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Construction, Validation and Sensitivity Analyses of a Job Exposure Matrix for Early Plutonium Workers at the Sellafield Nuclear Site, United Kingdom

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Plutonium is a radiologically significant alpha-particle emitter. The potential for adverse health effects from internal exposures due to plutonium intakes has been recognized since the 1940s. The workforce of the Sellafield nuclear facility (Cumbria, UK), includes one of the world's most important groups of plutonium-exposed workers for studying the potential health risks of this internal exposure. However, for several hundred workers employed at the start of plutonium work at the facility (1952–1963), historical monitoring records based on measurements of urinary excretion of plutonium are not sufficiently reliable to provide the accurate and unbiased exposure assessments needed for epidemiological studies. Consequently, these early workers have had to be excluded from such studies, significantly reducing their power. We constructed a population-specific quantitative job exposure matrix (JEM) to estimate the average intakes of "typical plutonium workers" in this period, from 1952–1963, and assessed its validity and sensitivity to exposure assessment decisions. We conducted internal cross-validation using an *a priori* 10% extracted sample to evaluate reliability of estimates, explored JEM sensitivity to assumptions in the exposure assessment, and assessed the impact of uncertainty in urinalysis measurements on the precision of annual intake estimates using Markov Chain Monte Carlo (MCMC) methodology. Pairwise correlations (R_P) of estimated (JEM) and measured (10% sample) annual intakes were moderate to high ($R_P > 0.4$) for 10 out of 13 JEM groups, while absolute differences were <20% for 11 out of 13 JEM groups. There was little evidence of a temporal trend in correlations ($P = 0.13$) or absolute differences ($P = 0.34$). The median JEM-derived cumulative intake of 95.2 (IQR, 55.0–130.0) Bq was comparable to those based on alternative assumptions in the exposure assessment (median range, 95.2–100.0 Bq; 75th percentiles, 130.0–146.0 Bq). Measurement error simulation resulted in a 40–60% reduced median cumulative intake but higher maximum cumulative intakes. The JEM finds a balance between reliability and precision that makes it useful for epidemiological purposes and is relatively insensitive to specific choices in the exposure assessment. This JEM will allow the inclusion of workers with longest follow-up and who could not be included up until now in epidemiological studies without introducing significant bias.

INTRODUCTION

The Sellafield site is the largest nuclear facility in the UK, located on the western coast of Cumbria next to the Lake District National Park. The first irradiated nuclear fuel reprocessing operations and the plutonium production plant started operations in February 1952 (*1, 2*). The workforce includes one of the world's most important groups of workers exposed to plutonium for studying the potential health risks of internal exposure from intakes of this alpha-particle emitter, and includes over 12,500 individuals who have been monitored for exposure to plutonium.

Plutonium can be hazardous to human health when it is taken into the body, primarily because its main isotopes undergo radioactive decay through alpha-particle emission; this has been recognized since its discovery in the 1940s (*3*). Epidemiological analyses of populations exposed to plutonium provide the potential to directly investigate any health effects of such internal exposures; studies of the heavily exposed plutonium workers at the Mayak installation in the former USSR have shown clear evidence of an excess risk of cancer in the lung, liver and bone, where plutonium is deposited. However, although the Sellafield plutonium

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worker cohort has also been the subject of epidemiological analyses, evidence of increased risks of cancer and other diseases in this worker population has up to now been limited (*4–7*), an important reason being the exclusion from the studies of those working during the period of 1952 to 1963, because of serious problems with the assessment of plutonium exposures for these workers (*8–10*).

Plutonium exposure estimates have always been largely based on measurements of urinary excretion of plutonium through a program of urine sample collection and analysis. The modern convention is that an individual's plutonium intake and dose are then estimated from these monitoring results using models of the biokinetics of plutonium from entry to the body through to excretion (*9*). However, for several hundred workers employed at the start of plutonium work at Sellafield, from 1952–1963, historical monitoring records of urine samples collected at the time lack sufficient information to provide the reliable and unbiased exposure assessments needed for risk analyses within epidemiological studies. This is because many results were recorded only as being less than a ''reporting level'', which was an operational exposure control measure used during this period when exposures were controlled by comparison with a maximum permissible body burden [a threshold level for plutonium intake below which it was believed, at that time, there would be no adverse health effects (*11*)], rather than against annual dose limits (*12*), and which pre-dates the modern concept of internal doses and their assessment. This reporting level was 20 times higher than the ''limit of detection'' of the analytical technique used at the time, which in turn is approximately five times higher than the limit of detection for later samples. From other records, available for some workers during this period, it is known that many routine monitoring results were actually below the analytical limit of detection at the time, and consequently, assessments based solely on below-reporting-level results produced untenably large minimum intake and dose estimates (*13*). As a result of these limitations, it has not been possible to include a significant proportion of the early workforce in epidemiological studies of plutonium workers, which has led to diminished statistical power within these studies and has, accordingly, hampered investigation of dose-response associations. Furthermore, inclusion of data for these early Sellafield plutonium workers is particularly important for epidemiological purposes because exposures tended to have been higher than at any subsequent time, and due to the passage of time, knowledge of health outcomes among these early workers is increasingly complete as this population ages.

Several methods to infer estimates of individual-level exposure where temporal monitoring data are not available have been used in occupational exposure assessment and epidemiology, and include exposures self-reported by study subjects, expert assessment (*14*), extra/interpolation of known exposures (*15*), qualitative (*16*) and quantitative job-exposure matrices (JEMs) (*17*) or combinations of these methodologies. JEMs are a well-established exposure assessment methodology in occupational epidemiology and have, for example, been used in the assessment of exposures to chemicals (*18*), as well as physical factors including radiation (*19, 20*). However, there has been limited application of JEMs within the field of internal radiation exposure assessment and they have mainly been developed using qualitative approaches (*21*). The goal of the current work was to mitigate the impact of the problems with plutonium exposure assessment for the early Sellafield workforce through the development of a historical and quantitative JEM. Here, we describe the development of the JEM using a novel methodology of ''exposure analogous'' to account for issues of plutonium retention, and we report on the benchmarking and validation of the JEM, as well as its application for reassessing plutonium doses in the early Sellafield plutonium workforce. The value of this population-specific JEM is its future utility in studies of potential health risks related to plutonium exposure in epidemiological studies based on, or including, the Sellafield worker cohort.

MATERIALS AND METHODS

The Sellafield Plutonium Exposure JEM

Six hundred and thirty plutonium workers employed during the 1952–1963 period for whom all urine sample results were recorded as less than the 46 mBq (20 pg) reporting level were assigned to JEM groups. [Note that original records report plutonium content by mass (pg); the alpha activity value in becquerels (Bq) that this represents is inferred using information about isotopic ratios in plant material at the time, and on this basis the assumption used is that 1 pg = 2.3 mBq plutonium alpha activity].

These workers were then matched to 330 workers who worked in one of these JEM groups in the same year as at least one of the JEM cases and for whom this was their first job with potential for plutonium exposure and who had better urinalysis records (i.e., they had urinalysis results that were only censored by the analytical limit of detection at the time); these workers have been termed ''exposure analogues''. Both groups were used in the construction of the JEM, and contributed a total of 4,906 annual work history records and 8,082 urinalysis results, which together with expert assessment and additional information on industrial activities at the Sellafield site throughout its history, were used to estimate average plutonium intake levels for each of 14 identified ''homogeneous plutonium exposure working groups'' for each year during the period of 1952–1963. A ''homogeneous plutonium exposure group'' describes a group of workers for whom exposure is believed to come from the same distribution (despite the fact that individual measurements may differ) and therefore, for whom long-term mean exposure is comparable (*22*). The 14 final homogenous plutonium exposure groups (henceforth ''JEM groups'') within the JEM are described in Table 1.

Average exposures were estimated using a modified version (''PumaXJEM'') of the ''PuMA'' plutonium mass assessment code (*23*). This code uses mathematical models of plutonium inhalation, absorption, distribution, metabolism and excretion to assess intakes. The principal underlying methodology used was similar to that used for the European Union Seventh Framework Programme SOLO project (*10*), and was based on the International Commission on Radiological Protection (ICRP) Publication 130 Human Respiratory Tract Model (HRTM) (*24*) (using Sellafield plutonium nitrate absorption parameters as defined for the SOLO project (*10*): fr =

TABLE 1
Number of Measurements in Validation Samples (N), Pearson Correlation Coefficients (R_P) and Absolute Differences (%) between Estimated and Measured Annual Intake Values for each JEM Group

Group code	Description	N	R_P[a]	|Difference| (%)[b]
General	Default/nonspecific	22	0.40	6.47
ZC04	Plutonium finishing	329	0.96	1.11
Z005	Health physics and safety	229	0.61	8.53
Z011	Non-scientific research and development	21	0.56	17.66
ZC15	Plutonium recovery	33	1.00	6.61
Z016	Mechanical maintenance	36	0.44	9.55
ZC20	Research and development	225	0.74	11.94
ZC24	Instrument maintenance	192	0.58	6.64
ZC31	Training	–	0.80	11.37
ZC36	Plant maintenance and construction	–	0.55	5.54
Z039	Primary separation process	27	0.34	29.92
Z042	Electrical maintenance main	8	–0.57	55.81
Z075	Decontamination centre	–	–	18.34.
Z076	Laundry	–	–	–

Notes. Cells containing only a minus sign (–) are based on pairwise comparisons for limited years only, because there were no workers in that work group/year combination in the 10% validation set [ZC31 (n = 5), ZC36 (n = 9), Z075 (n = 2), Z076 (n = 0)].

[a] Pearson coefficients for correlations between the estimated (based on the 90% JEM) and measured (in the 10% validation sample).

[b] Absolute relative differences (%) between the estimated (based on the 90% JEM) and measured (in the 10% validation sample).

0.17, sr = 1.0; ss = 0.0022; fb = 0.002, sb = 0.0; f1 = 0.0001) and the revised ICRP Publication 67 (*25*) systemic model for plutonium developed by Leggett *et al*. (*26*). The main difference between the estimation procedures in the SOLO project and this project was that we used maximum likelihood rather than Bayesian estimation to avoid potential bias from using a relatively strong prior intake with heavily censored data. Note that the JEM in this study produces estimates of intakes of ''total plutonium alpha activity''. This permits doses to be easily calculated for different time periods, as required by future epidemiological research, and for the JEM to be readily updated to reflect any potential changes to the underlying assumptions (e.g., with respect to HRTM parameters or isotopic ratios)

The average annual plutonium intakes for each of the 14 JEM groups are provided in the Supplementary Information (http://dx.doi.org/10.1667/RR15177.1.S1) and were used to estimate cumulative 1952–1963 plutonium intakes in those 630 workers for whom all urine sample results were recorded as less than the reporting level.

Validation and Sensitivity Analyses Procedures

Validation and assessment of sensitivity of the JEM to assumptions in the exposure assessment consisted of three components: 1. Internal cross-validation to evaluate stability of the estimates; 2. Inter/extrapolation of temporal trends to evaluate the impact of assumptions in the exposure assessment; and 3. Markov Chain Monte Carlo (MCMC) simulations to evaluate the impact of uncertainty in the urinalysis measurements on which the subsequent exposure assessment is based.

Internal cross-validation. Prior to any analyses, the dataset was split into two separate sets using a random allocation algorithm:

1. The ''JEM building'' dataset contained a random sample of 90% of all individuals (i.e., 574 JEM cases and 280 exposure analogues; contributing 4,487 annual work records and 6,899 urinalysis records) and was used to develop the JEM.
2. The ''validation'' dataset contained the remaining 10% of all individuals (i.e., 56 JEM cases and 50 exposure analogues; consisting of 419 annual work records and 1,183 urinalysis records).

For validation purposes, in the absence of an independent dataset, we conducted internal cross-validation to evaluate how the model results based on the 90% ''JEM building'' dataset generalize to the *a priori* 10% validation dataset. Annual intakes (in Bq) were estimated based on the 90% ''JEM building'' for the work group-year combinations included in the 10% validation sample. Differences between log-transformed measured values (i.e., in the 10% sample) and estimated values (from the JEM based on the 90% sample) were determined and aggregated absolute differences, expressed as percentages, and Pearson correlation coefficients were determined for each work group as well as per year across work groups.

Inter/extrapolation of temporal trends. Several of the 168 cells of the JEM did not have annual intake estimates because no measurements were recorded for those exposure groups in those years (Supplementary Information; http://dx.doi.org/10.1667/RR15177.1.S1). The most likely explanation was that there was deemed to be no potential for exposure in these locations during these specific periods, and therefore monitoring was unnecessary. Although this was considered the most plausible explanation based on expert review of the evidence, three sensitivity analyses were conducted to explore the impact of this and other exposure assessment assumptions:

1. Empty cells in the middle of the JEM were imputed (i.e., excluding empty cells at the start, 1952, or end, 1963, of the JEM period) using three different approaches; through linear interpolation between adjacent cells in the JEM and from maximum likelihood estimates from linear regression both with and without log-transformation of the data [a standard assumption in occupational epidemiology to account for the skewed distributions of exposures often encountered (*27*)]. This analysis specifically assessed the assumption that missing measurements, where they had been collected in years before and after that particular year, were not the result of there being no potential for intake, but instead were the result of missing (i.e., not collected) data.
2. Similar to no. 1 (above), but with linear extrapolation to empty cells at the start or end years of the JEM also similarly imputed.
3. All cells, both with an estimate and empty, were replaced by maximum likelihood estimates from linear regression models based on the data to assess the impact of non-negligible

TABLE 2
Pearson Correlation Coefficients (R_P) and Relative Absolute Differences (%) per Year of the JEM

Year	Number of comparisons	R_P[a]	|Difference| (%)[b]
1952	7	–0.06	–56.2
1953	10	0.48	9.0
1954	10	0.27	7.7
1955	9	0.16	7.8
1956	4	0.08	20.9
1957	4	–0.04	4.4
1958	6	0.30	1.0
1959	6	0.15	18.0
1960	10	–0.27	13.7
1961	7	–0.36	2.7
1962	8	0.41	5.7
1963	6	–0.47	5.6
P for trend		0.13	0.34

[a] Pearson coefficients for correlations between the estimated (based on the 90% JEM) and measured (in the 10% validation sample).

[b] Absolute relative differences (%) between the estimated (based on the 90% JEM) and measured (in the 10% validation sample).

measurement error. Replacement was done assuming linear as well as log linear trends (similar to no. 1, above).

The alternative intake estimates were, in all cases, subsequently used to re-estimate cumulative exposures for the 630 workers without useful urinalysis data, which are directly compared to the JEM (considered ''best estimates'').

Impact of Uncertainty in Urinalysis Measurements

MCMC simulation studies were conducted to assess the impact of uncertainty in the urinalysis measurements on the cumulative intakes. Coefficients of variation (CV) of each sample of urinalysis results that informed each of the cells of the JEM were calculated and averaged for each of the 14 homogeneous exposure groups. The natural logarithm of each JEM estimate (μ) was multiplied by the CV to obtain an estimate for the corresponding standard deviation (σ) of the assumed normal distributions. One hundred ''artificial'' total intakes for each worker were generated by adding together the single MCMC draws from $N(\ln(\mu), \sigma)$.

Study Approvals

The University of Manchester granted University Research Ethics approval for the study on February 17, 2014 (reference no. TPS170214). The project was approved by the NDA-PHE Epidemiology Governance Group, which provides independent governance and oversight of epidemiological research proposed or undertaken in relationship to workers of the former British Nuclear Fuels Limited (BNFL) sites.

RESULTS

Internal Cross-Validation

Table 1 shows the Pearson correlation coefficients (R_P) and relative (in %) differences in the absolute values between the annual intake estimates based on the 90% JEM building and the 10% validation datasets. R_P are only presented where pairwise comparisons could be made (i.e., no missing data in either dataset), and were moderate to high ($R_P > 0.4$) for the majority (10 of 13) of JEM groups. They were small or negative for groups with only few urinalysis data in the 10% validation sample: groups ZC31 (training), ZC36 (plant maintenance and construction), Z042 (electrical maintenance), Z075 (decontamination centre) and Z076 (laundry).

Relative absolute differences ranged from 1.1% to 55.8%, but were <20% for the majority (11 of 13) of JEM groups and <10% for approximately one half of the groups. Differences were high for groups Z039 (primary separation process, 29.9%) and Z042 (electrical maintenance, 55.8%), although these were based only on few (n = 27 and n = 8, respectively) measurements. Pearson correlation coefficients and relative absolute differences are also shown for each year in Table 2. R_P are poor and range from –0.36 to 0.48 (mean $R_P \sim 0.05$), which can be explained by the fact that different distributions of work groups contribute to the different estimates; however, importantly, there is little evidence of a significant trend in correlations over time ($P = 0.13$). Similarly, there is little evidence of a trend in the relative absolute difference ($P = 0.34$), but the range of differences is also large (range –56.2% to 20.9%), although for nine of the twelve years the relative absolute difference is <10%.

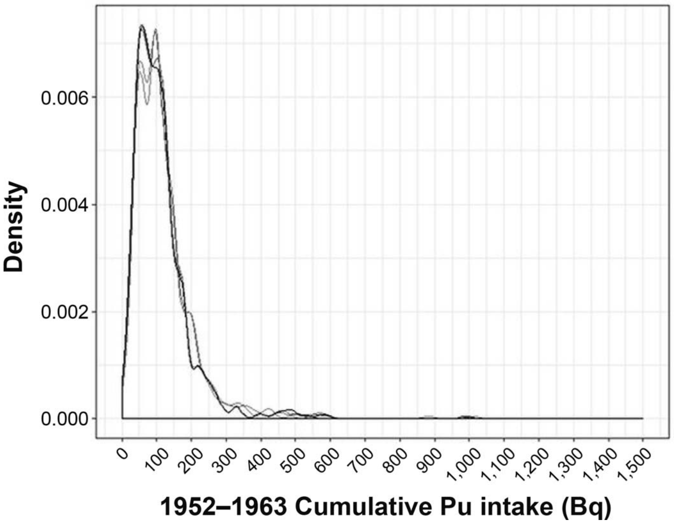

FIG. 1. Density plots of cumulative (total) individual intakes (Bq) from 1952–1963 of plutonium based on annual intake estimates from the final JEM (black) and the seven newly imputed JEMs (gray).

Interpolation and Extrapolation of Temporal Trends

Figure 1 shows the cumulative plutonium intakes from 1952–1963 for the 630 workers based on the JEM in comparison to cumulative intakes calculated using the seven JEMs based on alternative assumptions in the exposure assessment. As shown, these assumptions have minimal impact on the distribution of intakes from cumulative exposures for these workers. Median cumulative intake using the JEM is 95.2 Bq (interquartile range, 55.0–130.0 Bq), while for the alternative assumptions the median

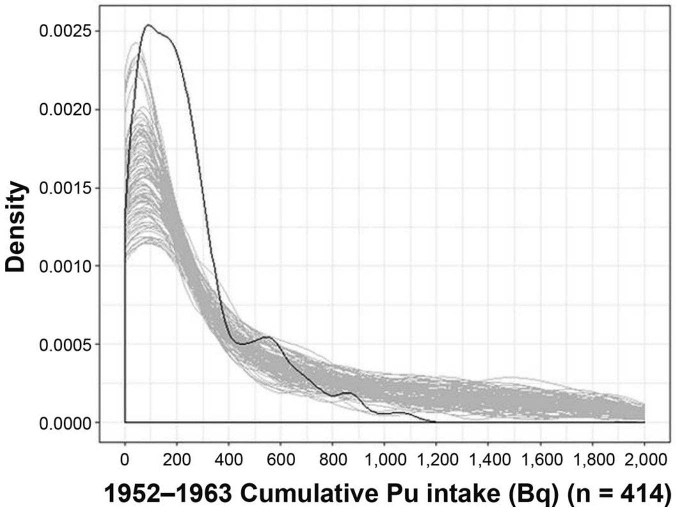

FIG. 2. Density plot of cumulative (total) doses from 1952–1963 plutonium intake estimates for the 414 workers with intakes based on the JEM (black) and for 100 MCMC simulated estimates (gray).

ranges from 95.2 to 100.0 Bq and the 75th percentiles from 130.0 to 146.0 Bq.

Impact of Uncertainty in Urinalysis Data

The impact of uncertainty in the urinalysis results on the cumulative 1952–1963 intakes is shown in Fig. 2. Inclusion of measurement error in the simulations results in reduced peak cumulative intake estimates from approximately 80–120 Bq to approximately 50 Bq, but in higher maximum cumulative intakes; the latter can be attributed to the absence of an upper limit to the distribution in our simulations. For illustration, histograms of log-transformed cumulative JEM intakes and based on simulated intakes 1–10 are presented in Fig. 3, and show comparable mean cumulative intakes, but with larger variability for the simulated intakes, as expected.

DISCUSSION

Here we have described the results of the construction, sensitivity and validation exercises for a plutonium intake job-exposure matrix for radiation workers employed at Sellafield from 1952–1963 who were potentially exposed to plutonium. A substantial review of all studies in the nuclear industry worldwide that employed some form of a JEM as part of the exposure assessment for epidemiology highlighted the importance of developing JEMs using a systematic approach, and quantitative information, where possible, and also the need for thorough validation and sensitivity analyses as part of this process (*21*). The current study follows these recommendations.

The use of a hybrid approach to JEM building for this pilot study has proven to be successful and has generated much more credible exposure estimates. Cumulative plutonium intakes for this group of workers yielded realistic estimates with median cumulative (total) 1952–1963 intake of 95 Bq (ranging from 6 Bq to 990 Bq), which is comparable to that of those workers in the same time period who had reliable urinalysis data. In comparison, exposure assessments based on conventional assessment methods range from 534 Bq to 36,700 Bq, with a median of 4,659 Bq, which is not plausible in this population (unpublished data). Internal cross-validation indicated that the JEM

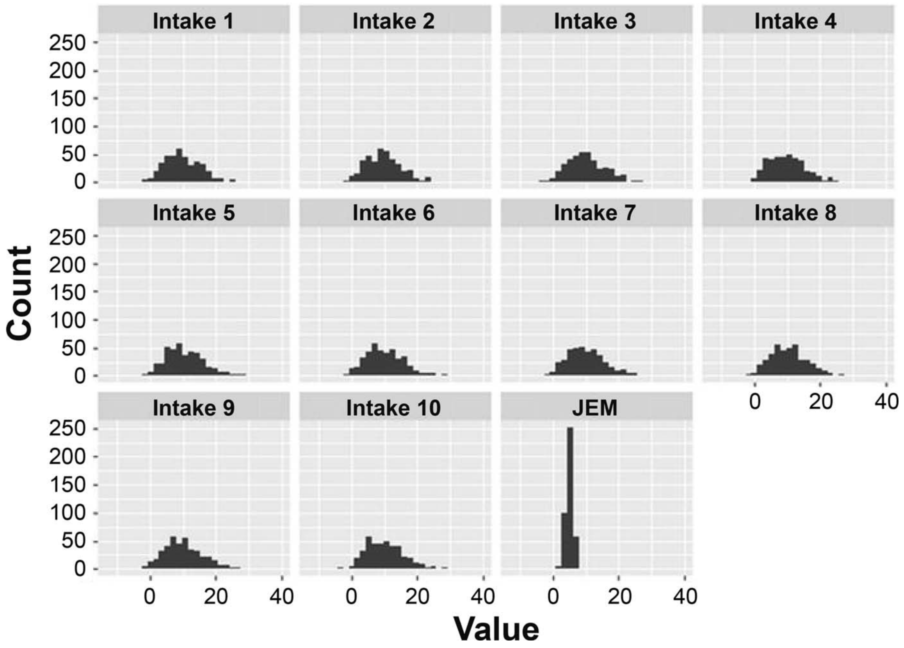

FIG. 3. Histograms of log-transformed cumulative 1952–1963 plutonium intake estimates for the 414 JEM cases with intakes based on the JEM and on 10 simulated intakes.

estimates were sufficiently accurate with differences between the JEM estimates of average plutonium intake in each homogeneous intake group and measured (from urinalysis samples) intakes generally less than 10%, while correlations within intake groups were moderate to good with no strong evidence of a temporal trend. Evaluation of the sensitivity of the JEM to assumptions in the exposure assessment and of the uncertainty in the urinalysis data on the 1952–1963 cumulative plutonium intake estimates indicated impacts were relatively minor and unlikely to have resulted in biased estimates. These results support the main underlying assumption of the JEM that workers' data can be aggregated into ''homogeneous exposure groups'' and also, importantly, that the cumulative intakes derived for these workers are of sufficient quality for use in future epidemiological studies, with little evidence of possible bias of the results (with respect to the factors evaluated here).

This study has some limitations. With respect to the validation of the JEM, the main limitations are that there are no additional urinalysis data available for this population that could be used for more extensive internal (cross-)validation, and similarly because this is a population-specific JEM, external data for external validation are not available.

Secondly, analyses have been based on estimates of average intakes for given homogeneous intake groups and years, and on the 1952–1963 cumulative intakes for individual workers estimated from these. There is significant variability in exposure at an individual level between different workers doing the same work or for a worker doing the same work on multiple occasions (i.e., within- and between-worker variability), and therefore, these will differ from the overall mean estimate at the aggregated level of the JEM (*28, 29*). Novel approaches to better appreciate the impact of classical and Berkson errors in radiation epidemiology have been pursued, specifically (*30, 31*), but the issue of estimation errors for individual workers is inherent to the use of JEMs (*29*).

However, the strength of this approach is that, in the absence of additional quantitative data, it enabled the development of a quantitative JEM for plutonium intake as well as the evaluation of the quality in terms of reliability, precision and sensitivity to expert decisions that had to be taken in the development of the JEM, for future epidemiological studies.

In conclusion, this evaluation of the impact of assumptions in the exposure assessment and complementary internal validation of the population-specific plutonium intake JEM for workers employed at Sellafield from 1952–1963, developed via the ''hybrid method'' using a mix of quantitative and qualitative data (*21*) combined with our novel approach of using ''exposure analogues'', indicates that the resulting JEM is able to find a balance between reliability and precision that makes it useful for epidemiological purposes, and that it is relatively insensitive to specific choices in the exposure assessment or to measurement error in the urinalysis measurements on which the JEM was based. As such, the JEM allows for a more dependable assessment of internal exposure to plutonium for workers employed at Sellafield between 1952 and 1963 with inadequate urinalysis data, thereby allowing the inclusion of these workers with longest follow-up (and for some with the highest plutonium intakes at Sellafield) that, up until now, could not be included in epidemiological studies without introducing significant bias.

Inclusion of these workers in future epidemiological studies of the Sellafield plutonium workers will increase statistical power to detect exposure/dose-response associations with less bias from early exposure assessments. Moreover, it is likely that imputation of the missing exposures with JEM-derived values will have considerable impact on risk estimates because early workers will usually have received some of the highest plutonium exposures and, due to the passage of time, health outcomes for these workers will now be largely known.

SUPPLEMENTARY INFORMATION

Table S1. The final plutonium intake (in Bq) of the Sellafield JEM.

Fig. S1. Direct comparisons between estimated intakes (based on the 90%-JEM) and measured intakes (in the 10% validation sample) for each year of the JEM groups, after log-transformation.

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REFERENCES

1. Arnold L, Gowing M. Independence and deterrence. Britain and atomic energy 1945–1952. Volume 1. Policy making. Basingstoke, UK: Palgrave Macmillan; 1974.
2. Gowing M. Independence and deterrence. Britain and atomic energy 1945–1952. Volume 2. Policy execution. Basingstoke, UK: Palgrave Macmillan; 1974.
3. Brues A, Lisco H, Finkel M. Carcinogenic action of some substances which may be a problem in certain future industries. Cancer Res 1946; 7:48.
4. Gillies M, Kuznetsova I, Sokolnikov M, Haylock R, O'Hagan J, Tsareva Y, et al. Lung cancer risk from plutonium: a pooled analysis of the Mayak and Sellafield Worker Cohorts. Radiat Res 2017; 188:645–60.

5. Grellier J, Atkinson W, Berard P, Bingham D, Birchall A, Blanchardon E, et al. Risk of lung cancer mortality in nuclear workers from internal exposure to alpha particle-emitting radionuclides. Epidemiology 2017; 28:675–84.
6. Omar RZ, Barber JA, Smith PG. Cancer mortality and morbidity among plutonium workers at the Sellafield plant of British Nuclear Fuels. Br J Cancer 1999; 79:1288–301.
7. Azizova TV, Batistatou E, Grigorieva ES, McNamee R, Wakeford R, Liu H, et al. An assessment of radiation-associated risks of mortality from circulatory disease in the cohorts of Mayak and Sellafield Nuclear Workers. Radiat Res 2018; 189:371–88.
8. Bingham D, Berard P, Birchall A, Bull R, Cardis E, Challeton-de Vathaire C, et al. Reconstruction of internal doses for the alpha-risk case-control study of lung cancer and leukaemia among European nuclear workers. Radiat Prot Dosimetry 2017; 174:485–94.
9. Riddell AE, Battersby WP, Peace MS, Strong R. The assessment of organ doses from plutonium for an epidemiological study of the Sellafield workforce. J Radiol Prot 2000; 20:275–86.
10. Riddell T, Birchall A, Puncher M, Efimov A, Vostrotin V. Report on the development and validation of plutonium dose assessment systems for epidemiological research. SOLO Sub-Project 3. Work Package 3.3 – Deliverable 3.3.1. 2015. (https://bit.ly/2OBgrUJ)
11. Beach S, Dolphin G. Determination of plutonium body burdens from measurements of daily urine excretion. In: Assessment of Radioactivity in Man. Vol. II. Vienna: International Atomic Energy Agency; 1964.
12. Britcher A, Dalton A, Riddell A, Battersby W. What do your plutonium in urine results tell you? A tour through 40 years of change at Sellafield. Radiat Prot Dosim 1994; 53:259–61.
13. Riddell AE. Development of an improved internal dose assessment methodology for plutonium. Birmingham: University of Birmingham; 2011.
14. Teschke K. Exposure surrogates: job-exposure matrices, self-reports, and expert evaluations. In: Nieuwenhuijsen MJ, editor. Exposure assessment in occupational and environmental epidemiology. Oxford: OUP; 2003. p. 119–32.
15. Dupree EA, Watkins JP, Ingle JN, Wallace PW, West CM, Tankersley WG. Uranium dust exposure and lung cancer risk in four uranium processing operations. Epidemiology 1995; 6:370–5.
16. Guseva Canu I, Paquet F, Goldberg M, Auriol B, Berard P, Collomb P, et al. Comparative assessing for radiological, chemical, and physical exposures at the French uranium conversion plant: Is uranium the only stressor? Int J Hyg Environ Health 2009; 212:398–413.
17. Hamra G, Nylander-French LA, Richardson D. Dose reconstruction for an occupational cohort at the Savannah River nuclear facility: evaluation of a hybrid method. Radiat Prot Dosimetry 2008; 131:188–97.
18. Ruttenber AJ, Schonbeck M, McCrea J, McClure D, Martyny J. Improving estimates of exposures for epidemiologic studies of plutonium workers. Occup Med 2001; 16:239–58.
19. Rooney C, Beral V, Maconochie N, Fraser P, Davies G. Case-control study of prostatic cancer in employees of the United Kingdom Atomic Energy Authority. BMJ 1993; 307:1391–7.
20. Wing S, Richardson D, Wolf S, Mihlan G. Plutonium-related work and cause-specific mortality at the United States Department of Energy Hanford Site. Am J Ind Med 2004; 45:153–64.
21. Liu H, Wakeford R, Riddell A, O'Hagan J, MacGregor D, Agius R, et al. A review of job-exposure matrix methodology for application to workers exposed to radiation from internally deposited plutonium or other radioactive materials. J Radiol Prot 2016; 36:R1–22.
22. Rappaport SM, Kromhout H, Symanski E. Variation of exposure between workers in homogeneous exposure groups. Am Ind Hyg Assoc J 1993; 54:654–62.
23. Riddell AE. Development of an improved internal dose assessment methodology for plutonium (Master of Philosophy thesis) Birmingham, UK: University of Birmingham; 2011. (https://bit.ly/2OEKjj9)
24. ICRP. Occupational intakes of radionuclides: Part 1. Publication 130. Ann ICRP 2015; 44.
25. ICRP. Age-dependent doses to members of the public from intake of radionuclides: Part 2. Ingestion dose coefficients. Publication 67. Ann ICRP 1993; 23.
26. Leggett RW, Eckerman KF, Khokhryakov VF, Suslova KG, Krahenbuhl MP, Miller SC. Mayak worker study: an improved biokinetic model for reconstructing doses from internally deposited plutonium. Radiat Res 2005; 164:111–22.
27. White E, Armstrong B, Saracci R. Principles of exposure assessment in epidemiology. 2nd ed. Oxford: OUP; 2010.
28. Kromhout H, Symanski E, Rappaport SM. A comprehensive evaluation of within- and between-worker components of occupational exposure to chemical agents. Ann Occup Hyg 1993; 37:253–70.
29. Kim HM, Richardson D, Loomis D, Van Tongeren M, Burstyn I. Bias in the estimation of exposure effects with individual- or group-based exposure assessment. J Expo Sci Environ Epidemiol 2011; 21:212–21.
30. Kukush A, Shklyar S, Masiuk S, Likhtarov I, Kovgan L, Carroll RJ, et al. Methods for estimation of radiation risk in epidemiological studies accounting for classical and Berkson errors in doses. Int J Biostat 2011; 7:15.
31. Masiuk SV, Shklyar SV, Kukush AG, Carroll RJ, Kovgan LN, Likhtarov IA. Estimation of radiation risk in presence of classical additive and Berkson multiplicative errors in exposure doses. Biostatistics 2016; 17:422–36.