

An Epidemiological Study of Rössing Uranium Mineworkers

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Key Messages

- This study investigated the potential link between radiation and other occupational exposures and the risk of developing cancer in the workforce at the Rössing Uranium Limited mine.
- Important differences were observed in risk of developing cancer by nationality/ethnicity, which was assessed to be likely due to differential likelihood of diagnosis and recording between different nationality/ethnicity groups.
- The suboptimal quality of the cancer registration and exposure data resulted in important uncertainties in the study.
- No association was observed between cumulative total radiation dose and risk of cancer.
- Subsequent analyses showed some associations with lung cancer for gamma radiation and long-lived radioactive dust, but the evidence was not strong.
- Based on the data provided by Rössing Uranium Ltd , the radiation doses were assessed to be low.
- This study does not provide strong evidence that radiation or other exposures at the Rössing mine caused an increased risk of cancers in the workforce.
- However, the suboptimal quality of the cancer registry data and considerable uncertainties in some of the dose estimates, particularly those to the lung from radioactive dust, mean that there are consequent uncertainties in the study findings and interpretation.

Who We Are

- A research team from The University of Manchester
 - Professor Raymond Agius, Emeritus Professor of Occupational and Environmental Medicine
 - Dr Evridiki Batistatou, Research Fellow & Statistician
 - Dr Matthew Gittins, Lecturer in Biostatistics
 - Professor Steve Jones, Visiting Professor (and Director, SJ Scientific Ltd)
 - Dr Hanhua Liu, Research Fellow (until September 2017)
 - Professor Roseanne McNamee, Emeritus Professor of Epidemiological Statistics
 - Dr Amir Rashid, Research Associate
 - Professor Martie van Tongeren, Professor of Occupational and Environmental Health & Director of Centre for Occupational and Environmental Health
 - Professor Richard Wakeford, Professor of Epidemiology

Funding

- The study was funded by Rio Tinto plc
- Rössing Uranium Ltd provided relevant data on the Rössing workforce and exposure monitoring
- Although the study was supported by Rio Tinto plc and Rössing Uranium Ltd, the study methodology was wholly under the control of the research team from The University of Manchester.
- There were no conflicts of interest.

Cancer Risks from Exposure to Ionising Radiation

- Exposure to external sources of penetrating γ -rays is known to increase the risk of most types of cancer.
- Inhaling the α -particle-emitting gas radon and its radioactive decay products is known to increase the risk of lung cancer.
- Uranium miners are exposed to both γ -rays and radon, and to radioactive dust.
- There is a clear link between radon exposure and lung cancer in underground uranium miners exposed to high levels of radon.
- However, the much lower ore grade exploited at Rössing (about 0.03% by weight uranium), together with the open pit design, mean that the radiation doses at Rössing would be expected to be much lower than those in underground mines.

Research Governance & Ethics

- External Advisory Committee
 - Representatives from community, Namibian government, industry, workforce and union
 - Scope was to
 - Provide guidance on ethical considerations that may arise from the study
 - Provide input on issues relevant to members of the community they represent
 - Be the liaison between Rio Tinto/Rössing and the communities and/or stakeholder
 - Provide guidance in support of a balanced outcome for the project.
- Ethics
 - Manchester – Ethical approval obtained 6th May 2016; first amendment approved
 - Namibia – Permission (including ethics) granted by the Ministry of Health and Social Services of the Republic of Namibia on 29th August 2016
 - South Africa – Ethical approval obtained from the Human Research Ethics Committee (Medical) of the University of Witwatersrand on 27th January 2017
- The University of Manchester conducted an independent study. However, during the project there was regular feedback and contact with the sponsor regarding the process.

Cohort and Case-cohort Study Design

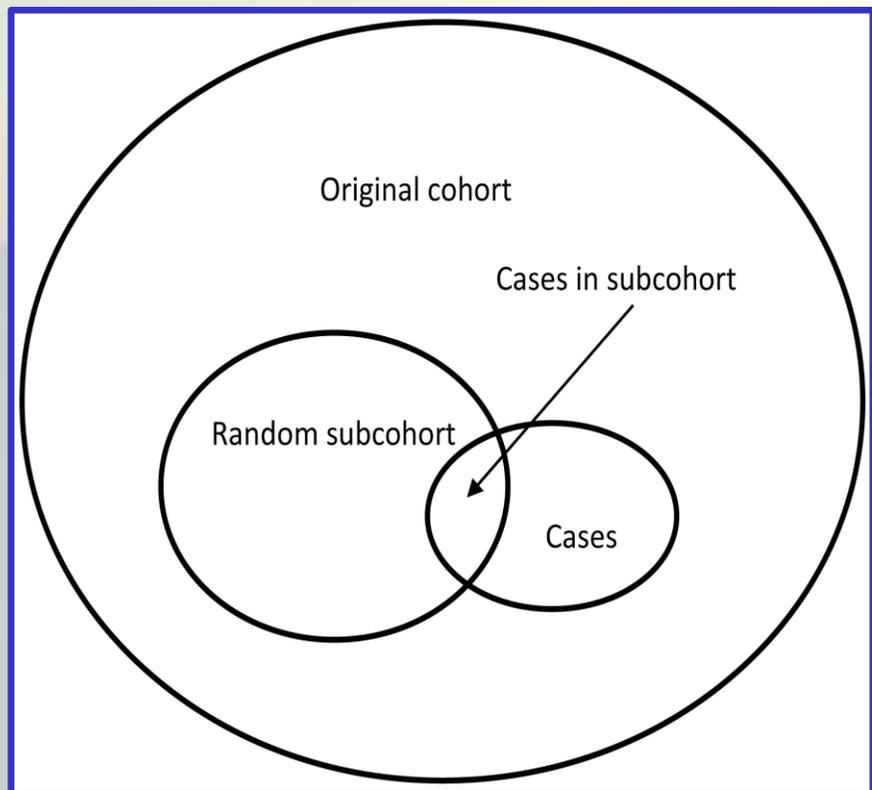
The Full Cohort: Individual workers employed by Rössing Uranium Limited between 1976 and 2010 inclusive, with at least one year's continual employment at the mine during this period, and excluding contract workers.

Case-Cohort study: exposure histories were ascertained for two groups selected from the full cohort: **cases** and the **sub-cohort**:

The **case group** included **all cancer cases of interest** in the full cohort

The **sub-cohort** is a stratified – by sex and decade of birth – random sample of the full cohort.

Since it is a random sample of the full cohort, the sub-cohort may include some cases, as shown.



Cancer Ascertainment in Full Rössing Cohort

Initially, all cases of cancer among the RUL workforce diagnosed by end-2015 were identified by linkage of workers' details with a number of sources

- Primary source was the Namibia National Cancer Registry (NNCR), but also
- South African National Cancer Registry (SANCR), and
- Records of the Rössing Uranium Limited occupational health provider, Medixx.
- Cancers of interest in relation to exposures at Rössing Uranium Mine are:
 - Lung cancer and cancers of the Extra-Thoracic (Upper) Airways – “ETA cancers”
 - Leukaemia
 - Brain cancer
 - Kidney cancer
- Only the workforce cancers of interest identified were retained to form the study case group.

Assessment of Radiation Doses at Rössing

- We used existing radiation exposure data from Rössing, collected for the purposes of radiological protection, to estimate the overall radiation exposure of workers over the years of their employment.
- Three components of radiation dose are assessed:
 - **External γ -ray** exposure (“**External Gamma**”)
 - **Internal** exposure from the inhalation of **Radon Decay Products** (“**RDP**”)
 - **Internal** exposure from inhalation of **Long-Lived Radioactive Dust** (“**LLRD**”)

Statistical Analyses

Main analyses – exposure categories:

workers classified into three **groups** – ‘**Low**’, ‘**Medium**’ or ‘**High**’ – based on tertiles of cumulative total radiation dose from all sources of exposure combined.

Analyses then estimated Rate Ratios (RRs) for **Medium vs Low** and for **High vs Low** dose groups, with adjustment for the following potential confounders:

age, period of birth, gender, smoking, socio-economic status, nationality/ethnicity, and other exposures as appropriate, including medical X-rays.

Secondary analyses – continuous exposure: analyses estimated Rate Ratio for **each increase of 10 mSv in cumulative total dose**, assuming a log-linear relationship between risk and dose (with same adjustments as above).

Further analyses estimated Rate Ratios for each of the **3 dose components**

Results: Organ/Tissue-specific Radiation Doses

Mean (median) cumulative organ/tissue-specific doses for the stratified randomly selected sub-cohort:

- Lung – 49.5 mSv (29.3 mSv)
 - Gamma: 4.5mSv (2.4 mSv); RDP: 33.9 mSv (20.4 mSv); LLRD: 11.0 mSv (5.4 mSv)
- ETA – 57.7 mSv (33.5 mSv)
 - Gamma: 4.7 mSv (2.4 mSv); RDP: 34.8 mSv (34.1 mSv); LLRD: 18.1 mSv (9.1 mSv)
- Leukaemia – 5.4 mSv (3.0 mSv)
 - Gamma: 4.9 mSv (2.6 mSv); LLRD: 0.54 mSv (0.29 mSv)
- Brain – 4.6 mSv (2.4 mSv)
 - Gamma: 4.6 mSv (2.3 mSv); LLRD: 0.02 mSv (0.01 mSv)
- Kidney – 5.2 mSv (2.7 mSv)
 - Gamma: 4.6 mSv (2.3 mSv); LLRD: 0.56 mSv (0.29 mSv)

The dose from RDP is zero for the organs/tissues of origin for leukaemia and brain and kidney cancers

Lung Cancer and ETA Cancer Rate Ratios by category of Cumulative Total Radiation Dose (5-year latency period)

Total Dose Category	Lung Cancer			Extra-thoracic Airways (ETA) Cancer		
	N of cases	N of sub-cohort	RR (95% CI)	N of cases	N of sub-cohort	RR (95% CI)
Low	11	456	1 (ref cat)	6	514	1 (ref cat)
Medium	11	437	1.42 (0.42, 4.77)	6	446	0.94 (0.20, 4.44)
High	10	228	1.22 (0.26, 5.68)	6	161	1.41 (0.19, 10.49)

Results from a weighted Cox proportional hazards analysis. RR: Rate Ratio; CI: Confidence Interval.

Lung cancer cumulative total radiation dose category: Low (<22.1mSv), Medium (≥22.1 to <80 mSv), High (≥80 mSv);

ETA cancer cumulative total radiation dose category: Low (<30 mSv), Medium (≥30 to <120 mSv), High (≥120 mSv).

Adjusted for gender, birth cohort, income category, smoking, medical X-ray exposure category and nationality/ethnicity category.

Brain, Leukaemia and Kidney Rate Ratios by category of Cumulative Total Radiation Dose (5-year latency for brain & kidney, 2 years for leukaemia)

Total Dose Category	Brain Cancer			Leukaemia			Kidney Cancer		
	N of cases	N of sub-cohort	RR (95% CI)	N of cases	N of sub-cohort	RR (95% CI)	N of cases	N of sub-cohort	RR (95% CI)
Low	3	417	1 (ref cat)	2	108	1 (ref cat)	3	525	1 (ref cat)
Medium	3	440	0.60 (0.11, 3.36)	3	333	0.61 (0.13, 2.86)	3	300	1.94 (0.30, 12.64)
High	3	264	0.60 (0.10, 3.39)	3	680	0.29 (0.04, 2.29)	3	296	1.82 (0.14, 24.40)

Results from a weighted Cox proportional hazards analysis. RR: Rate Ratio; CI: Confidence Interval.

Brain cancer cumulative total radiation dose category: Low (<1.5 mSv), Medium (≥1.5 to <5.8 mSv), High (≥5.8 mSv);
 Leukaemia cumulative total radiation dose category: Low (<0.01 mSv), Medium (≥0.01 to <2.0 mSv), High (≥2.0 mSv);
 Kidney cancer cumulative total radiation dose category: Low (<2.4 mSv), Medium (≥2.4 to <6.1 mSv), High (≥6.1 mSv).
 Adjusted for gender, birth cohort, income category, smoking, medical X-ray exposure category and nationality/ethnicity category.

Lung Cancer Rate Ratios per 10 mSv of Cumulative Radiation Dose: total dose model and models for each dose component separately (5-year latency).

<u>Continuous</u> Cumulative Dose	Lung Cancer		
	Number of cases	Number of sub-cohort	RR (95% CI) *
Total	32	1121	1.04 (0.95, 1.13)
Gamma	32	1121	1.63 (1.13, 2.34)
RDP	32	1121	1.02 (0.88, 1.19)
LLRD	32	1121	1.07 (1.003,1.14)

* Increase in RR per 10 mSv dose

Results from 4 separate weighted Cox proportional hazards analyses. RR: Rate Ratio; CI: Confidence Interval. Each analysis adjusted for gender, birth cohort, income category, smoking, medical X-ray exposure category and nationality/ethnicity.

Lung Cancer Rate Ratios per 10 mSv of Cumulative Radiation Dose, with Gamma, RDP and LLRD in the Same Model (5-year latency)

<u>Continuous</u> Cumulative Dose	Lung cancer			
	N of cases	N of sub-cohort	RR* (95% CI) with each dose component in the same model	RR** (95% CI) for each dose component in isolation
Gamma	32	1121	1.91 (1.09, 3.35)	1.63 (1.13, 2.34)
RDP	32	1121	0.97 (0.82,1.15)	1.02 (0.88, 1.19)
LLRD	32	1121	0.95 (0.79,1.15)	1.07 (1.003,1.14)

* Results from a weighted Cox proportional hazards ratio model which included all 3 dose components;

**Results from a weighted Cox proportional hazards ratio model which included only the selected dose component

RR: Rate Ratio; CI: Confidence Interval. Results are in terms of the change in RR per 10 mSv radiation dose.

Adjusted for gender, birth cohort, income category, smoking, medical X-ray exposure category and nationality/ethnicity.

Summary of Results

- For lung cancer:
 - No statistically significant association between cumulative total radiation dose and lung cancer risk
 - A statistically significant association was observed between gamma radiation dose and lung cancer when using the continuous variable for radiation
 - Elevated risk was observed for LLRD when using categorical variables (but not statistically significant). A statistically significant elevated risk was observed for LLRD when including as a continuous variable. However, this disappeared when adjusted for gamma radiation dose.

Summary of Results

- For **extra-thoracic (upper) airways (ETA) cancer**:
 - no statistically significant raised risk associated with radiation dose.
- For **leukaemia, brain cancer and kidney cancer**:
 - no statistically significant risk associated with radiation dose.

Conclusions

- There was no statistically significant relationship between the cumulative total radiation doses and the risks of any of the cancers of interest.
- Sensitivity analyses showed that when the radiation doses were included in the model as continuous variables, there was a statistically significant association for lung cancer with cumulative external gamma radiation and LLRD doses, but not for cumulative total or RDP doses.
- However, when including all three radiation dose metrics in the same model (as continuous variables) the increased risk associated with gamma dose remains, but there is no increased risk for LLRD dose.

Conclusions

- Estimated gamma radiation doses were similar to regional background levels and low compared to other epidemiological studies
 - Mean cumulative gamma dose to the lung in the RUL sub-cohort was 7 mSv.
 - Even for a large cohort study such as that of the ~100,000 Japanese atomic-bomb survivors there is considerable difficulty in finding an excess risk of all solid cancers combined below 100 mSv gamma dose.
- Owing to the estimated radiation doses based on data supplied to us, it could be considered improbable that exposure to external gamma radiation increased lung cancer risk in the RUL workforce.
- For LLRD dose and the lung, in particular, there are considerable uncertainties in the assessment. The observed association of lung cancer with LLRD dose may be due to a strong correlation with gamma radiation dose, but might have arisen from an underestimate of the dose or from some other cause that might have been associated with work.

Conclusions

- This study does not provide strong evidence that radiation or other exposures at the Rössing mine caused an increased risk of cancers in the workforce.
- However, there are important uncertainties in the study findings and interpretation due to
 - The suboptimal quality of the cancer registry data;
 - Considerable uncertainties in some of the dose estimates, particularly those to the lung from radioactive dust;
 - Uncertainty in some other key variables (e.g., smoking).

Concluding Thanks

- Thank you for listening and for your contribution to, and support for, this important project.
- Questions can be forwarded to us and we will attempt to answer them for you.