in order to clarify their role, if any, in the treatment of these patients.

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CHAPTER IV

Cost effectiveness of outpatient lumbar discectomy

Article 2

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Cost effectiveness of outpatient lumbar discectomy

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Abstract

Background: Microdiscectomy is the most commonly performed spine surgery and the first transitioning for outpatient settings. However, this transition was never studied, in what comes to cost-utility assessment. Accordingly, this economic study aims to assess the cost-effectiveness of outpatient lumbar microdiscectomy when compared with the inpatient procedure.

Methods: This is a cost utility study, adopting the hospital perspective. Direct medical costs were retrieved from the assessment of 20 patients undergoing outpatient lumbar microdiscectomy and 20 undergoing inpatient lumbar microdiscectomy. Quality-adjusted life-years were calculated from Oswestry Disability Index values (ODI). ODI was prospectively assessed in outpatients in pre and 3- and 6-month post-operative evaluations. Inpatient ODI data were estimated from a meta-analysis. A probabilistic sensitivity analysis was performed and incremental cost-effectiveness ratio (ICER) calculated.

Results: Outpatient procedure was cost-saving in all models tested. At 3-month assessment ICER ranged from €135753 to €345755/QALY, higher than the predefined threshold of €60000/QALY gained. At 6-month costs were lower and utilities were higher in outpatient, overpowering the inpatient procedure. Probabilistic sensitivity analysis showed that in 65% to 73% of simulations outpatient was the better option. The savings with outpatient were about 55% of inpatient values, with similar utility scores. No 30-day readmissions were recorded in either group.

Conclusion: This is the first economic study on cost-effectiveness of outpatient lumbar microdiscectomy, showing a significant reduction in costs, with a similar clinical outcome, proving it cost-effective.

Keywords: Discectomy; Intervertebral Disc Displacement; Outpatients; Patient Reported Outcome Measures; Cost-Benefit Analysis; Economics

Introduction/Background

Lumbar disc herniation results from disc degeneration, with protrusion or extrusion of the nucleus pulposus. It can be asymptomatic or lead to a myriad of symptoms, forcing patients to seek medical treatment [1,2]. While the conservative approach is the mainstay, upon its failure, surgery is associated with successful outcome [1]. Although many surgical procedures have been described for the treatment of herniated lumbar discs, lumbar discectomy is not only safe but also the simplest and most effective [3]. Due to its simplicity and low rate of complications, discectomy comprises 70–90% of all outpatient procedures performed in spinal surgery [4].

Many procedures have emerged from the traditional open discectomy, but microdiscectomy (MD) has been shown to provide a faster relief of pain, being nowadays the most common spinal surgery performed in United States, with more than 300,000 annual procedures [5]. As a result, MD represents a substantial burden to healthcare systems [67] and policies for cost reduction—such as ambulatory surgeries—are needed.

In fact, the literature depicts descriptions of outpatient discectomies since the 1980s [8] and MD was the first major spine surgery to transition to the ambulatory setting, with some centers performing almost half of these procedures in an outpatient basis [9]. However, many countries and centers still experience barriers in ambulatory transition. Actually, as described by the World Health Organization (WHO), economic advantages for hospitals from inpatient procedures, lack of educational programs, and absence of adapted facilities and community support can delay the progression to day surgeries [10]. Adequate scientific background and reassurance is needed to support this transition and reduce misinformation [10].

So, and although general outpatient procedures appear to be safe and effective [11], in the specific case of lumbar MD, a wider adoption of outpatient procedures may be precluded by insufficient evidence on the effectiveness, safety and economic savings of ambulatory MD compared to inpatient MD. Therefore, this cost-utility study aims to compare inpatient with outpatient lumbar MD regarding both its costs and effectiveness in adult patients with lumbar disc herniation and sciatica.

Methods

Study Design

This is a cost-utility study, corresponding to a full economic evaluation comparing both costs and effectivity in patients undergoing MD in the outpatient *versus* in the inpatient setting in a Portuguese National Healthcare System hospital. Effectivity is presented as quality-adjusted life-years (QALYs), with the number of QALYs calculated by the product between life years and utilities. We followed the hospital perspective, considering direct hospital costs.

Uncertainty was explored via an one-way deterministic sensitivity analysis and probability sensitivity analyses.

The study was approved by a hospital ethics committee in May 25th 2017.

Costs

Costs were assessed from two cohorts of patients treated in the same spine center of a central Portuguese hospital. Accordingly, specific data from 20 outpatients and 20 inpatients undergoing MD with single excision of herniated intervertebral disk was gathered. To be included in either group, patients had to present clinical complaints compatible with lumbar disc herniation and with confirmation of clinical findings by radiological studies (computed tomography and/or magnetic resonance imaging). Patients were excluded if they presented: 1) comorbidities precluding outpatient surgery; 2) social conditions precluding outpatient surgery (i.e. living alone or far from the hospital, psychiatric conditions); 3) need for additional spine surgical procedures other than single excision of herniated intervertebral

disk; or 4) previous lumbar spine surgery. Upon inclusion, all patients were submitted to a lumbar MD by the same surgical team.

Costs were defined as the sum of direct hospital costs related with inpatient and outpatient procedures. For outpatients, we quantified operatory room (OR) costs, including costs related with 1) staff and OR occupation; 2) used drugs; 3) supplies used in that particular intervention; and 3) other costs. In addition, we quantified costs related with eventual 30-days readmissions. Such costs were also quantified for inpatients, among whom costs related to hospital stay were also added. The latter include staff-, drug- and supplies- (i.e., bandages, disposable wearing, etc.) related costs. For both inpatients and outpatients, we retrieved other costs related with water supply, electricity, telephone services, administrative issues, etc. Both groups of patients had the first post-operative appointment 2 weeks after the surgery and follow a similar medical follow-up.

Regarding outpatients, we prospectively analyzed a consecutive sample of 20 patients, presenting to our spine center between 2017 and 2018, with clinical pain and disability due to radiologically-identified lumbar disc herniation that fulfilled the above-mentioned criteria. A pre-defined outpatient protocol was followed, with patients being submitted to a pre-operative anesthetic evaluation and provided with aseptic sponges to bath in the morning before the procedure. After surgery, all patients were discharged in the same day, less than 12 hours after the procedure and received a pre-defined analgesic protocol. To assess complications in the immediate post-operative period, a physician performed a telephone call up to 24 hours after discharge, with the patient being directed to an emergency appointment if any complication was suspected.

Assessed inpatients consisted of a sample of 20 individuals, fulfilling the above-mentioned criteria, with similar age and gender to those of outpatients, and who were retrospectively selected from patients submitted to MD in the same spine center.

Despite the literature describing a variable length of stay among MD patients in real life scenarios, there is an overall agreement among spine surgeons that an uncomplicated inpatient MD would only need a one-day admission [12]. As a result, we not only performed this economic evaluation study estimating inpatient costs as observed (irrespective of the admission time), but also performed a sensitivity analyses considering the scenario of all patients being only admitted for one day. To do so, costs for inpatients that stayed for longer periods were re-calculated for those expected in a one-day admission period.

Utilities

Utilities were estimated from the Oswestry Disability Index (ODI).

Outpatients were prospectively evaluated pre-operatively and three and six months post-operatively, with ODI being assessed in each evaluation, along with the overall visual analogue scale of pain (VAS), back pain VAS (BP-VAS), and leg pain VAS (LP-VAS).

Since inpatient data from our center were collected retrospectively, ODI data were retrieved from the literature. To do so, we performed a comprehensive search on MEDLINE from 2018 to 2020 (limited to humans and systematic reviews), using a combination of the search terms: “lumbar”, “hernia”, “protrusion”, “extrusion”, “discectomy” and “microdiscectomy”. We specifically searched for studies on lumbar MD, displaying ODI data on pre- and post-operative assessments at 3 and/or 6 months assessments after the surgical procedure. Of a

total of 110 retrieved references, we identified one systematic review with meta-analysis fulfilling all eligibility criteria and utilities were estimated from its data on ODI [13].

QALYs were estimated based on three and six-months utilities, adjusted for baseline values, using two different approaches – the area under the curve (AUC) and change from baseline (CfB) approach [14]. For outpatients, average and standard-deviation values for QALYs based on each approach were estimated using patient-level data. For inpatients, such values were estimated following Bayesian methods – a random-effects Bayesian meta-analysis was performed to obtain pooled baseline utilities and mean utilities differences, which were then used in the same Bayesian model to estimate the average and standard-deviation values for QALYs (via assessment of the posterior distributions) following the AUC and CfB approaches. Uninformative prior distributions were used in Bayesian models both for the effect size measures and for the tau parameters ($\text{dnorm}(0,0.00001)$ and $\text{dunif}(0,10)$, respectively).

Data analysis

Categorical variables were described using absolute and relative frequencies, while continuous variables were described using means and standard-deviations. Categorical variables were compared using the chi-square test, while continuous variables were compared using the independent samples t-test and its non-parametric counterparts.

To assess for cost-effectiveness, we estimated incremental cost-effectiveness ratios (ICER), consisting of the difference between costs (i.e., outpatient minus inpatient costs) dividing by the difference in QALYs (i.e., outpatient minus inpatient QALYs). To account for uncertainty, we performed one-way deterministic sensitivity analysis, testing the effect of

changing one variable at each time according to a prespecified range of values – observed minimum and maximum values were used for costs, while for QALYs (which were estimated by Bayesian values), the minimum and maximum values used for sensitivity analyses were obtained after 10,000 simulations based on their distributions. In addition, to explore uncertainty we conducted probabilistic sensitivity analysis via Monte Carlo simulation methods – we ran 10,000 simulations in which we allowed each input variable to vary according to a probability distribution. A treatment choice was regarded as cost-effective if its ICER was lower than the defined willingness to pay (WTP) per gained QALY. As indicated by WHO, The WTP was defined at 3 times the Portuguese per capita gross domestic product (GDP) [15]. Using the last available International Monetary Fund values (2019), this corresponds to a WTP value of €60000 [16]. This probability sensitivity analysis was performed for both inpatient's observed admission time and for one day only. Frequentist statistical analysis was performed using SPSS v26 (IBM SPSS Statistics, NY). Bayesian models were performed using rjags package for software R (version 4.0). Probabilistic sensitivity analysis was performed using TreeAgePro 2019 (TreeAge Software, Williamstown, MA).

Results

Costs Data

Costs were retrieved from 20 outpatients and 20 inpatients submitted to lumbar MD, in whom no significant differences were found for any assessed sociodemographic characteristics (Table 1). Inpatients length of stay averaged 2.5 days. No 30-day readmission was recorded. No loss of follow-up was observed in the six-month assessment period for the outpatients (Table 1).

	Setting		p value
	Inpatient (N=20)	Outpatient (N=20)	
Age at surgery	46.8±11.0	44.9±10.87	0.586
N of Females - N (%)	8 (40%)	10 (50%)	0.525
Level - N(%)			0.524
L2L3	1 (5%)		
L4L5	12 (60%)	11 (55%)	
L5S1	7 (35%)	9 (45%)	
Side - N(%)			0.626
Left	12 (60%)	12 (60%)	
Right	8 (40%)	8 (40%)	
Hospital stay (days)	2.5±0.89	0	<0.001
30-day readmissions - N (%)	0	0	-

Table 1. Demographic data of inpatient and outpatient. OR costs are costs related with the procedure. Hotel costs are costs related with hospital stay. N: number. OR: Operatory Room. Values are presented as mean±standard deviation.

Overall hospital costs averaged €630.1±18.4 per patient in outpatients and, €1477.7±207.0 per patient in inpatients ($p<0.001$). This represented an average save of €847.52 (95% confidence interval (CI)=€750.36-944.67), corresponding to a cost reduction of 55% (95%CI=35.8%-66.9%). OR costs were also significantly higher in inpatients compared to outpatients (average €883.7 *versus* €630.1, $p<0.001$) (Table 2).

Considering an inpatient admission time of one day the overall costs would be of €1128.2±25.5, with a mean hotel cost of €244.5±1.9.

	Setting		p value
	Inpatient (N=20)	Outpatient (N=20)	
Operatory Room Costs	€883.73	€630.14	<0.001
Drugs and related	€44.39	€24.63	<0.001
OR supplies	€79.54	€69.43	0.014
Staff	€560.08	€468.38	<0.001
Other costs	€199.72	€67.70	<0.001
Hotel Costs	€593.93	-	
Drugs and related	€39.73	-	
Medical supplies	€57.28	-	
Staff	€355.53	-	
Other costs	€112.57	-	
Diagnostic tests	€28.83	-	
Overall Costs	€1477.66	€630.14	<0.001

Table 2. Costs associated with inpatient and outpatient interventions. OR costs are costs related with the procedure. Hotel costs are costs related with hospital stay. N: number. OR: Operatory Room. Values are presented as mean.

Utility Data

Data on outpatient pre-operative, 3-month and 6-month assessments are available at Additional file 1. Between sequential assessments, a significant improvement was obtained in all outcomes (all $p < 0.001$), including ODI changes. All ODI and VAS inpatient changes were significantly higher than minimal clinical important differences. Inpatient ODI were retrieved from a systematic review and meta-analysis [17], with 6 primary studies displaying data at 3-month ODI, and 4 studies at 6-month ODI. Data on inpatient and outpatient utility values for the 3 and 6-month assessments are available at Table 3.

Utilities	Baseline	3 months	6 months
Outpatient	0.508±0.098	0.646±0.092	0.720±0.063
Inpatient at 3-month	0.492±0.065	0.678±0.088	-
Inpatient at 6-month	0.474±0.107	-	0.695±0.143

Table 3. Utilities estimated from inpatient and outpatient assessments. Values for inpatient are a result of meta-analysis including 6 studies at 3-months and 4 studies at 6-months. Values are presented as mean±standard deviation.

At the 3-month assessment, MD is associated with a gain of 0.14 or 0.02 QALY in the outpatient setting and 0.15 or 0.02 in the inpatient setting, respectively depending on whether the AUC or the CfB approach is being considered. At 6-months, these gains were of 0.32 (AUC) or 0.06 (CfB) QALY for inpatients, and 0.29 (AUC) or 0.06 QALY (CfB) for outpatients (Table 4).

Input variable	Mean±SD	Type of distribution	Information Source
Costs – Euro – ±2.5 days admission			Primary
Surgical costs in ambulatory setting	630.1±18.4	Gamma	(Our sample)
Surgical costs in hospitalization setting	883.7±26.9	Gamma	
Hotel costs in hospitalization setting	593.5±211.1	Gamma	
Costs – Euro – 1 day admission			Primary
Surgical costs in ambulatory setting	630.1±18.4	Gamma	(Our sample)
Surgical costs in hospitalization setting	883.7±26.9	Gamma	
Hotel costs in hospitalization setting	244.5±1.9	Gamma	
QALYs in ambulatory setting			Primary
Based on three months ODI data [AUC method]	0.144±0.022	Gamma	(Our sample)
Based on three months ODI data [CfB method]	0.017±0.010	Gamma	
Based on six months ODI data [AUC method]	0.315±0.040	Gamma	
Based on six months ODI data [CfB method]	0.061±0.026	Gamma	
QALYs in hospitalization setting			Meta-analysis
Based on three months ODI data [AUC method]	0.146±0.018	Gamma	
Based on three months ODI data [CfB method]	0.023±0.007	Gamma	
Based on six months ODI data [AUC method]	0.293±0.067	Gamma	
Based on six months ODI data [CfB method]	0.055±0.021	Gamma	

Table 4. Input variables included in economic evaluation model. OR costs are costs related with the procedure. Hotel costs are costs related with hospital stay. SD: standard deviations. OR: operator Room; AUC: Area under the curve; CfB: Change from Baseline; ODI: Oswestry Disability Index; QALY: Quality-adjusted life year.

Cost-utility analysis

Considering data from 3-month post-operative assessments, inpatient MD was associated both with higher costs and small QALY gains, resulting in an ICER of €345755.1/QALY gained (AUC approach) or €135753.2/QALY gained (CfB approach) (Table 5). In both cases, ICER are higher than the WTP threshold of €60000/QALY gained, rendering inpatient surgery not cost-effective.

	AUC	3-month CfB	6-month	
			AUC	CfB
Observed admission time				
ICER (outpatient vs inpatient)	€345755.1/QALY	€135753.2/QALY	-	-
% Simulations outpatient better than inpatient	65.2%	73.0%	68.9%	71.8%
1-day admission time				
ICER (outpatient vs inpatient)	€207541.7/QALY	€80338.7/QALY	-	-
% Simulations outpatient better than inpatient	58.4%	54.4%	66.3%	66.4%

Table 5. Cost-utility analysis for observed admission time and 1-day admission time. ICER values for 6-month assessment are not presented because, since outpatient is associated both with lower costs and higher utility gains, inpatient was dominated. AUC: Area under the curve; CfB: Change from Baseline; ICER: Incremental Cost-Effectiveness Ratio; QALY: Quality-adjusted life year.

One-way deterministic sensitivity analyses at 3-month assessments always resulted in ICER higher than the WTP threshold, indicating that the small utility gains in inpatient setting were not compensated by the underlying higher costs (Figure 1). At 6-month assessments, the inpatient setting was always found to be the dominated strategy – it was always found to be associated with lower utilities and higher costs when compared to the outpatient setting, translating in negative ICER values (Figure 2).

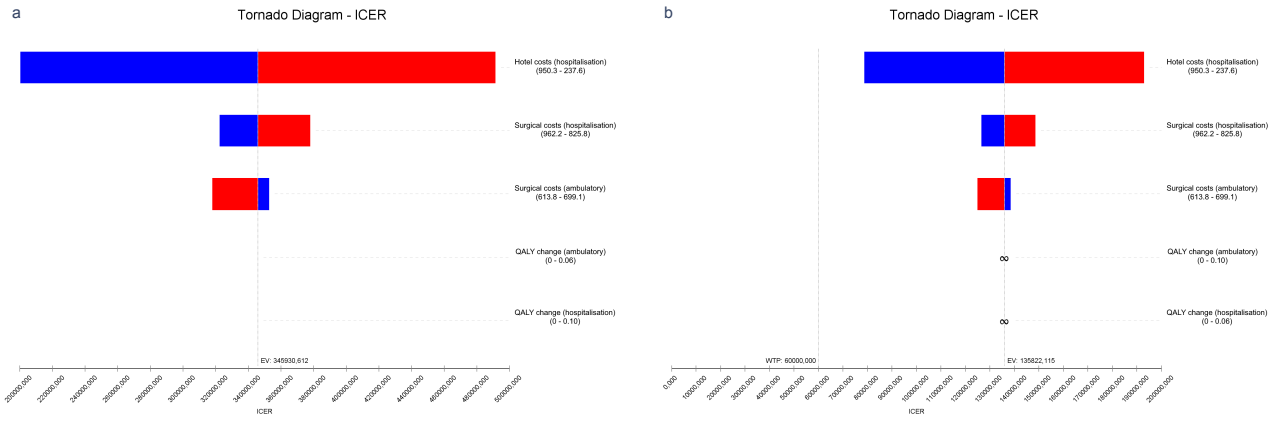


Figure 1. Incremental cost-effectiveness ratio (ICER) tornado diagram for one-way sensitivity analyses at 3-month assessment with inpatient costs calculated for the observed admission time. The minimum and maximum values for each input variable are presented in brackets and the dashed line represents the willingness-to-pay threshold. a: Sensitivity analyses with QALYs change computed based on the area under curve approach; b: Sensitivity analyses with QALYs change computed based on the change from baseline approach.

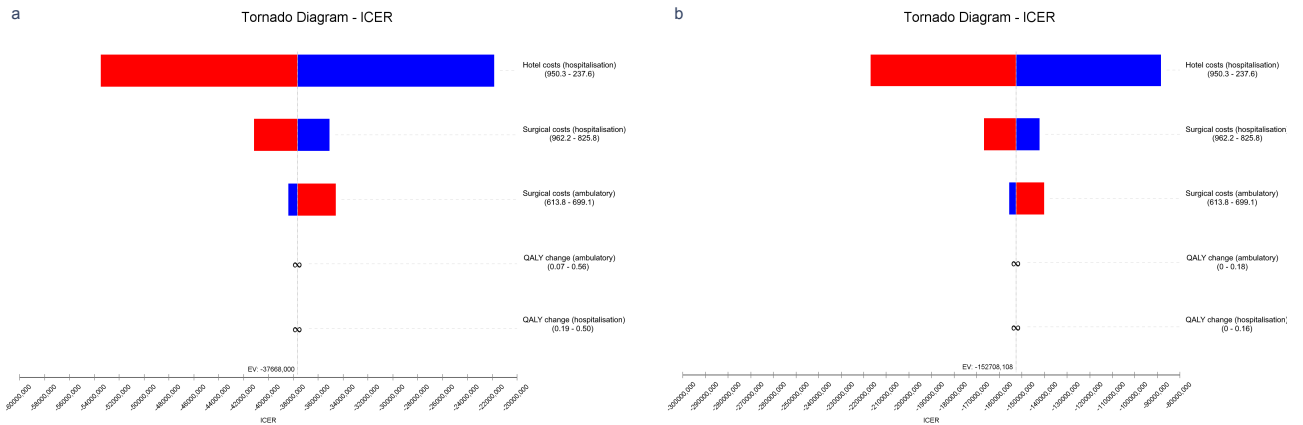


Figure 2. Incremental cost-effectiveness ratio (ICER) tornado diagram for one-way sensitivity analyses at 6-month assessment with inpatient costs calculated for the observed admission time. The minimum and maximum values for each input variable are presented in brackets and the dashed line represents the willingness-to-pay threshold. a: Sensitivity analyses with QALYs change computed based on the area under curve approach; b: Sensitivity analyses with QALYs change computed based on the change from baseline approach.

In probabilistic sensitivity analysis, ambulatory MD was found to be the best strategy in 65.2% (AUC approach) and 73.0% (CfB approach) simulations (Figure 3a and 3c, respectively, and Table 5).

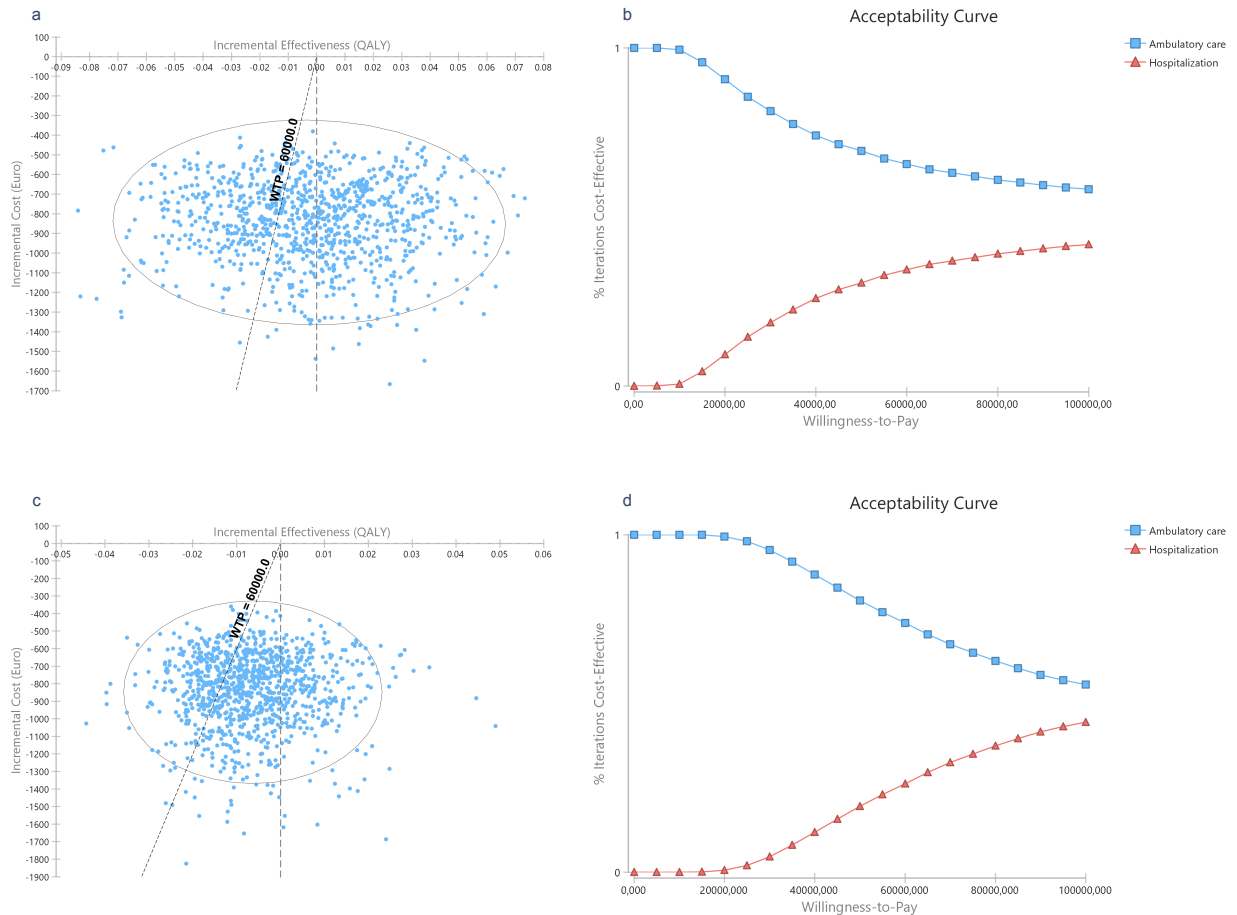


Figure 3 Results of probabilistic sensitivity analysis at 3-month assessment with inpatient costs calculated based in the observed admission time. a and b with QALYs computed based in area under curve; c and d based in change from baseline.

Right (a and c): Incremental cost-effectiveness ratio scatterplots and 95% confidence interval ellipse

- Each point represents a simulation, with indication of the mean incremental cost and effectiveness of outpatient compared to inpatient MD; the oblique dashed line represents the willingness-to-pay (WTP) threshold;

- Simulations represented to the left of the oblique dashed line (WTP line) represent those in which outpatient surgery was found to be less costly and less effective than inpatient surgery, with inpatient being the treatment of choice;
- Simulations to the right of the oblique dashed line (WTP line) and of the vertical line represent those in which outpatient surgery was found to be less costly and more effective than inpatient surgery with outpatient surgery being the treatment of choice.
- Between dashed lines are those in which outpatient was found to be less costly and less effective, but the effectiveness losses do not compensate the cost savings, and outpatient is the treatment of choice
- In this model, and according to €60000 WTP outpatient is better than inpatient in 65.2% (AUC) or 73.0% (CfB) of simulations.

Left (b and d): Cost-effectiveness acceptability curve of outpatient versus inpatient. The Y-axis represents the probability of each comparator being cost-effective at a given willingness-to-pay (WTP) threshold, and ranges between 0% and 100%. Outpatient MD has been identified as cost effective throughout all different WTP thresholds depicted

At 6-month assessments, outpatient MD, associated both with lower costs and higher QALY gains – no ICER was, thus, calculated, since inpatient MD was dominated (Table 5). In probabilistic sensitivity analysis, ambulatory MD was found to be the best strategy in 68.9% (AUC) and 71.8% (CfB) simulations (Figure 4a and 4c, respectively, and Table 5). Outpatient procedures remain cost-effective at 3 and 6-months, at any WTP between 0 and €100000/QALY gained (Figure 3b and 3d and Figure 4b and 4d, respectively).

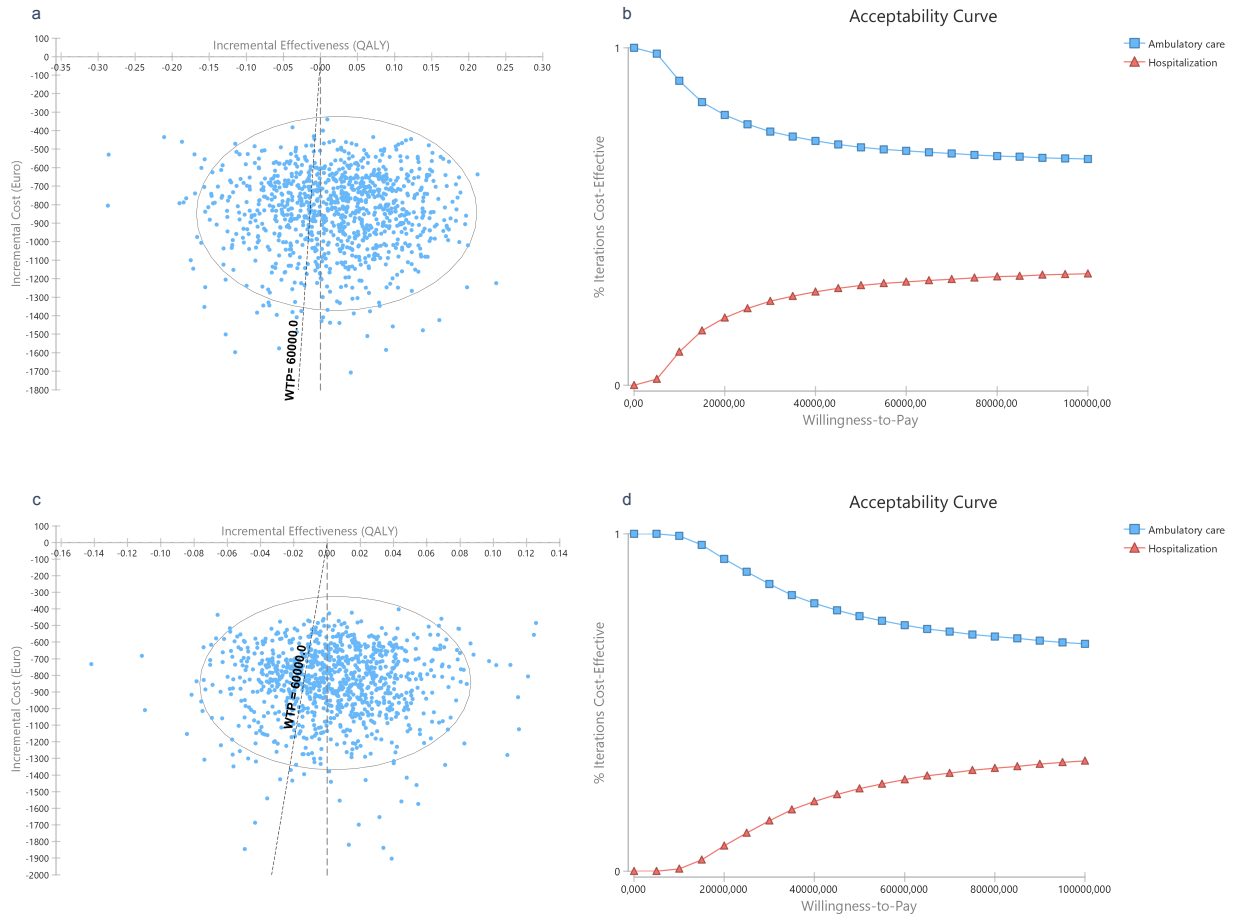


Figure 4. Results of probabilistic sensitivity analysis at 6-month assessment with inpatient costs calculated based in the observed admission time. a and b with QALYs computed based in area under curve; c and d based in change from baseline.

Right (a and c): Incremental cost-effectiveness ratio scatterplots and 95% confidence interval ellipse

- Each point represents a simulation, with indication of the mean incremental cost and effectiveness of outpatient compared to inpatient MD; the oblique dashed line represents the willingness-to-pay (WTP) threshold;
- Simulations represented to the left of the oblique dashed line (WTP line) represent those in which outpatient surgery was found to be less costly and less effective than inpatient surgery, with inpatient being the treatment of choice;

- Simulations to the right of the oblique dashed line (WTP line) and of the vertical line represent those in which outpatient surgery was found to be less costly and more effective than inpatient surgery with outpatient surgery being the treatment of choice.
- Between dashed lines are those in which outpatient was found to be less costly and less effective, but the effectiveness losses do not compensate the cost savings, and outpatient is the treatment of choice
- In this model, and according to €60000 WTP outpatient is better than inpatient in 68.9% (AUC) or 71.8% (CfB) of simulations.

Left (b and d): Cost-effectiveness acceptability curve of outpatient versus inpatient. The Y-axis represents the probability of each comparator being cost-effective at a given willingness-to-pay (WTP) threshold, and ranges between 0% and 100%. Outpatient MD has been identified as cost effective throughout all different WTP thresholds depicted

When inpatient costs for one admission day are considered, instead of costs for the observed admission period, 3-month ICER is of €207541.7/QALY gained (AUC approach) or €80338.7/QALY gained (CfB approach), remaining cost-effective at the defined WTP threshold of €60000/QALY gained. Outpatient MD is the best strategy in 58.4% (AUC approach) and 54.4% (CfB approach) simulations (Figure 5 and Table 5). At 6-month assessment, inpatient MD is still dominated, with MD being the best strategy in 66.3% (AUC) and 66.4% (CfB) simulations (Figure 6 and Table 5).

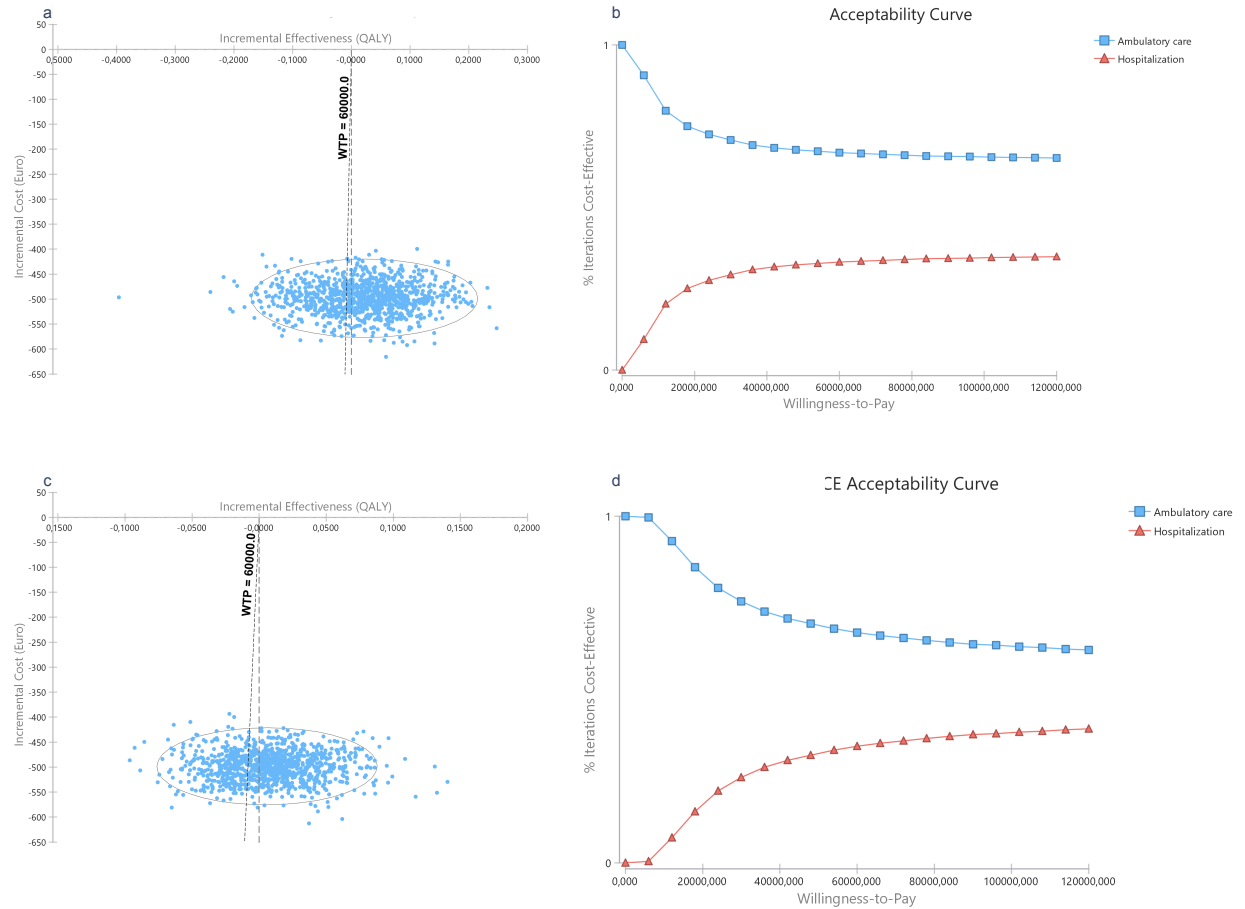


Figure 5. Results of probabilistic sensitivity analysis at 3-month assessment with inpatient costs calculated for one day of admission time. a and b with QALYs computed based in area under curve; c and d based in change from baseline.

Right (a and c): Incremental cost-effectiveness ratio scatterplots and 95% confidence interval ellipse

- Each point represents a simulation, with indication of the mean incremental cost and effectiveness of outpatient compared to inpatient MD; the oblique dashed line represents the willingness-to-pay (WTP) threshold;
- Simulations represented to the left of the oblique dashed line (WTP line) represent those in which outpatient surgery was found to be less costly and less effective than inpatient surgery, with inpatient being the treatment of choice;

- Simulations to the right of the oblique dashed line (WTP line) and of the vertical line represent those in which outpatient surgery was found to be less costly and more effective than inpatient surgery with outpatient surgery being the treatment of choice.
- Between dashed lines are those in which outpatient was found to be less costly and less effective, but the effectiveness losses do not compensate the cost savings, and outpatient is the treatment of choice
- In this model, and according to €60000 WTP outpatient is better than inpatient in 58.4% (AUC) or 54.4% (CfB) of simulations.

Left (b and d): Cost-effectiveness acceptability curve of outpatient versus inpatient. The Y-axis represents the probability of each comparator being cost-effective at a given willingness-to-pay (WTP) threshold, and ranges between 0% and 100%. Outpatient MD has been identified as cost effective at the €60000 WTP threshold.

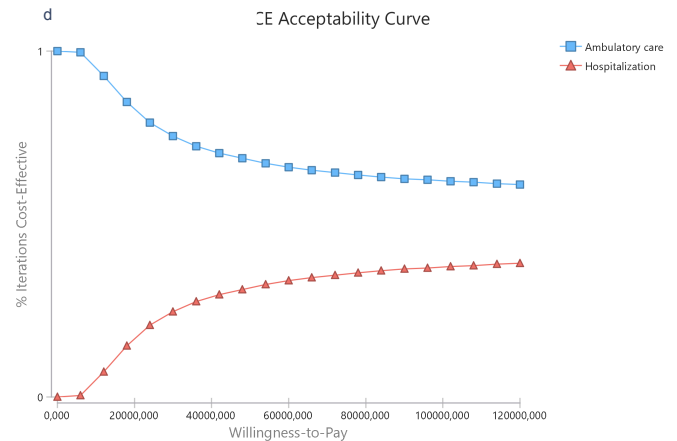
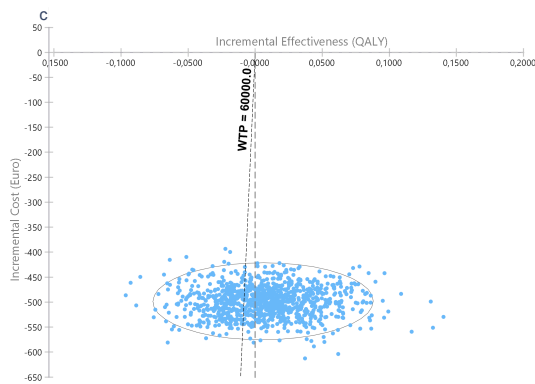
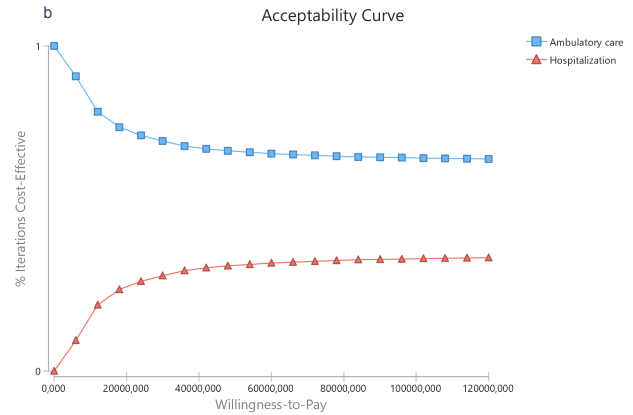
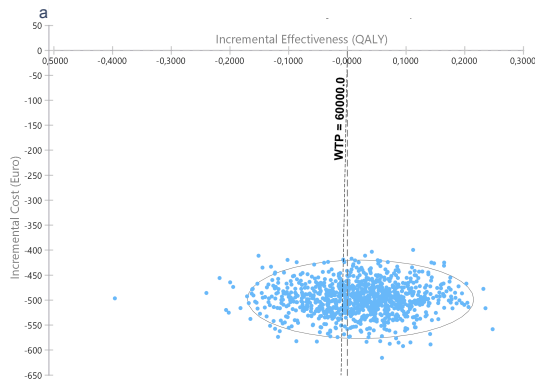


Figure 6. Results of probabilistic sensitivity analysis at 6-month assessment with inpatient costs calculated for one day of admission time. a and b with QALYs computed based in area under curve; c and d based in change from baseline.

Right (a and c): Incremental cost-effectiveness ratio scatterplots and 95% confidence interval ellipse

- Each point represents a simulation, with indication of the mean incremental cost and effectiveness of outpatient compared to inpatient MD; the oblique dashed line represents the willingness-to-pay (WTP) threshold;
- Simulations represented to the left of the oblique dashed line (WTP line) represent those in which outpatient surgery was found to be less costly and less effective than inpatient surgery, with inpatient being the treatment of choice;
- Simulations to the right of the oblique dashed line (WTP line) and of the vertical line represent those in which outpatient surgery was found to be less costly and more effective than inpatient surgery with outpatient surgery being the treatment of choice.
- Between dashed lines are those in which outpatient was found to be less costly and less effective, but the effectiveness losses do not compensate the cost savings, and outpatient is the treatment of choice
- In this model, and according to €60000 WTP outpatient is better than inpatient in 66.3% (AUC) or 66.4% (CfB) of simulations.

Left (b and d): Cost-effectiveness acceptability curve of outpatient versus inpatient. The Y-axis represents the probability of each comparator being cost-effective at a given willingness-to-pay (WTP) threshold, and ranges between 0% and 100%. Outpatient MD has been identified as cost effective throughout all different WTP thresholds depicted

Discussion

Low back pain and related affections carry a cost of more than 100 billion dollars each year, only in United States, with disc disorders playing a substantial role in this amount [18]. To the best of our knowledge, our study was the first to show that outpatient lumbar MD is cost-effective. We observed that ambulatory MD was associated with a significant reduction of costs, with no relevant utility loss, resulting in ICER expressively higher than the defined WTP threshold. These results were consistently found in all analysis performed, including with different QALY estimation methods, considered time periods and WTP.

At 3-month evaluation, QALYs gained were slightly higher in inpatient setting, but such gains in effectiveness were not sufficient to compensate for the additional costs, with ICER of €135753-345755/QALY gained. However, at the 6-month assessment, even QALYs gained were observed to be higher in the outpatient setting, with the inpatient setting being a dominated strategy. These differences in QALYs gained, however, might not be relevant, and may rather result from an expected variation due to sample variability and to the disparity of sources chosen for clinical data analysis. In fact, similar to previous studies, we showed significant gains in VAS and ODI in the 3- and 6- month assessments following lumbar discectomy [5, 13], and those gains are not expected to differ between inpatient or outpatient procedures.

Although no previous study displayed results on MD transition to the outpatient setting, there are some examples on other surgical procedures, such as knee arthroplasty [19]. For the latter procedure, although outpatient surgery was proven cost-effective for the defined WTP, the inpatient procedure was found to be more effective [19]. On the contrary, our study showed a similar effectiveness for outpatient and inpatient lumbar MD, with a significant cost

reduction associated with the former. This cost reduction agrees with the results of a former review that estimated average cost savings of 17.6% to 57.6% for outpatient orthopedic procedures when compared to similar procedures in hospitalized patients [20]. In fact, all analyzed costs were lower in outpatient setting, probably related with higher productivity rates and lower wasteful spending, leading to the decrease of individual costs depicted in Table 2.

This study has some limitations. We only considered direct medical costs, so that costs related with transportation, patient time, productivity and family assistance were not accounted. However, we expect no relevant differences in those indirect costs between compared groups, since all patients are walking and able to perform daily activities at discharge and acute complications are rare, what is reinforced by an absence of 30-day readmissions. Also, there is a limitation related with the observed admission time. Although it is expected that an inpatient submitted to an uncomplicated MD will only need one day of admission, many factors not directly related with the clinical condition and care may influence the length of stay [21]. To overcome these interferences, we computed the overall analysis for a hypothetical admission of one day, with outpatient surgery remaining cost-effective at both 3 and 6-month assessments. Another limitation is related with the fact that clinical data for inpatients were gathered from literature, based on a recent systematic review and meta-analysis [13]. Although we expect a small deviation from what would have happened in our sample, utilities were calculated from aggregated data from multiple studies that used similar samples and techniques. Nevertheless, the simulations performed under the probabilistic sensitivity analysis accounted for parameter uncertainty, as they considered the variability in the different variables included in the model, including the heterogeneity of

inpatient utilities (Table 4). Therefore, it would not be expected that variations of this variable would be so drastic in order to draw our results to favoring inpatient surgery.

Another limitation concerns the criteria used in assortment of patients for outpatient treatment – overall, patients indicated for outpatient treatment tend to be younger and healthier, an already recognized selection bias in studies with patients undergoing outpatient spine surgery [11]. To account for this issue, in the present study, we selected a set of matched patients submitted to inpatient treatment following the same criteria applied for outpatient eligibility (and making sure they were operated by the same surgeon). Nevertheless, one should bear in mind that day surgery is reserved for a group of selected patients, with no significant comorbidities [20], and that some patients will continue to require lumbar MD in inpatient settings. Further limitations include the absence of data for a period longer than 6 months, and the fact that costs data were retrieved from a single country. Although the absolute costs are expected to be different in other settings, a similar magnitude of savings is predictable, as already demonstrated in the literature [20].

Conclusion

In conclusion, we showed outpatient lumbar microdiscectomy to be cost-effective at the 3- and 6-months post-surgery, with a reduction of more than 50% costs when compared to the hospitalization setting, and similar utility gains. This is the first evidence of this clear benefit and should inform future health policies and clinical practice, advising for a global transition to ambulatory MD in patients eligible for this treatment modality.

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Additional File

Online Resource 1

	Assessments			p-value		p-value (variation vs MCID)	
	Pre-operative (N=20)	3-mth (N=20)	6-mth (N=20)	Pre to 3-mth	3 to 6-mth	Pre-3 mth	3-6 mth
ODI (%)	53.1±18.87	26.4±17.84	12.2±12.16	<0.001	<0.001	0.002	<0.001
Overall	7.75±2.22	3.40±2.06	1.35±1.14	<0.001	<0.001	<0.001	<0.001
VAS							
LP VAS	7.95±1.64	3.05±1.76	1.15±1.10	<0.001	<0.001	<0.001	<0.001
BP VAS	7.30±2.92	3.30±2.13	1.35±1.23	<0.001	<0.001	<0.001	<0.001

Outpatient Clinical Assessments. An improvement of leg pain (LP) VAS of 2 in 10 and a 15-point improvement in ODI were considered our minimal clinical important differences (MCID), as recommended by Federal Drug Administration.

mth: Months; N: number; ODI: Oswestry Disability Index; VAS: Visual Analog Scale; LP: Leg Pain; BP: Back Pain. Values are presented as mean±standard deviations.

CHAPTER V

Overall Discussion and Conclusions

OVERALL DISCUSSION

HEALTHCARE IMPACT AND FUTURE RESEARCH

Spine disorders and related disability are highly prevalent and pose a significant burden, with rising costs that do not necessarily correlate with improved outcomes⁵³. Complexity is added by the several treatment strategies available, turning spine care into an important target for cost reduction strategies⁵³.

This thesis goal is to contribute to the identification of strategies and interventions that may be eliminated or modified and simultaneously result in increased effectiveness and decreased costs in spine care. For this purpose, two models were specifically assessed, in which changes in care delivery for spine patients translate into an important impact in costs and effectiveness: one potentially dispensable practice – the use of orthosis in acute TL fractures of adults – and one change of paradigm – outpatient treatment of selected patients with lumbar disc herniation.

The first model concerns the conservative treatment of TL fractures with orthosis. Orthoses are used almost ubiquitously around the world in the conservative treatment of adult patients with acute TL fractures^{29,32}. However, different studies failed to demonstrate their benefit in the restoration of spinal alignment, prevention of vertebral collapse, reduction of pain, or improvement of disability^{34,35}. In fact, literature on the clinical and radiological impact of braces in patients with acute TL fractures had never been systematically reviewed and their use in clinical practice is still mostly based on the opinion of each physician. In this thesis, we conducted a systematic review and meta-analysis that found no clinical or radiological

differences between patients treated with or without an orthosis. To understand the role of bracing in adult patients with acute TL fractures, we selected randomized controlled trials, performing a comparison between orthosis and no orthosis, that included only patients with acute traumatic TL fractures submitted to primary conservative treatment. Articles including patients with non-acute fractures and with groups with differences other than orthosis use were excluded. Five studies matched our criteria, and despite their methodological and quality differences (with some not even reporting adequate numerical values), we were able to perform a meta-analysis for four main outcome measures.

In all included primary studies, outcomes were similar between patients treated with or without orthotic devices. Accordingly, no significant meta-analytical differences were found in pain (with follow-ups that ranged from 2 weeks to 10 years), quality-of-life assessments, and radiologic outcomes (kyphotic progression and loss of anterior height). On the other hand, the performed meta-analysis pointed to a significant difference in the length of hospital stay, higher in patients treated with an orthosis, on average 3.5 days.

Therefore, in this systematic review, we concluded that the use of orthosis seems to offer no advantages in clinical and radiological outcomes, but rather associates with increased length of stay. With this study, new evidence supports the decision of spine surgeons around the world of treating adult patients with acute TL fractures deemed for conservative approach with no external immobilization devices.

Following this first study, another question was raised, on what would be the impact if orthosis use was diminished or eliminated from daily practice. Therefore, we performed a survey study, targeting spine specialists in Europe and North America, and inquiring on the use of orthosis in their daily practice and on the direct costs of the device. One hundred and thirty specialists answered our questionnaire. Most specialists indicated the use of orthosis in

adult patients with acute TL fractures in their daily practice, but only a minority use it in all patients. The overall average cost of an orthosis was reported to be €546, with a wide variation between different regions. While these results only concern the direct costs of the device, more than one-third of the specialists stated that, in their institution, brace delivery requires admission of the patient. This implies there are other hospital costs related to brace use that are not negligible, so that the overall cost associated with the use of these devices is expected to be higher than the one found in this study.

The aggregated results of these two studies – a systematic review showing no advantage from orthosis use in patients with acute TL fractures, and a survey study pointing to an average associated cost with each device of more than €500 – highlight the need for a conscious and parsimonious use of these devices since they have no proven benefit and represent a significant burden for the healthcare system^{34,35}.

Future works on orthosis use in acute TL fractures are needed to understand if any difference in outcomes can be found among different types of fractures³⁴. Also, many questioned surgeons still base their decision on orthosis use in individual opinions and patients' feedback, most of those still lacking an adequate scientific background.

We present a systematic review showing no benefit from the use of these devices, reinforced by the already orthosis-free practice of many spine experts. Therefore, we believe that future consensus and subsequent guidelines should reflect this ongoing changing of paradigm, supporting specialists' decisions and avoiding fears related to possible litigations³⁵.

While orthosis used in patients with acute TL fractures are usually prescribed in emergency departments and are part of a conservative-treatment strategy, there is also space for improvement in elective procedures and surgical interventions. This was the focus of our

second model, which concerned the elective surgical treatment of patients with lumbar disc herniation. Although only a small percentage of patients with lumbar disc herniation need surgical treatment, this condition is highly prevalent, with discectomy being the most commonly performed spine procedure⁵. As a significant burden is associated with it, in this second model we tried to understand the cost-utility of an outpatient transition of MD. To do so, we performed a prospective assessment of patients referred for outpatient MD and calculated the costs of the procedure. A comparison group of demographically matched individuals, undergoing an inpatient MD, was retrospectively selected.

We found MD in outpatient basis to be cost-effective at 3- and 6-months, with average savings of €847, when compared with the inpatient procedure. These savings represented around 55% of inpatient costs, with the outpatient procedure being the better option in 65% to 73% of simulations. The ICER associated with the inpatient MD at 3 months was much higher than the willingness to pay threshold expected for Portugal, according to the WHO criteria⁶. At the 6-month assessment outpatient procedures associated both with less cost and higher utilities, with inpatient MD being the dominated strategy. Since inpatients were admitted for a mean period of 2.5 days we tried to understand what happened if their admission time was reduced to one day. Even in that scenario, the outpatient procedure remained cost-effective.

Pendharkar et al, on a review about outpatient spine surgery, had already proposed that lumbar decompression has strong evidence for safety in the outpatient setting, with favorable clinical outcomes³⁹. The authors emphasize the need for adequate patient selection and close follow-up in order to maximize cost reduction³⁹. In our study, patients submitted to outpatient MD followed a pre-defined protocol for ambulatory referral.

Outpatient transition implicates the development of protocols, standardized patient selection, and delivery of postoperative care³⁹. In the particular scenario of MD, the adequate patient selection will maximize the benefits and savings from ambulatory MD. Future studies should focus on identifying patients' characteristics that associate with poorer outcomes in outpatient treatment for lumbar disc hernia. Since outpatient MD should be the norm and not the exception for those suitable, it is important to understand what are the variables that turn a patient more prone to benefit from a hospital stay.

Previous reports on the cost-effectiveness of lumbar disc herniation treatment only compared discectomy with conservative treatment, and no previous study had ever presented the cost-utility of outpatient MD when compared with the inpatient procedure³⁷.

This thesis focuses on two models of HTA, in which small changes in current practices reflected a significant economic impact, maintaining the best clinical outcomes. These are only two examples in a myriad of spine practices that can be improved into a value-based care delivery. In fact, a 2020 evidence-based clinical guideline on diagnosis and treatment of low back pain released by North America Spine Society (NASS) assessed sixteen questions on cost-utility and found enough literature data to issue recommendations in only six of those questions. From those six, five had insufficient evidence to make a recommendation for or against¹⁷. Even for other orthopedic surgeries, Crawford et al showed that available data on inpatient versus outpatient surgeries is still scarce and has low quality⁵⁸. Nevertheless, these authors identified a representative group of selected orthopedic surgeries that, when performed on an outpatient basis, appear to be cost-effective and safe alternatives to inpatient

procedures⁵⁸. Future new and higher-quality studies addressing economic assessment on other orthopedic and, in particular, spine procedures are needed.

Spine Care – Portuguese Example

Portugal has an universal health coverage through a publicly financed National Health Service (NHS). In 2017, health expenses were around €2029 per capita, corresponding to 9.3% of Portuguese gross domestic product (GDP) and 66.4% of public expenses⁵⁹. No specific data on Portuguese public expenses are available for spine care. However, Azevedo et al found that, from those Portuguese individuals suffering from chronic pain, 42% localize it in the lumbar region⁶⁰, and Gouveia et al estimated that chronic low back pain is associated with an indirect cost of 739.85 million Euros, representing 0.4% of the Portuguese GDP⁶¹.

The two models described in this thesis present approaches to reduce the burden associated with spine diseases and it would be important to understand their impact on Portugal's healthcare system. Although the data needed for this assessment are not directly available for the Portuguese reality, one can extrapolate it from other European countries' published data. Portugal is included in the United Nations region of South Europe. According to the spine specialists from this region, surveyed in the second study of this thesis, it is expected that, if all acute TL fractures conservatively treated were braced, the orthosis cost per 100 fractures would be, on average, €24,113. This expense falls for €5,917 per 100 fractures if only a quarter of treated patients are braced.

No study on the incidence of acute spine fractures is available in the Portuguese population, but Brinke et al described it in the Netherlands, between 1997 and 2012. These authors found a rising incidence of these lesions, from 27/100,000 persons in 2007 to 58/100,000 persons in 2012, with expected increases for the forthcoming years⁶². From those fractures diagnosed each year, some would be surgically treated, but most are probably stable lesions, deemed for conservative treatment²⁹. Considering the cost of an orthosis and the considerable number

of fractures observed each year, a relevant burden associated with the use of these devices in Portugal can be anticipated.

While data on the incidence of TL fractures in Portugal are scarce, discectomies were more widely studied and specific data for the Portuguese population is available. A recent study on the state of spine surgeries in Portugal NHS identified that the number of yearly performed discectomies (other than cervical) in mainland ranged from 1945 in 2002 to 1650 in 2017⁶³. Considering a mainland Portuguese population of 9.8 million, this would represent an overall rate of 16.8 discectomies per 100,000 inhabitants^{63,64}. The discectomy numbers of this study are lower than those reported for other European countries, as Fjeld et al, in a study in Norway between 1999 and 2013, found an average stable number of 50 lumbar disc operations per 100,000 inhabitants⁶⁵. Nevertheless, since there is only available data for the Portuguese NHS (with no data on procedures undertaken in the private and social sectors), the real Portuguese results are expectedly higher, as is the burden associated with the treatment of lumbar disc herniation.

Not all patients with lumbar disc herniation can be treated on an outpatient basis. In the US, the percentage of procedures performed on an outpatient basis is as high as 40%, with some studies with pre-defined protocols showing even higher numbers of ambulatory-treated patients^{5,66}. In Portugal, a rise in outpatient procedures was observed after a governmental initiative in 2008 to increase efficiency, with financial incentives for hospitals and patients⁹. With this trend for outpatient transition, this thesis third study found an expected reduction in MD costs of an average of 55% of inpatient value, translated into savings of around €850 per procedure. Bearing in mind the number of annually performed discectomies in the Portuguese NHS, and the fact that a great amount of those patients can be treated on an

outpatient basis, the expected reduction from this transition would probably represent even greater savings for the healthcare system.

Considering both the reduction or, *in extremis*, the quasi-elimination of orthosis use in patients with acute TL fractures conservatively treated, and the transition of selected patients proposed for MD for outpatient treatment in Portuguese hospitals with spine dedicated units, the two models proposed in this thesis would eliminate, respectively, expenditures of around €500 and €850 per patient. The potential effect that these changes of current spine policies would represent on the burden of spine diseases for the NHS are more than enough for Portuguese spine surgeons to adopt a value-based care approach in the management of their patients.

Note: In the publication of the second study (Linhares D et al, Spine, 2020) costs are presented in dollars. Herein, they are presented in Euro for purposes of currency uniformization in this thesis. Since inflation was negligible, conversion was based on the average value from the first trimester of 2020.

STRENGTHS AND LIMITATIONS

The models described in this thesis show two of many spine care areas where lack of adequate assessment may result in unnecessary expenditure for the healthcare system. Presenting HTA in different spine fields, it focuses on two different domains and shows how small changes can result in substantial economic impacts without compromising, or even improving, the quality of the care delivered. The studies conducted were the first of their kind and their conclusions may support future policy modifications.

Nevertheless, this thesis has some limitations. No study was performed on the implementation of these proposed changes, and subsequent barriers can appear during this process, contradicting the expected advantages.

Additionally, the first model was based mainly on results from developed countries. We have few information on orthosis use in other world areas, and the real impact in spine care burden from the elimination of these devices may change with different bracing rates.

The second model presents direct results from a Portugal NHS hospital and absolute values are expected to fluctuate in different settings or locations. Nevertheless, it is expected that the magnitude of savings remains since it goes along with other literature reports from outpatient transition. Also, clinical data from a prospective assessment was combined with literature reports, introducing a source of heterogeneity. However, we performed both one-way deterministic and probabilistic sensitivity analyses to account for parameter uncertainty. No costs of the transition itself were calculated, and it was assumed that outpatient care was already a reality. If a particular caregiver needs to acquire new appliances, personal or surgical tools to fuel an outpatient transition the savings expected from this might be inexistent or diluted in the first years of practice.

CONCLUSIONS

In conclusion, this thesis presents two models of health technology assessment in which changes in established strategies of spine care reflect substantial cost reductions with no negative (or even positive) impacts on clinical outcomes.

The first model concludes that orthoses use in the treatment of acute thoracolumbar fractures in adult patients seems to bring no clinical or radiological benefits and are associated with substantial costs. In fact, many surgeons around the world already recognized that its use is most often not necessary and more international support is needed to implement a change of practice.

The second model shows that the microdiscectomy outpatient procedure is cost-effective. The observed substantial cost reduction with no negative clinical effects is highlighted, as is the support for the dissemination of this transition, relying on adequate patient selection.

These two models illustrate how outcomes and economic assessment can improve efficiency in spine care practice. The approaches presented in this thesis could and should be extended to other domains, emphasizing the need for value-based spine care, in order to increase its sustainability and inform healthcare improvement.

CHAPTER VI

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