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# Burn leads to long-term elevated admissions to hospital for gastrointestinal disease in a West Australian population based study

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ABSTRACT

*Background:* While the most obvious impact of burn is on the skin, systemic responses also occur after burn, including intestinal inflammation. The objective of this study was to assess if burns are associated with increased long-term admissions for gastrointestinal diseases.
*Methods:* A population-based longitudinal study using linked hospital morbidity and death data from Western Australia was undertaken of adults aged at least 15 years when hospitalized for a first burn (n=20,561) in 1980-2012. A frequency matched non-injury comparison cohort was randomly selected from Western Australia's birth registrations and electoral roll (n=80,960). Crude admission rates and summed days in hospital for digestive diseases were calculated. Negative binomial and Cox proportional hazards regression modeling were used to generate incidence rate ratios (IRR) and hazard ratios (HR), respectively.
*Results:* After adjustment for demographic factors and pre-existing health status, the burn cohort had 1.54 times (95% confidence interval (CI): 1.47–1.62) as many admissions and almost three times the number of days in hospital with a digestive system diagnosis (IRR, 95% CI: 2.90, 2.60–3.25) than the uninjured cohort. Significantly elevated adjusted post-burn incident rates were identified, with the risk decreasing with increasing time: in the first month (HR, 95% CI: 3.02, 1.89–4.82), from one month to five years (HR, 95% CI: 1.42, 1.31–1.54), and from five to twenty years after burn (HR, 95% CI: 1.13, 1.06–1.20).
*Conclusions:* Findings of increased hospital admission rates and prolonged length of hospital stay for gastrointestinal diseases in the burn cohort provide evidence to support that burns have effects that persist long after the initial injury.



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## 1. Introduction

While burn primarily affects the skin, the initial injury triggers a range of systemic responses, including inflammatory, immune and endocrine responses and hypermetabolism [1]. Although the injury presents a major insult to the body, evidence suggests that during the post-burn period the gastrointestinal tract plays a pivotal role in driving organ failure and immune dysfunction, and may be the primary source of inflammatory mediators found in systemic circulation [2–4]. Animal studies of burn have identified elevated cytokines, chemokines and neutrophils with correlations of these elevated inflammatory mediators with tissue damage of the gut [5–7]. The human colon provides a barrier against gut bacteria under healthy conditions; however, this barrier becomes disrupted after burn [8,9]. While the exact role in not known, the compromized gut barrier may play a key role in the processes that cause both organ and immune dysfunction. Evidence suggests that subsequent immune dysfunction may not be entirely the result of gut permeability changes and bacterial translocation, but the cytokine milieu induced by the interaction between the immune system with these bacteria that leads to the production of mediators that can cause organ and immune dysfunction [10].

To date, limited data have been available to examine the long-term health impacts of burns on the gastrointestinal tract. Population-based linked health administrative data provide a time and cost-effective resource to examine long-term morbidity trends expressed in the number of hospital admissions and length of stay for specific disease classifications [11]. The aim of this study was to use population-based linked health administrative data to determine if persons aged 15 years and older when hospitalized for a burn have increased long-term hospital use for digestive system diseases, after adjustment for socio-demographic factors and pre-existing comorbidities.

## 2. Methods

Our study formed part of the Western Australian Population-based Burn Injury Project– a retrospective cohort investigation – that uses administrative health data from the Western Australian Data Linkage System (WADLS), a validated linkage system that links several core datasets for the entire population of Western Australia [12]. The project was approved by the human research ethics committees of the University of Western Australia and the Western Australian Department of Health. Cohort selection and analytical methods have been reported previously [13]. Analyses were performed on a de-identified extraction of hospital morbidity records for all individuals who were aged at least 15 years when admitted to a hospital in Western Australia with a first burn between 1 January, 1980 and 30 June, 2012.

A first (index) burn was defined as the first hospital admission in a patient's medical record in which a burn was given as the principal diagnosis or an additional diagnosis, defined by International Classification of Diseases and Related Health (ICD) 9 CM 940–949 or ICD10 AM T20–T31. A population-based comparison cohort was randomly selected from Western Australia's birth registrations and electoral roll. Any person with an injury hospitalization during the study period was excluded from this cohort by WADLS staff. The resultant comparison cohort was frequency matched (4:1) on birth year and sex of each burn case 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 non-injured cohorts for the period 1980–2012.

Hospital admissions data included principal and additional diagnoses, age at admission, sex, and Aboriginal status, date of admission, date of discharge. Data supplied for the burn and non-injured cohorts also included place of residence and indices of geographical remoteness [14] and social disadvantage [15] derived from national census data. Geographical remoteness was classified into five categories: major cities, inner regional, outer regional, remote and very remote. The social disadvantage index was reclassified into quintiles (most to least disadvantaged). The mortality data included date of death and cause of death.

ICD9 940–949 and ICD10 T20–T31 codes were used to classify anatomical site, depth (full thickness, partial thickness, erythema or first degree, unspecified depth) and the percentage total body surface area (TBSA) burned (minor $<20\%$ TBSA; severe $\geq 20\%$ TBSA; unspecified TBSA). Smoke inhalation is not reported in this study since ICD coding for smoke is highly unreliable due to variable diagnosis, recording and coding [16].

Comorbidity (baseline) was assessed, with a five-year look-back period, using the Charlson comorbidity index (CCI) and the principal and additional diagnoses included in the hospital morbidity records (0 CCI=0; 1 CCI$\geq$1) [17,18]. A record of an existing congenital anomaly was identified using principal and additional diagnosis data (ICD9 740–759; ICD10 Q00–G99). The final discharge date for the index burn admission was used as the study start for follow-up for the burn cases and the respective frequency matched non-injury controls.

Categorical and non-parametric continuous variables were compared using $\chi^2$ and Kruskal Wallis tests respectively. A P-value of 0.05 or lower was considered statistically significant. The total number of admissions and the summed days in hospital for a principal diagnosis digestive system disease classified by ICD codes (ICD10: K20–K87) were used as outcome measures. ICD-10 codes were mapped to ICD-9 codes. The hospitalization of the first burn was not included in these outcomes. Crude yearly admission rates were calculated for these variables. Adjusted rate ratios (incidence rate ratio (IRR) and 95% confidence interval (CI)) between the burn and no injury cohorts and the outcome measures were generated using negative binomial regression. To adjust for the unequal distribution of factors between the burn and uninjured cohorts, socio-demographic factors (gender, Aboriginal status, 5-year age group, social disadvantage, remoteness of residence), health status information (comorbidity at baseline, previous admission for digestive disease, congenital abnormality) and year of study entry were included in all models to adjust for potential confounding effects. Additional analyses were carried out on data that excluded those with ICD coded burns to the gastrointestinal tract.

Survival analyses of incident hospital use for combined digestive system disease and sub-groups (i.e., ICD sub-chapter