Respiratory Morbidity After Childhood Burns: A 10-Year Follow-up Study

Janine M. Duke, PhD,[a] Sean M. Randall, BSc, (Hons),[b] Mark W. Fear, PhD,[a] James H. Boyd, BSc, (Hons),[b] Suzanne Rea, MB, BCh, PhD,[c] Fiona M. Wood, MBBS[c]

abstract

BACKGROUND AND OBJECTIVE: The systemic responses triggered by burns and resuscitative measures may cause pulmonary damage and edema in the acute phase. These effects may occur in the absence of inhalation injury. Currently, there is a paucity of data on the recovery of the respiratory system postburn. This study aimed to examine 10-year hospital service use for respiratory morbidity in children with cutaneous burns and no smoke inhalation injury.

METHODS: A population-based longitudinal study with 10-year follow-up using linked hospital and death from Western Australia for children <5 years when hospitalized for a first burn injury (n = 5290) between 1980 and 2012 and a frequency matched noninjury comparison cohort, randomly selected from Western Australia's birth registrations (n = 27 061). Multivariate negative binomial and Cox proportional hazards regression models were used to generate adjusted incidence rate ratios (IRR) and hazard ratios, respectively.

RESULTS: After adjustment for demographic factors and preexisting health status, the burn cohort had higher rates of admissions for influenza and viral pneumonia (IRR, 1.78; 95% confidence interval [CI], 1.10–2.87), bacterial pneumonia (IRR, 1.34; 95% CI, 1.06–1.70), and other respiratory infections (IRR, 1.65; 95% CI, 1.43–1.90. No significant difference was found for other upper respiratory tract conditions (IRR, 1.10; 95% CI, 0.98–1.23) or chronic lower respiratory diseases (IRR, 0.99; 95% CI, 0.80–1.23) compared with the uninjured cohort.

CONCLUSIONS: These findings demonstrated increased respiratory infection admissions after burns. These outcomes suggest that immune changes triggered by a burn injury may persist in some children for at least 10 years after wound healing.

[a]*Burn Injury Research Unit, School of Surgery, University of Western Australia, Perth, Western Australia, Australia;* [b]*Centre for Data Linkage, Curtin University, Perth, Western Australia, Australia; and* [c]*Burns Service of Western Australia, Fiona Stanley Hospital and Princess Margaret Hospital, Perth, Western Australia, Australia*

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Address correspondence to Janine M. Duke, PhD, Burn Injury Research Unit, School of Surgery, Faculty of Medicine, Dentistry and Health Sciences, M318, 35 Stirling Hwy, Crawley 6009, WA, Australia. E-mail: janine.duke@uwa.edu.au

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WHAT'S KNOWN ON THIS SUBJECT: Systemic responses triggered by burns and resuscitative measures may cause pulmonary damage and edema in the acute phase. These effects may occur in the absence of smoke inhalation. Little is known about the recovery of the respiratory system postburn.

WHAT THIS STUDY ADDS: Children with burns and no inhalation injury have higher hospital admission rates for respiratory infections for at least 10 years postinjury compared with noninjured children. This study provides the first evidence of clinically relevant sequelae of sustained immune suppression after burns.

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Despite a decline in the incidence of burn admissions in developed countries over the past few decades, children remain a vulnerable high-risk group.[1–3] The burden of burn injury is significant in terms of acute care and chronic health effects.[4] Burns initiate a range of acute systemic responses to restore tissue integrity and homeostasis, including activating the immune system, the blood coagulation cascade, and inflammatory pathways.[5,6] Postburn, there is an increased risk of infection,[7,8] primarily because of changes in skin and microflora,[9] innate proinflammatory responses,[10] and loss of adaptive immunity.[11,12] Additionally, pulmonary complications often occur.[13] Although smoke inhalation can cause lung damage,[14] inflammatory responses and resuscitative measures can also cause pulmonary damage in the acute phase in the absence of inhalation injury, with subsequent morbidity of pneumonia and acute respiratory distress syndrome.[15–17] Activation of coagulation and fibrinolysis by the burn can also contribute to pulmonary edema.[18]

Systemic effects of severe burns are well documented and have been shown to persist for up to 3 years[19,20]; however, recent evidence indicates longer-term immune dysfunction after both severe and minor burns.[21] Population-based research has identified long-term postburn cardiovascular[22,23] and musculoskeletal morbidity,[24,25] as well as increased incidence of cancers,[26,27] after severe and minor burns. Although the underlying mechanisms are not clear, postburn morbidity suggests persistent effects of acute inflammatory and immune system responses after wound healing. To date, there is a paucity of data on the recovery of the respiratory system postburn.

Using data of children hospitalized for cutaneous burns without smoke inhalation injury, we investigated respiratory morbidity in terms of hospitalizations and length of stay (LOS) for a 10-year period after burn discharge, controlling for sociodemographic factors and preexisting comorbidities.

METHODS

This study is part of the Western Australian Population-based Burn Injury Project, a retrospective cohort investigation that uses linked health administrative data from the Western Australian Data Linkage System (WADLS).[28] Quality and accuracy audits of data sets are undertaken routinely.[29] The project was approved by the human research ethics committees of the University of Western Australia and the Western Australian Department of Health. The project methodology has been reported previously.[22,30]

WADLS staff provided a de-identified extraction of hospital records for individuals <5 years of age when admitted to a hospital in Western Australia with a first burn between January 1, 1980 and June 30, 2012 by using *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes 940–949 or *International Classification of Diseases, Tenth Revision, Australian Modification* (ICD-10-AM) codes T20–T31. A first (index) burn injury was defined as the first hospital admission with a burn identified as the principal or additional diagnosis. A population-based comparison noninjured cohort was randomly selected from Western Australia's birth registrations; any child with an injury admission during the study period was excluded. The resultant comparison cohort was frequency matched 4:1 on birth year and sex burn cases for each year from 1980 to 2012.

Data from Western Australia's Hospital Morbidity Data System and death register were linked to the burn and noninjured cohorts for the period between 1980 and 2012. Hospital admissions data included principal and additional diagnoses, procedure and external causes, age, sex, indigenous status, dates of admission and discharge, and place of residence. Indices of geographical remoteness[31] and social disadvantage[32] (an index derived from principal components analysis of >40 census variables) were supplied for the burn and noninjured cohorts. The social disadvantage index was classified into quintiles (least to most disadvantage) and geographical remoteness was classified into major cities, inner regional, outer regional, remote, and very remote. The mortality data included date of death.

ICD-9-CM or ICD-10-AM burn disease and external cause codes were used to classify burn characteristics (depth, site, and cause). The percentage of total body surface area (TBSA) burned was derived by ICD codes (0%–9%, 10%–19%, etc) and classified: minor burns (<20% TBSA), severe burns (≥20% TBSA), and unspecified TBSA. The 20% TBSA cut-off was determined by burn surgeons (F.M.W., S.R.) based on differential responsive burn treatments and is the standard classification used in Western Australia Population-based Burn Injury Project studies.[24,33,34] Baseline comorbidity (yes/no) was assessed with a 5-year look-back period[35] using the Charlson comorbidity index[36] and the principal and additional diagnoses data in the hospital morbidity records. Congenital anomaly was identified using principal and additional diagnoses (ICD-10-AM: Q00–G99). Previous admission for any respiratory disease (5-year look-back period) was identified by using principal diagnosis data (ICD-10-AM: J00–J99). A record of ventilation was defined by procedure codes (ICD-10-AM: 92038-00, 92040-00, 92051-00, 13882-00, 13882-01, and 13882-02).

Given the inability to accurately identify children who had sustained smoke inhalation by using ICD-9-CM or ICD-10-AM codes,[37] to investigate the persistence of the systemic effects of burns, members of the pediatric burn cohort who were most likely to have sustained smoke inhalation were excluded. These children included those who had burns to the head and neck and/or respiratory tract and/or had a ventilation code during the index burn admission. To minimize confounding effects caused by smoking uptake during the teenage years, the study was restricted to children <5 years at burn admission with a 10-year follow-up after discharge. Tobacco sales to those <18 years of age is illegal in Australia.[38]

The final discharge date for the index burn admission was used as the starting point for follow-up for both the burn and uninjured cohorts. The total number of principal diagnosis admissions for respiratory diseases after burn discharge and summed hospital LOS for respiratory diseases were used as outcome measures. Categorical and nonparametric continuous variables were compared by using χ^2 and Kruskal–Wallis tests, respectively. A *P* value ≤.05 was considered statistically significant.

Analyses were conducted on combined respiratory diseases (J00–J47, J80–J99 excluding lung diseases due to external agents [J60–J70]), as well as selected ICD-9-CM or ICD-10-AM classified subgroups of respiratory disease (acute upper and lower respiratory tract infections [J00–J06, J20–J22]; influenza and pneumonia [J10–J18]; other diseases of upper respiratory tract [includes allergic and chronic rhinitis, sinusitis; J30–J39]; and chronic lower respiratory diseases [includes bronchitis, asthma; J40–J47]). ICD-9-CM codes were mapped to ICD-10-AM codes.[39]

Crude annual admission rates were calculated for respiratory admissions. Multivariate negative binomial regression was used to estimate adjusted incidence rate ratios (IRR) comparing the burn and uninjured cohorts while adjusting for potential confounders: indigenous status, social disadvantage and geographical remoteness, comorbidity, congenital anomaly, previous record of respiratory disease admission, record of ventilatory support, and year of admission (adjusting for time-related referral and treatment patterns). Age and sex were included in all models given data exclusions applied to different models. Analyses were conducted on subgroups defined by sex and TBSA.

Adjusted hazard ratios (HR) from Cox proportional hazards models were used to examine first-time (incident) hospital use after burn discharge for subgroups of respiratory disease (as specified above); models were adjusted for the covariates listed above. Analyses were conducted on the burn and uninjured cohorts excluding those with a record of previous respiratory admission, with additional exclusion to members of the burn cohort with a record of a principal diagnosis non–burn trauma admission (ICD-9-CM codes 800–999; ICD-10-AM codes S00–T99), to exclude potential confounding related to possible non–burn injury systemic effects.[21,40] The proportional hazard assumption for burn injured versus noninjured was tested by using standard diagnostic tests, and preliminary analyses did not reveal nonproportionality.[41]

Attributable risk percentage was used to estimate the proportion of post–burn incident admissions for respiratory diseases for which burn injury was an attributable component cause. Attributable risk percentage was calculated as 100 × (adjusted HR − 1)/(adjusted HR).[42] Statistical analyses were performed by using Stata, version 12 (Stata Corp, College Station, TX).

RESULTS

Cohort Characteristics

The burn cohort used in the analyses comprised 5290 children <5 years old when admitted with a first burn between 1980 and 2012; these children did not have a coded respiratory tract and/or head/neck burn and were not ventilated during the index burn admission. The noninjured comparison cohort comprised 27 061 children <5 years old. For both cohorts, the median age at study start was 1 year (interquartile range [IQR], 1–2 years), and males represented 59% of each cohort. Refer to Table 1 for other sociodemographic and health characteristics of each cohort.

In the burn cohort, 43% (*n* = 2275) had minor (<20% TBSA) burns, 1% (*n* = 38) had severe (≥20% TBSA) burns, and for 56% (*n* = 2977), the TBSA percentage was unspecified. Comparisons of median (IQR) LOS for the index burn admission suggested unspecified TBSA burns were most likely minor burns (<20% TBSA): 0% to 9% TBSA: 3 days (IQR, 1–8 days); 10% to 19% TBSA: 12 days (IQR, 6–20 days); ≥20% TBSA: 13 days (IQR, 1–38 days); and unspecified TBSA: 5 days (IQR, 2–11 days). Please refer to Table 2 for injury characteristics of the members of the burn cohort included in the analyses.

Admission Rates and Summed LOS

In our study period, there were 2042 hospital admissions after burn discharge with a respiratory condition as the principal or primary diagnosis. Influenza and pneumonia (viral and bacterial) admissions accounted for 14% (*n* = 278), other respiratory infections accounted for 33% (*n* = 670) of admissions, other diseases of the upper respiratory tract accounted for 19% (*n* = 393) of admissions, and chronic lower respiratory diseases accounted for 26% (*n* = 521) of admissions. The remaining 180 (9%) postburn respiratory admissions were for other conditions. In total, 5840 days were spent in the hospital with a respiratory diagnosis after burn discharge. The median LOS for the burn cohort was 2 days (IQR, 1–3 days) and was 1 day (IQR, 1–2 days) for the uninjured cohort. Refer to Table 3 for classification of respiratory admissions.

Unadjusted annual rates of admissions for combined and selected subgroups of respiratory diseases are shown in Figs 1 and 2, respectively. The burn cohort had higher rates of respiratory admissions over the study period, with this difference most prominent during the first years after burn discharge. After adjusting for sociodemographic and preexisting health factors, the burn cohort had 1.24-fold greater (IRR, 1.24; 95% confidence interval [CI], 1.13–1.36) hospital admissions for respiratory disease and had a 1.24 times greater hospital LOS (IRR, 1.24; 95% CI, 1.07–1.44).

After adjustment, the burn cohort had higher rates of admissions for influenza and pneumonia (IRR, 1.40; 95% CI, 1.13–1.74), but no significant difference in total hospital LOS (IRR, 1.11; 95% CI, 0.72–1.71) when compared with the uninjured cohort. Additional subgroup analyses of admissions for influenza and viral pneumonia (combined) (IRR, 1.78; 95% CI, 1.10–2.87), bacterial pneumonia (IRR, 1.34; 95% CI, 1.06–1.70), and other respiratory infections (IRR, 1.65; 95% CI, 1.43–1.90) showed significantly elevated adjusted admission rates for the burn cohort when compared with the uninjured cohort. No significant differences in admission rates for other upper respiratory tract conditions (IRR, 1.10; 95% CI, 0.98–1.23) or chronic lower respiratory diseases (IRR, 0.99; 95% CI, 0.80–1.23) were found.

Temporal trends in admissions for respiratory conditions identified less admissions in the earlier years of the study period for both the burn and uninjured cohorts when controlling for differing lengths of follow-up: admissions increased annually on average by 11% for influenza and viral pneumonia (IRR, 1.11; 95% CI, 1.08–1.13); 36% for bacterial pneumonia (IRR, 1.36; 95% CI, 1.08–1.71); and 5% for other respiratory infections (IRR, 1.05; 95% CI, 1.04–1.06).

Summed hospital LOS was greater in the burn cohort for other respiratory infections (a category that excludes influenza and pneumonia) (IRR, 1.86; 95% CI, 1.44–2.39) as well as other upper respiratory tract conditions (IRR, 1.22; 95% CI, 1.03–1.45); however, no significant difference was found for chronic respiratory conditions (IRR, 0.97; 95% CI, 0.75–1.25) compared with the uninjured cohort. Subcohort analyses by burn severity showed significantly elevated rates of combined respiratory diseases for minor burns and burns of unspecified TBSA; however, the elevated rate for severe burns was not statistically significant (refer to Table 4).

TABLE 1 Baseline Demographic and Preexisting Health Status Factors for the Burn Injury and Noninjury Cohort

Characteristics	No Injury, *N* (%)	Burn Injury, *N* (%)	*P*
Total	27 061	5290	
Demographic			
Indigenous			
Yes	1440 (5.3)	1058 (20.0)	<.001
Social disadvantage quintiles[a]			
Quintile 1 (most disadvantaged)	3517 (13.1)	1206 (23.1)	<.001
Quintile 2	6938 (25.8)	1753 (33.5)	
Quintile 3	4869 (18.13)	1029 (19.7)	
Quintile 4	4455 (16.5)	641 (12.2)	
Quintile 5 (least disadvantaged)	7158 T(26.6)	599 (11.5)	
Remoteness[b]			
Major city	17 881 (66.6)	2844 (54.3)	<.001
Inner regional	28007 (10.4)	527 (10.1)	
Outer regional	3250 (12.1)	775 (14.8)	
Remote	1842 (6.9)	584 (11.1)	
Very remote	1095 (4.1)	511 (9.8)	
Health status			
Any comorbidity (CCI ≥1)[c]	271 (1.0)	87 (1.6)	<.001
Previous admission for respiratory disease[d]	2200 (8.1)	897 (17.0)	<.001
Record of ventilation support before first postburn respiratory admission[e]	438 (1.6)	114 (2.2)	.022

[a] Socioeconomic Indices for Areas socioeconomic disadvantage quintiles; missing values: 1.2% burn, 0.5% no injury.
[b] Accessibility Remoteness Index of Australia remoteness classification; missing values: 0.9% burn, 0.7% no injury.
[c] Comorbidity based on Charlson Comorbidity Index (CCI) with 5-y look-back period.
[d] Principal diagnosis admission for respiratory disease with 5-y look-back period.
[e] Using procedure codes with 5-y look-back period.

Survival Analysis for First Respiratory Admissions After Burn

To investigate whether those with burns experienced increased rates of new or incident respiratory admissions, analyses were performed on the cohorts that excluded those with previous records of ventilation support and/or respiratory hospital admission and, in addition, excluded those in the burn cohort with a record of a principal (primary) diagnosis non–burn injury admission. This resultant burn cohort consisted of 3737 children, of which 579 had an incident respiratory admission after burn discharge. The resultant uninjured cohort contained 24 570 children, of which 3116 had an incident respiratory admission.

Results of multivariate Cox regression modeling showed an increased rate of first-time respiratory disease admissions over the 10-year study

TABLE 2 Injury Characteristics of Members of the Burn Cohort Included in the Analyses

Characteristics	*N* (%)[a]
Total	5290 (100)
Burn severity[b]	
Severe	38 (1)
Minor	2275 (43)
Unspecified	2977 (56)
Burn depth[c]	
Full thickness	377 (7)
Partial thickness	2319 (44)
Erythema	563 (11)
Unspecified	2015 (38)
Anatomic burn site[c]	
Trunk	1380 (26)
Upper limbs	4351 (82)
Wrist and hands	1412 (27)
Lower limbs/feet	1952 (49)
Eye	163 (3)
Internal organs	49 (1)
Multiple regions	464 (9)
Unspecified	184 (3)
External cause	
Flame	1271 (24)
Scalds	3013 (57)
Contact	1142 (22)
Electrical	70 (1)
Chemical	139 (3)
Explosions	5 (0.1)
Radiation	17 (0.3)
Unspecified	105 (2)
Other non–burn injury admission[d]	1486 (28)

[a] Excludes those with burns to head, neck, respiratory tract, and/or record of ventilation support during the index admission.
[b] Severe: ≥20% TBSA burned; minor: <20% TBSA burned.
[c] Some patients had multiple codes for burn site, depth, and cause.
[d] Principal diagnosis record of injury pre- and postburn admission (ICD-9-CM: 800–999; ICD-10-AM: S00–T98) in 10-y study period.

TABLE 3 Number of Admissions (%) for Respiratory Diseases Classified by ICD (ICD-9-CM or ICD-10-AM) Subchapter Codes in the Burn and Uninjured Cohorts

Respiratory Subconditions	Noninjury No. of Admissions (%)	Burn Injury No. of Admissions (%)
Total	2323 (100)	2042 (100)
Acute upper respiratory tract infections	525 (23)	497 (24)
Influenza and pneumonia	270 (12)	278 (14)
Influenza and viral pneumonia	52 (2)	28 (1)
Bacterial pneumonia	218 (9)	250 (12)
Other acute lower respiratory tract infections	221 (10)	173 (8)
Other diseases of the upper respiratory tract	559 (24)	393 (19)
Chronic lower respiratory diseases	581 (25)	521 (26)
Asthma	559 (24)	495 (24)
Suppurative and necrotic conditions of the lower respiratory tract	1 (0)	2 (0)
Intraoperative and postprocedural complications and disorders not elsewhere classified	10 (0)	0
Other diseases of the respiratory system	156 (7)	178 (9)

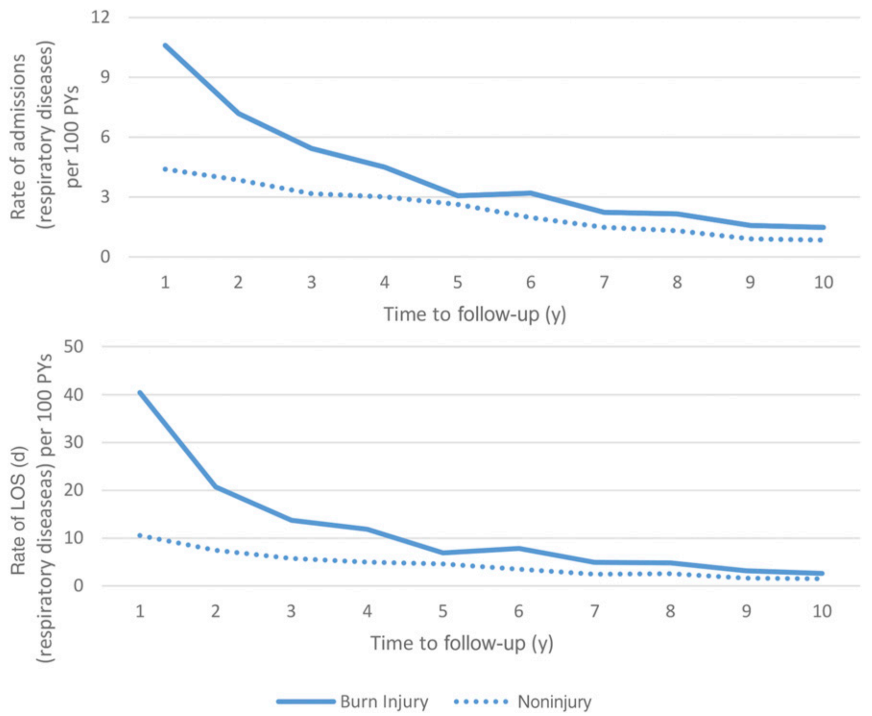

FIGURE 1
Unadjusted rates of hospital admissions and cumulative LOS (per 100 person years [PYs]) for respiratory conditions for burn injury versus noninjury cohorts.

period in the burn cohort (HR, 1.18; 95% CI, 1.08–1.28). Examination by TBSA severity showed elevated rates for each group; however, the result was significant for those with burns of unspecified TBSA only compared with uninjured controls (HR, 1.21; 95% CI 1.08–1.35 [unspecified TBSA]; HR, 1.20; 95% CI, 0.45–3.21 [≥20% TBSA]; and HR, 1.07; 95% CI, 0.93–1.25 [<20% TBSA]). Both males (HR, 1.14; 95% CI, 1.02–1.27) and females (HR, 1.25; 95% CI, 1.09–1.44) had increased rates of first respiratory admissions.

The burn cohort had 74 first admissions for influenza and pneumonia, 211 first admissions for other respiratory infections, 244 first admissions for upper respiratory tract diseases, and 111 first admissions for chronic lower respiratory disease. The uninjured cohort had 305 first admissions for influenza and pneumonia, 813 first admissions for other respiratory conditions, 1583 first admissions for upper respiratory tract disease, and 729 first admissions for chronic lower respiratory conditions. Results of Cox regressions of specific respiratory subconditions are shown in Table 5. The number of admissions were insuffcent to support subgroup analyses of incident admissions for influenza and viral pneumonia and bacterial pneumonia. The total number of first postburn admissions for respiratory

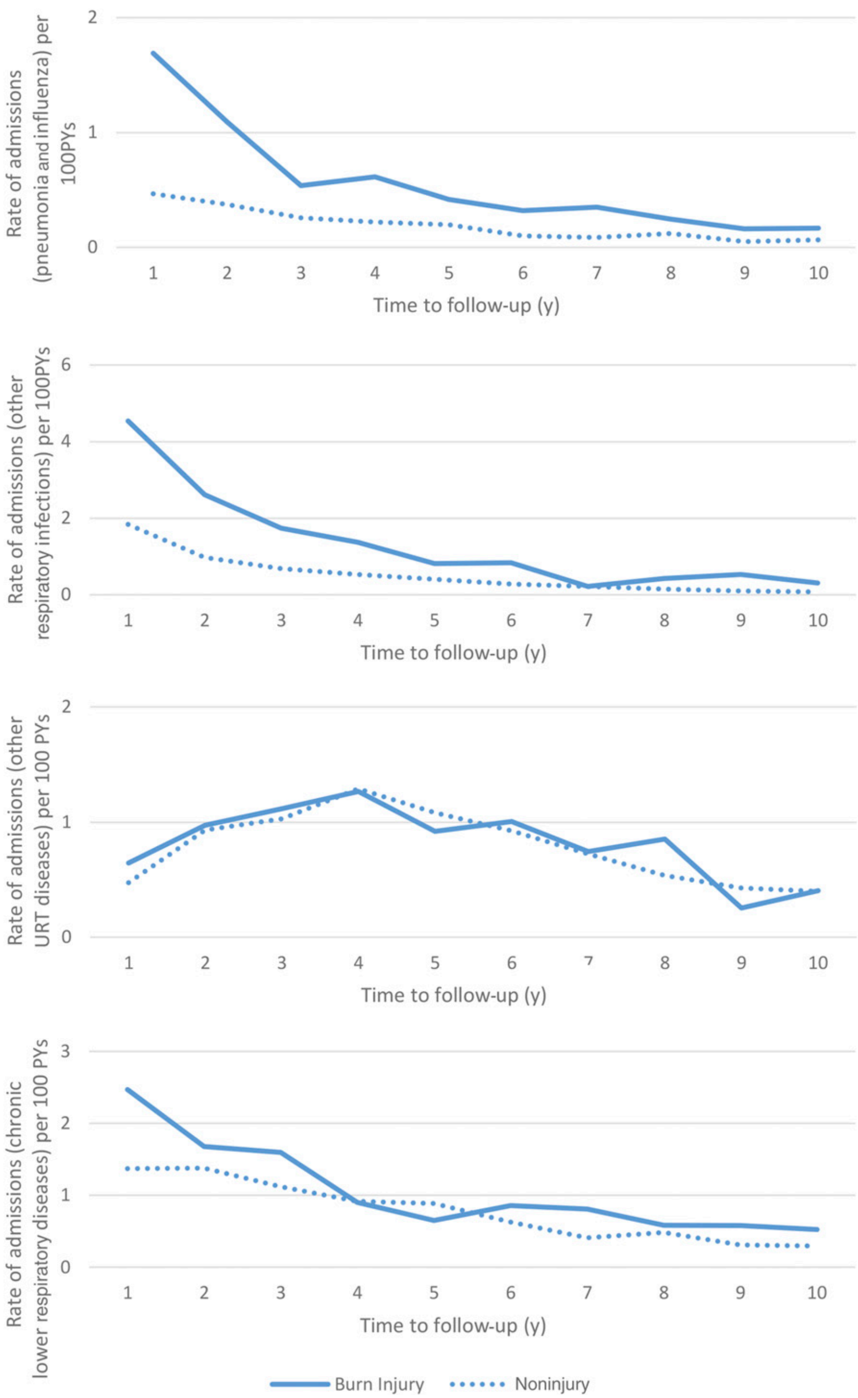

FIGURE 2
Unadjusted rates (per 100 person years [PYs]) of hospital admissions for respiratory subconditions for burn injury versus noninjury cohorts. URT, upper respiratory tract.

conditions that could be attributed to burns was 86.

DISCUSSION

This study estimated postburn respiratory morbidity in terms of hospital admissions for a population-based cohort of burn patients <5 years of age at the time of injury. Adjusted IRR analyses provided an overall picture of combined incident and prevalent admissions for respiratory conditions and found that the burn cohort experienced 1.24 times the rate of readmissions for respiratory diseases after burn discharge than the comparison uninjured cohort. Likewise, there was a 1.18-fold greater rate of incident admissions in the burn cohort when compared with the uninjured cohort.

Overall, the major driver of postburn respiratory admission rates was respiratory infections, with the burn cohort experiencing significantly greater admission rates for pneumonia (viral) and influenza, bacterial pneumonia, and other respiratory infections than the uninjured cohort.

Elevated admission rates for respiratory infections may possibly be related to persistence of immune dysfunction and inflammatory responses initiated by the burn.[43–45] Recent evidence demonstrates long-term changes in the immune response postburn, and these immune changes may have underlying roles in observed respiratory morbidity.[21] Impaired antimicrobial peptide production and systemic changes to epithelial function and integrity, at least in the acute postburn phase, may significantly increase the risk of respiratory infection after burns.[46,47] This long-term immune dysfunction also likely underpins the absence of any increase in chronic lower respiratory disease, which predominantly results in hospital presentations due to excessive inflammation. Together, the data suggest long-term immunosuppressive effects of burns. The hospital morbidity data do not include immunization status; however, the Australian government supports a national immunization program provided to all children through primary care, including Aboriginal Medical Services.

Record linkage provides an innovative and cost-effective opportunity to undertake long-term, population-level research that would otherwise not be possible. It provides a valuable method to study patient outcomes

TABLE 4 Adjusted IRRs and 95% CIs for Recurrent Admissions for Respiratory Subconditions by Burn Severity Versus No Injury

Respiratory Subcondition	Severe Burns ≥20% TBSA IRR (95% CI)[a]	Minor Burns <20% TBSA IRR (95% CI)[a]	Unspecified TBSA Burns IRR (95% CI)[a]
All	1.32 (0.61–2.86)	1.16 (1.01–1.32)	1.28 (1.13–1.44)
Influenza and pneumonia	No admissions	1.25 (0.92–1.70)	1.57 (1.19–2.06)
Other respiratory tract infections	2.32 (0.74–7.29)	1.24 (0.98–1.57)	1.83 (1.55–2.18)
Other upper respiratory conditions	No admissions	1.11 (0.93–1.33)	1.09 (0.95–1.26)
Chronic lower respiratory diseases	1.64 (0.48–5.63)	1.04 (0.77–1.40)	0.98 (0.74–1.31)

[a] All models were adjusted for sociodemographic (age at index, sex, indigenous status, social disadvantage, remoteness), index year, and health factors (comorbidity, congenital anomaly, previous respiratory disease, ventilation before respiratory admission).

TABLE 5 Results of Survival Analysis First or Incident Postburn Admissions for Respiratory Subconditions, Burn Cohort Versus No Injury Cohort

	HR (95% CI)	Attributable Risk %	No. of Admissions Attributable to Burn Injury
Influenza and pneumonia	1.36 (1.07–1.72)	26.5	20
Other respiratory infections	1.46 (1.26–1.69)	31.5	66
Other upper respiratory tract disease	1.07 (0.95–1.22)	n.s.	0
Chronic lower respiratory disease	0.97 (0.80–1.17)	n.s.	0
Total			86

All models were adjusted for sociodemographic (age at index, sex, indigenous status, social disadvantage, remoteness), index year, and health factors (comorbidity, congenital anomaly, previous respiratory disease, ventilation before respiratory admission). n.s., not significant.

in cases where prospective clinical studies face significant logistical hurdles. This allows the development of refined hypotheses that are more amenable to effective longitudinal testing in patients. The index of social disadvantage included in the models is highly correlated with lifestyle risk factors (eg, nutrition, smoking, alcohol, and physical activity),[48] and all models were adjusted for known confounding factors (health status, social disadvantage, access to services, and indigenous status). The year of inclusion in the study and length of follow-up were included in all models, allowing for adjustment for time-related referral and treatment patterns affecting both burn and uninjured cohorts.

Morbidity was measured in terms of respiratory admissions, which characteristically represent more serious conditions, and results may underestimate postburn respiratory morbidity in the community managed by primary care physicians. The elevated admission rates for those with severe burns in our study did not reach statistical significance, most likely reflecting the small number of severe burns. It is also possible that high levels of treatment and ongoing care associated with severe burns[49,50] lead to earlier diagnosis and management of pathologies via primary care, resulting in reduced admissions. The ICD (ICD-9-CM or ICD-10-AM) TBSA classification may have limited complete understanding of the effects of severe burns. A significant proportion of the study sample had burns of unspecified TBSA that were most likely minor burns. Increased admission rates were found for both minor burns and burns of unspecified TBSA. This is an interesting and important finding because the majority of burn admissions in Western Australia and other developed countries are for burns of <20% TBSA.[3,51] Additional research that links prescription and hospital data may provide a clearer picture of postburn respiratory pathologies and treatment pathways. Our findings are expected to be generalizable to other countries of similar demographics and health care systems.

CONCLUSIONS

After controlling for sociodemographic factors and preexisting comorbidities, increased hospital service use for respiratory infections was identified for children with burns when compared with the noninjured pediatric cohort. Our results identify the need for prolonged clinical care of pediatric burn patients and regular health assessments via primary care after discharge. Burns affect multiple systems of the body and the pathophysiological mechanisms are most likely wide-ranging. Future research to identify children at greatest risk and how burns trigger different mechanisms is important to inform early intervention, prevent long-term pathologies, and optimize the health of pediatric burn patients.

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ABBREVIATIONS

CI: confidence interval
HR: hazard ratio
ICD-9-CM: *International Classification of Diseases, Ninth Revision, Clinical Modification*
ICD-10-AM: *International Classification of Diseases, Tenth Revision, Australian Modification*
IQR: interquartile range
IRR: incidence rate ratio
LOS: length of stay
TBSA: total body surface area
WADLS: Western Australian Data Linkage System

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REFERENCES

1. Akerlund E, Huss FRM, Sjöberg F. Burns in Sweden: an analysis of 24,538 cases during the period 1987-2004. *Burns*. 2007;33(1):31–36
2. Spinks A, Wasiak J, Cleland H, Beben N, Macpherson AK. Ten-year epidemiological study of pediatric burns in Canada. *J Burn Care Res*. 2008;29(3):482–488
3. Duke J, Wood F, Semmens J, et al. A 26-year population-based study of burn injury hospital admissions in Western Australia. *J Burn Care Res*. 2011;32(3):379–386
4. Peck MD. Epidemiology of burns throughout the world. Part I: Distribution and risk factors. *Burns*. 2011;37(7):1087–1100
5. Eming SA, Martin P, Tomic-Canic M. Wound repair and regeneration: mechanisms, signaling, and translation. *Sci Transl Med*. 2014;6(265):265sr6
6. Gurtner GC, Werner S, Barrandon Y, Longaker MT. Wound repair and regeneration. *Nature*. 2008;453(7193):314–321
7. Sharma BR. Infection in patients with severe burns: causes and prevention thereof. *Infect Dis Clin North Am*. 2007;21(3):745–759, ix
8. Tran NK, Wisner DH, Albertson TE, et al. Multiplex polymerase chain reaction pathogen detection in patients with suspected septicemia after trauma, emergency, and burn surgery. *Surgery*. 2012;151(3):456–463
9. Barret JP, Herndon DN. Effects of burn wound excision on bacterial colonization and invasion. *Plas Reconstr Surg*. 2003;111(2):744–750
10. Hoover L, Bochicchio GV, Napolitano LM, et al. Systemic inflammatory response syndrome and nosocomial infection in trauma. *J Trauma*. 2006;61(2):310–316, discussion 316–317
11. Ni Choileain N, Redmond HP. Cell response to surgery. *Arch Surg*. 2006;141(11):1132–1140
12. Ni Choileain N, Redmond HP. The immunological consequences of injury. *Surgeon*. 2006;4(1):23–31
13. Herndon DN, Traber DL. Pulmonary circulation and burns and trauma. *J Trauma*. 1990;30(12 suppl):S41–S44
14. Traber DL, Hawkins HK, Enkhbaatar P, et al. The role of the bronchial circulation in the acute lung injury resulting from burn and smoke inhalation. *Pulm Pharmacol Ther*. 2007;20(2):163–166
15. Donnelly TJ, Meade P, Jagels M, et al. Cytokine, complement, and endotoxin profiles associated with the development of the adult respiratory distress syndrome after severe injury. *Crit Care Med*. 1994;22(5):768–776
16. Gross MA, Viders DE, Brown JM, et al. Local skin burn causes systemic (lung and kidney) endothelial cell injury reflected by increased circulating and decreased tissue factor VIII-related antigen. *Surgery*. 1989;106(2):310–316, discussion 316–317
17. Rue LW III, Cioffi WG, Mason AD Jr, McManus WF, Pruitt BA Jr. The risk of pneumonia in thermally injured patients requiring ventilatory support. *J Burn Care Rehabil*. 1995;16(3 pt 1):262–268
18. Kowal-Vern A, Walenga JM, McGill V, Gamelli RL. The impact of antithrombin (H) concentrate infusions on pulmonary function in the acute phase of thermal injury. *Burns*. 2001;27(1):52–60
19. Jeschke MG, Chinkes DL, Finnerty CC, et al. Pathophysiologic response to severe burn injury. *Ann Surg*. 2008;248(3):387–401
20. Jeschke MG, Gauglitz GG, Kulp GA, et al. Long-term persistance of the pathophysiologic response to severe burn injury. *PLoS One*. 2011;6(7):e21245
21. Valvis SM, Waithman J, Wood FM, Fear MW, Fear VS. The immune response to skin trauma is dependent on the etiology of injury in a mouse model of burn and excision. *J Invest Dermatol*. 2015;135(8):2119–2128
22. Duke JM, Boyd JH, Randall SM, Wood FM. Long term mortality in a population-based cohort of adolescents, and young and middle-aged adults with burn injury in Western Australia: a 33-year study. *Accid Anal Prev*. 2015;85:118–124
23. Duke JM, Randall SM, Fear MW, Boyd JH, Rea S, Wood FM. Understanding the long-term impacts of burn on the cardiovascular system. *Burns*. 2016;42(2):366–374
24. Duke JM, Randall SM, Fear MW, Boyd JH, Rea S, Wood FM. Increased admissions for musculoskeletal diseases after burns sustained during childhood and adolescence. *Burns*. 2015;41(8):1674–1682
25. Randall SM, Fear MW, Wood FM, Rea S, Boyd JH, Duke JM. Long-term musculoskeletal morbidity after adult burn injury: a population-based cohort study. *BMJ Open*. 2015;5(9):e009395
26. Duke J, Rea S, Semmens J, Edgar DW, Wood F. Burn and cancer risk: a state-wide longitudinal analysis. *Burns*. 2012;38(3):340–347
27. Duke JM, Bauer J, Fear MW, Rea S, Wood FM, Boyd J. Burn injury, gender and cancer risk: population-based cohort study using data from Scotland and Western Australia. *BMJ Open*. 2014;4(1):e003845
28. Holman CDJ, Bass AJ, Rouse IL, Hobbs MST. Population-based linkage of health records in Western Australia: development of a health services research linked database. *Aust N Z J Public Health*. 1999;23(5):453–459
29. Department of Health, Western Australia. Clinical Information Audit

Program, Hospital Activity Report. Available at: www.health.wa.gov.au/circularsnew/pdfs/12503.pdf.

30. Duke JM, Boyd JH, Rea S, Randall SM, Wood FM. Long-term mortality among older adults with burn injury: a population-based study in Australia. *Bull World Health Organ*. 2015;93(6):400–406

31. Glover J, Tennant S. *Remote Areas Statistical Geography in Australia: Notes on the Accessibility/Remoteness Index for Australia (Aria+ Version)*. Working Papers Series No. 9. Adelaide, SA, Australia: Public Health Information Development Unit, University of Adelaide; 2003

32. Trewin D. *Socio-economic Indexes for Areas (Information Paper, Census of Population and Housing)*. Canberra, ACT, Australia: Australian Bureau of Statistics; 2003

33. Duke JM, Randall SM, Fear MW, Boyd JH, Rea S, Wood FM. Long-term effects of pediatric burns on the circulatory system. *Pediatrics*. 2015;136(5). Available at: www.pediatrics.org/cgi/content/full/136/5/e1323

34. Duke JM, Rea S, Boyd JH, Randall SM, Wood FM. Mortality after burn injury in children: a 33-year population-based study. *Pediatrics*. 2015;135(4). Available at: www.pediatrics.org/cgi/content/full/135/4/e903

35. Preen DB, Holman CDAJ, Spilsbury K, Semmens JB, Brameld KJ. Length of comorbidity lookback period affected regression model performance of administrative health data. *J Clin Epidemiol*. 2006;59(9):940–946

36. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383

37. Kagan RJ. Documentation and coding of inhalation injury. *J Burn Care Res*. 2009;30(1):204–205

38. Australian Government Department of Health. A national approach for reducing access to tobacco in Australia by young people under 18 years of age. Available at: www.health.gov.au/internet/main/publishing.nsf/Content/tobacco-res-access. Accessed December 3, 2015

39. National Centre for Classification in Health. Australian Consortium for Classification Development. Mapping tables (ICD-10-AM/ACHI) backward and forward maps. Available at: www.accd.net.au/Downloads.aspx. Accessed July 27, 2015

40. Cameron CM, Purdie DM, Kliewer EV, McClure RJ. Ten-year health service use outcomes in a population-based cohort of 21,000 injured adults: the Manitoba injury outcome study. *Bull World Health Organ*. 2006;84(10):802–810

41. Hosmer DW, Lemeshow S. *Applied Survival Analysis: Regression Modeling of Time to Event Data*. New York, NY: Wiley; 1999

42. Gordis L. *Epidemiology*. 2nd ed. Philadelphia, PA: W.B. Saunders Company; 2000

43. D'Arpa N, Accardo-Palumbo A, Amato G, et al. Circulating dendritic cells following burn. *Burns*. 2009;35(4):513–518

44. O'Sullivan ST, O'Connor TP. Immunosuppression following thermal injury: the pathogenesis of immunodysfunction. *Br J Plast Surg*. 1997;50(8):615–623

45. Patenaude J, D'Elia M, Hamelin C, Bernier J. Selective effect of burn injury on splenic CD11c(+) dendritic cells and CD8alpha(+)CD4(-)CD11c(+) dendritic cell subsets. *Cell Mol Life Sci*. 2010;67(8):1315–1329

46. Cox RA, Jacob S, Andersen CR, et al. Integrity of airway epithelium in pediatric burn autopsies: association with age and extent of burn injury. *Burns*. 2015;41(7):1435–1441

47. Plichta JK, Droho S, Curtis BJ, Patel P, Gamelli RL, Radek KA. Local burn injury impairs epithelial permeability and antimicrobial peptide barrier function in distal unburned skin. *Crit Care Med*. 2014;42(6):e420–e431

48. Taylor AW, Dal Grande E, Wu J, Shi Z, Campostrini S. Ten-year trends in major lifestyle risk factors using an ongoing population surveillance system in Australia. *Popul Health Metr*. 2014;12(1):31

49. Armour AD, Billmire DA. Pediatric thermal injury: acute care and reconstruction update. *Plast Reconstr Surg*. 2009;124(1 suppl):117e–127e

50. Prasad JK, Bowden ML, Thomson PD. A review of the reconstructive surgery needs of 3167 survivors of burn injury. *Burns*. 1991;17(4):302–305

51. Kramer CB, Rivara FP, Klein MB. Variations in U.S. pediatric burn injury hospitalizations using the national burn repository data. *J Burn Care Res*. 2010;31(5):734–739

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Janine M. Duke, Sean M. Randall, Mark W. Fear, James H. Boyd, Suzanne Rea and Fiona M. Wood

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