

Central Australian Aboriginal Congress
'Aboriginal Health in Aboriginal Hands'

Precision Medicine in an Aboriginal Context

Sam Heard, Medical Director



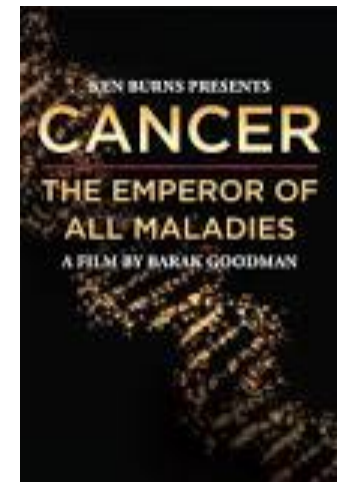
**Central Australian
Aboriginal Congress**

ABORIGINAL CORPORATION | ICN 7823



Cancer: my introduction to precision medicine

- **Using the genetic changes in a patient's tumour** to determine their treatment is known as precision medicine. Precision medicine is an approach to patient care that allows doctors to select treatments that are most likely to help patients based on a genetic understanding of their disease.
- Cancer: The Emperor of All Maladies
 - Siddhartha Mukherjee



One-size fits-all
medicine

Stratified medicine

Precision medicine



Stratification

Patients are grouped
by: Disease
Subtypes
Demographics
Clinical features
Biomarkers



Personalisation

Patient individual:
Preferences,
Clinical features
Medication history
Environment
Behaviours & habits
Biomarker



Precision medicine





Precision

- the quality, condition, or fact of being exact and accurate

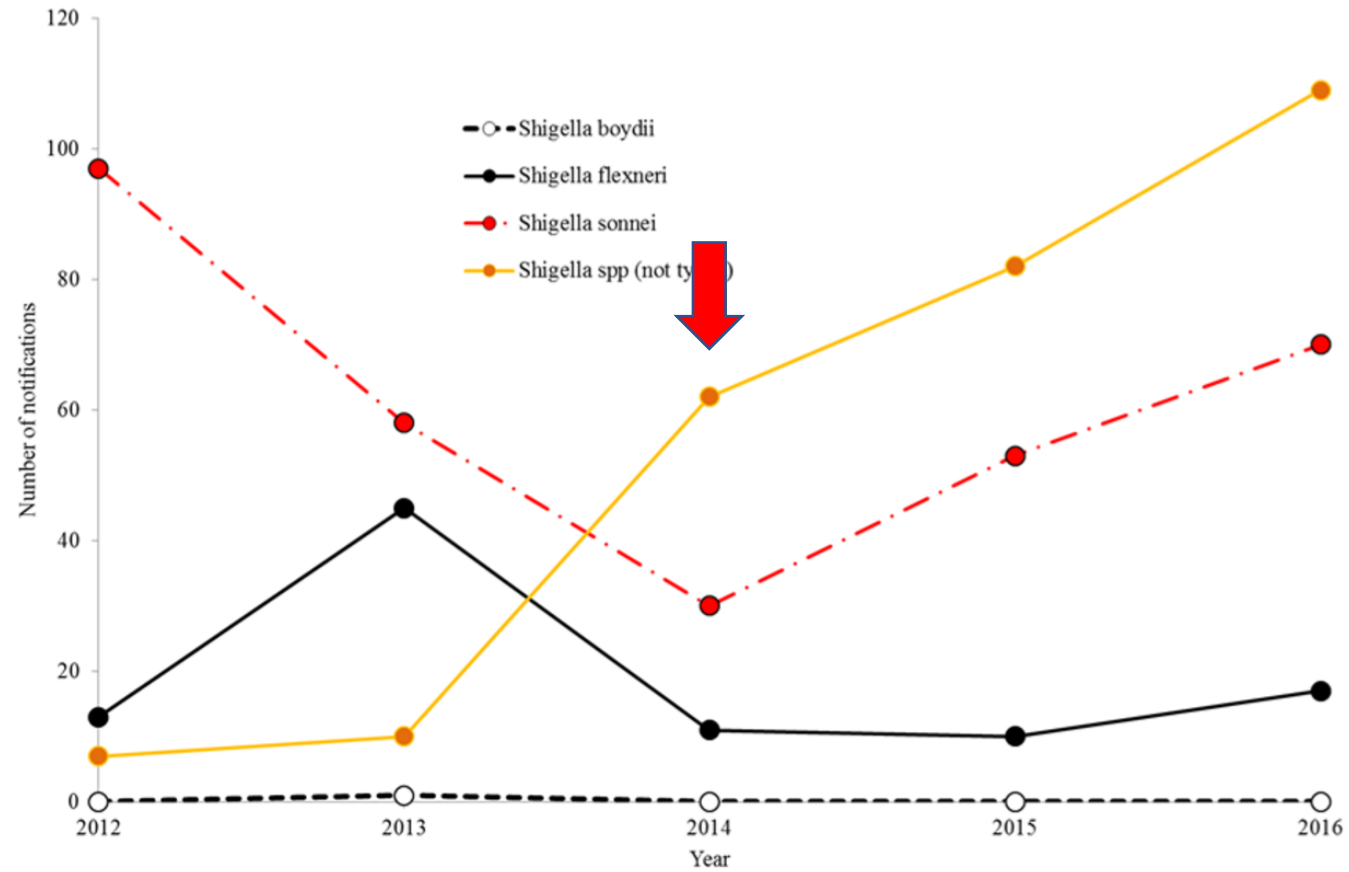
Precision v Accuracy

- Accuracy is correctness
- Precision is repeatability

Sensitivity	Conventional Method	Multiplex PCR
Enteric Protozoans	11 - 90%	100%
Enteric Bacteria	25 - 89%	100%

Shigella notifications

Figure 1. Shigellosis notifications by species in the Northern Territory, 2012-2016.



PCR Diagnosis



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Increase in antibiotic resistant Shigella

[2019 - Infectious disease alerts](#)

[2018 - Infectious disease alerts](#)

NSW Health has detected an increase in the number of shigellosis cases with resistance to key recommended antibiotics. Of the 60 notifications of shigellosis in April and May 2019, 59% were found to be resistant to multiple classes of antibiotics.

Related Links

[Immunisation Programs](#)

DNA and Aboriginality



Late in 2018 Massachusetts Senator Elizabeth Warren released a [video](#) strongly suggesting two things: she is running for US president in 2020, and she has Native American ancestry.

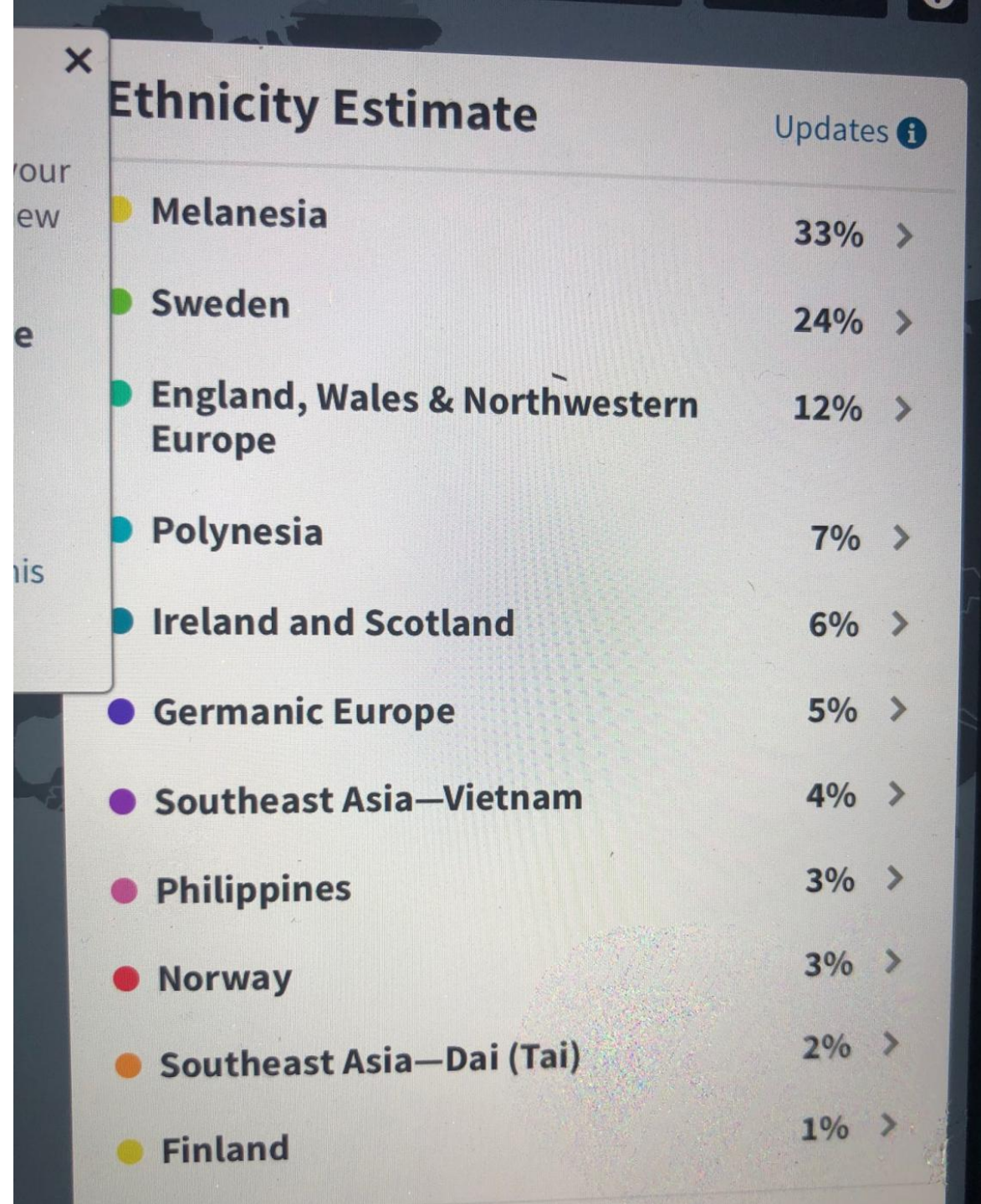
- Less data on DNA of Indigenous Australians
- Australian Indigenous people are far more accepting of people who discover their heritage later in life due to our history
- Tasmanian census
 - 1971 - 671 Identified as Indigenous
 - 2016 – 23,000

Larrakia DNA

Swedish Paternal Grandfather

Torres Strait Islander Paternal Grandmother

Larrakia Mother

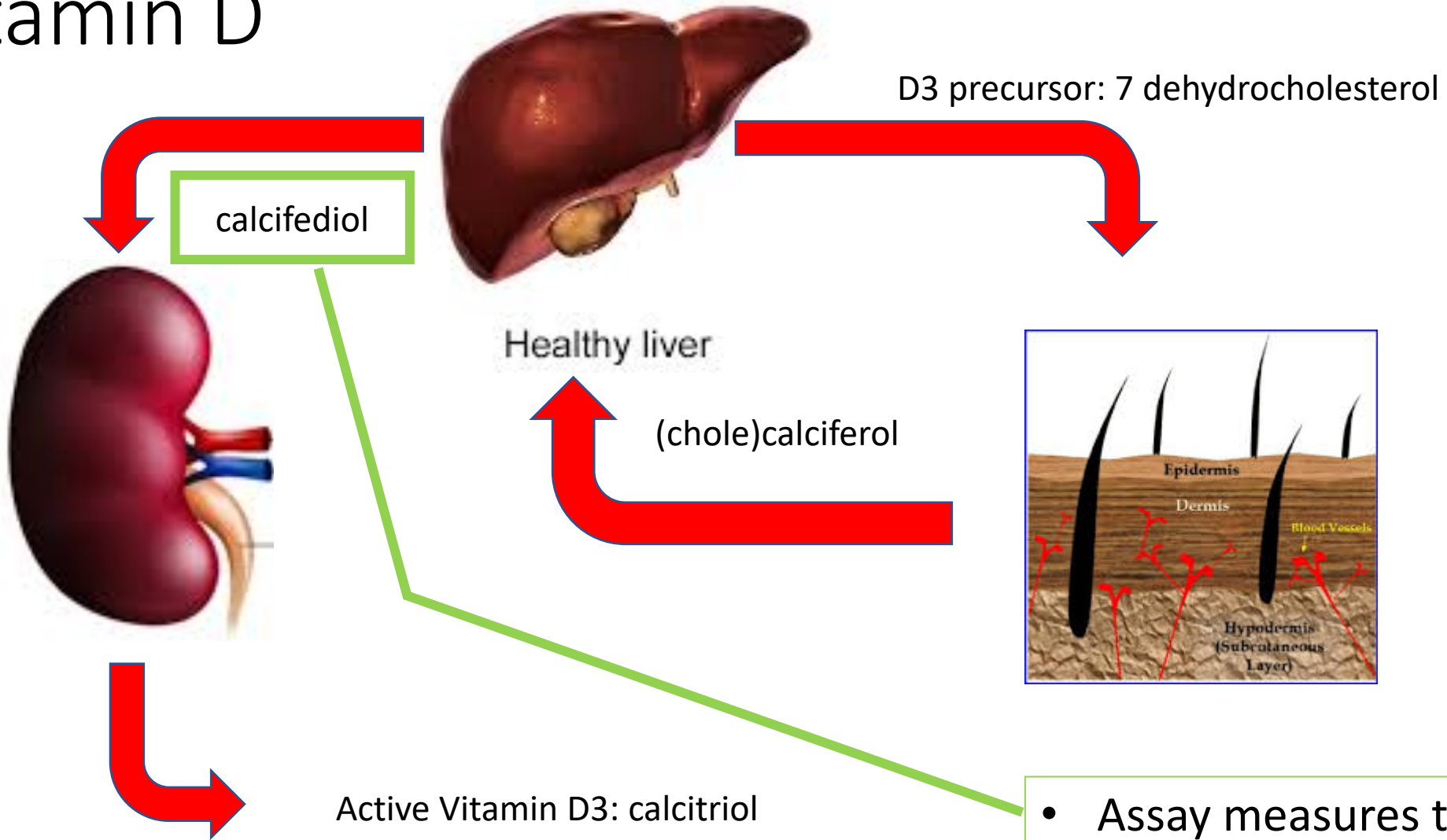




Vitamin D

- Vitamin D group of hormones
 - Vitamin D3
 - synthesized by the body
 - Manufactured pharmaceutically
 - Found in e.g. fish, liver, oils
 - Vitamin D2
 - Present in fruit and vegetables
 - Side chain variant
 - Not considered important
- Highly soluble and protein bound
 - 90% bound to DBP
 - 10% bound to albumin
- Calcifidiol
 - More easily measured
 - 99.96% protein bound
- Calcitriol (active)
 - 96%

Vitamin D



- Assay measures this
- 99.96% bound

Vitamin D

- Same molecule in all humans
- DBP (binding protein)
 - Varies in different groups
 - 1A1 variant in Aboriginal People is also found in South African Bantu
 - 4 fold affinity to Vit D than one variety and double the most common
 - Greater amounts of DBP if affinity is high
- Consequences for measurement
 - The majority of Aboriginal people have high affinity DBP
 - Incorrect status from assay – appear to be deficient

Vitamin D

“[In most studies] calcifediol levels, all assayed on Liaison immuno-analysers, are acceptably precise. As to accuracy however, the results of all studies will consistently show significant variance from those that would be obtained from a reference measurement procedure (RMP) analyser using mass spectrometry.”

“People with Aboriginal DBP, it can confidently be estimated that the true total in vivo calcifediol will be underestimated by as much as 40%.”

Normal values predicated on mass spectrometry results!

Vitamin D

- Liaison analysers give population mean of 57 with a high proportion below 50.
- Mass spectrometry gives a population mean of 87!
- Is this a non-disease?



Epigenetics

- Epigenetics is the study of heritable phenotype changes that do not involve alterations in the DNA sequence.
- The Greek prefix *epi-* (ἐπι- "over, outside of, around") in epigenetics implies features that are "on top of" or "in addition to" the traditional genetic basis for inheritance.

Epigenetics

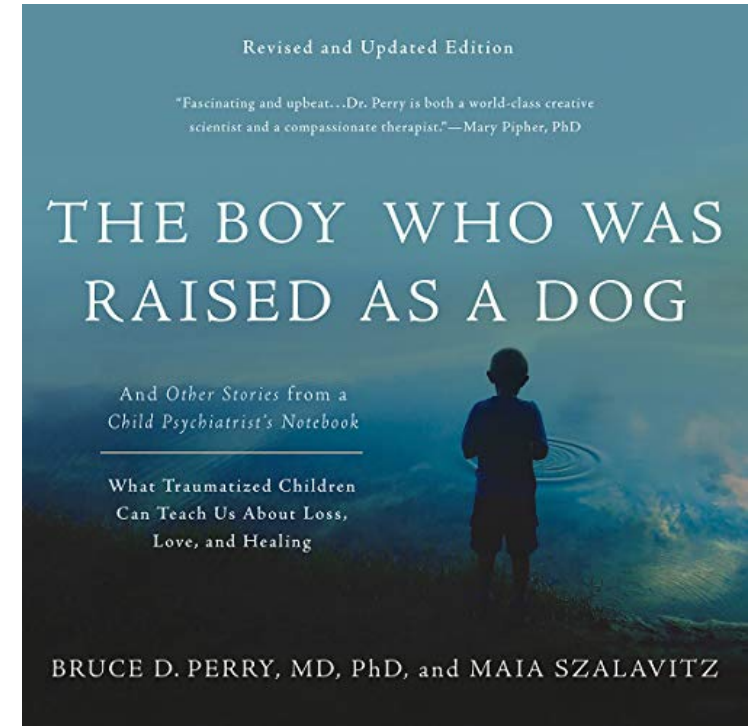
- Epigenetics most often denotes changes that affect gene activity and expression, but can also be used to describe any heritable phenotypic change.
- Such effects on cellular and physiological phenotypic traits may result from external or environmental factors, or be part of normal development.
- The standard definition of epigenetics requires these alterations to be heritable, in the progeny of either cells or organisms.

Psychological Epigenetics

- The following have been shown to have effects that can affect subsequent generations:
 - Early life stress
 - Addiction
 - Anxiety
 - Depression
 - Fear conditioning

The Boy Who Was Raised As a Dog

- Dr Bruce Perry
- The effect of trauma on development and intergenerational consequences
- Major trauma can be caused by the combination of:
 - Housing insecurity
 - Food insecurity
 - Racist taunts



Metabolic syndrome

- Condition characterized by a special constellation of reversible major risk factors for cardiovascular disease and type 2 diabetes.
- The main diagnostic components are:
 - Reduced HDL-cholesterol
 - Raised triglycerides, blood pressure and fasting blood glucose
- Related to weight gain, specifically intra-abdominal/ectopic fat
 - Increased waist circumference
- Affects 30-40% of people by age 65 driven by adult weight gain and
 - Genetic or epigenetic predisposition to abdominal fat accumulation
 - Related to poor intrauterine growth
- Doubles the risk of cardiovascular disease

Metabolic Syndrome

- Promoted by lack of:
 - Subcutaneous adipose tissue
 - Low skeletal muscle mass
 - Anti-retroviral drugs
- Remedied by weight loss
 - 5-10% is sufficient in many cases
 - Exercise increases muscle mass, reduces LDL, triglycerides, increases HDL
 - Bariatric surgery (BMI > 40)

Multimorbidity

- Major issue with application of research derived in populations without multimorbidity which is common in pharmaceutical trials
- In a study in NSW hospitals
 - Aboriginal people are 2.5 times more likely:
 - To have more than one chronic condition
 - To die within 12 months

Multimorbidity

Challenges for people with multimorbidity include:

- Communication with health professionals
 - Involvement in decision making
 - Coordination of care
 - Burden of disease
 - Focus on continuing care
-
- Probably the major opportunity for Precision Medicine



Poverty

Table S8.4: Age-specific total burden (DALY) rates, by life stage and socioeconomic group, 2015

Socioeconomic group	Age group (years)				
	Under 15	15–44	45–64	65–84	85+
1 (Lowest)	70.2	137.0	288.0	572.5	1,078.7
2	60.2	126.8	255.7	538.5	1,084.4
3	53.5	118.4	228.5	493.8	1,034.4
4	50.3	99.9	194.6	459.6	1,025.7
5 (Highest)	42.3	85.2	166.1	406.8	982.1

Note: DALY rate is expressed as DALY per 1,000 population.

39% of the gap between Indigenous and non-Indigenous health can be explained through social determinants

Poverty

Table S8.5: Age-standardised total burden (DALY) rates, selected diseases, by socioeconomic group, 2015

Disease	Socioeconomic group					
	1 (Lowest)	2	3	4	5 (Highest)	
Anxiety disorders	10.5	7.1	6.2	6.8	6.8	5.1
Coronary heart disease	20	15.5	13.5	11.5	9.8	8.5
Chronic kidney disease	5.2	3.0	2.4	2.0	1.6	1.3
COPD		8.4	7.4	6.5	6.1	5.1
Dementia		6.0	6.3	6.1	5.8	6
Depressive disorders	10.6	6.0	7.0	6.6	5.4	4
Lung cancer		7.5	6.9	5.8	4.8	3.8
Stroke		5.3	5.1	4.5	4.1	3.8
Suicide & self-inflicted injuries	8.7	7.1	6.0	6.3	5.1	4.3
Type 2 diabetes	9.2	5.7	4.0	3.9	3.0	2.3

Note: DALY rate is expressed as DALY per 1,000 population.

Poverty

Table S8.6: DALY age-standardised rate (DALY per 1,000 population) for risk factors, by socioeconomic group, 2015

Risk factor	Socioeconomic group				
	1 (Lowest)	2	3	4	5 (Highest)
Tobacco use	24.3	19.9	15.8	13.0	9.2
Overweight & obesity	20.4	16.6	14.9	12.6	10.1
Dietary risks	17.4	14.5	12.3	10.5	8.5
High blood pressure	12.5	11.3	9.6	8.4	7.3
Alcohol use	11.2	10.1	8.5	7.6	6.2
High blood plasma glucose	12.3	8.6	8.3	6.5	5.1
Illicit drug use	7.1	7.2	5.7	4.3	3.1
High cholesterol	7.0	6.0	5.0	4.2	3.7
Physical inactivity	5.7	4.8	4.3	3.7	3.1
Occupational exposures & hazards	4.4	4.1	3.6	3.1	2.7
Impaired kidney function	4.5	3.7	3.2	2.7	2.1
Intimate partner violence	2.0	1.8	1.6	1.4	0.8

Note: DALY rate is expressed as DALY per 1,000 population.

Site of Residence

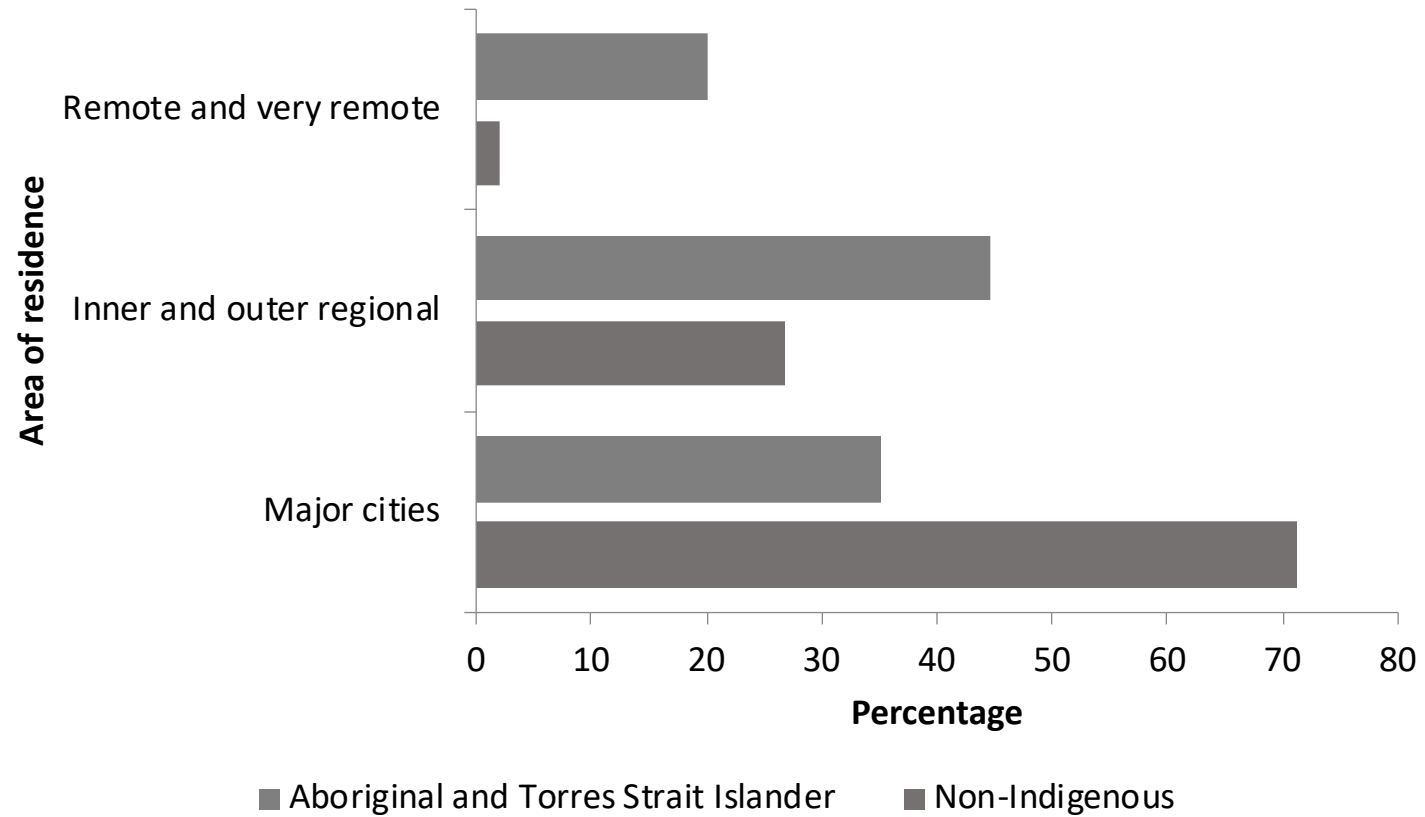




Figure 2.1.3 Number of notifications of hepatitis C infection, 2017, by Indigenous status, age and sex

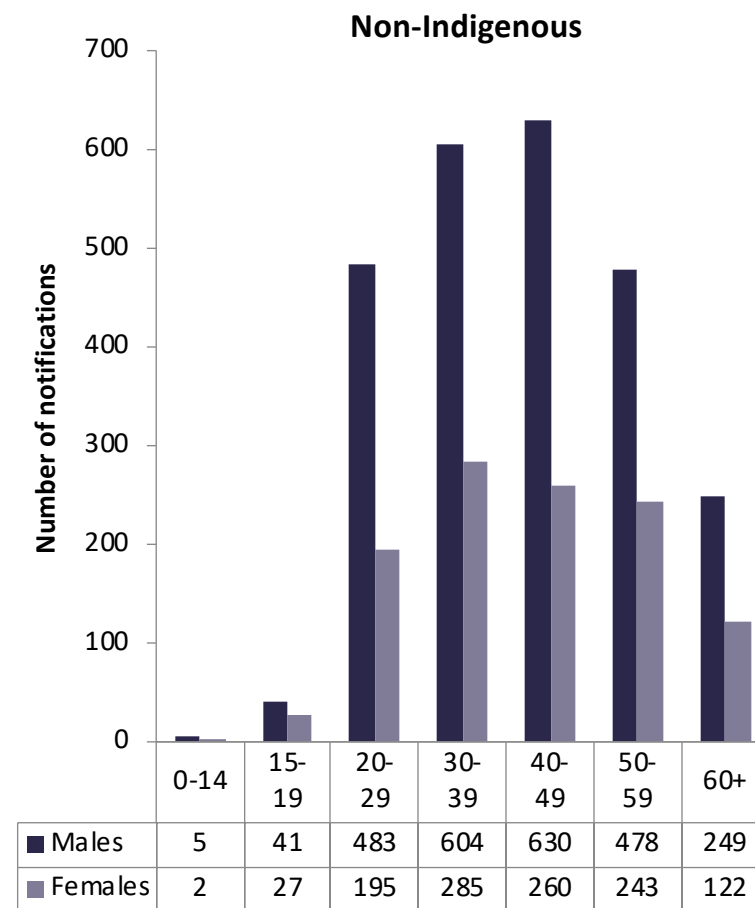
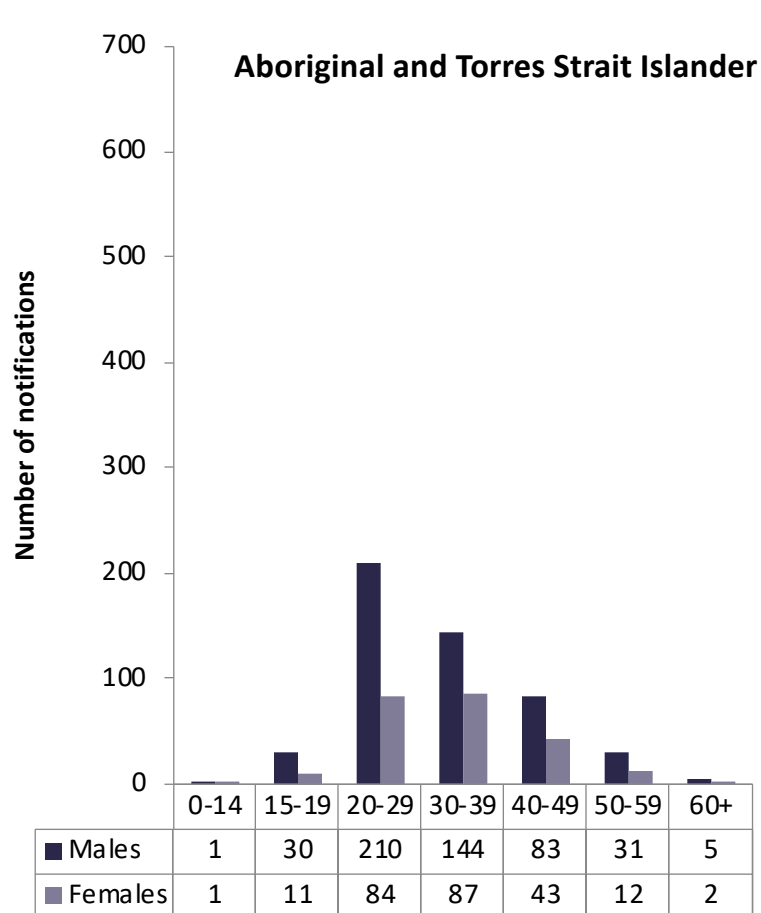


Figure 2.1.4 Hepatitis C notification rate per 100 000 population, 2017, by Indigenous status, sex and age group

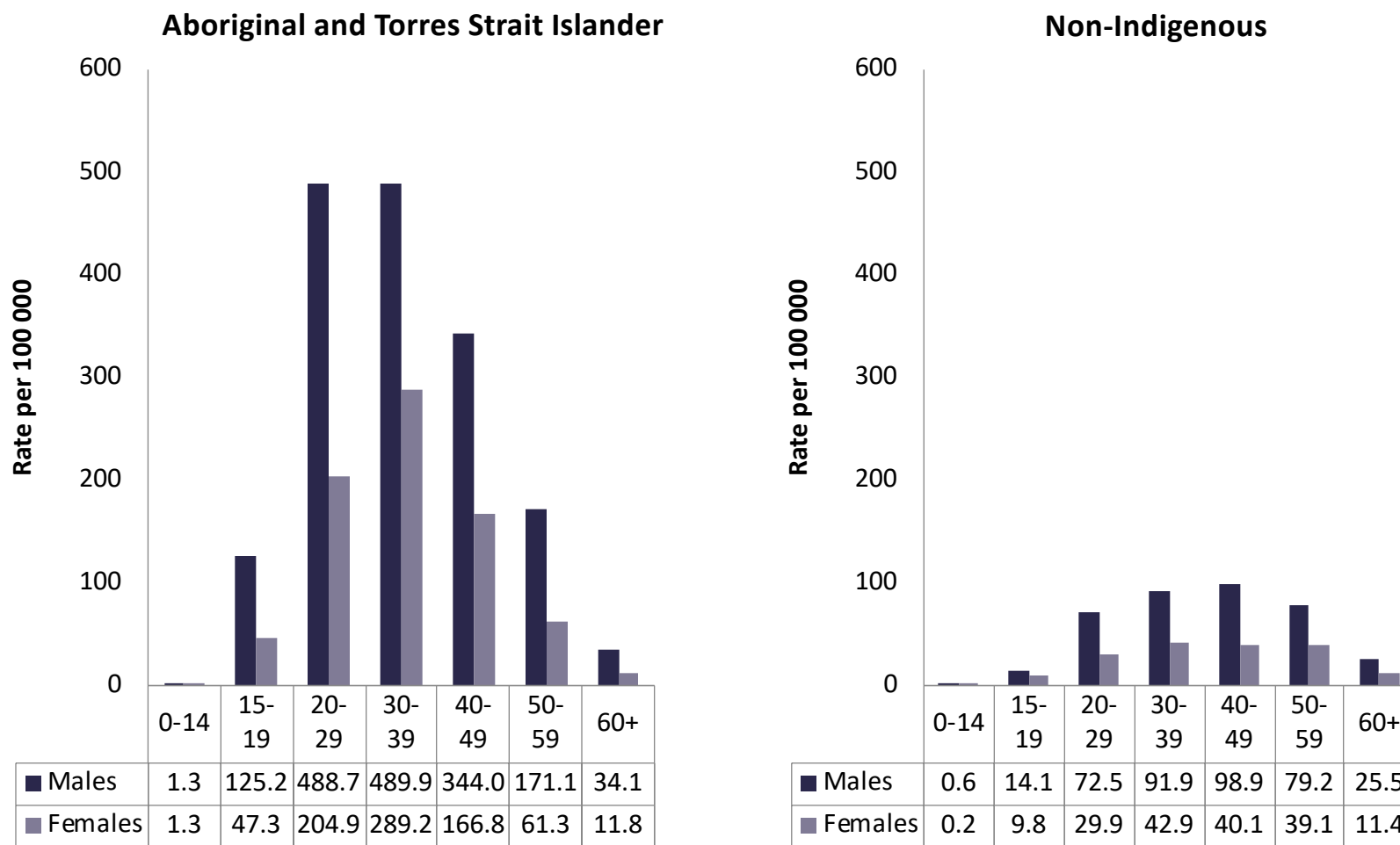
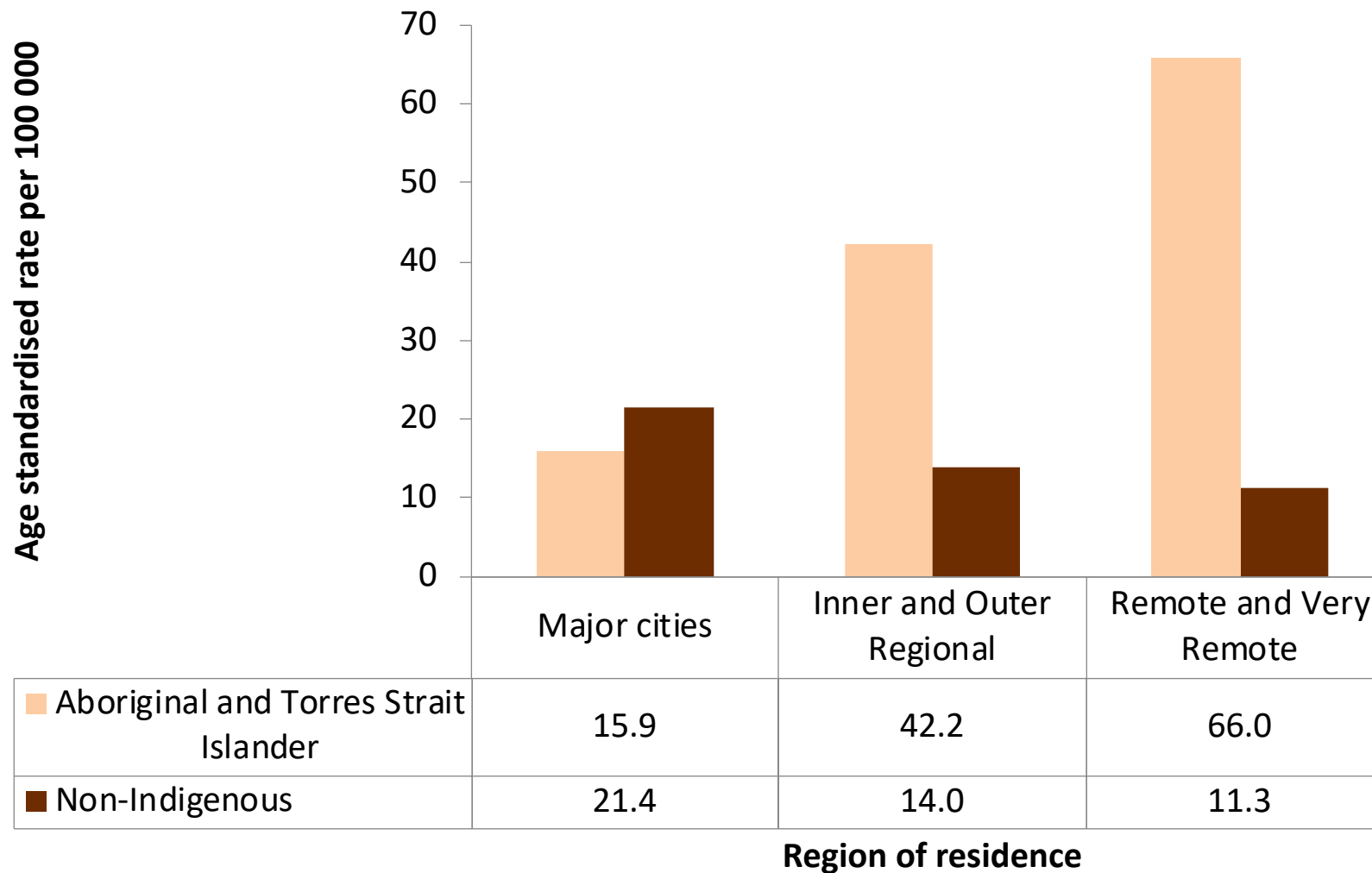


Figure 2.1.8 Hepatitis C notification rate per 100 000 population, 2017, by Indigenous status and area of residence



Figure 3.1.7 Hepatitis B notification rate per 100 000 population, 2017, by Indigenous status and area of residence



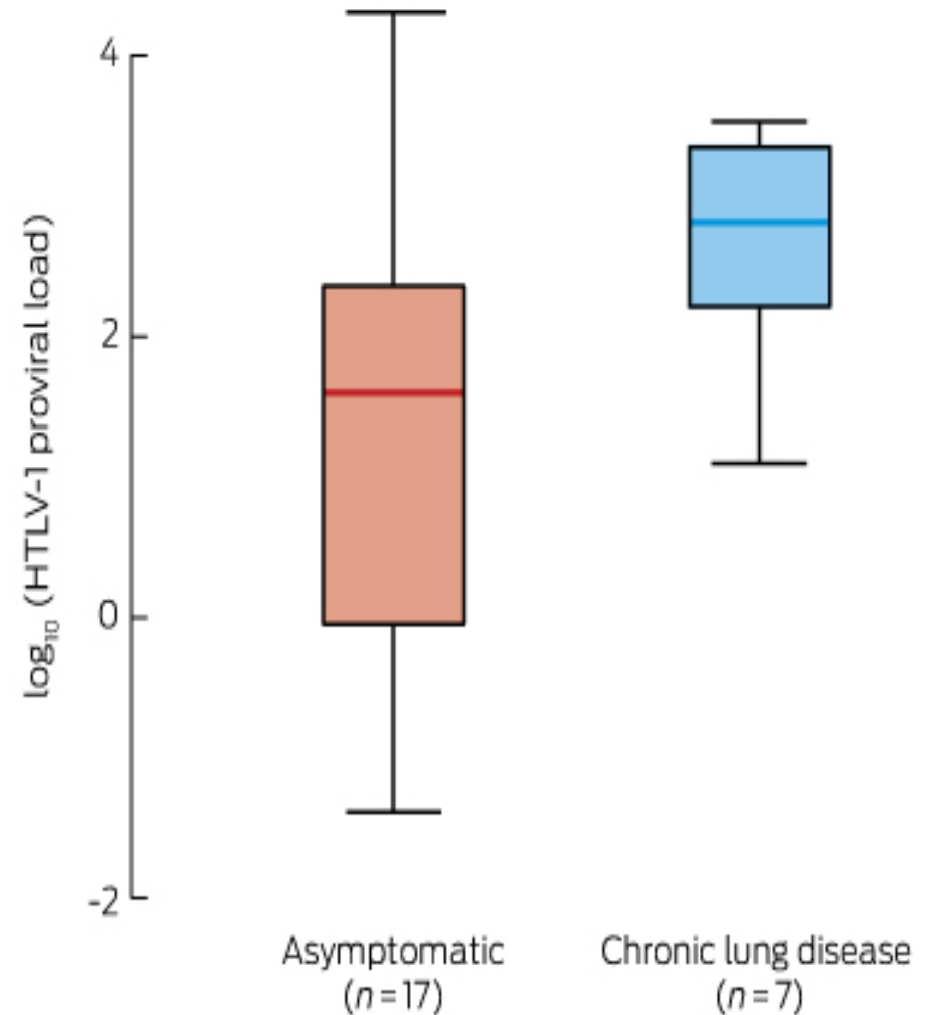
Human T-cell Leukaemic virus type 1

- Retrovirus of the human T-lymphotropic virus (HTLV) family
- 5-10million world wide: Southern Japan, Caribbean, Tropical Africa
- Implicated in:
 - very aggressive adult T-cell lymphoma (ATL)
 - Progressive myelopathy (Tropical Spastic Paresis)
 - Uveitis
 - Strongyloides stercoralis hyper-infection

International experience suggests about 1–5% of infected persons develop cancer as a result of the infection with HTLV-I over their lifetimes.

HTLV1

- First reported in Central Australia in 1988
- Greater than 30% of Aboriginal adults admitted to Alice Springs Hospital
- Similar to southern Japan
- HTLV1c – specific subtype
- Bronchiectasis
- Crusted Scabies



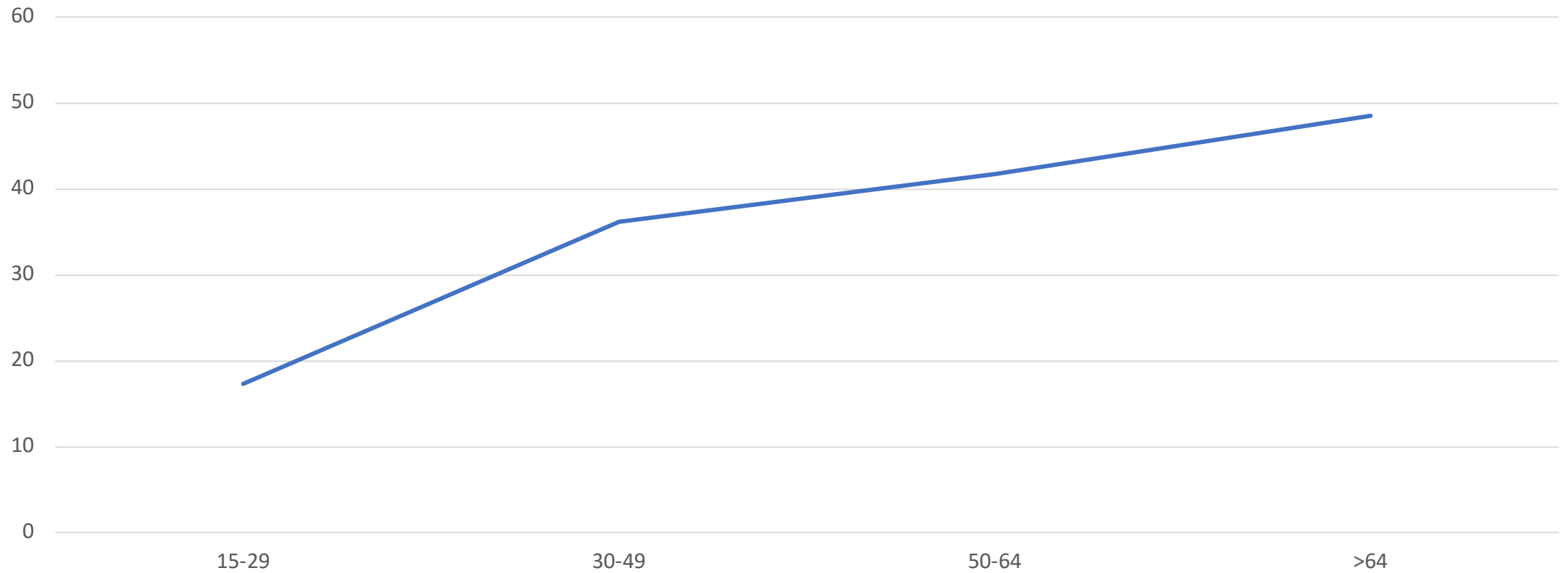
HTLV1

Dr Lloyd Einsiedel

“There is irrevocable evidence that the transmission of HTLV-1 could also be averted. For example, the implementation of universal antenatal care HTLV-1 screening and avoidance of breast feeding in Japan has reduced the HTLV-1 prevalence from 20% to 2.5% since 1987” ASHM Report 2018

Prevalence Rates

Prevalence % by Age Group



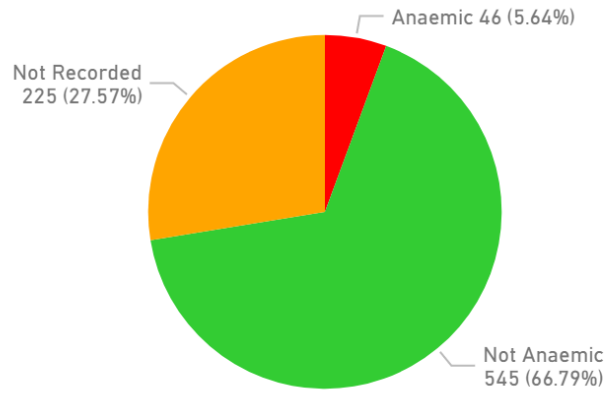


Precision Medicine and Iron Deficiency

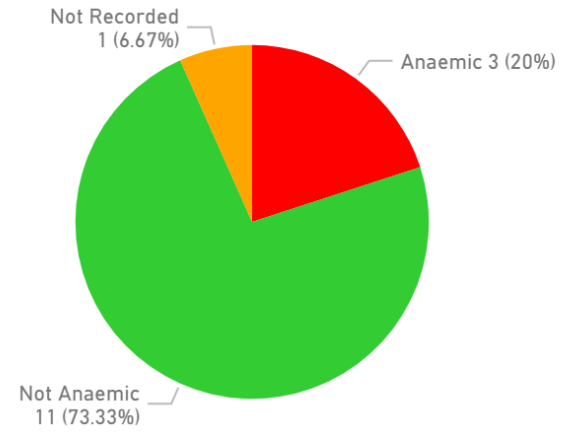
- High Rates of Iron Deficiency ~ 40%
- Expressed as Anaemia
- Concern about:
 - Developmental delay
 - Infections
 - Growth

Last Updated
31/08/2019

A Anaemia

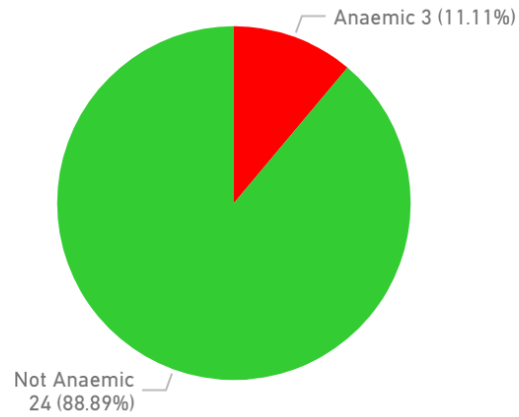


B Anaemia

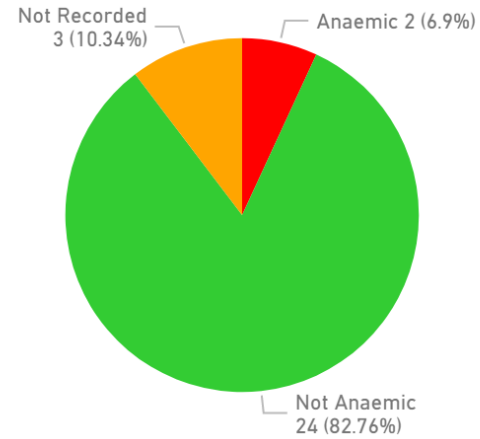


Anaemia Rates for children aged 6 months - 2 years (reflects a Hb test in the past 12 months as per the NTKPI definition)

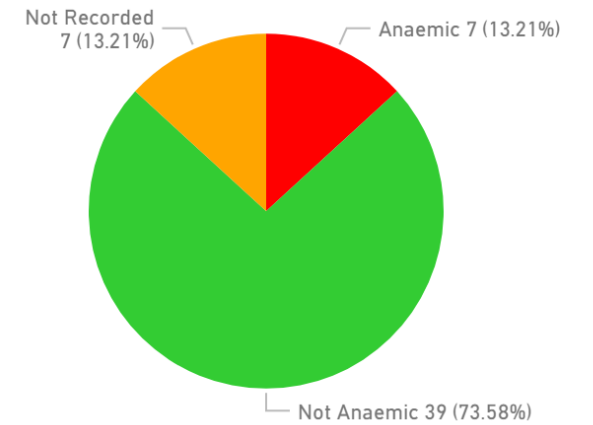
C Anaemia



D Anaemia



E Anaemia



Anaemia or Iron Deficiency

- Treatment protocols for children
 - Not acceptable for clinicians in mainstream
 - Staining/painful
 - Persisting with ineffective oral treatments
- Treatment for pregnant women with Iron Infusion
- Remove “infusion pumps”
- Change to anaemia indicates iron deficiency

Kidney Disease

- 400 people on Dialysis
- the wonderful Purple House, taking dialysis out bush

Dr Christine Jeffries-Stokes was a chief investigator for the Western Desert Kidney Health Project

- 5 Western Desert Indigenous communities and 5 towns in WA's Goldfields
- 1,000 people screened for type 2 diabetes and renal disease over three years
- Aboriginal participants 35% microalbuminuria
- non-Aboriginal participants 26% microalbuminuria

