Ethnic Disparities in Rates of Severe Infection in New Zealand

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Background
• Inequality
  – Between group difference in health status

• Equity
  – An ethical concept of justice: everyone has enough to meet their minimum requirements

• Inequity
  – Disparity through maldistribution of resource that is avoidable, unnecessary, unfair and unjust

• Racism
  – Institutionalised
  – (Interpersonal)
  – (Internalised)
Figure 4: Neighbourhood deprivation distribution (NZDep 2006), Māori and non-Māori, 2006

Source: Salmond et al 2007

Tatau Kahukura 2nd edition
Ethnic Disparities - Viewpoints

“Racialised expression of Biology”

Differences in health status are derived from within the group

“Biologic expression of Racism”

Differences in health status shaped by social environment and heirarchy
From Socioeconomic Disadvantage to Infection

• Classic Pathways
  – Overcrowding
  – Malnutrition
  – Smoking
  – Alcoholism
  – Skin disease
  – Dental health
  – Lack of access to healthcare
  – Adherence to healthcare recommendations
  – Infectious complications of excess morbidity
    • Cancer
    • Respiratory disease
    • Rheumatic fever
Severe infection

• What are we talking about?
  – Severe sepsis
    • infection associated with severe illness, organ failure and/or death

• Why are we talking about it?
  – Mortality and morbidity burden
  – Indicator of poor health and prognosis
  – Higher incidence amongst Maori living in the Waikato DHB catchment
  – Maybe we’ve forgotten about it?
1900---- **Exotoxin**: species specific heat sensitive toxins

**Endotoxin**: common bacterial pathogens
=> animal models of endotoxic shock

1926 First detailed description of **disseminated intravascular coagulation** in endotoxic shock

1970---- **Cytokine biology**: IL-1 and TNFa

1990s---- “**PAMPs and PRRs**”
Infection by bacteria can lead to sepsis. Key components include:

- Complement system
- Lipopolysaccharide
- Lipoproteins
- DNA
- Outer membrane protein
- Fimbriae
- sCD14
- CSA (C5a receptor 1)
- Tissue factor
- Coagulation

The diagram illustrates the following processes:

1. **Inflammation**:
   - Moderate: beneficial alarm signal
   - Severe: deleterious effects
   - Organ dysfunction

2. **Inflammation down-regulation**:
   - Increased susceptibility to nosocomial infection

**Figure 1: From bacteria to disease**

- Barred lines: inhibition
- Arrows: activation or consequences

Te Hanga Whaioranga Mo Te Iwi – Building Healthy Communities

Waikato District Health Board
My definition of severe infection/sepsis.....

• Justice Potter Stewart

• “I shall not today attempt further to define [obscene/pornography]....; and perhaps I could never succeed in intelligibly doing so. But I know it when I see it.”
What am I “seeing”?

- Hypotension  Systolic BP<90mmHg
- Lactate  >4 mmol/L
- Creatinine  >176.8 μmol/L
- Bilirubin  > 34.2 μmol/L
- Platelet Count  < 1000,000 μL
- INR  > 1.5
- Intensive care admission
- Mechanical ventilation
- Urgent surgery
- **Death**
Am I seeing more?

Figure 1: Annual rate of infectious and non-infectious diseases and all-cause hospital admissions in New Zealand (1989-2008)

*Lancet* 2012; 379: 1112-19
Severe Sepsis Study – Waikato Region 2007-2012

Primary Infection Code - 10% of all admissions

Organ Failure Code - 8% of infections - 1674 individual episodes

• Population 370000
• 20% Maori
• 9.5% of NZ population
• 14% of NZ Maori
Infection with evidence of organ failure

Figure 1: Annual admission rate adjusted for age and sex, per 100,000 person-years, stratified by age. Vertical bars indicate 95% confidence intervals.

Huggan P. Unpublished
Incidence rates by age, ethnicity

Rate, per 100,000 person-years

Age (years)

Non-Maori
Maori
<table>
<thead>
<tr>
<th>Risks for ICU admission</th>
<th>Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>1.75 (1.21-2.53)</td>
<td>0.003</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>3.38 (1.37-8.33)</td>
<td>0.008</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>13.97 (10.18-19.18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multi-organ failure</td>
<td>1.42 (1.06-1.9)</td>
<td>0.018</td>
</tr>
<tr>
<td>Risks for in-hospital death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per year)</td>
<td>1.04 (1.03-1.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson score ≥1</td>
<td>1.72 (1.32-2.23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU admission</td>
<td>3.58 (1.71-3.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>1.81 (1.15-2.84)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>2.94 (1.29-6.72)</td>
<td>0.01</td>
</tr>
<tr>
<td>Multi-organ failure</td>
<td>1.5 (1.15-1.95)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Survivorship – long term increase in risk of death

Figure 1 Kaplan-Meier curves and 95% CIs for long-term survival after sepsis. Sepsis versus non-sepsis. Includes 970 sepsis and 28 694 non-sepsis individuals. Analysis censored at 6 years.

Wang et al BMJ Open 2014; 4: e004283
## Mortality within 1 year of Severe Sepsis Diagnosis

<table>
<thead>
<tr>
<th>Age Group</th>
<th>1 year Mortality per 100000/yr [Total Population]</th>
<th>1 year Mortality Per 100000/yr [Maori Population]</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td>0.97</td>
<td>1.87</td>
<td>1.9</td>
</tr>
<tr>
<td>20-59</td>
<td>9.4</td>
<td>28</td>
<td>2.99</td>
</tr>
<tr>
<td>≥ 60</td>
<td>183</td>
<td>250</td>
<td>1.4</td>
</tr>
</tbody>
</table>
Survivorship - Cognitive Disability

Iwashyna et al. JAMA 2010; 304: 1787-94
Iwashyna et al. JAMA 2010; 304: 1787-94
Figure 1 Regional variation in sepsis mortality, United States, 1999-2005. Excludes Alaska and Hawaii.

http://www.ij-healthgeographics.com/content/9/1/9
The heavy concentration of strokes in the southeast has given that region the nickname "the stroke belt."
(Source: CDC, 2010a.)
The REGARDS Study

- “Reasons for Geographic and Racial Disparity in Stroke”
- One of the largest ongoing prospective cohort studies in the USA - >30,000 community dwelling patients >45
- Health events and hospitalisations coded
- Baseline risks associated with sepsis events
  - Chronic disease
  - Lower education and income
  - Alcohol and Tobacco use  
    - Wang HE. PLoS ONE 2012
  - Waist circumference  
    - Wang HE. Obesity 2013
  - hsCRP  
    - Wang HE. PLoS ONE 2013
Figure 1. Adjusted risk of incident sepsis versus number of chronic medical conditions. Total of 975 incident sepsis events among 30,239 participants in the REGARDS cohort. Chronic medical conditions included hypertension, diabetes, dyslipidemia, coronary artery disease, atrial fibrillation, myocardial infarction, stroke, deep vein thrombosis, peripheral artery disease, chronic kidney disease and chronic lung disease. Hazard ratios adjusted for age, sex, race, education, income, geographic region, smoking status and alcohol use. P-value for test of trend <0.001.
doi:10.1371/journal.pone.0048307.g001
• Birth Cohort Studies
  – Burden of ill health experienced in childhood is carried into adulthood
    • *Lancet* 2002; 360: 1640
  – Childhood social disadvantage predicts increased chronic disease and cardiometabolic risk
    • *Am J Epidemiol* 2014; doi:10.1093/aje/kwu127
  – Childhood maltreatment predicts systemic inflammation in adulthood
    • *PNAS* 2007; 104: 1319
From Socioeconomic Disadvantage to Infection

**Classic Pathways**
- Overcrowding
- Malnutrition
- Smoking
- Alcoholism
- Skin disease
- Dental health
- Lack of access to healthcare
- Adherence to healthcare recommendations
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**Alternate Pathways**
Chronic morbidities predisposing to severe infection
- Diabetes
- Obesity
- Renal disease
- Liver disease
- Atrial fibrillation
- Heart Failure
- Hypertension
- Dyslipidemia
- Vascular disease
The right to security, food, shelter, education and healthcare for every child in New Zealand.