BMJ Open

Chronic Wounds in a Multi-Ethnic Asian Population. A Cost of Illness Study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065692
Article Type:	Original research
Date Submitted by the Author:	17-Jun-2022
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Keywords:	GENERAL MEDICINE (see Internal Medicine), HEALTH ECONOMICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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Chronic Wounds in a Multi-Ethnic Asian Population. A Cost of Illness Study.

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Words. 2620

Abstract

Objective. To estimate the 'cost of illness' arising from chronic wounds in Singapore.

Design. Incidence based cost of illness study using evidence from a range of sources.

Setting: Singapore health services.

Participants. We consider 3.49 million Singapore citizens and permanent residents. There are 16,752 new individuals with a chronic wound in 2017, with 598 venous ulcers, 2,206 arterial insufficiency ulcers, 6,680 diabetic ulcers and 7,268 pressure injuries.

Outcome measures: number of acute care bed days used; costs of acute care bed days; costs of non-acute health care services; costs of outpatients services; reduced health related quality of life as measured by Quality Adjusted Life Years; value of lost Quality Adjusted Life Years.

Results: Total annual cost of illness was $350 million (range $78 to 1,479 million). With 168,419 acute bed days used annually (range 144,050 to 196,789) that incurred costs of $138 million (range 118 to 162 million). Total costs to health services were $185 million (range $121 to $991. Total annual costs of lost health were 2,071 QALYS (range -2,296 to 26,656) valued at $166 million (range -184 to 2,052 million).

Conclusions. The costs of chronic wounds are large to Singapore, but many of them could be avoided by making positive investments in integrated and comprehensive wound prevention and treatment programmes.

Strengths and limitations of this study

- Reliable and relevant data sources were used to update the results
- First study to quantify the national cost of chronic wounds in a multi-ethnic Asian population
- Some important costs were excluded as no data were available
- The sample size for the preference based utility weights for QALYS were small
- Some outcomes were not adjusted for co-morbidities and so likely overstate the true costs.

Introduction

Chronic wounds are those that fail to heal in a time sufficient for normal healing. They tend to present as a co-morbid rather than primary condition among older individuals. Other risk factors are diabetes, poor nutrition, incontinence and reduced mobility [1]. They have been described as causing a 'silent epidemic' that affects a large proportion of the world's population [2]. Chronic wounds are prevalent among vulnerable individuals living at home and residents of long-term care facilities. They are commonly associated with extended hospital stays yet patient safety programmes have reduced nosocomial events [3].

The burden of cost is particularly large [4] with 3% of the total NHS budget [5] and 4% of health care expenditure in Scandinavian countries used to manage the consequences of chronic wounds [6]. Evidence from the United States suggests the annual healthcare cost of diabetic foot ulcer alone approximates the costs of treating cancer [7]. Yet, the goal of reducing the prevalence of chronic wounds has failed to attract sustained investment from those who pay for health services [8]. This contrasts with other major diseases, where payers are prepared to invest in 'cancer moonshots' for example [9], that will hopefully lead to better outcomes the future. This inequity is irrational as the technology for reducing chronic wounds is available now, saves more than it costs to implement [10] and will cause large and certain gains in health outcomes.

Ulcers of the skin are the most common type of chronic wounds and include venous ulcers, arterial ulcers, diabetic foot ulcers and pressure ulcers or injuries. There are associated with a wide range of economic costs [2]. Affected individuals require frequent evidence-based treatments and if the condition becomes overwhelming an admission to hospital is inevitable. Many patients will be admitted for other reasons, and the wound may independently prolong hospital stay [11]. Debridement, minor amputations, and major amputations are very common among higher risk groups [12, 13]. Chronic wounds are prevalent in aged care facilities and will incur additional costs for staff time and consumables. Home nursing services as well as charities and volunteer groups that support the frail and elderly in their homes will also have to manage many patients [14]. Out of pocket expenditures will arise for patients and family members who travel to access services and purchase consumable items [15]. Productivity losses will arise as the patients are unable to perform their normal activities, be they paid or unpaid, and family members will have to take time from economically productive activity. Health-related quality of life - which has monetary value [16] - will be reduced. All these relevant costs can be structured by a 'cost of illness' method [17]. Estimates arise from information on the incidence and prevalence of the disease.

The aim of this study is to estimate the 'cost of illness' arising from chronic wounds in Singapore. Our results could be used to encourage decision makers to invest in known prevention and management programmes. The findings will also aid researchers who wish to model the cost savings or the cost-effectiveness of specific interventions.

Method

Scope of the analysis

We include all resident Singapore Citizens and Permanent Residents (n=3.49M), excluding resident foreign nationals and long-term employment pass holders (n=526,000) in 2017 [18]. Singapore has a multi-ethnic Asian population comprising of residents who are 76% Chinese, 15% Malay and 7.5% Indian descent [19].

Incident cases of chronic wounds

We used published incidence rates for 2017 from a population-based study of wounds among those admitted to acute care hospitals from 2000 to 2017 [20]. For this work the authors identified relevant ICD-10 codes for for occurrences of venous ulcers, arterial insufficiency ulcers, diabetic ulcers, and pressure ulcers or injuries, see Appendix 1, and applied them to the Singapore Ministry of Health central claims database, which includes records of all admissions to public and private acute care hospitals. The incidence rates by age band are reported alongside the at-risk population enabling the number of incident cases to be estimated, see Appendix 2.

Reduced health related quality of life

We used EQ-5D-5L data to estimate the impact of chronic wounds on health-related quality of life. This instrument includes preference based valuations of health states expressed as 'health utilities' on a scale between zero, the worst possible health state, and one, the best possible health state [21]. Multiplying the relevant health utility score by the time individuals spend in that health state provides an estimate of the number of quality adjusted life years (QALYs). QALYs are a recognised outcome measure that reveal the health benefits of new innovations and therapies [22]. Many governments are willing to pay money for services that increase the number of QALYs in a population, given a programme achieves a marginal QALY below a designated cost [23].

We used EQ-5D-5L data from 799 individuals with relevant wounds from the Singapore national wound care registry. Responses were recorded at entry into the registry, when the wound was first assessed in the hospital setting and then at 1, 3 and 6 months, see Appendix 3. We used a Singapore EQ-5D-3L value set [24] that was then mapped onto the EQ-5D-5L version using the SAS code in Appendix 1A. The utility outcomes for the wound patients were compared to population norms for the EQ-5D index informed by Singapore preference weights for appropriate age bands [25] to estimate a decrement to health utility from the wound.

The mean duration of wounds in days for the specific wound types was extracted from the Singapore Wound Registry, see Appendix 4. The economic value of one QALY was set at the mean gross domestic product per

capita for Singapore, which is USD $59,798 or approximately SGD $80,000 [26]. This approach assumes one year of perfect quality of life does not exceed the per capita gross domestic product [27].

Admissions to hospitals

A population cohort of all inpatient admissions to acute hospitals in Singapore between 2012 and 2019 was obtained from the Singapore Ministry of Health. We identified all inpatient episodes with any occurrences of Venous ulcers, Arterial insufficiency ulcers, Diabetic ulcers and Pressure injury or any combination of these wounds as a primary or secondary diagnosis using the ICD-9 codes in Appendix 1. We extracted the length of hospital stay and relevant co-variate information that could be used to explain variation in the length of stay, see Appendix 5.

A parsimonious multivariable generalised linear model (GLM) with a gamma link function was used to accommodate the skew typical of lengths of stay data [28]. The outcome of interest was the excess length of stay associated with chronic wound management in the inpatient setting. Other covariates included were age, gender, race, and comorbid chronic diseases. The statistical model generated a coefficient for 'wound type' expressed as a rate ratio, that showed the amount of increase in length of stay associated with the presence of wound, given that other factors that predicted length of stay had been accounted for. This rate ratio was used to moderate the mean length of stay for the entire sample and an excess length of stay associated with the wound was estimated, see Appendix 6. The cost per bed-day in 2017 was estimated to be $823 (95% CI $817 to 829) based on information from Singapore's Ministry of Health.

Other Health Services

The same population cohort for 2012 to 2019 who were admitted as inpatients was used to identify their use of 'other' health services in Singapore. Information was available for attendances at the Emergency Departments of acute hospitals, visits to community-based Polyclinics and use of community health assist scheme (CHAS). CHAS is a mechanism for funding all Singapore Citizens to attend medical and/or dental care at participating General Practitioner (GP) and dental clinics. CHAS is particularly designed to support the management of chronic diseases.

We sought to estimate the excess use of these services associated with any chronic wound. For the analysis each patient is counted only once, and those with wounds are only counted when they first appear with any wound, and the number of 12-month visits from the incidence date is the outcome variable. For those without wounds, their 12-month use starts from the first visit during the study period. A parsimonious generalised linear model with a log link Poisson function was used for all regressions. The outcome of interest was a count of the use of the services. Other covariates included were age, gender, race Charlson comorbidity index and presence of comorbid conditions, see Appendix 7. The ensuing statistical models

generated a coefficient for 'any wound' expressed as a rate ratio, that showed the change in the number of visits associated with the presence of wound, given that other factors that predicted variation in these outcomes. As before, the rate ratio was used to moderate the mean counts for the entire sample and an excess number of visits was estimated for all wounds, see Appendix 8. For the costs of health services, we use estimates before any subsidies were paid, from the Singapore Ministry of Health, see Table 1.

Use of outpatient services

The Singapore national wound care registry was interrogated to identify the annual number of visits for those with chronic wounds and the costs incurred per visits, this information was available by wound type. There were 573 individuals for whom these data were reported. Visits were for specialist consultations specifically for their wound, and for podiatry visit or medical tests. See Appendix 6a.

Parameters, Uncertainty & Model Evaluation

The parameters used for the cost of illness model estimations are shown in Table 1.

Table 1. All parameters used for modelling cost of illness of chronic wounds

Parameter	Estimate	Distribution used for uncertainty	Source
Number admissions to hospital			
Arterial	14,536	fixed	[20]
Venous	19,210	fixed	
Diabetic	16,999	fixed	
Pressure injury	49,879	fixed	
Utility outcomes (baseline)			+
Arterial	0.44	Beta (0.24:0.30)	
Venous	0.57	Beta (0.60:0.46)	
Diabetic	0.64	Beta (0.21:0.12)	
Pressure	-0.18	Normal (-0.18:0.50)	
Utility outcomes (month 1)			
Arterial	0.52	Beta (0.23:0.21)	
Venous	0.68	Beta (0.89:0.41)	
Diabetic	0.71	Beta (0.04:0.02)	
Pressure	0.00	Normal (0.00:0.56)	
Utility outcomes (month 3)			
Arterial	0.54	Beta (0.13:0.11)	
Venous	0.74	Beta (0.81:0.28)	
Diabetic	0.72	Beta (0.28:0.11)	
Pressure	0.18	Normal (0.18:0.54)	
Utility outcomes (month 6)			
Arterial	0.58	Beta (0.16:0.12)	
Venous	0.74	Beta (0.83:0.28)	
Diabetic	0.74	Beta (0.05:0.02)	
Pressure	0.11	Normal (0.11:0.59)	
Durations of Arterial wounds (days)			
<40	133	Normal(133,92)	+
40-49	129	Normal(129,109)	
50-59	331	Normal(331,394)	
60-69	223	Normal(223,269)	
70-79	307	Normal(307,438)	
≥80	205	Normal(205,153)	
Durations of Venous wounds (days)			
<40	133	Normal(133,92)	

40-49	129	Normal(129,109)	+
50-59	331	Normal(331,394)	
60-69	223	Normal(223,269)	
70-79	307	Normal(307,438)	
≥80	205	Normal(205,153)	
Durations of Diabetic wounds (days)			
<40	177	Normal(177,88)	+
40-49	325	Normal(325,550)	
50-59	224	Normal(224,216)	
60-69	314	Normal(314,430)	
70-79	256	Normal(256,305)	
≥80	160	Normal(160,138)	
Durations of Pressure injury (days)			
<40	55	Normal(55,11)	+
40-49	86	Normal(86,24)	
50-59	115	Normal(115,1)	
60-69	103	Normal(103,59)	
70-79	105	Normal(105,115)	
≥80	62	Normal(62,52)	
Excess length of acute hospital stay admission			
Arterial	2.365	Gamma(757,0.003)	Appendix 6
Venous	0.788	Gamma(84,0.009)	
Diabetic	2.259	Gamma(742,0.003)	
Pressure injury	1.613	Gamma(724,0.002)	
Excess use of Poly clinic visit	0.91	Gamma(24161,0.05)	Appendix 6
Excess use of CHAS services	3.54	Gamma(157196,0.092)	
Excess use of ED visit	0.63	Gamma(35860,0.15)	
Outpatient visits number (with consult)			#
Arterial	8.2	Gamma (1.82:4.52)	
Venous	5.9	Gamma (0.98:5.99)	
Diabetic	8.1	Gamma (1.70:4.76)	
Pressure	6.5	Gamma (1.93:3.37)	
Outpatient visits number (without consult)			
Arterial	8.5	Gamma (1.77:4.79)	
Venous	23.6	Gamma (1.55:15.25)	
Diabetic	14.2	Gamma (0.08:185.15)	
Pressure	9.7	Gamma (0.81:12.00)	
Outpatient visits costs per visit (with consult)			
Arterial	110.4	Gamma (5.60:19.74)	
Venous	133.2	Gamma (2.70:49.30)	
Diabetic	112.0	Gamma (2.86:39.20)	
Pressure	111.0	Gamma (4.05:27.43)	
Outpatient visits costs per visit (without consult)			
Arterial	117.3	Gamma (5.60:19.74)	
Venous	106.8	Gamma (2.70:49.30)	
Diabetic	114.9	Gamma (2.86:39.20)	
Pressure	124.1	Gamma (4.05:27.43)	
Economic value per QALY	$80,000	Fixed	[26]
Cost per bed day	$823	Normal(823,0.78)	#
Cost per Poly clinic visit	$147	Normal(147,2.5)	
Cost per CHAS use	$56	Normal(56,1.14)	
Cost per ED visit	$352	Normal(352,.14)	

+ Skin Research Institute of Singapore, *Singapore Wound Registry, Agency for Science Technology and Research.* Accessed in 2021
# Ministry of Health, *Administrative database*, Ministry of Health (MOH). Accessed in 2021.

Uncertainty for the outcomes was assessed by taking 5,000 random resamples from all prior distributions. Model evaluation was completed by combining the stated parameters to estimate: the number and costs of the excess bed days used for all wound types; the observed annual number of outpatients' consultations; the number and costs of excess visits to polyclinics, CHAS services and ED; the number and value of QALYS foregone.

Patient and Public Involvement

The data came from the Singapore Wound Registry and from the Ministry of Health. It was routinely reported data collected for the purpose of managing and planning health services. It was not possible to develop the research question or outcome measures based on the priorities, experience, and preferences of the patients. Patients were not involved patients in the design, recruitment and conduct of the study. Patients who are interested will be able to read the paper.

Results

There are 16,752 new cases for 2017, with 598 venous ulcers, 2,206 arterial insufficiency ulcers, 6,680 diabetic ulcers and 7,268 pressure injuries. The mean and minimum and maximum values obtained from the model parameters for these incident cases are shown in Table 2.

Table 2. Annual cost outcomes for incident cases (n=16,752), Singapore dollars

	mean (min:max)
Bed days arterial	34,397 (30385:38,632)
Bed days venous	15,150 (9,632:22,590)
Bed days diabetic	38,403 (33,829:42,930)
Bed days pressure	80,470 (70,203:92,637)
Costs bed days arterial	$28,308,066 ($24,932,371:$31,821,962)
Costs bed days venous	$12,468,507 ($7,941,748:$18,655,204)
Costs bed days diabetic	$31,605,197 ($27,722,430:$35,350,126)
Costs bed days pressure	$66,225,760 ($57,852,994:$76,198,768)
Costs Polyclinic visits	$2,249,594 ($711,389:$5,127,710)
Costs CHAS episodes of care	$3,301,201 ($1,653,310:$5,815,975)
Costs Outpatients arterial	$4,150,483 ($25,476:$40,260,866)
Costs Outpatients venous	$1,997,965 ($9,318:$22,903,331)
Costs Outpatients diabetic	$16,333,239 ($11,130:$563,220,045)
Costs Outpatients pressure	$14,297,952 ($124,731:$177,747,006)
Costs ED visits	$3,721,208 ($301,938:$13,612,955)
QALYS arterial	537 (-361:5,802)
QALYS venous	77 (-135:1,119)
QALYS diabetic	854 (-1239:13,177)
QALYS pressure	602 (-560:5,557)
Value QALYS arterial	$42,994,791 (-$28,897,531:$464,173,798)
Value QALYS venous	$6,187,275 (-$10,822,288:$89,547,619)
Value QALYS diabetic	$68,316,063 (-$99,119,920:$1,054,186,965)
Value QALYS pressure	$48,199,106 (-$44,839,589:$444,575,871)
Total Costs - Arterial	$76,674,669 ($4,460,814:$497,501,523)
Total Costs - Venous	$20,984,759 ($1,890,303:$105,689,456)
Total Costs - Diabetic	$119,951,394 (-$60,215,105:$1,089,348,943)
Total Costs - Pressure	$132,745,584 ($27,551,116:$531,071,502)
Total Cost of Illness	$350,356,406 ($77,685,675:$1,478,865,185)

Based on our estimates pressure injuries account for 48% of the 168,415 bed days lost to chronic wounds and 39% of the outpatients costs. For the non-hospital sector, the costs of CHAS services and ED visits account for most of the burden. The QALY burdens are large for diabetic foot, arterial and pressure injury with venous having smaller impact. Box plots for all the outcomes except for 'Total Costs' are shown in Appendix 9. Box plots for the 'Total Costs' outcomes are shown in Figure 1.

FIGURE 1 HERE

There is a large probability that the costs of chronic wounds are positive with the most likely value suggesting an annual cost of Singapore $350 million. The findings are uncertainty with the range of total costs between $78 million and $1.48 billion. More than half of the total costs arise from use of health services ($185 million, 53%) with outpatients accounting for $37 million (10%) and the use of acute bed days accounting for $139 million (40%). The value of the lost health by QALYs is substantial at $165 million, 47% of the total burden.

Discussion

Our findings reveal the costs of chronic wounds to Singapore are extensive. The total cost burden accounts for 3.14% of the 2019 Government Health Expenditure on services [29] and 2.3% of total economy-wide expenditure on services. Our estimates align findings from other countries. In Australia 2% of the total national health expenditure is allocated to chronic wounds, 3% of the total national health expenditure in the UK [5] is used, 2% of the European health budget [30]; and, for Scandinavian countries, the costs were 2 to 4% of the total health care expenditure [6]. While the findings are lower than the expected annual costs of diabetes, estimated to be US $787 million in 2010 [31], the policy response to diabetes has been considerable with a 'War on Diabetes' declared in 2016, to mobilise a national programme to reduce the problem of diabetes [32].

This study likely underestimates the extent of the costs of chronic wounds as relevant information was not available for many costs we suspect are present. Our data came primarily from patients who were admitted to the hospital for their wounds. Thus patients with less serious wounds managed in the community are excluded. We were also unable to identify and include estimates of the private costs incurred by patients and family members. Other studies have found that such costs can be substantial. For the German setting Purwins et al. [33] found patients with leg ulcers in a given year spent €424 on topical treatments and drugs, €486 on out of pocket incidentals, €254 on drug prescriptions and €740 on non-drug treatments. Although no data were available on the time away from work and other production losses, we addressed this by estimating and valuing lost quality adjusted life years (QALYs). We assume that time in reduced health states has a relationship with an ability to be economically productive. Thus, the dollar valuations of the lost QALYs can be thought of as representing lost production from chronic wounds. Importantly we did not consider the costs of lost production for informal carers, which we expect to be substantial.

This recurring and unnecessary cost burden is a deadweight loss to Singapore health services, and society in general. It could be reduced if evidence-based and relatively simple prevention and management programmes were implemented. The international evidence [10] reveals that using optimal prevention practices for diabetic foot ulcers [34] was likely to be cost-saving in Peru [35], Australia [36], Thailand [37]

and China [38]. For the prevention of pressure injury nursing led interventions, a quality improvement collaborative and the standardised use of pressure injury bundles were found to be cost-saving in Denmark [39], the US and UK [40-43]. And for the prevention of venous leg ulcers, compression therapy, clinical assessments and use of guidelines were found to be cost-saving in the UK [44, 45] and US [46, 47].

There are several limitations to our study. Regarding the estimation of QALY losses, the sample sizes for EQ5D were quite small for Pressure injury with only 51 patients providing data. It is possible the estimate would change with a larger and more representative sample. It should be noted that the lowest health utilities arise from this sample; for example, the values for baseline were -0.18 indicating a health state valued worse than death, and a value of 0.00, the worst possible health state, was observed for month 1. Values remained low at 0.18 and 0.11 for the 3 month and 6 month follow-ups. We assumed that the observed decrement between the population norms for health utility and the estimates from the wound registry were wholly attributable to the presence of a wound. These QALY estimates did not adjust for the other health conditions that patients may have, and as such may overstate the QALY losses.

Despite these limitations, our findings serve an important purpose of providing baseline information for researchers who wish to model the cost-effectiveness of programmes that will improve wound outcomes in the future. Understanding the baseline of costs and QALY outcomes form a useful start-point for evaluation of intervention studies. These can reveal the potential cost effectiveness of increasing investment in good quality wound prevention programmes, and can also help bolster arguments for greater investments in these interventions.

Conclusions.

The costs of chronic wounds are large to Singapore, but many of them could be avoided by making positive investments in integrated and comprehensive wound prevention and treatment programmes.

Authors contributions. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. Drafting the work or revising it critically for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. NG; GG; KB; OG; HP; TC; PB; DC; SA; JL; EY; FB; WZ; KH.

A competing interests statement. None

Funding. We would like to acknowledge the funding supported from the Agency for Science, Technology and Research (A*STAR) under its Industry Alignment Fund-Pre-Positioning Programme (IAF-PP) grant number H1901a00Y9/ and H17/01/a0/0CC9 as part of the Wound Care Innovation for the Tropics (WCIT) Programme.

Data availability statement. No data from the wound registry or MoH administrative databases are available. This is due to the privacy considerations of the Singapore MOH and the Singapore wound registry.

Ethics Approval

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

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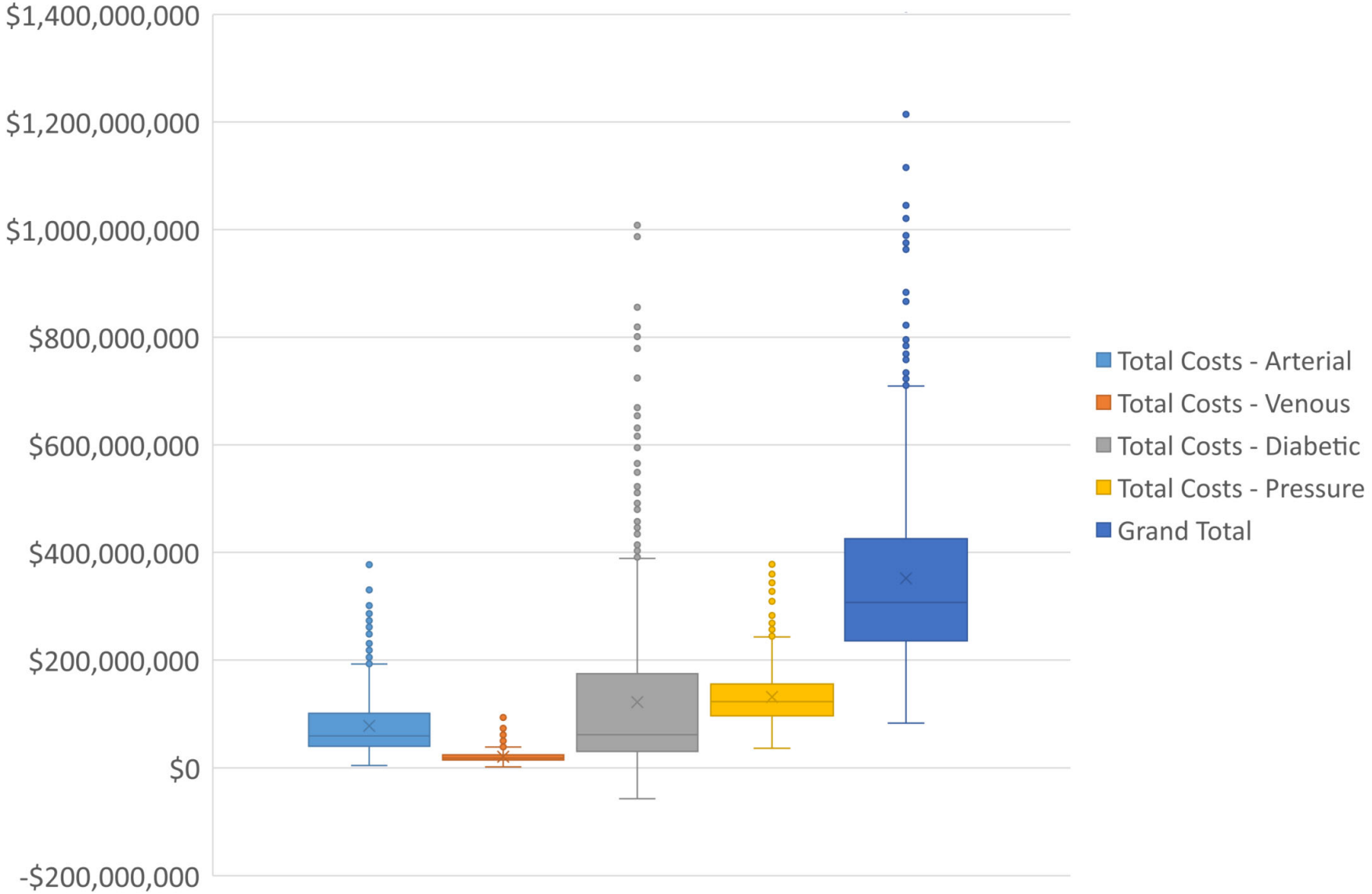
Figure 1. Total cost outcomes for the cost of Illness by wound type


$1,400,000,000
$1,200,000,000
$1,000,000,000
$800,000,000
$600,000,000
$400,000,000
$200,000,000
$0
-$200,000,000
Total Costs - Arterial
Total Costs - Venous
Total Costs - Diabetic
Total Costs - Pressure
Grand Total

Appendix 1. ICD-9 codes used to identify chronic wounds from national claims dataset

Venous ulcers – *ICD-9-AM: 4540, 4532, 4591; ICD-10-AM: I83.0, I83.2, I87.0.*

Arterial insufficiency ulcers – *ICD-9-AM: 44023, 44024; ICD-10-AM: I70.23, I70.24*

Diabetic ulcers – *ICD-9-AM: 7071, 7078, 7079, 7854 & one of 25070, 25071, 25072 or 25073; ICD-10-AM: E10.73, E11.73, E13.73, E14.73, E10.52, E11.52, E13.52, E14.52, E09.02, E09.52, E10.69, E11.69, E13.69, E14.69*

Pressure ulcers – *ICD-9-AM: 7070; ICD-10-AM: L89.0, L89.1, L89.2, L89.3, L89.4, L89.5, L89.6, L89.7, L89.8, L89.9*

Appendix 1A - SAS code for calculating the local EQ-5D index score from EQ-5D-3L

```
*** coding of EQ-5D data: 1 = no problems, 2 = some/moderate problems, 3 = extreme problems;
*** mo = mobility, sc = self-care, ua = usual activity, pd = pain/discomfort, ad = anxiety/depression;

data new; set new;
    if mo=2 then m2=1; else m2=0;
    if mo=3 then m3=1; else m3=0;
    if sc=2 then s2=1 page ; else s2=0;
    if sc=3 then s3=1; else s3=0;
    if ua=2 then u2=1; else u2=0;
    if ua=3 then u3=1; else u3=0;
    if pd=2 then p2=1; else p2=0;
    if pd=3 then p3=1; else p3=0;
    if ad=2 then a2=1; else a2=0;
    if ad=3 then a3=1; else a3=0;
    if mo=3 or sc=3 or ua=3 or pd=3 or ad=3 then n3=1; else n3=0;
    EQ_index = 1 - 0.1678*m2 - 0.3040*m3 - 0.1615*s2 - 0.3465*s3 - 0.2555*u2 - 0.3209*u3 - 0.1462*p2 - 0.2291*p3 - 0.1501*a2 - 0.2784*a3 - 0.2905*n3;
    if mo =. or sc=. or ua=. or pd=. or ad =. then EQ_index =. ;
    drop m2 m3 s2 s3 u2 u3 p2 p3 a2 a3 n3; run;
```

Appendix 2. The incidence rates by age band, at risk population and incident cases

	age band	at risk population	incidence rate per 100,000	annual incident cases
Venous	<40	1,957,020	1.2	23
	40-49	614,941	7	43
	50-59	614,492	19.9	122
	60-69	466,620	37.5	175
	70-79	211,447	66.7	141
	≥80	101,276	91.8	93
	total	3,965,796		598
Arterial	<40	1,957,020	1.1	22
	40-49	614,941	15.6	96
	50-59	614,492	67.5	415
	60-69	466,620	143.4	669
	70-79	211,447	246.4	521
	≥80	101,276	477.9	484
	total	3,965,796		2,206
Diabetic	<40	1,957,020	5.8	114
	40-49	614,941	56.6	348
	50-59	614,492	175.8	1,080
	60-69	466,620	368.6	1,720
	70-79	211,447	758.6	1,604
	≥80	101,276	1791.1	1,814
	total	3,965,796		6,680
Pressure	<40	1,957,020	4.8	94
	40-49	614,941	22	135
	50-59	614,492	74.4	457
	60-69	466,620	236.4	1,103
	70-79	211,447	844.2	1,785
	≥80	101,276	3646.5	3,693
	total	3,965,796		7,268

Appendix 3. EQ-5D scores by type of wound and time from Singapore Wound Registry

Mean (Std. Dev.)	Baseline	month 1	month 3	month 6
Venous	0.57 (0.34) (n=255)	0.68 (0.31) (n=235)	0.74 (0.30) (n=242)	0.74 (0.30) (n=243)
Arterial	0.44 (0.40) (n=354)	0.52 (0.42) (n=311)	0.54 (0.45) (n=303)	0.58 (0.44) (n=291)
Diabetic	0.64 (0.42) (n=139)	0.71 (0.44) (n=128)	0.72 (0.38) (n=129)	0.74 (0.43) (n=126)
Pressure	-0.18 (0.50) (m=51)	0.00 (0.56) (n=43)	0.18 (0.54) (n=38)	0.11 (0.59) (n=40)

Appendix 4. Mean duration of wounds in days, by age band; Mean (Standard Deviation)

Age Band	Venous (n=150)	Diabetic (n=245)	Pressure (n=24)
<40	133 (92)	177 (88)	55 (11)
40-49	129 (109)	325 (550)	86 (24)
50-59	331 (394)	224 (216)	115 (1)
60-69	223 (269)	314 (430)	103 (59)
70-79	307 (438)	256 (305)	105 (115)
≥80	205 (153)	160 (138)	62 (52)

values for Diabetic were used to proxy 'Arterial' wounds

Appendix 5. Cohort of all hospital admissions for a relevant chronic wound 2012 to 2019

	All	No wound	Arterial	Venous	Diabetic	Pressure
Number	5,196,899	5,047,162	14,536	19,210	16,999	49,879
Age, mean (st dev)	50.4 (26.9)	49.6 (26.8)	75 (13.3)	72.1 (17.1)	72.4 (15.7)	81.7 (13)
Male	49%	48%	56%	57%	58%	50%
CCI score (mean)	4.1	4.1	6.1	4.7	5.9	4.4
Chinese	64%	64%	63%	60%	54%	71%
Malay	14%	14%	17%	16%	21%	13%
Indian	10%	10%	11%	13%	13%	6%
Others	12%	12%	9%	11%	12%	10%
COPD	7%	7%	6%	5%	5%	8%
Diabetes Mellitus	42%	42%	82%	57%	100%	40%
Hypertension	69%	68%	92%	77%	88%	76%
Dyslipidemia	61%	61%	84%	67%	86%	59%
Heart Failure	14%	14%	33%	21%	27%	14%
Renal Failure	24%	23%	49%	30%	44%	21%
Stroke	17%	17%	27%	19%	20%	40%
Dementia	6%	6%	7%	5%	4%	33%
Major Depression	6%	6%	5%	5%	6%	8%
Parkinson	3%	3%	2%	2%	1%	17%
Schizophrenia	4%	4%	1%	3%	2%	4%
Length of Stay, mean (st dev)	6.5(17)	6.3 (16.7)	16.2 (20.2)	9.8 (16)	14 (18.6)	16.8 (25.2)

Appendix 6. Results of generalised linear model (GLM) with a gamma link function to estimate excess length of stay

	All	No wound	Arterial	Venous	Diabetic	Pressure
Number	5,196,899	5,054,937	14,536	19,210	16,999	49,879
Length of Stay, mean (st dev)	6.5 (17)	6.3 (16.7)	16.2 (20.2)	9.8 (16)	14 (18.6)	16.8 (25.2)
Coefficient (95% CI)	-	-	0.722 (0.690,0.754)	0.303 (0.272,0.333)	0.701 (0.669,0.733)	0.543 (0.516,0.570)
Rate ratio of length of stay (95% CI)	-	-	2.059 (1.993,2.126)	1.353 (1.993,2.126)	2.015 (1.952,2.081)	1.722 (1.676,1.769)
Estimated mean length of stay (95% CI)	-	-	2.233 (2.215,2.252)	2.232 (2.215,2.252)	2.226 (2.208,2.245)	2.234 (2.216,2.253)
Expected length of stay (95% CI)	-	-	4.598 (4.414,4.788)	3.02 (4.414,4.788)	4.485 (4.31,4.672)	3.847 (3.714,3.986)
Excess length of stay (95% CI)	-	-	2.365 (2.199,2.536)	0.788 (2.199,2.536)	2.259 (2.102,2.427)	1.613 (1.498,1.733)

Appendix 6a – usage and costs of outpatient services for patients with chronic wounds

	with consult		without consult	
Total annual costs	mean (sd)	95% CI	mean (sd)	95% CI
Costs of Outpatient with Consult - Arterial	$908.13 ($778.27)	($815.39, $1000.86)	$992.01 ($1241.53)	($844.08, $1139.94)
Costs of Outpatient with Consult - Venous	$685.73 ($575.30)	($603.62, $767.84)	$2381.98 ($2449.41)	($2024.72, $2739.24)
Costs of Outpatient with Consult - Diabetic	$918.06 ($823.40)	($752.11, $1084.01)	$1068.85 ($905.06)	($888.33, $1249.36)
Costs of Outpatient with Consult - Pressure	$702.40 ($525.63)	($368.43, $1036.37)	$1111.98 ($1330.34)	(-$118.38, $2342.34)
Annual visits	mean (sd)	95% CI	mean (sd)	95% CI
No. of Visits of Outpatient with Consult - Arterial	8.249 (6.107)	(7.521, 8.977)	8.454 (6.362)	(7.696, 9.212)
No. of Visits of Outpatient with Consult - Venous	5.874 (5.932)	(5.028, 6.721)	23.639 (18.989)	(20.870, 26.409)
No. of Visits of Outpatient with Consult - Diabetic	8.102 (6.209)	(6.857, 9.347)	14.172 (51.225)	(4.008, 24.336)
No. of Visits of Outpatient with Consult - Pressure	6.5 (4.681)	(3.526, 9.474)	9.714 (10.797)	(-0.271, 19.700)
Cost per Visit	mean (sd)	95% CI	mean (sd)	95% CI
Costs per Visit of Outpatient with Consult - Arterial	$110.44 ($46.69)	($104.88, $116.01)	$117.28 ($87.66)	($106.84, $127.73)
Costs per Visit of Outpatient with Consult - Venous	$133.24 ($81.05)	($121.67, $144.80)	$106.81 ($105.11)	($91.48, $122.14)
Costs per Visit of Outpatient with Consult - Diabetic	$112.00 ($66.26)	($98.64, $125.35)	$114.93 ($39.31)	($107.08, $122.77)
Costs per Visit of Outpatient with Consult - Pressure	$111.04 ($55.19)	($75.97, $146.10)	$124.14 ($38.92)	($88.14, $160.13)

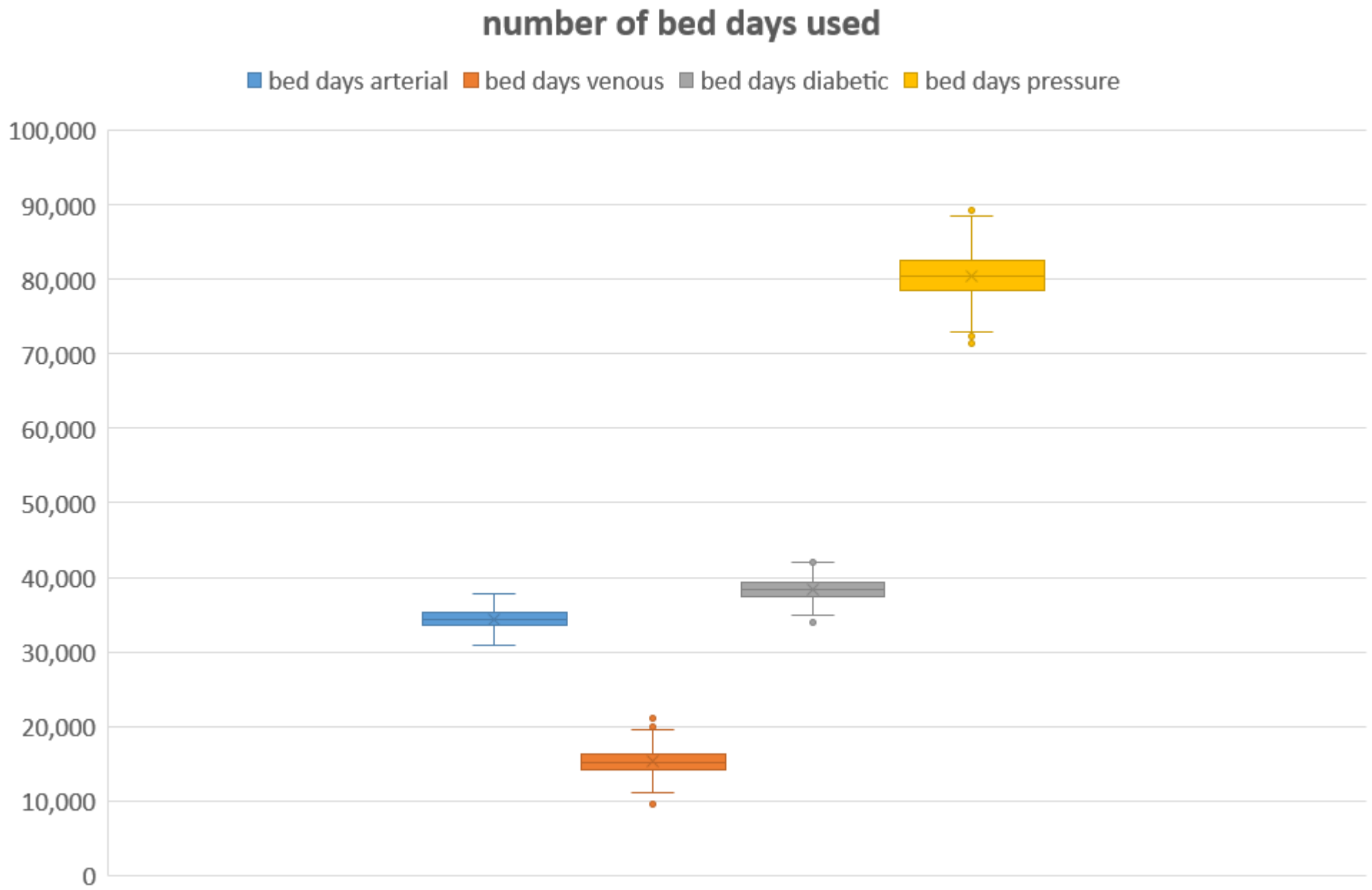
Appendix 7. Cohort of all patients who accessed CHAS, Polyclinic or Emergency departments (ED) 2012 to 2019

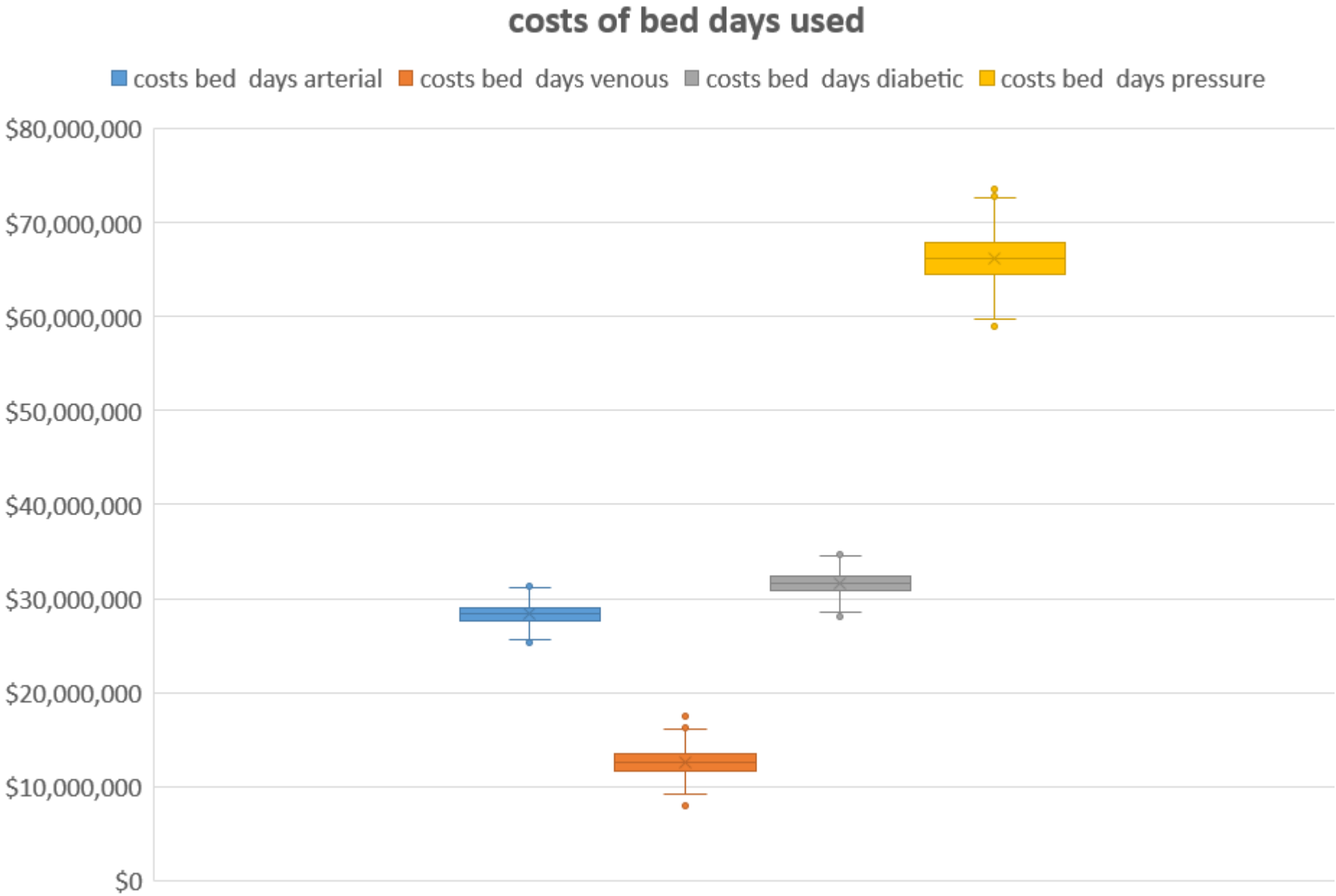
	CHAS		Polyclinic		ED	
	No Wound	Any Wound	No Wound	Any Wound	No Wound	Any Wound
Number	1,013,104	3,463	2,600,153	1,441	2,964,540	7,403
Age	49.4	67.9	37	65	36	68
Male	46%	45%	51%	57%	56%	52%
CCI score	2.6	4.0	2.1	4.3	2.0	5.0
Chinese	72%	78%	64%	61%	52%	61%
Malay	14%	10%	12%	13%	10%	17%
Indian	6%	8%	10%	20%	9%	13%
Others	9%	5%	14%	6%	30%	9%
COPD	3%	4%	2%	5%	3%	5%
Diabetes Mellitus	32%	55%	28%	68%	30%	70%
Hypertension	64%	82%	55%	81%	56%	83%
Dyslipidemia	61%	72%	50%	78%	51%	77%
Heart Failure	4%	13%	3%	15%	4%	22%
Renal Failure	10%	24%	7%	26%	8%	39%
Stroke	8%	16%	7%	17%	8%	26%
Dementia	2%	6%	1%	6%	2%	16%
Major Depression	3%	3%	2%	4%	2%	7%
Parkinson	1%	3%	1%	2%	1%	6%
Schizophrenia	2%	2%	2%	3%	2%	3%
Average no. of episodes in 12 months from wound/first visit	3.1	6.2	1.8	2.8	1.4	2.6

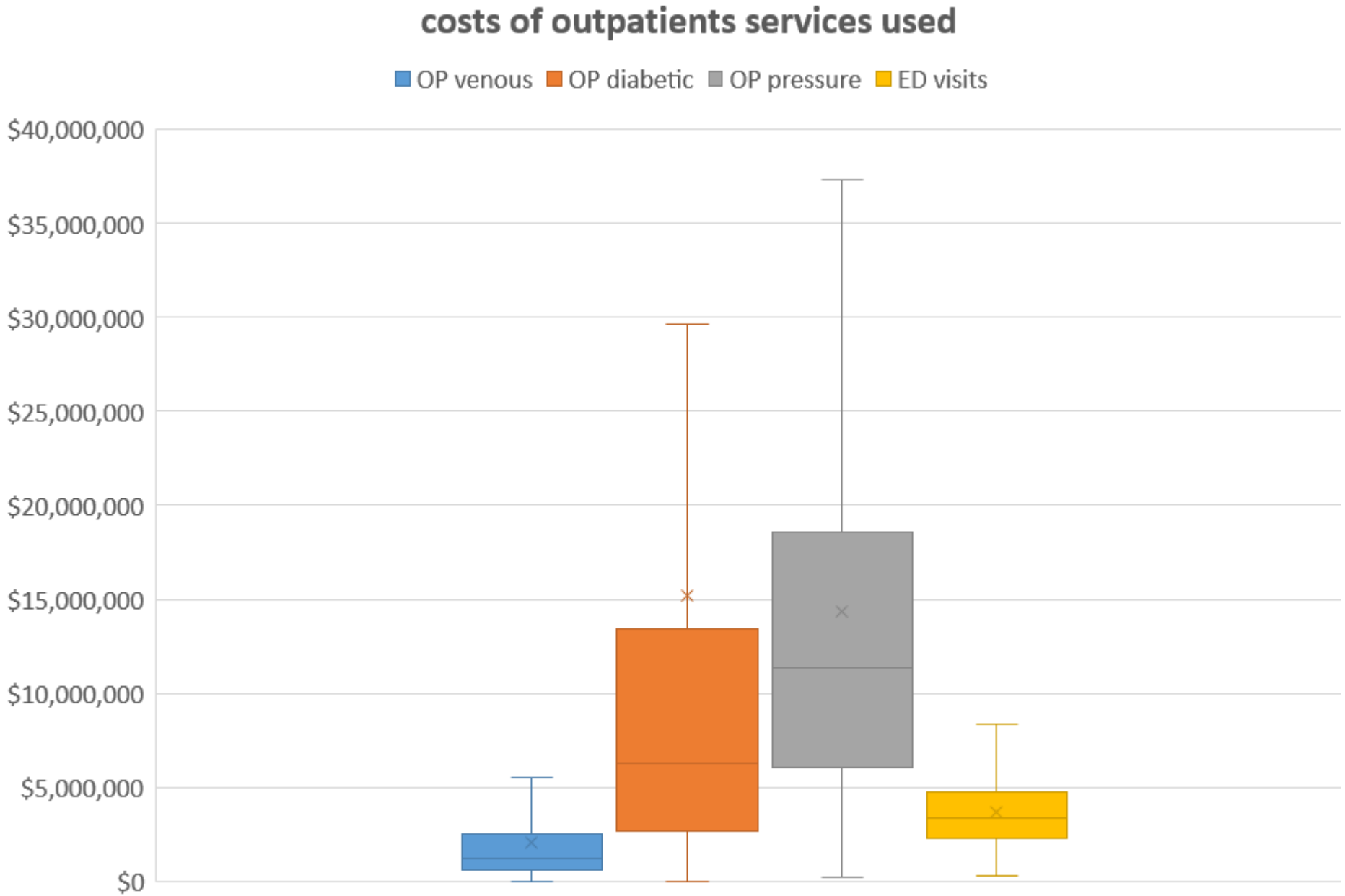
Appendix 8. Results of generalised linear model (GLM) with a Poisson link function to estimate excess use of poly-clinic services, CHAS and ED.

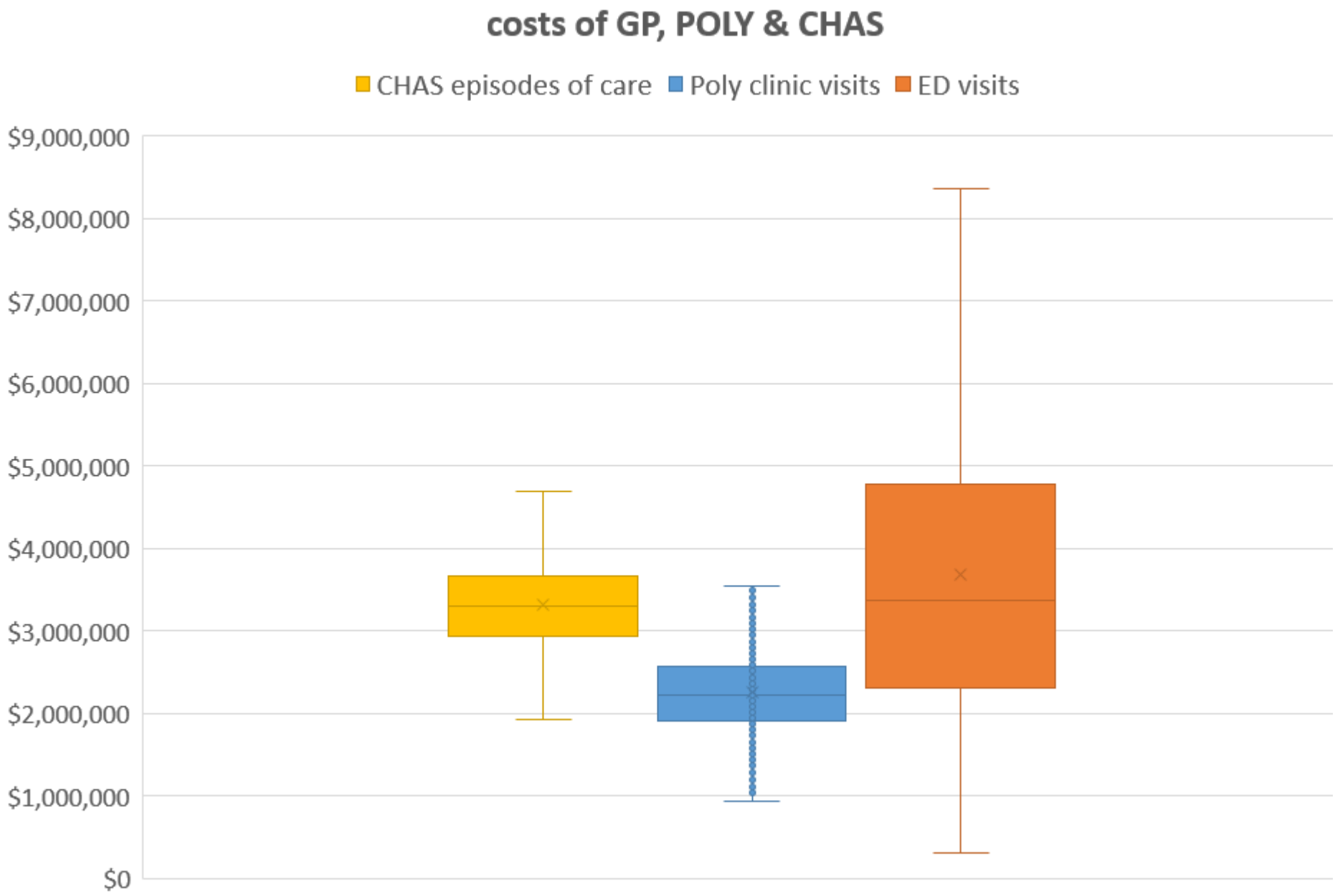
Polyclinic	All	No wound	Any wound
Number	2601594	2600153	1441
Mean no. of episodes in 12 months, SD	1.85(1.78)	1.85(1.77)	1.85(1.78)
Median 12 month utilisation, IQR	1 (1-2)	1 (1-2)	2 (1-3)
Coefficient			0.352 (0.288,0.416)
Rate ratio of Episodes, CI			1.423 (1.333,1.513)
Estimated mean Episodes, CI			2.157 (2.13,2.184)
Expected Episodes, CI			3.069 (3.031 ,3.108)
Excess Episodes, CI			0.912 (0.901 ,0.924)
CHAS	All	No wound	Any wound
Number	1016567	1013104	3463
Mean no. of episodes in 12 months, SD	3.13 (3.75)	3.12 (3.73)	6.18 (7.30)
Median 12 month utilisation, IQR	2 (1 - 4)	2 (1 - 4)	4(2 -8)
Coefficient			0.685 (0.669 , 0.701)
Rate ratio of Episodes, CI			1.984 (1.952 , 2.016)
Estimated mean Episodes, CI			3.596 (3.578 , 3.614)
Expected Episodes, CI			7.134 (7.099 , 7.169)
Excess Episodes, CI			3.538 (3.521 , 3.556)
ED	All	No wound	Any wound
Number	2971943	2964540	7403
Mean no. of episodes in 12 months, SD	1.38(1.17)	1.38(1.16)	1.38(1.17)
Median 12 month utilisation, IQR	1 (1-1)	1 (1-1)	2 (1-3)
Coefficient			0.343 (0.319 ,0.367)
Rate ratio of Episodes, CI			1.410 (1.376 ,1.444)
Estimated mean Episodes, CI			1.531 (1.515 ,1.547)
Expected Episodes, CI			2.159 (2.136 ,2.181)
Excess Episodes, CI			0.628 (0.621 ,0.634)

Appendix 9 Boxplots of all outcomes estimated from COI model








costs of GP, POLY & CHAS
CHAS episodes of care
Poly clinic visits
ED visits
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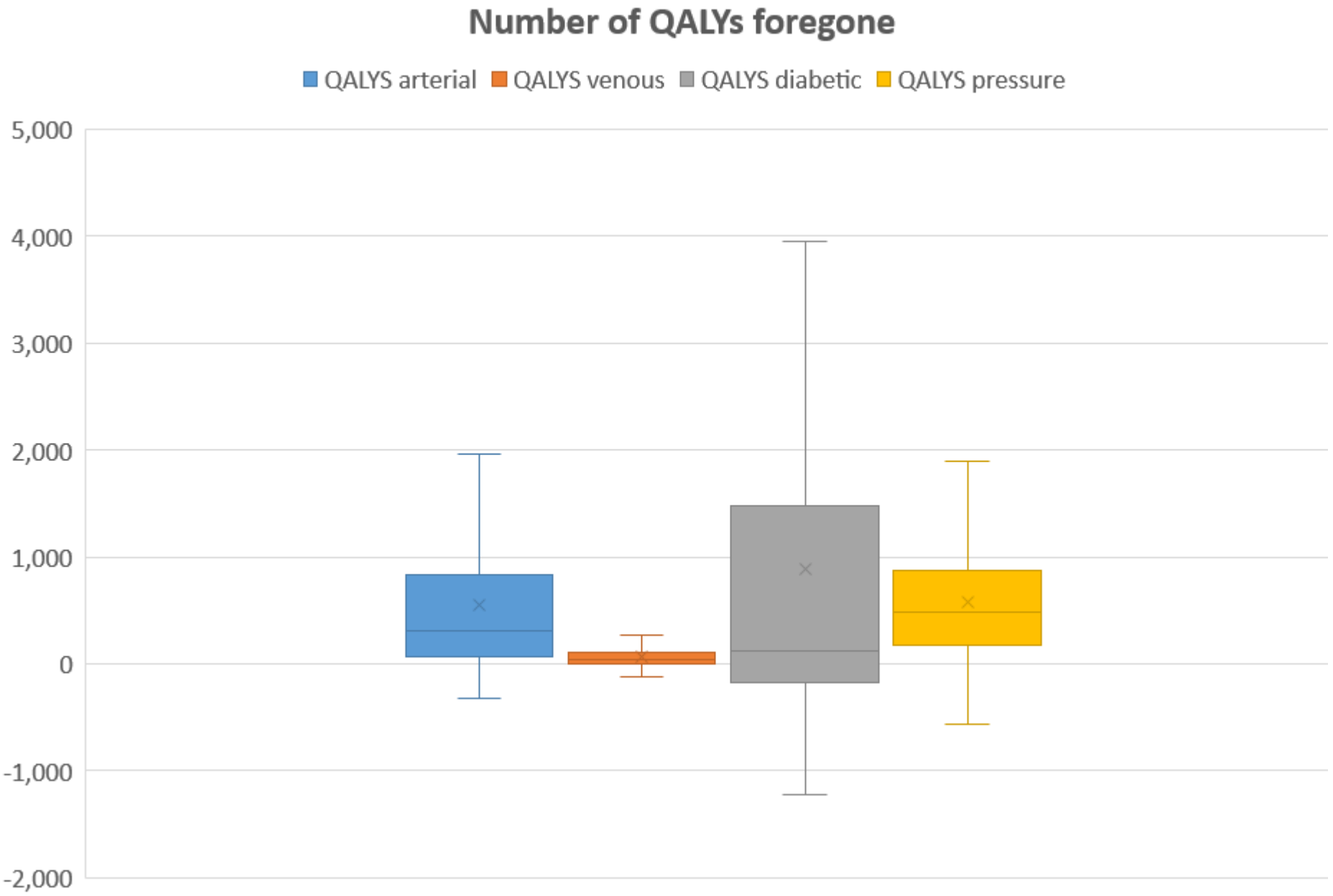
Number of QALYs foregone
QALYS arterial
QALYS venous
QALYS diabetic
QALYS pressure
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3,000
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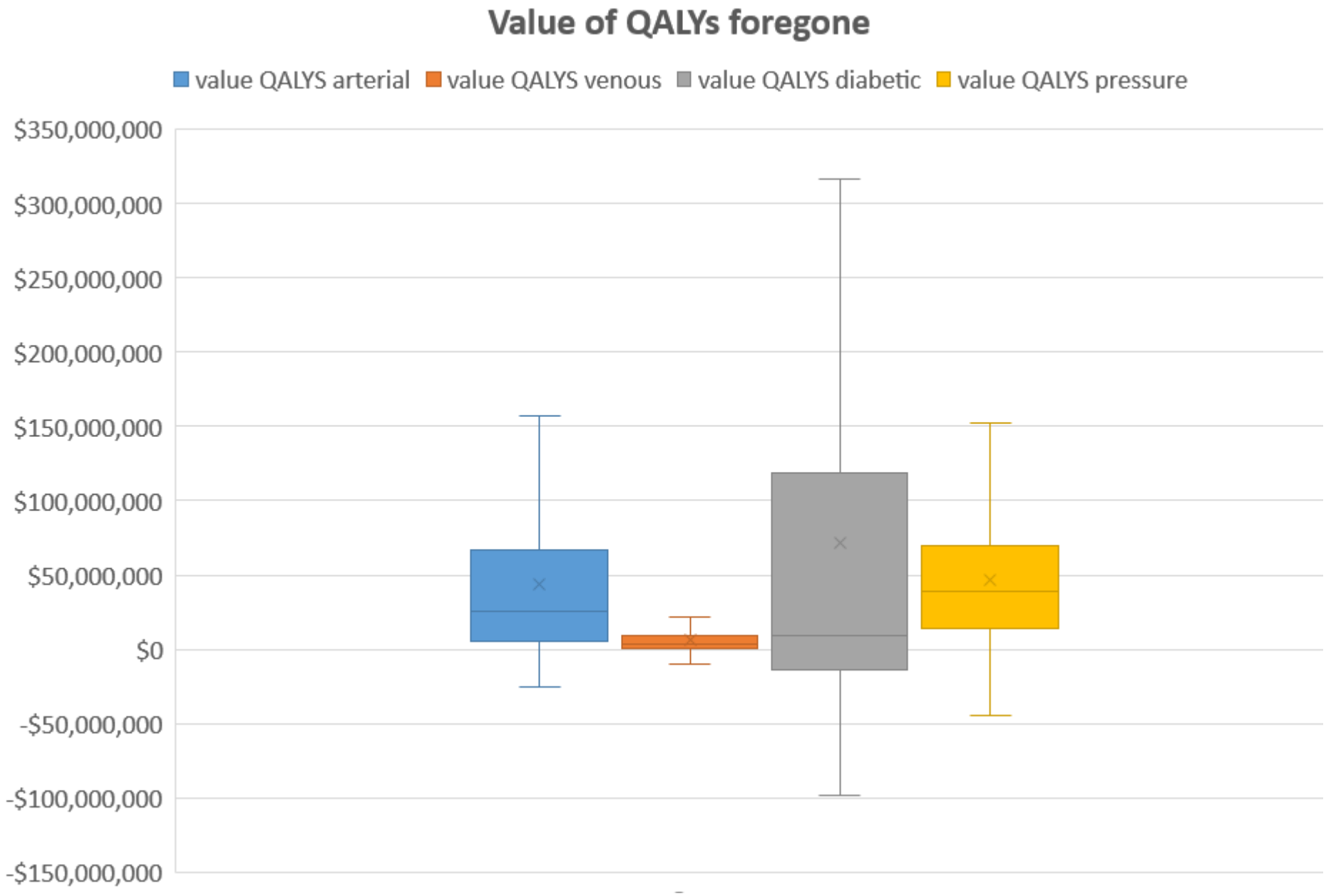
-2,000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BMJ Open

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Manuscript ID	bmjopen-2022-065692.R1
Article Type:	Original research
Date Submitted by the Author:	05-Jan-2023
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Primary Subject Heading:	Health economics
Secondary Subject Heading:	Health policy, Health services research, Epidemiology
Keywords:	GENERAL MEDICINE (see Internal Medicine), HEALTH ECONOMICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, WOUND MANAGEMENT

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Chronic Wounds in a Multi-Ethnic Asian Population. A Cost of Illness Study.

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Words. 3500

Abstract

Objective. To estimate the 'cost of illness' arising from chronic wounds in Singapore.

Design. Incidence based cost of illness study using evidence from a range of sources.

Setting: Singapore health services.

Participants. We consider 3.49 million Singapore citizens and permanent residents. There are 16,752 new individuals with a chronic wound in 2017, with 598 venous ulcers, 2,206 arterial insufficiency ulcers, 6,680 diabetic ulcers and 7,268 pressure injuries.

Primary outcome measures expressed in monetary terms are the: value of all hospital bed days lost for the population; monetary value of QALYs lost in the population; costs of all outpatient visits; and, costs of all poly clinic, use of community health assist scheme (CHAS) and emergency departments (ED) visits. Intermediate outcomes that inform the primary outcomes are also estimated.

Results: Total annual cost of illness was $350 million (range $72 to 1,779 million). With 168,503 acute bed days taken up annually (range 141,966 to 196,032) that incurred costs of $139 million (range 117 to 161 million). Total costs to health services were $184 million (range $120 to $1,179 million). Total annual costs of lost health were 2,077 QALYS (range -2,657 to 29,029) valued at $166 million (range -212 to 2,399 million).

Conclusions. The costs of chronic wounds are large to Singapore. Many of them could be avoided by making positive investments in integrated and comprehensive wound prevention and treatment programmes.

Strengths and limitations of this study

- Reliable and relevant data sources were used to update the results
- First study to quantify the national cost of chronic wounds in a multi-ethnic Asian population
- Some important costs were excluded as no information was available
- The sample size for the preference based utility weights for QALYS were small
- Some outcomes were not adjusted for co-morbidities and so might overstate the true costs.

Introduction

Chronic wounds are those that fail to heal in a time sufficient for 'normal' healing. They tend to present as a co-morbid rather than primary condition among older individuals. Other risk factors are diabetes, poor nutrition, incontinence and reduced mobility [1]. They have been described as causing a 'silent epidemic' that affects a large proportion of the world's population [2]. Chronic wounds are prevalent among vulnerable individuals living at home and residents of long-term care facilities. They are commonly associated with extended hospital stays but patient safety programmes have reduced healthcare associated events [3].

The burden of cost is particularly large [4] with 3% of the total NHS budget [5] and 4% of health care expenditure in Scandinavian countries used to manage the consequences of chronic wounds [6]. The goal of reducing the prevalence of chronic wounds has failed to attract sustained investment from those who pay for health services [7]. This contrasts with other major diseases, where payers are prepared to invest in 'cancer moonshots' for example [8], that will hopefully lead to better outcomes the future. This inequity is puzzling as the technology for reducing chronic wounds is available now, saves more than it costs to implement [9], and will cause large and certain gains in health outcomes.

Ulcers of the skin are the most common type of chronic wounds and include venous ulcers, arterial ulcers, diabetic foot ulcers and pressure ulcers or injuries. There are associated with a wide range of economic costs [2]. Affected individuals require frequent evidence-based treatments and if the condition becomes overwhelming an admission to hospital is inevitable. Many patients will be admitted for other reasons, and the wound may independently prolong hospital stay [10]. Debridement, minor amputations, and major amputations are common among higher risk groups [11, 12]. Chronic wounds are prevalent among residents of aged care facilities and will incur additional costs for staff time and consumables. Home nursing services as well as charities and volunteer groups that support the frail and elderly in their homes also manage patients [13]. Out of pocket expenditures will arise for patients and family members who travel to access services and purchase consumable items [14]. Productivity losses will arise as the patients are unable to perform their normal activities, be they paid or unpaid, and family members will have to take time from waged and unwaged productive activity. Health-related quality of life, which has monetary value [15], will be reduced. All these costs can be structured by a 'cost of illness' method [16].

The aim of this study is to estimate the 'cost of illness' arising from chronic wounds in Singapore. Our results could be used to stimulate decision makers to invest in known prevention and management programmes. The findings will also aid researchers who wish to model the cost savings or the cost-effectiveness of specific interventions.

Method

Scope of the Analyses

We include all resident Singapore Citizens and Permanent Residents (n=3.49M) and exclude resident foreign nationals and long-term employment pass holders (n=526,000) in 2017 [17]. Singapore has a multi-ethnic Asian population comprising of residents who are 76% Chinese, 15% Malay and 7.5% Indian descent [18]. The perspective for this analysis includes the costs incurred by health services and the losses to health benefits, expressed as QALYs foregone. We do not represent the 'societal' perspective as there are no data on private out of pocket costs, but we do review this omission in the Discussion. We estimate the expected annual costs arising from incident cases of venous ulcers, arterial insufficiency ulcers, diabetic ulcers and pressure injury.

Scope of the Modelling

We use statistical models to estimate four primary outcomes for the year 2017, see Figure 1.

FIGURE 1 HERE

First, are the monetary '*value of all hospital bed days lost for the population'*. The information used is summarised in Part A of Figure 1 and is labelled Inpatient 'Acute Sector Costs'. Second, are the '*monetary value of QALYs lost in the population'*. The information used is summarised in Part B of Figure 1 and is labelled 'Lost Heath Outcomes'. Third, are the '*costs of all outpatient visits'*. The information used is summarised in Part C of Figure 1 and is labelled 'Outpatient Clinics Costs'. Fourth, are the *'costs of all poly clinic, use of community health assist scheme (CHAS) and emergency departments (ED) visits'*. The information used is summarised in Part D of Figure 1 and is labelled 'Primary Care and ED costs'. CHAS is a mechanism for funding all Singapore Citizens to attend medical and or dental care at participating General Practitioner (GP) and dental clinics. CHAS is particularly designed to support the management of chronic diseases.

Data, Parameters and Assumptions

A. Inpatient Acute Sector Costs

Two outcomes, shown by blue boxes in Figure 1, are estimated: '*Number of bed days lost per case'* and '*Value of all hospital bed days lost for population ($)'*. To estimate the '*Number of bed days lost per case'* we combined information on the '*Number of admissions to hospital with wounds*' with information on '*Excess acute hospital stay due to a wound'*. To estimate the '*Number of admissions to hospital with wounds*' we retrieved a population cohort of all inpatient admissions to acute hospitals in Singapore between 2012 and 2019 from the Singapore Ministry of Health, and applied the cases from 2017. From the entire

dataset we identified all inpatient episodes with any occurrence of Venous ulcers, Arterial insufficiency ulcers, Diabetic ulcers and Pressure injury or any combination of these wounds as a primary or secondary diagnosis based on the ICD-9 codes in Appendix 1.

To estimate '*Excess acute hospital stay due to wound'* we extracted the length of hospital stay and relevant co-variate information that could be used to explain variation in the length of stay, see Appendix 2. A parsimonious multivariable generalised linear model (GLM) with a gamma link function was used to accommodate the skew typical of lengths of stay data [19]. The outcome of interest was the length of stay associated with chronic wound management in the inpatient setting. Other covariates included were age, gender, race, and comorbid chronic diseases. The statistical model generated a coefficient for 'wound type' expressed as a rate ratio, that showed the amount of increase in length of stay associated with the presence of wound, given that other factors that predicted length of stay had been accounted for. This rate ratio was used to moderate the mean length of stay for the entire sample and an excess length of stay associated with the wound was estimated. In Appendix 3 we show a summary of the results of the multivariable generalised linear model and in Appendix 4 we show the full model results.

To estimate the '*Value of all hospital bed days lost for population ($)'* we combined the *'Number of bed days lost per case'* with the *'Cost per bed day ($)'*.

All the data inputs used for this part of the model are shown in Table 1.

Table 1. Data inputs used to estimate the outcomes for the 'Inpatient Acute Sector Costs'

Parameter	Estimate	Distribution used for uncertainty	
Excess acute hospital stay due to wound (days)			
Arterial	2.37	Gamma (757, 0.0031)	Estimated by multivariable generalised linear model
Venous	0.79	Gamma (84, 0.0094)	
Diabetic	2.26	Gamma (742, 0.003)	
Pressure	1.61	Gamma (724, 0.0022)	
Number of admissions to hospital with wounds			
Arterial	14,536	Fixed	#
Venous	19,210	Fixed	
Diabetic	16,999	Fixed	
Pressure	49,879	Fixed	
Cost per bed day ($)	823	Normal(823, 2.78)	#

Ministry of Health, *Administrative database*, Ministry of Health (MOH). Accessed in 2021.

B. Lost Health Outcomes

Five outcomes, shown by blue boxes in Figure 1, are estimated: *Annual cases by wound type; Number of QALYs lost per case (by age group); Utility decrement; Number of QALYS lost in population; and, Monetary value of QALYS lost in the population ($).* The first four are intermediate outcomes that contribute information to the primary outcome of '*Monetary value of QALYs lost in the population ($)'*.

To estimate *'Annual cases by wound type'* we apply the incidence rates for each wound type to the *'Total at risk population'*. We used published incidence rates for 2017 from a population-based study of wounds among those admitted to Singapore acute care hospitals from 2000 to 2017 [20]. For this work the authors identified relevant ICD-10 codes for for occurrences of venous ulcers, arterial insufficiency ulcers, diabetic ulcers, and pressure ulcers or injuries, see Appendix 1, and applied them to the Singapore Ministry of Health central claims database, which includes records of all admissions to public and private acute care hospitals. The incidence rates by age band are reported alongside the at-risk population enabling the number of incident cases to be estimated, see Appendix 5 for more detail.

To estimate the '*Number of QALYs lost per case (by age group)'* we use EQ-5D-5L data. This instrument includes preference based valuations of health states expressed as 'health utilities' on a scale between zero, the worst possible health state, and one, the best possible health state [21]. We used EQ-5D-5L data from 799 individuals with relevant wounds from the Singapore wound care registry to inform the '*Health utility for cases with specific wound type'*. Responses were recorded at entry into the registry, when the wound was first assessed in the hospital setting and then at 1, 3 and 6 months, see Appendix 6. We used a Singapore EQ-5D-3L value set [22] that was then mapped onto the EQ-5D-5L version using the SAS code in Appendix 7. The utility outcomes for the wound patients are compared to population norms for the EQ-5D index informed by Singapore preference weights for appropriate age bands [23], this informs the '*Population normal Utility (by age)'*. Using the information described above we are able to estimate the '*Utility Decrement'* from having a wound. The '*Duration of Wound'* was informed by the mean durations of wounds in days for the specific wound types from the Singapore Wound Registry, see Appendix 8. The '*Number of QALYs lost in population'* is the product of the '*Number of QALYS lost per case'* and the '*Annual cases by wound type'*. The '*Monetary value of QALYs lost in the population'* is the product of the '*Number of QALYS lost in population*' and the *'Value of one QALY'*, which is set at the mean gross domestic product per capita for Singapore of SGD $80,000 [24]. This approach assumes the value of one year of perfect quality of life does not exceed the per capita gross domestic product [25].

All the data inputs used for this part of the model are shown in Table 2.

Table 2. Data inputs used to estimate the outcomes for the 'Lost Health Outcomes'

Parameter	Estimate	Distribution used for uncertainty	
Health utility for cases with specific wound type			
Arterial – baseline	0.44	Beta (0.24, 0.30)	Singapore Wound Registry
Venous – baseline	0.57	Beta (0.60, 0.46)	
Diabetic – baseline	0.64	Beta (0.21, 0.12)	
Pressure – baseline	-0.18	Normal (-0.18, 0.50)	
Arterial – month 1	0.52	Beta (0.23, 0.21)	
Venous – month 1	0.68	Beta (0.89, 0.41)	
Diabetic – month 1	0.71	Beta (0.04, 0.02)	
Pressure – month 1	0.00	Normal (0.00, 0.56)	
Arterial – month 3	0.54	Beta (0.13, 0.11)	
Venous – month 3	0.74	Beta (0.81, 0.28)	
Diabetic – month 3	0.72	Beta (0.28, 0.11)	
Pressure – month 3	0.18	Normal (0.18, 0.54)	
Arterial – month 6	0.58	Beta (0.16, 0.12)	
Venous – month 6	0.74	Beta (0.83, 0.28)	
Diabetic – month 6	0.74	Beta (0.05, 0.02)	
Pressure – month 6	0.11	Normal (0.11, 0.59)	
Population normal utility (by age group)			
<40	0.980	Beta (350, 7)	[23]
40-49	0.950	Beta (636, 33)	
50-59	0.940	Beta (535, 34)	
60-69	0.960	Beta (193, 8)	
70-79	0.890	Beta (189, 23)	
≥80	0.890	Beta (189, 23)	
Value of one QALY ($)	80,000	Fixed	[24]
Durations of Arterial wounds in days (by age group)			
<40	133	Normal(133,92)	Singapore Wound Registry
40-49	129	Normal(129,109)	
50-59	331	Normal(331,394)	
60-69	223	Normal(223,269)	
70-79	307	Normal(307,438)	
≥80	205	Normal(205,153)	
Durations of Venous wounds in days (by age group)			
<40	133	Normal(133,92)	
40-49	129	Normal(129,109)	
50-59	331	Normal(331,394)	
60-69	223	Normal(223,269)	
70-79	307	Normal(307,438)	
≥80	205	Normal(205,153)	
Durations of Diabetic wounds in days (by age group)			
<40	177	Normal(177,88)	
40-49	325	Normal(325,550)	
50-59	224	Normal(224,216)	
60-69	314	Normal(314,430)	
70-79	256	Normal(256,305)	
≥80	160	Normal(160,138)	
Durations of Pressure injury in days (by age group)			
<40	55	Normal(55,11)	
40-49	86	Normal(86,24)	
50-59	115	Normal(115,1)	
60-69	103	Normal(103,59)	
70-79	105	Normal(105,115)	
≥80	62	Normal(62,52)	

C. Outpatient Clinics costs

Only one outcome, '*Costs of all outpatient visit ($)',* was estimated. Information was used for the '*Annual cases by wound type', 'Cost per outpatient visit ($)' and 'Outpatient visits per case'*

To estimate *'Cost per outpatient visit ($)'* we interrogated the Singapore wound care registry to identify the annual number of visits for those with chronic wounds and the reported costs per visits, this information was available by wound type. There were 573 individuals for whom these data were reported. Visits were for specialist consultations specifically for their wound, and for podiatry visit or medical tests, see Appendix 9. All the data inputs used for this part of the model are shown in Table 3.

Table 3. Data inputs used to estimate the outcomes for the 'Outpatient Clinic Costs'

	Estimate	Distribution used for uncertainty	Source
Outpatient visits per case (with consult)			Singapore Wound Registry
Arterial	8.2	Gamma (1.82:4.52)	
Venous	5.9	Gamma (0.98:5.99)	
Diabetic	8.1	Gamma (1.70:4.76)	
Pressure	6.5	Gamma (1.93:3.37)	
Outpatient visits per case (without consult)			
Arterial	8.5	Gamma (1.77:4.79)	
Venous	23.6	Gamma (1.55:15.25)	
Diabetic	14.2	Gamma (0.08:185.15)	
Pressure	9.7	Gamma (0.81:12.00)	
Cost per outpatient visit (with consult) ($)			
Arterial	110	Gamma (5.60:19.74)	
Venous	133	Gamma (2.70:49.30)	
Diabetic	112	Gamma (2.86:39.20)	
Pressure	111	Gamma (4.05:27.43)	
Cost per outpatient visit (without consult) ($)			
Arterial	117	Gamma (5.60:19.74)	
Venous	106	Gamma (2.70:49.30)	
Diabetic	114	Gamma (2.86:39.20)	
Pressure	124	Gamma (4.05:27.43)	

D. Primary Care and ED costs

Only one outcome '*Costs of all POLY, CHAS & ED visits ($)*' was estimated. Information was used for the '*Annual cases by wound type', 'Cost per POLY, CHAS & ED visit ($)'* and *'Excess POLY, CHAS & ED visits per case due to wound*'.

For the '*Cost per POLY, CHAS & ED visit ($)* we use estimates reported by the Singapore Ministry of Health. To estimate *Excess POLY, CHAS & ED visits per case due to wound*' the same population cohort for 2012 to 2019 who were admitted as inpatients were interrogated. We identify the use of the Emergency Departments (ED) of acute hospitals and all visits to community-based Polyclinics (POLY) and use of community health assist scheme (CHAS).

We sought to estimate the excess use of these services associated with any chronic wound. For the analysis each patient is counted only once, and those with wounds are only counted when they first appear with any wound, and the number of 12-month visits from the incidence date is the outcome variable. For those without wounds, their 12-month use starts from the first visit during the study period. A parsimonious generalised linear model with a log link Poisson function was used for all regressions. The Poisson distribution was chosen over the negative binomial distribution based on fitting the model then doing model

checks with diagnostic plots and relevant statistics. The outcome of interest was a count of the use of the services. Other covariates included were age, gender, race, Charlson comorbidity index and presence of comorbid conditions, see Appendix 10. The ensuing statistical models generated a coefficient for 'any wound' expressed as a rate ratio, that showed the change in the number of visits associated with the presence of wound, given that other factors that predicted variation in these outcomes. As before, the rate ratio was used to moderate the mean counts for the entire sample and an excess number of visits was estimated for all wounds, see Appendix 11. All the data inputs used for this part of the model are shown in Table 4.

Table 4. Data inputs used to estimate the outcomes for the 'Primary care and ED Costs'

Parameter	Estimate	Distribution used for uncertainty	Source
Excess visits for Polyclinics (all wounds)	0.91	Gamma (18.33, 0.049)	Estimated by multivariable generalised linear model
Excess visits for CHAS (all wounds)	3.54	Gamma (38.51, 0.091)	
Excess visits for ED (all wounds)	0.63	Gamma (4.18, 0.15)	
Cost per Poly clinic visit	$147	Normal(147,2.5)	Ministry of Health, Administrative database, Ministry of Health (MOH). Accessed in 2021
Cost per CHAS use	$56	Normal(56,1.14)	
Cost per ED visit	$352	Normal(352,.14)	

Uncertainty & Model Evaluation

Uncertainty for all the outcomes shown in Figure 1 was assessed by probabilistic sensitivity analysis. We take 5,000 Monte Carlo resamples from all the parameters described in Tables 1 to 4. We report the number of 'acute care bed days lost' and the number of 'QALYs lost to chronic wounds'. We then report the findings from the resamples for the primary model outcomes: *Value of all bed days lost for population; Monetary value of QALYS lost in the population; Costs of all outpatient visit; and, Costs of all POLY, CHAS & ED visits.* We sum these four primary outcomes to report the '*Total Costs of Illness for each wound type'.* These processes are shown in Figure 1.

Patient and Public Involvement

The data came from the Singapore Wound Registry and from the Ministry of Health. It was routinely reported data collected for the purpose of managing and planning health services. It was not possible to develop the research question or outcome measures based on the priorities, experience, and preferences of the patients. Patients were not involved patients in the design, recruitment and conduct of the study. Patients who are interested will be able to read the paper.

Results

There were 16,752 'new' or 'incident' cases for 2017, with 598 venous ulcers, 2,206 arterial insufficiency ulcers, 6,680 diabetic ulcers and 7,268 pressure injuries. The values obtained from the model for 'acute care bed days lost' and the number of 'QALYs lost to chronic wounds' are shown in Table 5.

Table 5. Annual outcomes for bed days lost and QALYs lost for incident cases (n=16,752)

Number of QALYS lost	mean (min:max)
Arterial	544 (-340:5,436)
Venous	75 (-127:0,971)
Diabetic	856 (-1670:16,962)
Pressure	602 (-520:6,631)
Number of Bed days lost	
Arterial	34,389 (29269:38,674)
Venous	15,161 (10,044:22,166)
Diabetic	38,423 (33,445:43,573)
Pressure	80,530 (69,208:91,619)

The values obtained from the model for the four primary outcomes are shown in Table 6.

Table 6. Annual cost outcomes for the primary outcomes (n=16,752)

Value of all bed days lost for population	mean (min:max)
Arterial	$28,302,139 ($24,148,856:$31,912,933)
Venous	$12,477,776 ($8,243,954:$18,212,629)
Diabetic	$31,622,397 ($27,431,880:$35,693,113)
Pressure	$66,276,250 ($57,237,092:$75,718,807)
Monetary value of QALYS lost in the population	
Arterial	$43,491,588 (-$27,170,499:$434,890,646)
Venous	$5,975,553 (-$10,153,391:$77,645,170)
Diabetic	$68,498,429 (-$133,624,494:$1,356,989,736)
Pressure	$48,199,291 (-$41,617,890:$530,453,557)
Costs of all outpatient visit	
Arterial	$4,233,236 ($84,899:$35,360,192)
Venous	$2,017,189 ($8,957:$27,539,296)
Diabetic	$16,337,217 ($3,058:$785,613,392)
Pressure	$13,859,689 ($42,824:$142,991,574)
Primary care & ED costs	
Costs Polyclinic visits - all wounds	$2,245,437 ($877,197:$5,715,449)
Costs CHAS episodes of care - all wounds	$3,296,040 ($1,849,062:$5,930,304)
Costs ED visits - all wounds	$3,730,682 ($235,741:$14,456,940)

The aggregate of these cost outcomes are the 'Total Costs of Illness for each wound type' and are shown in Table 7.

Table 7. Annual total costs of illness for each wound type (n=16,752)

Total Costs of Illness for each wound type	mean (min:max)
Arterial	$77,247,993 ($6,047,354:$469,696,045)
Venous	$20,801,577 ($5,388,353:$91,673,830)
Diabetic	$120,155,304 (-$97,359,748:$1,395,843,120)
Pressure	$132,358,039 ($42,035,656:$624,864,715)
Total Cost of Illness	$350,562,913 ($72,814,108:$1,779,366,924)

Based on our estimates pressure injuries account for 48% of the 168,503 bed days lost to chronic wounds and 38% of the $28.4M outpatients costs. For the non-hospital sector, the costs of CHAS services and ED visits account for most of the burden. The QALY burdens are large for diabetic foot, arterial and pressure injury with venous ulcers having lesser impact. Box plots for the 'Total Costs' outcomes are shown in Figure 2.

FIGURE 2 HERE

There is a 100% probability that the costs of chronic wounds are positive with the most likely value suggesting an annual cost to Singapore of $350 million. The findings are uncertain with the range of total costs between $79 million and $1.78 billion. More than half of the total costs arise from use of health services ($185 million, 53%) with outpatients accounting for $37 million (10%) and the use of acute bed days accounting for $139 million (40%). The value of the lost health by QALYs is substantial at $165 million, 47% of the total burden.

Discussion

These findings suggest the costs of chronic wounds to Singapore are large. The total cost burden accounts for 3.14% of the 2019 Government Health Expenditure on services [26] and 2.3% of total economy-wide expenditure on services. Our estimates roughly align with those from other countries. In Australia 2% of the total national health expenditure is used for chronic wounds and in the UK 3% of the national health expenditure is taken up [27]. Two percent of the European health budget [28] is for care of chronic wounds and for Scandinavian countries the costs were found to be 2 to 4% of the total health care expenditure [6].

While the findings are lower than the annual costs of diabetes in Singapore, estimated to be US $787 million in 2010 [29], the policy response to diabetes has been considerable with a 'War on Diabetes' declared in 2016 to mobilise a national programme to reduce the problem of diabetes [30]. We found two other studies reporting costs of chronic venous leg and neuro-ischemic ulcers in Singapore, but neither study were at a population level instead focusing on average costs per patient [31, 32].

This study likely underestimates the extent of the costs of chronic wounds as relevant information was not available for many costs we suspect are present. Our data came primarily from patients who were admitted to the hospital for their wounds. Thus patients with less serious wounds managed in the community are excluded. We were also unable to identify and include estimates of the private costs incurred by patients and family members. Other studies have found that such costs can be substantial. For the German setting Purwins et al. [33] found patients with leg ulcers in a given year spent €424 on topical treatments and drugs, €486 on out of pocket incidentals, €254 on drug prescriptions and €740 on non-drug treatments.

Although no data were available on the time away from work and other production losses, we addressed this by estimating and valuing lost quality adjusted life years (QALYs). We assume that time in reduced health states has a relationship with an ability to be economically productive. Thus, the dollar valuations of the lost QALYs can be thought of as representing lost production from chronic wounds. Most governments are willing to pay money for services that increase the number of QALYs in a population, given a programme achieves a marginal QALY below a designated cost [34]. Importantly we did not consider the costs of lost production for informal carers, which we expect are substantial.

There are further limitations to our study. Regarding the estimation of QALY losses, the sample sizes for EQ5D were quite small for Pressure injury with only 51 patients providing data. It is possible the estimate would change with a larger and more representative sample. It should be noted that the lowest health utilities arise from this sample. For example, the values for baseline were -0.18 indicating a health state valued worse than death, and a value of 0.00, the worst possible health state, was observed for month 1. Values remained low at 0.18 and 0.11 for the 3 month and 6 month follow-ups. We assumed that the observed decrement between the population norms for health utility and the estimates from the wound registry were wholly attributable to the presence of a wound. These QALY estimates did not adjust for the other health conditions that patients may have, and as such may overstate the QALY losses.

To attribute excess acute bed days to the presence of a chronic wound we developed generalised linear regression models with the outcome of length of stay. While did not have an exhaustive list of control variables we did find that factors such as race, age, gender, myocardial infarction, cancer, liver disease, peptic ulcer disease, peripheral vascular disease, renal disease, COPD, dementia, diabetes, heart failure, hyperlipidemia, lymphoproliferative disease, major depression, Parkinson's, schizophrenia and stroke all played a role in explaining variation in the observed length of stay. We fitted the best models possible, but acknowledge there may be some covariate information missing.

In summary, this recurring and unnecessary cost burden is a deadweight loss to Singapore health services, and society in general. It could be reduced if evidence-based and relatively simple prevention and management programmes were implemented. International evidence [9] reveals that using optimal prevention practices for diabetic foot ulcers [35] was cost-saving in Peru [36], Australia [37], Thailand [38]

and China [39]. For the prevention of pressure injury nursing led interventions, a quality improvement collaborative and the standardised use of pressure injury bundles were found to be cost-saving in Denmark [40], the US and UK [41-44]. And for the prevention of venous leg ulcers, compression therapy, clinical assessments and use of guidelines were found to be cost-saving in the UK [45, 46] and US [47, 48].

Our findings provide fundamental information for researchers who wish to model the cost-effectiveness of programmes that will improve wound outcomes in the future. Understanding the baseline of costs and QALY outcomes form a useful start-point for any evaluation of interventions.

Conclusions.

The costs of chronic wounds are large to Singapore, but many of them could be avoided by making positive investments in integrated and comprehensive wound prevention and treatment programmes.

Authors contributions.

Nicholas Graves, Ganga Ganesan, Kelvin Tan, Orlanda Qi Mei Goh, Jackie Ho, Chong Tze Tec, Priya Bishnoi, David Carmody, Ang Shin Yuh, Ng Yi Zhen, Zhiwen Lo, Yong Enming, Fazila Binte, Abu Bakar Aloweni, Wang Zifei and Keith Harding made substantial contributions to the: conception and design of the paper, the acquisition, analysis, and interpretation of data; drafting and reviewing versions of the manuscript; and, final approval of the version submitted. All authors are accountable for all aspects of the work.

A competing interests statement. None

Funding. We would like to acknowledge the funding supported from the Agency for Science, Technology and Research (A*STAR) under its Industry Alignment Fund-Pre-Positioning Programme (IAF-PP) grant number H1901a00Y9/ and H17/01/a0/0CC9 as part of the Wound Care Innovation for the Tropics (WCIT) Programme.

Data availability statement. No data from the wound registry or MoH administrative databases are available. This is due to the privacy considerations of the Singapore MOH and the Singapore wound registry.

Ethics Approval

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

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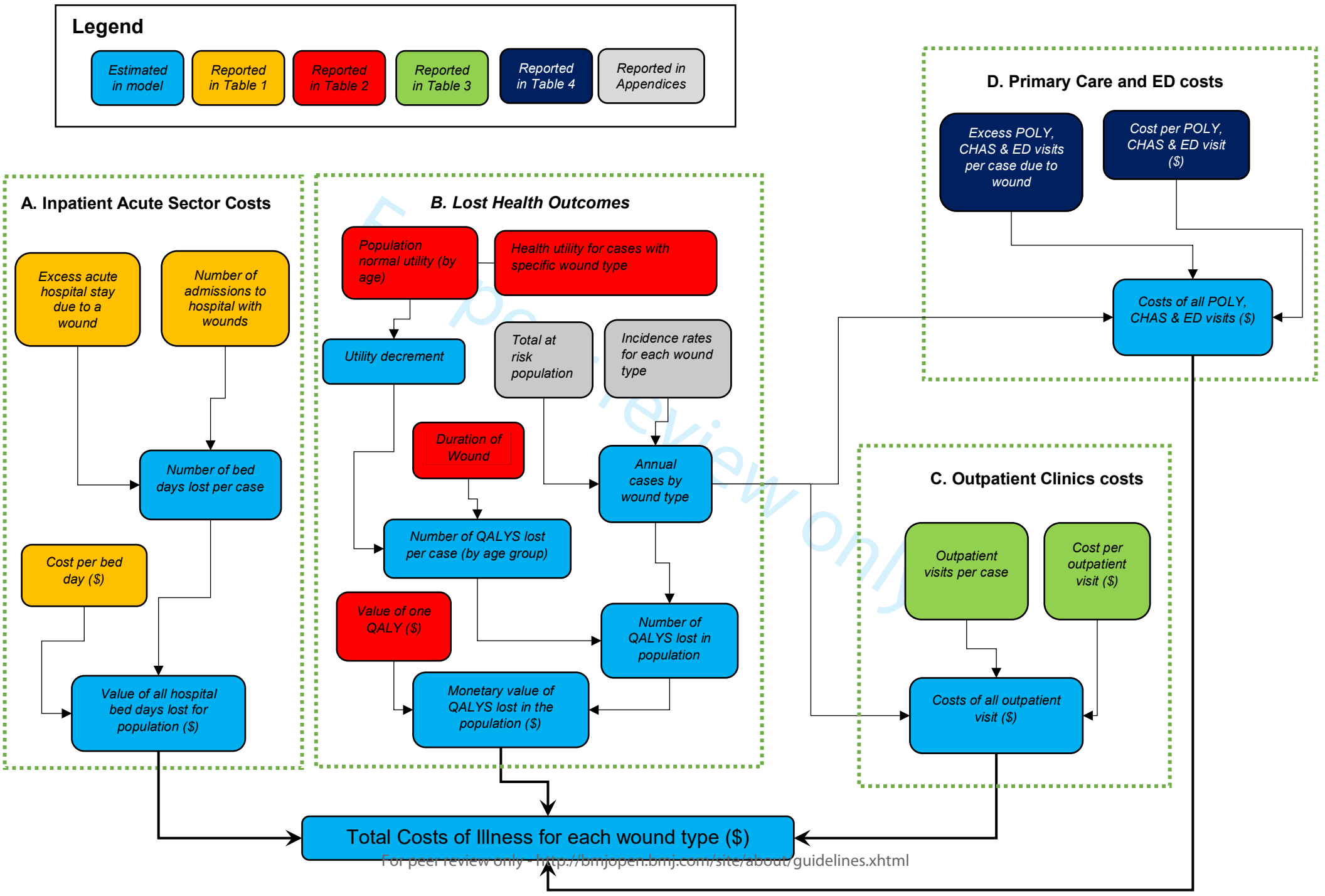
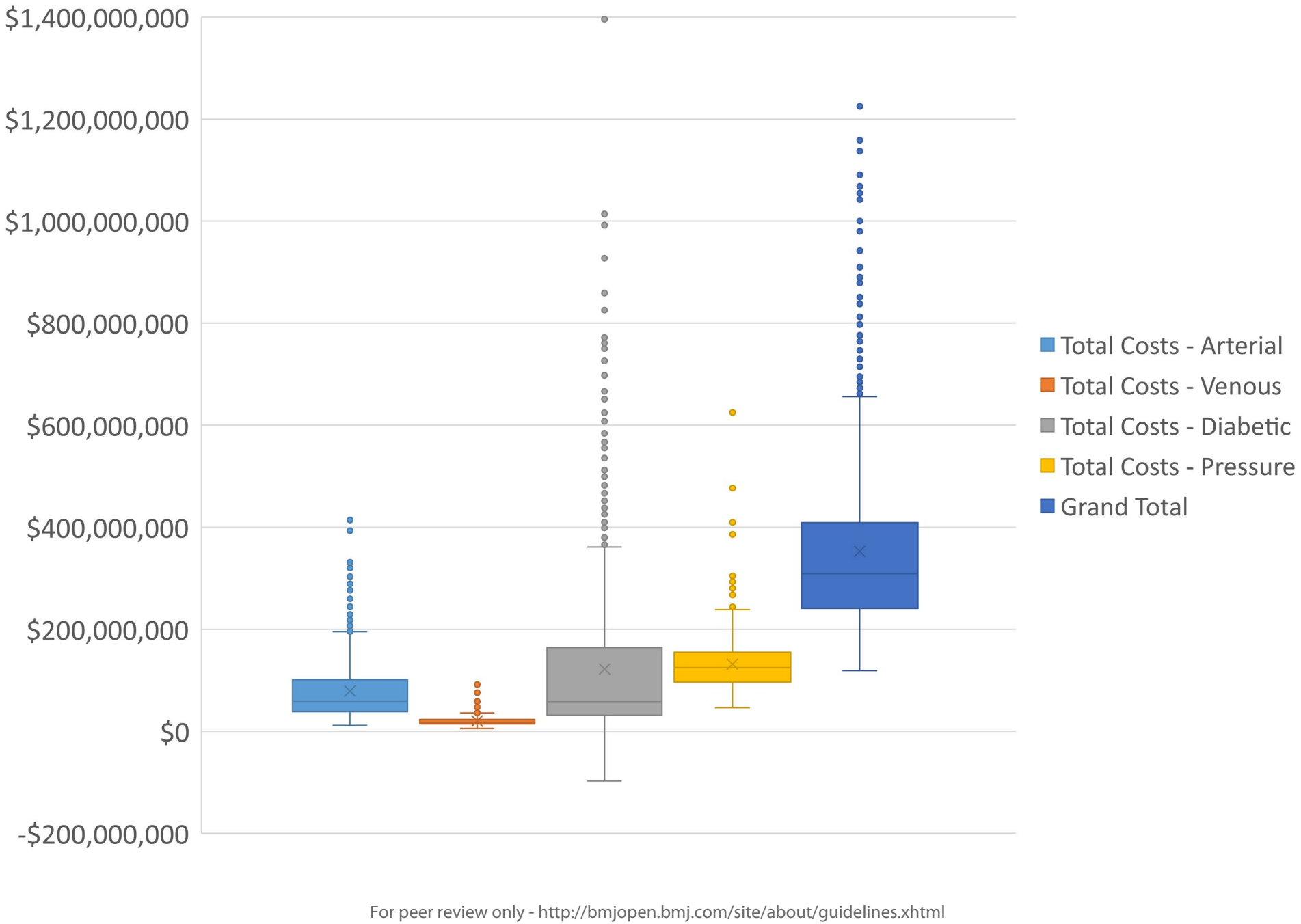
Figure 1. A diagram to show how the various parameters update the outcomes

Figure 2. Total cost outcomes for the cost of Illness by wound type





Appendix 1. ICD-9 codes used to identify chronic wounds from national claims dataset

Venous ulcers – *ICD-9-AM: 4540, 4532, 4591; ICD-10-AM: I83.0, I83.2, I87.0.*

Arterial insufficiency ulcers – *ICD-9-AM: 44023, 44024; ICD-10-AM: I70.23, I70.24*

Diabetic ulcers – *ICD-9-AM: 7071, 7078, 7079, 7854 & one of 25070, 25071, 25072 or 25073; ICD-10-AM: E10.73, E11.73, E13.73, E14.73, E10.52, E11.52, E13.52, E14.52, E09.02, E09.52, E10.69, E11.69, E13.69, E14.69*

Pressure ulcers – *ICD-9-AM: 7070; ICD-10-AM: L89.0, L89.1, L89.2, L89.3, L89.4, L89.5, L89.6, L89.7, L89.8, L89.9*

Appendix 2. Cohort of all hospital admissions for a relevant chronic wound 2012 to 2019

	All	No wound	Arterial	Venous	Diabetic	Pressure
Number	5,196,899	5,047,162	14,536	19,210	16,999	49,879
Age, mean (st dev)	50.4 (26.9)	49.6 (26.8)	75 (13.3)	72.1 (17.1)	72.4 (15.7)	81.7 (13)
Male	49%	48%	56%	57%	58%	50%
CCI score (mean)	4.1	4.1	6.1	4.7	5.9	4.4
Chinese	64%	64%	63%	60%	54%	71%
Malay	14%	14%	17%	16%	21%	13%
Indian	10%	10%	11%	13%	13%	6%
Others	12%	12%	9%	11%	12%	10%
COPD	7%	7%	6%	5%	5%	8%
Diabetes Mellitus	42%	42%	82%	57%	100%	40%
Hypertension	69%	68%	92%	77%	88%	76%
Dyslipidemia	61%	61%	84%	67%	86%	59%
Heart Failure	14%	14%	33%	21%	27%	14%
Renal Failure	24%	23%	49%	30%	44%	21%
Stroke	17%	17%	27%	19%	20%	40%
Dementia	6%	6%	7%	5%	4%	33%
Major Depression	6%	6%	5%	5%	6%	8%
Parkinson	3%	3%	2%	2%	1%	17%
Schizophrenia	4%	4%	1%	3%	2%	4%
Length of Stay, mean (st dev)	6.5(17)	6.3 (16.7)	16.2 (20.2)	9.8 (16)	14 (18.6)	16.8 (25.2)

Appendix 3. Summary results of generalised linear model (GLM) with a gamma link function to estimate excess length of stay

	All	No wound	Arterial	Venous	Diabetic	Pressure
Number	5,196,899	5,054,937	14,536	19,210	16,999	49,879
Length of Stay, mean (st dev)	6.5 (17)	6.3 (16.7)	16.2 (20.2)	9.8 (16)	14 (18.6)	16.8 (25.2)
Coefficient (95% CI)	-	-	0.722 (0.690,0.754)	0.303 (0.272,0.333)	0.701 (0.669,0.733)	0.543 (0.516,0.570)
Rate ratio of length of stay (95% CI)	-	-	2.059 (1.993,2.126)	1.353 (1.993,2.126)	2.015 (1.952,2.081)	1.722 (1.676,1.769)
Estimated mean length of stay (95% CI)	-	-	2.233 (2.215,2.252)	2.232 (2.215,2.252)	2.226 (2.208,2.245)	2.234 (2.216,2.253)
Expected length of stay (95% CI)	-	-	4.598 (4.414,4.788)	3.02 (4.414,4.788)	4.485 (4.31,4.672)	3.847 (3.714,3.986)
Excess length of stay (95% CI)	-	-	2.365 (2.199,2.536)	0.788 (2.199,2.536)	2.259 (2.102,2.427)	1.613 (1.498,1.733)

Appendix 4. Full results of generalised linear model (GLM) with a gamma link function to estimate excess length of stay

Co-variate	**Exponentiated coefficients; 95% confidence intervals in brackets**							
los_cens	Arterial		Venous		Diabetic		Pressure	
d_ulcer	2.059***		1.353***		2.015***		1.722***	
95CI	1.993	2.126	1.993	2.126	1.952	2.081	1.676	1.769
age	1.013***		1.013***		1.013***		1.013***	
95CI	1.013	1.013	1.013	1.013	1.013	1.013	1.013	1.013
male	1.019***		1.020***		1.019***		1.020***	
95CI	1.016	1.023	1.016	1.023	1.015	1.023	1.016	1.024
1.Race	1		1		1		1	
2.Race	0.989***		0.989***		0.987***		0.988***	
95CI	0.983	0.994	0.983	0.994	0.982	0.992	0.983	0.993
3.Race	0.903***		0.902***		0.902***		0.904***	
95CI	0.898	0.909	0.898	0.909	0.897	0.908	0.898	0.910
4.Race	0.935***		0.935***		0.934***		0.935***	
95CI	0.927	0.942	0.927	0.942	0.926	0.941	0.928	0.943
dCCI_AMI	0.941***		0.943***		0.942***		0.943***	
95CI	0.936	0.946	0.936	0.946	0.937	0.948	0.938	0.948
dCCI_Cancer	1.099***		1.099***		1.099***		1.099***	
95CI	1.094	1.105	1.094	1.105	1.093	1.105	1.094	1.105
dCD_DM	1.094***		1.096***		1.091***		1.098***	
95CI	1.090	1.099	1.090	1.099	1.087	1.096	1.093	1.102
dCD_Hyp	1.076***		1.077***		1.077***		1.078***	
95CI	1.071	1.082	1.071	1.082	1.071	1.083	1.072	1.084
dCD_LPD	0.919***		0.919***		0.918***		0.920***	
95CI	0.914	0.923	0.914	0.923	0.914	0.923	0.916	0.925
dCD_HeartFail	1.040***		1.040***		1.041***		1.041***	
95CI	1.034	1.046	1.034	1.046	1.035	1.046	1.036	1.047
dCCI_Renal	1.113***		1.115***		1.113***		1.115***	
95CI	1.108	1.118	1.108	1.118	1.108	1.118	1.110	1.121
dCD_Stroke	1.153***		1.153***		1.154***		1.150***	
95CI	1.148	1.159	1.148	1.159	1.149	1.159	1.144	1.155
dCD_Dementia	1.144***		1.143***		1.143***		1.132***	

95CI	1.135	1.152	1.135	1.152	1.134	1.151	1.124	1.141
dCD_MajDepression	1.086***		1.086***		1.086***		1.085***	
95CI	1.078	1.095	1.078	1.095	1.077	1.094	1.077	1.094
dCD_Parkinson	1.155***		1.154***		1.154***		1.143***	
95CI	1.142	1.168	1.142	1.168	1.141	1.168	1.130	1.156
dCD_Schizophrenia	1.475***		1.474***		1.476***		1.474***	
95CI	1.459	1.492	1.459	1.492	1.460	1.493	1.458	1.491
dCD_COPD	0.971***		0.970***		0.970***		0.971***	
95CI	0.965	0.977	0.965	0.977	0.964	0.977	0.965	0.978
dCCI_ModLiver	1.003		1.002		1.003		1.003	
95CI	0.990	1.016	0.990	1.016	0.990	1.016	0.991	1.017
dCCI_PUD	0.969***		0.969***		0.969***		0.969***	
95CI	0.964	0.975	0.964	0.975	0.964	0.975	0.963	0.975
dCCI_PVD	1.226***		1.244***		1.234***		1.248***	
95CI	1.217	1.235	1.217	1.235	1.225	1.243	1.238	1.257
dCCI_SevereLiver	1.015		1.014		1.016		1.014	
95CI	0.999	1.032	0.999	1.032	0.999	1.033	0.998	1.031
_cons	2.233***		2.232***		2.226***		2.234***	
	2.215	2.252	2.215	2.252	2.208	2.245	2.216	2.253
N	1908832		1908832		1908832		1908832	
	10790634.3		10794131.0		10790860.0	1.8	10791675.1	9.0
BIC	10790933.4		10794430.1		10791159.1		10791974.2	

Appendix 5. The incidence rates by age band, at risk population and incident cases

	age band	at risk population	incidence rate per 100,000	annual incident cases
Venous	<40	1,957,020	1.2	23
	40-49	614,941	7	43
	50-59	614,492	19.9	122
	60-69	466,620	37.5	175
	70-79	211,447	66.7	141
	≥80	101,276	91.8	93
	total	3,965,796		598
Arterial	<40	1,957,020	1.1	22
	40-49	614,941	15.6	96
	50-59	614,492	67.5	415
	60-69	466,620	143.4	669
	70-79	211,447	246.4	521
	≥80	101,276	477.9	484
	total	3,965,796		2,206
Diabetic	<40	1,957,020	5.8	114
	40-49	614,941	56.6	348
	50-59	614,492	175.8	1,080
	60-69	466,620	368.6	1,720
	70-79	211,447	758.6	1,604
	≥80	101,276	1791.1	1,814
	total	3,965,796		6,680
Pressure	<40	1,957,020	4.8	94
	40-49	614,941	22	135
	50-59	614,492	74.4	457
	60-69	466,620	236.4	1,103
	70-79	211,447	844.2	1,785
	≥80	101,276	3646.5	3,693
	total	3,965,796		7,268

Appendix 6. EQ-5D scores by type of wound and time from Singapore Wound Registry

Mean (Std. Dev.)	Baseline	month 1	month 3	month 6
Venous	0.57 (0.34) (n=255)	0.68 (0.31) (n=235)	0.74 (0.30) (n=242)	0.74 (0.30) (n=243)
Arterial	0.44 (0.40) (n=354)	0.52 (0.42) (n=311)	0.54 (0.45) (n=303)	0.58 (0.44) (n=291)
Diabetic	0.64 (0.42) (n=139)	0.71 (0.44) (n=128)	0.72 (0.38) (n=129)	0.74 (0.43) (n=126)
Pressure	-0.18 (0.50) (m=51)	0.00 (0.56) (n=43)	0.18 (0.54) (n=38)	0.11 (0.59) (n=40)

Appendix 7 - SAS code for calculating the local EQ-5D index score from EQ-5D-3L

```
*** coding of EQ-5D data: 1 = no problems, 2 = some/moderate problems, 3 = extreme problems;
*** mo = mobility, sc = self-care, ua = usual activity, pd = pain/discomfort, ad = anxiety/depression;

data new; set new;
    if mo=2 then m2=1; else m2=0;
    if mo=3 then m3=1; else m3=0;
    if sc=2 then s2=1 page; else s2=0;
    if sc=3 then s3=1; else s3=0;
    if ua=2 then u2=1; else u2=0;
    if ua=3 then u3=1; else u3=0;
    if pd=2 then p2=1; else p2=0;
    if pd=3 then p3=1; else p3=0;
    if ad=2 then a2=1; else a2=0;
    if ad=3 then a3=1; else a3=0;
    if mo=3 or sc=3 or ua=3 or pd=3 or ad=3 then n3=1; else n3=0;
    EQ_index = 1 - 0.1678*m2 - 0.3040*m3 - 0.1615*s2 - 0.3465*s3 - 0.2555*u2 - 0.3209*u3 - 0.1462*p2 - 0.2291*p3 - 0.1501*a2 - 0.2784*a3 - 0.2905*n3;
    if mo =. or sc=. or ua=. or pd=. or ad =. then EQ_index =. ;
    drop m2 m3 s2 s3 u2 u3 p2 p3 a2 a3 n3; run;
```

Appendix 8. Mean duration of wounds in days, by age band; Mean (Standard Deviation)

Age Band	Venous (n=150)	Diabetic (n=245)	Pressure (n=24)
<40	133 (92)	177 (88)	55 (11)
40-49	129 (109)	325 (550)	86 (24)
50-59	331 (394)	224 (216)	115 (1)
60-69	223 (269)	314 (430)	103 (59)
70-79	307 (438)	256 (305)	105 (115)
≥80	205 (153)	160 (138)	62 (52)

values for Diabetic were used to proxy 'Arterial' wounds

Appendix 9 – usage and costs of outpatient services for patients with chronic wounds

	with consult		without consult	
Total annual costs	mean (sd)	95% CI	mean (sd)	95% CI
Costs of Outpatient with Consult - Arterial	$908.13 ($778.27)	($815.39, $1000.86)	$992.01 ($1241.53)	($844.08, $1139.94)
Costs of Outpatient with Consult - Venous	$685.73 ($575.30)	($603.62, $767.84)	$2381.98 ($2449.41)	($2024.72, $2739.24)
Costs of Outpatient with Consult - Diabetic	$918.06 ($823.40)	($752.11, $1084.01)	$1068.85 ($905.06)	($888.33, $1249.36)
Costs of Outpatient with Consult - Pressure	$702.40 ($525.63)	($368.43, $1036.37)	$1111.98 ($1330.34)	(-$118.38, $2342.34)
Annual visits	mean (sd)	95% CI	mean (sd)	95% CI
No. of Visits of Outpatient with Consult - Arterial	8.249 (6.107)	(7.521, 8.977)	8.454 (6.362)	(7.696, 9.212)
No. of Visits of Outpatient with Consult - Venous	5.874 (5.932)	(5.028, 6.721)	23.639 (18.989)	(20.870, 26.409)
No. of Visits of Outpatient with Consult - Diabetic	8.102 (6.209)	(6.857, 9.347)	14.172 (51.225)	(4.008, 24.336)
No. of Visits of Outpatient with Consult - Pressure	6.5 (4.681)	(3.526, 9.474)	9.714 (10.797)	(-0.271, 19.700)
Cost per Visit	mean (sd)	95% CI	mean (sd)	95% CI
Costs per Visit of Outpatient with Consult - Arterial	$110.44 ($46.69)	($104.88, $116.01)	$117.28 ($87.66)	($106.84, $127.73)
Costs per Visit of Outpatient with Consult - Venous	$133.24 ($81.05)	($121.67, $144.80)	$106.81 ($105.11)	($91.48, $122.14)
Costs per Visit of Outpatient with Consult - Diabetic	$112.00 ($66.26)	($98.64, $125.35)	$114.93 ($39.31)	($107.08, $122.77)
Costs per Visit of Outpatient with Consult - Pressure	$111.04 ($55.19)	($75.97, $146.10)	$124.14 ($38.92)	($88.14, $160.13)

Appendix 10. Cohort of all patients who accessed CHAS, Polyclinic or Emergency departments (ED) 2012 to 2019

	CHAS		Polyclinic		ED	
	No Wound	Any Wound	No Wound	Any Wound	No Wound	Any Wound
Number	1,013,104	3,463	2,600,153	1,441	2,964,540	7,403
Age	49.4	67.9	37	65	36	68
Male	46%	45%	51%	57%	56%	52%
CCI score	2.6	4.0	2.1	4.3	2.0	5.0
Chinese	72%	78%	64%	61%	52%	61%
Malay	14%	10%	12%	13%	10%	17%
Indian	6%	8%	10%	20%	9%	13%
Others	9%	5%	14%	6%	30%	9%
COPD	3%	4%	2%	5%	3%	5%
Diabetes Mellitus	32%	55%	28%	68%	30%	70%
Hypertension	64%	82%	55%	81%	56%	83%
Dyslipidemia	61%	72%	50%	78%	51%	77%
Heart Failure	4%	13%	3%	15%	4%	22%
Renal Failure	10%	24%	7%	26%	8%	39%
Stroke	8%	16%	7%	17%	8%	26%
Dementia	2%	6%	1%	6%	2%	16%
Major Depression	3%	3%	2%	4%	2%	7%
Parkinson	1%	3%	1%	2%	1%	6%
Schizophrenia	2%	2%	2%	3%	2%	3%
Average no. of episodes in 12 months from wound/first visit	3.1	6.2	1.8	2.8	1.4	2.6

Appendix 11. Results of generalised linear model (GLM) with a Poisson link function to estimate excess use of poly-clinic services, CHAS and ED.

Polyclinic	All	No wound	Any wound
Number	2601594	2600153	1441
Mean no. of episodes in 12 months, SD	1.85(1.78)	1.85(1.77)	1.85(1.78)
Median 12 month utilisation, IQR	1 (1-2)	1 (1-2)	2 (1-3)
Coefficient			0.352 (0.288,0.416)
Rate ratio of Episodes, CI			1.423 (1.333,1.513)
Estimated mean Episodes, CI			2.157 (2.13,2.184)
Expected Episodes, CI			3.069 (3.031 ,3.108)
Excess Episodes, CI			0.912 (0.901 ,0.924)
CHAS	All	No wound	Any wound
Number	1016567	1013104	3463
Mean no. of episodes in 12 months, SD	3.13 (3.75)	3.12 (3.73)	6.18 (7.30)
Median 12 month utilisation, IQR	2 (1 - 4)	2 (1 - 4)	4(2 -8)
Coefficient			0.685 (0.669 , 0.701)
Rate ratio of Episodes, CI			1.984 (1.952 , 2.016)
Estimated mean Episodes, CI			3.596 (3.578 , 3.614)
Expected Episodes, CI			7.134 (7.099 , 7.169)
Excess Episodes, CI			3.538 (3.521 , 3.556)
ED	All	No wound	Any wound
Number	2971943	2964540	7403
Mean no. of episodes in 12 months, SD	1.38(1.17)	1.38(1.16)	1.38(1.17)
Median 12 month utilisation, IQR	1 (1-1)	1 (1-1)	2 (1-3)
Coefficient			0.343 (0.319 ,0.367)
Rate ratio of Episodes, CI			1.410 (1.376 ,1.444)
Estimated mean Episodes, CI			1.531 (1.515 ,1.547)
Expected Episodes, CI			2.159 (2.136 ,2.181)
Excess Episodes, CI			0.628 (0.621 ,0.634)

BMJ Open

Chronic Wounds in a Multi-Ethnic Asian Population. A Cost of Illness Study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065692.R2
Article Type:	Original research
Date Submitted by the Author:	21-Apr-2023
Complete List of Authors:	Graves, Nicholas; Duke-NUS Medical School Ganesan, Ganga; Ministry of Health Singapore Tan, Kelvin; Ministry of Health Singapore, Policy Research & Evaluation Division Goh, Orlanda; Singapore General Hospital, Department of Internal Medicine Ho, Jackie; National University of Singapore Chong, Tze; Singapore General Hospital, Bishnoi, Priya; A*STAR, Carmody, David; Singapore General Hospital, Department of Internal Medicine Yuh, Ang Shin; Singapore General Hospital Ng, Yi Zhen; Skin Research Institute of Singapore, Lo, Zhiwen; National Healthcare Group Woodlands Health Campus Enming, Yong; Tan Tock Seng Hospital Abu Bakar Aloweni, Fazila; Singapore General Hospital, Nursing Division Zifei, Wang; Skin Research Institute of Singapore Harding, Keith; A*STAR
Primary Subject Heading:	Health economics
Secondary Subject Heading:	Health policy, Health services research, Epidemiology
Keywords:	GENERAL MEDICINE (see Internal Medicine), HEALTH ECONOMICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, WOUND MANAGEMENT

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Chronic Wounds in a Multi-Ethnic Asian Population. A Cost of Illness Study

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Words. 3500

Abstract

Objective. To estimate the 'cost of illness' arising from chronic wounds in Singapore.

Design. Incidence based cost of illness study using evidence from a range of sources.

Setting: Singapore health services.

Participants. We consider 3.49 million Singapore citizens and permanent residents. There are 16,752 new individuals with a chronic wound in 2017, with 598 venous ulcers, 2,206 arterial insufficiency ulcers, 6,680 diabetic ulcers and 7,268 pressure injuries.

Primary outcome measures expressed in monetary terms are the: value of all hospital bed days lost for the population; monetary value of QALYs lost in the population; costs of all outpatient visits; and, costs of all poly clinic, use of community health assist scheme (CHAS) and emergency departments (ED) visits. Intermediate outcomes that inform the primary outcomes are also estimated.

Results: Total annual cost of illness was $350 million (range $72 to 1,779 million). With 168,503 acute bed days taken up annually (range 141,966 to 196,032) that incurred costs of $139 million (range 117 to 161 million). Total costs to health services were $184 million (range $120 to $1,179 million). Total annual costs of lost health were 2,077 QALYS (range -2,657 to 29,029) valued at $166 million (range -212 to 2,399 million).

Conclusions. The costs of chronic wounds are large to Singapore. Many of them could be avoided by making positive investments in integrated and comprehensive wound prevention and treatment programmes.

Strengths and limitations of this study

- Reliable and relevant data sources were used to update the results
- First study to quantify the national cost of chronic wounds in a multi-ethnic Asian population
- Some important costs were excluded as no information was available
- The sample size for the preference based utility weights for QALYS were small
- Some outcomes were not adjusted for co-morbidities and so might overstate the true costs.

Introduction

Chronic wounds are those that fail to heal in a time sufficient for 'normal' healing. They tend to present as a co-morbid rather than primary condition among older individuals. Other risk factors are diabetes, poor nutrition, incontinence and reduced mobility [1]. They have been described as causing a 'silent epidemic' that affects a large proportion of the world's population [2]. Chronic wounds are prevalent among vulnerable individuals living at home and residents of long-term care facilities. They are commonly associated with extended hospital stays but patient safety programmes have reduced healthcare associated events [3].

The burden of cost is particularly large [4] with 3% of the total NHS budget [5] and 4% of health care expenditure in Scandinavian countries used to manage the consequences of chronic wounds [6]. The goal of reducing the prevalence of chronic wounds has failed to attract sustained investment from those who pay for health services [7]. This contrasts with other major diseases, where payers are prepared to invest in 'cancer moonshots' for example [8], that will hopefully lead to better outcomes the future. This inequity is puzzling as the technology for reducing chronic wounds is available now, saves more than it costs to implement [9], and will cause large and certain gains in health outcomes.

Ulcers of the skin are the most common type of chronic wounds and include venous ulcers, arterial ulcers, diabetic foot ulcers and pressure ulcers or injuries. There are associated with a wide range of economic costs [2]. Affected individuals require frequent evidence-based treatments and if the condition becomes overwhelming an admission to hospital is inevitable. Many patients will be admitted for other reasons, and the wound may independently prolong hospital stay [10]. Debridement, minor amputations, and major amputations are common among higher risk groups [11, 12]. Chronic wounds are prevalent among residents of aged care facilities and will incur additional costs for staff time and consumables. Home nursing services as well as charities and volunteer groups that support the frail and elderly in their homes also manage patients [13]. Out of pocket expenditures will arise for patients and family members who travel to access services and purchase consumable items [14]. Productivity losses will arise as the patients are unable to perform their normal activities, be they paid or unpaid, and family members will have to take time from waged and unwaged productive activity. Health-related quality of life, which has monetary value [15], will be reduced. All these costs can be structured by a 'cost of illness' method [16].

The aim of this study is to estimate the 'cost of illness' arising from chronic wounds in Singapore. Our results could be used to stimulate decision makers to invest in known prevention and management programmes. The findings will also aid researchers who wish to model the cost savings or the cost-effectiveness of specific interventions.

Method

Scope of the Analyses

We include all resident Singapore Citizens and Permanent Residents (n=3.49M) and exclude resident foreign nationals and long-term employment pass holders (n=526,000) in 2017 [17]. Singapore has a multi-ethnic Asian population comprising of residents who are 76% Chinese, 15% Malay and 7.5% Indian descent [18]. The perspective for this analysis includes the costs incurred by health services and the losses to health benefits, expressed as QALYs foregone. We do not represent the 'societal' perspective as there are no data on private out of pocket costs, but we do review this omission in the Discussion. We estimate the expected annual costs arising from incident cases of venous ulcers, arterial insufficiency ulcers, diabetic ulcers and pressure injury.

Scope of the Modelling

We use statistical models to estimate four primary outcomes for the year 2017, see Figure 1.

FIGURE 1 HERE

First, are the monetary '*value of all hospital bed days lost for the population'*. The information used is summarised in Part A of Figure 1 and is labelled Inpatient 'Acute Sector Costs'. Second, are the '*monetary value of QALYs lost in the population'*. The information used is summarised in Part B of Figure 1 and is labelled 'Lost Heath Outcomes'. Third, are the '*costs of all outpatient visits'*. The information used is summarised in Part C of Figure 1 and is labelled 'Outpatient Clinics Costs'. Fourth, are the *'costs of all poly clinic, use of community health assist scheme (CHAS) and emergency departments (ED) visits'*. The information used is summarised in Part D of Figure 1 and is labelled 'Primary Care and ED costs'. CHAS is a mechanism for funding all Singapore Citizens to attend medical and or dental care at participating General Practitioner (GP) and dental clinics. CHAS is particularly designed to support the management of chronic diseases.

Data, Parameters and Assumptions

A. Inpatient Acute Sector Costs

Two outcomes, shown by blue boxes in Figure 1, are estimated: '*Number of bed days lost per case'* and '*Value of all hospital bed days lost for population ($)'*. To estimate the '*Number of bed days lost per case'* we combined information on the '*Number of admissions to hospital with wounds*' with information on '*Excess acute hospital stay due to a wound'*. To estimate the '*Number of admissions to hospital with wounds*' we retrieved a population cohort of all inpatient admissions to acute hospitals in Singapore between

2012 and 2019 from the Singapore Ministry of Health, and applied the cases from 2017. From the entire dataset we identified all inpatient episodes with any occurrence of Venous ulcers, Arterial insufficiency ulcers, Diabetic ulcers and Pressure injury or any combination of these wounds as a primary or secondary diagnosis based on the ICD-9 codes in Appendix 1.

To estimate '*Excess acute hospital stay due to wound'* we extracted the length of hospital stay and relevant co-variate information that could be used to explain variation in the length of stay, see Appendix 2. A parsimonious multivariable generalised linear model (GLM) with a gamma link function was used to accommodate the skew typical of lengths of stay data [19]. The outcome of interest was the length of stay associated with chronic wound management in the inpatient setting. Other covariates included were age, gender, race, and comorbid chronic diseases. The statistical model generated a coefficient for 'wound type' expressed as a rate ratio, that showed the amount of increase in length of stay associated with the presence of wound, given that other factors that predicted length of stay had been accounted for. This rate ratio was used to moderate the mean length of stay for the entire sample and an excess length of stay associated with the wound was estimated. In Appendix 3 we show a summary of the results of the multivariable generalised linear model and in Appendix 4 we show the full model results.

To estimate the '*Value of all hospital bed days lost for population ($)'* we combined the *'Number of bed days lost per case'* with the *'Cost per bed day ($)'*.

All the data inputs used for this part of the model are shown in Table 1.

Table 1. Data inputs used to estimate the outcomes for the 'Inpatient Acute Sector Costs'

Parameter	Estimate	Distribution used for uncertainty	
Excess acute hospital stay due to wound (days)			
Arterial	2.37	Gamma (757, 0.0031)	Estimated by multivariable generalised linear model
Venous	0.79	Gamma (84, 0.0094)	
Diabetic	2.26	Gamma (742, 0.003)	
Pressure	1.61	Gamma (724, 0.0022)	
Number of admissions to hospital with wounds			
Arterial	14,536	Fixed	#
Venous	19,210	Fixed	
Diabetic	16,999	Fixed	
Pressure	49,879	Fixed	
Cost per bed day ($)	823	Normal(823, 2.78)	#

Ministry of Health, *Administrative database*, Ministry of Health (MOH). Accessed in 2021.

B. Lost Health Outcomes

Five outcomes, shown by blue boxes in Figure 1, are estimated: *Annual cases by wound type; Number of QALYs lost per case (by age group); Utility decrement; Number of QALYS lost in population; and, Monetary value of QALYS lost in the population ($).* The first four are intermediate outcomes that contribute information to the primary outcome of '*Monetary value of QALYs lost in the population ($)'*.

To estimate *'Annual cases by wound type'* we apply the incidence rates for each wound type to the *'Total at risk population'*. We used published incidence rates for 2017 from a population-based study of wounds among those admitted to Singapore acute care hospitals from 2000 to 2017 [20]. For this work the authors identified relevant ICD-10 codes for for occurrences of venous ulcers, arterial insufficiency ulcers, diabetic ulcers, and pressure ulcers or injuries, see Appendix 1, and applied them to the Singapore Ministry of Health central claims database, which includes records of all admissions to public and private acute care hospitals. The incidence rates by age band are reported alongside the at-risk population enabling the number of incident cases to be estimated, see Appendix 5 for more detail.

To estimate the '*Number of QALYs lost per case (by age group)'* we use EQ-5D-5L data. This instrument includes preference based valuations of health states expressed as 'health utilities' on a scale between zero, the worst possible health state, and one, the best possible health state [21]. We used EQ-5D-5L data from 799 individuals with relevant wounds from the Singapore wound care registry to inform the '*Health utility for cases with specific wound type'*. Responses were recorded at entry into the registry, when the wound was first assessed in the hospital setting and then at 1, 3 and 6 months, see Appendix 6. We used a Singapore EQ-5D-3L value set [22] that was then mapped onto the EQ-5D-5L version using the SAS code in Appendix 7. The utility outcomes for the wound patients are compared to population norms for the EQ-5D index informed by Singapore preference weights for appropriate age bands [23], this informs the '*Population normal Utility (by age)'*. Using the information described above we are able to estimate the '*Utility Decrement'* from having a wound. The '*Duration of Wound'* was informed by the mean durations of wounds in days for the specific wound types from the Singapore Wound Registry, see Appendix 8. The '*Number of QALYs lost in population'* is the product of the '*Number of QALYS lost per case'* and the '*Annual cases by wound type'*. The '*Monetary value of QALYs lost in the population'* is the product of the '*Number of QALYS lost in population*' and the *'Value of one QALY'*, which is set at the mean gross domestic product per capita for Singapore of SGD $80,000 [24]. This approach assumes the value of one year of perfect quality of life does not exceed the per capita gross domestic product [25].

All the data inputs used for this part of the model are shown in Table 2.

Table 2. Data inputs used to estimate the outcomes for the 'Lost Health Outcomes'

Parameter	Estimate	Distribution used for uncertainty	
Health utility for cases with specific wound type			
Arterial – baseline	0.44	Beta (0.24, 0.30)	Singapore Wound Registry
Venous – baseline	0.57	Beta (0.60, 0.46)	
Diabetic – baseline	0.64	Beta (0.21, 0.12)	
Pressure – baseline	-0.18	Normal (-0.18, 0.50)	
Arterial – month 1	0.52	Beta (0.23, 0.21)	
Venous – month 1	0.68	Beta (0.89, 0.41)	
Diabetic – month 1	0.71	Beta (0.04, 0.02)	
Pressure – month 1	0.00	Normal (0.00, 0.56)	
Arterial – month 3	0.54	Beta (0.13, 0.11)	
Venous – month 3	0.74	Beta (0.81, 0.28)	
Diabetic – month 3	0.72	Beta (0.28, 0.11)	
Pressure – month 3	0.18	Normal (0.18, 0.54)	
Arterial – month 6	0.58	Beta (0.16, 0.12)	
Venous – month 6	0.74	Beta (0.83, 0.28)	
Diabetic – month 6	0.74	Beta (0.05, 0.02)	
Pressure – month 6	0.11	Normal (0.11, 0.59)	
Population normal utility (by age group)			
<40	0.980	Beta (350, 7)	[23]
40-49	0.950	Beta (636, 33)	
50-59	0.940	Beta (535, 34)	
60-69	0.960	Beta (193, 8)	
70-79	0.890	Beta (189, 23)	
≥80	0.890	Beta (189, 23)	
Value of one QALY ($)	80,000	Fixed	[24]
Durations of Arterial wounds in days (by age group)			
<40	133	Normal(133,92)	Singapore Wound Registry
40-49	129	Normal(129,109)	
50-59	331	Normal(331,394)	
60-69	223	Normal(223,269)	
70-79	307	Normal(307,438)	
≥80	205	Normal(205,153)	
Durations of Venous wounds in days (by age group)			
<40	133	Normal(133,92)	
40-49	129	Normal(129,109)	
50-59	331	Normal(331,394)	
60-69	223	Normal(223,269)	
70-79	307	Normal(307,438)	
≥80	205	Normal(205,153)	
Durations of Diabetic wounds in days (by age group)			
<40	177	Normal(177,88)	
40-49	325	Normal(325,550)	
50-59	224	Normal(224,216)	
60-69	314	Normal(314,430)	
70-79	256	Normal(256,305)	
≥80	160	Normal(160,138)	
Durations of Pressure injury in days (by age group)			
<40	55	Normal(55,11)	
40-49	86	Normal(86,24)	
50-59	115	Normal(115,1)	
60-69	103	Normal(103,59)	
70-79	105	Normal(105,115)	
≥80	62	Normal(62,52)	

C. Outpatient Clinics costs

Only one outcome, '*Costs of all outpatient visit ($)',* was estimated. Information was used for the '*Annual cases by wound type', 'Cost per outpatient visit ($)' and 'Outpatient visits per case'*

To estimate *'Cost per outpatient visit ($)'* we interrogated the Singapore wound care registry to identify the annual number of visits for those with chronic wounds and the reported costs per visits, this information was available by wound type. There were 573 individuals for whom these data were reported. Visits were for specialist consultations specifically for their wound, and for podiatry visit or medical tests, see Appendix 9. All the data inputs used for this part of the model are shown in Table 3.

Table 3. Data inputs used to estimate the outcomes for the 'Outpatient Clinic Costs'

	Estimate	Distribution used for uncertainty	Source
Outpatient visits per case (with consult)			Singapore Wound Registry
Arterial	8.2	Gamma (1.82:4.52)	
Venous	5.9	Gamma (0.98:5.99)	
Diabetic	8.1	Gamma (1.70:4.76)	
Pressure	6.5	Gamma (1.93:3.37)	
Outpatient visits per case (without consult)			
Arterial	8.5	Gamma (1.77:4.79)	
Venous	23.6	Gamma (1.55:15.25)	
Diabetic	14.2	Gamma (0.08:185.15)	
Pressure	9.7	Gamma (0.81:12.00)	
Cost per outpatient visit (with consult) ($)			
Arterial	110	Gamma (5.60:19.74)	
Venous	133	Gamma (2.70:49.30)	
Diabetic	112	Gamma (2.86:39.20)	
Pressure	111	Gamma (4.05:27.43)	
Cost per outpatient visit (without consult) ($)			
Arterial	117	Gamma (5.60:19.74)	
Venous	106	Gamma (2.70:49.30)	
Diabetic	114	Gamma (2.86:39.20)	
Pressure	124	Gamma (4.05:27.43)	

D. Primary Care and ED costs

Only one outcome '*Costs of all POLY, CHAS & ED visits ($)*' was estimated. Information was used for the '*Annual cases by wound type', 'Cost per POLY, CHAS & ED visit ($)'* and *'Excess POLY, CHAS & ED visits per case due to wound*'.

For the '*Cost per POLY, CHAS & ED visit ($)* we use estimates reported by the Singapore Ministry of Health. To estimate *Excess POLY, CHAS & ED visits per case due to wound*' the same population cohort for 2012 to 2019 who were admitted as inpatients were interrogated. We identify the use of the Emergency Departments (ED) of acute hospitals and all visits to community-based Polyclinics (POLY) and use of community health assist scheme (CHAS).

We sought to estimate the excess use of these services associated with any chronic wound. For the analysis each patient is counted only once, and those with wounds are only counted when they first appear with any wound, and the number of 12-month visits from the incidence date is the outcome variable. For those without wounds, their 12-month use starts from the first visit during the study period. A parsimonious generalised linear model with a log link Poisson function was used for all regressions. The Poisson

distribution was chosen over the negative binomial distribution based on fitting the model then doing model checks with diagnostic plots and relevant statistics. The outcome of interest was a count of the use of the services. Other covariates included were age, gender, race, Charlson comorbidity index and presence of comorbid conditions, see Appendix 10. The ensuing statistical models generated a coefficient for 'any wound' expressed as a rate ratio, that showed the change in the number of visits associated with the presence of wound, given that other factors that predicted variation in these outcomes. As before, the rate ratio was used to moderate the mean counts for the entire sample and an excess number of visits was estimated for all wounds, see Appendix 11. All the data inputs used for this part of the model are shown in Table 4.

Table 4. Data inputs used to estimate the outcomes for the 'Primary care and ED Costs'

Parameter	Estimate	Distribution used for uncertainty	Source
Excess visits for Polyclinics (all wounds)	0.91	Gamma (18.33, 0.049)	Estimated by multivariable generalised linear model
Excess visits for CHAS (all wounds)	3.54	Gamma (38.51, 0.091)	
Excess visits for ED (all wounds)	0.63	Gamma (4.18, 0.15)	
Cost per Poly clinic visit	$147	Normal(147,2.5)	Ministry of Health, Administrative database, Ministry of Health (MOH). Accessed in 2021
Cost per CHAS use	$56	Normal(56,1.14)	
Cost per ED visit	$352	Normal(352,.14)	

Uncertainty & Model Evaluation

Uncertainty for all the outcomes shown in Figure 1 was assessed by probabilistic sensitivity analysis. We take 5,000 Monte Carlo resamples from all the parameters described in Tables 1 to 4. We report the number of 'acute care bed days lost' and the number of 'QALYs lost to chronic wounds'. We then report the findings from the resamples for the primary model outcomes: *Value of all bed days lost for population; Monetary value of QALYS lost in the population; Costs of all outpatient visit; and, Costs of all POLY, CHAS & ED visits.* We sum these four primary outcomes to report the *'Total Costs of Illness for each wound type'.* These processes are shown in Figure 1.

Patient and Public Involvement

The data came from the Singapore Wound Registry and from the Ministry of Health. It was routinely reported data collected for the purpose of managing and planning health services. It was not possible to develop the research question or outcome measures based on the priorities, experience, and preferences of the patients. Patients were not involved patients in the design, recruitment and conduct of the study. Patients who are interested will be able to read the paper.

Results

There were 16,752 'new' or 'incident' cases for 2017, with 598 venous ulcers, 2,206 arterial insufficiency ulcers, 6,680 diabetic ulcers and 7,268 pressure injuries. The values obtained from the model for 'acute care bed days lost' and the number of 'QALYs lost to chronic wounds' are shown in Table 5.

Table 5. Annual outcomes for bed days lost and QALYs lost for incident cases (n=16,752)

Number of QALYS lost	mean (min:max)
Arterial	544 (-340:5,436)
Venous	75 (-127:0,971)
Diabetic	856 (-1670:16,962)
Pressure	602 (-520:6,631)
Number of Bed days lost	
Arterial	34,389 (29269:38,674)
Venous	15,161 (10,044:22,166)
Diabetic	38,423 (33,445:43,573)
Pressure	80,530 (69,208:91,619)

The values obtained from the model for the four primary outcomes are shown in Table 6.

Table 6. Annual cost outcomes for the primary outcomes (n=16,752)

Value of all bed days lost for population	mean (min:max)
Arterial	$28,302,139 ($24,148,856:$31,912,933)
Venous	$12,477,776 ($8,243,954:$18,212,629)
Diabetic	$31,622,397 ($27,431,880:$35,693,113)
Pressure	$66,276,250 ($57,237,092:$75,718,807)
Monetary value of QALYS lost in the population	
Arterial	$43,491,588 (-$27,170,499:$434,890,646)
Venous	$5,975,553 (-$10,153,391:$77,645,170)
Diabetic	$68,498,429 (-$133,624,494:$1,356,989,736)
Pressure	$48,199,291 (-$41,617,890:$530,453,557)
Costs of all outpatient visit	
Arterial	$4,233,236 ($84,899:$35,360,192)
Venous	$2,017,189 ($8,957:$27,539,296)
Diabetic	$16,337,217 ($3,058:$785,613,392)
Pressure	$13,859,689 ($42,824:$142,991,574)
Primary care & ED costs	
Costs Polyclinic visits - all wounds	$2,245,437 ($877,197:$5,715,449)
Costs CHAS episodes of care - all wounds	$3,296,040 ($1,849,062:$5,930,304)
Costs ED visits - all wounds	$3,730,682 ($235,741:$14,456,940)

The aggregate of these cost outcomes are the 'Total Costs of Illness for each wound type' and are shown in Table 7 for the entire population of Singapore, and for the average individual.

Table 7. Annual total costs of illness for each wound type (n=16,752)

Total Costs of Illness for each wound type	mean (min:max)	
	population	individual
Arterial	$77,247,993 ($6,047,354:$469,696,045)	$35,364 ($383:$257,207)
Venous	$20,801,577 ($5,388,353:$91,673,830)	$35,023 ($9,064:$162,054)
Diabetic	$120,155,304 (-$97,359,748:$1,395,843,120)	$18,095 (-$17,094:$231,815)
Pressure	$132,358,039 ($42,035,656:$624,864,715)	$18,161 ($3,829:$73,175)
Total Cost of Illness	$350,562,913 ($72,814,108:$1,779,366,924)	$21,002 ($2,664:$100,366)

Based on our estimates pressure injuries account for 48% of the 168,503 bed days lost to chronic wounds and 38% of the $28.4M outpatients costs. For the non-hospital sector, the costs of CHAS services and ED visits account for most of the burden. The QALY burdens are large for diabetic foot, arterial and pressure injury with venous ulcers having lesser impact. Box plots for the 'Total Costs' outcomes are shown in Figure 2.

FIGURE 2 HERE

There is a 100% probability that the costs of chronic wounds are positive with the most likely value suggesting an annual cost to Singapore of $350 million. The findings are uncertain with the range of total costs between $79 million and $1.78 billion. More than half of the total costs arise from use of health services ($185 million, 53%) with outpatients accounting for $37 million (10%) and the use of acute bed days accounting for $139 million (40%). The value of the lost health by QALYs is substantial at $165 million, 47% of the total burden.

Discussion

These findings suggest the costs of chronic wounds to Singapore are large and account for approximately 0.07% of GDP. The total cost burden accounts for 3.14% of the 2019 Government Health Expenditure on services [26] and 2.3% of total economy-wide expenditure on services. Our estimates roughly align with those from other countries. In Australia 2% of the total national health expenditure is used for chronic wounds and in the UK 3% of the national health expenditure is taken up [27]. Two percent of the European health budget [28] is for care of chronic wounds and for Scandinavian countries the costs were found to be 2 to 4% of the total health care expenditure [6].

While the findings are lower than the annual costs of diabetes in Singapore, estimated to be US $787 million in 2010 [29], the policy response to diabetes has been considerable with a 'War on Diabetes' declared in 2016 to mobilise a national programme to reduce the problem of diabetes [30]. We found two other studies

reporting costs of chronic venous leg and neuro-ischemic ulcers in Singapore, but neither study were at a population level instead focusing on average costs per patient [31, 32].

This study likely underestimates the extent of the costs of chronic wounds as relevant information was not available for many costs we suspect are present. Our data came primarily from patients who were admitted to the hospital for their wounds. Thus patients with less serious wounds managed in the community are excluded. We were also unable to identify and include estimates of the private costs incurred by patients and family members. Other studies have found that such costs can be substantial. For the German setting Purwins et al. [33] found patients with leg ulcers in a given year spent €424 on topical treatments and drugs, €486 on out of pocket incidentals, €254 on drug prescriptions and €740 on non-drug treatments.

Although no data were available on the time away from work and other production losses, we addressed this by estimating and valuing lost quality adjusted life years (QALYs). We assume that time in reduced health states has a relationship with an ability to be economically productive. Thus, the dollar valuations of the lost QALYs can be thought of as representing lost production from chronic wounds. Most governments are willing to pay money for services that increase the number of QALYs in a population, given a programme achieves a marginal QALY below a designated cost [34]. Importantly we did not consider the costs of lost production for informal carers, which we expect are substantial.

There are further limitations to our study. Regarding the estimation of QALY losses, the sample sizes for EQ5D were quite small for Pressure injury with only 51 patients providing data. It is possible the estimate would change with a larger and more representative sample. It should be noted that the lowest health utilities arise from this sample. For example, the values for baseline were -0.18 indicating a health state valued worse than death, and a value of 0.00, the worst possible health state, was observed for month 1. Values remained low at 0.18 and 0.11 for the 3 month and 6 month follow-ups. We assumed that the observed decrement between the population norms for health utility and the estimates from the wound registry were wholly attributable to the presence of a wound. These QALY estimates did not adjust for the other health conditions that patients may have, and as such may overstate the QALY losses.

To attribute excess acute bed days to the presence of a chronic wound we developed generalised linear regression models with the outcome of length of stay. While did not have an exhaustive list of control variables we did find that factors such as race, age, gender, myocardial infarction, cancer, liver disease, peptic ulcer disease, peripheral vascular disease, renal disease, COPD, dementia, diabetes, heart failure, hyperlipidemia, lymphoproliferative disease, major depression, Parkinson's, schizophrenia and stroke all played a role in explaining variation in the observed length of stay. We fitted the best models possible, but acknowledge there may be some covariate information missing.

In summary, this recurring and unnecessary cost burden is a deadweight loss to Singapore health services, and society in general. It could be reduced if evidence-based and relatively simple prevention and management programmes were implemented. International evidence [9] reveals that using optimal prevention practices for diabetic foot ulcers [35] was cost-saving in Peru [36], Australia [37], Thailand [38] and China [39]. For the prevention of pressure injury nursing led interventions, a quality improvement collaborative and the standardised use of pressure injury bundles were found to be cost-saving in Denmark [40], the US and UK [41-44]. And for the prevention of venous leg ulcers, compression therapy, clinical assessments and use of guidelines were found to be cost-saving in the UK [45, 46] and US [47, 48].

Our findings provide fundamental information for researchers who wish to model the cost-effectiveness of programmes that will improve wound outcomes in the future. Understanding the baseline of costs and QALY outcomes form a useful start-point for any evaluation of interventions.

Conclusions.

The costs of chronic wounds are large to Singapore, but many of them could be avoided by making positive investments in integrated and comprehensive wound prevention and treatment programmes.

Authors contributions.

Nicholas Graves, Ganga Ganesan, Kelvin Tan, Orlanda Qi Mei Goh, Jackie Ho, Chong Tze Tec, Priya Bishnoi, David Carmody, Ang Shin Yuh, Ng Yi Zhen, Zhiwen Lo, Yong Enming, Fazila Binte, Abu Bakar Aloweni, Wang Zifei and Keith Harding made substantial contributions to the: conception and design of the paper, the acquisition, analysis, and interpretation of data; drafting and reviewing versions of the manuscript; and, final approval of the version submitted. All authors are accountable for all aspects of the work.

A competing interests statement. None

Funding. We would like to acknowledge the funding supported from the Agency for Science, Technology and Research (A*STAR) under its Industry Alignment Fund-Pre-Positioning Programme (IAF-PP) grant number H1901a00Y9/ and H17/01/a0/0CC9 as part of the Wound Care Innovation for the Tropics (WCIT) Programme.

Data availability statement. No data from the wound registry or MoH administrative databases are available. This is due to the privacy considerations of the Singapore MOH and the Singapore wound registry.

Ethics Approval

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

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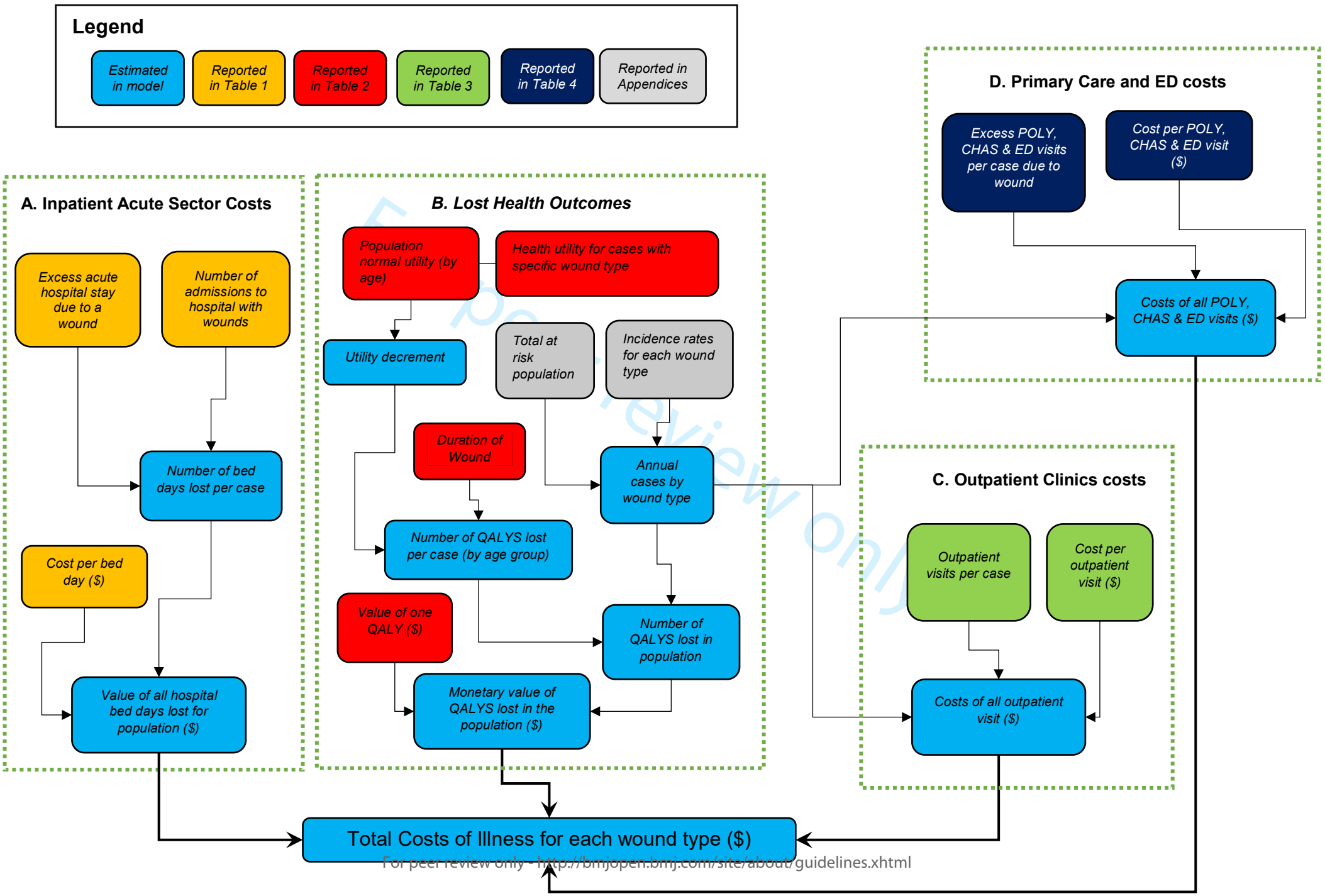
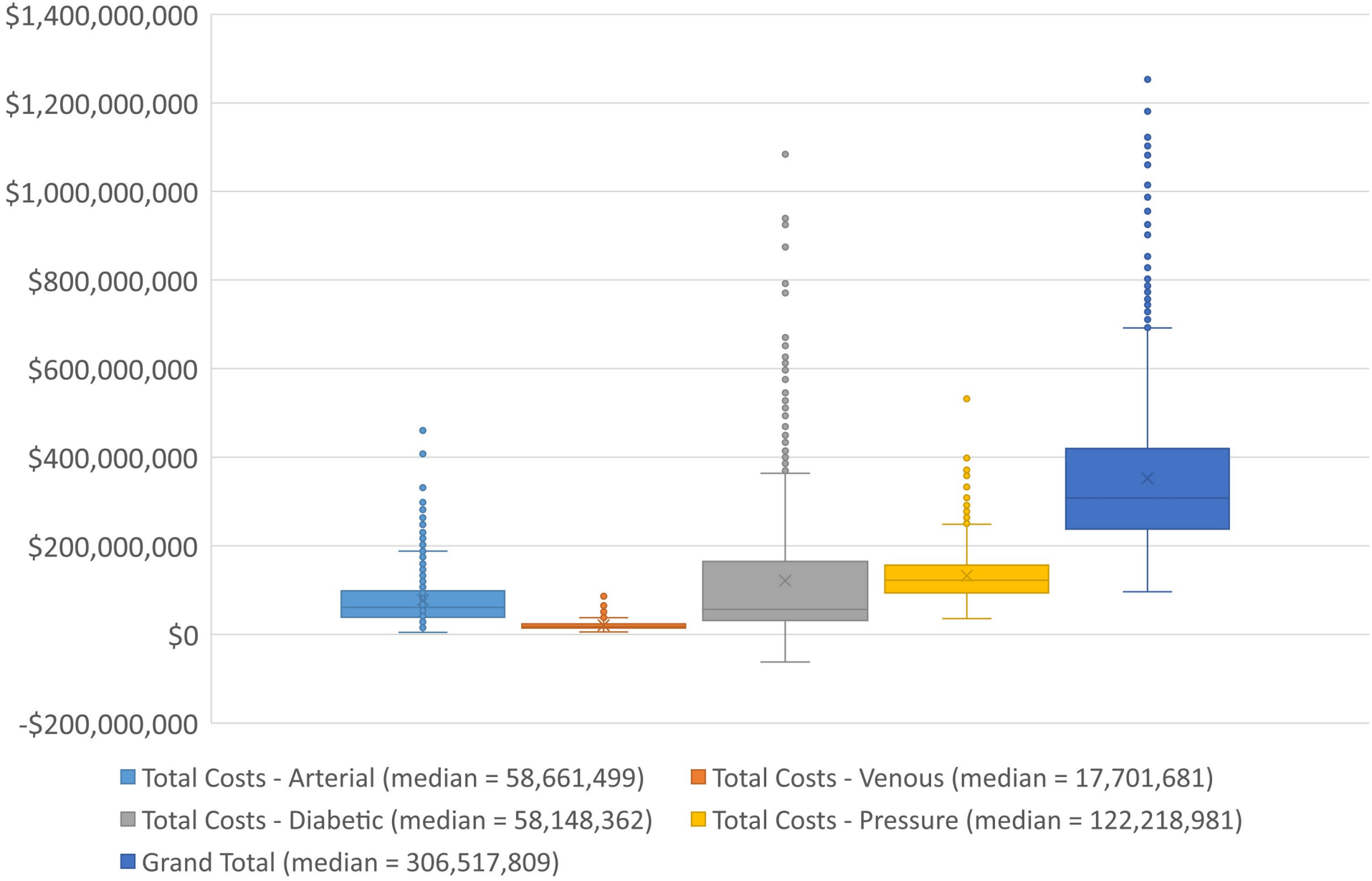
Figure 1. A diagram to show how the various parameters update the outcomes

Figure 2. Total cost outcomes for the cost of Illness by wound type




$1,400,000,000
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$1,000,000,000
$800,000,000
$600,000,000
$400,000,000
$200,000,000
$0
-$200,000,000
Total Costs - Arterial (median = 58,661,499)
Total Costs - Venous (median = 17,701,681)
Total Costs - Diabetic (median = 58,148,362)
Total Costs - Pressure (median = 122,218,981)
Grand Total (median = 306,517,809)

Appendix 1. ICD-9 codes used to identify chronic wounds from national claims dataset

Venous ulcers – *ICD-9-AM: 4540, 4532, 4591; ICD-10-AM: I83.0, I83.2, I87.0.*

Arterial insufficiency ulcers – *ICD-9-AM: 44023, 44024; ICD-10-AM: I70.23, I70.24*

Diabetic ulcers – *ICD-9-AM: 7071, 7078, 7079, 7854 & one of 25070, 25071, 25072 or 25073; ICD-10-AM: E10.73, E11.73, E13.73, E14.73, E10.52, E11.52, E13.52, E14.52, E09.02, E09.52, E10.69, E11.69, E13.69, E14.69*

Pressure ulcers – *ICD-9-AM: 7070; ICD-10-AM: L89.0, L89.1, L89.2, L89.3, L89.4, L89.5, L89.6, L89.7, L89.8, L89.9*

Appendix 2. Cohort of all hospital admissions for a relevant chronic wound 2012 to 2019

	All	No wound	Arterial	Venous	Diabetic	Pressure
Number	5,196,899	5,047,162	14,536	19,210	16,999	49,879
Age, mean (st dev)	50.4 (26.9)	49.6 (26.8)	75 (13.3)	72.1 (17.1)	72.4 (15.7)	81.7 (13)
Male	49%	48%	56%	57%	58%	50%
CCI score (mean)	4.1	4.1	6.1	4.7	5.9	4.4
Chinese	64%	64%	63%	60%	54%	71%
Malay	14%	14%	17%	16%	21%	13%
Indian	10%	10%	11%	13%	13%	6%
Others	12%	12%	9%	11%	12%	10%
COPD	7%	7%	6%	5%	5%	8%
Diabetes Mellitus	42%	42%	82%	57%	100%	40%
Hypertension	69%	68%	92%	77%	88%	76%
Dyslipidemia	61%	61%	84%	67%	86%	59%
Heart Failure	14%	14%	33%	21%	27%	14%
Renal Failure	24%	23%	49%	30%	44%	21%
Stroke	17%	17%	27%	19%	20%	40%
Dementia	6%	6%	7%	5%	4%	33%
Major Depression	6%	6%	5%	5%	6%	8%
Parkinson	3%	3%	2%	2%	1%	17%
Schizophrenia	4%	4%	1%	3%	2%	4%
Length of Stay, mean (st dev)	6.5(17)	6.3 (16.7)	16.2 (20.2)	9.8 (16)	14 (18.6)	16.8 (25.2)

Appendix 3. Summary results of generalised linear model (GLM) with a gamma link function to estimate excess length of stay

	All	No wound	Arterial	Venous	Diabetic	Pressure
Number	5,196,899	5,054,937	14,536	19,210	16,999	49,879
Length of Stay, mean (st dev)	6.5 (17)	6.3 (16.7)	16.2 (20.2)	9.8 (16)	14 (18.6)	16.8 (25.2)
Coefficient (95% CI)	-	-	0.722 (0.690,0.754)	0.303 (0.272,0.333)	0.701 (0.669,0.733)	0.543 (0.516,0.570)
Rate ratio of length of stay (95% CI)	-	-	2.059 (1.993,2.126)	1.353 (1.993,2.126)	2.015 (1.952,2.081)	1.722 (1.676,1.769)
Estimated mean length of stay (95% CI)	-	-	2.233 (2.215,2.252)	2.232 (2.215,2.252)	2.226 (2.208,2.245)	2.234 (2.216,2.253)
Expected length of stay (95% CI)	-	-	4.598 (4.414,4.788)	3.02 (4.414,4.788)	4.485 (4.31,4.672)	3.847 (3.714,3.986)
Excess length of stay (95% CI)	-	-	2.365 (2.199,2.536)	0.788 (2.199,2.536)	2.259 (2.102,2.427)	1.613 (1.498,1.733)

Appendix 4. Full results of generalised linear model (GLM) with a gamma link function to estimate excess length of stay

Co-variate	**Exponentiated coefficients; 95% confidence intervals in brackets**							
los_cens	Arterial		Venous		Diabetic		Pressure	
d_ulcer	2.059***		1.353***		2.015***		1.722***	
95CI	1.993	2.126	1.993	2.126	1.952	2.081	1.676	1.769
age	1.013***		1.013***		1.013***		1.013***	
95CI	1.013	1.013	1.013	1.013	1.013	1.013	1.013	1.013
male	1.019***		1.020***		1.019***		1.020***	
95CI	1.016	1.023	1.016	1.023	1.015	1.023	1.016	1.024
1.Race	1		1		1		1	
2.Race	0.989***		0.989***		0.987***		0.988***	
95CI	0.983	0.994	0.983	0.994	0.982	0.992	0.983	0.993
3.Race	0.903***		0.902***		0.902***		0.904***	
95CI	0.898	0.909	0.898	0.909	0.897	0.908	0.898	0.910
4.Race	0.935***		0.935***		0.934***		0.935***	
95CI	0.927	0.942	0.927	0.942	0.926	0.941	0.928	0.943
dCCI_AMI	0.941***		0.943***		0.942***		0.943***	
95CI	0.936	0.946	0.936	0.946	0.937	0.948	0.938	0.948
dCCI_Cancer	1.099***		1.099***		1.099***		1.099***	
95CI	1.094	1.105	1.094	1.105	1.093	1.105	1.094	1.105
dCD_DM	1.094***		1.096***		1.091***		1.098***	
95CI	1.090	1.099	1.090	1.099	1.087	1.096	1.093	1.102
dCD_Hyp	1.076***		1.077***		1.077***		1.078***	
95CI	1.071	1.082	1.071	1.082	1.071	1.083	1.072	1.084
dCD_LPD	0.919***		0.919***		0.918***		0.920***	
95CI	0.914	0.923	0.914	0.923	0.914	0.923	0.916	0.925
dCD_HeartFail	1.040***		1.040***		1.041***		1.041***	
95CI	1.034	1.046	1.034	1.046	1.035	1.046	1.036	1.047
dCCI_Renal	1.113***		1.115***		1.113***		1.115***	
95CI	1.108	1.118	1.108	1.118	1.108	1.118	1.110	1.121
dCD_Stroke	1.153***		1.153***		1.154***		1.150***	
95CI	1.148	1.159	1.148	1.159	1.149	1.159	1.144	1.155
dCD_Dementia	1.144***		1.143***		1.143***		1.132***	

95CI	1.135	1.152	1.135	1.152	1.134	1.151	1.124	1.141
dCD_MajDepression	1.086***		1.086***		1.086***		1.085***	
95CI	1.078	1.095	1.078	1.095	1.077	1.094	1.077	1.094
dCD_Parkinson	1.155***		1.154***		1.154***		1.143***	
95CI	1.142	1.168	1.142	1.168	1.141	1.168	1.130	1.156
dCD_Schizophrenia	1.475***		1.474***		1.476***		1.474***	
95CI	1.459	1.492	1.459	1.492	1.460	1.493	1.458	1.491
dCD_COPD	0.971***		0.970***		0.970***		0.971***	
95CI	0.965	0.977	0.965	0.977	0.964	0.977	0.965	0.978
dCCI_ModLiver	1.003		1.002		1.003		1.003	
95CI	0.990	1.016	0.990	1.016	0.990	1.016	0.991	1.017
dCCI_PUD	0.969***		0.969***		0.969***		0.969***	
95CI	0.964	0.975	0.964	0.975	0.964	0.975	0.963	0.975
dCCI_PVD	1.226***		1.244***		1.234***		1.248***	
95CI	1.217	1.235	1.217	1.235	1.225	1.243	1.238	1.257
dCCI_SevereLiver	1.015		1.014		1.016		1.014	
95CI	0.999	1.032	0.999	1.032	0.999	1.033	0.998	1.031
_cons	2.233***		2.232***		2.226***		2.234***	
	2.215	2.252	2.215	2.252	2.208	2.245	2.216	2.253
N	1908832		1908832		1908832		1908832	
	10790634.3		10794131.0		10790860.0	1.8	10791675.1	9.0
BIC	10790933.4		10794430.1		10791159.1		10791974.2	

Appendix 5. The incidence rates by age band, at risk population and incident cases

	age band	at risk population	incidence rate per 100,000	annual incident cases
Venous	<40	1,957,020	1.2	23
	40-49	614,941	7	43
	50-59	614,492	19.9	122
	60-69	466,620	37.5	175
	70-79	211,447	66.7	141
	≥80	101,276	91.8	93
	total	3,965,796		598
Arterial	<40	1,957,020	1.1	22
	40-49	614,941	15.6	96
	50-59	614,492	67.5	415
	60-69	466,620	143.4	669
	70-79	211,447	246.4	521
	≥80	101,276	477.9	484
	total	3,965,796		2,206
Diabetic	<40	1,957,020	5.8	114
	40-49	614,941	56.6	348
	50-59	614,492	175.8	1,080
	60-69	466,620	368.6	1,720
	70-79	211,447	758.6	1,604
	≥80	101,276	1791.1	1,814
	total	3,965,796		6,680
Pressure	<40	1,957,020	4.8	94
	40-49	614,941	22	135
	50-59	614,492	74.4	457
	60-69	466,620	236.4	1,103
	70-79	211,447	844.2	1,785
	≥80	101,276	3646.5	3,693
	total	3,965,796		7,268

Appendix 6. EQ-5D scores by type of wound and time from Singapore Wound Registry

Mean (Std. Dev.)	Baseline	month 1	month 3	month 6
Venous	0.57 (0.34) (n=255)	0.68 (0.31) (n=235)	0.74 (0.30) (n=242)	0.74 (0.30) (n=243)
Arterial	0.44 (0.40) (n=354)	0.52 (0.42) (n=311)	0.54 (0.45) (n=303)	0.58 (0.44) (n=291)
Diabetic	0.64 (0.42) (n=139)	0.71 (0.44) (n=128)	0.72 (0.38) (n=129)	0.74 (0.43) (n=126)
Pressure	-0.18 (0.50) (m=51)	0.00 (0.56) (n=43)	0.18 (0.54) (n=38)	0.11 (0.59) (n=40)

Appendix 7 - SAS code for calculating the local EQ-5D index score from EQ-5D-3L

```
*** coding of EQ-5D data: 1 = no problems, 2 = some/moderate problems, 3 = extreme problems;
*** mo = mobility, sc = self-care, ua = usual activity, pd = pain/discomfort, ad = anxiety/depression;

data new; set new;
    if mo=2 then m2=1; else m2=0;
    if mo=3 then m3=1; else m3=0;
    if sc=2 then s2=1 page; else s2=0;
    if sc=3 then s3=1; else s3=0;
    if ua=2 then u2=1; else u2=0;
    if ua=3 then u3=1; else u3=0;
    if pd=2 then p2=1; else p2=0;
    if pd=3 then p3=1; else p3=0;
    if ad=2 then a2=1; else a2=0;
    if ad=3 then a3=1; else a3=0;
    if mo=3 or sc=3 or ua=3 or pd=3 or ad=3 then n3=1; else n3=0;
    EQ_index = 1 - 0.1678*m2 - 0.3040*m3 - 0.1615*s2 - 0.3465*s3 - 0.2555*u2 - 0.3209*u3 - 0.1462*p2 - 0.2291*p3 - 0.1501*a2 - 0.2784*a3 - 0.2905*n3;
    if mo =. or sc=. or ua=. or pd=. or ad =. then EQ_index =. ;
    drop m2 m3 s2 s3 u2 u3 p2 p3 a2 a3 n3; run;
```

Appendix 8. Mean duration of wounds in days, by age band; Mean (Standard Deviation)

Age Band	Venous (n=150)	Diabetic (n=245)	Pressure (n=24)
<40	133 (92)	177 (88)	55 (11)
40-49	129 (109)	325 (550)	86 (24)
50-59	331 (394)	224 (216)	115 (1)
60-69	223 (269)	314 (430)	103 (59)
70-79	307 (438)	256 (305)	105 (115)
≥80	205 (153)	160 (138)	62 (52)

values for Diabetic were used to proxy 'Arterial' wounds

Appendix 9 – usage and costs of outpatient services for patients with chronic wounds

	with consult		without consult	
Total annual costs	mean (sd)	95% CI	mean (sd)	95% CI
Costs of Outpatient with Consult - Arterial	$908.13 ($778.27)	($815.39, $1000.86)	$992.01 ($1241.53)	($844.08, $1139.94)
Costs of Outpatient with Consult - Venous	$685.73 ($575.30)	($603.62, $767.84)	$2381.98 ($2449.41)	($2024.72, $2739.24)
Costs of Outpatient with Consult - Diabetic	$918.06 ($823.40)	($752.11, $1084.01)	$1068.85 ($905.06)	($888.33, $1249.36)
Costs of Outpatient with Consult - Pressure	$702.40 ($525.63)	($368.43, $1036.37)	$1111.98 ($1330.34)	(-$118.38, $2342.34)
Annual visits	mean (sd)	95% CI	mean (sd)	95% CI
No. of Visits of Outpatient with Consult - Arterial	8.249 (6.107)	(7.521, 8.977)	8.454 (6.362)	(7.696, 9.212)
No. of Visits of Outpatient with Consult - Venous	5.874 (5.932)	(5.028, 6.721)	23.639 (18.989)	(20.870, 26.409)
No. of Visits of Outpatient with Consult - Diabetic	8.102 (6.209)	(6.857, 9.347)	14.172 (51.225)	(4.008, 24.336)
No. of Visits of Outpatient with Consult - Pressure	6.5 (4.681)	(3.526, 9.474)	9.714 (10.797)	(-0.271, 19.700)
Cost per Visit	mean (sd)	95% CI	mean (sd)	95% CI
Costs per Visit of Outpatient with Consult - Arterial	$110.44 ($46.69)	($104.88, $116.01)	$117.28 ($87.66)	($106.84, $127.73)
Costs per Visit of Outpatient with Consult - Venous	$133.24 ($81.05)	($121.67, $144.80)	$106.81 ($105.11)	($91.48, $122.14)
Costs per Visit of Outpatient with Consult - Diabetic	$112.00 ($66.26)	($98.64, $125.35)	$114.93 ($39.31)	($107.08, $122.77)
Costs per Visit of Outpatient with Consult - Pressure	$111.04 ($55.19)	($75.97, $146.10)	$124.14 ($38.92)	($88.14, $160.13)

Appendix 10. Cohort of all patients who accessed CHAS, Polyclinic or Emergency departments (ED) 2012 to 2019

	CHAS		Polyclinic		ED	
	No Wound	Any Wound	No Wound	Any Wound	No Wound	Any Wound
Number	1,013,104	3,463	2,600,153	1,441	2,964,540	7,403
Age	49.4	67.9	37	65	36	68
Male	46%	45%	51%	57%	56%	52%
CCI score	2.6	4.0	2.1	4.3	2.0	5.0
Chinese	72%	78%	64%	61%	52%	61%
Malay	14%	10%	12%	13%	10%	17%
Indian	6%	8%	10%	20%	9%	13%
Others	9%	5%	14%	6%	30%	9%
COPD	3%	4%	2%	5%	3%	5%
Diabetes Mellitus	32%	55%	28%	68%	30%	70%
Hypertension	64%	82%	55%	81%	56%	83%
Dyslipidemia	61%	72%	50%	78%	51%	77%
Heart Failure	4%	13%	3%	15%	4%	22%
Renal Failure	10%	24%	7%	26%	8%	39%
Stroke	8%	16%	7%	17%	8%	26%
Dementia	2%	6%	1%	6%	2%	16%
Major Depression	3%	3%	2%	4%	2%	7%
Parkinson	1%	3%	1%	2%	1%	6%
Schizophrenia	2%	2%	2%	3%	2%	3%
Average no. of episodes in 12 months from wound/first visit	3.1	6.2	1.8	2.8	1.4	2.6

Appendix 11. Results of generalised linear model (GLM) with a Poisson link function to estimate excess use of poly-clinic services, CHAS and ED.

Polyclinic	All	No wound	Any wound
Number	2601594	2600153	1441
Mean no. of episodes in 12 months, SD	1.85(1.78)	1.85(1.77)	1.85(1.78)
Median 12 month utilisation, IQR	1 (1-2)	1 (1-2)	2 (1-3)
Coefficient			0.352 (0.288,0.416)
Rate ratio of Episodes, CI			1.423 (1.333,1.513)
Estimated mean Episodes, CI			2.157 (2.13,2.184)
Expected Episodes, CI			3.069 (3.031 ,3.108)
Excess Episodes, CI			0.912 (0.901 ,0.924)
CHAS	All	No wound	Any wound
Number	1016567	1013104	3463
Mean no. of episodes in 12 months, SD	3.13 (3.75)	3.12 (3.73)	6.18 (7.30)
Median 12 month utilisation, IQR	2 (1 - 4)	2 (1 - 4)	4(2 -8)
Coefficient			0.685 (0.669 , 0.701)
Rate ratio of Episodes, CI			1.984 (1.952 , 2.016)
Estimated mean Episodes, CI			3.596 (3.578 , 3.614)
Expected Episodes, CI			7.134 (7.099 , 7.169)
Excess Episodes, CI			3.538 (3.521 , 3.556)
ED	All	No wound	Any wound
Number	2971943	2964540	7403
Mean no. of episodes in 12 months, SD	1.38(1.17)	1.38(1.16)	1.38(1.17)
Median 12 month utilisation, IQR	1 (1-1)	1 (1-1)	2 (1-3)
Coefficient			0.343 (0.319 ,0.367)
Rate ratio of Episodes, CI			1.410 (1.376 ,1.444)
Estimated mean Episodes, CI			1.531 (1.515 ,1.547)
Expected Episodes, CI			2.159 (2.136 ,2.181)
Excess Episodes, CI			0.628 (0.621 ,0.634)

CHEERS 2022 Checklist

Title			
Title	1	Identify the study as an economic evaluation and specify the interventions being compared.	N/A
Abstract			
Abstract	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	P2
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	P3
Methods			
Health economic analysis plan	**4**	**Indicate whether a health economic analysis plan was developed and where available.**	**P4 TO 9**
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	P4
Setting and location	6	Provide relevant contextual information that may influence findings.	P3 TO 4
Comparators	7	Describe the interventions or strategies being compared and why chosen.	N/A
Perspective	8	State the perspective(s) adopted by the study and why chosen.	P4
Time horizon	9	State the time horizon for the study and why appropriate.	P4

(continued)

Discount rate	10	Report the discount rate(s) and reason chosen.	N/A
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	FIGURE 1
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	P4 TO 9
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	P4 TO 9
Measurement and valuation of resources and costs	14	Describe how costs were valued.	P4 TO 9
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	P4
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	P9
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	P4 TO 9
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	P4 TO 9
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	P4 TO 9

(continued)

Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	P9
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	P9
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	P4 TO 9
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	P10 TO 11
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	N/A
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	N/A
Discussion			

(continued)

Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	P11 TP 13
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	P13
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	P13

From: Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health 2022;25. doi:10.1016/j.jval.2021.10.008