



Cost-Effectiveness of the Use of Autologous Cell Harvesting Device Compared to Standard of Care for Treatment of Severe Burns in the United States

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ABSTRACT

Introduction: When introducing a new intervention into burn care, it is important to consider both clinical and economic impacts, as the financial burden of burns in the USA is significant. This study utilizes a health economic modeling approach to estimate cost-effectiveness and burn center budget-impact for the use of the RECELL[®] Autologous Cell Harvesting Device to prepare autologous skin cell suspension (ASCS) compared to standard of care (SOC)

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split-thickness skin graft (STSG) for the treatment of severe burn injuries requiring surgical intervention for definitive closure.

Methods: A hospital-perspective model using sequential decision trees depicts the acute burn care pathway (wound assessment, debridement/excision, temporary coverage, definitive closure) and predicts the relative differences between use of ASCS compared to SOC. Clinical inputs and ASCS impact on length of stay (LOS) were derived from clinical trials and real-world use data, American Burn Association National Burn Repository database analyses, and burn surgeon interviews. Hospital resource use and unit costs were derived from three US burn centers. A budget impact calculation leverages Monte Carlo simulation to estimate the overall impact to a burn center.

Results: ASCS treatment is cost-saving or cost-neutral (< 2% difference) and results in lower

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LOS compared to SOC across expected patient profiles and scenarios. In aggregate, ASCS treatment saves a burn center 14–17.3% annually. Results are sensitive to, but remain robust across, changing assumptions for relative impact of ASCS use on LOS, procedure time, and number of procedures.

Conclusions: Use of ASCS compared to SOC reduces hospital costs and LOS of severe burns in the USA.

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Keywords: Autologous cell harvesting device; Budget impact; Burn care; Cost-effectiveness; Dermatology; Skin graft; Split-thickness

INTRODUCTION

Burn injuries represent approximately 1% of non-fatal injuries among US civilians [1], with nearly 500,000 burn victims seeking medical care and approximately 40,000 patients requiring hospitalization [2]. As a result of complex and individualized treatment, the management of severe burns requires a high intensity of healthcare resource utilization and long inpatient stays that lead to high medical care costs. The economic burden of burns in the USA is significant, estimated at over \$7.9 billion per year (2018, inflated from 2010) for hospitalizations, emergency department visits, and deaths [3].

Burn management has evolved with the integration of new technologies and treatment paradigms into routine care, resulting in significant declines in the number of burn fatalities [4]. In past decades, mortality was common for burns greater than 20% total body surface area (TBSA) [4]. Today, new interventions have allowed patients with burns covering 90% of their bodies to survive [5]. However, there remain limited alternatives for effectively managing patients, minimizing morbidity, and mitigating the substantial cost of burn injury for severe burns requiring surgical intervention [6].

RECELL[®] Autologous Cell Harvesting Device (ACHD) (AVITA Medical, Valencia, CA, USA) is an innovative technology recently FDA-

approved that allows the rapid preparation of autologous skin cell suspension (ASCS) at the point-of-care for treatment of acute thermal burn wounds [7, 8]. ASCS may be applied either as a primary intervention for deep partial-thickness (DPT) burns with confluent dermis, or as an adjunct to widely meshed split-thickness skin grafts (STSG) for mixed-depth and full-thickness (FT) burns (hereafter named FT/mixed-depth). Published clinical trials, compassionate use data, and real-world evidence point to economic and clinical benefits of ASCS use in burn care. Recent clinical trials illustrate that use of ASCS significantly minimizes donor skin harvesting requirements, enhances re-epithelialization of widely meshed skin grafts, and may decrease the need for follow-up reconstructive procedures [8–10]. Furthermore, when compared to STSG, analysis of real-world burn center records demonstrates that use of ACHD-generated ASCS, in isolation and in combination with STSG, can reduce hospital length of stay (LOS) for severe burn patients [7, 11].

In the current environment of healthcare resource scarcity, hospitals must increasingly consider both clinical efficacy as well as budget-impact when deciding whether to adopt new products. However, the complexity of burn care presents a challenge when evaluating value for money for new interventions. Numerous aspects of practice patterns vary, including the timing of burn-depth diagnosis, excision technique and timing, use of temporary dressings, dermal substitutes, autografting technique, intensity of inpatient rehabilitation, and criteria for patient discharge and outpatient follow-up [12]. As a result, it is difficult to design and implement randomized controlled trials (RCTs) or other direct studies of interventions that are applicable across the spectrum of patient profiles, burn types, and provider practice patterns. In this complex clinical scenario, therefore, it can be useful to apply modeling methods to explore the possible range of expected health impact and economic outcomes.

To the authors' knowledge, there is no validated economic model of the inpatient burn care pathway available for assessment of health economic impact of new interventions versus current standard of care (SOC). Recognizing the

importance of both the economic and clinical impacts of ASCS use in burn care, this study utilizes a health economic modeling approach to represent current inpatient management of burns and to capture the expected impact of ASCS compared to SOC. Specifically, we estimate the cost-effectiveness and burn center budget-impact for the use of ASCS compared to conventional STSG.

METHODS

Structure

A burn center perspective cost-effectiveness model (CEM) of the burn care pathway (Fig. 1), known as the Burn-MCM (medical counter measure) Effectiveness Assessment Cost Outcomes Nexus (BEACON) model, evaluates a single inpatient stay for the management of a severe burn.

The model takes patient characteristics as input and then utilizes linked, sequential decision trees across multiple modules to estimate

the clinical and economic outcomes associated with each phase of care, and overall, during inpatient care. Each module represents a sequential progression through key clinical phases of burn care, including wound assessment, debridement/excision, temporary coverage, and definitive closure. An overview of the burn care pathway and core assumptions is detailed in supplementary materials. In brief, a cohort of patients enters the model at the time of wound assessment, and the depth of wound is determined. To simplify these analyses, it is assumed that all patients are diagnosed correctly in the wound assessment phase. Following wound assessment, a patient moves to debridement/excision where the wound is cleaned and may also be excised for removal of necrotic tissue. For subsequent phases of burn care, management options vary on the basis of burn depth. A patient diagnosed with DPT or FT/mixed-depth burn may receive temporary coverage during the waiting period before the next treatment takes place or for dermal regeneration. For this ASCS-focused analysis, we do not explicitly model temporary coverage interventions.

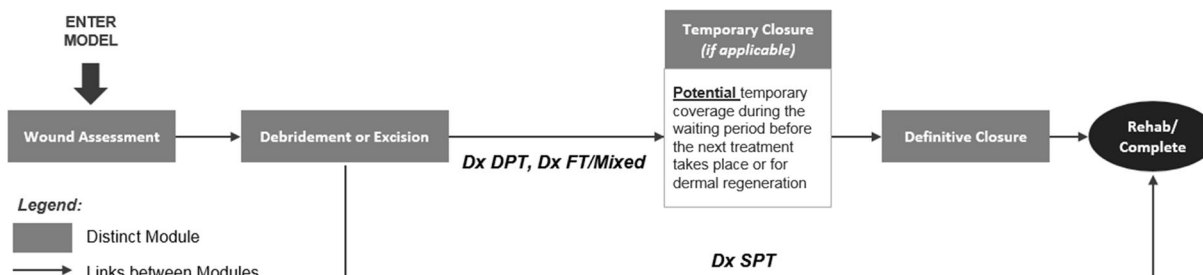


Fig. 1 Burn model diagram. *Wound assessment*—the depth of wound is assessed, and a patient’s wounds are diagnosed in terms of depth. *Debridement or excision*—per US standard practice, DPT and FT/mixed-depth burns are surgically excised in the operating room until viable bleeding tissue is reached to prepare the wound for definitive closure. SPT burns are assumed to be debrided to remove devitalized tissue and treated using conservative management without surgery. *Temporary closure*—for this ASCS-focused analysis, we implicitly capture the impact of temporary coverage on LOS and cost through predictive equations derived from burn center data. However, we do not explicitly model the individual unit costs or

performance of potential temporary coverage (including dermal regeneration) interventions. Note that interventions for temporary coverage are not explicitly modeled at this time; however, their impact on total cost and length of stay is implicitly considered with the NBR predictive equations. *Definitive closure*—in this phase of burn care, wounds that are diagnosed as requiring surgery for definitive closure (DPT, FT/mixed-depth) and receive STSG or treatment with ASCS (with or without STSG). *Rehabilitation*—though not a discrete phase, the model evaluates resources to capture key inpatient rehabilitation cost as well as the proportion of patients requiring contracture operations

For phases of burn care not impacted by ASCS treatment (namely, wound assessment, debridement/excision, temporary coverage), non-differential SOC was assumed to provide an evidence-based benchmark for patient outcomes under SOC in current clinical practice (as outcomes such as LOS and total cost are affected by all phases of care) and to isolate the incremental impact of ASCS use within the overall context of burn care management.

The budget impact model (BIM) builds on the CEM to capture the impact of interventions on costs and patient outcomes for a burn center overall, accounting for key drivers specific to the burn center, such as the expected patient mix by burn depth, TBSA burned, and other individual patient characteristics. The model compares costs for the two treatment pathways (with and without the use of ASCS) to isolate the likely shift in costs related to ASCS.

The BIM samples from normal distributions around patient and burn characteristics from the American Burn Association National Burn Repository (NBR) to generate 200 proxy patient profiles representing a real-world population of patients treated annually in the inpatient setting. For each unique patient profile, the detailed CEM estimates patient-level outcomes (e.g., LOS, cost, number of surgical operations). A Monte Carlo simulation is then used to generate the 200 profiles 100 times, enhancing the stability and precision of results. The combination of a Monte Carlo approach and sampled patient profiles enables the model to test the impact of an intervention, given variation in patient characteristics (e.g., input variability). The BIM aggregates results across the profiles to calculate the total fiscal impact to a burn center for two treatment pathways, considering the likely number of patients in each unique profile.

This article does not contain any new studies with human or animal subjects performed by any of the authors.

Patient Profile

The target population for the model is adults (average 42 years of age), with severe burns of TBSA $\geq 10\%$ receiving inpatient care, where

DPT and FT/mixed-depth burns are eligible for ASCS.

Model inputs for additional factors that influence patient outcomes, such as inhalation injury, infection [hospital-acquired infection (HAI) and other infections], and sex, were derived from analysis of the NBR. The NBR includes 10 years of cumulative data from burn centers, representing the largest data resource for burn injuries in the USA including demographic, injury, and outcome information. Leveraging the NBR data (version 8.0, 2002–2011), analyses were performed on a sample of 21,175 surviving patients for whom key data points were available. All analyses leveraging the NBR were based on patients with TBSA between 10% and 60% to reduce a tail effect where outlier patients with high TBSA may skew predicted estimates. The NBR includes only relative burn size information (as % TBSA). Therefore, the National Health and Nutrition Survey (NHANES) [13] 2014–2016 was analyzed to determine the average absolute body surface areas (BSA, cm^2) for male and female subjects in the USA to convert percentage TBSA from the NBR to an average size of burns in terms of square centimeters, needed for cost calculations in the model.

Clinical Inputs

Clinical inputs were derived from RCTs, a survey of eight burn surgeons, NBR database analyses, and in-depth interviews with four experienced burn surgeons. Further, all model assumptions were vetted by one or more burn surgeons, and the output of the model was benchmarked against real-world data to validate the modeling structure and ensure clinical validity [14] (Table 1).

To ensure the model accurately accounts for patient characteristics when predicting outcomes and costs, patient LOS associated with STSG treatment was estimated using the NBR. LOS was predicted via a regression controlling for TBSA, TBSA of partial-thickness burn, age (linear, squared and cubed to account for non-linearity), HAI, other infection, inhalation injury, sex, whether or not they had one or

Table 1 Key clinical inputs

| Variable | Patient profile | Input | References |
|---|-----------------|------------|--------------------------------------|
| Wound assessment | | | |
| Time until wound depth diagnosed/first procedure | TBSA 10–20% | 4.938 days | Burn surgeon survey (data on file) |
| | TBSA 21%+ | 4.525 days | |
| Debridement/excision | | | |
| Average number of non-excisional debridement procedures (FT/mixed-depth) | TBSA 10% | 0.48 | NBR database analyses (data on file) |
| | TBSA 20% | 0.32 | |
| | TBSA 30% | 0.30 | |
| | TBSA 40% | 0.32 | |
| Average number of non-excisional debridement procedures (DPT) | TBSA 10% | 0.56 | |
| | TBSA 20% | 0.47 | |
| | TBSA 30% | 0.52 | |
| | TBSA 40% | 0.62 | |
| Time per debridement procedure (mins) | TBSA 10% | 19 | Burn centers (data on file) |
| | TBSA 20% | 38 | |
| | TBSA 30% | 47 | |
| | TBSA 40% | 62 | |
| Average number of excision procedures (FT/mixed-depth) | TBSA 10% | 2.49 | NBR database analyses (data on file) |
| | TBSA 20% | 2.98 | |
| | TBSA 30% | 3.57 | |
| | TBSA 40% | 4.27 | |
| Average number of excision procedures (DPT) | TBSA 10% | 2.18 | |
| | TBSA 20% | 2.37 | |
| | TBSA 30% | 2.64 | |
| | TBSA 40% | 3.03 | |
| Average time per excision procedure (mins) | TBSA 10% | 38 | Burn centers (data on file) |
| | TBSA 20% | 75 | |
| | TBSA 30% | 90 | |
| | TBSA 40% | 120 | |
| Definitive closure | | | |
| Conservative approximation: number of autograft operations (STSG, FT/mixed-depth & DPT) | TBSA 10–20% | 1 | Assumption |
| | TBSA 21%+ | 2 | |

Table 1 continued

| Variable | Patient profile | Input | References |
|---|-----------------|--------------|--------------------------------------|
| NBR national average: number of autograft operations (STSG, FT/mixed-depth) | TBSA 10% | 2.46 | NBR database analyses (data on file) |
| | TBSA 20% | 3.14 | |
| | TBSA 30% | 3.83 | |
| | TBSA 40% | 4.54 | |
| NBR national average: number of autograft operations (STSG, DPT) | TBSA 10% | 2.23 | |
| | TBSA 20% | 2.69 | |
| | TBSA 30% | 3.15 | |
| | TBSA 40% | 3.63 | |
| Donor site size for STSG treatment (% of burn) | TBSA 10–39% | 61.1% | Gravante [9] |
| | TBSA 40%+ | 25% | Holmes [8] |
| Donor site size for ASCS treatment (% of burn) | All TBSA | 1.3% | Gravante [9] |
| Donor site size ASCS + STSG (% of burn)* | TBSA 10–39% | 41.5% | Holmes [8] |
| | TBSA 40%+ | 17% | Holmes [8] |
| Autograft operative time (mins) | Burn wound site | 1.6 per TBSA | Burn surgeon survey (data on file) |
| | Donor site | 2.1 per TBSA | |
| Other | | | |
| Odds ratio for LOS for ASCS relative to SOC (up to 40% TBSA) | DPT | 0.70 | Park [11] |
| | FT/Mixed | 0.98 | Park [11] |
| Odds ratio for LOS for ASCS relative to SOC (over 40% TBSA) | DPT & FT/mixed | 0.53 | Holmes [19] |
| Proportion of patients requiring contracture procedures (%) | STSG | 37.5% | Gravante [9] |
| | ASCS | 28.6% | |
| Blood requirements per % TBSA (ml) | Excision | 20.51 | Luo [22] |
| | STSG | 32.83 | |

*Assumption based on meshing ratio of 4:1 for STSG and for ASCS + STSG, relative reduction in donor site size for ASCS + STSG from Holmes 2018 [8]

more grafting procedures, and diabetes status [15]. Similarly, the numbers of non-excisional debridements (ICD-9: 86.28) and excisional debridements (ICD-9: 86.22) are predicted using predictive equations derived from the NBR, based on patient characteristics.

Definitive Closure

The impact of the use of ASCS is modeled in the definitive closure module. In this phase of care, wounds diagnosed as requiring surgery for timely closure (DPT, FT/mixed-depth) can receive ASCS or SOC. For burns treated with

ASCS, the model assumes ASCS alone for DPT burns and ASCS with meshed STSG for FT/mixed-depth burns, while all SOC patients receive conventional STSG.

Other key differences in patient management for ASCS versus SOC include number of definitive closure procedures, procedure time, size of donor site, and LOS. In all scenarios considered in the model, definitive closure (healing) using ASCS is assumed to require one surgical procedure (i.e., healing is achieved with a single ASCS treatment for a given patient) [7–10]. As outlined below, model assumptions for the number of procedures for SOC were developed to capture the variability in practice patterns.

As highlighted during burn surgeon interviews and analysis of NBR data, surgical practices for definitive closure vary on the basis of surgeon preference, as well as patient and burn center characteristics. Therefore, estimated cost-effectiveness of ASCS is presented for two scenarios to account for likely real-world variation in SOC STSG practices: (1) a conservative approximation, and (2) an NBR-based national average. The conservative approximation SOC scenario assumes a single conventional autografting procedure with STSG for patients with TBSA $\leq 20\%$ and two conventional autografting procedures with STSG for patients with TBSA $> 20\%$. For the NBR national average scenario, the number of procedures to achieve definitive closure via conventional autografting with STSG (by burn depth and TBSA) was predicted using NBR data, with conventional autografting procedures identified via ICD-9 codes 86.61, 86.62, 86.63, and 86.69 [16]. It was assumed that multiple codes were performed in the same operation, and therefore the maximum count of a single conventional autografting ICD-9 procedure code represented would estimate the number of SOC definitive closure procedures.

Information on donor site size harvested for ASCS and SOC STSG, as well as the proportion of patients requiring a contracture release procedure associated with ASCS treatment, is based on RCTs [8–10]. The number of ACHD devices used to prepare ASCS is determined by the percentage TBSA burned. On the basis of product

information [17] one device can be used to prepare up to 24 ml of ASCS, which treats up to 1920 cm² of burn wound. For patients with TBSA up to 40%, Gravante et al. demonstrated that average donor site per percent TBSA of burn was 61.1% for SOC STSG and 1.25% for ASCS [9]. For patients with TBSA over 40%, size of donor site per percent TBSA was estimated at 25% based on a survey of eight practicing surgeons for SOC STSG, with a 32% reduction (relative to SOC STSG) due to use of ASCS based on randomized clinical data [10]. Impact of reduced donor site in the model is captured via reduced time to harvest donor skin and reduced time and resources to dress the donor site. In addition to reducing size of the donor site per percent TBSA, use of ASCS is associated with reduced patient pain related to donor site harvesting and reduced number of additional procedures arising from limited availability of donor sites to support SOC STSG [10].

The impact of ASCS on LOS was derived from published, real-world evidence from Australia [11] as the device for preparation of ASCS has only recently become available outside of clinical trials in the USA [18]. Specifically, to estimate the effect of ASCS on LOS, odds ratios (OR) for DPT (0.7) and FT/mixed-depth (0.98) burn depths were applied to SOC-based LOS, as estimated by the NBR equation for burns up to 40% TBSA [11]. For burns with TBSA $\geq 40\%$, compassionate use data from the USA was used to inform the impact of ASCS treatment on LOS (OR 0.53) [19]. Routine daily patient care outside of the operating room was assumed the same for ASCS and STSG. As such, changes in LOS costs are representative of reduced LOS only and conservatively do not assume any change in costs per day outside of key procedures. Daily care included daily dressing changes for both the burn wounds and donor sites, performed by one nurse and one technician with an estimated 1 min of staff time per square centimeter of burn, as estimated by a survey of eight burn surgeons. For operating room costs, key differences related to ASCS use include reduced number of procedures as well as reduced time for donor skin harvesting and donor skin wound dressings.

After definitive closure, the model accounts for inpatient rehabilitation costs. On the basis of burn surgeon input, for all patients, one physical therapy and one occupational therapy appointment was assumed for each day of inpatient stay. The model also accounts for the proportion of patients requiring surgery for contracture release, with rates for ASCS and SOC based on published clinical data [8, 9]. For patients requiring contracture release, we assumed a 3-day hospital stay for the procedure but do not assume rehabilitation costs, thereby presenting a conservatively low estimate of the cost of contracture.

Costs and Resource Use

Key cost elements include staffing (nurses, scrub technicians), costs per day (or bed costs), operating room time and related resources, wound-related resources (e.g., wound dressings), and the price of the device(s) used to prepare ASCS. The model results presented herein conservatively assumed that burn surgeon and anesthesiologist time is billed separately and does not represent a cost to the burn center. As a result of limitations in obtaining nuanced data on anesthesia cost by each inpatient procedure, a non-differential lump sum anesthesia cost was conservatively applied to all patients undergoing surgery regardless of receiving SOC or ASCS. The cost of ASCS use (per 1920 cm² of burn wound) is based on the \$7500 list price of the ACHD used to prepare ASCS. Hospital resource use (e.g., materials, procedure time) and unit costs were derived from survey data obtained from three US burn centers. All unit costs represent 2017 USD and are reflective of average costs reported by surgery centers (Table 2).

Analyses

Cost-Effectiveness Analysis

The BEACON model is fully customizable to support use of individual burn center data. The results presented are based on national aggregate trends. The model predicts outcomes for patients with any TBSA; however, results presented herein focus on TBSA ranges that are

Table 2 Key cost and resource use inputs

| Provider resource use element | Unit | Cost (USD 2017) |
|--|---------------------|-----------------|
| Cost per day for burn patients | Per day | \$6795.00 |
| Burn surgery operating room time | Per hour | \$3720.00 |
| Nurse time | Per hour | \$56.10 |
| Scrub tech time | Per hour | \$39.00 |
| Blood transfusion (packed cells, whole blood) | Per liter | \$117.00 |
| Escharotomy | Per excision | \$500.00 |
| Wound dressings inpatient | Per cm ² | \$0.09 |
| Physical therapy | Per session | \$21.75 |
| Occupational therapy | Per session | \$15.75 |
| Contracture surgery first | 100 cm ² | \$100.00 |
| Contracture surgery subsequent | 100 cm ² | \$50.00 |
| Anesthesiology | Per patient | \$2694.00 |
| List price for Autologous Cell Harvesting Device for preparation of ASCS | Per device | \$7500.00 |

common in real-world care [20]. Specifically, results are reported for adult patients (average age 42 years) with TBSA 10%, 20%, 30%, and 40% for DPT and FT/mixed-depth, controlling for comorbidities as derived from NBR data. The selected patient profiles for TBSA and burn depths were chosen to illustrate a range of cost-effectiveness outcomes with ASCS use.

While overall patient characteristics were held consistent across model runs for DPT and FT/mixed-depth burn depths, underlying model inputs were varied (per Table 1) to account for

the impact of wound depth on LOS and amount of donor skin harvested (and associated impact on surgery time). Two scenarios were analyzed—assuming a conservative approximation and using NBR-based national averages to predict number of SOC STSG procedures. One-way sensitivity analysis (OWSA) was conducted for each patient profile (Table 3).

Budget Impact Analysis

To estimate budget impact, a burn center treating 200 patients annually was simulated. Consistent with the CEM, individual patient characteristics were extracted from the NBR, including average age, sex, and comorbidities. This information represents national aggregate

data on the mix of patient types, burn depth, and TBSA for a burn center. As highlighted in Table 3, the BIM includes the full range of patient and burn characteristics expected to present in the USA. Therefore, while the target CEM profiles described above highlight the range in outcomes across potential patient and burn types, the BIM considers the relative mix of TBSA ranges.

The BIM requires categorization of patients into discrete burn depths of superficial partial-thickness (SPT), DPT, and FT/mixed-depth. Burn depth is not a discrete variable in the NBR; however, continuous variables of TBSA of FT and PT are reported. These variables were used to categorize a patient as FT/mixed-depth if

Table 3 Cost-effectiveness and budget impact patient profiles *Source: Inputs based on analysis of NBR data*

| Details of patient profiles for the cost-effectiveness model | | | | |
|--|--|--|---|--------|
| | TBSA | | | |
| Patient characteristics | 10% | 20% | 30% | 40% |
| Female (%) | 26% | 23% | 27% | 27% |
| BSA (cm ²) | 19,808 | 19,856 | 19,788 | 19,783 |
| Size of burn (cm ²) | 1981 | 3971 | 5936 | 7913 |
| Comorbidities | | | | |
| Inhalation injury (%) | 4% | 9% | 13% | 25% |
| Hospital-acquired infection (HAI) (%) | 1% | 3% | 4% | 9% |
| Other infection (%) | 2% | 5% | 4% | 5% |
| Diabetes (%) | 6% | 6% | 3% | 4% |
| Details of default settings for a burn center with 200 adult patient annually | | | | |
| | Full-thickness/mixed-depth No. Patients (%) | Deep partial-thickness No. Patients (%) | Superficial partial-thickness^a No. Patients (%) | |
| Wound depth distribution | 40 (20%) | 58 (29%) | 102 (51%) | |
| Proportion of burns | | | | |
| TBSA 40% + (average 48%) | 5 (13%) | 5 (8%) | 7 (7%) | |
| TBSA 21–40% (average 28%) | 15 (38%) | 20 (35%) | 26 (25%) | |
| TBSA 10–20% (average 15%) | 19 (49%) | 33 (57%) | 69 (68%) | |

^a Superficial partial-thickness patients receive no STSG or ASCS, as they are assumed to heal within 21 days. Note: May not sum to 100% because of rounding of number of patients in simulation

50%+ of their burn was FT depth and as SPT if they had zero surgical procedures in the NBR, with remaining burns classified as DPT.

RESULTS

Cost-Effectiveness Analysis

In the conservative approximation scenario of ASCS use, spend was cost-neutral (< 2%) or cost-saving in all profiles. Using the NBR national averages to predict number of STSG operations in an alternate scenario, all patient profiles showed cost savings with use of ASCS. In both scenarios, reduced number of definitive closure procedures enabled through use of ASCS use was driven by reduced need for donor skin. Accordingly, mitigating availability of donor skin as a limiting factor, fewer surgical operations were required to achieve definitive closure. A key finding was that cost savings increase as burn size increases owing to overall reduction in the number of operations, dressing time, and associated costs (Table 4).

LOS was reduced for all patient profiles modeled, but the relative shift in LOS was most favorable for large burns. The OR for LOS with ASCS, relative to NBR-derived SOC estimates, was most favorable for DPT burns as well as for burns with TBSA of 40% or more, which led to greater reductions in LOS and associated inpatient costs for these patients. Notably, for FT/mixed-depth burns of 40% TBSA, the projected reduction in LOS was almost 28 days (SOC, 59 days; ASCS, 31 days). Further, large relative LOS reductions were seen across all TBSA ranges for DPT, with ASCS-reductions in LOS increasing along with increases in TBSA percentages. Across all patient profiles, the use of ASCS translates to roughly a 20% reduction in rehabilitation costs (~ \$2000 savings per acute care stay), due to a reduced proportion of patients requiring surgical procedures for contracture release and reduced number of days as inpatients with physical therapy and occupational therapy visits.

In OWSA, the OR for ASCS impact on LOS for each strategy is the primary driver of results for all depths and burn sizes. Additional influential

variables include the size of the donor site and the number of operations for SOC. Nevertheless, for all patient profiles, the use of ASCS consistently led to cost savings or cost-neutral results when varying model inputs across expected high and low ranges, which suggests that model results remain robust across expected uncertainties or variations in individual model parameters. OWSA diagrams can be found in supplementary materials.

Budget Impact Analysis

Aggregating patient profiles to view results for a burn center, use of ASCS is expected to reduce overall costs by an estimated 14–17.3% annually. Under the conservative scenario for estimating SOC STSG procedures, use of ASCS reduced costs by an estimated 14% (\$5.3 million for the burn center, average \$26.6 thousand per patient). When estimating SOC STSG procedures per NBR averages, overall relative savings increased to 17.3% (\$6.8 million for the burn center, \$34.1 thousand per patient). Reductions in costs are driven by reduced number and duration of procedures performed for definitive closure, change in LOS, and reduced rehabilitation needs (Table 5). Notably, use of ASCS led to an estimated 32% and 37% reduction in definitive closure procedures relative to SOC for the conservative and NBR scenarios, respectively.

DISCUSSION

This study evaluated the impact of ASCS on patient LOS, number and duration of definitive closure procedures, inpatient resource use, and the estimated cost impact to a burn center for treatment of severe burns in the USA. At a patient level, use of ASCS for burn treatment (regardless of burn depth) was predicted to be cost saving or cost neutral vs SOC when applying the conservative approximation (for SOC procedures) and consistently cost saving for all patient profiles when applying the NBR predictive equations (for SOC procedures). All sensitivity analyses continued to show cost-saving or at least cost-neutral results, demonstrating that

Table 4 Cost and effect results by depth and TBSA

| Burn depth | TBSA | Results measure | Conservative approximation scenario | | | NBR-based national average scenario | | |
|----------------|------|-----------------|-------------------------------------|-----------|------------------------|-------------------------------------|-----------|------------------------|
| | | | SOC | ASCS | Difference \$/days (%) | SOC | ASCS | Difference \$/days (%) |
| FT/mixed-depth | 10% | Total costs | \$174,857 | \$176,031 | \$1174 (0.7%) | \$181,560 | \$176,031 | -\$5529 (- 3.0%) |
| | | Total LOS | 21.2 | 20.8 | - 0.4 (- 2.0%) | 21.2 | 20.8 | - 0.4 (- 2.0%) |
| | | No. procedures | 1.0 | 1.0 | 0 (0.0%) | 2.5 | 1.0 | - 1.5 (- 59.3%) |
| | 20% | Total costs | \$281,679 | \$286,001 | \$4322 (1.5%) | \$301,386 | \$286,001 | -\$15,385 (- 5.1%) |
| | | Total LOS | 32.4 | 31.8 | - 0.6 (- 2.0%) | 32.4 | 31.8 | - 0.6 (- 2.0%) |
| | | No. procedures | 1.0 | 1.0 | 0 (0.0%) | 3.1 | 1.0 | - 2.1 (- 68.2%) |
| | 30% | Total costs | \$416,268 | \$410,249 | -\$6019 (- 1.4%) | \$438,191 | \$410,249 | -\$27,942 (- 6.4%) |
| | | Total LOS | 45.0 | 44.1 | - 0.9 (- 2.0%) | 45.0 | 44.1 | - 0.9 (- 2.0%) |
| | | No. procedures | 2.0 | 1.0 | - 1 (- 50.0%) | 3.8 | 1.0 | - 2.8 (- 73.9%) |
| | 40% | Total costs | \$549,200 | \$335,830 | -\$213,370 (- 38.9%) | \$579,292 | \$335,830 | -\$243,462 (- 42.0%) |
| | | Total LOS | 59.4 | 31.3 | - 28.2 (- 47.4%) | 59.4 | 31.3 | - 28.2 (- 47.4%) |
| | | No. procedures | 2.0 | 1.0 | - 1 (- 50.0%) | 4.5 | 1.0 | - 3.5 (- 78.0%) |
| DPT | 10% | Total costs | \$133,693 | \$102,714 | -\$30,979 (- 23.2%) | \$139,348 | \$102,714 | -\$36,634 (- 26.3%) |
| | | Total LOS | 15.6 | 10.9 | - 4.7 (- 30.0%) | 15.6 | 10.9 | - 4.7 (- 30.0%) |
| | | No. procedures | 1.0 | 1.0 | 0 (0.0%) | 2.2 | 1.0 | - 1.2 (- 55.1%) |
| | 20% | Total costs | \$193,573 | \$151,560 | -\$42,013 (- 21.7%) | \$209,089 | \$151,560 | -\$57,529 (- 27.5%) |
| | | Total LOS | 21.2 | 14.9 | - 6.4 (- 30.0%) | 21.2 | 14.9 | - 6.4 (- 30.0%) |
| | | No. procedures | 1.0 | 1.0 | 0 (0.0%) | 2.7 | 1.0 | - 1.7 (- 62.8%) |
| | 30% | Total costs | \$276,670 | \$205,882 | -\$70,788 (- 25.6%) | \$290,407 | \$205,882 | -\$84,525 (- 29.1%) |
| | | Total LOS | 28.1 | 19.7 | - 8.4 (- 30.0%) | 28.1 | 19.7 | - 8.4 (- 30.0%) |
| | | No. procedures | 2.0 | 1.0 | - 1 (- 50.0%) | 3.1 | 1.0 | - 2.1 (- 68.2%) |
| | 40% | Total costs | \$359,875 | \$228,723 | -\$131,152 (- 36.4%) | \$379,182 | \$228,723 | -\$150,459 (- 39.7%) |
| | | Total LOS | 37.0 | 19.5 | - 17.5 (- 47.4%) | 37.0 | 19.5 | - 17.5 (- 47.4%) |
| | | No. procedures | 2.0 | 1.0 | - 1 (- 50.0%) | 3.6 | 1.0 | - 2.6 (- 72.5%) |

Note that only differential definitive closure procedures are shown in the main results table, as SOC before definitive closure was assumed non-differential (see Table 1 for information on number of debridement and excision procedures)

Table 5 Budget impact model results

| Costs by category (200 patients) | Conservative approximation scenario | | | NBR-based national average scenario | | |
|----------------------------------|-------------------------------------|--------------|----------------------|-------------------------------------|--------------|----------------------|
| | SOC | ASCS | Difference \$ (%) | SOC | ASCS | Difference \$ (%) |
| Wound assessment | \$481,550 | \$481,550 | \$0 (0.0%) | \$482,821 | \$482,821 | \$0 (0.0%) |
| Debridement/excision | \$2141,040 | \$2141,040 | \$0 (0.0%) | \$2,142,983 | \$2,142,983 | \$0 (0.0%) |
| Definitive closure | \$4496,118 | \$3895,555 | -\$600,562 (-13.4%) | \$6,047,354 | \$3,936,108 | -\$2111,246 (-34.9%) |
| Rehabilitation | \$995,604 | \$772,729 | -\$222,875 (-22.4%) | \$996,079 | \$773,201 | -\$222,877 (-22.4%) |
| LOS | \$29,153,546 | \$24,665,265 | -\$4488,281 (-15.4%) | \$29,220,479 | \$24,736,277 | -\$4484,202 (-15.3%) |
| Other ^a | \$547,355 | \$547,355 | \$0 (0.0%) | \$547,213 | \$547,213 | \$0 (0.0%) |
| Total costs | \$37,815,213 | \$32,503,495 | -\$5311,718 (-14.0%) | \$39,436,928 | \$32,618,602 | -\$6818,326 (-17.3%) |
| Average cost per patient | \$189,076 | \$162,517 | -\$26,559 (-14.0%) | \$197,185 | \$163,093 | -\$34,092 (-17.3%) |

^a Other includes costs for anesthesia and escharotomy. Note: Results may differ in phases outside of definitive closure because of randomization in the Monte Carlo simulation

the core model results remain robust across expected uncertainties in individual model parameters.

Results of the CEM illustrate consistent cost-saving results across a range of individual patient profiles, as highlighted by the burn depth and TBSA ranges presented. Leveraging the individual patient results from the CEM, the BIM considered the mix of patients and burn characteristics expected to present in the USA annually, concluding projected net savings to a burn center overall.

The underlying clinical driver associated with ASCS use is the reduced requirement for harvesting of donor skin, which leads to a reduced number of procedures and faster healing time [8–10]. While favorable results were observed across a range of patient profiles, the modeled impact of ASCS on LOS is likely conservative. Using the Australian real-world data, use of ASCS alone for DPT burns allowed for a greater reduction in LOS (OR 0.7) compared to ASCS with meshed-STSG for FT/mixed depth burns (OR 0.98) [11]. However, the higher relative OR for FT/mixed depth burns (0.98) may be conservatively biased given the majority of patients (92%) had TBSA less than 20%. The number of procedures needed for definitive closure for SOC increases with TBSA and, therefore, the benefits of a single procedure for ASCS also increased at the same time as expected LOS reductions. This trend of increased ASCS benefits with higher TBSA for FT/mixed depth wounds was also supported by US-based compassionate use data. Specifically, for patients with an average TBSA of 62% (range 40–91%) use of ASCS with meshed-STSG showed an OR of 0.53 compared to SOC [19]. Therefore, it is expected that the impact of ASCS on LOS for FT/mixed depth burns may be greater than estimated in this analysis.

As with any modeling exercise, this study is subject to limitations relevant to interpretation of results. The primary limitation is that data comparing LOS for ASCS treatment versus SOC, outside of compassionate use and within-in patient controls, was not available in the USA. Therefore, we estimated the LOS for SOC patients in the US setting, and then applied the OR derived from a real-world study from

Australia to estimate the impact of ASCS versus SOC for burns less than 40% TBSA. While the use of a relative effect in the form of an odds ratio follows best practices for modeling, it should be noted that we do not explicitly address any underlying differences between the US and Australian health systems that may impact the ASCS-related shift in LOS. For patients with 40%+ TBSA, data from a single burn center were used that found a 47% reduction in LOS for patients receiving ASCS treatment compared to age and burn severity matched controls in a limited compassionate use sample (~ 10 adult patients) [19]. Nevertheless, results and assumptions have been verified by US burn surgeons. Furthermore, substantial and consistent clinical and financial benefits from use of ASCS in compassionate use experience in the USA has been reported [19].

Secondly, information about the costs and timing of procedures were obtained from a small sample of burn centers or from a survey of burn surgeons. These represent average costs as reported by the centers and, therefore, do not explicitly address the likely range in true paid costs when considering the mix of insurance types across patients. As mentioned earlier, surgical management of burns varies across burn centers and surgeons. Accordingly, staff and healthcare costs, as well as definitive closure procedure times, may also vary. Conclusions from the OWSA suggest that results remain robust across expected, known variations as well as potential shifts in costs due to insurance status of patients. Furthermore, the use of random sampling from distributions in the BIM highlights that conclusions also remain robust across variations in key inputs. The authors also conducted an external benchmark against predicted costs across patient profiles in the NBR to check validity of final results, concluding that predicted costs for SOC were consistent with NBR data [15].

Finally, several simplifying assumptions were made to develop a transparent, flexible model. First, individual unit costs and temporary coverage interventions (e.g., allograft, xenograft, skin substitute, or dermal analogs) were not explicitly considered. Temporary closure costs and patient impacts are only implicitly captured

via the NBR-based predictive equations. Next, as is the case with clinical practice, the model assumes correct diagnosis when determining pathways for a diagnosed burn. Accuracy of burn depth diagnosis varies on the basis of burn center practices as well as timing of diagnosis, and published literature suggests that inaccurate diagnosis can occur, especially for SPT and DPT burns [21]. The most important impact of this assumption on model results is that the number of DPT burns eligible for ASCS (either misdiagnosed SPT or true DPT burns) may be uncertain. However, given that the use of ASCS is expected to result in savings for DPT burns, some amount of inherent misdiagnosis likely leads to an underestimate of cost savings for any incorrectly diagnosed SPT burns. Further, the NBR does not code diagnosis changes (i.e., burn depth conversion) over time and, therefore, does not highlight whether diagnoses were correct or incorrect. However, the predictive equations derived from the NBR implicitly capture the effects of how incorrectly diagnosed patients impact average outcomes for procedures and LOS. Also, the model assumes only one procedure for a patient with ASCS. While this is consistent with trends seen in real-world use in Australia as well as early clinical trial data [7], there may be instances when patients undergo more than one procedure given very high TBSA or provider preferences. Finally, the model does explicitly consider the cost of retreatment for ASCS or SOC, but the impact of retreatment on LOS may be implicitly captured in the NBR predictive equations for LOS.

Although the aforementioned limitations exist, best-practice modeling methods were used, and key assumptions were validated by burn surgeons, thereby ensuring that the analytic conclusions are clinically valid and useful to the burn community.

CONCLUSIONS

The BEACON model was developed to facilitate evaluation of cost-effectiveness of new interventions within burn care, as measured by the clinical outcomes and relative costs for management of burns in the USA. As a first step, the

model was used to estimate the potential impact of treatment with ASCS for inpatient burn management for individual patient profiles and for burn centers, given current SOC practice patterns and the distribution of patient characteristics seen nationally. Overall, ASCS use reduces costs associated with the current treatment of severe burns, with greater savings seen in larger FT/mixed-depth burns and across all DPT burns. The cost savings are due to reductions in LOS, the number of operations required to close the burn wound, the donor site size, and associated donor site wound care.

Future analyses should seek to replace LOS parameters with real-world data for the USA across a broader range of patient profiles, and to obtain more data on costs and the timing of procedures from more hospitals to improve generalizability. Furthermore, information from individual burn centers could be integrated to identify how ASCS treatment is likely to impact costs and resource use given their current SOC practices. Finally, given that the model captures the full spectrum of burn care, future analyses could leverage the modeling framework to evaluate additional new interventions, alone or in combination with ASCS treatment, and thereby estimating the synergistic impacts of different interventions on the cost of burn care.

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Data availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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