EDITORIAL

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Nuclear worker studies: promise and pitfalls

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The publication in this issue of *BJC* of the findings of an updated study of Canadian nuclear industry workers by Zablotska *et al* (2014) invites enquiry into the background of this and similar studies. Nearly 40 years ago, the Royal Commission on Environmental Pollution (1976) opined that it would be desirable to conduct epidemiological studies of nuclear workers to directly assess risks to health from protracted occupational exposure to ionising radiation, to test the appropriateness of the assumptions made in setting radiation protection standards based largely on the experience of the acutely exposed Japanese survivors of the atomic bombings of Hiroshima and Nagasaki. The next year, the study by Mancuso *et al* (1977) on nuclear workers at Hanford, WA, appeared to show that cancer risks among these workers were greater than expected; the methodology of this study was heavily criticised (Hutchison *et al,* 1979), but it received much publicity.

In the United Kingdom, the National Registry for Radiation Workers (NRRW) was established in 1976 (Kendall *et al*, 1992), and nuclear worker studies were initiated in other countries, notably the United States of America (Gilbert *et al*, 1989) and Canada (Gribbin *et al*, 1993). However, it was recognised that international collaboration was highly desirable to increase the statistical power of the worker studies, and in 1988 the International Agency for Research on Cancer (IARC) agreed to coordinate such a collaboration, the first fruits of which appeared in 1995 and involved three countries and seven groups of workers, three from the United States of America (including Hanford), three from the United Kingdom (including Sellafield) and one from Canada (the workers of Atomic Energy of Canada Limited, AECL) (Cardis *et al*, 1995). The combined data showed a positive association between the risk of mortality from leukaemia (excluding chronic lymphocytic leukaemia, CLL) and the cumulative recorded dose of radiation from external sources, which was of marginal statistical significance, and a (non-significantly) negative association for the risk of all other cancers combined, results that were compatible with conventional risk estimates (Cardis *et al*, 1995). For AECL workers, the estimates of the excess relative risk (ERR) per sievert were as follows: leukaemia excluding CLL (5 deaths), 48.40 (95% confidence interval (CI): 2.8, >100); all other cancers (324 deaths), 0.13 (95% CI: <0, 2.1) (Cardis *et al*, 1995).

The IARC-coordinated collaborative study was later extended to 15 countries, and the first report from this study was published in 2005 (Cardis *et al*, 2005). Although the trend of risk with cumulative external dose was positive for mortality from leukaemia excluding CLL, somewhat surprisingly given the findings of the three-country study it was not statistically significant; but the association with dose for all other cancers was both positive and significant – the ERR/Sv was 0.97 (95% CI: 0.14, 1.97). Moreover, the risk estimate for the group of all other cancers was only just compatible with the prediction of standard risk models, leading to controversial suggestions that the risk of cancer resulting from protracted exposure to radiation in the workplace has been underestimated.

The interpretation of the 15-country study was not, however, straightforward, and one aspect of the findings that troubled both me (Wakeford, 2005, 2009a) and others (United Nations Scientific Committee on the Effects of Atomic Radiation, 2008; Boice, 2010) was the surprisingly large influence of the Canadian workers on the risk estimate for all other cancers – although the Canadian workers contributed around 4% of the deaths, the exclusion of these workers caused a $\sim$40% reduction in the risk estimate (Wakeford, 2005). In fact, the ERR/Sv for the Canadian workers, 6.65 (90% CI: 2.56, 13.0), was notably and significantly larger than the ERR/Sv estimate for the combined workers from the other 14 countries, 0.58 (90% CI: -0.10, 1.39) (Cardis *et al*, 2007). Of course, this does not mean that the Canadian data are necessarily wrong, but scrutiny of previous findings of studies of Canadian workers, including the three-country study (Cardis *et al*, 1995), reveals an apparent upward step-change in risk estimates for the group of all other cancers that coincides with the start of the use of Canadian National Dose Registry (NDR) data in the analyses (Wakeford, 2009a).

Ashmore *et al* (2010) examined the NDR data for the AECL workers, the group of workers who seemed to be the primary reason for the upward change in the Canadian risk estimates. They identified a number of possible deficiencies in the AECL worker data used in the 15-country study, in particular those relating to the data before 1971. They called for a thorough examination of the Canadian worker data, and if appropriate, a new analysis of Canadian worker risks based on revised NDR data.

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The Canadian worker data contributing to the 15-country study were those used in the study of Zablotska *et al* (2004) of workers from AECL and three Canadian electricity-generating companies. Now, Zablotska *et al* (2014) report the findings of an updated study of 45 656 Canadian nuclear industry workers, following a detailed check of dosimetry and employment records, which resulted in a number of changes in the AECL data in the NDR. These revisions led to a reduction in the ERR/Sv for mortality from all solid cancers from 2.80 (95% CI: −0.04, 7.13) to 1.77 (95% CI: −0.42, 5.30), the latter risk estimate being driven by the AECL workers, 3.25 (95% CI: 0.11, 8.85). However, also revealed was a notable difference in the solid cancers ERR/Sv for 3088 (19%) of the AECL workers first employed during 1956–1964, 7.87 (95% CI: 1.88, 19.5), and those first employed after 1964, −1.03 (95% CI: < −1.66, 5.76). Zablotska *et al* (2014) conclude that the finding for the early AECL workers is likely to be due to remaining data inaccuracies, probably missing dose information, rather than a real effect of radiation exposure, and they believe that use of the pre-1965 AECL worker data cannot be justified until further investigation is undertaken.

So, it would appear that the most reliable results from the 15-country study are for the combined 14 countries excluding Canada, which are not exceptional (see above). For Canada, Zablotska *et al* (2014) propose that until the findings of further investigations of the AECL data are available, the ERR/Sv estimates should be taken to be those using the post-1964 AECL worker data combined with the data for the workers of the three generating companies: leukaemia excluding CLL (12 deaths), 14.4 (95% CI: < −1.49, 146), and all other cancers (347 deaths), −1.36 (95% CI: < −1.47, 1.98).

Zablotska *et al* (2014) have indicated that it is intended to further investigate the data for pre-1965 AECL workers with the intention of eventually including them in future studies. Hopefully, this investigation will prove fruitful as the earlier studies of all AECL workers based on an AECL dosimetry database rather than the NDR suggested that these early workers could contribute valuable data – for example, it was pointed out above that a statistically significant positive trend with dose for mortality from leukaemia excluding CLL, was previously reported for all AECL workers (Cardis *et al*, 1995). It is generally the case that early nuclear workers will have accumulated larger radiation doses than later workers, not only because they have worked longer, but also and importantly because doses received in the early years of the industry were greater (sometimes much greater) than those received in recent years. Consequently, the inclusion of such early workers will considerably improve statistical power, and this is especially the case for workforces in countries with nuclear programmes starting in the 1940s and 1950s, such as Canada. By way of illustration, the recently published third analysis of the NRRW included greater than 10 000 workers with cumulative external radiation doses exceeding 100 mSv (i.e., moderate doses), but at the time of the analysis only about one-quarter of these workers had died (Muirhead *et al*, 2009), suggesting that substantial information is still to come.

Studies on radiation workers have the potential to provide valuable evidence on the risks from protracted exposure to low-level radiation. International collaboration remains the obvious way of extracting as much information out of the available data as possible, and these collaborations should certainly continue (Wakeford, 2009b), but the difficulties in conducting such studies and interpreting the results should not be underestimated. The latest Canadian worker study by Zablotska *et al* (2014) illustrates the care that must be exercised in collating worker data, and the problems that can arise, especially when using data that may have been collected for purposes other than epidemiology.

REFERENCES

Ashmore JP, Gentner NE, Osborne RV (2010) Incomplete data on the Canadian cohort may have affected the results of the study by the International Agency for Research on Cancer on the radiogenic cancer risk among nuclear industry workers in 15 countries. *J Radiol Prot* **30**: 121–129.

Boice JD (2010) Uncertainties in studies of low statistical power. *J Radiol Prot* **30**: 115–120.

Cardis E, Gilbert ES, Carpenter L, Howe G, Kato I, Armstrong BK, Beral V, Cowper G, Douglas A, Fix J, Fry SA, Kaldor J, Lavé C, Salmon L, Smith PG, Voelz GL, Wiggs LD (1995) Effects of low doses and low dose rates of external ionizing radiation: cancer mortality among nuclear industry workers in three countries. *Radiat Res* **142**: 117–132.

Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M, Hill C, Howe G, Kaldor J, Muirhead CR, Schubauer-Berigan M, Yoshimura T, Bermann F, Cowper G, Fix J, Hacker C, Heinmiller B, Marshall M, Thierry-Chef I, Utterback D, YO Ahn, Amoros E, Ashmore P, Auvinen A, Bae JM, Solano JB, Biau A, Combalot E, Deboodt P, Diez Sacristan A, Eklof M, Engels H, Engholm G, Gulis G, Habib R, Holan K, Hyvonen H, Kerekes A, Kurtinaitis J, Malker H, Martuzzi M, Mastauskas A, Monnet A, Moser M, Pearce MS, Richardson DB, Rodriguez-Artalejo F, Rogel A, Tardy H, Telle-Lamberton M, Turai I, Usel M, Veress K (2005) Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries. *Br Med J* **331**: 77.

Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M, Hill C, Howe G, Kaldor J, Muirhead CR, Schubauer-Berigan M, Yoshimura T, Bermann F, Cowper G, Fix J, Hacker C, Heinmiller B, Marshall M, Thierry-Chef I, Utterback D, Ahn YO, Amoros E, Ashmore P, Auvinen A, Bae JM, Bernar J, Biau A, Combalot E, Deboodt P, Diez Sacristan A, Eklöf M, Engels H, Engholm G, Gulis G, Habib RR, Holan K, Hyvonen H, Kerekes A, Kurtinaitis J, Malker H, Martuzzi M, Mastauskas A, Monnet A, Moser M, Pearce MS, Richardson DB, Rodriguez-Artalejo F, Rogel A, Tardy H, Telle-Lamberton M, Turai I, Usel M, Veress K (2007) The 15-Country Collaborative Study of Cancer Risk among Radiation Workers in the nuclear industry: estimates of radiation-related cancer risks. *Radiat Res* **167**: 396–416.

Gilbert ES, Fry SA, Wiggs LD, Voelz GL, Cragle DL, Petersen GR (1989) Analyses of combined mortality data on workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Nuclear Weapons Plant. *Radiat Res* **120**: 19–35.

Gribbin MA, Weeks JL, Howe GR (1993) Cancer mortality (1956-1985) among male employees of Atomic Energy of Canada Limited with respect to occupational exposure to external low-linear-energy-transfer ionizing radiation. *Radiat Res* **133**: 375–380.

Hutchison GB, MacMahon B, Jablon S, Land CE (1979) Review of report by Mancuso, Stewart and Kneale of radiation exposure of Hanford workers. *Health Phys* **37**: 207–220.

Kendall GM, Muirhead CR, MacGibbon BH, O'Hagan JA, Conquest AJ, Goodill AA, Butland BK, Fell TP, Jackson DA, Webb MA, Haylock RGE, Thomas JM, Silk TJ (1992) Mortality and occupational exposure to radiation: first analysis of the National Registry for Radiation Workers. *Br Med J* **304**: 220–225.

Mancuso TF, Stewart A, Kneale G (1977) Radiation exposures of Hanford workers dying from cancer and other causes. *Health Phys* **33**: 369–385.

Muirhead CR, O'Hagan JA, Haylock RG, Phillipson MA, Willcock T, Berridge GL, Zhang W (2009) Mortality and cancer incidence following occupational radiation exposure: third analysis of the National Registry for Radiation Workers. *Br J Cancer* **100**: 206–212.

Royal Commission on Environmental Pollution (Chairman: Sir Brian Flowers) (1976) *Sixth Report. Nuclear Power and the Environment*. Her Majesty's Stationery Office: London.

United Nations Scientific Committee on the Effects of Atomic Radiation (2008) *Effects of Ionizing Radiation. Volume I: UNSCEAR 2006 Report to the General Assembly, with Scientific Annexes. Annex A: Epidemiological Studies of Radiation and Cancer*. pp 13–322. United Nations: New York.

Wakeford R (2005) Cancer risk among nuclear workers. *J Radiol Prot* **25**: 225–228.

Wakeford R (2009a) Radiation in the workplace-a review of studies of the risks of occupational exposure to ionising radiation. *J Radiol Prot* **29**: A61–A79.

Wakeford R (2009b) More on the risk of cancer among nuclear workers. *J Radiol Prot* **29**: 1–4.

Zablotska LB, Ashmore JP, Howe GR (2004) Analysis of mortality among Canadian nuclear power industry workers after chronic low-dose exposure to ionizing radiation. *Radiat Res* **161**: 633–641.

Zablotska LB, Lane RSD, Thompson PA (2014) A reanalysis of cancer mortality in Canadian nuclear workers (1957–1994) based on revised exposure and cohort data *Br J Cancer* **110**(1): 214–223.

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