## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Non-communicable diseases, infection and survival in a retrospective cohort of Indigenous and non-Indigenous adults in central Australia. |
| **AUTHORS** | Einsiedel, Lloyd; Fernandes, Liselle; Joseph, Sheela; Brown, Alex; Woodman, Richard |

## VERSION 1 - REVIEW

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| **REVIEWER** | Dr.Srinivas Kondalsamy-Chennakesavan<br>Epidemiologist, Rural Clinical School<br>The University of Queensland<br>Australia |
| **REVIEW RETURNED** | 03-May-2013 |

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| **THE STUDY** | Indigenous patients admitted to the hospital with blood stream infections may not be representative of Indigenous Australians. |
| **GENERAL COMMENTS** | It is a well written manuscript evaluating the association between NCDs and risk of blood stream infection among residents of central Australia.<br>My comments:<br>1. Their current hypothesis states that "rising prevalence rates of non-communicable diseases (NCDs) increases infection risk and worsens outcomes among socially disadvantaged Indigenous Australians undergoing a rapid epidemiological transition". Using retrospective data will help evaluate the association and causal relationship can not be attributed.<br>2. In fig 2, they have presented the survival plots. However, they haven't mentioned about the median follow-up for the overall group and the specified sub-groups. Also, if they censor their analyses at the end of five years, that will improve the presentation of fig 2. |

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| **REVIEWER** | Dr Katie Panaretto<br><br>Population Health Medical Officer<br>Director, Preventative Health Unit<br>Queensland Aboriginal and Islander Health Council<br>21 Buchanan St, West End Q 4101 \|PO Box 3205 South Brisbane Q 4101<br><br>No competing interests |
| **REVIEW RETURNED** | 09-May-2013 |

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| **THE STUDY** | Aspects of the particpants could be expanded upon<br>1. The actual demographics are minimal. For example tobacco use may be of interest, marital status, education status, nutritional status, |

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| | why they were in town<br>2. Duration of the co morbidities may be of interest possibly esp duration of alcohol use, diabetes<br>3. The context - this work has occurred in a complex environment of attempts at harm minimisation related to alcohol use in the Northern Territory. Some reference to this would be helpful - so were these participants followed at a time of Alcohol management plans in the remote communities, so pre, post or during times of 'dry communities'.<br>4. the charactersitics of the remote community residents could be more detailed. Were these particpants also harmful users of alcohol or were they in town visiting relatives or came to town knowing they needed hospital care.<br>5. Context of the hospilisation - were they referred in due to the failure of oral antibiotics by primary health care teams? |
| **RESULTS & CONCLUSIONS** | There is a clinical issue explored - how is mortality related to NCDs and infection in Indigenous Australians?<br>But the social context is not explored in great detail and yet the title refers to 'rapid epidemiological transition'. A couple of additional sentences here may help explore this as noot all readers may be familiar with these concepts.<br>And whilst the participants may be typical of the Indigenous patients of Central Australia, the findings may not be translate to the Indigenous community living in the regional cities along the east coast for example.<br>Perhaps the title could include a reference to location |
| **REPORTING & ETHICS** | Could the ethics line have any further information. Who convenes the Committee? What organisations might be representated on the Board |
| **GENERAL COMMENTS** | The paper is a well written paper. It does address an important aspect of the health of Indigenous Australians. However it has an arguably fairly narrow clinical focus. The key message appaers to be that Indigenous Australians with NCDs are a high risk of bacteraemia/septicaemia particularly if they use alcohol in a harmful way. Is this new?<br><br>An international audience may be unaware of the complex environment in which these participants live. This is in part explored in the discussion with respect to the impact of siocial disadvantage but this is even more complicated in remote Indigenous Australia by policy and legislative frameworks attempting to minimise the exposure to and harm of alcohol use.<br>In addition there is no exploration of any aspects of prevention - do these participants ever use local primary health care services, would PHC intervention have helped? There is no mention of the robust Aboriginal Community Controlled Health Service in Alice Springs. Do they run outreach services to the river bed community? What role do they play in the complex alcohol environemnt - prevention, rehab etc - that may impact ion these findings in the future? |

**VERSION 1 – AUTHOR RESPONSE**

Reviewer: Dr.Srinivas Kondalsamy-Chennakesavan Epidemiologist, Rural Clinical School The University of Queensland Australia

Indigenous patients admitted to the hospital with blood stream infections may not be representative of Indigenous Australians.

Response: We agree that the Indigenous population of Australia is heterogeneous. Infection rates in central Australia are among the highest worldwide; far higher than those of their peers in the tropical north of the Northern Territory or Indigenous Australians elsewhere (at least for Staphylococcus aureus BSI). We also agree that Indigenous Australians presenting with a BSI may not be representative of the Indigenous community of central Australia more generally. However, the main aim of the study was to explore possible interactions between types of infection and comorbidities within those infected. It was for this reason that patients presenting with blood stream infections were chosen as the study population. We have now changed the title to better reflect this aim. The other major aim of the study was to demonstrate the effect of residence on infection rates for which we used population based rates given that Alice Springs Hospital is where the majority of admissions for BSI's occur.

It is a well written manuscript evaluating the association between NCDs and risk of blood stream infection among residents of central Australia.
My comments:
1. Their current hypothesis states that "rising prevalence rates of non-communicable diseases (NCDs) increases infection risk and worsens outcomes among socially disadvantaged Indigenous Australians undergoing a rapid epidemiological transition". Using retrospective data will help evaluate the association and causal relationship can not be attributed.

Response: We agree with the reviewer that a causal relationship cannot be attributed. This has been made clear in the Abstract and Key Points where the hypothesis is referred to.

2. In fig 2, they have presented the survival plots. However, they haven't mentioned about the median follow-up for the overall group and the specified sub-groups. Also, if they censor their analyses at the end of five years, that will improve the presentation of fig 2.

Response: The median duration of follow-up for data presented in Fig 2 has been included in the figure legend and Fig 2 has now been censored at five years as suggested.

Reviewer: Dr Katie Panaretto

Population Health Medical Officer
Director, Preventative Health Unit
Queensland Aboriginal and Islander Health Council

No competing interests

Aspects of the particpants could be expanded upon
Response: Our stated aim is to study the effects of non-communicable diseases on infection risk and outcomes in a socially disadvantaged Indigenous population. To achieve this we were forced to rely on available retrospective administrative and clinical data sources which are unfortunately limited in terms of individual demographics.

1. The actual demographics are minimal. For example tobacco use may be of interest, marital status, education status, nutritional status, why they were in town

Response: We agree that this information would be of interest and would further define our study population. However, much of this information is not collected by ASH. This is a limitation of our retrospective study and has now been clearly included in the paragraph on study limitations (page 22, para 2, line 6). Moreover, with the exception of nutritional status and health literacy (which are difficult to quantify) these factors have are unlikely to affect infection risk . Indeed, obtaining accurate data for these parameters from a hospital data-base would be exceptionally difficult. In contrast to alcohol usage, which is a major and direct cause of hospital presentation in central Australia, an ICD-10 code for other factors would only be recorded where these require consideration during hospital admission. In the case of tobacco usage, for example, this would certainly be recorded for patients admitted with COPD, but this would be unlikely for admissions with gastroenteritis. Similarly, nutritional status is very difficult to retrospectively define in our setting from the given data sources. Micronutrient deficiencies are likely to be common, though seldom tested for, and gross malnutrition is only occasionally recorded as an ICD-10 code where this complicates the hospital admission. This is a further limitation of our retrospective study and has been included in a paragraph detailing such limitations in the discussion (page 22, para 2, line 18). Other information, such as educational attainment, marital status and the reasons for visiting Alice Springs, would be difficult to obtain even in a prospective study due to language difficulties and a reluctance to discuss such issues with strangers in an acute care setting. English is generally the second or third language spoken. In our prospective study of self-discharge in this population (Einsiedel et al. Aust Health Rev; 2012; reference 17 in the current study), for example, interpreters capable of speaking ten different languages were required. In that study ensuring that an appropriate interpreter was available for a particular patient was rendered still more difficult due to cultural obligations and the need to respect avoidance relationships. This would make any prospective study comparable in size to our current retrospective study difficult to perform and prohibitively expensive. Instead, we have included more demographic detail related to our study population derived from Australian Bureau of Statistics data relating to education and employment (Introduction, page 9, line 8).

2. Duration of the co morbidities may be of interest possibly esp duration of alcohol use, diabetes

Response: We agree that the duration of co-morbid conditions would be of interest; however, it would be exceptionally difficult to obtain any meaningful data in our setting. We could, for example, determine the date of diagnosis by contacting all remote clinics in this area of 1,000,000 km2, but this would not allow us to determine the date of onset and would be dependent on clinic attendance and therefore subject to significant bias. Young Indigenous men in particular are less likely to engage with health services in our setting (see Reference 17; Einsiedel et al, Aust Health Rev., 2012).

3. The context - this work has occurred in a complex environment of attempts at harm minimisation related to alcohol use in the Northern Territory. Some reference to this would be helpful - so were these participants followed at a time of Alcohol management plans in the remote communities, so pre, post or during times of 'dry communities'.

Response: As noted by the reviewer, NT and Australian Federal Government policy regarding the management of alcohol and attempts at harm minimisation are extremely complex. Our data was collected during a period in which a variety of different interventions, including ‘dry’ communities, were implemented to control alcohol use in our region. Although any discussion of Government policy in relation to alcohol control is beyond the scope of our paper, we have now acknowledged this complexity in the Introduction (page 9, line 11) and provided a recent reference to which the reader may refer. Regarding alcohol use in particular communities, as is noted in the section on limitations (Discussion, page 22, line 7), our study population is highly mobile. This significantly weakens past

attempts to restrict alcohol consumption by outlawing the consumption of alcohol in particular ‘dry’ communities.

4. the charactersitics of the remote community residents could be more detailed. Were these particpants also harmful users of alcohol or were they in town visiting relatives or came to town knowing they needed hospital care.

Response: As noted above, determining why our patients were visiting Alice Springs is impossible in this retrospective study and would be very difficult to determine in an acute care setting even in a prospective study. The objective of our paper was to determine the infection risks (type, previous number of infections and survival) associated with NCDs. All analyses presented in our study were however adjusted for the 3 broad places of residence, which might confound and/or predict the associations with NCD.

5. Context of the hospilisation - were they referred in due to the failure of oral antibiotics by primary health care teams?

Response: The issue of management in the primary health care setting is an important one; however, it was not the aim of this study and, unfortunately, the referral path is impossible to retrospectively ascertain using the hospital data-base.

There is a clinical issue explored - how is mortality related to NCDs and infection in Indigenous Australians?
But the social context is not explored in great detail and yet the title refers to 'rapid epidemiological transition'. A couple of additional sentences here may help explore this as noot all readers may be familiar with these concepts.

Response: An introductory paragraph has been included, which explores the concept of the ‘epidemiological transition’ (page 7, para 1).

And whilst the participants may be typical of the Indigenous patients of Central Australia, the findings may not be translate to the Indigenous community living in the regional cities along the east coast for example.
Perhaps the title could include a reference to location

Response: We agree that the results of this study are unlikely to be relevant to Indigenous Australians living in the more developed regions of the east coast of Australia or in urban settings in major Australian cities. They are; however, very likely to be relevant to other socially deprived populations in resource poor areas elsewhere. A reference to location has been included in the title.

Could the ethics line have any further information. Who convenes the Committee? What organisations might be representated on the Board

Response: the Central Australian Human Research Ethics Committee is a nationally supervised HREC details of which can be obtained from the website, the address has now been included in the methods section.

The paper is a well written paper. It does address an important aspect of the health of Indigenous Australians. However it has an arguably fairly narrow clinical focus. The key message appaers to be that Indigenous Australians with NCDs are a high risk of bacteraemia/septicaemia particularly if they use alcohol in a harmful way. Is this new?

Response: Our findings are new in the context of Indigenous Health in Australia. This is perhaps not surprising given the failure to integrate NCD management in the NT, an approach that is not peculiar to Australia and which has been recently criticised internationally (De Maeseneer et al, Lancet, 2012). Our findings are however important as they quantify the extent of the problem amongst the Indigenous and non-Indigenous populations and the magnitude of the independent effects of NCD's, including alcohol, and residence on infection risk. As noted in our discussion, our findings also have relevance to other socially disadvantaged populations in resource poor areas where sophisticated microbiological diagnostics are unavailable and where demonstrating such an association is consequently likely to be very difficult.

An international audience may be unaware of the complex environment in which these participants live. This is in part explored in the discussion with respect to the impact of siocial disadvantage but this is even more complicated in remote Indigenous Australia by policy and legislative frameworks attempting to minimise the exposure to and harm of alcohol use.

Response: The failure of Australian Government policy to control alcohol use undoubtedly contributes to the high rates of alcohol consumption in our study and it is these high rates in the setting of social deprivation that has allowed us to demonstrate an association with increased infection risk so conclusively. As noted in our conclusion, our findings illustrate the need for an integrated response to the NCD crisis. This must include the empowerment of affected populations in accord with the National Aboriginal Health Strategy. Significantly, the proposals of the NAHS are also consistent with recent calls by De Maeseneer et al (Lancet, 2012) to empower affected populations. This has been made clear in the conclusion (Page 24, line 2).

In addition there is no exploration of any aspects of prevention - do these participants ever use local primary health care services, would PHC intervention have helped? There is no mention of the robust Aboriginal Community Controlled Health Service in Alice Springs. Do they run outreach services to the river bed community? What role do they play in the complex alcohol environemnt - prevention, rehab etc - that may impact ion these findings in the future?

Response: We agree that improving outcomes in our setting will require the provision of appropriate health services. Our data has therefore been provided to the Tangengtyerre Council who run the town camps with a view to improving the provision of health care to town camp residents. The provision of health services to those who camp while visiting Alice Springs is more problematic because many of these people are from remote communities. However, ours is a retrospective study that was specifically designed to identify disease associations that might be amenable to public health and clinical intervention in the future and was not designed to also assess the potential mitigating impact of the local primary health care services.