

## ORIGINAL ARTICLE

# The burden of costs on health services by patients with neuro-ischaemic ulcers in Singapore

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## Abstract

The economic burden of neuro-ischaemic ulcers (NIU) is expected to increase because of rising prevalence of comorbidities in an aging population. We aim to estimate healthcare resources consumed by NIU patients, and to quantify the extent to which factors explain variation in cost-related outcomes. We analysed retrospective patient-level cohort data for NIU patients from a tertiary hospital registry in Singapore, from 2013 to 2017, using generalised linear regression models. The outcome variables were the length of stay per admission; inpatient and outpatient bill per admission; and, if they had an Emergency Department visit. Cost outcomes were reported in Singapore dollars (S\$). A total of 1682 patients were included, and the mean age was 69.9 years ( $\pm 13.0$ ). An average patient incurred a length of stay of 38.7 days, 7.9 inpatient dressing sessions, an inpatient bill of S\$33 096, 11.3 outpatient dressing sessions, and an outpatient bill of S\$8780. Inpatient services per patient cost 73.5% higher than outpatient services. NIU patients with multiple ( $>3$ ) comorbid conditions, peripheral artery disease, or chronic kidney disease incurred longer hospitalisation and higher inpatient bill. Patients with diabetes mellitus and coronary artery disease had higher odds of incurring an ED visit. Patients with coronary artery disease, hyperlipidaemia, kidney complications, or obesity incurred higher outpatient bills. NIU treatment imposes a significant economic burden, especially with inpatient services.

## KEYWORDS

chronic wound, economic burden, neuro-ischemic ulcer

## Key Messages

- This study provides insights on the use of healthcare resources by patients with Neuro-ischaemic ulcers (NIU) which neuropathic, ischaemic or ulcers with both components.
- Average cost of inpatient services per patient was found to be substantial, being 73.5% higher than outpatient services

- NIU patients with >3 comorbid conditions, peripheral artery disease or chronic kidney disease incurred longer hospitalization and higher inpatient bills.
- NIU patients with coronary artery disease, hyperlipidaemia, kidney complications, or obesity incurred higher outpatient bills.
- Good quality cost information relevant to the Asian settings are useful to update economic arguments for alternate models of care

## 1 | INTRODUCTION

Chronic leg ulcers emerge below the knee and remain unhealed for more than 3 months giving rise to health-care costs and reducing patients' quality of life.<sup>1,2</sup> These ulcers overall affect 0.6% to 3% of those aged above 60 years with prevalence rising with age.<sup>3</sup> The rising incidence of chronic leg ulcers attributed to an aging population and growing prevalence of comorbidities such as obesity and diabetes, is expected to inflate healthcare costs.<sup>1,4</sup> A retrospective analysis conducted on Medicare 5% dataset for the year 2014 reported 8.2 million individuals, approximately 15% of the beneficiaries, had at least one type of chronic wound or infection, and the total expenditures ranged from US\$28.1 to US\$96.8 billion depending on wound type.<sup>5</sup> UK's National Health Service (NHS) estimated an annual cost of £1.94 billion for the treatment of 731 000 leg ulcers based on data from 2012.<sup>6</sup>

Neuro-ischemic ulcer (NIU) is one of the main subtypes of chronic leg ulcers and is associated with patients with diabetes (DM) and/or peripheral artery disease (PAD).<sup>7</sup> NIU consists of a spectrum that can be predominantly neuropathic (those with diabetes only), predominantly ischaemic (those with the peripheral arterial disease only) or has both components (those with both diabetes and peripheral arterial disease).<sup>8,9</sup> The prevalence of diabetic foot ulcers (DFUs) among DM patients is 4% to 10%,<sup>10</sup> and an estimated 50% of patients with foot ulceration are diagnosed with PAD in developed countries, while neuropathic ulcers are more prevalent in developing countries.<sup>8</sup>

As Singapore's population is rapidly aging, both DM and PAD are found to be prevalent.<sup>11,12</sup> Therefore, the prevalence and incidence of NIU may increase, posing substantial economic challenges to healthcare systems. An approximate 95% increase in wound episodes per 1000 inpatient admissions was observed in 2017 compared with 2013 based on a Singapore study.<sup>13</sup> Good quality cost information relevant to Asian settings can be imperative in informing economic arguments for alternate models of care and even prevention programmes. Two studies were found to estimate the economic burden of chronic wound treatments in Singapore. A 2013 retrospective study estimated annual direct and indirect costs to be S\$4.59 million and S\$0.86 million respectively,

across various chronic wound categories.<sup>14</sup> The annual direct gross cost was estimated as S\$1.68 million for DFUs and S\$0.43 million for ischaemic ulcers. Another study based on data from 2013 to 2017 reported the average gross charge per wound episode as approximately US \$13 000.<sup>13</sup> With the significant economic burden of chronic leg ulcers on individuals and healthcare systems arising from prolonged hospital care, high resource utilisation, loss of productivity, and reduced quality of life,<sup>15,16</sup> it is important to understand the gross costs and factors that explain variation in cost outcomes of NIUs. The first aim of this study is to estimate the costs and resources consumed by patients with NIUs. The second aim is to quantify the extent to which predictors explain variation in selected cost-related outcomes. The findings will be useful for clinicians, researchers and policy-makers focused on improving wound management and treatment.

## 2 | MATERIALS AND METHODS

### 2.1 | Study data

This study is an analysis using retrospective data from a cohort of patients. Data were retrieved from a data registry from the National University Hospital (NUH) of Singapore, for the period 1 January 2013 to 31 October 2017. Patients with NIUs were included if they were aged 21 and above, and if the admission diagnosis International Classification of Disease (ICD) codes suggested diabetes, or PAD, or both conditions. The ICD codes listed in Appendix A were used to identify patients to be included in analysis.

The information available for analysis included socio-demographic characteristics, lifestyle behaviour, medical history, and outpatient and inpatient treatments provided. Socio-demographic characteristics included age, gender, and race. Lifestyle behaviour included obesity and current smoking habit. Patients' medical history included diabetes mellitus, venous insufficiency, PAD, coronary artery disease, congestive heart failure, hypertension, hyperlipidemia, or chronic kidney disease/end-stage renal failure. Data on healthcare service consumption included number of admissions, length of stay of each admission, number of podiatrist and nurse dressing

sessions, and type of surgical procedures (including debridement, skin grafting, amputation, and arterial revascularization procedures). Amputation procedures included amputation of toes, feet, and lower limbs. Data on outpatient treatment included the number of outpatient visits, number of emergency department (ED) visits and number of outpatient podiatrist dressing sessions. The outpatient visits included visits to vascular surgery clinic, diabetic clinic, orthopaedic clinic, and podiatrist clinic. The total inpatient and total outpatient bill was the gross amount incurred by patients before government subsidy and was provided in Singapore dollars (S\$).

## 2.2 | Study outcomes

The length of follow-up varied among the cohort as patients could enter and leave the registry at any point during the study period. Patients with a hospital admission or an outpatient visit in 2013, the first year of the cohort data, were found to have the longest length of follow-up duration. For the first aim of this study, to estimate the costs and resources consumed by patients with NIUs, we only included patients who were admitted in 2013. As for the study's second aim, we used the entire cohort data to evaluate these outcomes: length of stay per admission; inpatient bill per admission; and outpatient bill per visit (not inclusive of ED charges). Independent variables were also analysed against a binary outcome variable which includes if a patient had an ED visit. All costs are reported in Singapore dollars (S\$).

## 2.3 | Statistical methods

Patients' characteristics are summarised using frequencies with corresponding percentages for categorical variables, means and standard deviations for normally distributed continuous variables, or medians and 1st quartile-3rd quartile ranges for skewed variables.

For the study's second aim of quantifying the extent to which predictors explain variation in cost-related outcomes, a generalised linear modelling (GLM) was used. This approach uses maximum-likelihood estimation to summarise the relationship between explanatory variables and cost-related outcomes used in the analysis. Outcomes that are continuous variables were heavily positively skewed, thus a gamma distribution was chosen to characterise the outcome and a log link function to specify the relationship with explanatory variables.<sup>17</sup> GLM results were reported as beta coefficients and 95% confidence intervals (CI) inclusive of P-values. Coefficients were converted to the original units such as length of stay (days) and costs (S\$), by multiplying the mean of the outcome variable. For the binary outcome, if a patient

had an ED visit, multivariable logistic regression model with a logit link function was used. Results were reported as odds ratios (OR) and 95% CIs.

The variable selection process was guided by theory and clinical knowledge.<sup>18-22</sup> Thereafter statistical significance was used for a stepwise selection approach where candidate variables were included as predictors. Variables were checked for multi-collinearity via variance inflation factor (VIF) and no major violation was observed. Models which yielded the best residuals in the quantile-quantile (Q-Q) plots of the residuals and lowest Akaike information criterion (AIC) were preferred. Statistical analysis was performed using R Statistical software (R Core Team [2020]. R: A language and environment for statistical computing. R. Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>).

## 2.4 | Ethics

This research study has been approved by the NHG Domain Specific Review Board (DSRB 2019/00917).

# 3 | RESULTS

## 3.1 | Patient characteristics

Data on 1722 NIU patients were available for analysis. Fourteen patients who did not incur outpatient treatments and 26 patients who had prolonged inpatient stays with large bills likely caused by other medical conditions that co-exist with a NIU wound, were removed from analysis. A total of 1682 patients were included in the analysis. The statistical distributions of the outcomes analysed are presented in Appendix B (Figures B1-B3).

Patient characteristics are presented in Table 1. Mean age was 69.9 ( $\pm 13.0$ ), and 58.1% were male. Most were of Chinese ethnicity (47.2%). Diabetes mellitus was highly prevalent in the cohort (92.4%), followed by hypertension (82.7%) and hyperlipidaemia (71.7%). A large majority had more than 3 comorbid conditions (70.8%) and had incurred at least 1 ED visit (75.6%).

## 3.2 | Costs and resources arising from cases of NIU

For 836 patients with an inpatient admission in 2013, the total length of stay, inpatient dressing sessions, and inpatient bill amounted to 32 372 (95% CI: 35.1-42.3), 6638 (95% CI: 7.1-8.8) and S\$27 668 492 (95% CI: 29 764.2-36 428.4) respectively. Mean inpatient dressing sessions, mean length of stay, and mean inpatient bill for

TABLE 1 Characteristics of the study cohort

Variable	N = 1682
Socio-demographic characteristics	
Age (years)	69.9 ( $\pm$ 13.0)
Gender	
Male	977 (58.1)
Female	705 (41.9)
Race	
Chinese	793 (47.2)
Malay	401 (23.8)
Indian	278 (16.5)
Others	210 (12.5)
Medical history	
Presence of more than 3 comorbidities <sup>a</sup>	1191 (70.8)
Diabetes mellitus	1555 (92.4)
Venous insufficiency	51 (3.0)
Peripheral arterial disease	1044 (62.1)
Coronary artery disease	544 (32.3)
Congestive heart failure	333 (19.8)
Hypertension	1391 (82.7)
Hyperlipidaemia	1206 (71.7)
Chronic kidney disease/end-stage renal failure	1070 (63.6)
Lifestyle factors	
Obesity	57 (3.4)
Smoking	488 (29.0)
Treatment of wound	
Debridement	358 (21.3)
Skin grafting	88 (5.2)
Amputation <sup>b</sup>	626 (37.2)
Arterial revascularization procedure	587 (34.9)
Emergency department visits	1272 (75.6)
Variables adjusted for length of follow-up	
Number of inpatient dressing sessions <sup>c</sup> per admission	2.0 (1.0-4.0)
Length of stay per admission (days)	10.0 (4.7-19.0)
Inpatient bill per admission (S\$)	9239.4 (3579.2-19 593.9)
Number of outpatient podiatrist dressing sessions per visit	0.2 (0.0-0.5)
Outpatient bill per visit (S\$)	209.5 (145.3-294.4)

Note: Data presented as n (%) for categorical variables, mean ( $\pm$ SD) for normally distributed continuous variables, or as median (Q1 – Q3) for non-normally distributed continuous variables.

<sup>a</sup>Includes diabetes mellitus, venous insufficiency, peripheral arterial disease, coronary artery disease, congestive heart failure, hypertension, hyperlipidaemia, chronic kidney disease/end-stage renal failure and neuropathy.

<sup>b</sup>Includes amputation of toes, feet and lower limbs.

<sup>c</sup>Includes podiatrist and nurse dressing sessions.

TABLE 2 Factors associated with length of stay per inpatient admission: multivariable generalised linear model

Variable	Coefficient (95% CI)	P value
Age (year)	1.00 (1.00-1.01)	.190
Female gender	0.99 (0.90-1.08)	.781
Race		
Malay vs Chinese	1.07 (0.95-1.20)	.258
Indian vs Chinese	0.93 (0.82-1.06)	.265
Others vs Chinese	1.07 (0.93-1.23)	.358
Presence of more than 3 comorbidities <sup>a</sup>	1.18 (1.01-1.38)	.043
Diabetes mellitus	0.81 (0.67-0.97)	.023
Venous insufficiency	0.80 (0.63-1.04)	.090
Peripheral arterial disease	1.25 (1.10-1.41)	<.001
Hyperlipidaemia	0.81 (0.72-0.92)	<.001
Chronic kidney disease/end-stage renal failure	1.23 (1.09-1.38)	<.001
Neuropathy	0.87 (0.73-1.05)	.126
Minor surgery <sup>b</sup>	1.28 (1.15-1.43)	<.001
Amputation <sup>c</sup>	1.57 (1.43-1.73)	<.001
Arterial revascularization procedure	0.92 (0.82-1.03)	.132
Number of inpatient dressing sessions per admission <sup>d</sup>	1.11 (1.09-1.12)	<.001

<sup>a</sup>Includes diabetes mellitus, venous insufficiency, peripheral arterial disease, coronary artery disease, congestive heart failure, hypertension, hyperlipidaemia, chronic kidney disease/end-stage renal failure and neuropathy.

<sup>b</sup>Includes debridement and skin grafting.

<sup>c</sup>Includes amputation of toes, feet and lower limbs.

<sup>d</sup>Includes podiatrist and nurse dressing sessions.

an average patient were 7.9, 38.7, and S\$33 096, respectively. For 928 patients with an outpatient visit in 2013, the total number of outpatient podiatrist dressing sessions and outpatient bills amounted to 10 523 (95% CI: 10.2-12.5) and S\$8 148 117 (95% CI: 8259.3-9301.3), respectively. This translates to an average patient incurring 11.3 outpatient dressing sessions and an outpatient bill of S\$8 780.

### 3.3 | Predictors explain variation in selected cost-related outcomes - inpatient services

The results from GLM regression for the length of stay and inpatient bill are presented in Tables 2 and 3. The presence of more than 3 comorbid conditions, diabetes mellitus, PAD, hyperlipidaemia or chronic kidney disease/end-stage renal failure, minor surgery, amputation, and number of inpatient dressing sessions were significantly associated with length of stay (Table 2). Patients

with more than 3 comorbid conditions had longer inpatient stay by 2.7 days per admission (95% CI: 0.2-5.7) compared with their counterparts. Similarly, patients with PAD and kidney disease incurred an additional 3.7 (95% CI: 1.5-6.1) and 3.4 (95% CI: 1.3-5.7) inpatient days per admission, respectively, compared with their counterparts. Conversely, patients with diabetes mellitus and hyperlipidaemia incurred a shorter inpatient stay by 19% compared with patients without. An amputation procedure ensued in a longer inpatient stay by 8.5 (95% CI: 6.4-10.9) more days per admission.

Factors associated with inpatient bill per admission are shown in Table 3. The presence of various comorbidities such as diabetes mellitus, venous insufficiency, PAD, coronary artery disease, hyperlipidemia, kidney disease, and neuropathy were significantly associated with inpatient bill. NIU patients with PAD, coronary artery disease or kidney disease incurred a higher inpatient bill per admission by S\$4916 (95% CI: 1902.8-8721.2), S\$3489 (95% CI:

**TABLE 3** Factors associated with inpatient bill per admission: multivariable generalised linear model

Variable	Coefficient (95% CI)	P value
Age (year)	1.00 (0.99-1.00)	.187
Female gender	0.98 (0.86-1.12)	.810
Race		
Malay vs Chinese	1.09 (0.94-1.26)	.263
Indian vs Chinese	0.79 (0.67-0.94)	.006
Others vs Chinese	1.08 (0.90-1.31)	.385
Presence of more than 3 comorbidities <sup>a</sup>	1.21 (0.98-1.49)	.082
Diabetes mellitus	0.67 (0.52-0.85)	.001
Venous insufficiency	0.65 (0.48-0.93)	.012
Peripheral arterial disease	1.31 (1.12-1.55)	<.001
Coronary artery disease	1.22 (1.07-1.40)	.003
Hyperlipidaemia	0.80 (0.68-0.93)	.005
Chronic kidney disease/end-stage renal failure	1.20 (1.03-1.39)	.021
Neuropathy	0.75 (0.59-0.96)	.015
Smoking	0.89 (0.78-1.03)	.118
Minor surgery <sup>b</sup>	1.25 (1.08-1.44)	.002
Amputation <sup>c</sup>	1.46 (1.29-1.66)	<.001
Arterial revascularization procedure	1.11 (0.96-1.29)	.164
Number of inpatient dressing sessions per admission <sup>d</sup>	1.11 (1.09-1.12)	<.001

<sup>a</sup>Includes diabetes mellitus, venous insufficiency, peripheral arterial disease, coronary artery disease, congestive heart failure, hypertension, hyperlipidaemia, chronic kidney disease/end-stage renal failure and neuropathy.

<sup>b</sup>Includes debridement and skin grafting.

<sup>c</sup>Includes amputation of toes, feet and lower limbs.

<sup>d</sup>Includes podiatrist and nurse dressing sessions.

1109.9-6342.7) and S\$3171 (95% CI: 475.7-6184.1), respectively, compared with their counterparts. In addition, Indian patients (vs Chinese) were found to incur 21% lower inpatient bill per admission. Patients who had to undergo minor surgery (ie, debridement or skin grafting) or amputation incurred a higher inpatient bill by S\$3964 (95% CI: 1268.5-6976.9) and S\$7294 (95% CI: 4598.5-10 465.5), respectively. The presence of more than 3 comorbidities was found to result in higher inpatient bill by 21%, although this was less precisely estimated.

### 3.4 | Predictors explain variation in selected cost-related outcomes - outpatient services

GLM regression results for outpatient bills are presented in Table 4. Patients with coronary artery disease, hyperlipidaemia, and chronic kidney disease/end-stage renal failure incurred S\$26 (95% CI: 4.8-50.5), S\$29 (95% CI: 7.2-52.9), and S\$60 (95% CI: 36.1-86.6) more per outpatient visit, respectively, compared with their counterparts. Although less precisely estimated, patients with PAD incur a higher bill by 6% (95% CI: 0.98-1.15) compared with their counterparts. Age, obesity, and smoking were also found to be significantly associated with outpatient bill.

### 3.5 | Predictors explain variation in selected cost-related outcomes—emergency department

GLM regression results for ED visits are presented in Table 5. ED visit was significantly associated with age,

**TABLE 4** Factors associated with outpatient bill per visit: multivariable generalised linear model

Variable	Coefficient (95% CI)	P value
Age (year)	1.00 (0.99-1.00)	.002
Female gender	1.04 (0.96-1.14)	.341
Race		
Malay vs Chinese	0.96 (0.87-1.06)	.389
Indian vs Chinese	1.02 (0.92-1.14)	.689
Others vs Chinese	1.02 (0.91-1.15)	.749
Peripheral arterial disease	1.06 (0.98-1.15)	.156
Coronary artery disease	1.11 (1.02-1.21)	.014
Hyperlipidaemia	1.12 (1.03-1.22)	.010
Chronic kidney disease/end-stage renal failure	1.25 (1.15-1.36)	<.001
Obesity	1.36 (1.09-1.66)	.007
Smoking	1.10 (1.00-1.20)	.046



**TABLE 5** Factors associated with ED visit (no or yes): multivariable generalised linear model

Variable	Coefficient (95% CI)	P value
Age (year)	1.01 (1.00-1.02)	.027
Female gender	1.24 (0.99-1.58)	.072
Race		
Malay vs Chinese	1.39 (1.15-2.32)	.033
Indian vs Chinese	1.62 (1.03-1.88)	.007
Others vs Chinese	1.17 (0.81-1.70)	.393
Diabetes mellitus	2.18 (1.47-3.22)	<.001
Congestive heart failure	1.39 (1.01-1.92)	.045
Hypertension	0.65 (0.46-0.91)	.015
Ischemic heart disease	0.82 (0.63-1.07)	.143
Chronic kidney disease/ end-stage renal failure	1.18 (0.91-1.52)	.220
Neuropathy	1.47 (0.90-2.53)	.150
Obesity	1.85 (0.90-4.31)	.120

Malay and Indian ethnicity (vs Chinese), and the presence of diabetes mellitus, congestive heart failure, and hypertension. The odds of incurring an ED visit were higher at 1.39 times (95% CI: 1.15-2.32) and 1.62 (95% CI: 1.03-1.88) times in Malay and Indian ethnicity, respectively, as compared with Chinese. In addition, the odds of incurring an ED visit were higher at 2.18 times (95% CI: 1.47-3.22) and 1.39 times (95% CI: 1.01-1.92), in patients with diabetes mellitus and congestive heart failure, respectively, as compared with their counterparts.

## 4 | DISCUSSION

This study provides insights into the use of healthcare resources by patients with NIU. The cost of inpatient services was found to be substantial, with the length of stay and inpatient bill for an average patient amounting to 38.7 days and S\$33 096. The hospitalisation cost and resources incurred by NIU patients were observed to be considerably higher compared with a similar study conducted on retrospective data of venous leg ulcer patients, where the average length of stay and inpatient bill per patient was 3.0 days and S\$7886, respectively.<sup>23</sup> It was also reported in another Singapore study that a 54% increase in NIU wound episodes per 1000 inpatient admissions was observed in 2017 compared with 2013, and that NIU patients compared with other wound groups (ie, venous leg ulcers, pressure injuries, and surgical site infections) were in the poorest of health with the highest number of comorbid conditions. This suggests

that management and treatment of NIU results in higher consumption of healthcare resources and longer duration, compared with other wound types.

In this study, the cost of inpatient services per NIU patient was 73.5% higher than outpatient bill. Although not specific to NIUs, high hospitalisation cost arising from DFUs and chronic leg ulcers has been highlighted in previously published studies. For an average DFU patient, a Spanish study reported a cost of €7633 per admission,<sup>24</sup> and a 2008 Eurodiale study estimated a range between €7147 and €18 790 depending on wound complications.<sup>16</sup> A prospective study on DFU conducted in a multidisciplinary hospital-based care setting comprising of inpatient and outpatient services, reported the cost of inpatient care to be more than thrice the cost of outpatient care.<sup>25</sup> However, the study demonstrated that despite the high cost, favourable outcomes are attainable as the limb salvage rate was 95% in the first year of study. While our study estimates the average length of stay for an NIU patient as 38.7 days for the duration the patient is present in the cohort data, another Singapore study reported the average length of stay as 15.8 days and gross charge as US\$11 045 (S\$14 949) per NIU wound episode for a single year.<sup>13</sup> Understanding the high costs associated with NIU is important as the incidence of NIU is expected to rise due to higher prevalence of asymptomatic PAD and diabetes in a rapidly aging population.<sup>26,27</sup> Furthermore, a study reported patients with ischemic DFU patients with PAD to have more severe wound and clinical features resulting in poor health outcomes compared with neuropathic DFU patients.<sup>8</sup>

Findings of this study also showed that NIU patients with more than 3 medical comorbidities, kidney disease complications or coronary artery disease have incurred longer lengths of stay and higher patient bills. Furthermore, patients with diabetes mellitus had higher odds of incurring an ED visit compared with their counterparts. A recent systematic review on the severity of DFU discovered advanced age and other comorbidities in diabetes patients to be repeated predicting factors in various studies.<sup>28</sup> These findings are particularly concerning and relevant as a large majority of our study cohort were diagnosed with diabetes mellitus (92.4%) and had more than 3 comorbidities (70.8%). Similarly, a study conducted with over a million patients with type 2 diabetes had 88.5% of the cohort with at least two comorbid conditions.<sup>29</sup> The study also reported chronic kidney disease and cardiovascular disease to be among the most common conditions co-existing with diabetes, and a six-fold increase in the co-prevalence of these conditions was observed from the youngest to the oldest patient. Our findings on these comorbid conditions are of high importance as these factors are potentially modifiable through interventions targeted at patients with early onset of diabetes.

In addition, this study reports important associations between the presence of PAD and cost outcomes. NIU patients with PAD incurred longer inpatient stay and higher inpatient bill. In our study cohort, 62% of patients with NIU were diagnosed with PAD. In diabetic patients with foot ulcers, there is an increasing prevalence of PAD,<sup>30</sup> and coexistence of these conditions affects the healing process and often leads to amputation.<sup>31</sup> A 2004 review on economic consequences of DFUs reported infected ulcers with no amputations to cost approximately US\$17 500, whereas lower limb amputations to be between US\$3000 to US\$33 500.<sup>32</sup> This is demonstrated in our study where NIU patients who had to undergo amputation incurred an additional 8.5 days and S\$7294, in inpatient stay and bill, respectively. A systematic review on the economic burden of chronic wounds showed the median cost per hospitalisation to be higher for diabetes-related amputations compared with treating heart failure patients.<sup>2</sup> This highlights the importance of lowering the risk of amputation among NIU patients, through various interventions such as multi-disciplinary approach in wound care, patient education on foot self-care habits and suitable footwear, timely deliverance of treatment options, and prompt referral system. The systematic review also highlighted that a cost-saving of approximately US\$85 000 to US\$1 100 000 per year can be achieved through the use of appropriate interventions.<sup>2</sup>

There are a few limitations to this study. First, is lack of information on the actual wound conditions such as size, severity, and duration of healing as these could not be extracted through an electronic coding system. This could have explained more of the variation in cost-related outcomes. Second, we analysed factors associated with direct costs and did not incorporate productivity costs such as work-loss days and loss of health-related quality of life. The total societal costs involved in the management and treatment of NIU patients would have been higher if these were included.

## 5 | CONCLUSION

In this study, we found the cost of inpatient services for an average patient with NIU to have incurred 38.7 inpatient days, 7.9 inpatient dressings, and a bill amount of S\$33 096. For outpatient services, mean dressing sessions per patient and bill per patient was 11.3 and S\$8780, respectively. This study also showed increased cost outcomes to be associated with NIU patients with multiple (>3) comorbid conditions, amputation, presence of PAD, chronic kidney disease, or coronary artery disease. Further research is important to inform how care approaches can achieve improved health outcomes while mitigating costs.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## APPENDIX A

List of International Classification of Disease (ICD) codes used for identifying eligible patients for study analysis.

Category	Diagnosis description	ICD-10 codes
Section A – Wounds related to diabetes	Type 2 diabetes mellitus with foot ulcer because of multiple causes	E1173
	Unspecified diabetes mellitus with foot ulcer because of multiple causes	E1473
	Other specified diabetes mellitus with foot ulcer because of multiple causes	E1373
	Type 1 diabetes mellitus with foot ulcer because of multiple causes	E1073
Section B - Wounds related to peripheral artery disease	Atherosclerosis of arteries of extremities with ulceration	I7023
	Atherosclerosis of arteries of extremities with gangrene	I7024



Category	Diagnosis description	ICD-10 codes
Section C - Wounds related to both diabetes and peripheral artery disease	'Type 1 diabetes mellitus with peripheral angiopathy, with gangrene'	E1052
	'Type 2 diabetes mellitus with peripheral angiopathy, with gangrene'	E1152
	'Unspecified diabetes mellitus with peripheral angiopathy, with gangrene'	E1452
Section D - Peripheral arterial disease	'Atherosclerosis of arteries of extremities, unspecified'	I7020
	'Impaired glucose regulation with peripheral angiopathy, without gangrene'	E0951
	Other specified peripheral vascular diseases	I738
	'Peripheral vascular disease, unspecified'	I739
	Atherosclerosis of arteries of extremities with intermittent claudication	I7021
Section E - Both diabetes and peripheral arterial disease	'Type 1 diabetes mellitus with peripheral angiopathy, without gangrene'	E1051
	'Type 2 diabetes mellitus with peripheral angiopathy, without gangrene'	E1151
	'Unspecified diabetes mellitus with peripheral angiopathy, without gangrene'	E1451
	'Other specified diabetes mellitus with peripheral angiopathy, without gangrene'	E1351

Patients were included in analysis if there were fell into:

1. Section A only
2. Section B only
3. Section C only
4. Section A and D
5. Section B and E

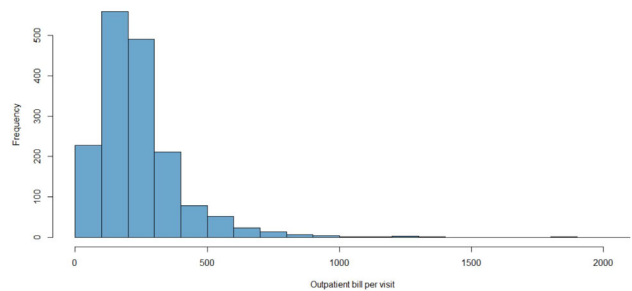


FIGURE B3 Histogram distribution of outcome: outpatient bill (\$\$) per visit

APPENDIX B

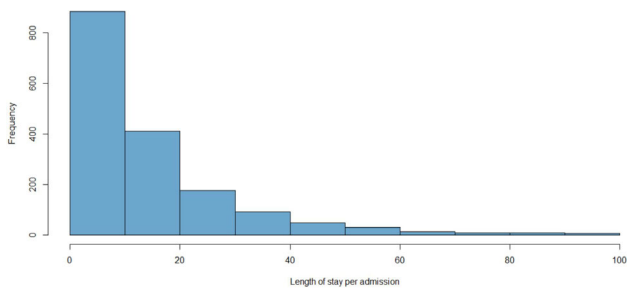


FIGURE B1 Histogram distribution of outcome: length of stay per inpatient admission

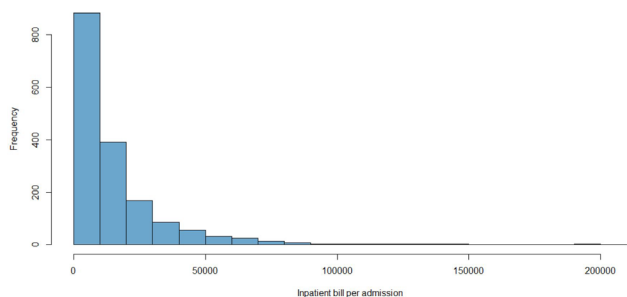


FIGURE B2 Histogram distribution of outcome: inpatient bill (\$\$) per admission