

Gunbalanya-Kakadu disease cluster investigation.

Final Report

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Acronyms	Full form
ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
CDR	Chronic Disease Register
CHC	Community Health Centre
CIP	Community Informant Panel
G-K	Gunbalanya-Kakadu
HGA Pap test	High-grade Abnormal Papanicolaou test
HPV	Human Papillomavirus
NT	Northern Territory
OSS	Office of the Supervising Scientist
PCIS	Primary Care Information System
PDC	Perinatal Data Collection
PTR	Pap Test Register
SGA	Small for Gestational Age
SIR	Standardised Incidence Ratio
SNAPE	Smoking, Nutrition, Alcohol, Physical active, Emotional assessments

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- Australian Radiation Protection and Nuclear Safety Agency (ARPANSA)
- NT Department of Primary Industry and Resources (formerly the Department of Mines and Energy)
- Energy Resources of Australia
- NT Public Health Network
- Aboriginal Medical Services Alliance of the Northern Territory
- Red Lily Health Board
- Alligator Rivers Region Advisory Committee
- Alligator Rivers Region Technical Committee
- NT Registry of Births, Deaths and Marriages
- Gundjeihmi Aboriginal Corporation
- Northern Land Council
- Jabiru Community Health Centre
- Gunbalanya Community Health Centre
- Public Health Association of Australia, NT Branch
- Independent reviewers Professor Bruce Armstrong and Professor Elizabeth Sullivan

2. Overview

In October 2014 the operators of the Ranger uranium mine, Energy Resources of Australia, lodged a Draft Environmental Impact Statement with the Northern Territory (NT) Environment Protection Authority and the Commonwealth Department of the Environment for their proposal to expand the open-cut Ranger mine by commencing underground mining. Concern had previously been expressed that cancer incidence might be higher than expected in the Aboriginal population living in the vicinity of the Ranger mine. Consequently, the NT Department of Health prepared a submission to the Environment Protection Authority's assessment of the Draft Environmental Impact Statement about cancer incidence and fetal deaths (stillbirth - weighing at least 400 grams or having a gestational age of 20 weeks or more) for the Aboriginal population of the Gunbalanya-Kakadu (G-K) area. This report found that the fetal death rate and the incidence of head and neck cancers, lung cancer and all-cancers combined were higher for Aboriginal residents of the G-K area than for the rest of the Aboriginal population of the Top End of the NT.

In response to this finding, the NT Chief Health Officer initiated a disease cluster investigation to investigate cancer incidence and the fetal death rate more rigorously and, if excess rates were confirmed, to investigate the causes of this disease cluster. The 2014 report that was submitted to the Environment Protection Authority was designated as Stage One of the cluster investigation.

Stage Two of the cluster investigation consisted of a retrospective cohort study of long-term Aboriginal residents of the G-K area, to measure cancer incidence and the fetal death rate in people who were known to be long-term residents of the area for most of the period 1991-2014. A cohort of Aboriginal people who had lived in Jabiru, the surrounding Kakadu National Park, Gunbalanya or its outstations for more than 50% of the period 1991-2014 was established using data from several Department of Health administrative and clinical data sources. Residential status was verified by senior Aboriginal community informant panels in the relevant communities. This cohort was then matched to the NT Cancer Register to ascertain cases of cancer in cohort members and matched to the Perinatal Data Collection to ascertain cases of fetal and neonatal death in babies born to women in the cohort. Cancer incidence and fetal death rates were calculated for the cohort and compared to the Aboriginal population of the Top End (excluding cohort members). This cohort study confirmed the findings of Stage One that cancer incidence and the fetal death rate were higher than expected in the G-K cohort.

Stage Three consisted of three components:

- 3.1 a study of the prevalence of risk factors for fetal death for births to G-K cohort members compared to births to other Aboriginal women resident in the Top End;
- 3.2 a study of the prevalence of risk factors for cancer in adult members of the G-K cohort compared to other Aboriginal adults in the Top End; and
- 3.3 a 'worst-case scenario' study of the possible excess of cancers that could have arisen in this population if it had been continuously exposed to maximum levels of environmental ionising radiation in the area (based on long-term monitoring by the Office of the Supervising Scientist).

Study 3.1 found that the prevalence of three fetal death risk factors was higher than expected for G-K births. Smoking prevalence was 12% higher for G-K than comparison births, but this explained only a very small part of the excess fetal deaths in G-K births. The prevalence of first birth was 13% higher for G-K than comparison births, but this did not explain any of the excess of fetal deaths. The prevalence of small for gestational age (SGA) in live births was 33% higher for G-K than comparison births; the contribution of

higher SGA prevalence to the excess of fetal deaths could not be investigated because fetal death before the onset of labour can reduce the weight of the fetus and data on fetal weight before fetal death was not available.

Study 3.2 found that the prevalence of several cancer risk factors was higher than expected in the G-K population, but that this higher prevalence did not explain any of their higher cancer incidence. This somewhat surprising lack of association of cancer incidence in the G-K population with their higher exposure to smoking and alcohol than the comparator population could have been due to the small size of the G-K population and, in consequence, the comparatively small number of cancers observed in it, and the comparatively short period of follow-up time remaining after the risk factor data became available. That is, Study 3.2 had insufficient statistical power to observe other than a very strong relationship between known risk factors for cancer and cancers known to be associated with those risk factors.

Study 3.3 found that the level of environmental radiation exposure under the worst-case scenario would have produced a very small increase in cancer incidence compared to a population exposed to average levels of environmental radiation. Even under the worst-case scenario, exposure to environmental ionizing radiation, including any originating in the mine, could explain little, if any, of the higher incidence of cancers in the G-K population.

In summary, the G-K cluster investigation has confirmed that the fetal death rate and the incidence of all-cancers combined, head and neck cancers and lung cancer was higher than expected when compared to the Top End Aboriginal population excluding cohort members. Lower birthweight (i.e. higher SGA prevalence) might explain part of this excess but this could not be directly investigated, and higher prevalence of smoking might explain a small part of the excess. There was evidence that the fetal death rate for G-K births decreased between 1991 and 2014 by a similar amount to the decrease for comparison births (about 38%). No certain explanation for the higher incidence of cancers was found. The incidence of lung cancer and head and neck cancers is higher for Aboriginal than other Australians, and particularly for Aboriginal people where smoking prevalence is very high. The investigation found that the prevalence of alcohol consumption and smoking was even higher for the G-K cohort than for Aboriginal people elsewhere in the Top End. While these differences could explain the higher incidence of lung cancer and head and neck cancers in the G-K population, our limited capacity to adjust for these differences did not suggest that they did. A worst-case-scenario estimate of exposure of members of the G-K population to ionising radiation suggested that little if any of the increased risk of cancer in this population could be explained by ionising radiation originating in the mine. Notwithstanding the lack of evidence that higher prevalence of smoking and alcohol consumption explained the excess of cancers in the G-K population, reduction in alcohol consumption and smoking should reduce the incidence of these and several other cancers in this population and have other positive health effects such as reducing the incidence of cardiac and respiratory disease.

This investigation has only partially explained the higher incidence of fetal deaths and has not explained the higher incidence of cancers in the G-K population. However, high levels of smoking and alcohol consumption in this population point to actions that could be taken to improve the overall health of the G-K population that would continue the decline in fetal death rates and decrease cancer incidence.

3. Background

This investigation was initiated by the NT Chief Health Officer under the provisions of the Public and Environmental Health Act to investigate a potentially serious public health issue, namely a finding that all-cancer incidence and the fetal death rate were higher for Aboriginal residents of the G-K area than for the rest of the Aboriginal population of the Top End of the NT.⁽¹⁾ This finding was the result of an analysis undertaken by the NT Department of Health for a submission to the NT Environment Protection Authority in relation to the assessment of the Draft Environmental Impact Statement for the proposed extension of the Ranger uranium mine in Kakadu National Park.⁽²⁾

Concern about excessive cancer incidence in the G-K Aboriginal population was first raised by Professor Colin Tatz in 2006.⁽³⁾ When approval for the Ranger mine was being considered in the late 1970s, Professor Tatz led a project investigating the potential social impact of the proposed mine on the Aboriginal population of the area. In 1978 the Australian Government commissioned the Australian Institute of Aboriginal and Torres Strait Islander Studies to undertake this project. In 1984 the final report of the Uranium Impact Project Steering Committee, which oversaw the social impact study, recommended the establishment of permanent monitoring of the social impact of the mine.⁽⁴⁾ The Australian Government supported the recommendation but did not fund the monitoring process. In 2004 Professor Tatz looked into whether the social impact of the mine could be investigated retrospectively. Suitable existing data sources were limited, but analysis of data from the NT Cancer Register found that the incidence of all-cancers combined in 1994-2003 was higher for the Aboriginal population living in the area around the Ranger uranium mine (the Kakadu national park including the town of Jabiru and the nearby Gunbalanya community) than for the NT total Aboriginal population.

Cancer incidence is higher in the Top End than Central Australian Aboriginal populations, consistent with the higher prevalence of smoking in the Top End than Central Australia.⁽⁵⁾ The NT Department of Health therefore compared cancer incidence for G-K Aboriginal residents with other Aboriginal residents of the Top End of the NT. This analysis found that there was no strong evidence that all-cancer incidence was higher for the G-K Aboriginal population when compared to other Top End Aboriginal residents; in 2011 the Department of Health repeated this analysis with similar results.¹

In October 2014 the operators of the Ranger uranium mine, Energy Resources of Australia, lodged a Draft Environmental Impact Statement (2) with the NT Environment Protection Authority and the Commonwealth Department of the Environment for their proposal to expand the open-cut Ranger mine by commencing underground mining (named the 'Ranger 3 Deeps' mine). Because of the previous concerns about cancer incidence in the G-K population, the NT Department of Health repeated the analysis of cancer incidence (for the period 1991-2011), as part of a submission to the NT Environment Protection Authority's assessment of the Ranger 3 Deeps Draft Environmental Impact Statement. This analysis found that there was now evidence of an excess of all cancers combined and of all head and neck cancers combined, but not of any specific cancer site, in the Aboriginal population of the G-K area.

The 2014 analysis also found evidence of an excess of fetal deaths (also known as stillbirths) to Aboriginal women living in the G-K area during this period. Fetal deaths were investigated because of the potential link between exposure to environmental ionizing radiation and increased risk of congenital malformations

¹ Unpublished departmental documents.

in babies. At the time there was no data source about congenital malformations in babies born in the NT, so the occurrence of fetal deaths was investigated as a less specific indicator for which reliable data was available, while recognising that risk of fetal death is not directly related to environmental radiation exposure.

The data sources available for this analysis (the NT Cancer Register and the NT Perinatal Data Collection) could only classify place of residence at the time of the cancer diagnosis or the birth; they could not identify long-term residents of the G-K area. They were not designed for long-term monitoring of health status of small populations within the NT or for monitoring of potentially harmful exposures that might cause particular health problems. Consequently, the 2014 study might have missed cases in long-term G-K residents because their place of residence was recorded in the Cancer Register and Perinatal Data Collection as being elsewhere in the NT, perhaps because they were temporarily living elsewhere or because an error was made when recording place of residence. Conversely, the 2014 study might have included short-term residents or visitors as G-K residents because they were temporarily living in the G-K area at the time of the cancer diagnosis or fetal death.

As a result of the 2014 study, the NT Chief Health Officer commissioned this disease cluster investigation. The investigation was conducted in three stages:

1. The 2014 study of cancer incidence and fetal death rate was designated as **Stage One**.
2. **Stage Two** aimed to assess cancer incidence and the fetal death rate in long-term residents of the G-K area more rigorously than could be done in Stage One, by:
 - a. establishing a cohort of long-term residents of the G-K area
 - b. ascertaining all cancer cases diagnosed in, and births to, members of this G-K cohort by linking the cohort to the NT Cancer Register and the NT Perinatal Data Collection.
 - c. Calculating cancer incidence (for all cancers combined and for specific cancer sites) and the fetal death rate in the G-K cohort for the period 1991-2014
 - d. Comparing cancer incidence and the fetal death rate for the G-K cohort to that for a comparison population, the Aboriginal population of the Top End of the NT excluding the G-K cohort members.
3. After Stage Two confirmed the findings of Stage One, **Stage Three** aimed to investigate the cause of the excess of cancers and fetal deaths by:
 - a. A study comparing the prevalence of cancer risk factors for the G-K cohort with that for other Aboriginal residents of the Top End.
 - b. A study comparing the prevalence of fetal death risk factors for the G-K cohort with that for other Aboriginal residents of the Top End.
 - c. A 'worst-case scenario' study of the potential excess of cancers that could have been produced by environmental radiation exposure to long-term residents of the G-K area who had been continuously exposed to the highest plausible levels of environmental ionising radiation in this area, which included any exposure from the Ranger mine.

The investigation was conducted by epidemiologists within the Innovation and Research Branch (previously the Health Gains Planning Branch) of the NT Department of Health. The study protocols and reports for each stage were reviewed by independent experts engaged by the Department: Professor Bruce Armstrong, one of Australia's most experienced cancer epidemiologist was the overall project

reviewer; and Professor Elizabeth Sullivan, one of Australia's leading perinatal epidemiologists, was the specialist reviewer for the fetal death components of Stages Two and Three.

This report summarises the overall disease cluster investigation. More details about each stage of the investigation, including study protocols and reports of the conduct and findings of each stage, are available in separate reports for each stage.

4. Investigation Team

An investigation team was assembled consisting of staff members from the Innovation and Research Branch (formerly Health Gains Planning Branch), NT Department of Health:

- Dr Steven Guthridge (Investigation leader), Director, Health Gains Planning Branch
- Professor John Condon, Medical Epidemiologist
- Mark Ramjan, Investigation Project Officer
- Jonathon Hall, Research Officer/Epidemiologist
- Dr Xiaohua Zhang, Health Economist
- Dr Nick Georges, Public Health Registrar
- Shu Qin Li, Senior Epidemiologist
- Fiona Johnson, Epidemiologist
- Natrisha Barnett, Health Economist

Independent reviewers

Suitably qualified cancer and perinatal epidemiologists, who are experts in cancer and fetal death cluster investigations, were appointed to independently review the project:

- Professor Bruce Armstrong, overall project reviewer, appointed on 11/11/2016
Consultant – Environmental Epidemiology, Environmental Health and Health Services
Adjunct Professor, School of Population Health, The University of Western Australia, and
Emeritus Professor, School of Public Health, The University of Sydney.
- Professor Elizabeth Sullivan, specialist reviewer for perinatal epidemiology, appointed 1/8/2017
Consultant - Medical Epidemiologist, perinatal, maternal, sexual and reproductive health
Professor of Public Health and Deputy Head, Faculty of Health and Medicine,
University of Newcastle.

The independent reviewers analysed the scope, design and conduct of the investigation and provided advice on the following aspects of the investigation:

- project design and implementation,
- data analysis and interpretation,
- implications of findings.

Investigation Stakeholder Group

To ensure transparency of the investigation, a key stakeholder group was established in order to keep stakeholders informed of progress of the investigation, and to provide an opportunity for stakeholders to raise questions, discuss and have input into the investigation process. The Chief Health Officer of the NT Department of Health chaired the stakeholder meetings. Stakeholder meetings were held on 16 February 2017, 26 May 2017 with a final meeting planned for early 2020 to consider the final report.

Feedback during the project was also provided to the Red Lily Health Board and the Alligator Rivers Regional Advisory Committee.

Table 1 Members of the stakeholder group

Name	Title	Organisation
Hugh Heggie	Chief Health Officer	NT Department of Health
Steven Guthridge	Director, Health Gains Planning	NT Department of Health
Stephanie Miller	Manager of Health, Safety, Environment, Communities & Water	Energy Resources of Australia Ltd, Jabiru
Forrest Egerton	A/General Manager, Operations	Energy Resources of Australia Ltd, Jabiru
Rhonda Powell	Assistant General Manager, Top End Health Services	NT Department of Health
Che Doering	Senior Research Scientist / Team Leader	Commonwealth Department of the Environment and Energy
Rick Van Dam	Senior Principal Research Scientist/ Director	Commonwealth Department of the Environment and Energy
Keith Tayler	A/Assistant Secretary Supervising Scientist Branch (Northern Territory)	Commonwealth Department of the Environment and Energy
Tania Dhu	Manager, Geophysics and Remote Sensing	NT Geological Survey, Department of Mines and Energy
Bruce Armstrong	Independent Reviewer	Consultant
John Condon	Investigation Project Manager	NT Department of Health
Justin O'Brien	Chief Executive Officer	Gundjeihmi Aboriginal Corporation
Andrew Bell	Remote Medical Practitioner Gunbalanya, Medical Advisor to Red Lily Health Board	NT Department of Health
Joanne Carroll	Transitional Manager, Red Lily Health Board	Aboriginal Medical Services Alliance of the Northern Territory
Mark Ramjan	Investigation Project Officer	NT Department of Health
Reuben Cooper	Chair	Red Lily Health Board
Michael Fonda	Representative	Public Health Association of Australia, NT Branch
Colin Tatz	Professor of Politics (retired)	Previously Australian Institute of Aboriginal and Torres Strait Islander Studies.

5. History and population of the Gunbalanya-Kakadu region

Aboriginal people have lived in the G-K area for tens of thousands of years with little contact with people from other parts of the world. Makassan sailors from the southwest corner of Sulawesi, Indonesia, visited the coast of northern Australia to collect and process trepang from the eighteenth century until the trade was banned in 1907.(6) Goods were exchanged from the Macassans with Aboriginal people, with the Macassans trading goods such as tobacco, cloth, axes, steel knives and dugout canoes.(7) Europeans colonised eastern Australia in the late 1700s. Colonisation of the Northern Territory occurred almost 100 years later with the establishment of Darwin in 1869, after four failed attempts to establish colonies on the north coast from 1824 including one in 1827 at Raffles Bay on the Coburg Peninsula north of Gunbalanya.

There was only sporadic interaction between European colonisers (particularly buffalo hunters) and Aboriginal people in western Arnhem Land until about 1906 when Paddy Cahill (previously a buffalo hunter in the area) took up a pastoral lease at the base of the escarpment country to the east of the East Alligator river. In 1925 Cahill's farm was taken over by the Church of England's Church Missionary Society and became the Oenpelli Mission.(6) In 1974 the Church Missionary Society returned control of the Oenpelli community to Aboriginal people, who subsequently renamed it Gunbalanya (Figure 1). The lifestyle of the Aboriginal people in this region changed significantly over this period of time.

The main language spoken in Gunbalanya is Kunwinjku, which is used by many residents as a first language. The traditional owners of the land where the Gunbalanya community is located are the Mandjurlngunj clan. There are 25 clan groups in Gunbalanya in total. Some clans migrated to the Gunbalanya area in the early 1900s to work on buffalo settlements, live in the mission, or to gain access to western goods such as tobacco, flour and sugar.

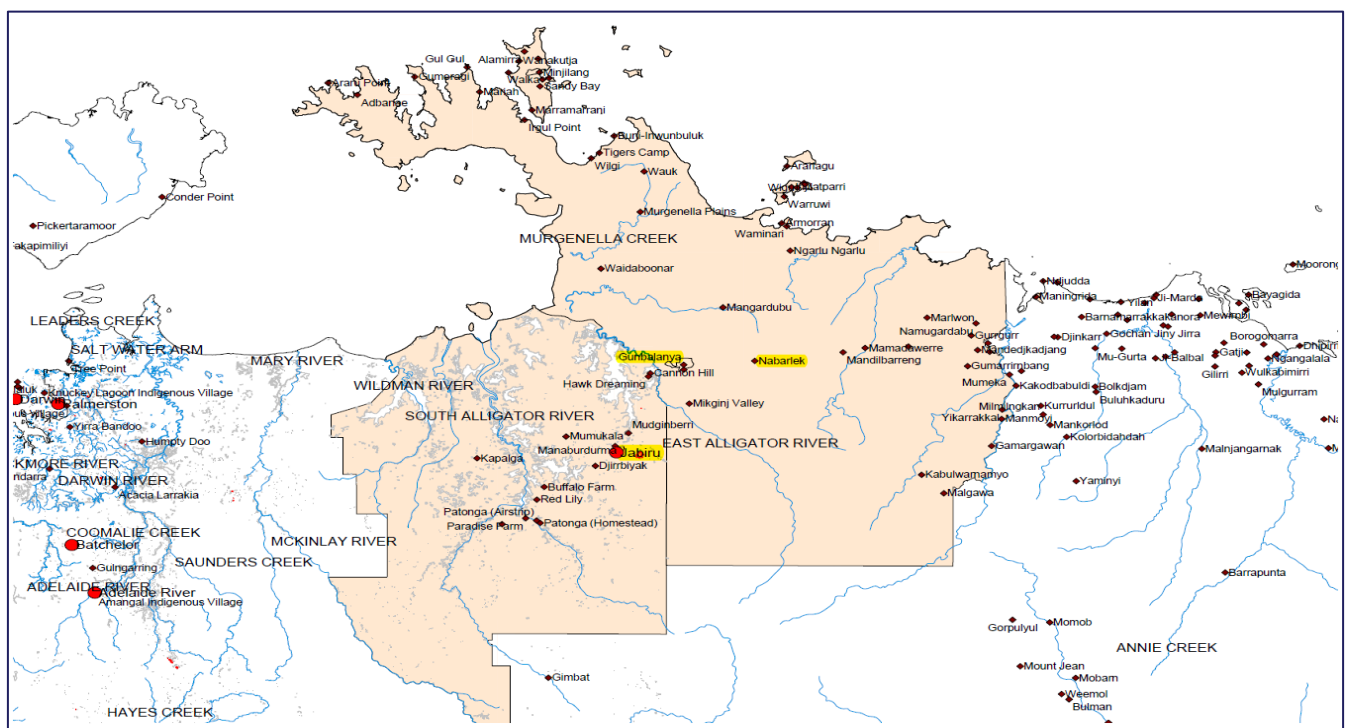


Figure 1 Map of area used to compile Gunbalanya - Kakadu potential long-term residents list.

The Mirarr are the traditional owners of much of the land to the south and west of Gunbalanya, including the sites of the Jabiru township and the Ranger uranium mine.(8) Aboriginal land to the west of the East Alligator River became (with the agreement of Aboriginal leaders) the Kakadu National Park, under the National Parks and Wildlife Conservation Act 1975, in stages commencing in 1979.(9) Aboriginal residents of the Kakadu area live either in Jabiru or in outstations in, or to the north of, the national park.

The first uranium was found in Kakadu at Coronation Hill in 1953. More uranium was found in this region in 1954 and 1956 and small-scale mining began in the years between 1956 and 1964. In 1969-1970 uranium was discovered 30km east of Gunbalanya (at Narbalek) and also 60 km to the south-west at the present location of Jabiru. Queensland Mines Limited commenced mining at Narbalek in 1979 and milling took place through to 1988. Rehabilitation of the mine site was completed in 1995. Mining of the Ranger deposit was also proposed. The Mirarr opposed the mining of uranium on their land, but the 1977 Ranger Uranium Environmental Inquiry (known as the Fox Inquiry) concluded that whilst the development of the mine had the potential for negative environmental and social impact on the region, these impacts could be minimised and the mine development should proceed with safeguards in place.(10) The Inquiry recommended the establishment of a comprehensive system of environmental monitoring and research, overseen by a coordinating committee representing all the agencies involved, and chaired by a supervising scientist. It also recommended the granting of Aboriginal title to a substantial part of the region and the creation of a national park. In 1980 the Ranger uranium mine commenced operation in the northern part of the Kakadu National Park and the town of Jabiru was built to house the workforce for the mine.

Jabiru became the regional centre for the Alligator Rivers region. It is 250km east of Darwin; Gunbalanya lies a further 60km north-east. There are many Aboriginal outstations in and around the Kakadu National Park and to the north and east of Gunbalanya, some permanent and others occupied seasonally. At the 2016 Census the Usual Resident Count of Aboriginal people for Gubalanya was 983 with another 346 in the area to the east and north.(11) For Jabiru, the Usual Resident Count was 263 Aboriginal people with another 217 people in and around the national park. (12) In February 2017 there were 1,394 Aboriginal people listed as usual clients of the Gunbalanya Community Health Centre (CHC) and 510 for Jabiru CHC.²

The non-Aboriginal population of the G-K area is predominantly short-medium term residents associated with the Ranger uranium mine, tourism and associated support services. The Aboriginal population of the area is predominantly a long-term resident population, albeit with a high level of migration between neighbouring communities and the two nearest regional centres (Darwin and Katherine).

² Unpublished source: NT Department of Health, Primary Care Information System Traffic Light Report, Feb. 2017

6. Stage One: cancer incidence and fetal death prevalence in the Gunbalanya-Kakadu Aboriginal population

In the 2014 study, prepared as part of the assessment of the Draft Environmental Impact Statement, population health monitoring data sources were used to compare the occurrence of cancers and fetal deaths for the Aboriginal population of the G-K area with that for the Aboriginal population elsewhere in the Top End of the NT. The population included in this analysis was people living in the town of Jabiru (adjacent to the Ranger uranium mine), the surrounding Kakadu National Park, and the town of Gunbalanya (60 km north-east of the Ranger mine).

Based on the available data sources, there appeared to be an excess of cancers and fetal deaths in the Aboriginal population of the G-K area. The excess of cancers was for all-cancers combined and for lip, mouth and pharynx cancers combined but not for any specific cancer and the overall pattern observed was not consistent with ionising radiation exposure as a cause.

6.1. Observed number and types of cancers

Data on NT residents diagnosed with cancer was obtained from the NT Cancer Register, which is a high quality statutory collection of all cancers diagnosed in NT residents (including cancers diagnosed interstate).⁽¹³⁾ In the Aboriginal population of the G-K area in the 21-year period 1991-2011 there were 79 cases of cancer diagnosed (Table 2). The number of cancer cases diagnosed in the G-K Aboriginal population was compared with the number that would have been expected if the G-K Aboriginal population had the same cancer incidence as the Aboriginal population of the rest of the Top End. In the Aboriginal population of the G-K area in the 21-year period 1991-2011 there were (Table 3):

- no cases of leukaemia and only two cases of lymphoma diagnosed.
- four cases of thyroid cancer diagnosed compared to 1.8 expected cases. Of these four, none were aged less than 20 at the time of diagnosis. The 95% confidence interval for the incidence rate ratio included 1.0 indicating that this excess number of cases could be due to random variation rather than a true excess.³
- 15 cases of lung cancer diagnosed compared to 11.5 expected. Similarly, this excess number of cases could be due to random variation rather than a true excess.
- seven cases of breast cancer diagnosed in females compared to 4.4 expected. This excess number of cases could be due to random variation rather than a true excess. Six of these seven cases were diagnosed in the most recent years (2007-2011).
- 16 cases of cancers of the lip, mouth & pharynx compared to 5.5 expected. With an incidence rate ratio (IRR) of 2.93 and a 95% confidence interval (95%CI) of 1.67 to 4.75, this excess is unlikely to be due to random variation.

There also was a likely true excess of all cancers combined, with 79 cases diagnosed compared to 54.1 expected. The number diagnosed was 48% more than expected (IRR 1.48) and the 95%CI (1.17-1.85) did not include 1.0. The excess was greater for males (60%) than females (33%). For males, there were more cases diagnosed than expected throughout the period 1991-2011, but for females the excess occurred only in recent years (2007-2011) (Table 4).

³ While thyroid cancer can be taken as an indicator of radiation induced cancer, this is only the case when it occurs in childhood. The most recent relevant report on thyroid cancer in atomic bomb survivors found no excess in people aged 20 years or more at the time of the bombing. 14. Furukawa K, Preston D, Funamoto S, Yonehara S, Ito M, Tokuoka S, et al. Long-term trend of thyroid cancer risk among Japanese atomic-bomb survivors: 60 years after exposure. *International Journal of Cancer*. 2012;132:1222-6.

Cancers of the lip, mouth & pharynx were the most common cancers in the G-K area Aboriginal population. These cancers are not considered to be caused by ionising radiation. Specifically, the most recent relevant report on risk of solid cancers in atomic bomb survivors did not find an increased risk of these cancers;(15) nor did the International Agency for Research on Cancer, in its review of all relevant evidence in 2009 find sufficient or limited evidence that ionising radiation caused any of them.(16) A high proportion of these cancers are known to be caused by smoking tobacco and/or alcohol consumption, and some are caused by infection with the Human Papillomavirus. The 10.5 excess cases of lip, mouth and pharynx cancers accounted for 42% of the excess number (24.9 cases) of all cancers combined.

There were no other cancer sites with a high proportion of cases (Table 2): there were five cases of colorectal cancer and four of liver cancer, all other sites had three or less cases diagnosed in the 21-year period.

The study found that the number of cases of all cancers combined was higher than expected and it is unlikely that this excess was due to random variation. This excess, however, was not due to any specific cancer; there were only a small number of cases for each cancer site. Cancers of the lip, mouth and pharynx as a group accounted for 42% of these excess cases; this grouping includes 14 specific sites, some of which are associated with tobacco smoking and alcohol consumption and some with Human Papillomavirus (HPV) infection. 59 of the 79 cancer cases lived in Gunbalanya at the time their cancer was diagnosed. There was no indication of an excess of cancers considered to be associated with exposure to ionising radiation in the G-K Aboriginal population based on cancer registrations data. There were no registered cases of leukaemia or thyroid cancer before 20 years of age and the higher than expected numbers of lung and of breast cancer cases were consistent with random variation in each case.

6.2. Fetal deaths

Data on fetal deaths among babies born in the NT was obtained from the NT Perinatal Data Collection, a statutory collection of information about each pregnancy and birth (not including miscarriages before 20 weeks of gestation) in the NT.(17) Fetal deaths (also known as stillbirths) are defined as the birth of a dead baby that is of 20 or more weeks gestation or has a birth-weight of 400 or more grams.

The fetal death rate for the G-K Aboriginal population was higher than that for the Top End Aboriginal population. In the period 2000-2013 the fetal death rate for the NT Aboriginal population was 13.4 (95%CI 11.8-15.1) fetal deaths per 1000 births (256 fetal deaths in 19,072 total births). In the G-K area for the same period the fetal death rate was 28.7 (13.3-44.1) per 1,000 births (13 fetal deaths in 453 total births). The odds ratio comparing these two fetal death rates was 2.17 (1.13-3.82), indicating that the higher fetal death rate in the G-K Aboriginal population is unlikely to be due to random variation. There may, however, be bias in this result because the Perinatal Data Collection does not distinguish long-term residents of the G-K area from short term residents.

Table 2 Number of cancer cases diagnosed in the Gunbalanya-Kakadu area by site, 1991-2011

Cancer site	Indigenous	Non-Indigenous
Lip, oral cavity & pharynx	16	4
Oesophagus & Stomach	3	2
Colon & rectum	5	7
Anus	0	1
Liver	4	0
Pancreas	3	1
Larynx	1	0
Trachea, bronchus & lung	15	3
Bone	1	0
Melanoma of skin	0	9
Breast	7	6
Vulva	1	0
Cervix uteri	2	0
Uterus	0	1
Penis	1	0
Prostate	1	6
Kidney	0	1
Bladder	0	2
Brain	2	0
Thyroid	4	1
Unknown primary site	8	1
Lymphoma	2	4
Leukaemia	0	2
Others*	3	1
All cancers combined	79	52

Table 3 Gunbalanya-Kakadu area Aboriginal population, observed and expected number of cancer cases for selected sites¹ and all-cancers combined

Cancer site	Observed cases	Expected cases	SIR (95%CI) ²
Trachea, bronchus and lung	15	11.5	1.33 (0.74-2.19)
Breast (female)	7	4.4	1.60 (0.64-3.29)
Thyroid	4	1.8	2.25 (0.61-5.77)
Lip, mouth & pharynx	16	5.5	2.93 (1.67-4.75)
All cancers combined			
Persons	79	54.1	1.48 (1.17-1.85)
Male	44	27.3	1.60 (1.16-2.14)
Female	35	26.3	1.33 (0.94-1.88)

1. Leukaemia was not included because no cases were diagnosed in Aboriginal residents of the Gunbalanya-Kakadu area in 1991-2011.

2. standardised incidence ratio (i.e. ratio of number of observed cases to number expected) and 95% confidence interval

Table 4 Gunbalanya-Kakadu area Aboriginal population, observed and expected number of cancer cases for selected sites¹ and all-cancers combined, by time period

Cancer site	Period	Observed cases	Expected cases	SIR	(95%CI) ²
<i>Trachea, bronchus and lung</i>					
	1991-1996	3	2.9	1.04	(0.21-3.04)
	1997-2001	1	1.6	0.62	(0.02-3.47)
	2002-2006	3	2.7	1.12	(0.23-3.26)
	2007-2011	8	4.4	1.85	(0.80-3.64)
<i>Breast (female)</i>					
	1991-1996	0	0.5	0.00	(0.00-8.04)
	1997-2001	1	0.9	1.14	(0.03-6.37)
	2002-2006	0	1.2	0.00	(0.00-3.00)
	2007-2011	6	1.9	3.22	(1.18-7.01)
<i>Thyroid</i>					
	1991-1996	0	0.4	0.00	(0.00-11.00)
	1997-2001	0	0.3	0.00	(0.00-12.00)
	2002-2006	1	0.6	1.66	(0.04-9.22)
	2007-2011	3	0.6	5.14	(1.06-15.00)
<i>Lip, oral cavity & pharynx</i>					
	1991-1996	1	0.8	1.24	(0.03-6.91)
	1997-2001	2	1.1	1.91	(0.23-6.88)
	2002-2006	7	1.5	4.70	(1.89-9.69)
	2007-2011	6	2.2	2.78	(1.02-6.04)
<i>All cancers combined</i>					
<i>Persons</i>					
	1991-1996	15	10.5	1.43	(0.80-2.36)
	1997-2001	12	9.0	1.34	(0.69-2.33)
	2002-2006	17	13.7	1.24	(0.72-1.99)
	2007-2011	35	20.9	1.68	(1.17-2.33)
<i>Male</i>					
	1991-1996	8	5.2	1.55	(0.67-3.05)
	1997-2001	8	4.6	1.74	(0.75-3.43)
	2002-2006	12	6.2	1.92	(0.99-3.36)
	2007-2011	16	11.3	1.42	(0.81-2.30)
<i>Female</i>					
	1991-1996	7	5.3	1.32	(0.53-2.71)
	1997-2001	4	4.3	0.94	(0.26-2.40)
	2002-2006	5	7.2	0.70	(0.23-1.63)
	2007-2011	19	9.6	1.99	(1.20-3.11)

1. Leukaemia was not included because no cases were diagnosed in Aboriginal residents of the Kakadu and Gunbalanya area in 1991-2011. Note that there were only 3 blood or lymphatic cancers diagnosed in the Gunbalanya-Kakadu cohort (Table 5).

2. standardised incidence ratio (i.e. ratio of number of observed cases to number expected) and 95% confidence interval

7. Stage Two: retrospective cohort study

The purpose of Stage Two was to measure cancer incidence and the fetal death rate in long-term Aboriginal residents of the G-K area (the 'G-K cohort'), and compare them to those of the Aboriginal population of the Top End (excluding the G-K area) more rigorously than was possible in Stage One. Stage Two expanded the investigation of fetal deaths to also include neonatal deaths because the risk factors for neonatal death (the death of a baby in the first 27 completed days after birth) are similar to those for fetal death (the death of a baby of at least 400 grams birthweight or 20 weeks' gestation before or during birth). The combination of fetal and neonatal deaths is referred to as 'perinatal deaths'.

The null hypotheses tested by the Stage Two investigation were:

1. The incidence of all-cancers combined in Aboriginal long-term residents of the G-K area is not greater than that in Aboriginal people living elsewhere in the Top End.
2. The incidence of head and neck cancers and of cancers of other specific sites in Aboriginal long-term residents of the G-K area is not greater than those of Aboriginal people living elsewhere in the Top End.
3. The perinatal death rate for births to Aboriginal women who are long-term residents of the G-K area is not greater than for births to Aboriginal women resident elsewhere in the Top End.

The 'G-K cohort' consisted of Aboriginal people who had lived in the G-K area for more than 50% of the study period (1991-2014), or 50% of their time alive during the study period for those who were born or died during the study period. The G-K cohort was defined as those Aboriginal (including Torres Strait Islander) people who were a resident in the G-K defined area for:

- More than half of the period of time between 1 January 1991 and 31 December 2014, or
- More than half of the person's lifetime if born after 1 January 1991, or:
- For any person who died before 31 December 2014, more than half of the time between 1 January 1991 and their date of death.

The comparison population was the total dynamic Aboriginal population of the Top End (excluding the G-K area), rather than a cohort of individuals.

7.1. G-K retrospective population cohort development

The first component of Stage Two consisted of the establishment of the G-K cohort. The investigation team were unable to locate any historical population records for the G-K area from 1991 onwards. Instead, a list of potential G-K area residents was compiled from Department of Health clinical data sources:

- The hospital inpatient dataset: all persons with any inpatient episodes since 1991 with a place of residence recorded as the West Arnhem area.
- The Perinatal Data Collection: all babies born since 1986 with the mother's place of residence recorded as the West Arnhem area plus all mothers who gave birth since 1986 with place of residence recorded as the West Arnhem area.
- The clinical information system (the Primary Care Information System, PCIS) used in remote Community Health Centres (CHC): all persons with their usual community health centre recorded as one of the four West Arnhem area CHCs.
- The Chronic Disease Registers (CDR) maintained by District Medical Officers until about 2010 (when they were replaced by PCIS): all people with Gunbalanya, Waruwi and Minjilang CHCs as their usual CHC (there was no CDR for Jabiru CHC because District Medical Officers did not work there).

For the purposes of this study and due to population movement for cultural and family reasons, the West Arnhem area included Jabiru and the Kakadu National Park, Gunbalanya, Waruwi, Minjilang and associated outstations. It did not include Maningrida.

The 'potentials' list needed to be very inclusive so that all people who might have been residents of the G-K area since 1991 were included in the list. The residential status of people in the list was confirmed in two ways:

1. Examination of utilisation of primary care services in the four West Arnhem CHCs since 2000, using data from the CDRs and PCIS (from 2010); examination of place of residence recorded at each hospital inpatient episode since 1991, and examination of place of residence recorded in the Perinatal Data Collection since 1986. The potential G-K residents list contained 4,799 persons.
2. The investigation team then worked with senior community members (Community Informant Panels or CIPs), to identify people on the potentials list who met the G-K cohort definition.

At the conclusion of the CIP process, the G-K cohort consisted of 2,228 persons who were assessed by the CIPs as meeting the criteria for long-term Aboriginal residents of the G-K area during the study period. It was later found that there were some duplicate records in the database of potential cohort members considered by the CIPs; the final G-K cohort therefore consisted of 2,216 persons. Further information about the development of the G-K cohort is available in the report on the cohort development process. (18)

After the long-term resident G-K population cohort was identified, cohort members were matched to the NT Cancer Register and the NT Perinatal Data Collection to identify G-K residents diagnosed with cancer or G-K resident women who had suffered a perinatal death. Cancer incidence and the perinatal death rate were then calculated and compared with the Aboriginal population of the Top End of the NT.(19)

7.2. Cancer incidence in the G-K cohort.

Ninety-five members of the G-K cohort were diagnosed with cancer between 1/1/1991 and 31/12/2014 (Table 5). Three of these people were each diagnosed with cancer at two different sites, so that there was a total of 98 cancer cases (Table 6). The number of cases of all cancers combined was 1.8 times higher in the G-K cohort than expected on the basis of cancer incidence rates in the comparison population, and higher than expected for both males and females. The lower bounds of the confidence intervals for the Standardised Incidence Ratios (SIRs) were above 1.0, indicating that the higher than expected number of cases in the G-K cohort was unlikely to be due to random variation in the number of cases in this relatively small cohort.

For specific cancer sites, the number of cases was 3.7 times higher than expected for mouth and throat cancers and 2.2 times higher for lung cancer; the lower bound of the confidence interval of the SIRs was above 1.0 for these cancers. For thyroid and cervix cancers, the number of cases was higher than expected (2.8 and 2.2 times higher respectively) but the lower bounds of the SIR confidence intervals were just below 1.0, indicating that each of these apparently higher rates may have been due to random variation.

The numbers of cases of bowel and breast cancer were also higher than expected (1.5 and 1.2 times higher respectively), but the SIR confidence intervals were wide and included 1.0 indicating that there is no strong evidence that the incidence of these cancers was higher than expected. The incidence of blood and lymphatic cancers was lower than expected.

Table 5 Cancer incidence, all cancers combined and selected cancer sites¹, Gunbalanya-Kakadu cohort (1991-2014)

Site	Number of cases		Ratio ²	(95% CI)
	Observed	Expected		
All cancers ³	95	53.2	1.8	(1.4-2.2)
Male	52	25.6	2.0	(1.5-2.7)
Female	43	27.5	1.6	(1.1-2.1)
Mouth & throat	20	5.5	3.7	(2.2-5.6)
Bowel	5	3.4	1.5	(0.5-3.5)
Lung	25	11.4	2.2	(1.4-3.2)
Breast (female)	7	5.6	1.2	(0.5-2.6)
Cervix	5	2.3	2.2	(0.7-5.1)
Thyroid	5	1.8	2.8	(0.9-6.4)
Blood and lymphatic	3	4.2	0.7	(0.1-2.1)
Other cancer sites	28	19.9	1.4	(0.9-2.0)

1. Cancer sites or site groups with more than five cases in the G-K cohort in the study period (plus blood and lymphatic cancers).
2. Standardised incidence ratio, G-K cohort compared to comparison population.
3. The sum of the number of observed cases for individual cancer sites is greater than the number for all cancers combined because three people had multiple cancers and the number of cases for all cancers combined is the number of persons with one diagnosed cancer (based on their first cancer diagnosis).

Table 6 Cancer cases diagnosed in the Gunbalanya-Kakadu cohort (1991-2014)

Site	ICD10 codes	Number of cases
Mouth and throat	C01-C14	20
Oesophagus	C15	1
Stomach	C16	1
Bowel	C18-C20	5
Anus	C21	1
Liver	C22	4
Gallbladder & bile ducts	C23-C24	3
Pancreas	C25	3
Larynx	C32	2
Lung	C34	25
Other thoracic and respiratory organs	C37	1
Breast	C50	7
Vulva	C51	1
Cervix	C53	5
Penis	C60	1
Prostate	C61	1
Brain	C71	1
Thyroid	C73	5
Unknown	C80	8
Blood and lymphatic cancers	C81-C96, D45, D46, D47.1, D47.3-D47.5	3
Total	C00-C97, D45, D46, D47.1, D47.3-D47.5	98

7.3. Perinatal deaths in the G-K cohort

There were 890 births to members of the G-K cohort between 1/1/1991 and 31/12/2014, with 27 perinatal deaths. The baby was born dead in 20 of these births (fetal death) and seven live-born babies died within 28 days after birth (neonatal death) (Table 7).

The fetal death rate was higher in the G-K cohort than in the comparison population (Table 7); the odds ratio (OR) was 1.84 (95%CI; 1.10, 2.93) with a 95% confidence interval that did not include 1.0 (Table 8), providing strong evidence that the number of fetal deaths in the G-K cohort was higher than expected.

In contrast to fetal deaths, there was no evidence of excess neonatal deaths in the G-K cohort; the neonatal death rate was lower for the cohort than for the comparison population (Table 7; OR 0.68, 95%CI 0.27, 1.42). The 95% CI, however, is wide and it is unlikely that the neonatal death rate was truly lower in the G-K cohort than in the comparison population.

Table 7 Perinatal deaths, Gunbalanya-Kakadu cohort and other Top End Aboriginal population, 1991-2014.

	G-K cohort		Other Top End	
	Number	Rate	Number	Rate
Perinatal deaths ¹	27	30.3	486	24.0
Fetal deaths ¹	20	22.5	249	12.3
Neonatal deaths ²	7	8.0	237	11.9
Births				
Live births	870		19,984	
Total births	890		20,233	

1. rate as number of deaths per 1,000 total births

2. rate as number of deaths per 1,000 live births

Table 8 Odds ratios for fetal, neonatal and perinatal deaths, Gunbalanya-Kakadu cohort compared with other Top End Aboriginal population, 1991-2014.

	G-K cohort	Other Top End	Odds Ratio	(95%CI)
Fetal deaths	20	249	1.84	(1.10, 2.93)
Live births	870	19,984		
Neonatal deaths	7	237	0.68	(0.27, 1.42)
Other live births	863	19,747		
Perinatal deaths	27	486	1.27	(0.82, 1.89)
Other births	863	19,747		

Causes of perinatal death

Nationally, in 2012-2016, only 56% of perinatal deaths had a known cause of death. This is because cause of death frequently cannot be determined for fetal deaths, which comprised 71% of perinatal deaths in that period. For the G-K cohort, 67% of perinatal deaths had a known cause (Table 9). Among those with a known cause, the only categories of cause of death with more than two perinatal deaths in the G-K cohort were: 'disorders related to gestation and fetal growth' with nine deaths, of which three were caused by extreme prematurity and five by prematurity, and all but one were fetal deaths; and 'respiratory and cardiovascular disorders' with six deaths, of which five were caused by intrauterine hypoxia or birth asphyxia, and four of the six were fetal deaths. There was one perinatal death classified as caused by a congenital malformation.

Table 9 Causes of perinatal death, Gunbalanya-Kakadu cohort (1991-2014) and total Australia (2012-2016)¹.

Category	G-K cohort				Australia
	Fetal n ²	Neonatal n	Perinatal		Perinatal %
	n		n	%	%
Disorders related to length of gestation and fetal growth (P05-P08)	8	1	9	33.3	18.1
Birth trauma (P10-P15)	0	0	0	0.0	0.0
Respiratory and cardiovascular disorders specific to the perinatal period (P20-P29)	4	2	6	22.2	5.0
Infections specific to the perinatal period (P35-P39)	0	0	0	0.0	1.6
Haemorrhagic and haematological disorders of fetus and newborn (P50-P61)	0	0	0	0.0	2.2
Transitory endocrine and metabolic disorders specific to fetus and newborn (P70-P74)	0	0	0	0.0	1.1
Digestive system disorders of fetus and newborn (P75-P78)	0	0	0	0.0	0.6
Conditions involving the integument and temperature regulation of fetus and newborn (P80-P83)	0	0	0	0.0	0.9
Other disorders originating in the perinatal period (P90-P96)	0	0	0	0.0	5.3
Fetal death of unspecified cause (P95)	8	1	9	33.3	43.4
CHAPTER XVII Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)	0	1	1	3.7	20.0
Sudden Infant Death Syndrome (R95)	0	2	2	7.4	0.2
Other (Chapters 1-15, 18 and 20, excluding R95)	0	0	0	0.0	1.6
Total	20	7	27	100.0	100.0

1. source: Australian Bureau of Statistics, Deaths Australia 2016. Table 14.9.

<http://www.abs.gov.au/AUSSTATS/abs@.nsf/allprimarymainfeatures/47E19CA15036B04BCA2577570014668B?op=endocument>

2. number of deaths.

8. Stage 3a: cancer risk factor prevalence study

The aim of the cancer risk factor prevalence study was to assess whether the G-K cohort (i.e. Aboriginal long-term residents of the Gunbalanya-Kakadu area) had greater exposure to cancer risk factors than other Aboriginal people living in the Top End of the NT. Stage Two of the cluster investigation found strong evidence that the G-K cohort had an excess of all-cancers combined, of mouth and throat cancers and of lung cancer. 'Mouth and throat cancers' is a grouping of different types of cancer that occur in the tongue, tonsils, other parts of the mouth, the oropharynx, nasopharynx, the parotid gland, other salivary glands or related structures; these cancers do not all have the same risk factors. There was also an indication, but not strong evidence, of an excess of cervix and thyroid cancers. The cancer risk factor study therefore focused, when possible, on risk factors that are shared by several cancers and risk factors that are specific to mouth and throat, lung, cervix and thyroid cancers. They were:

- Smoking
- Alcohol
- Poor nutrition
- Low levels of physical activity
- Overweight and obesity
- Diabetes
- Infection with oncogenic (i.e. cancer-causing) types of Human Papillomavirus (HPV)
- Exposure to ionizing radiation
- Chemical exposures.

For most cancer risk factors, prolonged exposure over many years is required before cancer is diagnosed. Ideally, exposure to cancer risk factors should be measured during the entire period of known excess cancer occurrence (from 1991) and for 10-20 years before that; this would require data that was recorded multiple times in a consistent manner over the past 40 years, and for which comparable data is available for a comparison population. No consistent data is available from 1991 (or before) about cancer risk factors for the Aboriginal population of the Top End, so cumulative exposure cannot be measured from data recorded contemporaneously. This study therefore investigated recent (between 2012 and 2017) rather than life-long exposure to relevant risk factors. The study design is described in detail in the scientific protocol (20) and is described here in summary.

Existing clinical records from the NT Department of Health's Primary Care Information System (PCIS) and the NT Pap Test Register (PTR) for Top End Aboriginal residents were used as the main source of information about exposure to cancer risk factors. More information about cancer risk factors and these data sources is available in the scientific protocol for this study.(20) Data was available from primary health care records since May 2012 for the cohort and for a comparison population of other Top End Aboriginal residents, so this study focused on prevalence of cancer risk factors in recent years. This is informative about future risk of cancer and provides indirect evidence about past exposures if exposure has not changed to a large extent over time.

The comparison population for this study was current Aboriginal residents of the 22 Top End communities that use the NT Department of Health's PCIS electronic medical records system, excluding G-K cohort members.

A high grade abnormal (HGA) Pap test result is an indication of an oncogenic (i.e. cancer-causing) HPV infection of the cervix. Female members of the G-K cohort and of the comparison population who were aged 18 years and over on 31/12/2015 were matched to the NT PTR to obtain information on Pap tests performed for these women in the period 1/1/1997 to 31/12/2017. The linked dataset was used to calculate and compare the prevalence of HGA Pap tests in screened women in each group.

No data was available about individual exposure to environmental ionizing radiation. Exposure to environmental ionizing radiation was assessed by development of a 'worst case scenario' for the G-K population based on measurement of environmental radiation levels, consumption of bush tucker (plant, marine and animal foods gathered or hunted locally) and airborne exposure to radon gas. This was investigated in a separate study (see section 10). There is no data source about individual exposure (current or cumulative) to chemicals. Consultation with the Gunbalanya Council and other organisations found no useful records about use of chemicals in the Gunbalanya community or surrounding area. Exposure to carcinogenic chemicals could not be assessed in this study.

A multi-variable analysis of the contribution of each cancer risk factor to the excess cancer incidence in the G-K cohort compared with the comparison population (Aboriginal clients of other PCIS CHCs) was performed adjusting for sex, age and each risk factor individually to see whether any risk factor appeared to explain part or all of the difference in cancer risk between the G-K cohort and comparison population. This analysis was limited to persons for whom risk factor data was available. Persons who died before 1/5/2014 (two years after PCIS risk factor data was first available) were excluded to allow sufficient time for Smoking, Nutrition, Alcohol, Physical Activity, Emotional (SNAPE) assessments to have occurred, as were persons alive after that date but with no PCIS risk factor data. This analysis had low statistical power because only nine cancers were diagnosed in the eligible G-K cohort members (and 50 in the comparison group) between 1/5/2012 (the first date for which cancer risk factor data was available) and 31/12/2015 (the last date for which cancer diagnosis data was available).

8.1. Cancer risk factor prevalence

When adjusted for age and sex, the prevalence of current alcohol consumption was 21% higher in the G-K cohort than in the comparison group, current smoking was 8% higher and infrequent vegetable consumption 8% higher, while the prevalence of sugary drink consumption was 19% lower (Table 10). There was no strong evidence that the prevalence of other risk factors was different for the G-K cohort than the comparison group.

The rate ratio comparing cancer incidence for the G-K cohort with the comparison group was 1.52 (0.75-3.09), adjusted only for age (at 31/12/2017) and sex. When each risk factor was included in the regression model individually, there was little or no change in the rate ratio; the largest change was a decrease to 1.49 when adjusted for infrequent vegetable consumption and for infrequent physical activity (Table 11).

Human Papillomavirus infection

A different sub-group was used for multivariable analysis of HGA Pap test, which was restricted to women born on or before 31/12/1997 (so that they turned 18 years old at least two years before 31/12/2017, the last date for which Pap test data was available) who had had a Pap test since 1/1/1997. There were 3,741 women included in this analysis (G-K cohort 429; comparison 3,312). The prevalence of any HGA Pap test was similar for the G-K cohort and the comparison group (prevalence ratio 0.97, 95%CI 0.66-1.42).

Table 10 For each risk factor separately, the ratio of the prevalence in the G-K cohort to that in the comparison group.

Risk factor	Prevalence ratio and 95% CI	
Alcohol (current)	1.21	(1.13-1.31)
Smoking (current)	1.08	(1.04-1.13)
Frequent fatty foods	0.87	(0.72-1.05)
Infrequent fruit	0.97	(0.92-1.02)
Infrequent vegetables	1.08	(1.02-1.14)
Sugary drinks	0.81	(0.71-0.93)
Infrequent activity	1.01	(0.98-1.04)
Overweight/obese	1.01	(0.93-1.10)
Diabetes	1.08	(0.95-1.22)

Table 11. For each risk factor individually, the risk of cancer incidence in the G-K cohort to that in the comparison cohort, adjusted for the risk factor¹.

Risk factor	Cancer incidence ratio and 95% CI	
Unadjusted	1.52	(0.75-3.09)
Alcohol (current)	1.54	(0.76-3.15)
Smoking (current)	1.53	(0.75-3.12)
Frequent fatty foods	1.50	(0.74-3.07)
Infrequent fruit	1.52	(0.74-3.11)
Infrequent vegetables	1.49	(0.73-3.06)
Sugary drinks	1.51	(0.74-3.08)
Infrequent activity	1.49	(0.73-3.03)
Overweight/obese	1.50	(0.74-3.05)
Diabetes	1.52	(0.75-3.09)

1. In a Poisson regression model adjusted for sex and age

8.2. Apparent effects of individual cancer risk factors on cancer risk in the two cohorts combined

There was little evidence that the risk factors investigated in this study were associated with increased risk of cancer in study participants in the period 1/5/2012 and 31/12/2015 (the period for which risk factor data was available from PCIS). The risk ratio for several risk factors was below 1.0; for others, the risk ratio was above 1.0 but with a wide confidence interval that included 1.0 (Table 12).

Table 12 For each risk factor separately, the ratio¹ of cancer incidence in all persons (G-K cohort and comparison group combined) with the risk factor compared to those without, adjusted for age and sex.

Risk factor	Risk ratio and 95% CI	
Alcohol (current)	0.61	(0.32-1.13)
Smoking (current)	0.78	(0.46-1.34)
Frequent fatty foods	0.59	(0.18-1.90)
Infrequent fruit	1.37	(0.79-2.38)
Infrequent vegetables	1.03	(0.61-1.73)
Sugary drinks	1.66	(0.87-3.19)
Infrequent activity	0.73	(0.42-1.26)
Overweight/obese	0.67	(0.38-1.21)
Diabetes	1.25	(0.74-2.14)
HGA Pap test ²	1.70	(0.52-5.62)

1. estimated using Poisson regression model including adjustment for sex and age (at 31/12/2017)

2. women only, adjusted for age.

9. Stage 3b: fetal death risk factor prevalence study

Most fetal death risk factors involve exposure during pregnancy. Exposure to these risk factors must be measured during pregnancy and, for women who have had more than one pregnancy, must be measured separately for each pregnancy. The study was therefore a retrospective study of the prevalence of risk factors during each pregnancy in members of the G-K cohort and the comparison population who birthed during the study period using clinical data recorded at the time of each birth. The Perinatal Data Collection was the data source for this study; it contains information about each birth in the NT since 1986, including data about many, but not all, fetal death risk factors.(21)

The study design is described in detail in the scientific protocol. (22) In brief, the study compared the prevalence of each risk factor individually (univariate analysis) for births to women in the G-K cohort ('G-K births') and births to other Aboriginal women who were resident in the Top End of the NT ('comparison births') at the time of each birth. Fetal death is a binomial outcome (yes or no for each birth). Modified Poisson regression using generalised estimating equations with adjustment for clustering (because many mothers had more than one birth) was used to model the prevalence of fetal death (i.e. the proportion of births that resulted in a fetal death). Multivariable analysis assessed the extent to which higher prevalence of some risk factors for G-K than comparison births contributed to the excess of fetal deaths for G-K births.

9.1. Fetal deaths

Between 1991 and 2014 the fetal death rate was 86% higher in G-K than comparison births (Table 13). In the comparison group, the fetal death rate was similar for births to women living in urban (11.6 per 1,000 in Darwin, Palmerston and hinterland) and remote (12.2 per 1,000) areas. This indicates that the excess of fetal deaths is specific to the G-K cohort rather than to remote areas residents in general. The fetal death rate fluctuated considerably over time for G-K births (Table 14) because of the small number of births and fetal deaths each year in the G-K cohort. In regression analysis, the fetal death rate decreased by 2.1% per year (rate ratio 0.979 per year, 95%CI 0.960-0.997), or by 38% between 1991 and 2014. The rate of decline was similar for G-K and comparison births.

Table 13 Fetal deaths number and rate, G-K cohort and comparison births, 1991-2014

	G-K	Comparison ¹	Rate ratio (95%CI)
Fetal death	20	243	
Live birth	870	19,867	
Total	890	20,110	
Fetal death rate ²	22.5	12.1	1.86 (1.18-2.92)

1. The comparison group includes slightly fewer births than in Stage Two (see section 7.3) because births to women with 'uncertain' membership of the G-K cohort were not transferred to the comparison group for the fetal death risk factor prevalence study

2. Per 1,000 total births

Table 14 Fetal death rate¹ by period, G-K cohort and comparison births, 1991-2014

Period	G-K	Comparison	Rate ratio	95%CI
1991-1995	23	16	1.41	(0.52-3.84)
1996-2000	15	13	1.15	(0.36-3.66)
2001-2005	40	9	4.48	(2.04-9.86)
2006-2010	24	13	1.90	(0.70-5.16)
2011-2014	11	10	1.17	(0.28-4.83)
1991-2014	23	12	1.86	(1.18-2.92)

1. per 1,000 births

9.2. Risk factor prevalence

For most risk factors, prevalence was not higher for G-K than comparison births (Table 15). There was weak or no evidence that G-K births had higher prevalence of: preterm birth; post-term birth; older maternal age >35 years; maternal overweight and obesity; pre-existing hypertension or pre-eclampsia; pre-existing diabetes; no antenatal care; maternal anaemia; maternal syphilis infection; maternal urinary tract infection; placental abruption; alcohol consumption during pregnancy; or injury hospitalisation during pregnancy.

There was strong evidence that G-K births had a higher prevalence of:

- Small for gestational age births
The proportion of births that were SGA was higher for G-K than comparison births (27% and 20% respectively), with an adjusted prevalence ratio of 1.33 (1.17-1.52).
- Maternal age at birth <18 years and lower mean maternal age
The proportion of mothers aged less than 18 years at the time of birth was higher for G-K than comparison births (16.7% and 12.5% respectively), with an adjusted prevalence ratio of 1.35 (1.15-1.58).
- Low maternal BMI
The proportion of mothers with low BMI was higher for G-K than comparison births (23.8% and 13.6% respectively), with an adjusted prevalence ratio of 1.85 (1.30-2.65).
- Maternal smoking during pregnancy
The proportion of mothers who smoked during pregnancy was higher for G-K than comparison births (60.4% and 54.7% respectively), with an adjusted prevalence ratio of 1.12 (1.03-1.21).
- First birth
The proportion of births that were the mother's first birth was higher for G-K than comparison births: (35.0% and 31.0% respectively), with a prevalence ratio of 1.13 (1.03-1.24).
- Gestational diabetes
The proportion of births where the mother had gestational diabetes was higher for G-K than comparison births: (13.0% and 9.3% respectively), with a prevalence ratio of 1.43 (1.09-1.88).
- Late first antenatal visit
The proportion of G-K births where the first antenatal visit was in trimester two or three was higher for G-K than comparison births (67% and 61.5% respectively), with an adjusted prevalence ratio of 1.11 (1.05-1.17).

The risk factor 'small for gestational age' (SGA) is based on gestational age and birthweight. Data for SGA was available from 1991-2014 but was reliable only for live births because a fetal death before the onset of labour can reduce the weight of the fetus before birth occurs. Fetal weights estimated by obstetric

ultrasound before fetal death were not available from the PDC, so only livebirth data was included in the SGA analyses. Although the prevalence of 'maternal age at birth <18 years', 'low maternal BMI' and 'gestational diabetes' was higher for G-K than comparison births, these are not risk factors for fetal death (unlike older maternal age, high BMI and pre-existing diabetes).

Table 15 Prevalence (%) of fetal death risk factors, G-K and comparison (other Top End Aboriginal mothers) births, 1991-2014

Risk factor	G-K	Comparison	p-value ¹	Ratio ²	(95%CI)
<i>Gestational age at birth</i>					
<37 weeks	15.2%	15.6%	0.942	1.00	(0.83-1.21)
37-41 weeks	83.7%	83.3%		1.00	(0.97-1.04)
42+ weeks	1.0%	1.1%		0.93	(0.45-1.91)
Mean gestational age (weeks)	38.2 wks	38.1 wks	0.897		
Small for gestational age	27.0%	20.0%	0.000	1.33	(1.17-1.52)
<i>Maternal age at birth</i>					
<18 years	16.7%	12.5%	.001	1.35	(1.15-1.58)
18-34 years	77.9%	81.3%		0.96	(0.92-0.99)
35-39 years	4.7%	5.3%		0.86	(0.60-1.24)
40+ years	0.7%	0.9%		0.76	(0.34-1.72)
Mean maternal age (years)	23.2	24.1	<0.001	na	
<i>Overweight and obesity³</i>					
BMI <18.5	23.8%	13.6%	0.019	1.85	(1.30-2.65)
BMI 18.5-24	40.0%	39.7%		0.99	(0.77-1.27)
BMI 25-29	19.1%	26.3%		0.73	(0.49-1.11)
BMI 30+	17.1%	20.4%		0.78	(0.48-1.25)
Mean BMI (BMI units)	23.8	25.4	0.007		
<i>Maternal smoking³</i>					
In early pregnancy	60.1%	54.3%	0.006	1.12	(1.03-1.21)
In late pregnancy	55.1%	48.5%	0.004	1.17	(1.07-1.28)
Any time during pregnancy	60.4%	54.7%	0.007	1.12	(1.03-1.21)
First birth	35.0%	31.0%	0.013	1.13 ⁴	(1.03-1.24)
<i>Maternal hypertension</i>					
Pre-existing	1.5%	1.3%	0.665	1.17	(0.62-2.22)
Pre-eclampsia ³	3.6%	5.1%	0.085	0.72	(0.46-1.12)
<i>Maternal diabetes³</i>					
Pre-existing	1.0%	1.6%	0.154	0.67	(0.33-1.36)
Gestational	13.0%	9.3%	0.010	1.43	(1.09-1.88)
<i>First antenatal visit</i>					
Trimester one	31.4%	36.6%	0.108	0.84	(0.74-0.94)
Trimester two or three	67.0%	61.5%		1.11	(1.05-1.17)
None	1.6%	2.2%		0.72	(0.40-1.28)
Mean number of antenatal visits	9.3	8.7	0.001	na	
Maternal anaemia	10.4%	10.3%	0.924	1.00	(0.75-1.35)
Maternal syphilis ³	2.1%	3.2%	0.108	0.74	(0.43-1.30)
Urinary tract infection ³	8.4%	7.1%	0.314	1.18	(0.86-1.61)
Placental abruption ³	0.2%	0.7%	0.144	0.26	(0.04-1.87)
<i>Alcohol consumption³</i>					
First antenatal visit	10.8%	10.4%	0.806	1.07	(0.81-1.41)
36 weeks gestation	7.1%	6.9%	0.858	1.04	(0.72-1.51)
Any alcohol consumption	10.9%	10.7%	0.886	1.05	(0.79-1.38)
Alcohol-related hospitalisation	4.5%	5.7%	0.298	0.75	(0.43-1.32)
Injury hospitalisation	0.2%	0.7%	0.128	0.23	(0.03-1.62)

1. P-value of chi squared test for prevalences, t-test for means.

2. Ratio of the proportion or mean value for the G-K cohort to that for the comparison group, estimated by individual regression model (adjusted for clustering by mother) for each risk factor.

3. Only for years during which data for this risk factor was collected; see (21)

4. Not adjusted for clustering, because regression models adjusted for clustering would not converge

9.3. Multivariable analysis of risk factors that explain excess fetal deaths in G-K births.

Risk factors that were associated with increased risk of fetal death in univariate analysis (23) were included in a multivariable model to assess the extent to which these risk factors in combination explained the excess risk of fetal death in G-K births (Table 16). The deviance of the multivariable model was only 5.2% lower than that of the simple model containing only the G-K:comparison term and the G-K:comparison prevalence ratio was not lower in the multivariable model than the simple model, indicating that the risk factors included in the multivariable model explained little, if any, of the excess risk of fetal death for G-K births.

Table 16 Multivariable analysis of risk factors for fetal death (prevalence ratio), G-K and comparison births 1991-2014

Risk factor	Simple model		Final model ¹	
	Ratio ²	(95%CI)	Ratio ²	(95%CI)
<i>G-K:comparison</i>	1.85	(1.08-3.16)	1.88	(1.10-3.19)
<i>Pre-existing hypertension</i>			2.16	(1.00-4.67)
<i>Pre-existing diabetes</i>				
Yes			2.04	(0.89-4.65)
Unknown			0.55	(0.19-1.60)
<i>No antenatal care</i>				
None			4.42	(3.13-6.25)
Unknown			1.85	(1.27-2.71)
<i>Placental abruption</i>				
Yes			10.05	(5.62-17.96)
Unknown			1.09	(0.65-1.83)
<i>Alcohol consumption during pregnancy</i>				
Yes			1.90	(1.21-3.00)
Unknown			1.82	(1.31-2.52)
<i>Alcohol-related hospitalisation</i>				
Yes			2.27	(1.40-3.68)
unknown			0.92	(0.57-1.51)
<hr/>				
Regression model statistics				
Pseudo-likelihood	-1408.6		-1337.7	
Deviance	2817.3		2675.4	

1. modified Poisson model adjusted for clustering by mother; final model after backwards stepwise elimination of risk factors with little or no evidence of association with risk of fetal death in G-K and comparison births.

2. prevalence ratio

9.4. Trends in selected risk factors

There was strong evidence that the prevalence of SGA, alcohol consumption during pregnancy and no antenatal care decreased over time but the prevalence of pre-existing hypertension increased over time, while there was little change in the prevalence of smoking.

There was strong evidence that SGA prevalence decreased by 2.4% per year, which was a decrease of 43% between 1991 and 2014 (prevalence ratio 0.976 per year, CI 0.972-0.980). The rate of decline was similar for G-K (2.7% per year) and comparison (2.4% per year) births.

There was strong evidence that the prevalence of no antenatal care decreased over time; the prevalence of no antenatal care decreased by 6.1% per year (prevalence ratio 0.939 per year, CI 0.929-0.949). The proportion of mothers who received no antenatal care decreased from 3.6% in 1991-1995 to 1.2% in 2001-2014 (excluding births with missing data about antenatal care). There was no strong evidence that the decrease was greater for G-K than comparison births.

There was also evidence that early commencement of antenatal care increased over time; the prevalence of antenatal first visit in trimester two or three (among births with any antenatal care and excluding births with missing data) was lower in 2011-2014 than it had been in previous years (Table 17). However, the trimester in which antenatal care commenced was unknown for a very high proportion of births in earlier years (Table 17) so this time trend may not be reliable.

The prevalence of smoking during pregnancy did not decrease over time for either G-K or comparison births (prevalence ratio 1.011 per year, CI 1.008-1.014).

There was strong evidence that the prevalence of pre-existing hypertension increased for both G-K and comparison births (prevalence ratio 1.027 per year, CI 1.008-1.060). There was no strong evidence that this increase was different for G-K than comparison births.

There was strong evidence that the prevalence of alcohol consumption during pregnancy decreased by 1.5% per year (prevalence ratio 0.985 per year, CI 0.976-0.994), a decrease of 24% between 1996 and 2014 (data on alcohol consumption during pregnancy was not available for 1991-1995).

The prevalence of alcohol consumption during pregnancy (amongst births with data on alcohol consumption available) decreased considerably for G-K births between 1996 and 2014, while there was little change for comparison births until the last period (Table 18). There was weak evidence that the rate of decline was greater for G-K than comparison births; the prevalence of alcohol consumption during pregnancy decreased by 1.3% per year for comparison births and by 5.2% per year for G-K births, but the confidence interval for the interaction term 'G-K by year' bordered on 1.0 (prevalence ratio 0.961, CI 0.921, 1.002) (Table 19). It was estimated that prevalence was 47% higher for G-K than comparison births in 1996 (prevalence ratio 1.47, CI 0.94-2.30) (Table 19) but 29% lower in 2014 (prevalence ratio 0.713, CI 0.44-1.16), although the confidence interval for both prevalence ratios was wide and included 1.0.

The proportion of births with missing data about alcohol consumption decreased from over 30% in 1996-2000 to just over 10% in 2011-2014. Improvement in data availability might have contributed to the changes in the proportion of births with alcohol consumption recorded but it is not plausible that this fully explains these time trends; for comparison births, the prevalence of alcohol consumption was stable for the first three periods when most of the improvement in data availability occurred, while for G-K births there was little change in prevalence between the first and second periods when the largest improvement in data availability occurred but then a large decrease in prevalence in each of the third and fourth periods when there was less change in data availability.

Table 17 Prevalence of first antenatal visit in trimester two or three¹ by period, G-K and comparison births, 1991-2014

Years	Prevalence (%) ¹		Proportion unknown ² (%)	
	G-K births	Comparison	G-K births	Comparison
1991-1995	20.1	19.1	33.0	30.7
1996-2000	23.8	22.1	55.3	46.7
2001-2005	20.6	22.6	10.6	15.9
2006-2010	18.2	22.5	1.1	4.6
2011-2014	17.3	13.7	0.0	2.1

1. excluding births for which trimester of first antenatal visit was not recorded.

2. Proportion of births with data not recorded for trimester of first antenatal visit.

Table 18 Prevalence of alcohol consumption during pregnancy by period, G-K and comparison births, 1996-2014

Years	Prevalence (%) ¹		Proportion unknown ² (%)	
	G-K births	Comparison	G-K births	Comparison
1996-2000	15.8	11.5	39.7	31.4
2001-2005	14.7	11.1	18.8	19.1
2006-2010	9.7	11.4	18.8	17.3
2011-2014	4.5	8.5	12.4	11.0

1. Prevalence of alcohol consumption at any time during pregnancy, excluding births for which alcohol consumption was not recorded.

2. Proportion of births with data not recorded for alcohol consumption during pregnancy.

Table 19 Prevalence of alcohol consumption during pregnancy, regression analysis¹ of time trends for G-K and comparison births, 1996-2014

	Prevalence ratio	(95%CI)
G-K compared with comparison births (in 1996)	1.466	(0.935-2.300)
<i>Trend in prevalence of maternal alcohol consumption (per year) by year of infant's birth</i>		
G-K births	0.948	(0.910-0.988)
Comparison births	0.987	(0.977-0.996)

1. modified Poisson regression adjusted for clustering by mother.

10. Stage 3c: environmental ionizing radiation study

Environmental ionizing radiation is a risk factor for cancer and for congenital malformations, some of which cause fetal death. There is one active and several old uranium mines in the Alligator Rivers Region in which the Aboriginal population of Gunbalanya and Kakadu live. There are no historical or contemporary data sources about radiation exposure to individuals living in the Alligator Rivers Region. The Supervising Scientist (a statutory office that is part of the Australian Government Department of the Environment) monitors potential environmental contamination from the Ranger uranium mine by monitoring water quality, sampling air and dust and sampling marine animals in water bodies up- and down-stream of the mine; it does not monitor people directly.

The G-K cluster investigation assessed the feasibility of conducting a survey of current residents of the G-K area for biomarkers of radiation damage. This was found not to be feasible because there are currently no scientifically validated methods to measure biological damage arising from very low levels of exposure to environmental ionizing radiation, as distinct from exposure to non-environmental sources such as nuclear fuels, or high-dose medical irradiation such as cancer radiotherapy.

In consultation with the Supervising Scientist, the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) and the independent reviewer Professor Armstrong, the G-K cluster investigation developed a worst-case scenario to assess the highest potential exposure from environmental sources (including locally caught or harvested bush foods, water and air) and assess the maximum increase in cancer incidence that could have occurred if the entire population had experienced the worst-case exposure level. (24) The Supervising Scientist analysed information based on environmental monitoring data for living and recreation areas, and a survey of Aboriginal residents' hunting and gathering practices to determine residents' maximum plausible exposure to ingestion of radio-nuclides from bush tucker. (24)

ARPANSA assessed the findings of the cohort study (Stage Two) and the worst-case scenario and estimated the excess occurrence of cancer that could plausibly arise from the extent to which ionizing radiation exposure under the worst-case scenario was higher than average background levels of environmental radiation exposure. ARPANSA's advice was: (24)

On the basis of the two new reports provided, ARPANSA advises that, with regard to the increased incidence rate of cancer generally, [and] specifically for lung cancer:

- *Inhalation of radon and its progeny is known to cause lung cancer*
- *All mine-related ionising radiation exposures to hypothetical individuals living at Manaburduma and Mudginberri settlements are a fraction of the typical Australian and global background radiation levels*
- *Although inhalation of mine-related radon was the dominate [sic]⁴ exposure pathway, the measured average mine-related radon levels were very small*
- *The predicted increased frequency of lung cancer to hypothetical individuals living at Manaburduma and Mudginberri settlements from mine-related radon exposures is very small and would not be observable in either hypothetical⁵ settlement above baseline lung cancer rates*
- *Attributing risk from other mine-related ionising radiation exposure for other cancer types or*

⁴ Should be 'dominant'

⁵ 'hypothetical' here refers to the experience of the 'hypothetical' population of Manaburduma and Mudginberri under the worst-case scenario.

fetal death is not recommended due to the negligible levels and doses predicated by Supervising Scientist for all other exposure pathways

- *The available information does not support the hypothesis that the cancer rates in the Aboriginal resident cohort of the Alligator Rivers Region have been impacted by radiological releases from the Ranger uranium operation*

Based on the findings of the worst-case scenario and ARPANSA's estimation of the potential excessive occurrence of cancer in a population exposed to environmental radiation under that scenario, it is highly unlikely that the excess occurrence of cancer in the G-K population is caused by excessive exposure to environmental ionizing radiation.

12. Discussion

This disease cluster investigation confirmed the initial finding from 2014 that there is strong evidence of an excess of head and neck cancers, lung cancer and all-cancers combined, and of fetal deaths, in Aboriginal long-term residents of the Gunbalanya-Kakadu area. It did not establish an explanation for these excesses but, given that alcohol and tobacco use are established causes of these cancers, it is highly likely that they have contributed to the higher levels in the G-K cohort. Similarly, the higher prevalence of alcohol consumption and smoking during pregnancy is likely to have contributed to the higher fetal death rate for G-K births.

12.1. Cancer

The cohort study (Stage Two) confirmed the findings of Stage One of this investigation. It found strong evidence that the G-K cohort has an excess of all-cancers combined (for both men and women), mouth, throat and lung cancers, and weak evidence of an excess of cervical and thyroid cancers. There was little evidence of an excess of bowel or breast cancers.

There was strong evidence that the prevalence of three cancer risk factors was higher for the G-K cohort than the comparison group: alcohol, 21% higher; smoking, 8% higher; and infrequent vegetable consumption, 8% higher. The information available about alcohol consumption and smoking consisted only of whether the person consumed alcohol or tobacco; there was no information available about the frequency of consumption or amount consumed. Surprisingly, in the whole study population (G-K cohort and Top End comparison cohort combined), cancer incidence was not higher in those who consumed alcohol or smoked compared to those who did not (Table 12) (although the confidence intervals about the incidence rate ratios were wide) and the higher prevalence of alcohol consumption and smoking in the G-K cohort did not appear to explain any of their higher incidence of all-cancers combined. Infrequent vegetable consumption is not a direct risk factor for cancer; it was used here as an indicator of poor nutrition. Here again, in the whole study population (Table 12), cancer incidence was not higher in those with infrequent compared to frequent vegetable consumption. In multivariable analysis of the excess of cancer incidence in the G-K cohort compared to the comparison population, adjustment for these risk factors did not reduce the excess cancer incidence in G-K cohort members (Table 11), suggesting that their higher prevalence of these risk factors does not explain their higher cancer incidence compared with that in the comparison cohort.

The 'worst case scenario' strongly suggests that exposure to environmental ionizing radiation does not explain the excess of cancers in Aboriginal long-term residents of the G-K area. Exposure to chemicals could not be assessed.

12.2. Fetal deaths

The cohort study (Stage Two) also confirmed the findings of Stage One in regard to the higher fetal death rate in G-K than comparison births.

The prevalence of three risk factors for fetal death was higher for G-K than comparison births: small for gestational age (SGA, 35% higher), maternal smoking during pregnancy (12% higher) and first birth (13% higher). The prevalence of gestational diabetes and late first antenatal visit was also higher for G-K than comparison births, but these factors did not appear to increase the risk of fetal death. The risk of fetal death is known to be much higher for SGA than other births, but the contribution of SGA to the excess of fetal deaths in G-K births could not be directly assessed so there is only indirect evidence that higher SGA prevalence contributed to the higher fetal death rate for G-K births. SGA prevalence decreased over time for both G-K and comparison births, but there was no strong evidence that prevalence decreased more for G-K than comparison births, so it is likely that higher SGA prevalence continues to contribute to higher risk

of fetal death for G-K births. Unfortunately, no data was available about maternal nutrition, which might have played a role in the higher SGA prevalence for G-K babies. The prevalence of low maternal BMI was higher for G-K than comparison births (23.8% compared with 13.6%), indicating that maternal nutrition may be less than optimal for G-K mothers. However, low maternal weight of itself is not a recognised risk factor for fetal death and there were no fetal deaths among G-K births with low maternal BMI.

Smoking prevalence was 12% higher for G-K than comparison births, but there was no direct evidence that this contributed to the excess of fetal deaths in G-K births. There was no evidence that the prevalence of smoking during pregnancy decreased over time for either G-K or comparison births.

The prevalence of alcohol consumption during pregnancy was similar for G-K and comparison births. Higher prevalence of alcohol consumption during pregnancy did not appear to contribute directly to the excess of fetal deaths in G-K births. The prevalence of alcohol consumption during pregnancy decreased for both G-K and comparison births between 1996 and 2014, and there was weak evidence that the rate of decline was greater for G-K than comparison births. Whether or not the decline was greater for G-K than comparison births, the evidence from this study of decreasing prevalence of this risk factor indicates that the risk of fetal death caused by alcohol consumption during pregnancy has decreased for all Top End Aboriginal women, including G-K residents.

There was little direct evidence that the higher prevalence of risk factors identified by this study contributed to the excess fetal deaths in G-K births; other factors may also be involved. Several risk factors (poor maternal nutrition, folate deficiency, illicit drug use, and low education) could not be investigated because data was not available from existing data sources and could not be obtained retrospectively. One or more of these risk factors might have been more prevalent for G-K than comparison births and contributed to the higher SGA prevalence for G-K births or been associated with their higher fetal death rate.

The fetal death rate decreased by 38% between 1991 and 2014. This reduction was similar for G-K and comparison births, so that the excess of fetal deaths for G-K births apparently continued until 2014, although this can only be inferred from analysis of long-term trends; the evidence about the excess in recent years is weak because of the small size of the G-K cohort and consequently small number of births and fetal deaths each year.

12.3. Strengths and limitations

A strength of this investigation was the ability to establish a cohort of long-term residents of the area, based on community informant panels, and the availability of data for most (but not all) fetal risk factors over the entire 24-year study period. However, the study has several limitations.

Data was only available for some cancer risk factors; other risk factors such as chemical exposures could not be investigated. Data on most cancer risk factors was only available from May 2012 and was only available (except for HGA Pap tests) for persons with a PCIS record. Among them, risk factor data was not available for 15-22% (depending on the risk factor) of G-K cohort members and 10-13% of the comparison group. It is possible that people with no available risk factor data have different risk factor exposure and different risk of cancer to the people included in the cancer risk factor study. No data about individual exposure to environmental radiation was available so the prevalence of such exposure in the G-K cohort could not be compared to that in the comparison group. However, data was available to assess the potential impact of environmental ionizing radiation exposure for the worst-case scenario.

Similarly, data was not available for some fetal death risk factors (such as estimated fetal weight for gestational age before onset of labour; maternal nutrition), so these risk factors could not be investigated as potential explanations. For other risk factors, the only available data was a 'yes or no' indicator of exposure to the risk factor with no information about magnitude of that exposure; alcohol and tobacco

consumption are good examples, where the available data indicated that a mother smoked or consumed alcohol during pregnancy but provided no information about the frequency of consumption or amount consumed. There is also no certainty that the risk factor data was collected consistently over the 24 years from 1991 to 2014, or consistently by all clinicians (midwives, Aboriginal Health Workers and doctors) providing antenatal and obstetric care throughout the Top End. Guidelines for providing and documenting antenatal care were standardised throughout the NT for the entire period, including a standardised antenatal care record used in most primary health care services for Aboriginal women, applying to both G-K and comparison births; this would have reduced variations in practice to some (unknown) extent. The primary analysis was a comparison of risk factor prevalence in two groups (G-K and comparison births) using data from the same data source that had been collected by the same processes; if these processes had varied over time, these changes applied to both G-K and comparison births.

The precision of estimates of risk factor prevalence and associated risk of cancer and fetal death was restricted by the relatively small size of the G-K cohort and small number of G-K births; the lack of risk factor data for some cohort members/births; and the small number of cohort members/births exposed to individual risk factors.

12.4. Implications

Although the analysis of association between risk factor prevalence and risk of cancer/fetal death provided little useful information because of the limitations described above, the estimates of risk factor prevalence provide some useful, albeit limited, evidence to inform the G-K population about actions to take to reduce the risk of cancer and fetal death.

The prevalence of smoking (including during pregnancy) is much higher for the Aboriginal population of the NT than for other Australians, and even higher in the G-K cohort than in the Aboriginal population elsewhere in the Top End. The prevalence of alcohol consumption is considerably higher for the G-K cohort than for other Top End Aboriginal residents (although not for pregnant women). As well as being risk factors for cancer, smoking and excessive alcohol consumption are harmful to health in many ways. This study provides no evidence of volume and frequency of consumption. The fetal death risk factor study indicated that consumption of alcohol during pregnancy decreased over 24 years, but that smoking during pregnancy did not, for pregnant women in the G-K cohort.

There is national evidence that the prevalence of smoking is decreasing in the Aboriginal and Torres Strait Islander population, which is encouraging and to be encouraged for the G-K communities. The 21% higher prevalence of alcohol consumption in the G-K cohort is a cause for serious concern; if frequency and volume of consumption are also high, this would be causing major health and social problems for the G-K population.

This study did not find direct evidence that higher prevalence of smoking or alcohol consumption in members of the G-K cohort contributed to their higher cancer incidence or fetal death rate. However, alcohol and smoking cause a wide range of disease, and excessive alcohol consumption causes a wide range of injury, economic and social damage in this population as elsewhere in the NT. The evidence that alcohol and tobacco consumption is even more frequent in the G-K population than elsewhere indicates that these two factors may be causing more damage to the G-K population than elsewhere, regardless of whether that includes cancer or not.

This study has explained only a small part of the excess of fetal deaths in G-K births, but it does provide direction on several health promotion and prevention actions that can be taken to further reduce the risk of fetal death for G-K women in future pregnancies: increasing the age at birth (fewer teenage pregnancies); reducing smoking during pregnancy; provision of early antenatal care to all pregnant women; and further reducing alcohol consumption during pregnancy. Continuing improvement in the birthweight

of G-K babies (measured as weight for gestational age) would appear to be the most sensitive indicator that their risk of fetal death is declining.

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