

# Under-nutrition Affects Time to Recurrence of Gastroenteritis among Aboriginal and Non-Aboriginal Children

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## ABSTRACT

This study investigated whether under-nutrition affected time to hospitalization for recurrence of gastroenteritis in Australian children. Linked hospitalization records of all infants, born in 1995 and 1996 in Western Australia, who were admitted for gastroenteritis during their first year of life (n=1,001), were retrieved. A survival frailty model was used for determining the factors influencing the recurrent times over the subsequent seven years. Aboriginality and under-nutrition were significantly associated with an increased risk of recurrence (hazard ratios of 2.59 and 1.28). Hospitalizations due to gastroenteritis were common among Aboriginal children who had a higher mean re-admission rate and much shorter intervals between re-admissions than other patients. The proportion of patients with recurrence was also significantly higher for Aboriginals (38.5%) than for other patients (14.2%). Gastroenteritis remains a serious problem in Aboriginal children. This presents a complex challenge to be addressed with public-health principles, political determination and commitment, and adequate resources.

**Key words:** Gastroenteritis; Diarrhoea, Infantile; Aborigines; Infant nutrition disorders; Retrospective studies; Cohort studies; Australia

## INTRODUCTION

Gastroenteritis is common worldwide even in industrialized countries, such as the United States where approximately 200 million episodes of acute diarrhoea occur each year (1). It is much more serious and life-threatening among infants and young children in tropical and developing countries, often in association with malnutrition (2-4). It is also prevalent and much more severe in other disadvantaged groups, particularly those living in over-crowded and unhygienic conditions in otherwise affluent, hygienic and healthy societies. This is so for Australian Aboriginal infants and children, particularly

those who live in remote and tropical regions (5-7). Although deaths from gastroenteritis are now rare in Aboriginal children, their hospitalization rates in Western Australia are several times higher than those for their non-Aboriginal peers (5-7).

The bi-directional interactions between infection and under-nutrition have been recognized for more than 30 years (8). Infection negatively affects nutritional status by suppressing dietary intake, increasing catabolism and, especially in the case of diarrhoeal infections, increasing the losses of nutrients that are needed for growth and tissue maintenance. Conversely, malnutrition can increase the risk of infection because of negative impacts on immune protective mechanisms, for example at the gastrointestinal mucosa (9). These interrelationships are very complex and difficult to disentangle, partly because of the possible effects of confounding variables. Under-nutrition has been linked to prolonged diarrhoea, its severity, and the likelihood of subsequent death, particularly in developing countries (9).

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Western Australia is a good location for a study on recurrent gastroenteritis and under-nutrition in Aboriginal children because of its accurate and comprehensive demographic information, its efficient hospitalization data recording, the routine identification, during hospitalization, of Aboriginal status, and the capacity to link these data with other characteristics, such as co-morbidities of patients, and with maternal information (10).

To investigate the effects of clinical and aetiological factors on the incidence, prevalence, and recurrence of childhood gastroenteritis in Western Australia, linked hospitalization records were retrieved to derive the outcome measures, associated co-morbidities, and other demographic variables for a cohort of children. Specifically, all infants, born in Western Australia in 1995 and 1996, who were admitted for gastroenteritis during their first year of life were included in the cohort. Census date was set at 31 May 2002. Figure 1 depicts the incidence (index episode) and recurrence (re-admissions due to gastroenteritis) pattern over time for a typical gastroenteritis patient and the associated outcome measures.

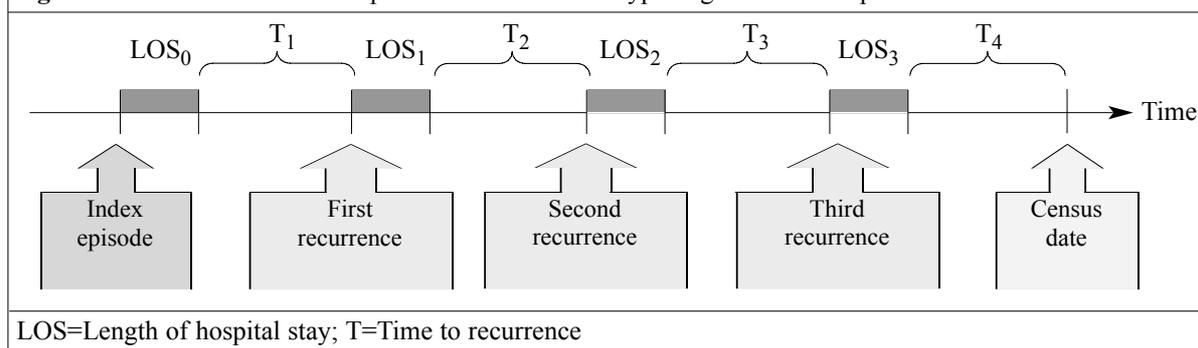
providers to improve strategic planning and resourcing of prevention of diarrhoea, related health promotion, and clinical and infrastructure services to help lessen the burden of gastroenteritis in communities and at primary and secondary healthcare levels.

## MATERIALS AND METHODS

### Linked hospitalization data

The sources of data for this retrospective cohort study were the Western Australia Hospital Morbidity Data System (14), the Western Australia Midwives' Notification of Births, and the mortality database of Australian Bureau of Statistics. A cohort-study design was chosen because information on hospital separations is routinely collected for all episodes of hospitalizations throughout Western Australia. The Health Information Centre of the Department of Health, Western Australia, extracts linked hospitalization and birth-records of each individual. Record linkage is used for retrieving the medical history of each patient from the diagnostic information

**Fig. 1.** Incidence and recurrence pattern over time for a typical gastroenteritis patient



Previous studies by our group have examined factors that influence the number of recurrent episodes of gastroenteritis causing re-admission (11), and the length of time that infants and children stay in hospital using a baseline model for repeated length of hospital stay records (12) and advanced frailty models allowing autocorrelation between observations (10) and clustering of patients within health districts in a multi-level setting (13). Previously-published studies by ourselves and others, however, have paid less attention to the possible impact of under-nutrition on the risk of hospitalization for recurrence of gastroenteritis episodes in vulnerable groups. The aim of the present study was to analyze the duration between successive hospitalizations of infants and children for recurrent gastroenteritis, i.e. the recurrence times  $T_i$  between episodes as shown in Figure 1. The determination of pertinent factors affecting recurrent hospitalizations is required by health planners and

recorded on hospital separation summaries. A unique patient number (anonymous) is attached by record linkage to all hospital separation records for the same individual to facilitate retrieval of the patient's information. The quality of the hospital morbidity-data linkage has been assessed, with the proportions of invalid and missed links estimated to be 0.11% (15).

All infants, born in 1995 and 1996, who had an index gastroenteritis admission during their first year of life were included in our cohort. This group was followed up until 31 May 2002 to document their recurrent hospitalizations for gastroenteritis. There were no deaths in this group through the study interval that were attributed to gastroenteritis or its complications. The total number of patients was 1,001 after removing eight deaths from other causes that occurred during the observation period.

In this study, admissions due to gastroenteritis were defined according to the ICD9-CM codes (before July 1999) and ICD10-AM codes (after July 1999) for principal diagnoses of diarrhoeal diseases which were: bacterial and viral diarrhoea, diarrhoea not otherwise specified, protozoal intestinal diseases, salmonellosis, shigellosis, bacterial food-poisoning, acute amoebic dysentery, chronic amoebic dysentery, non-dysenteric amoebic colitis, and candidal enteritis. Acute hospital-discharge data on age, sex, indigenous status, place of residence, admission type, birth-weight, and co-morbidities were extracted from the linked records for each patient in the cohort.

The birth-weights were checked and recorded measurements of midwives. Trained hospital staff obtained these weights using standard methods and with standardized calibrated equipment, i.e. Avery digital and checked electronic scales. There was only one birth-weight recorded for each individual in the Western Australia Midwives' Notification of Births registry. The nutritional status was assessed based on body mass measurements taken with standardized digital scales (to 100 g) after initial rehydration and in light clothing, and according to age, sex, and body length (to 2 years) or height using standard methodology (16). Under-nutrition was classified according to the ICD9-CM (263.9) and ICD10-AM (E46) codes. Gastrointestinal sugar intolerance was detected and recorded if the patient had persistent fluid diarrhoea when on a diet containing sugars, most often lactose, and with evidence of acidic stools, a positive Clinitest examination of the fluid part of a fresh stool specimen, and a clinical response to elimination of lactose or other relevant carbohydrates from the diet (17). Infections were documented, on clinical and microbiological grounds, indicating the presence of otitis media, scabies and/or infections involving the genitourinary tract. Iron-deficiency anaemia was documented on the basis of iron-deficiency (plasma fer-ritin <10 mg/L, elevated transferrin saturation, mean corpuscular volume, and mean corpuscular haemoglobin readings), and a haemoglobin value <110 g/L.

### Statistical modelling

Linked hospitalization records enabled determination of multiple hospital admissions for each patient during the observation period. For this data setting, the use of Cox's proportional hazards model that assumes independence of observations becomes inappropriate. By pooling the hospital re-admission episodes, a proportional hazards frailty modelling approach (18) was adopted to determine the factors influencing the recurrence times  $T_i$ . The method is a generalization of the Cox's regression model for time-to-event outcomes in survival analysis but adjusting the within-patient correlation among

hospital re-admissions of the same child. This approach has been previously employed to analyze length of hospital stay (12,19). The model-fitting procedure has been built into the S-Plus statistical package (20).

The proportional hazards frailty method is applicable to time-to-event data in the presence of both censored and repeated observations. In this study, the time from the hospital separation date of each patient's last episode of gastroenteritis to the census date (31 May 2002) was considered censored. The frailty approach preserves the semi-parametric nature of the Cox's regression model and, hence, is robust to mis-specification of the baseline hazard function. It improves statistical power by incorporating all available information, including random patient variations. The differences in patient characteristics as a source of extra-variation are accommodated and adjusted in the random component of the frailty model. Effects of potential risk factors on the repeated outcomes can be assessed through the adjusted hazard ratio, with a hazard ratio exceeding 1 implying a higher risk of recurrence relative to its reference category. Determination of pertinent factors would benefit health professionals and clinicians to assess the risk of recurrent gastroenteritis after adjusting for case-mix and the inherent dependency of observations.

## RESULTS

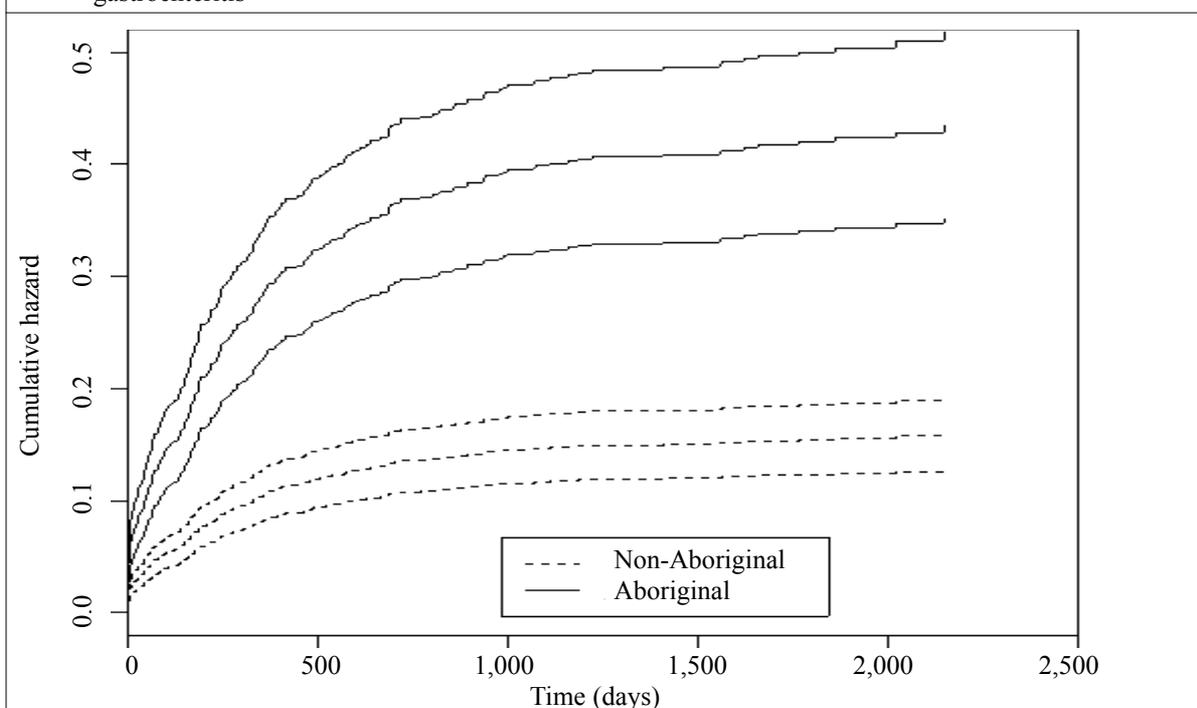
There were 1,001 patients—317 (32%) of Aborigines and 684 (68%) non-Aborigines—among 1,295 total gastroenteritis-related admissions monitored, of which 38.3% were for Aboriginal and 61.7% for non-Aboriginal children (Table 1). Hence, the re-admission rates were higher in the former ethnic group by a differential of 38.5% to 14.2% ( $p < 0.001$ ). The mean number of re-admissions and the mean re-admission rate among Aboriginal patients were much higher ( $p < 0.001$  for each measure), whereas their mean elapsed time to re-admission was significantly shorter ( $p < 0.001$ ). The average birth-weight of Aboriginal patients was significantly less than that of other patients ( $p < 0.001$ ). There was a highly significant trend for Aboriginal patients to reside in non-metropolitan areas, and their rate of low birth-weight was higher ( $p < 0.05$ ). The non-Aboriginal patients were more frequently admitted non-urgently ( $p < 0.01$ ). Dehydration, under-nutrition, and infections, such as otitis media, or those involving the genitourinary tract or the skin, were significantly more common among Aboriginal patients ( $p < 0.001$ ), and they had significantly higher rates of gastrointestinal sugar intolerance ( $p < 0.01$ ).

Figure 2 shows the cumulative hazard of recurrent gastroenteritis by indigenous status. The cumulative

**Table 1.** Demographic and descriptive statistics about patients

Characteristics	Overall	Aboriginal	Non-Aboriginal	p value*
Number of admissions due to gastroenteritis	1,295	496	799	
Number of patients	1,001	317	684	
Number of patients hospitalized once	782	195	587	0.000
Number of patients with re-admissions (%)	219 (22)	122 (38.5)	97 (14.2)	0.000
Maximum number of re-admissions	5	5	4	
Mean number of re-admissions (SD)	0.294 (0.649)	0.568 (0.889)	0.167 (0.448)	0.000
Mean re-admission rate (SD)	0.055 (0.122)	0.106 (0.166)	0.031 (0.084)	0.000
Mean re-admission time (days) (SE)	1,964 (25.63)	1,644 (48.6)	2,158 (26.2)	0.000
Proportion of censored observations (%)	77.3	63.91	85.61	0.000
Average birth-weight (kg) (SD)	3.148 (0.656)	3.015 (0.606)	3.210 (0.671)	0.000
Proportion of patients (%)				
Male	55.64	58.36	54.39	0.111
Aboriginal	31.67	100	0	
Non-metropolitan residence	49.05	78.23	35.53	0.000
Low birth-weight ( $\leq 2.5$ kg)	12.63	16.73	10.73	0.012
Proportion of admissions (%)				
Non-urgent	8.73	6.05	10.39	0.007
Dehydration	28.26	35.69	23.65	0.000
Gastrointestinal sugar intolerance	6.72	9.48	5.01	0.002
Under-nutrition	7.03	12.50	3.63	0.000
Iron-deficiency anaemia	3.40	7.46	0.88	0.000
Infection (genitourinary/scabies/otitis media)	13.44	23.99	6.88	0.000

\*Difference between Aboriginal and non-Aboriginal children  
SD=Standard deviation; SE=Standard error

**Fig. 2.** Cumulative hazard (with 95% CI) of Aboriginal versus non-Aboriginal children for recurrent gastroenteritis

CI=Confidence interval

hazard of recurrence of gastroenteritis was, in general, higher for Aboriginals, especially during the first three years following hospitalization from the previous episode. In the framework of proportional hazards frailty modelling, adjusted gastroenteritis re-admission hazard ratios are shown in Table 2. The effects of confounding factors have been incorporated in the statistical model, while observations with missing birth-weight values were removed in the analysis. Older children experienced a lower risk of recurrent gastroenteritis, with a reduced hazard of 3.7% per month of age or equivalently

nutritional disorders, and reduced life expectancy (5,21-23). This study has shown that young Aboriginal patients experienced a much shorter duration between re-admissions for these infectious diarrhoeal diseases. Approximately, 32% of patients and 38% of hospital admissions came from this numerically small minority group. Re-admissions were also significantly much more frequent among Aboriginal patients, and their average time to re-admission was much shorter than that for other patients, especially in the first three years after their previous episode of hospitalization (Fig. 2).

**Table 2.** Adjusted hazard ratios (95% CI) for factors affecting recurrent times from fitting a proportional hazards frailty model\*

Factor	Reference category	Hazard ratio	95% CI	p value
<b>Demographic</b>				
Admission age (months)		0.963	0.944-0.982	0.000
Sex: male	Female	1.268	0.975-1.649	0.077
Indigenous status: Aboriginal	Non-Aboriginal	2.593	1.910-3.519	0.000
Admission type: non-urgent	Emergency	0.900	0.546-1.483	0.680
Area of residence: non-metro	Metropolitan	1.288	0.948-1.750	0.110
Birth-weight (kg)		0.993	0.812-1.215	0.950
Year of birth: 1995	1996	1.110	0.858-1.436	0.430
<b>Co-morbidity†</b>				
Dehydration		1.001	0.871-1.150	0.990
Gastrointestinal sugar intolerance		1.148	0.717-1.837	0.570
Under-nutrition		1.640	1.088-2.471	0.018
Iron-deficiency anaemia		0.898	0.489-1.650	0.730
Infection		1.096	0.783-1.534	0.590
Variance of random effect=0.237				
*Based on 1,153 observations owing to missing values on birth-weight; †Absence of condition taken as reference category				
CI-Confidence interval				

reduced by 36.4% per year of age. Aboriginality and the presence of under-nutrition were significantly associated with a higher risk of recurrence, with hazard ratios of 2.59 (95% confidence interval [CI] 1.91-3.52) and 1.64 (95% CI 1.09-2.47) respectively. The random component variance estimate of 0.237 suggests moderate extra-variation among the repeated observations from some patients. Such variations in frailty among patients have demonstrated the usefulness of applying the frailty modelling approach to analyze the time to recurrent event data.

**DISCUSSION**

Aboriginal people comprise only 3.2% of Western Australia's population of 1.85 million (Australian Bureau of Statistics' 2001 Census of Population and Housing). Compared to the rest of the population, they generally have much more serious health problems, including high infant mortality, very high rates of infections and

There were some other important characteristics that were different between the two groups of patients. The mean birth-weight of Aboriginals was significantly lower, and more of them resided in non-metropolitan locations in this vast state (area=2.5 million sq km). Complicating medical conditions, such as dehydration, under-nutrition, and gastrointestinal sugar intolerance, were significantly more common in the Aboriginal cohort, whereas clinically-important co-morbidities, including iron-deficiency anaemia and a wide range of infections of the skin, ears, and genitourinary tracts, were very significantly more common among Aboriginal patients. Although these are not new observations, they help explain why Aboriginal patients were hospitalized and re-hospitalized more frequently than non-Aboriginal patients for gastrointestinal infections and parasitic infestations. This may also help explain why proportionately more non-Aboriginal patients were hospitalized non-urgently; that is, because there were relatively fewer complications or co-existing

diseases among them. Re-admission was significantly associated with indigenous status of patients and the existence of under-nutrition (Table 2). The positive association between pre-existing under-nutrition and later hospitalization for recurrent episodes of gastroenteritis suggests that compromised nutritional status is a contributing factor to recurrent episodes of infectious diarrhoea, notwithstanding the complex interacting synergistic and antagonistic relationships between nutrition and infection that were first proposed by Scrimshaw in the late 1960s (8) and have been reviewed by him recently (24).

Several limitations should be considered when interpreting the findings of this study. First, it is possible that inadequate primary healthcare services closer to home may help explain the excess hospitalization rates of rural Aboriginal children. Regrettably, information was not available on the distance from the children's homes to the nearest primary healthcare facility. Second, only episodes of infectious diarrhoea or gastroenteritis requiring hospitalizations were included. Data on children attending outpatient clinics are not captured by the Hospital Morbidity Data System. Third, information on such factors, as feeding patterns, dietary adequacy, and micronutrient deficiencies that are typically obtained by nutritional surveys, was not available from the accessible databases.

Our experience shows that diarrhoeal diseases are prevalent in infants and children of this particular ethnic group, namely Australian Aborigines. Others working with other ethnic groups, including indigenous populations, have reported similar experience. For example, results of pioneering work of Mata among Mayan children in the Guatemalan highlands showed that their early lives were punctuated by repeated episodes of infections, including those involving the gastrointestinal tract and that these were associated with under-nutrition and growth failure (25). Sack, Santosham, and their colleagues showed that diarrhoeal diseases were major public-health problems among native American Apache children living in reservations in southwestern parts of the United States; they remarked that the epidemiologic and microbiological patterns of disease were similar to those found in developing countries (26,27). Later work among American Indian and Alaskan native children demonstrated that diarrhoea-related hospitalizations for these children from 1980 to 1995 declined to levels similar to those in the national US population (28). Such improvements have not occurred among Aboriginal infants and children in Western Australia over recent years (6). Examples of other ethnic groups in which diarrhoeal diseases have been well-documented include children in northeastern Brazil (29), in the West African nation

of Gambia (30), and in Pakistan (31) and many other parts of the Indian sub-continent, including India and Bangladesh. Many of these studies have concentrated on particular aspects of childhood diarrhoeal illnesses, such as their epidemiology, aetiologic agents, the causes of persistent diarrhoea (32), co-morbidities, methods of treatment, and preventive public-health measures, including the use of vaccines. In the vast literature on childhood infectious diarrhoeas, few authors have focused on this issue as a particular problem of indigenous populations within generally affluent and otherwise healthy nations, such as Australia.

The heavy burden of infectious diarrhoeas among Australian Aboriginal infants and children is very complex and multi-factorial. Many of these infections are transmitted by the faecal-oral route and, therefore, are prevalent where living conditions are overcrowded and unhygienic, where sewage and waste disposal are inadequate, and where personal, family and community levels of hygiene behaviour are risky for the transmission of infecting microorganisms or disease-carrying vectors, such as flies (6,33,34). Understanding about transmission of infectious diseases and prevention of related illnesses among members of affected families is often poor. This increases their risk of exposure to a range of infectious illnesses, including diarrhoea, particularly among infants and young children. This can result in delayed transfer to clinic or hospital, thus necessitating hospitalization rather than brief treatment as an outpatient or in a day clinic or at home under supervision (6,21). Furthermore, Aboriginal people in remote parts of Australia tend to live long distances from hospitals and have limited access to primary and secondary healthcare compared to other Australians. These factors and health and nutrition promotion and provision of clinical services at primary and secondary levels are needed to help overcome this serious problem.

#### ACKNOWLEDGEMENTS

The authors thank Diana Rosman, William Pyper, and Peter Somerford of the Department of Health, Western Australia, for providing data and coding information, and Dr. Valerie Burke, Department of Medicine, University of Western Australia, for statistical advice. Thanks are also due to the Editor and anonymous reviewers for their constructive comments and suggestions. The authors are grateful to the Office of Aboriginal Health of the Department of Health, Western Australia, for supporting this project. This research was supported financially by research grants from the Australian Research Council (Project ID DP0559204) and the Research Grants Council of Hong Kong SAR.

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