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Compression Therapy Is Cost-Saving in the Prevention of Lower Limb Recurrent Cellulitis in Patients with Chronic Edema

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Abstract

Background: Cellulitis is a common and often recurrent infection that causes substantial financial burden and morbidity. Compression therapy reduces the risk of recurrent cellulitis episodes for adults with chronic edema; however, little is known about the cost-effectiveness of the intervention.

Methods and Results: A cost analysis was undertaken during a randomized controlled trial (RCT) involving 84 participants with lower limb chronic edema and a history of recurrent cellulitis. The intervention group received compression therapy and education, while the control group received education only. A clinical audit and survey were used to measure health service and patient resource use for (1) the most recent episode of cellulitis, and (2) compression therapy over 18 months. Australian reference costs were used to calculate cellulitis and compression therapy costs, and the mean expenditure in both the RCT groups. Of the 84 RCT participants, 43 were surveyed and audited on the cost of cellulitis, and 40 on the cost of compression therapy. The mean cost of a hospitalized and nonhospitalized episode of cellulitis was \$9071 and \$506 from a health service perspective, and \$4496 and \$1320 from a patient perspective. The mean cost of compression therapy per participant over 18 months was \$1905 and \$421 from health service and patient perspectives, respectively. During the RCT, the mean annual cost per participant was \$4972 in the experimental group and \$26,382 in the control group, giving a cost-saving of \$21,483 (95% confidence interval, 3136–48,176) per participant.

Conclusion: For patients with lower limb chronic edema and recurrent cellulitis, compression therapy is both efficacious and cost-saving. Trial Registration: ACTRN12617000412336.

Keywords: cellulitis, edema, lymphedema, recurrence, compression, cost

Introduction

CELLULITIS IS A common bacterial infection of the skin and subcutaneous tissue. It frequently reoccurs, with up to 47% of patients experiencing another infection within

3 years.¹ Cellulitis causes considerable financial burden for both patients and health services. Within the Australian emergency departments, cellulitis is the fourth most-common principal diagnosis, and the third most-common presentation requiring hospital admission.² In 2017–2018, there were

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128,129 emergency department presentations² and 72,150 hospital admissions³ for cellulitis, which cost the Australian health system ~90 million and 327 million AUD, respectively.^{3,4} Although only 7%–20% of cellulitis episodes require hospitalization,^{5,6} it has been reported that 83% of medical expenditure for cellulitis is related to hospital admissions.⁶

Chronic edema, where swelling persists for 3 or more months, increases the risk of cellulitis and cellulitis recurrence.^{1,7,8} There is a cyclical relationship between cellulitis and chronic edema, through which chronic edema increases the risk of cellulitis, and cellulitis can cause or worsen chronic edema.⁹ An international cross-sectional study of patients with lower limb chronic edema observed that the lifetime prevalence of cellulitis was 37%, with 16% suffering an episode in the past 12 months.¹⁰ Furthermore, controlled swelling was associated with reduced risk of cellulitis.¹⁰ Two linked clinical trials investigating the impact of prophylactic penicillin on cellulitis recurrence found that preexisting edema was present in 46% of participants with a history of cellulitis, and 59% of participants with recurrent cellulitis.^{11,12} Thus, as both chronic edema and cellulitis are common comorbid conditions, there is an urgent need to manage both conditions to improve health and relieve financial burden.

Compression therapy is the main modality used to manage chronic edema. Our recent randomized controlled trial (RCT) demonstrated that for patients with lower limb chronic edema experiencing recurrent cellulitis, compression therapy reduced the risk of further cellulitis episodes by 77% (hazard ratio, 0.23; 95% confidence interval [CI], 0.09–0.59; $p=0.002$).¹³ The RCT was designed to enroll 164 participants, however, it was stopped for efficacy following a planned interim analysis. As such, the trial had a total of 84 participants with a median follow-up time of 186 days instead of the planned 3 years.¹³

While we now know compression therapy is effective in preventing cellulitis, there is limited information on the associated costs involved. A retrospective cohort study conducted in Australia during the 2012–2013 financial year found that the mean hospital admission cost for an episode of cellulitis was \$5196 for inpatient admissions and \$5873 for hospital-in-the-home admissions. However, as patients hospitalized for cellulitis with concurrent edema have longer admissions,¹⁴ hospital costs are likely to be higher in this population. While we have some knowledge of hospital admission costs for cellulitis, information on the broader health service and patient costs relating to cellulitis is scarce. Furthermore, chronic edema is considered a hidden epidemic, despite being very common, and the expense to the health system and patient is largely unknown. Improved knowledge of these costs is essential to guide policy and resource allocation.

Compression therapy can break the cycle of edema and cellulitis, but there is no information on the cost-effectiveness of this intervention. As part of the clinical trial assessing the impact of compression therapy on cellulitis recurrence, a cost analysis was undertaken¹⁵ with the aim to describe and compare the cost of a recurrent cellulitis episode and the cost of compression therapy (over 18 months) from both health service and patient perspectives. Furthermore, the total costs arising in the experimental and control groups during the RCT were compared.

Methods

During the RCT, a cost analysis was undertaken to determine and compare the costs of cellulitis and compression therapy in patients with chronic edema who are experiencing recurrent cellulitis. Cellulitis and compression therapy costs were measured from both health service and patient perspectives. These costs were then applied to the experimental and control RCT groups, allowing comparison of costs.

RCT methods

The RCT protocol and results have been previously published,^{11,13} but are summarized briefly here. The primary outcome of the RCT was time to cellulitis recurrence. Following enrollment, participants were randomized to receive either education on the prevention of cellulitis (control group) or the same education plus compression therapy (experimental group).¹³ Trial group assignment was concealed, but after randomization therapists and participants were not blinded to treatment allocation for ethical and logistical reasons. To replicate standard clinical practice, participants were followed up six monthly, with the experimental group participants attending extra appointments to complete compression therapy with qualified lymphedema physiotherapists.

Following an episode of recurrent cellulitis, participants in the control group were crossed over to receive compression therapy. The trial was planned to continue for 3 years, or until 45 episodes of cellulitis occurred, and a planned interim analysis with stopping rules was completed after the 23rd episode of cellulitis. Although the trial was stopped early for efficacy, participants were followed up until 18 months postrandomization, allowing the cost of compression therapy to be measured across this time frame.

Participants

The cost analysis included two subsets of participants from the RCT who were surveyed regarding resource use: one group in relation to their most recent episode of cellulitis (cellulitis group), and the other regarding the use of compression therapy over 18 months (compression group). Participants were excluded from the cellulitis group if their most recent episode of cellulitis was over a year before enrollment in the trial.

Participants met the inclusion criteria for the RCT, which included having chronic edema and a history of two or more episodes of cellulitis in the same leg in the 2 years before trial referral. Exclusion criteria comprised the following: being <18 years of age; being medically unstable; receiving end-of-life care; having a chronic wound or wound requiring specialist treatment; being unable to tolerate compression; or already wearing effective compression garments regularly.

Outcomes

The primary outcomes of the costs analysis were the cost of an episode of cellulitis, and the cost of compression therapy over 18 months. Costs were categorized as health service or patient expenses. Paper surveys were developed to measure participant resource use and piloted on relevant patients before use in the trial. Participants were also asked to complete the Self-Administered Comorbidity Questionnaire, and to provide demographic information to allow description and comparison of the samples.

The cellulitis group participants were surveyed consecutively following enrollment into the trial. The survey captured resource use relating to their most recent episode of cellulitis, including medical appointment attendances, health service utilization, length of stay (LOS) in hospital, participant and family time away from work and leisure activities, duration that the participants required assistance with activities of daily living (ADLs), and use of antibiotics and pain relief. Medical records were audited at both the Australian Capital Territory (ACT) public hospitals to verify the details of reported hospital admissions. Participants' data were excluded if they reported hospitalization for cellulitis, but the medical record indicated that their admission was primarily for another condition.

The compression group participants were consecutively surveyed during a scheduled follow-up appointment after 18 months of compression therapy. The survey obtained information regarding participant and family time away from work and assistance provided for ADLs that were related to their compression therapy. Medical records were audited to determine the cost of prescribed compression garments, the number of appointments attended, and the number of compression bandages applied.

Resource costs

Australian national reference costs for the 2017/2018 financial year were applied to all resource items. Medications were costed using the Australian Pharmaceutical Benefit Scheme¹⁶ (PBS) with the assumption that pension age participants (≥ 66 years) paid the concession price, with the PBS funding the surplus.^{17,18} Health Information Services at the two local hospitals individually costed reported hospital admissions using the Australian Refined Diagnosis Related Groups¹⁹ (AR-DRGs). For the three reported hospital admissions that occurred outside of the ACT, admission costs were calculated using a standard algorithm that incorporates the 2017/2018 National Efficient Price, the average price weights for the two cellulitis AR-DRGs (J64A: Cellulitis, Major Complexity; and J64B: Cellulitis, Minor Complexity), and the hospital LOS. Emergency department presentations were costed based on the National Hospital Cost Data Collection Cost Report.⁴

General practitioner appointment costs were based on the Medicare Benefits Scheme (MBS) prices,²⁰ while hospital outpatient, pathology, and allied health appointments were based on the Independent Hospital Pricing Authorities' (IHPA) Tier 2 Non-Admitted Services Classification prices.³ The national average patient cocontribution was used for general practitioner and outpatient appointments.²¹ Time off work was priced on the average Australian weekly earnings reported by the Australian Bureau of Statistics.²² The National Disability Insurance Scheme price guide²³ was used to assign costs for assistance with ADLs. For participants reporting they required both assistance with ADLs and family to take time away from work, family time off work was subtracted from the number of days ADL assistance was provided to avoid doubling up on costs.

Travel for all appointments was assumed to be a 10 km round trip, with the price per km based on the Australian Tax Office's work-related car expenses.²⁴ The compression

bandage and compression garment costs were recorded for each participant. A full list of the resource costs can be found in Supplementary Appendix Table S1.

The health service perspective included all costs related to government-funded health services, being hospital admissions, emergency department presentations, public outpatient services, and MBS and PBS rebates for appointments and medications. The patient perspective included all costs incurred by the participants and their family, including costs relating to appointments, travel, medications, assistance with ADLs, and the inability to work. Leisure time missed was recorded but not priced. Tables 2 and 3 show which costs were assigned to either the health service perspective or the patient perspective.

Descriptive analysis

Resource use and associated costs were reported as mean and standard deviation (SD). Costs were calculated and presented using Australian reference costs for the 2017–2018 financial year, with high-level costs being translated into US dollars (USD) using the average conversion rate for that financial year²⁵ to allow easier international comparison. Although some trial data collection and outcomes occurred before and after this time frame, due to the limited follow-up duration of the trial, discounting was considered redundant.

Mean total costs for compression therapy were given over 18 months, as well as over 0–6 and 7–18 months to show how treatment costs change over time. Mean total costs for cellulitis were also presented separately for hospitalized and nonhospitalized participants due to the large difference in resource use for these participants. The sensitivity analysis assessed the impact of outlier values. Winsorization was used, with all variable outliers over 3.29 SDs from the mean being replaced with the closest nonoutlier value.²⁶ All analyses were performed using R software (version 3.6.0).

Application of measured costs to the RCT

The outcomes from the costs analysis were used to calculate the total cost of the intervention and the cellulitis episodes for each trial group during the RCT. For both the RCT groups (experimental and control), the intervention cost was calculated for each participant based on the individual follow-up time frame, before being censored for an episode of cellulitis or the trial's cessation. For the experimental group participants, their follow-up duration within the initial 6-month period, and the subsequent 7- to 18-month period was costed separately based on mean compression therapy costs for these periods, before being summated. For the control group, the intervention cost was based on the number of appointments attended for education on cellulitis prevention. Hospitalized and nonhospitalized episodes of cellulitis occurring during the trial were costed separately.

Due to the large discrepancy in follow-up time between the two trial groups arising from more control group participants being censored following cellulitis episodes, the trial costs were presented per participant per year to allow direct comparison. Due to the small sample size and skewed data, non-parametric bootstrap sampling with 1000 samples was used to calculate the mean annual cost per participant for each trial group, and subsequently the mean intergroup difference and 95% CIs.

Results

Participant characteristics

Data were obtained on the cost of compression therapy for 40 participants (compression group) and the cost of an episode of cellulitis for 43 participants (cellulitis group), with 18 participants contributing data to both groups. The majority of participants surveyed regarding compression therapy costs were those randomized to the experimental group, however, three control group participants who completed 18 months of compression therapy following crossover were also surveyed. Of participants surveyed on the cost of cellulitis, 21 were from the experimental group, and 22 were from the control group. The patient demographics of the compression and cellulitis groups in the cost analysis are shown in Table 1, and are similar to those of the RCT participants.¹³

For both groups, the mean number of cellulitis episodes per leg in the 2 years before referral to the trial was 2, the mean Self-Administered Comorbidity Questionnaire Score was 9 (out of a maximum score of 45), and obesity was the most common reported factor contributing to chronic edema. For the compression group, the mean age and body mass index (BMI) were 66 (SD: 12.9) and 39 (SD: 9.9), respectively, and chronic edema was bilateral in 78% of participants. The cellulitis group's mean age and BMI were 64 (SD: 14) and 42 (SD: 9.6), and 81% had bilateral chronic edema.

Cellulitis group costs

The resource use and costs associated with an episode of cellulitis are shown in Table 2. Of the 43 cellulitis group participants, 27 (63%) presented to the emergency department, 24 (56%) were admitted to hospital, 41 (95%) had one or more general practitioner appointments, 23 (53%) required nonprescription pain relief, and 15 (35%) required prescription pain relief for their most recent episode of cellulitis. The total mean cost for a nonhospitalized episode of cellulitis was \$1826, whereas the mean cost for a hospitalized episode was 7.4 times higher, being \$13,567.

Health service costs. The mean cost to health services for an episode of cellulitis was \$5287 (\$4289 USD). However, on average, cellulitis episodes requiring hospitalization cost \$9071, which is almost 18 times higher than nonhospitalized episodes, which cost an average of \$506. The highest cellulitis-related costs were for hospital utilization, with emergency department presentations costing a mean of \$640 per participant and the average hospital admission costing \$7057 per hospitalized participant. General practitioner and other health care appointments were the next biggest contributor to cost, with antibiotics and pain relief medications adding comparatively minimal expense. Resource use and costs were generally positively skewed (Supplementary Appendix Table S2), with a few participants with substantially higher resource utilization increasing mean values. For example, 22 of 24 hospital admissions cost between \$3300 and \$7500, however, 2 admissions costing more than \$24,000 resulted in the mean and median costs for hospitalization being \$7057 and \$5831.

Patient costs. The mean patient cost for an episode of cellulitis was \$3092 (\$2509 USD), with hospitalized patient

TABLE 1. BASELINE CHARACTERISTICS OF THE PARTICIPANTS

<i>Characteristic</i>	<i>Compression (N=40)</i>	<i>Cellulitis (N=43)</i>
Female sex, <i>n</i> (%)	19 (48)	17 (40)
Age		
Mean (SD)	66 (12.9)	64 (14)
Median (IQR)	69 (55–75)	65 (52–73)
Pension age (≥66 years), <i>n</i> (%)	23 (58)	21 (48)
Spousal status (single or <i>de facto</i>)		
<i>De facto</i> , <i>n</i> (%)	28 (70)	28 (65)
Body mass index		
Mean (SD)	39 (9.9)	42 (9.6)
Median (IQR)	39 (31–45)	41 (34–48)
Self-Administered Comorbidity Questionnaire		
Mean (SD)	9 (4.4)	9 (5.2)
Median (IQR)	9 (5–11)	9 (5–12)
Chronic edema: bilateral, <i>n</i> (%)	31 (78)	35 (81)
Duration of edema, <i>n</i> (%)		
1–5 Years	17 (43)	13 (30)
>5 Years	23 (58)	30 (70)
Episodes of cellulitis per leg in 2 years before trial referral		
Mean (SD)	2 (1.4)	2 (1.3)
Median (IQR)	2 (0–2)	2 (0–2)
Hospital admission for cellulitis in 2 years before trial referral		
Mean (SD)	1 (0.9)	1 (0.7)
Median (IQR)	1 (0–1)	1 (0.5–1)
Prophylactic antibiotics, <i>n</i> (%)	2 (5)	2 (5)
Factors contributing to chronic edema, <i>n</i> (%)		
Obesity	26 (65)	30 (70)
Surgery/trauma	14 (35)	13 (30)
Venous hypertension	11 (28)	14 (33)
Immobility	4 (10)	4 (9)
Primary lymphedema	3 (8)	3 (7)
Cancer	0 (0)	0 (0)
Other	6 (15)	5 (12)
Comorbidities, <i>n</i> (%)		
Tinea pedis	14 (35)	15 (35)
Diabetes	10 (25)	14 (33)
Chronic venous insufficiency	10 (25)	13 (30)
Congestive heart failure	7 (18)	11 (26)

IQR, interquartile range; SD, standard deviation.

costs being \$4496, compared with \$1320 for nonhospitalized patients. The highest costs were for patient and family time off work and assistance with ADLs, and general practitioner and other health care appointments were the next biggest contributor. Patient and family time off work, assistance with ADLs, and the overall combined resource costs were positively skewed (Supplementary Appendix Table S2). A total of 17 (40%) participants were employed, with 13 reporting they required time off work. Those who were employed took a mean of 15 days off work (range 0–45 days). Furthermore, 26 (60%) participants needed assistance with ADLs or family to take time off work.

TABLE 2. MEASURED RESOURCE USE AND COST FOR RECURRENT CELLULITIS EPISODES

Measured resources (per episode of cellulitis)	Cellulitis episodes, n=43			
	Number, mean (SD)	Health service costs (\$), mean (SD)	Patient costs (\$), mean (SD)	Total cost (\$), mean (SD)
Hospital utilization				
Emergency department Presentations	1 (0.6)	640 (516)	—	640 (516)
Hospital LOS for cellulitis episodes requiring admission (days) ^a	8 (7.9)	7057 (5883)	—	7057 (5883)
Health care appointments				
General practitioner	3 (3.1)	105 (116)	106 (117)	211 (233)
Other	2 (4.9)	614 (1208)	66 (144)	680 (1296)
Antibiotics (prescriptions purchased)	2 (1.3)	11 (15)	34 (29)	46 (27)
Pain relief (days used)				
Prescription	5 (8.6)	8 (22)	20 (47)	28 (55)
Nonprescription	5 (8.4)	—	4 (7)	4 (7)
Travel for health care (number of trips)	7 (6.7)	—	43 (44)	43 (44)
Assistance with ADLs ^b (days)	8 (11.3)	—	644 (991)	644 (991)
Time off work (days)				
Patient	6 (11.2)	—	1945 (3715)	1945 (3715)
Family	1 (2.3)	—	238 (758)	238 (758)
Leisure time missed (days)				
Patient	14 (18.7)	—	—	—
Family	4 (8.9)	—	—	—
Combined resources per episode of cellulitis				
All episodes (n=43)	—	5287 (6344)	3092 (4483)	8379 (8442)
Hospitalized episodes (n=24)	—	9071 (6254)	4496 (5493)	13,567 (7944)
Nonhospitalized episodes (n=19)	—	506 (842)	1320 (1551)	1826 (2106)

All costs are in 2017–2018 Australian dollars. The average exchange rate for the 2017–2018 financial year: \$1 AUD=\$0.8113 USD.²⁵

^aLOS calculations only included patients who were hospitalized (n=24).

^bFor ADL assistance calculations, reported family time away from work was subtracted from the reported number of days that ADL assistance was required to avoid doubling up on costs.

ADLs, activities of daily living; LOS, length of stay.

Compression group costs

The mean resource use and costs for compression therapy are shown in Table 3. Of the 40 compression group participants, 23 (58%) received compression bandaging to reduce their edema before the provision of compression garments. These participants attended extra appointments, usually early on in their treatment course. The total mean cost for compression therapy over 18 months was \$2326 (\$1887 USD), with \$1229 attributed to the first 6 months and \$1117 to the following 12 months. These figures indicate that compression therapy is more expensive during the initial intensive treatment phase, and after 6 months, ongoing maintenance costs for compression therapy are reduced for both the health service and the patient.

Health service costs. Health service costs for compression therapy are greatest in the first 6 months of treatment, after which ongoing maintenance costs were 57% lower. The mean health service cost of compression therapy was \$1905 (\$1546 USD) per participant over 18 months, with \$1038 of that expenditure occurring within the first 6 months and \$887 occurring in the following 12 months. The greatest expense was for lymphedema service appointments, being \$1045 over 18 months, however, appointment costs reduced substantially after the initial 6-month period. Compression garments were the second biggest expense, costing \$795 per participant over

18 months. For the 65% of participants for whom compression garments were government funded, the mean cost of compression garments was 1.5 times higher, being \$1223 per participant. Participants with unilateral edema cost 36% less than those with bilateral edema.

Patient costs. The mean patient cost for compression therapy was \$421 (\$342 USD) per participant over 18 months, with the first 6 months costing \$191 and the following 12 months costing \$230. Although only 35% of compression garments were patient funded, they were still the greatest contributor to the overall cost for participants. The mean patient cost for compression garments was \$242, with \$118 being spent in the first 6 months and \$124 in the following 12 months. The mean patient cost for compression garments was much higher among self-funding participants, being \$691 over 18 months. Assistance with ADLs and time off work costs were positively skewed, with the mean sitting above the interquartile range (Supplementary Appendix Table S3).

Only four participants required up to 1 day off work, and two participants required assistance with ADLs for compression therapy. Of these two participants, one required 10 minutes of assistance per day over the 18-month period to apply and remove compression garments, which substantially positively skewed the total patient expenditure, particularly for those with unilateral edema.

TABLE 3. MEASURED RESOURCE USE AND COST FOR COMPRESSION THERAPY OVER 18 MONTHS

Measured resources (per participant)	Compression therapy, n=40			
	Number, mean (SD)	Health service costs (\$), mean (SD)	Patient costs (\$), mean (SD)	Total cost (\$), mean (SD)
Garment sets purchased				
0–6 Months	2 (0.2)	292 (259)	118 (189)	410 (180)
7–18 Months	3 (1.2)	503 (543)	124 (205)	627 (456)
Compression bandages applied				
0–6 Months	3 (3.1)	59 (73)	—	59 (73)
7–18 Months	0 (0.8)	6 (19)	—	6 (19)
Lymphedema service appointments				
0–6 Months	4 (2.1)	686 (325)	—	686 (325)
7–18 Months	2 (1.4)	378 (223)	—	378 (223)
Travel for health care (number of trips)				
0–6 Months	4 (2.1)	—	29 (14)	29 (14)
7–18 Months	2 (1.4)	—	16 (9)	16 (9)
Assistance with ADLs ^a (hours)				
0–6 Months	1 (4.8)	—	37 (219)	37 (219)
7–18 Months	2 (9.6)	—	74 (437)	74 (437)
Time off work (days)				
Patient	0 (0.2)	—	23 (78)	23 (78)
Family	0 (0)	—	0 (0)	0 (0)
Leisure time missed (days)				
Patient	0 (1.4)	—	—	—
Family	0 (0.1)	—	—	—
Combined resources per participant All participants (n=40)				
0–18 Months	—	1905 (1097)	421 (825)	2326 (1169)
0–6 Months	—	1038 (539)	191 (320)	1229 (582)
7–18 Months	—	887 (708)	230 (515)	1117 (737)
Participants with unilateral edema (n=9)				
0–18 Months	—	1322 (592)	740 (1548)	2062 (1566)
Participants with bilateral edema (n=31)				
0–18 Months	—	2074 (1158)	328 (455)	2403 (1046)

All costs are in 2017–2018 Australian dollars. The average exchange rate for the 2017–2018 financial year: \$1 AUD=\$0.8113 USD.²⁵

^aFor ADL assistance calculations, reported family time away from work was subtracted from the reported number of days that ADL assistance was required to avoid doubling up on costs.

Sensitivity analysis

After winsorizing all identified outlier values, no mean total health service costs changed by more than 5%. For an episode of cellulitis, the average patient cost among hospitalized participants changed from \$4496 to \$4250 (5% change). For compression therapy, the patient cost over 18 months reduced from \$421 to \$317 (25% change). This change was particularly large for participants with unilateral edema, where the average patient cost for compression therapy over 18 months reduced from \$740 to \$315 (57% change). This reduction in the cost of compression therapy for patients was related to one participant with unilateral edema who required high levels of assistance with ADLs (daily assistance for garment application and removal).

RCT outcomes and costs

RCT outcomes. During the RCT, 23 episodes of cellulitis occurred before the interim analysis and subsequent stopping of the trial for efficacy. Six episodes of cellulitis occurred in the experimental group, and 17 occurred in the control group, giving an incidence rate ratio of 0.21 (95% CI:

0.08–0.55, *p*=0.0005). Of those participants who experienced cellulitis, three and six required hospital admission in the experimental and control groups, respectively.

Measured costs applied to the RCT. The mean annual costs per participant for both the experimental and control groups are shown in Table 4. The mean annual health service cost per person was \$3616 in the experimental group and \$14,527 in the control group, giving a mean intergroup difference of \$10,963 (95% CI, \$1000–\$24,590). The mean yearly patient costs were \$1356 and \$11,856 per person in the experimental and control groups, respectively, providing a mean intergroup difference of \$10,521 (95% CI, \$1806–\$24,933). The mean total (health service and patient) annual cost per person was \$4972 (\$4034 USD) for the experimental group and \$26,382 (\$21,404 USD) for the control group, giving an intergroup difference of \$21,483 (95% CI, \$3136–\$48,176). Therefore, the mean total expenditure per participant was 81% lower in the experimental group. This reflects the higher incidence and costs related to cellulitis management in the control group (90% of total costs) versus the experimental group (48% of total costs).

TABLE 4. MEASURED COSTS APPLIED TO THE RANDOMIZED CONTROLLED TRIAL

Perspective	Mean annual cost per participant (\$)		Mean intergroup difference, \$ (95% CI)
	Experimental group, n=41	Control group, n=43	
Health service	3616	14,527	10,963 (1000–24,590)
Patient	1356	11,856	10,521 (1806–24,933)
Total (health+patient)	4972	26,382	21,483 (3136–48,176)

The mean annual cost per participant, and the mean intergroup difference and 95% CI were calculated using nonparametric bootstrap sampling with 1000 samples. All costs are in 2017–2018 Australian dollars. The average exchange rate for the 2017–2018 financial year: \$1 AUD=\$0.8113 USD.²⁵

CI, confidence interval.

Discussion

This is the first analysis to demonstrate that compression therapy is a cost-saving treatment for preventing cellulitis in patients with recurrent cellulitis and comorbid lower limb chronic edema. While this trial assessed costs in Australian currency (AUD), the cost-savings presented may be proportionate to other countries with similar health systems. Daily costs incurred during the trial were 81% lower in the experimental group than in the control group. Compared with the control group, health service and patient-specific costs in the experimental group were 75% and 89% lower, respectively. These results provide strong justification for health care systems to invest in compression therapy for these patients, as the benefits are clear from both health and economic perspectives.

During the RCT, total expenditure on cellulitis was calculated to be \$147,648, of which 83% related to hospitalized participants. The reported mean LOS for cellulitis-related hospitalizations varies from 4.7 to 12.1.^{5,6} The mean and median hospital LOS of 8 and 6.5 observed in the cellulitis group is on the higher end of reported Australian statistics,^{3,27} however, an above-average LOS in this population was expected as research has shown that edema is a risk factor for increased LOS for cellulitis-related admissions.¹⁴ In addition, hospital admissions have been observed to be longer for recurrent versus primary episodes of cellulitis.²⁸ The increased LOS found in this population, and the high expenditure related to hospitalization, highlights the importance of preventing cellulitis infections in this patient group.

Total expenditure on compression therapy during the RCT was \$50,551 across 41 participants, with health services funding 84% and patients funding the remaining 16%. Government funding schemes differ between countries, and therefore, the proportion of compression therapy expenditure funded by health services may also vary. Health service and patient costs for compression therapy were substantially higher in the first 6 months compared with the following 12 months. This was expected as initiating compression therapy involves multiple appointments for education, and for measurement and fitting of compression garments. Furthermore, some patients also require a series of compression bandages to reduce limb volume before optimal measurement and fit of compression garments. Although these interventions may be required on an ongoing basis to manage chronic edema, the frequency and consequently cost are usually much lower after the initial intensive treatment phase. After the initial 6-month period, the measured 12-month cost of compression therapy per patient, being \$887 and \$230

from health service and patient perspectives, respectively, may be indicative of ongoing annual costs. Thus, provision of compression therapy has high upfront costs, but ongoing maintenance costs appear to be lower.

In addition to preventing cellulitis, compression therapy provides many other health benefits for patients with chronic edema or venous disease. Compression therapy is a primary treatment modality for both chronic edema²⁹ and chronic venous insufficiency,³⁰ a common condition³¹ and a known cause of chronic edema.³² Compression therapy has been found to increase the rate of healing for venous ulcers,³³ reduce the rate of venous ulcer recurrence,³⁴ reduce limb volume,¹³ improve skin condition,²⁹ improve quality of life for patients with chronic venous disease,³⁵ and may prevent post-thrombotic syndrome.³⁶ Furthermore, it is used to manage conditions that mimic cellulitis, such as lipodermatosclerosis.³⁷ Therefore, the health and financial benefits of compression therapy for patients with chronic edema and cellulitis may be greater than that found in our trial. Thus, we believe our analysis presents a conservative perspective on the cost-savings of compression therapy in these patients.

A limitation of this trial was the early cessation for efficacy, as this limited the sample size and duration of the follow-up period. Although outliers were identified, they were accurate, and we believe they would occur in standard practice. Therefore, although we assessed their impact in the sensitivity analysis, their inclusion in the primary analysis is appropriate.

This cost analysis indicates that compression therapy is cost-saving from both a patient and health service perspective for patients with chronic edema and recurrent cellulitis. The health and economic benefits demonstrated by this research provide clinicians, health services, and policy makers with strong justification to support the funding of compression therapy in the prevention of lower limb recurrent cellulitis. Further research with more participants and a longer follow-up duration will allow for a robust analysis of its longer term cost-effectiveness.

Ethics Approval

The study was approved by the ACT Health, Calvary Public Hospital Bruce, and the University of Canberra Human Research Ethics Committees. The trial was registered before commencement (ACTRN12617000412336). All participants were given written and verbal information on the trial, and signed a consent form before participating in the trial.

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Authors' Contributions

E.W.: trial design and implementation, funding acquisition, contribution of original material, analysis and interpretation of data, creating initial draft, and approving the final article. V.M. and B.B.: trial implementation support, contribution of original material, and interpretation of data. T.N.: trial design input, trial implementation support, and statistical support. V.M., B.B., T.N., F.B., and E.P. provided supervision, contributed to refinement of the article, and approved the final article.

Author Disclosure Statement

The authors have no competing interests to declare.

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Calvary Public Hospital Bruce was the primary sponsor, funding clinician time to initiate and manage the trial. Haddenham Healthcare was a secondary sponsor, providing two sets of free compression garments for each trial participant. Haddenham Healthcare had no role in designing this trial, trial implementation, analyses, data interpretation, or publication or dissemination of results. Haddenham Healthcare had no access to trial data.

Supplementary Material

Supplementary Appendix Table SA1
Supplementary Appendix Table SA2
Supplementary Appendix Table SA3

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