Adv Ther
https://doi.org/10.1007/s12325-023-02686-9

ORIGINAL RESEARCH

Economic Evaluation of a Bioinductive Implant for the Repair of Rotator Cuff Tears Compared with Standard Surgery in Italy

Carla Rognoni · Leo M. Nherera · Raffaele Garofalo · Enrico Guerra · Umile Giuseppe Longo · Ettore Taverna · Rosanna Tarricone

Received: July 28, 2023 / Accepted: September 8, 2023
© The Author(s) 2023

ABSTRACT

Introduction: Rotator cuff tear (RCT) is a painful, progressive condition resulting from damage to the rotator cuff tendons and is the leading cause of shoulder-related disability. Surgical repair of rotator cuff is an established standard of care (SOC); however, failure of the procedure can occur. In this context, the use of collagen-based bioinductive implant REGENETEN showed long-term improvements in clinical scores. The aim of the study was to assess the cost-effectiveness of REGENETEN combined with SOC (SOC + REGENETEN) compared to SOC alone from both National Healthcare Service (NHS) and societal perspectives in Italy.

Methods: A decision analytic model was developed to estimate the number of tears healed and costs for the two considered treatment strategies over 1 year. Clinical data were retrieved from the literature, and the clinical pathways for the management of patients with RCTs were retrieved from four key opinion leaders in Italy.

Results: Over a 1-year time horizon, healed lesions were 90.70% and 72.90% for surgical repair of RCTs with and without REGENETEN, respectively. Considering the NHS perspective, mean costs per patient were €7828 and €4650

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12325-023-02686-9.

C. Rognoni (✉) · R. Tarricone
Centre for Research on Health and Social Care Management (CERGAS), SDA Bocconi School of Management, Bocconi University, Via Sarfatti 10, 20136 Milan, Italy
e-mail: carla.rognoni@unibocconi.it

L. M. Nherera
Smith & Nephew, Fort Worth, TX, USA

R. Garofalo
Ospedale Generale Regionale 'F. Miulli', Bari, Italy

E. Guerra
IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy

U. G. Longo
Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy

U. G. Longo
Università Campus Bio-Medico di Roma, Rome, Italy

E. Taverna
IRCCS Ospedale Galeazzi – Sant'Ambrogio, Milan, Italy

R. Tarricone
Department of Social and Political Science, Bocconi University, Milan, Italy

Published online: 28 September 2023

for the two strategies, respectively, leading to an incremental cost-effectiveness ratio (ICER) of €17,857 per healed tear. From the societal perspective, the mean costs per patient were €12,659 for SOC and €11,784 for REGENETEN, thus showing savings of €4918 per healed tear when the bioinductive implant is used. The sensitivity analyses confirmed the robustness of the model results.

Conclusion: In the context of paucity of cost-effectiveness studies, our findings provide additional evidence for clinicians and payers regarding the value of a new treatment option that supports a tailored approach for the management of patients with RCTs.

PLAIN LANGUAGE SUMMARY

The rotator cuff refers to a group of four muscles, with tendons connected to the upper arm bone, which act together to allow lifting and rotating the shoulder. A tear of the rotator cuff can affect either a single tendon or multiple tendons. Typical first-line treatment includes conservative therapies, which aim to alleviate pain and reduce functional impairment, but are often ineffective. Persisting disease is usually managed through conventional surgical repair. Recently, REGENETEN, a collagen-based bioinductive implant derived from purified bovine Achilles tendon, positioned over the site of the damaged rotator cuff, achieved successful rotator cuff tendon repair with an increase in healed tears of 17.80% at 1 year compared to conventional surgery. Considering the National Healthcare Service perspective in Italy, the cost needed to achieve one additional healed tear using REGENETEN compared to conventional surgery is €17,857. From the societal perspective, which includes patients' productivity losses from hospital admission to return to work, the use of REGENETEN may be cost-saving compared to conventional surgery. The findings of our study provide evidence for clinicians and payers to support the value of a new treatment option for patients with rotator cuff lesions.

Keywords: Cost-effectiveness; Bioinductive implant; Standard surgery; Rotator cuff disease

Key Summary Points

Rotator cuff tears, resulting from damage to the rotator cuff tendons, are a leading cause of shoulder-related disability. These lesions are generally managed through conventional surgical repair (standard of care, SOC).

Surgical intervention using REGENETEN, a collagen-based bioinductive implant, showed an increase in healed tears of 17.80% at 1 year compared to SOC.

Considering the National Healthcare Service (NHS) perspective in Italy, mean costs per patient over 1 year were €7828 and €4650 for REGENETEN and SOC, respectively. The incremental cost-effectiveness ratio was €17,857 per healed tear.

From the societal perspective, the analyses showed savings of €4918 per healed tear when the bioinductive implant is used.

These findings provide evidence for clinicians and payers to support the value of a new treatment option for patients with rotator cuff lesions.

INTRODUCTION

Rotator cuff disease is a painful, progressive condition resulting from damage to the rotator cuff tendons and is the leading cause of shoulder-related disability [1]. Rotator cuff tears (RCTs) are unlikely to spontaneously heal, and disease progression is typical. The socioeconomic burden of rotator cuff surgery is growing and heavily affecting the working population, with 390,001 RC repairs performed in Italy from 2001 to 2014 [2].

Typical first-line treatment includes conservative therapies, which aim to alleviate pain and reduce functional impairment, but are often ineffective [3]. Persisting disease is often treated using surgical interventions. Surgical repair of rotator cuff is an established standard of care (SOC); however, failure of the procedure is possible [4] with reported incidence up to 30% [5].

The REGENETEN implant is a collagen-based bioinductive implant that can be used to treat all stages of rotator cuff disease progression. The implant uses highly porous, purified collagen derived from bovine Achilles tendon and is gradually integrated over a 6-month period, ensuring long-term biocompatibility and an excellent safety profile (so far, only two cases of subacromial-subdeltoid bursitis with rice bodies have been reported [6]). The clinical value of the REGENETEN implant for the treatment of both partial- and full-thickness tears is supported by observational trials and real-world evidence. A prospective study [7] of 30 patients with partial or complete rotator cuff tears treated with REGENETEN showed, 6 months after surgery, complete integration of the implant and absence of inflammatory or foreign body reactions. Bokor and colleagues [8] examined 11 patients and showed a statistically significant improvement in clinical scores after 5 years from the intervention with REGENETEN compared to preoperative values, with most repaired tendons intact at 5 years. Another study [9] collected outcomes data prospectively for 1 year on 173 patients treated with REGENETEN in partial- (52%) and full-thickness (48%) cuff tears; the study showed statistically significant improvements in standardized outcomes/scales (visual analogue scale, single-assessment numeric evaluation, Veterans RAND 12-Item, American Shoulder and Elbow Surgeons and Western Ontario Rotator Cuff) in both groups. Thon and colleagues [10] assessed the safety, outcomes and healing rates in large and massive rotator cuff repairs using a bioinductive collagen scaffold patch in a single-arm study on 23 patients. The authors reported 96% healing rate and no adverse events attributed to the implant.

Compared with conventional surgery, the REGENETEN implant may reduce overall direct and indirect costs associated with treatment of rotator cuff tears by enabling faster patient recovery and durable repair. Direct treatment costs compared with conventional surgery may be reduced as a result of reduced requirements for pain relief and physical therapy [9, 11, 12]. Rapid postoperative patient recovery and earlier return to work with the REGENETEN implant versus conventional surgery may reduce workers' productivity losses [11]. Low postoperative re-tear rates with the REGENETEN implant may translate into low requirements for revision surgery and reduced long-term costs for healthcare providers [8, 10].

Currently, only one study [13] assessed the cost-effectiveness of REGENETEN compared to standard of care; the study estimated an incremental cost-effectiveness ratio (ICER) of $13,061 per healed rotator cuff tear with REGENETEN used during standard surgery compared to conventional surgery alone from the payor's perspective in the US, and considering patients' productivity losses, REGENETEN was found to be cost-saving.

At this time, in Italy, the cost of the bioinductive implant is not covered by the current Diagnosis-Related Group (DRG) reimbursement but is sustained by the clinical centers themselves. Therefore, the generation of further evidence is needed to show Italian decision-makers the value of the clinical and economic benefits associated with the use of REGENETEN in clinical practice [14, 15].

METHODS

The aim of the study was to assess the cost-effectiveness of REGENETEN combined with conventional surgery (SOC + REGENETEN) compared to conventional surgery alone (SOC) from both National Healthcare Service (NHS) and societal perspectives in Italy.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Table 1 Clinical inputs used in the model

Item	Baseline value	Lower confidence interval	Upper confidence interval	References
SOC re-tear rates				
Medium	0.190	0.152	0.227	[18, 19]
Large	0.287	0.23	0.345	
Massive	0.501	0.401	0.601	
Combined	0.271	0.217	0.325	
SOC + REGENETEN re-tear rates				
Medium	0.072	0.057	0.086	[8, 20, 21]
Large	0.119	0.095	0.142	[10, 20, 21]
Massive	0.093	0.074	0.112	
Combined	0.0928	0.074	0.111	
Events following re-tear/failure				
Revision surgery	25.20%	20.20%	30.30%	[17]
Reverse total shoulder arthroplasty	3.90%	3.10%	4.70%	
Conservative management	70.90%	59.80%	89.70%	

SOC standard of care

The Model

A cost-effectiveness analysis (CEA) has been performed to compare surgical repair of RCTs with or without the use of REGENETEN from both NHS and societal perspectives in Italy. The analysis followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) [16]. The CHEERS checklist is reported in the Supplementary Material.

The decision analytic model developed by McIntyre and colleagues [13] was adapted for the purpose of the present study. The model, created with Microsoft Excel, consisting of a decision tree representing the possible patients' clinical pathways, was developed to estimate the number of tears healed and costs associated with SOC + REGENETEN and SOC alone in an adult population with full-thickness RCTs. If a lesion does not heal, revision, reverse total shoulder arthroplasty and conservative management options are allowed.

The clinical inputs considered in the model were healing failure (re-tear) rates for the different lesion sizes (medium, large and massive) and frequencies of subsequent events (revision, reverse total shoulder arthroplasty and conservative management) for the management of healing failures. A literature search was performed, starting from the references reported in the study by McIntyre and colleagues [13], to retrieve re-tear rates at 1 year for SOC and SOC + REGENETEN. The study by Parikh and colleagues [17] was the source of data for the management of healing failures. Table 1 reports the clinical inputs used in the model (a more detailed description of the clinical inputs is reported in [13]). The base case model considers a combination of the different tear sizes (medium, large and massive).

A time horizon of 1 year was applied for baseline analysis considering a population with mean age equal to 58 years as reported in [13], and no discount rate was applied to model

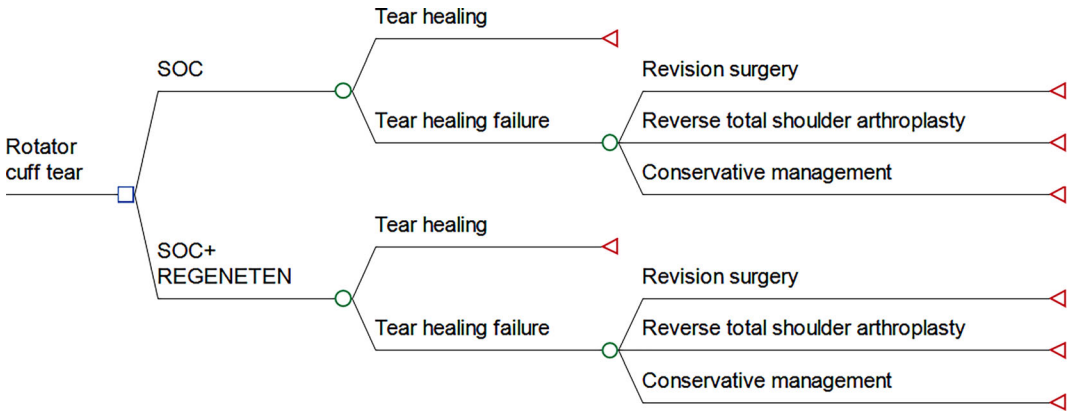

Fig. 1 CEA model representation. The figure is reproduced from "Arthroscopy, Sports Medicine, and Rehabilitation, 5(2), McIntyre LF, Nherera LM, Schlegel TF, Resorbable Bioinductive Collagen Implant Is Cost Effective in the Treatment of Rotator Cuff Tears, e367–e374", Copyright Elsevier (2023). *CEA* cost-effectiveness analysis, *SOC* standard of care

outcomes because of the short period analyzed. Figure 1 shows the structure of the decision model.

Data Collection

The clinical pathways for the management of patients with rotator cuff full-thickness lesions were retrieved from four key opinion leaders (RG, EG, UGL, ET) in Italy belonging to clinical centers, geographically distributed in Italy, performing a high volume of procedures annually (Ospedale Generale Regionale 'F. Miulli'—Bari, IRCCS Istituto Ortopedico Rizzoli—Bologna, Fondazione Policlinico Universitario Campus Bio-Medico—Rome, IRCCS Ospedale Galeazzi—Sant'Ambrogio—Milan). A Delphi approach [22] was applied since experts were independently interviewed through online meetings lasting 30–60 min in February–March 2023. Clinicians were asked to refer to the typical cohort of patients with RCTs and to report data on healthcare resource utilization based on their clinical experience. Data collected were related to type and frequency of examinations and visits performed before primary surgical intervention and before subsequent options for the management for non-healing lesions, frequency and type of visits, examinations, drugs and physiotherapy sessions related to conservative management, healthcare services performed in the follow-up and reimbursement modalities for the different options. Experts were also asked to report the DRGs applied for the different types of surgical interventions (obtained from the hospitals administrative offices). For each item, a weighted mean was calculated on the basis of the number of responders. Mean values of healthcare resource use were subsequently shared with the clinicians through email in April 2023 to obtain a final validation. All the clinicians confirmed the validity of the data presented.

Healthcare Resource Utilization and Costs

When healthcare services were paid for by the NHS, we considered national DRG reimbursement rates for hospitalizations and official tariffs for outpatient healthcare services. As the cost of REGENETEN is in general borne by the hospitals, which, however, obtain funds from Regional Health Authorities, also this cost has been considered in the analysis.

Table 2 reports the summary of healthcare resources used according to the different types of treatment options as obtained from the KOL responses.

From the investigation of DRGs, basically three DRGs are applied for reimbursement purposes. For the primary intervention both DRGs 223 (MAJOR SHOULDER/ELBOW PROC, OR

Table 2 Healthcare resource consumption

Items	Mean value per patient
Visits/examinations pre-surgery	
Primary intervention/revision	
Specialist visit	1.00
Radiography of the shoulder	0.50
Magnetic resonance imaging without contrast	0.75
Magnetic resonance imaging with contrast	0.25
Reverse total shoulder arthroplasty	
Visit	1.00
Magnetic resonance imaging without contrast	0.50
Radiography of the shoulder	0.50
Bone computed tomography	1.00
Conservative management (1 year)	
Specialist visit	1.67
Radiography of the shoulder	0.33
Magnetic resonance imaging without contrast	0.33
Physiotherapy (no. sessions)	19.00
Hydrokinesitherapy (no. sessions)	24.00
Laser/tecar (no. sessions)	20.00
Visits/examinations post-surgery (in the same year)	
Visit	2.00
Radiography of the shoulder	0.34
Magnetic resonance imaging with contrast	0.13

Table 3 Unit costs used in the model

Items	Costs (€)	References
Specialist visit	20.66	Code 89.7
Radiography of the shoulder	17.82	Code 88.21
Magnetic resonance imaging without contrast	133.28	Code 88.92.8
Magnetic resonance imaging with contrast	204.15	Code 88.94.2
Bone computed tomography	81.81	Code 88.38.3
Physiotherapy (1 session)	8.83	Code 93.16
Hydrokinesitherapy (1 session)	8.83	Code 93.16
Laser/tecar (1 session)	3.10	Code 99.99.1
REGENETEN implant (mean value)	3484	Data provided by the producer[a]
Primary intervention/ revision	3041	DRG 223, National tariff
	4391	DRG 224, National tariff
Reverse total shoulder arthroplasty	8565	DRG 491, National tariff

DRG Diagnosis-Related Group
[a]Includes VAT 4% (implantable device)

OTHER UPPER EXTREMITY PROC W CC) and 224 (SHOULDER, ELBOW OR FOREARM PROC, EXC MAJOR JOINT PROC, W/O CC) are used in clinical practice (50% each), without differentiating the use of REGENETEN. For the revision, the DRG of the primary intervention is applied, while for the reverse total shoulder arthroplasty the DRG applied in all clinical centers is 491 (MAJOR JOINT & LIMB REATTACHMENT PROCEDURES OF UPPER EXTREMITY). For arthroplasty, the intervention is intended to be performed with the implant of a standard shoulder prosthesis, without the use of REGENETEN or other biological implants; therefore, the cost is assumed covered by the DRG reimbursement rate for this type of intervention (DRG 491). Table 3 reports the summary of costs used in the model (€, 2023).

Regarding post-surgery physiotherapy sessions, we referred to the data reported in the

literature of 25 sessions, which were considered for both REGENETEN and SOC [20, 21, 23].

The analysis from the societal perspective included patients' productivity losses, which were estimated based on the weeks missed for the return to work after surgery. These were 14 for SOC [11, 24] and 6.91 for REGENETEN [20]. Working time lost was valued through the mean gross salary in Italy (annual value of €29,748€ and €572 per week) [25]. Table 3 reports the summary of costs used in the model.

The mean cost per patient for visits and examinations performed in the pre-surgery period was €181 and €178 for primary intervention/revision and reverse total shoulder arthroplasty, respectively. The mean cost per patient for visits/examinations and physical therapy in the post-surgical period was €288. The conservative management accounted for €526 per patient. The cost of REGENETEN bio-inductive implant was estimated as €3484 (mean cost for Italy provided by the producer).

Cost-Effectiveness Analysis

A cost-effectiveness analysis was performed by estimating the incremental cost-effectiveness ratio (ICER) as the difference in the mean expected costs between surgical repair of RCTs with or without the use of REGENETEN divided by the difference in the mean expected healed lesions between these options, considering a time horizon of 1 year:

$$\begin{aligned}\text{ICER} = {} & (\text{Cost}_{\text{SOC+REGENETEN}} - \text{Cost}_{\text{SOC}})/ \\ & (\%\ \text{Healed lesions}_{\text{SOC+REGENETEN}} \\ & - \%\ \text{Healed lesions}_{\text{SOC}})\end{aligned}$$

The ICER represents the cost needed to achieve one additional healed tear with the use of REGENETEN compared to SOC alone. To clearly interpret the comparison of clinical outcomes between the two treatment options, the number needed to treat (NNT) was also estimated [26]. This represents the number of patients needed to be treated with REGENETEN to achieve one additional healed lesion over a time period of 1 year.

In the base case analysis, medium, large and massive tears were combined together while the variations in tear sizes were explored in scenario analyses. Additional scenario analyses were performed considering the impact of risk factors for lesions re-tearing like age (relative risk 2.12 if age > 60 years), hypertension (relative risk 2.05), obesity (relative risk 2.4) and alcohol consumption (relative risk 2) [27].

Deterministic and probabilistic sensitivity analyses (PSA) were performed to test the robustness of the model. The PSA was performed by assigning distributions to model parameters (beta for probabilities of events and gamma for healthcare resource use and costs, with a standard deviation of 20% of the baseline value); then, all parameters were randomly sampled from their assigned distributions considering 3000 Monte Carlo simulations. Results have been presented graphically as acceptability curves. One-way sensitivity analyses were performed on the model parameters by applying a variation of ± 20% of their baseline values. Regarding the probability of revision or reverse total shoulder arthroplasty, these were varied individually, and the probability of conservative management was calculated by difference to obtain a total probability of events always equal to 1. The results of these analyses are shown in a tornado diagram for the ICER.

RESULTS

Cost-Effectiveness Analysis

Over a 1-year time horizon, healed lesions were 90.70% and 72.90% for surgical repair of RCTs with and without REGENETEN, respectively. The NNT was 5.6, meaning that 5.6 patients should be treated with REGENETEN to obtain one additional healed tear over a time horizon of 1 year.

Considering the NHS perspective, mean costs per patient were €7828 and €4650 for the two strategies, respectively. The ICER was €17,857 per healed tear. From the societal perspective, the mean costs per patient were €12,659 for SOC and €11,784 for REGENETEN, thus showing savings of €4918 per healed tear

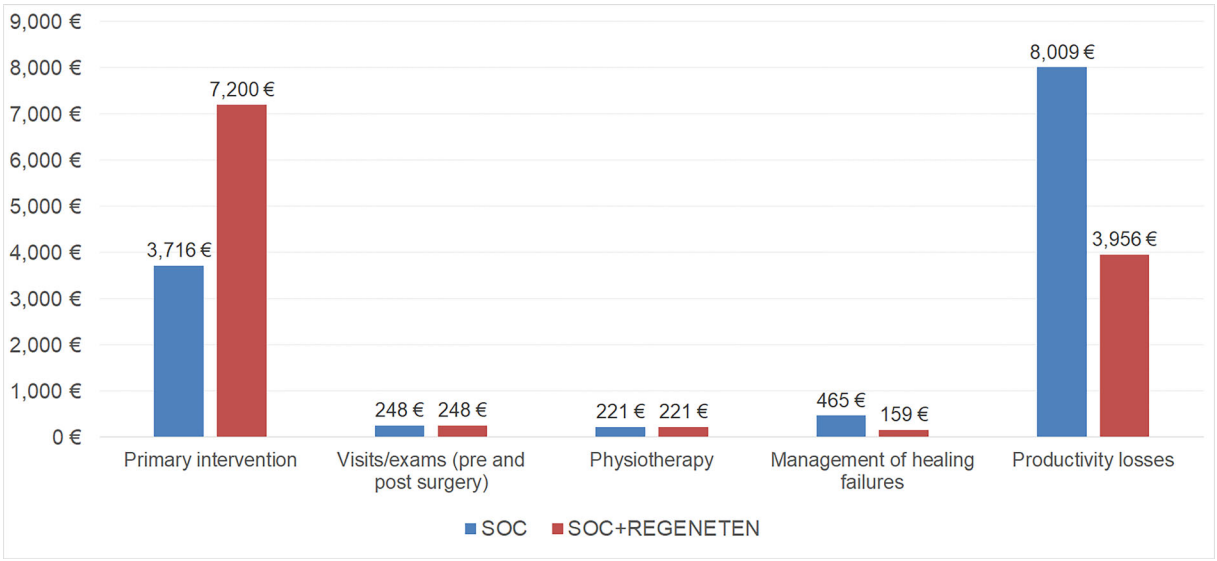

Fig. 2 Details for the different cost categories. *SOC* standard of care

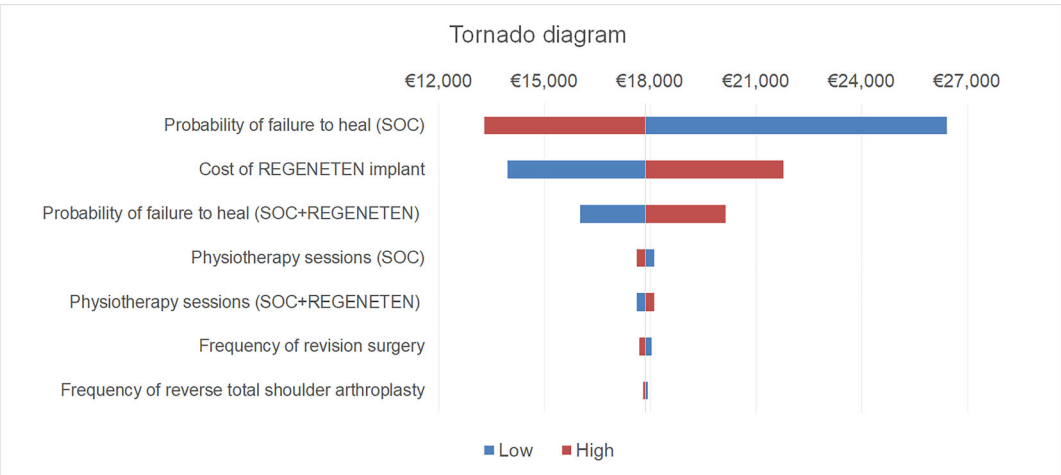

Fig. 3 Tornado diagram reporting one-way sensitivity analyses on the model parameters for the NHS perspective (base case ICER €17,857/healed tear). *ICER* incremental cost-effectiveness ratio, *NHS* National Healthcare Service, *SOC* standard of care

when the bioinductive implant is used. Figure 2 shows the cost details for the different categories. The cost of REGENETEN represents 44.5% of the total cost from the NHS perspective and 29.6% of the cost from the societal perspective.

One-way sensitivity analyses highlighted that the cost of REGENETEN implant and the probabilities of healing failure are the parameters most impacting the model results considering the NHS perspective (Fig. 3). From the societal perspective, the number of weeks off work for SOC is the parameter possibly leading to the loss of dominance of SOC + REGENETEN; for a number of weeks lost equal to 11.2, the ICER becomes €4082 per healed tear.

The results of the scenario analyses are reported in Table 4. Notably, the most cost-effective scenario for using REGENETEN from the

Table 4 Results for scenario analyses

Impact	Delta costs		Delta healed tears (%)	ICER (cost or saving per healed tear)	
	NHS perspective (€)	Societal perspective (€)		NHS perspective (€)	Societal perspective (€)
Medium tears	3282	− 772	11.80	27,894	− 6559
Large tears	3194	− 859	16.90	18,935	− 5095
Massive tears	2863	− 1190	36.10	7926	− 3295
Age > 60 years	2836	− 1218	37.70	7515	− 3228[a]
Hypertension	2857	− 1196	36.50	7831	− 3279
Obesity	2750	− 1304	42.70	6438	− 3052
Alcohol consumption	2872	− 1181	35.60	8069	− 3318

ICER incremental cost-effectiveness ratio, *NHS* National Healthcare Service

[a]The result is valid considering a patients' age till retirement (< 67 years). For patients > 67 years old, the result for the societal perspective is equivalent to the result for the NHS perspective

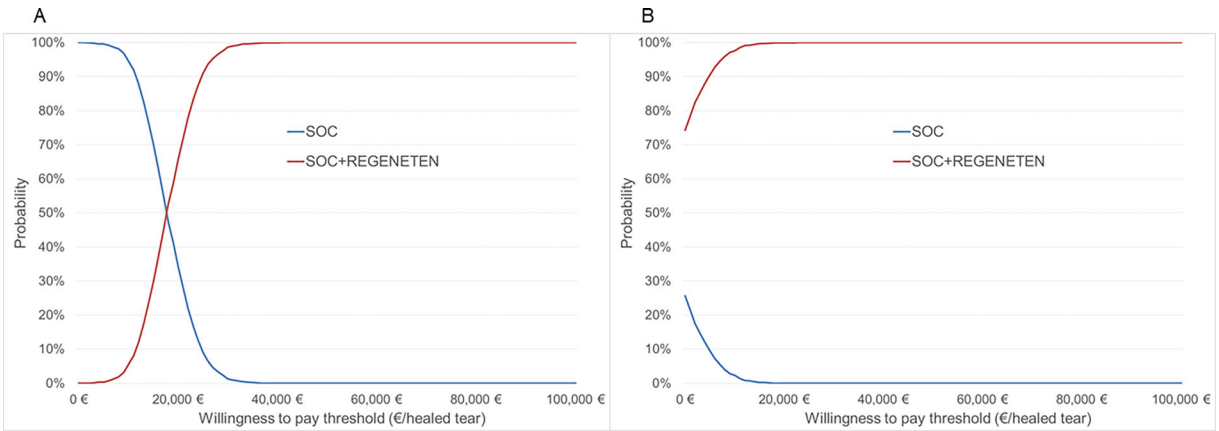

Fig. 4 Acceptability curves for the ICER for NHS (**A**) and societal (**B**) perspectives. *ICER* incremental cost-effectiveness ratio, *NHS* National Healthcare Service, *SOC* standard of care

NHS perspective is the one considering obese patients. In this context, the use of REGENETEN implies an additional cost; therefore; the most cost-effective scenario is the one reporting the lowest cost per healed tear (€6438). However, the most cost-saving scenario from the societal perspective is the one that considers the use of REGENETEN for the repair of medium-sized lesions as it has the biggest saving per healed tear (− €6559).

The PSA showed that surgical repair of RCTs with REGENETEN may be cost-effective in the totality of simulations considering a WTP threshold > €41,000/healed tear and €19,000/healed tear for NHS and societal perspectives, respectively (Fig. 4).

DISCUSSION

Rotator cuff disease is a significant and costly problem [8, 28, 29] that causes constant pain and limits patients' mobility [30, 31]. Progressive in nature, small tears tend to grow in size and severity over time, eventually requiring surgery. The REGENETEN bioinductive implant stimulates the body's natural healing response to support new tendon growth and disrupt disease progression [8, 32]. Derived from highly purified bovine Achilles tendon, it creates an environment favorable to healing [8, 32]. As REGENETEN is a novel technology, there is limited evidences on its cost-effectiveness profile compared to standard care. Accurate information regarding the cost-effectiveness of a novel surgical implant is vital to inform policy and ensure scarce resources are used to optimal benefit.

In the context of a paucity of comparative studies, our analysis, based on real-world data [33], showed that, from the NHS perspective, REGENETEN leads to an ICER of €17,857 per healed tear considering a 1-year time horizon. From the societal perspective, REGENETEN shows a cost-saving profile. The sensitivity analyses confirmed the robustness of the model results and that the cost of the new technology is one of the cost drivers together with the probabilities of failure to heal. Our results are in line with those presented by McIntyre and colleagues [13], who compared the use of REGENETEN to standard of care for the treatment of full-thickness RCT in the US. That study estimated an ICER of $13,061 (about €12,097, exchange rate $1 = €0.93) per healed RCT with SOC + REGENETEN compared to SOC from the payor's perspective (Medicare/Medicaid services or insurance companies), while REGENETEN was found to be cost-saving from the societal perspective. Both studies considered the same clinical inputs but differ concerning the assessment of costs; the US study obtained resource use data and cost information from the published literature, while our study relied on expert opinions to identify the use of healthcare resources since published data in the Italian context were not available.

The present study has some limitations that need to be discussed. For the identification and measurement of healthcare resource consumption, we asked expert surgeons using a Delphi panel. Each individual patient's clinical pathway is complex since it starts from the hospital admission for surgery till the follow-up in outpatient settings (i.e., visits/examinations and physiotherapy). Administrative data are not available to reconstruct the entire clinical pathway; therefore, we deferred to expert opinions to retrieve the number and type of healthcare resources used, according to their clinical practice. In this context, the Delphi methodology seemed appropriate, as it is suggested when administrative data are not readily available or when access to them may be very difficult, costly or time-consuming [34, 35]. Another point relates to the limited sample size of the Delphi panel, which may not guarantee representativeness of costing data. That said, the experts are key opinion leaders in the field and were chosen across Italy to obtain results representing the context as broadly as possible. Moreover, when empirical data are either limited or missing, evidence, often in the form of expert judgments, is usually collected to integrate the data collection [36, 37]. For future studies, we recommend the collection of cost data from specifically developed multicenter registries to allow more accurate results.

Second, the model considered a short time horizon in accordance with the different clinical studies available in the literature used to extrapolate re-tear frequencies. Recently, Bushnell and colleagues [38] reported re-tear rates of 13.2% at 2 years with supplemented double-row repair technique for the bioinductive implant. This study, and possible future clinical trials, will be able to highlight the long-term advantages of the bioinductive implant allowing a longer time horizon for the analyses.

Third, the analysis on societal perspective was limited to considering productivity losses in the post-surgical period; however, patients may bear costs for physical treatments, anti-inflammatory drugs, formal care and informal care, which may be significant. In the future, the collection of these specific data directly from

the patients might provide a more comprehensive view of the cost-effectiveness profile of REGENETEN implants. Fourth, the model did not consider aspects related to patients' quality of life. The literature reports different studies that have evaluated the quality of life of patients who underwent surgery for repair of rotator cuff lesions. Nevertheless, these studies were not specifically focused on the use of REGENETEN but generally evaluated differences before and after surgery [39–41]. Also in this case, specific evidence generation from patients would be crucial to measure quality-adjusted life years for comparative purposes with the standard of care.

Medical devices show particular challenges for health technology assessments caused by the rapid innovation, outcomes influenced by training, competence of final users and dynamic pricing [15, 42]. It has been demonstrated that clinical outcomes and resource consumption related to patients managed with new technologies, such as REGENETEN, may be influenced by the underlying learning curve of the healthcare personnel [43]. Moreover, centers executing a higher number of procedures may obtain better surgical performances and produce better health outcomes at lower procedure costs [43]. Regular data collection and monitoring could offer more robust data for an iterative evaluation of the technology as long as new evidence on these features accrue.

CONCLUSIONS

Considering healed tears as the outcome, our findings showed the cost-effectiveness profile of REGENETEN and that it may be a cost-saving choice compared to SOC from the societal perspective. These findings provide additional evidence for clinicians and payers on the value of a new treatment option for patients with rotator cuff lesions. currently, decision-makers can use these preliminary results to support a tailored approach in defining and treating the targeted patient populations. Future studies comparing standard and innovative approaches are recommended to increase the clinical evidence to confirm or reject the validity of this preliminary evaluation.

Author Contributions. Carla Rognoni and Rosanna Tarricone contributed to the study conception and design. Material preparation, data collection and analysis were performed by Carla Rognoni. Leo M. Nherera developed the cost-effectiveness model. Raffaele Garofalo, Enrico Guerra, Umile Giuseppe Longo and Ettore Taverna provided clinical advice and contributed to data collection on healthcare resource use. Rosanna Tarricone supervised the study. The first draft of the manuscript was written by Carla Rognoni and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding. Open access funding provided by Università Commerciale Luigi Bocconi within the CRUI-CARE Agreement. This study was funded by Smith & Nephew through an unrestricted grant. No interferences occurred in carrying out the research project and in writing the manuscript for which the authors take the sole responsibility. The study sponsor has also funded the journal's Rapid Service and Open Access Fees.

Data Availability. All data generated or analyzed during this study are included in this published article.

Declarations

Conflict of Interest. Leo M. Nherera is an employee of Smith & Nephew. Carla Rognoni, Raffaele Garofalo, Enrico Guerra, Umile Giuseppe Longo, Ettore Taverna and Rosanna Tarricone have nothing to disclose.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Open Access. This article is licensed under a Creative Commons Attribution-Non-Commercial 4.0 International License, which

permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc/4.0/.

REFERENCES

1. Dang A, Davies M. Rotator cuff disease: treatment options and considerations. Sports Med Arthrosc Rev. 2018;26:129–33.

2. Longo UG, Salvatore G, Rizzello G, Berton A, Ciuffreda M, Candela V, et al. The burden of rotator cuff surgery in Italy: a nationwide registry study. Arch Orthop Trauma Surg. 2017;137:217–24.

3. Pedowitz RA, Yamaguchi K, Ahmad CS, Burks RT, Flatow EL, Green A, et al. Optimizing the management of rotator cuff problems. J Am Acad Orthop Surg. 2011;19:368–79.

4. Lee S, Gumucio J, Mendias C, Bedi A. What is the role of systemic conditions and options for manipulation of bone formation and bone resorption in rotator cuff tendon healing and repair? Tech Shoulder Elb Surg. 2017;18:113–20.

5. Longo UG, Carnevale A, Piergentili I, Berton A, Candela V, Schena E, et al. Retear rates after rotator cuff surgery: a systematic review and meta-analysis. BMC Musculoskelet Disord. 2021;22:749.

6. Root KT, Wright JO, Mandato N, Stewart BD, Moser MW. Subacromial-subdeltoid bursitis with rice bodies after rotator cuff repair with a collagen scaffold implant: a case report. JBJS Case Connect. 2023;13(1): e22.

7. Camacho-Chacon JA, Cuenca-Espierrez J, Roda-Rojo V, Martin-Martinez A, Calderon-Meza JM, Alvarez-Alegret R, et al. Bioinductive collagen implants facilitate tendon regeneration in rotator cuff tears. J Exp Orthop. 2022;9:53.

8. Bokor DJ, Sonnabend D, Deady L, Cass B, Young A, Van Kampen C, et al. Evidence of healing of partial-thickness rotator cuff tears following arthroscopic augmentation with a collagen implant: a 2-year MRI follow-up. Muscles Ligaments Tendons J. 2016;6:16–25.

9. McIntyre LF, Bishai SK, Brown PB, Bushnell BD, Trenhaile SW. Patient-reported outcomes after use of a bioabsorbable collagen implant to treat partial and full-thickness rotator cuff tears. Arthrosc J Arthrosc Relat Surg Off Publ Arthrosc Assoc N Am Int Arthrosc Assoc. 2019;35:2262–71.

10. Thon SG, O'Malley L, O'Brien MJ, Savoie FH. Evaluation of healing rates and safety with a bioinductive collagen patch for large and massive rotator cuff tears: 2-year safety and clinical outcomes. Am J Sports Med. 2019;47:1901–8.

11. Acevedo DC, Paxton ES, Williams GR, Abboud JA. A survey of expert opinion regarding rotator cuff repair. J Bone Jt Surg Am. 2014;96: e123.

12. Arshi A, Kabir N, Cohen JR, Lord EL, Wang JC, McAllister DR, et al. Utilization and costs of postoperative physical therapy after rotator cuff repair: a comparison of privately insured and medicare patients. Arthrosc J Arthrosc Relat Surg Off Publ Arthrosc Assoc N Am Int Arthrosc Assoc. 2015;31: 2392-2399.e1.

13. McIntyre LF, Nherera LM, Schlegel TF. Resorbable bioinductive collagen implant is cost effective in the treatment of rotator cuff tears. Arthrosc Sports Med Rehabil. 2023;5(2):e367–74.

14. Tarricone R, Amatucci F, Armeni P, Banks H, Borsoi L, Callea G, et al. Establishing a national HTA program for medical devices in Italy: overhauling a fragmented system to ensure value and equal access to new medical technologies. Health Policy. 2021;125:602–8.

15. Tarricone R, Torbica A, Drummond M, MedtecHTA Project Group. Key recommendations from the MedtecHTA project. Health Econ. 2017;26(Suppl 1): 145–52.

16. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated health economic evaluation reporting standards (CHEERS) 2022 explanation and elaboration: a report of the ISPOR CHEERS II good practices task force. Value Health J Int Soc Pharmacoeconomics Outcomes Res. 2022;25:10–31.

17. Parikh N, Martinez DJ, Winer I, Costa L, Dua D, Trueman P. Direct and indirect economic burden

associated with rotator cuff tears and repairs in the US. Curr Med Res Opin. 2021;37:1199–211. https://doi.org/10.1080/03007995.2021.1918074.

18. Hein J, Reilly JM, Chae J, Maerz T, Anderson K. Retear rates after arthroscopic single-row, double-row, and suture bridge rotator cuff repair at a minimum of 1 year of imaging follow-up: a systematic review. Arthrosc J Arthrosc Relat Surg. 2015;31:2274–81.

19. Rashid MS, Cooper C, Cook J, Cooper D, Dakin SG, Snelling S, et al. Increasing age and tear size reduce rotator cuff repair healing rate at 1 year. Acta Orthop. 2017;88(6):606–11.

20. McIntyre LF, McMillan S, Trenhaile SW, Bishai SK, Bushnell BD. Full-thickness rotator cuff tears can be safely treated with a resorbable bioinductive bovine collagen implant: one-year results of a prospective, multicenter registry. Arthrosc Sports Med Rehabil. 2021;3:e1473–9.

21. Bushnell BD, Connor PM, Harris HW, Ho CP, Trenhaile SW, Abrams JS. Retear rates and clinical outcomes at 1 year after repair of full-thickness rotator cuff tears augmented with a bioinductive collagen implant: a prospective multicenter study. JSES Int. 2021;5:228–37.

22. Trevelyan EG, Robinson PN. Delphi methodology in health research: how to do it? Eur J Integr Med. 2015;7:423–8.

23. Dickinson RN, Kuhn JE, Bergner JL, Rizzone KH. A systematic review of cost-effective treatment of postoperative rotator cuff repairs. J Shoulder Elb Surg. 2017;26:915–22.

24. Haunschild ED, Gilat R, Lavoie-Gagne O, Fu MC, Tauro T, Forsythe B, et al. Return to work after primary rotator cuff repair: a systematic review and meta-analysis. Am J Sports Med. 2021;49:2238–47. https://doi.org/10.1177/0363546520975426.

25. Istat.it Lavoro e retribuzioni [Internet]. [cited 2023 May 2]. Available from: https://www.istat.it/it/lavoro-e-retribuzioni?dati

26. Mendes D, Alves C, Batel-Marques F. Number needed to treat (NNT) in clinical literature: an appraisal. BMC Med. 2017;15:112.

27. Gumina S, Passaretti D, Candela V. Epidemiology and demographics of the rotator cuff tear. In: Gumina S, editor. Rotator cuff tear pathog eval treat. Cham: Springer; 2017. p. 53–9. https://doi.org/10.1007/978-3-319-33355-7_4.

28. Washburn R, Anderson TM, Tokish JM. Arthroscopic rotator cuff augmentation: surgical technique using bovine collagen bioinductive implant. Arthrosc Tech. 2017;6:e297-301.

29. Mather RC, Koenig L, Acevedo D, Dall TM, Gallo P, Romeo A, et al. The societal and economic value of rotator cuff repair. J Bone Jt Surg Am. 2013;95:1993–2000.

30. Lin JC, Weintraub N, Aragaki DR. Nonsurgical treatment for rotator cuff injury in the elderly. J Am Med Dir Assoc. 2008;9:626–32.

31. Franceschi F, Longo UG, Ruzzini L, Rizzello G, Denaro V. Arthroscopic management of calcific tendinitis of the subscapularis tendon. Knee Surg Sports Traumatol Arthrosc Off J ESSKA. 2007;15:1482–5.

32. Schlegel TF, Abrams JS, Bushnell BD, Brock JL, Ho CP. Radiologic and clinical evaluation of a bioabsorbable collagen implant to treat partial-thickness tears: a prospective multicenter study. J Shoulder Elb Surg. 2018;27:242–51.

33. Pongiglione B, Torbica A, Blommestein H, de Groot S, Ciani O, Walker S, et al. Do existing real-world data sources generate suitable evidence for the HTA of medical devices in Europe? Mapping and critical appraisal. Int J Technol Assess Health Care. 2021;37: e62.

34. Powell C. The Delphi technique: myths and realities. J Adv Nurs. 2003;41:376–82.

35. Thorn JC, Brookes ST, Ridyard C, Riley R, Hughes DA, Wordsworth S, et al. Core items for a standardized resource use measure: expert Delphi consensus survey. Value Health. 2018;21:640–9.

36. Soares MO, Sharples L, Morton A, Claxton K, Bojke L. Experiences of structured elicitation for model-based cost-effectiveness analyses. Value Health. 2018;21:715–23.

37. Cao Q, Postmus D, Hillege HL, Buskens E. Probability elicitation to inform early health economic evaluations of new medical technologies: a case study in heart failure disease management. Value Health J Int Soc Pharmacoeconomics Outcomes Res. 2013;16:529–35.

38. Bushnell BD, Connor PM, Harris HW, Ho CP, Trenhaile SW, Abrams JS. Two-year outcomes with a bioinductive collagen implant used in augmentation of arthroscopic repair of full-thickness rotator cuff tears: final results of a prospective multicenter study. J Shoulder Elb Surg. 2022;31:2532–41.

39. Renfree KJ, Hattrup SJ, Chang Y-HH. Cost utility analysis of reverse total shoulder arthroplasty. J Shoulder Elb Surg. 2013;22:1656–61.

40. Vitale MA, Vitale MG, Zivin JG, Braman JP, Bigliani LU, Flatow EL. Rotator cuff repair: an analysis of utility scores and cost-effectiveness. J Shoulder Elb Surg. 2007;16:181–7.

41. Bushnell BD, Bishai SK, Krupp RJ, McMillan S, Schofield BA, Trenhaile SW, et al. Treatment of partial-thickness rotator cuff tears with a resorbable bioinductive bovine collagen implant: 1-year results from a prospective multicenter registry. Orthop J Sports Med. 2021;9:23259671211027850.

42. Drummond M, Griffin A, Tarricone R. Economic evaluation for devices and drugs–same or different? Value Health J Int Soc Pharmacoeconomics Outcomes Res. 2009;12:402–4.

43. Tarricone R, Callea G, Ogorevc M, Prevolnik RV. Improving the methods for the economic evaluation of medical devices. Health Econ. 2017;26(Suppl 1):70–92.