Decreased mobility, lack of social support, haemosiderosis and use of antidepressant medications may predict recurrent venous leg ulcers within 12 months of healing: A prospective longitudinal study

KJ Finlayson, PhD\textsuperscript{1,2}, CN Parker, PhD\textsuperscript{1,2}, C Miller, PhD\textsuperscript{3}, HE Edwards, PhD\textsuperscript{1,2} and J Campbell, PhD\textsuperscript{4}

Abstract

\textbf{Aim:} To identify clinical, medical and psychosocial predictors of venous leg ulcer recurrence within 12 months of healing. \\
\textbf{Methods:} A multi-site study was conducted in Australia in community and hospital outpatient settings. Adults with venous leg ulcers were recruited within 4 weeks of healing and data were collected on preventative treatments and health, medical, clinical and psychosocial factors. Follow-up data on recurrences were collected every 3 months until ulcer recurrence, or until 12 months after healing pending which occurred first. Factors associated with time to recurrence were analysed using a Cox proportional hazards regression model. \\
\textbf{Design:} Secondary data analysis of a multi-site, prospective longitudinal study to validate a risk assessment tool for recurrence. \\
\textbf{Results:} A sample of 143 participants was recruited (51\% male, $M_{\text{age}} = 73$ years, SD 13.6). Almost half (49.6\%) had an ulcer recurrence within 12 months, with a mean time to ulcer recurrence of 37 weeks ($SE = 1.63$, 95\% CI 33.7–40.1). Factors measured at the time of healing that were significant independent predictors of recurrence were: prescribed antidepressant medications ($p = .035$), presence of haemosiderosis ($p = .006$), decreased mobility (longer sitting times) ($p = .007$) and lower social support scale scores ($p = .002$). Participants who wore compression systems providing 20 mmHg or higher for at least 5 days/week were less likely to recur, although not reaching statistical significance ($p = .06$). \\
\textbf{Conclusion:} Results provide evidence that antidepressant medications, haemosiderosis, decreased mobility and lack of social support are risk factors associated with ulcer recurrence; therefore, these variables are modifiable and could guide early intervention.

Keywords \\
Recurrence, venous leg ulcers, predictors, prospective longitudinal study

Introduction

Chronic venous insufficiency develops as a result of venous hypertension, venous reflux and/or calf muscle pump incompetence, leading to inflammatory changes and ulceration.\textsuperscript{1} Clinical manifestations may include leg pain, oedema, ankle flare, haemosiderosis, atrophie blanche, venous eczema and lipodermatosclerosis.\textsuperscript{2,3} Venous leg ulcers are open lesions or wounds that occur on the lower leg between the knee and ankle joint and tend to occur on lateral and medial aspects of the leg in the presence of venous insufficiency.\textsuperscript{2}
Venous leg ulcers are estimated to affect around 1–2% of adults and increase in incidence with age, with reported prevalence of 3% of those aged over 80 years, and a doubling of incidence in adults over 65 years compared to younger adults. The prevalence of venous leg ulcers and venous insufficiency is expected to increase further as the population ages. Venous ulcers are the most common type of ulceration in the lower extremity, accounting for up to 70% of all leg ulcers.

In the United Kingdom (UK), it is estimated that 1 in 500 people have a venous leg ulcer, costing an estimated £400–600 million in health care costs. In the United States (US), an estimated 500,000–600,000 people have a venous leg ulcer costing nearly US$1 billion in treatment costs annually. In Germany, the mean annual cost of venous leg ulcer care was €9569, although this study published in 2010 is likely an underestimate of current cost. The global cost of venous leg ulcer treatment is expected to reach US$4.8 billion by 2026. In Australia, the weekly cost of guideline-based optimal care was estimated to be Au$295.00, with the total direct cost of treating venous leg ulcers (in hospital and residential aged care settings) estimated to be US$802.55 million, although this estimate did not include the cost in community settings such as general practitioner visits.

There is significant morbidity resulting from venous leg ulcers, which are associated with moderate to severe pain in up to half of adults with the condition, sleep disturbance, lower limb oedema, decreased mobility, decreased quality of life and significant health care costs. Complications of venous disease also encompass considerable morbidity and occasionally mortality, including the impacts from dermatitis, atrophie blanche, lipodermatosclerosis, cellulitis and sepsis, and malignancy. Wound healing can take many months or even years, involving burdensome therapies and costs; compounding this challenge is frequent recurrence once healing has been achieved. Overall, venous leg ulcer recurrence rates are high, reported as ranging from 50% to 78%, while rates within 12 months of healing are reported as ranging from 33% to 57%. Despite the high recurrence rates, health professionals have limited evidence on risk factors and early signs predicting venous leg ulcer recurrence. Previous studies have found that a history of deep vein thrombosis, deep vein reflex, multiple past ulcers, longer ulcer duration, reduced lower limb or ankle movement and increasing age are risk factors for recurrence. There are few studies, however, that have examined predictors of recurrence and some rely on retrospective analysis which can limit the types of variables that can be examined as predictors of recurrence.

The aim of this study was to identify clinical, medical and psychosocial predictors of ulcer recurrence within the first year after healing.

**Methods**

**Design**

Secondary analysis of data collected in a prospective longitudinal study was undertaken to identify predictors of venous leg ulcer recurrence. Funding for the study was received from the Wound Management Innovations Collaborative Research Centre (Australia). Ethics approval for the study was received from each participating institution’s Human Research Ethics Committee.

**Sample**

Study sites included a nurse practitioner-led community-based wound clinic (Queensland (QLD), Australia), medical practitioner-led outpatient chronic wound clinic (QLD, Australia), and two community nursing services (QLD, Australia; Victoria, Australia). Inclusion criteria were a healed lower leg ulcer of primarily venous aetiology which was classified as a wound that had maintained 100% epithelialisation of the wound bed for at least 14 days and an Ankle Brachial Pressure Index ≥0.8 and <1.3. Persons were excluded from this study if they had cognitive impairment or were unavailable for regular data collection during the study period.

Data for this study were derived from a risk assessment validation study that recruited 143 participants. This sample size exceeds the requirements for a Cox proportional hazards regression analysis, using a power calculator and parameters of 80% power, 5% Type 1 error rate, and expected event rate of 0.5, (n = 122).

**Procedure**

Potential participants were provided with the study information by the attending clinician. Research assistants contacted the person to confirm eligibility and interest in participating, obtained written informed consent and attended to all subsequent data collection. Data collection was attended either in a clinic or home-based setting as per their current or prior to healing service provision arrangements. Telephone follow-up was conducted if the participant missed a face-to-face visit.

Data collection involved a face-to-face visit with the participant and was attended at baseline and every 3 months for a 12 month follow-up period, or until ulcer recurrence occurred, if this happened prior to 12 months. Research assistants completed training regarding the study procedures to standardise research practices across sites and site fidelity checks were undertaken by the study investigators. The data collection process followed previously tested processes in prior studies by this research team.
**Data collection and measures**

The primary outcome measure was time to ulcer recurrence. Venous leg ulcer recurrence was defined as a new area of skin or tissue loss that was in the same lower leg as a previous venous leg ulcer and was diagnosed as venous in aetiology by a clinician. Baseline data included information on sociodemographic characteristics, medical history and co-morbidities, Body Mass Index (BMI), mobility, venous history (including previous venous surgical treatments) and prior ulcer history. As data collection occurred in community-based settings, including home care by community nursing services, the facilities and resources to obtain data on the degree of venous insufficiency were unavailable.

Clinical appraisal during data collection included assessing the participant’s level of lower leg oedema, venous eczema and skin condition, ankle brachial pressure index, ankle and calf circumferences (to calculate calf/ankle ratio), and ankle range of motion (measured via a goniometer). The research assistant further documented the participant’s concordance with preventive strategies such as compression therapy use, including type/level of compression mmHg and duration of use; leg elevation (above the level of the heart, frequency, duration); conduct of ankle and calf exercises (frequency and duration); and skin care.

At each data collection, participants completed a self-report inventory that included measures of physical activity (Yale Physical Activity Scale (YPAS)\(^{26}\)), symptoms of malnutrition (Malnutrition Screening Tool\(^{25}\)), wellbeing and general health (Short Form Health Survey (SF-12)\(^{28}\)), depressive symptoms (Geriatric Depression Scale (GDS)\(^{29}\)), perceptions of social support (MOS Social Support\(^{30}\)), and perceptions of self-efficacy (General Self-Efficacy Scale\(^{11}\)).

**Analysis**

Data were analysed with the IBM SPSS Statistics for Windows (Version 23.0) software. Descriptive statistics were used to describe sample variables (means and standard deviations or medians and interquartile range as appropriate for continuous variables; and frequencies and percentages for categorical variables). A \(p\) value less than .05 was considered statistically significant. A survival analysis approach was used to identify factors associated with time to ulcer recurrence, using Kaplan Meier survival curves for bivariate testing and a Cox proportional hazards multivariable regression model to control for potential confounders and identify significant relationships with ulcer recurrence.

**Results**

A sample of 143 participants was recruited (51% male, \(M_{\text{age}}\) 73 years, \(SD = 13.6\)). Sixteen participants were unable to complete the full 12 months follow-up, due to illness (\(n = 4\)), death (\(n = 1\)), change of address (\(n = 1\)), withdrew from the study (\(n = 2\)) or were lost to follow-up (\(n = 8\)). The most frequent comorbid conditions were hypertension (66%) and osteoarthritis (56%), and most frequent signs of chronic venous disease were varicose veins (74%), history of recurrent leg ulcers (66%), and haemosiderosis (62%). Further details of the sample characteristics are shown in Table 1.

Half (49.6%, 63/127) experienced an ulcer recurrence within 12 months, with a mean time to ulcer recurrence of 37 weeks (SE 1.63, 95% CI 33.7–40.1). Males had slightly shorter mean times to recurrence of 33.5 weeks (SE 2.31, 95% CI 29–38) compared to females who recurred in a mean time of 40.5 weeks (SE 2.22, 95% CI 36–45), \((p = .051)\).

Looking at preventative strategies, within the sample of 143 participants 49% moisturised the skin on their legs at least once/day, 60% moved around on their feet for at least 3 h/day (as measured by the YPAS Moving Index), 41% elevated their legs for at least 30 min/day and 65% wore compression of 20 mmHg or more, for five or more days a week. Participants who wore compression of 20 mmHg or more for five or more days a week had a mean longer time to recurrence (39.3 weeks, 95% CI 35–43) than those who did not wear this level of compression (33.6 weeks, 95% CI 28–39, \(p = .091\)).

Although not statistically significant, participants who required mobility aids had a mean shorter time to recurrence (33.7 weeks, SE = 2.62, 95% CI 29–39) than those who did not require a mobility aid (40.4 weeks, SE = 1.91, 95% CI 37–44, \(p = .055\)). Participants who used non-steroidal anti-inflammatories had a longer time without recurrence (mean 47.7 weeks, SE = 2.08, 95% CI 44–52) compared to those who did not take non-steroidal anti-inflammatories (mean 34.8 weeks, SE = 1.85, 95% CI 31–38, \(p = .035\)).

The following factors were not significantly related to recurrence: age, living alone, income, history of cardiac disease and use of steroids. History of either lower limb surgery or leg trauma and history of deep vein thrombosis were also not related to recurrence, along with lower limb characteristics such as oedema, venous eczema, atrophie blanche, lipodermatosclerosis and range of ankle motion (see Table 2). However, presence of haemosiderosis was associated with higher risk of recurrence, while elevating the legs for at least 30 min/day and higher levels of social support were significantly associated with decreased risk of ulcer recurrence (see Table 2).

To examine these data further a multivariable Cox proportional hazards regression was undertaken (see Table 3) to control for potential confounding and to identify factors independently associated with ulcer recurrence. Four factors were identified as significantly related to recurrence; the presence of haemosiderosis in the affected leg, use of antidepressants and higher YPAS sitting index scores were
Table 1. Characteristics of the study sample.

| Factor                                      | Total = 143 |
|---------------------------------------------|-------------|
| Age (years), M (SD)                         | 73 (13.6)   |
| Body mass index (BMI), M (SD)               | 32 (10.1)   |
| Gender n (%)                                |             |
| Male                                        | 73 (51%)    |
| Female                                      | 70 (49%)    |
| Lives alone n (%)                           | 63 (44%)    |
| Income N (%)                                |             |
| Pension; aged/disability/veteran            | 110 (77%)   |
| Employed/self-funded/retired                | 32 (23%)    |
| Mobilise with aid n (%)                     | 67 (47%)    |
| MSTa score ≥ 2 (at-risk)                    | 14 (10%)    |
| Medical history n (%)                       |             |
| Hypertension                                | 94 (66%)    |
| Osteoarthritis                              | 79 (56%)    |
| Cardiac disease                             | 65 (46%)    |
| Diabetes                                    | 31 (22%)    |
| Cardiovascular accident                     | 22 (15%)    |
| Rheumatoid arthritis                        | 12 (8%)     |
| Varicose veins in study leg                 | 102 (74%)   |
| Surgery or trauma to study leg              | 63 (46%)    |
| Deep vein thrombosis in study leg           | 25 (18%)    |
| BMI ≤ 22 (kg/m²)                            | 16 (11%)    |
| History of previous leg ulcers (>1)         | 95 (66%)    |
| Haemosiderosis                              | 89 (62%)    |
| Atrophie blanche                            | 40 (28%)    |
| Medications n (%)                           |             |
| Antihypertensives                           | 94 (66%)    |
| Anticoagulants                              | 75 (52%)    |
| Diuretics                                   | 55 (39%)    |
| Antidepressants                             | 26 (18%)    |
| Respiratory                                 | 24 (27%)    |
| Non-steroidal anti-inflammatories           | 23 (16%)    |
| Steroids                                    | 15 (11%)    |
| Clinical lower limb characteristics n (%)    |             |
| Oedema                                      | 36 (25%)    |
| Lymphoedema                                 | 7 (5%)      |
| Venous eczema                               | 14 (10%)    |
| Haemosiderosis                              | 89 (62%)    |
| Atrophie blanche                            | 40 (28%)    |
| Lipodermatosclerosis                        | 15 (10%)    |
| Lifestyle/preventive strategies n (%)       |             |
| Current smoker                              | 13 (9%)     |
| Skin care – moisturised at least once/day   | 64 (49%)    |
| YPASb moving index: Moving on feet at least 3/h per day | 85 (60%) |
| Elevating legs for 30 min/day               | 57 (41%)    |
| Compression ≥ 20 mmHg for five or more days/weeka | 89 (65%) |
| Total YPAS activity index, mean (SD.)       | 32 (22.8)   |
| Psychosocial measures                       |             |
| Total GDSc score, med. (IQR)                | 1.09 (2.0)  |
| Total MOS social support scored, M(SD)      | 67.1 (28.8) |
| General self – efficacy scale score, M(SD)  | 31.9 (5.63) |
| SF-12 physical component score, M(SD)       | 43.2 (10.2) |
| SF - 12 mental component score, M(SD)       | 49.9 (8.65) |

aMalnutrition Screening Tool.27
bYale Physical Activity Scale (YPAS).26
cGeriatric Depression Scale (GDS).29
dMedical Outcomes Study Social Support Scale.30
BMI: body mass index.
Table 2. Survival analysis of mean time to recurrence by participant characteristics.

| Factor                              | Mean time to recurrence (weeks) (95% confidence interval) | Log rank Chi-square value | P    |
|-------------------------------------|----------------------------------------------------------|---------------------------|------|
| **Age**                             |                                                          |                           |      |
| <70 years                           | 34.5 (29–40)                                             | 2.52                      | .112 |
| 70 years and older                  | 38.1 (34–42)                                             |                           |      |
| **Gender**                          |                                                          |                           |      |
| Male                                | 33.5 (29–38)                                             | 3.81                      | .051 |
| Female                              | 40.5 (36–45)                                             |                           |      |
| **Lives alone**                     |                                                          |                           |      |
| Yes                                 | 34.4 (30–39)                                             | 3.51                      | .061 |
| No                                  | 38.9 (35–43)                                             |                           |      |
| **Mobilises with aid**              |                                                          |                           |      |
| Yes                                 | 33.7 (29–39)                                             | 3.68                      | .055 |
| No                                  | 40.4 (37–44)                                             |                           |      |
| **Cardiac disease**                 |                                                          |                           |      |
| Yes                                 | 37.8 (33–43)                                             | 0.19                      | .660 |
| No                                  | 36.3 (32–41)                                             |                           |      |
| **Diabetes**                        |                                                          |                           |      |
| Yes                                 | 33.8 (26–41)                                             | 0.26                      | .613 |
| No                                  | 37.9 (34–41)                                             |                           |      |
| **Chronic pulmonary disease**       |                                                          |                           |      |
| Yes                                 | 33.3 (26–40)                                             | 0.59                      | .443 |
| No                                  | 37.9 (34–41)                                             |                           |      |
| **Osteoarthritis**                  |                                                          |                           |      |
| Yes                                 | 37.9 (34–42)                                             | 0.32                      | .572 |
| No                                  | 35.6 (31–41)                                             |                           |      |
| **Autoimmune disease**              |                                                          |                           |      |
| Yes                                 | 32.3 (22–43)                                             | 1.87                      | .171 |
| No                                  | 37.4 (34–41)                                             |                           |      |
| **Depression**                      |                                                          |                           |      |
| Yes                                 | 32.0 (22–42)                                             | 1.54                      | .214 |
| No                                  | 37.4 (34–41)                                             |                           |      |
| **Salbutamol**                      |                                                          |                           |      |
| Yes                                 | 39.9 (32–48)                                             | 1.23                      | .267 |
| No                                  | 36.4 (33–40)                                             |                           |      |
| **Diuretics**                       |                                                          |                           |      |
| Yes                                 | 34.5 (29–40)                                             | 1.55                      | .213 |
| No                                  | 38.4 (35–42)                                             |                           |      |
| **Non-steroidal anti-inflammatories** |                                                        |                           |      |
| Yes                                 | 47.7 (44–52)                                             | 4.46                      | .035 |
| No                                  | 34.8 (31–38)                                             |                           |      |
| **Steroids**                        |                                                          |                           |      |
| Yes                                 | 42.3 (35–49)                                             | 0.72                      | .398 |
| No                                  | 36.3 (33–39)                                             |                           |      |
| **Antidepressants**                 |                                                          |                           |      |
| Yes                                 | 32.2 (24–40)                                             | 3.11                      | .078 |
| No                                  | 37.9 (34–41)                                             |                           |      |
| **History surgery or trauma in leg**|                                                          |                           |      |
| Yes                                 | 34.5 (29–39)                                             | 2.98                      | .084 |
| No                                  | 39.7 (35–44)                                             |                           |      |
| **Previous deep vein thrombosis**   |                                                          |                           |      |
| Yes                                 | 37.7 (29–46)                                             | 1.05                      | .305 |
| No                                  | 36.9 (33–40)                                             |                           |      |
| **Previous venous surgery**         |                                                          |                           |      |
| Yes                                 | 35.6 (28–44)                                             | 0.23                      | .630 |
| No                                  | 37.4 (34–41)                                             |                           |      |
| **Oedema**                          |                                                          |                           |      |
| Yes                                 | 35.9 (29–43)                                             | 0.21                      | .650 |
| No                                  | 37.3 (34–41)                                             |                           |      |
| **Haemosiderosis**                  |                                                          |                           |      |
| Yes                                 | 34.5 (30–39)                                             | 3.80                      | .051 |
| No                                  | 40.9 (36–46)                                             |                           |      |
| **Lymphoedema**                     |                                                          |                           |      |
| Yes (n = 7)                         | 12.9 (0.8–25)                                             | 16.99                     | <.001|
| No                                  | 38.3 (35–41)                                             |                           |      |
| **Venous eczema**                   |                                                          |                           |      |
| Yes                                 | 37.6 (27–48)                                             | 0.39                      | .528 |
| No                                  | 36.9 (34–40)                                             |                           |      |
| **Atrophie blanche**                |                                                          |                           |      |
| Yes                                 | 35.8 (29–42)                                             | 0.02                      | .963 |
| No                                  | 37.4 (34–41)                                             |                           |      |
| **YPASb moving on feet at least 3 h/day** |                     |                           |      |
| Yes                                 | 39.5 (36–43)                                             | 2.86                      | .091 |
| No                                  | 33.3 (28–39)                                             |                           |      |
| **Wearing compression ≥ 20 mmHg at least 5 days/week** | |                           |      |
| Yes                                 | 39.3 (35–43)                                             | 2.86                      | .091 |
| No                                  | 33.6 (28–39)                                             |                           |      |

(continued)
associated with ulcer recurrence; while increased social support (measured by the MOS Social Support Scale) was associated with fewer recurrences. Compression hosiery equal to or greater than 20 mmHg worn for at least five or more days per week was associated with longer times to recurrence clinically, although was not statistically significant (p = .061).

### Discussion

The aim of this study was to investigate predictors of venous leg ulcer recurrence in patients attending outpatient wound care services. This prospective study found the incidence of venous ulcer recurrence in the first 12 months after healing was high, with 50% of this sample of community living adults experiencing an ulcer recurrence. This is consistent with previous studies from European and Asia-Pacific areas, although higher than reported rates by Probst, Bobbink, Gohel, Mora, which ranged between 28 and 33%. Using survival analysis, the mean time to ulcer recurrence found in this study was 37 weeks (SE 1.63, 95% CI 33.7–40.1). There is inconsistency in methods reporting recurrence, thus limited studies with similar methods and follow-up time in the literature; however, this study’s findings are similar to the previously reported times of 42 weeks or 48 weeks, although longer than the mean time of 77.9 days reported by Kapp et al.

The incidence of one in two patients experiencing a recurrence within a year after healing signifies an exceptional burden for both patients and the healthcare system, and it further underscores the magnitude of this health issue. Further research that identifies risk and preventative factors is required to inform approaches that can intervene in the cycle of healing and recurrence that is characteristic of this clinical population.

In this study, the presence of haemosiderosis, decreased mobility and use of antidepressants at the time of ulcer healing, were significantly associated with time to ulcer recurrence within 12 months of healing. The presence of haemosiderosis at the time of ulcer healing was the only lower limb clinical indicator found to be associated with subsequent ulcer recurrence. The amount of oedema (calf-ankle circumference ratio), lymphoedema, presence of venous eczema, erythema, hyperkeratosis, atrophie blanche and lipodermatosclerosis were not observed to be associated with an ulcer recurrence. Although six out of seven participants with lymphoedema recurred, the small number of participants in this sample with this condition did not allow further analysis to be progressed. There is limited evidence in the literature on clinical signs predicting future recurrence. One retrospective cohort study investigating risk factors for incidence of a first venous leg ulcer reports a slightly higher risk of leg ulceration if oedema was present, and another study using secondary analysis of data from combined longitudinal studies found the presence of lower limb erythema, venous eczema and reduced ankle range of motion at the time of healing, were significantly associated with increased risk of recurrence within 12 months. These findings are inconsistent with the current study’s results and, given the brevity of evidence available, further studies are required to consolidate a consistent evidence base regarding which clinical indicators

### Table 2. (continued)

| Factor | Mean time to recurrence (weeks) (95% confidence interval) | Log rank Chi-square value | P |
|--------|----------------------------------------------------------|----------------------------|---|
| Elevating legs for at least 30 min/day | Yes 42.8 (38–47) | 9.73 | .002 |
| | No 33.6 (29–38) |  | |
| Score ‘at-risk’ on GDS | Yes 30.2 (19–41) | 2.55 | .110 |
| | No 37.9 (34–42) |  | |

aMalnutrition Screening Tool.27
bYale Physical Activity Scale (YPAS).26
cGeriatric Depression Scale (GDS).29
dMedical Outcomes Study Social Support Scale.30
could facilitate identification of people who are at greatest risk of ulcer recurrence.

Measures of mobility vary in studies with persons with venous leg ulcers, including range of ankle motion, the need for aids to mobilise, or scales measuring walking time or distance.18,38 Reduced mobility has been found to be associated with delayed healing of venous leg ulcers,38–40 yet few studies on ulcer recurrence have reported this measure. The ones that have, however, support the findings in this investigation,18,34 suggesting that a greater emphasis on lower limb exercise would be advisable for adults with chronic venous insufficiency.

The use of antidepressants by participants in this study was associated with ulcer recurrence. Depression or use of antidepressants is rarely reported in recurrence studies. One study analysing data from 250 patients found significantly higher GDS (measuring depressive symptoms) scores in those who recurred at the bivariate level, however, when controlling for all variables in a multivariable model, GDS did not retain a significant relationship.18,19 An association has also been reported between delayed healing of venous leg ulcers and depression.41 The processes involved in the relationship between depression and recurrence are unclear as to the direction of effect and whether this association reflects a mediator or moderator pathway. For example, depression may be associated with a range of physiological and psychosocial risk factors which are linked to ulcer recurrence. The current study did not determine GDS scores (measuring depressive symptoms) to be a significant predictor of recurrence, however, the use of antidepressants was associated with recurrence. Antidepressant drugs may have been prescribed for reasons other than depression, thus the potential role of antidepressant medications, associated conditions, depression and ulcer recurrence warrants further investigation.

With respect to the sociodemographic characteristics in the current study, the mean age and gender distribution was consistent with other venous leg ulcers studies.18,19 The mean BMI of people in this study was 32 which is classified as obese42 and is slightly higher than the figures reported in the literature of ~30 in Europe.19 The only sociodemographic variable that remained significant on multivariate analysis was the MOS social support scale, indicating that increased social support was significantly associated with longer time to venous leg ulcer recurrence.

Living with chronic venous insufficiency can place significant restrictions on daily activities and decrease quality of life. These impacts may be lessened by social support. Relationships between health and social isolation or loneliness are complex, with research demonstrating links between less loneliness and improved physical health.43 Living alone has previously been found to have a significant relationship with delayed healing of venous leg ulcers44 and while living alone was not significantly related to recurrence in this study, higher levels of support as measured on the Medical Outcomes Social Support scale, including tangible support, emotional support and information/educational support subscales, were all significantly associated with longer time to recurrence (see Table 2). The MOS Social Support Survey was designed for chronically ill patients and contains 19 items measuring the self-reported availability of four dimensions of social support: tangible support (material aid or behavioural assistance); affectionate support; positive social interaction; and emotional/informational support (empathetic understanding, advice guidance and feedback).30 The importance, therefore, for clinicians to conduct social support appraisals of patients and consider actions that address social support needs are suggested from these results and implied in the literature, although would benefit from further exploration.

Surprisingly, the use of compression therapy was not statistically significantly related to recurrence, however, a clinical difference of longer time to recurrence for those wearing compression (of moderate or high level) at least 5 days/week was observed (see Table 2). Systematic reviews and clinical guidelines support the use of compression to prevent recurrence.45–47 This item relied on self-report for wearing time which may have had inaccuracies.

### Table 3. Factors associated with venous leg ulcer recurrence – Cox proportional hazards regression.

| Factor                                      | β      | Hazard ratio | 95% CI      | p value |
|---------------------------------------------|--------|--------------|-------------|---------|
| Antidepressants                             | 0.77   | 2.16         | 1.06–4.42   | .035    |
| Non-steroidal anti-inflammatories           | -0.82  | 0.44         | 0.17–1.13   | .089    |
| History of surgery/trauma in study leg      | 0.51   | 1.67         | 0.94–2.97   | .083    |
| Haemosiderosis in study leg                 | 0.91   | 2.47         | 1.29–4.71   | .006    |
| YPAS sitting Index                          | 0.39   | 1.47         | 1.11–1.95   | .007    |
| Compression hosiery ≥20 mmHg for 5 or more days/week | -0.57  | 0.57         | 0.31–1.03   | .061    |
| MOS social support scale                    | -0.015 | 0.98         | 0.97–0.99   | .002    |

*aYPAS: Yale Physical Activity Survey Sitting Index (higher scores indicate increased length of time/day sitting).
*bMOS: Medical Outcomes Study Social Support Scale, Scale 0–100, where higher scores indicated increased social support.*
Overall, these findings reveal that the predictors of venous leg ulcer recurrence are complex and inter-related, requiring clinicians and care providers to be cognisant of the need for ongoing specialist care, with a focus on shared decision making with the patient.

**Limitations**

The results of this study were reliant on the variables collected, however, other variables such as degree of chronic venous insufficiency and calf muscle function may add further understanding of recurrence. While validated scales were utilised where possible, the self-report nature of a number of variables, including adherence to compression therapy, may have introduced an element of response bias. A prospective approach enabled the inclusion of a number of relevant measures, however, the time period of three-monthly appraisal does not eliminate the potential for recall bias. While the sample size calculation indicated sufficient sample to enable a Cox proportional hazards model analysis, there were, however, some variables that lacked sufficient incidence of events to enable inclusion in the model, such as the presence of lymphoedema. Further studies with a larger sample size and increased incidence of such relevant events for co-variates would enable a more comprehensive exploration of their relationship with ulcer recurrence.

**Conclusion**

This study found a high rate of ulcer recurrence with one in two patients experiencing a recurring ulcer within 12 months after healing. This finding underscores the importance of further work and need for interventions to break the cycle of healing and recurrence. A strength of this study was the number of participants across multiple sites in community and hospital settings. This secondary analysis followed people who had a healed venous leg ulcer for 12 months where antidepressant medications, presence of haemosiderosis, decreased mobility and lower social support were found to be significant predictors of recurrence. There is a paucity and lack of consistent literature in relation to many of these variables, hence, the investigation of these variables for recurrence provides guidance for the clinical management of people with venous leg ulcers that heal. While some variables are not modifiable, physical activity is and should be promoted by health care clinicians.

**Acknowledgements**

We would like to acknowledge all staff from Queensland University of Technology, Royal District Nursing Service, BlueCare and Royal Women’s and Brisbane Hospital, Australia, who assisted and contributed to the original research study.

**Contributorship**

KF researched literature and KF and HE conceived the study. KF, CP, CM, and HE were involved in protocol development, obtaining ethical and governance approvals, participant recruitment and data analysis. KF, CP, CM, HE and JC contributed to drafts of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

**Declaration of conflicting interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Wound Management Innovation CRC (established and supported under the Australian Government’s Cooperative Research Centres Program).

**Ethical approval**

Ethical approval was received from the Queensland University of Technology Human Research Ethics Committee (HREC) (Ref. No.1100001442), the Royal Brisbane and Women’s Hospital HREC (12/QRBW/57), UnitingCare Queensland HREC, and Royal District Nursing Services HREC (no.125).

**Guarantor**

KF.

**ORCID iD**

KJ Finlayson https://orcid.org/0000-0002-5743-2731

**References**

1. Van Gent WB, Wilschut ED and Wittens C. Management of venous ulcer disease. *BMJ* 2010; 341: c6045.
2. Chamanga E. Understanding venous leg ulcers. *Comm Wound Care* 2018; 23: S6–S15.
3. Ratliff CR, Yates S, McNichol L, et al. Compression for primary prevention, treatment, and prevention of recurrence of venous leg ulcers. *J Wound Ostomy Cont Nurs* 2016; 43: 347–364.
4. Guest JF, Ayoub N, McIlwraith T, et al. Health economic burden that wounds impose on the National Health Service in the UK. *BMJ Open* 2015; 5: e009283.
5. Margolis DJ, Bilker W, Santanna J, et al. Venous leg ulcer: incidence and prevalence in the elderly. *J Am Acad Dermatol* 2002; 46: 381–386.
6. Posnett J, Gottstrup F, Lundgren H, et al. The resource impact of wounds on health-care providers in Europe. *J Wound Care* 2009; 18: 154.
7. Berenguer Pérez M, López-Casanova P, Sarabia Lavin R, et al. Epidemiology of venous leg ulcers in primary health
care: incidence and prevalence in a health centre-A time series study (2010–2014). Int Wound J 2019; 16: 256–265.
8. O'Donnell TF and Passman MA. Clinical practice guidelines of the society for vascular surgery (SVS) and the American venous forum (AVF)-management of venous leg ulcers. J Vasc Surg 2014; 60: 1S–2S.
9. Sen CK. Human wound and its burden: updated 2020 compendium of estimates. Adv Wound Care 2021; 10(5): 281–292.
10. Purwins S, Herberger K, Debis ES, et al. Cost-of-illness of chronic leg ulcers in Germany. Int Wound J 2010; 7: 97–102.
11. Barnsbee L, Cheng Q, Tulleners R, et al. Measuring costs and quality of life for venous leg ulcers. Int Wound J 2018; 16(1): 112–121.
12. Graves N, et al. Modelling the economic benefits of gold standard care for chronic wounds in a community setting. Wound Pract Res 2014; 22(3): 163–168.
13. Kapp S and Santamaria N. The financial and quality-of-life cost to patients living with a chronic wound in the community. Int Wound J 2017; 14: 1108–1119.
14. Edwards H, Finlayson K, Skerman H, et al. Identification of symptom clusters in patients with chronic venous leg ulcers. J Pain Symptom Manage 2014; 47(5): 867–875.
15. Graves N and Zheng H. Modelling the direct health care costs of chronic wounds in Australia. Wound Pract Res J Aust Wound Manag Assoc 2014; 22(1): 20–33.
16. Pugliese DJ. Infection in venous leg ulcers: considerations for optimal management in the elderly. Drugs Aging 2016; 33: 87–96.
17. Barron GS, Jacob SE and Kirschner RS. Dermatologic complications of chronic venous disease: medical management and beyond. Ann Vasc Surg 2007; 21: 652–662.
18. Finlayson K, Wu ML and Edwards HE. Identifying risk factors and protective factors for venous leg ulcer recurrence using a theoretical approach: a longitudinal study. Int J Nurs Stud 2015; 52: 1042–1051.
19. Gethin G, Vellinga A, Tawfick W, et al. The profile of patients with venous leg ulcers: a systematic review and global perspective. J Tissue Viability 2021; 30: 78–88. DOI: 10.1016/j.jtv.2020.08.003.
20. Lo ZJ, Lim X, Eng D, et al. Clinical and economic burden of wound care in the tropics: a 5-year institutional population health review. Int Wound J 2020; 17: 790–803.
21. Probst S, Bobbink P, Séchaud L, et al. Venous leg ulcer recurrences-The relationship to self-efficacy, social support and quality of life-a mixed method study. J Adv Nurs 2021; 77: 367–375.
22. Sermathamiasawadi N, Jieciamprasertbun J, Pruekprasert K, et al. Factors that influence venous leg ulcer healing and recurrence rate after endovenous radiofrequency ablation of incompetent saphenous vein. J Vasc Surg Venous Lymphat Disord 2020; 8(3): 452–457.
23. Labropoulos N, Wang ED, Lanier ST, et al. Factors associated with poor healing and recurrence of venous ulceration. Plast Reconstr Surg 2012; 129(1): 179–186.
24. Finlayson KJ, Parker CN, Miller C, et al. Predicting the likelihood of venous leg ulcer recurrence: the diagnostic accuracy of a newly developed risk assessment tool. Int Wound J 2018; 15: 686–694. DOI: 10.1111/iwj.12911.
25. Hyloewn Consulting LLC. Power and sample size calculators. Hyloewn Consulting LLC, 2013, powerandsamplesize.com/calculator/test-time-to-event-data/Cox-PH-Equivalence. Accessed 19/10/2020.
26. Dipietro L, Caspersen CJ, Ostfeld AM, et al. A survey for assessing physical activity among older adults. Med Sci Sports Exerc 1993; 25(5): 628–642.
27. Rubenstein LZ, Harker JO, Salva A, et al. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol Ser A Biol Sci Med Sci 2001; 56(6): M366–M372.
28. Ware JE, Jr, Kosinski M and Keller SD. A 12-item short-form health survey. Med Care 1996; 34(3): 220–23.
29. Brink TL, Yesavage JA, Lum O, et al. Screening tests for geriatric depression. Clin Gerontol 1982; 1(1): 37–43.
30. Sherbourne CD and Stewart AL. The MOS social support survey. Soc Sci Med 1991; 32(6): 705–714.
31. Schwarz R and Jerusalem M. The general self-efficacy scale. http://userpage.fu-berlin.de/~health/engscal.htm (1993, accessed 7 July 2008).
32. Milic DJ, Zivic SS, Bogdanovic DC, et al. A randomized trial of class 2 and class 3 elastic compression in the prevention of recurrence of venous ulceration. J Vasc Surg Venous Lymphat Disord 2018; 6(6): 717–723.
33. Gohel MS, Mora J, Szigeti M, et al. Long-term clinical and cost-effectiveness of early endovenous ablation in venous ulceration. JAMA Surg 2020; 155: 1113. DOI: 10.1001/jamasurg.2020.3845.
34. Brooks J, Ersser SJ, Lloyd A, et al. Nurse-led education sets out to improve patient concordance and prevent recurrence of leg ulcers. J Wound Care 2004; 13(3): 111–116.
35. Kapp S, Miller C and Donohue L. The clinical effectiveness of two compression stocking treatments on venous leg ulcer recurrence. Int J Lower Extrem Wounds 2013; 12(3): 189–198.
36. Darwin E, Liu G, Kirschner RS, et al. Examining risk factors and preventive treatments for first venous leg ulceration: a cohort study. J Am Acad Dermatol 2020; 84(1): 76–85.
37. Finlayson K and Edwards H. Clinical and psychosocial predictors of venous leg ulcer recurrence: results from prospective, longitudinal cohort studies. In: vWINter international meeting in phlebology & lymphology. Cortina d’Ampezzo, Italy: vWIN Foundation; 2019.
38. Parker CN, Finlayson KJ, Shuter P, et al. Risk factors for delayed healing in venous leg ulcers: a review of the literature. Int J Clin Pract 2015; 69(9): 967–977.
39. Meagher H, Ryan D, Clarke-Moloney M, et al. An experimental study of prescribed walking in the management of venous leg ulcers. J Wound Care 2012; 21: 421–430.
40. Simka M. Calf muscle pump impairment and delayed healing of venous leg ulcers: air plethysmographic findings. J Dermatol 2007; 34(8): 537–544.

41. Finlayson KJ, Courtney MD, Gibb MA, et al. The effectiveness of a four-layer compression bandage system in comparison with class 3 compression hosiery on healing and quality of life in patients with venous leg ulcers: a randomised controlled trial. Int Wound J 2014; 11(1): 21–27.

42. Commonwealth of Australia National Health and Medical Research Council. Australian dietary guidelines. Canberra: NHMRC: Australian Government, 2013.

43. Victor CR and Bowling A. A longitudinal analysis of loneliness among older people in Great Britain. J Psychology 2012; 146(3): 313–331.

44. Parker CN, Finlayson KJ and Edwards HE. Ulcer area reduction at 2 weeks predicts failure to heal by 24 weeks in the venous leg ulcers of patients living alone. J Wound Care 2015; 25(11): 626–634.

45. Health Quality Ontario. Compression stockings for the prevention of venous leg ulcer recurrence: a health technology assessment. Ont Health Technol Assess Series 2019; 19(2): 1–86.

46. AWMA. Australian and New Zealand Clinical Practice Guidelines for Prevention and Management of Venous Leg Ulcers. Treloar Cres, Australia: AWMA, Barton, ACT, 2011.

47. Nelson EA and Bell-Syer SE. Compression for preventing recurrence of venous ulcers. Cochrane Database Systematic Reviews 2014; 2014(9): CD002303.