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# Assessing the reliability of dose coefficients for exposure to radioiodine by members of the public, accounting for dosimetric and risk model uncertainties

M Puncher<sup>1,4</sup>, W Zhang<sup>1</sup>, J D Harrison<sup>1,2</sup> and R Wakeford<sup>3</sup>

<sup>1</sup> Centre for Radiation, Chemical and Environmental Hazards, Public Health England, Chilton, Didcot, OX11 0RQ, United Kingdom

<sup>2</sup> Faculty of Health and Life Sciences, Oxford Brookes University, Headington Road, Oxford, OX3 0BP, United Kingdom

<sup>3</sup> Centre for Occupational and Environmental Health, The University of Manchester, Ellen Wilkinson Building, Oxford Road, Manchester, M13 9PL, United Kingdom

E-mail: [wei.zhang@phe.gov.uk](mailto:wei.zhang@phe.gov.uk)

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## Abstract

Assessments of risk to a specific population group resulting from internal exposure to a particular radionuclide can be used to assess the reliability of the appropriate International Commission on Radiological Protection (ICRP) dose coefficients used as a radiation protection device for the specified exposure pathway. An estimate of the uncertainty on the associated risk is important for informing judgments on reliability; a derived uncertainty factor, UF, is an estimate of the 95% probable geometric difference between the best risk estimate and the nominal risk and is a useful tool for making this assessment. This paper describes the application of parameter uncertainty analysis to quantify uncertainties resulting from internal exposures to radioiodine by members of the public, specifically 1, 10 and 20-year old females from the population of England and Wales. Best estimates of thyroid cancer incidence risk (lifetime attributable risk) are calculated for ingestion or inhalation of <sup>129</sup>I and <sup>131</sup>I, accounting for uncertainties in biokinetic model and cancer risk model parameter values. These estimates are compared with the equivalent ICRP derived nominal age-, sex- and population-averaged estimates of excess

<sup>4</sup> Deceased; this paper is dedicated to Matthew Puncher, who died suddenly before it was completed.



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thyroid cancer incidence to obtain UFs. Derived UF values for ingestion or inhalation of  $^{131}\text{I}$  for 1 year, 10-year and 20-year olds are around 28, 12 and 6, respectively, when compared with ICRP Publication 103 nominal values, and 9, 7 and 14, respectively, when compared with ICRP Publication 60 values. Broadly similar results were obtained for  $^{129}\text{I}$ . The uncertainties on risk estimates are largely determined by uncertainties on risk model parameters rather than uncertainties on biokinetic model parameters. An examination of the sensitivity of the results to the risk models and populations used in the calculations show variations in the central estimates of risk of a factor of around 2–3. It is assumed that the direct proportionality of excess thyroid cancer risk and dose observed at low to moderate acute doses and incorporated in the risk models also applies to very small doses received at very low dose rates; the uncertainty in this assumption is considerable, but largely unquantifiable. The UF values illustrate the need for an informed approach to the use of ICRP dose and risk coefficients.

Keywords: reliability, dose coefficients, radioiodine, risk uncertainties

## 1. Introduction

The International Commission on Radiological Protection (ICRP) publishes effective dose coefficients (sievert per becquerel intake) for radionuclides that enter the body by inhalation or ingestion ('internal emitters') (ICRP 1994, 1996). Although these dose coefficients are intended as point values, applied without consideration of uncertainties, it is nevertheless recognised that it is important to understand sources of uncertainty in the derivation of these quantities (Committee Examining Radiation Risks of Internal Emitters (CERRIE) 2004, Committee on Medical Aspects of Radiation in the Environment (COMARE) 2004, National Council on Radiation Protection and Measurements (NCRP) 2009). Puncher and Harrison (2012) discuss this issue and describe a framework in which the quantification of uncertainties on doses and risk can be used to assess the *reliability* of dose coefficients as a protection device. Knowledge of the uncertainty on the best estimate of risk—how well the risk can be determined—is a prerequisite to making a judgment on reliability. In this regard it is uncertainty on the location of the mean value of risk per unit dose (the risk coefficient) with respect to the nominal risk associated with the dose coefficient that is required (Puncher and Harrison 2012).

This paper describes the application of parameter uncertainty analysis to quantify uncertainties in estimates of thyroid cancer risk (specifically, the lifetime attributable risk, LAR) resulting from intakes of radioiodine species by members of the public, based on the population of England and Wales. Exposures to both iodine-131 and iodine-129 can occur in the UK:  $^{131}\text{I}$  is released into the atmosphere as a result of nuclear power generation, and  $^{129}\text{I}$  is released during spent nuclear fuel reprocessing and potentially from radioactive waste repositories (White and Smith 1984). Intakes by ingestion can occur as a result of the presence of these radioisotopes in food and water. Inhaled radioiodine is likely to be gaseous, with methyl iodide gas being the primary form (Collins *et al* 2004).

Epidemiological studies show significant age-at-exposure and sex differences in susceptibility to radiation-induced thyroid cancer. Excess risks are greatest for those exposed as young children and are also greater for females than males (National Research Council (NRC) 2006, United Nations Scientific Committee on the Effects of Atomic Radiation

(UNSCEAR 2008, 2013, ICRP 2007, NCRP 2008). It is therefore expected that thyroid cancer risks for exposed young females will be higher than the ICRP age-, sex- and population-averaged nominal risk estimates, where the ICRP population averaging is in terms of composite European-American and Asian populations (ICRP 2007). In the work described here, best estimates of cancer risk were calculated for 1 year old, 10-year old and adult (20-year old) females. Account was taken of uncertainties in the population mean values of parameters in the biokinetic model used to estimate doses to the thyroid from radioisotopes of iodine, and also higher thyroid doses resulting from greater iodine uptake by the thyroid expected for a UK population known to have a mild to moderate dietary iodine deficiency (Vanderpump *et al* 2011). Best estimates of cancer risk were calculated taking account of uncertainties in thyroid cancer risk model parameter values; differences between risk models and baseline incidence rates were also considered. The distribution of calculated risk coefficients provided an estimate of the population mean thyroid cancer incidence risk for the age groups considered. These were compared with ICRP nominal values to derive 'uncertainty factors' (UFs), which provide a measure of the 95% probable geometric difference between the best estimate and nominal value (Puncher 2014).

## 2. Methods

### 2.1. The biokinetic model for iodine

Current ICRP dose coefficients for inhalation and ingestion of radioisotopes of iodine were calculated using a simple three-compartment model, consisting of blood, soft tissues (excluding thyroid) and thyroid gland, with recycling of iodine occurring between thyroid and blood (ICRP 1989). This model is based on an earlier version derived by Riggs (1952), and was extended by ICRP (1989) to incorporate age dependent differences in uptake and retention of iodine by the thyroid. There do not appear to be significant differences in thyroid retention by males and females (Leggett 2010), and so it is reasonable to use the model to estimate doses for both male and female subjects.

Leggett (2010) provided a more physiologically realistic model, which includes additional soft tissue compartments and a more detailed representation of iodine uptake and retention by the thyroid gland. Compared to the ICRP (1989) model, this revised model predicts identical absorbed doses to the thyroid for  $^{131}\text{I}$  and small differences (20%) for the longer lived  $^{129}\text{I}$ ; but greater differences (around a factor of 3) are observed for radioisotopes with very short half-lives, such as  $^{122}\text{I}$  (half-life 3.6 min) (Leggett 2010). An uncertainty analysis showed no differences in the mean values or ranges of effective dose for ingestion and inhalation of  $^{131}\text{I}$  calculated using the original or revised model, and small but expected (20%) differences in mean values for  $^{129}\text{I}$  (Puncher and Harrison 2013). For this study, the current ICRP (1989) model was assumed to adequately represent retention of iodine in subjects of varying age, with appropriate modification for dietary iodine insufficiency, as discussed below.

For intakes by ingestion, the systemic model for iodine was coupled with the ICRP Publication 30 alimentary tract model (ICRP 1979). For intakes by inhalation, the systemic model was used in conjunction with the revised human respiratory tract model published by ICRP (2015).

## 2.2. Cancer risk models for the thyroid

Empirical models that predict excess risks of developing thyroid cancer following irradiation have been published by ICRP (2007), UNSCEAR (2008), the US NRC in the BEIR VII Report (NRC 2006), the Japanese/US Radiation Effects Research Foundation (RERF) (Preston *et al* 2007) and the US Environmental Protection Agency (EPA) (EPA 2011, Pawel and Puskin 2012). These risk models are based on thyroid cancer incidence data from the Life Span Study (LSS) of the Japanese survivors of the atomic bombings of Hiroshima and Nagasaki (Preston *et al* 2007), but also considered (to varying extents) data from studies of those exposed to external sources of photons for medical purposes (Ron *et al* 1995). Excess relative risk (ERR) models are preferred because the number of radiation-induced thyroid cancers predicted by ERR models will be less susceptible to variations in thyroid screening intensity and therefore to variations in background thyroid cancer incidence rates (ICRP 2007), but ERR/excess absolute risk (EAR) model combinations were also used where equivalent EAR models were available. All these models assume a linear no-threshold dose response at low doses.

There has been some debate over the past 30 years or so as to whether the thyroid cancer risk from internal exposure to  $^{131}\text{I}$  (and by extension,  $^{129}\text{I}$ ) is lower than that incurred from photon exposures from external sources, by anything up to a factor of 4 (ICRP 1991), although this might be due to dose protraction (and therefore accounted for by using a dose rate effectiveness factor (DDREF); see below) (NCRP 1985, Boice 2005). More recent evidence from large studies of exposure to  $^{131}\text{I}$  in childhood following the Chernobyl accident suggested the risks are comparable (Cardis *et al* 2005, Little *et al* 2014, 2015). There was also a suggestion (Cardis *et al* 2005) that the iodine-deficient thyroid is more susceptible to radiogenic cancer per unit dose than the normal thyroid, although this is a factor that may be accounted for by using an ERR model to estimate excess risk because iodine deficiency is positively correlated with an elevation in baseline thyroid cancer risk (Szybiński *et al* 2003, Zimmermann and Galetti 2015).

The present analysis assumes that the empirical models derived for thyroid cancer can be applied to calculate risks arising from internal exposure to radioiodine and uses primarily the ERR model for radiation-induced thyroid cancer presented in the BEIR VII Report (NRC 2006). BEIR VII provides statistical uncertainty estimates for the dose response parameter,  $\beta$ , which directly affects the estimates of risk. The effect of using different risk models is addressed by comparing the BEIR VII estimates with those derived for the same individuals using a number of alternative risk models: the UNSCEAR (2008), ICRP (2007), RERF (Preston *et al* 2007) and EPA (EPA 2011, Pawel and Puskin 2012) ERR models. To examine the influence of assuming a 100% ERR model, estimates were also performed using 50/50 ERR/EAR model combinations with the ERR and EAR thyroid cancer models presented by ICRP (2007), UNSCEAR (2008), and RERF (Preston *et al* 2007); BEIR VII (NRC 2006) and EPA (2011) provide ERR models only, and therefore it is not possible to calculate excess risks using ERR/EAR model combinations. The data sources for these different risk models were primarily the LSS database for the Japanese atomic bomb survivors, but the BEIR VII and EPA risk models also considered data from studies of external photon exposure for medical purposes (Ron *et al* 1995, NCRP 2008). There are limited sources of data on which to build risk models, and this is likely to result in an underestimation of the overall uncertainty of the derived risks. However, by comparing risk estimates from different models, the uncertainty associated with empirical risk modelling is assessed, which is essential for a comprehensive analysis of uncertainty.

In this paper, best estimates of LAR of thyroid cancer incidence following internal exposure to radioiodine were calculated. These are based on 2001 cancer incidence data for the population of England and 2003 mortality data for the population of England and Wales (Office for National Statistics (ONS) 2004a, 2004b). To investigate the sensitivity of LAR estimates to the use of these particular datasets for England and Wales, the composite European–American and Asian populations as presented by ICRP (2007) were adopted to provide alternative risk estimates.

### 2.3. Derivation of uncertainties in the biokinetic model for iodine

**2.3.1. Iodine retention in the thyroid.** A number of studies have been published describing the application of parameter uncertainty analysis to calculate uncertainties on doses resulting from ingestion and inhalation of iodine compounds, as reviewed by Puncher and Harrison (2012). The effective dose per unit ingestion of radioisotopes of iodine is determined by the amount of radioiodine taken up by the thyroid. The fraction of ingested iodine taken up by the thyroid in 24 h (the  $U_{24}$  value) is closely related to the amount of stable iodine present in the diet. Published uncertainty studies centre their distributions of thyroid uptake on values of 25%–30%. The current ICRP model (ICRP 1989, 1996) predicts a  $U_{24}$  value for  $^{129}\text{I}$  (serving as a surrogate for stable iodine) of 28%. These values are applicable to a population, such as that of the United States, with a relatively high dietary intake of stable iodine. However, a recent study by Vanderpump *et al* (2011) of daily urinary excretion of iodine by UK schoolgirls aged 14–15 years suggested that the UK population may suffer from mild iodine deficiency and thus have a higher average  $U_{24}$  value and hence higher thyroid dose compared with a similar US population. From the median urinary concentration of stable iodine determined by Vanderpump *et al* (2011) and using empirical relationships between  $U_{24}$  and urinary excretion of stable iodine described by Stanbury (1954) and Leggett (2010), it can be inferred that the mean  $U_{24}$  value for a UK population is more likely to be around 40%, although there is significant uncertainty on this value. For the present study, it was assumed that uncertainty on the average  $U_{24}$  value for a UK population can be reasonably represented by multiplying the rate constant from blood to thyroid in the ICRP (1989) model for iodine by a random variable sampled from a lognormal distribution with median value of 2 and geometric standard deviation (GSD) of 1.4. These assumptions resulted in a mean value for  $U_{24}$  of 42% and a 95% range of 27%–61% for ingested  $^{129}\text{I}$  (serving as a surrogate for stable iodine) in Monte Carlo simulations; the simulated predictions followed a normal distribution. The value of 27% probably represents a conservative lower bound (a value more consistent with a population with optimum levels of dietary iodine, ~30%) and 61% a conservative upper bound in the absence of more specific data.

Puncher and Harrison (2012) discussed the importance of attempting to distinguish between variability and uncertainties in assessing data and analyses relating to the biokinetics and resulting doses from radioisotopes of iodine. It was noted that while the distributions obtained by Hamby and Benke (1999) were smaller than those of Apostoaei and Miller (2004), in part because account had been taken of the relationship between dietary iodine levels and thyroid mass (e.g. Zvonova 1989), both may overestimate uncertainties by inclusion of variability.

To model uncertainty on the rate of loss of radioiodine from the thyroid, it is reasonable to assume that this process is dominated by secretion of thyroid hormone. Reference values for the rate of secretion collated by Leggett (2010) suggest a central range of 55–85  $\mu\text{g d}^{-1}$  for adults. In this study, uncertainty on the rate of removal of iodine from the thyroid was modelled by multiplying the model reference rates of loss of iodine from the thyroid by a random variable sampled from a lognormal distribution with a median value of unity and

GSD of 1.2. Assuming thyroidal iodine stores of 10 mg, this assumption resulted in a predicted rate of secretion of between 60 and 124  $\mu\text{g d}^{-1}$  (the 95% range of simulated predictions).

**2.3.2. Absorption from the alimentary tract.** The data relating to the absorption of iodine from the alimentary tract was reviewed by Harrison *et al* (2001), who suggested a 90% confidence interval of 0.9–1.0 for all members of the public. Because existing data suggest that the fraction absorbed from the alimentary tract to blood, the  $f_1$  value, for iodine in food is likely to be closer to unity, uncertainty on the population mean value was assumed to be represented by a triangular distribution with minimum of 0.9 and maximum value and vertex of unity.

**2.3.3. Deposition of methyl iodide vapour in the lungs.** It was considered that exposures via inhalation will occur primarily in the form of iodine vapour, most likely methyl iodide gas ( $\text{CH}_3\text{I}$ ) (Collins *et al* 2004) released as a result of nuclear power generation ( $^{131}\text{I}$ ) and fuel reprocessing ( $^{129}\text{I}$ ). ICRP (1995) assumes that methyl iodide behaves as a 'class SR-1' vapour: 70% of the inhaled vapour is assumed to be deposited in the thoracic and extra-thoracic airways (except  $\text{ET}_1$ ) and absorbed instantaneously to blood. Thus there is a 100% correlation between the fraction deposited in the airways and thyroid dose per Bq of inhaled radioiodine. Morgan and Morgan (1967) performed studies on human volunteers exposed to methyl iodide gas which suggested that the amount deposited varied between 50% and 90%, with a mean value of 70%. For the present study, uncertainty on the mean value was assumed to follow a normal distribution with a mean of 70% and standard deviation of 15% (which gives a >95% range of values of between 40% and 100%); this range is likely to overestimate uncertainty on the population mean value but accounts for the possibility that inhaled chemical forms may include other iodine species in addition to methyl iodide.

The distributions and parameters used in the assessment of uncertainties in the iodine biokinetic model, as derived from the literature reviewed in this section, are summarised in table 1.

#### 2.4. Derivation of uncertainties in the estimation of cancer risk

**2.4.1. Uncertainty in the dose response parameter.** The BEIR VII solid cancer risk models (NRC 2006) take the general form

$$\text{ERR} = \beta_S D \exp[\gamma(e - 30)](a/60)^\eta,$$

where  $D$  is the dose (Sv),  $e$  is the age at exposure (years), and  $a$  is the attained age (years).

Uncertainties arise in estimates of cancer risk model parameters—these are the sex-dependent linear dose response parameter ( $\beta_S$ ), and the parameters for age at exposure ( $\gamma$ ) and attained age at diagnosis ( $\eta$ )—as a result of statistical uncertainties in the epidemiological data. In an uncertainty analysis of cancer risk estimates described in the BEIR VII Report, uncertainties in statistical parameters were confined to the dose response parameter,  $\beta_S$ ; this was primarily because uncertainty in this parameter was expected to dominate uncertainty on the LAR for each cancer site (NRC 2006). The same approach was adopted in the risk code RadRAT for the same reasons (Berrington de Gonzalez *et al* 2012). In the present study, lognormal distributions were assumed for values of  $\beta_S$  for the BEIR VII thyroid cancer risk model, which has  $\eta = 0$  (i.e. no attained age dependence) and a different value of  $\beta_S$  for each sex, the value for females,  $\beta_F$ , being twice that for males,  $\beta_M$  (NRC 2006). The LAR estimates of thyroid cancer ERR were multiplied by a lognormally distributed variable with

**Table 1.** Probability distributions for iodine biokinetic parameters.

Parameter	Distribution	Median	GSD	
<i>ICRP (1979) systemic model</i>				
Blood to thyroid	Lognormal	2	1.4	
Thyroid to 'rest of body'	Lognormal	1	1.2	
<i>ICRP (1979) alimentary tract model</i>				
Fractional absorption to blood, $f_1$	Triangular	0.9 <sup>a</sup>	1 <sup>b</sup>	1 <sup>c</sup>
<i>ICRP (1995) respiratory tract model (methyl iodide vapour)</i>				
Regional lung deposition	Normal	0.7 <sup>d</sup>	0.15 <sup>e</sup>	

GSD—geometric standard deviation.

<sup>a</sup> Minimum value of triangular probability density function (pdf).

<sup>b</sup> mode of triangular pdf.

<sup>c</sup> maximum value of triangular pdf.

<sup>d</sup> Mean of a normal pdf.

<sup>e</sup> Standard deviation of a normal distribution.

median of unity and GSD of 1.93; this approach is equivalent to sampling  $\beta_F$ , the dose response parameter for females, from a lognormal distribution with a median value of 1.05 and 95% range of values between 0.28 and 3.9 (NRC 2006).

#### 2.4.2. Transfer of risk from high acute external exposure to low protracted internal exposure.

Estimates of risk of solid cancers are reduced by a factor of two by ICRP (2007) to account for the likelihood that radiation risks per unit dose are reduced at low doses and/or when exposure is fractionated or chronic, compared with the risk incurred from moderate-to-high acute doses; this factor is the dose and dose rate effectiveness factor (DDREF). The empirical models used to fit the epidemiological data for solid cancers in the A-bomb survivors assume a simple linear relationship between risk and dose (NRC 2006, ICRP 2007, UNSCEAR 2008), and there does not appear to be strong evidence from these data to suggest that this relationship departs from linearity at low doses (NCRP 2012), although the slope of the dose response is modified by factors such as age at exposure and sex. Evidence that the risk of cancer induction is reduced (and thus the slope of the dose-response is decreased) at low doses and/or dose rates comes from radiobiological studies (NRC 2006). Linear-quadratic dose response models fit animal tumour induction data, and the data also indicate that a dose delivered over a protracted time has less of an effect than the same dose delivered acutely for a range of radiobiological endpoints. Attempts have been made to infer DDREF more directly from epidemiological studies. For example, Jacob *et al* (2009) derived risk estimates for populations that were subject to protracted low-level exposures to low LET external radiation; ratios of cancer risk per unit dose for these groups and for the Japanese A-bomb survivors ostensibly provided an estimate of DDREF. This analysis resulted in a DDREF close to unity (Jacob *et al* 2009). However, limitations of the approach have been discussed by a report of the US National Council on Radiation Protection and Measurements (NCRP 2012), which noted that the results were sensitive to the inclusion of different exposed population groups in the analysis. Furthermore,

there was the potential that some of the population groups may have also been exposed to high LET internal emitters, which could reduce the inferred DDREF.

In this study it is assumed that the distribution derived in the BEIR VII Report to represent uncertainty on DDREF (NRC 2006), namely a lognormal distribution with median value of 1.5 and GSD of 1.35, is applicable for low-level exposure of the thyroid. The distribution assumed in BEIR VII defines a central value and 95% range that is:

- (i) informed predominantly by the most recent epidemiological data: the 95% range, assuming a median of 1.5 and GSD of 1.35, is 0.83–2.7, in good agreement with the likelihood profile for DDREF derived directly from the BEIR VII analysis of the A-bomb survivor data; and
- (ii) the range is compatible with more recent epidemiological studies (e.g. Jacob *et al* 2009) which suggest a DDREF for cancer risk resulting from low protracted exposures to low LET radiation of around unity.

The analysis of thyroid cancer risk conducted by Ron *et al* (1995) using pooled data from seven epidemiological studies found that for exposure to radiation during childhood, the dose response was linear down to doses of  $\sim 100$  mGy. Recently, Veiga *et al* (2016) updated this pooled analysis using data from 12 studies, and found that for those exposed in childhood to doses  $< 100$  mGy, the ERR of thyroid cancer increased significantly with dose with no detectable departure from linearity. Lubin *et al* (2017) examined in greater detail thyroid cancer risks among those exposed as children to doses  $< 200$  mGy in 9 of the 12 studies considered by Veiga *et al* (2016) having subjects with doses  $< 200$  mGy. They confirmed the findings of Veiga *et al* (2016) that for dose ranges  $< 200$  mGy and  $< 100$  mGy the ERR increased significantly with dose and that the trend was consistent with linearity. Nonetheless, although Lubin *et al* (2017) found no reliable evidence for a threshold in the dose response, they could not exclude the possibility of a threshold below  $\sim 40$  mGy. At the very low doses ( $\mu\text{Sv}$  range) and dose rates of relevance in the current study, the uncertainty on the shape of the dose response is substantial and the distribution of the DDREF derived by BEIR VII from comparatively high exposures will under-represent this uncertainty.

**2.4.3. Additional uncertainties.** In an uncertainty analysis of radiation-induced thyroid cancer risk, the US EPA (EPA 2011, Pawel 2013) multiplied estimates of risk by a factor sampled from a lognormal distribution with median of unity and GSD of 1.3. This represents the composite of other more minor sources of uncertainty including selection bias, disease misclassification, incomplete follow-up and errors in dosimetry. Although derived for the follow-up studies of the A-bomb survivors, this distribution was considered to be reasonably representative of similar uncertainties in the medically exposed cohorts that were also considered by Ron *et al* (1995) to derive estimates of thyroid cancer risk (EPA 2011). The same assumption is made here. The present analysis also assumes that the relative biological effectiveness for  $^{129}\text{I}$  and  $^{131}\text{I}$  beta particle emissions is not significantly different from unity, which is supported by a comparison of the thyroid cancer risk estimates obtained from studies of children exposed to  $^{131}\text{I}$  released during the Chernobyl accident and those exposed to external sources of photons (Little *et al* 2014, 2015).

The distributions and parameters used in the assessment of uncertainties in the thyroid cancer risk model, as derived from the literature reviewed in this section, are summarised in table 2.

**Table 2.** Probability distributions derived for thyroid cancer risk model parameters.

Parameter	Distribution	Median	GSD
<i>Epidemiology</i>			
Statistical uncertainty ( $\beta_F$ )	Lognormal	1	1.93
Selection bias	Lognormal	1	1.1
Disease misclassification	Lognormal	1	1.05
Errors in dosimetry	Lognormal	1	1.16
Incomplete follow-up	Lognormal	1	1.2
<i>Extrapolation to low-level exposure</i>			
Dose and dose rate effectiveness factor (DDREF)	Lognormal	1.5	1.35

GSD—geometric standard deviation

 $\beta_F$ —slope of the dose response for females.

## 2.5. Parameter uncertainty analysis

**2.5.1. Monte Carlo methods.** Monte Carlo calculations were performed using a software tool developed to analyse uncertainties on doses (Puncher and Birchall 2008). This code samples parameter values from defined distributions and can be interfaced with the dosimetry codes, IMBA Professional Plus (Birchall *et al* 2007) and PLEIADES (Fell *et al* 2007), to calculate doses. The code has been extended to calculate uncertainties on cancer risk estimates from sampled doses using a risk code developed by the UK Health Protection Agency (Wall *et al* 2011). Doses to the thyroid were calculated assuming ICRP reference masses for the female thyroid (ICRP 2001a, 2001b).

The Latin Hyper-cube sampling algorithm (McKay *et al* 1979) was used to sample parameter values. A Latin Hyper-cube matrix of 500 variates was constructed for dose and risk model parameters using the distributions derived above; up to three separate simulations were performed to monitor convergence of the calculated distributions of risk coefficients. In each simulation, the following steps were performed for each vector of sampled parameters following ingestion or inhalation of 1 Bq of  $^{131}\text{I}$  or  $^{129}\text{I}$ :

1. The biokinetic parameter values were set in the dosimetry code PLEIADES.
2. The average absorbed dose received by the thyroid in each year following an acute intake of 1 Bq at 1, 10 or 20 years of age to age 70 years was calculated.
3. The lifetime attributable risk (%LAR) up to an attained age of 89 years was calculated using the BEIR VII ERR model for thyroid cancer (NRC 2006), taking as input the doses from (2) and sampled risk model parameter values.

The above steps were repeated for each of the 500 vectors of parameters in the Latin Hyper-cube matrix. Final distribution statistics were calculated from the combined runs (1500 iterations in total).

**2.5.2. Calculation of nominal ICRP values of cancer incidence.** For comparison with best estimates of cancer risk, nominal ICRP cancer incidence values were also calculated. ICRP committed equivalent doses to the thyroid for each age group were used (ICRP 1989, 1993, 1995), considering intakes by ingestion and by inhalation of methyl iodide. Nominal values of excess thyroid cancer incidence were then obtained by multiplying the committed doses by nominal incidence risk coefficients from ICRP Recommendations in Publications 60

(ICRP 1991) and 103 (ICRP 2007); thyroid cancer incidence risks based on Publication 60 ( $R60_{\text{inc}}$ ) and Publication 103 ( $R103_{\text{inc}}$ ) were obtained as follows:

$$R60_{\text{inc}} = \frac{R_D w_T}{l(2-k)} \cdot \left(1 + \frac{(1-k)}{k}\right), \quad (1)$$

$$R103_{\text{inc}} = \frac{R_D w_T}{l(k + q(1-k))}, \quad (2)$$

where

$w_T$  is the tissue weighting factor for the thyroid: 0.05 (ICRP 1991) and 0.04 (ICRP 2007);

$k$  is the thyroid cancer lethality fraction: 0.1 (ICRP 1991) and 0.07 (ICRP 2007);

$l$  is the relative life lost weighting factor for thyroid cancer: 1 (ICRP 1991) and 1.29 (ICRP 2007);

$R_D$  is the detriment-adjusted total stochastic effects nominal risk coefficient, % Sv<sup>-1</sup>: 7.3 (ICRP 1991) and 5.7 (ICRP 2007);

$q$  is the adjusted lethality fraction, obtained from:

$$q = q_{\text{min}} + k(1 - q_{\text{min}}), \quad (3)$$

where

$q_{\text{min}}$  is the minimum weight for non-lethal cancers (0.2 for the thyroid, 0 for skin and 0.1 for all other tissues);

equations (1)–(3) are derived from equations (A.143), (A.141) and (A.144), respectively, of ICRP Publication 103 (ICRP 2007).

**2.5.3. Risk model structure uncertainty.** To obtain an indicative assessment of the effect of the choice of risk model on the estimate of excess thyroid cancer risk, the point estimate from the risk calculation described above using the BEIR VII ERR model was repeated using the ERR models of UNSCEAR, ICRP, RERF and EPA (UNSCEAR 2008, ICRP 2007, Preston *et al* 2007, EPA 2011), and the influence of selecting a 100% ERR model was examined by using 50/50 ERR/EAR model combinations with ERR and EAR models taken from UNSCEAR (2008), ICRP (2007) and RERF (Preston *et al* 2007); EAR models were not presented by BEIR VII or EPA.

**2.5.4. Baseline incidence rate uncertainty.** Excess risks derived from ERR models, unlike those based upon EAR models, depend on background incidence rates. Therefore, in order to assess the sensitivity of the radiation-induced excess thyroid cancer risk to the choice of background incidence rates, in addition to the incidence rates for the population of England in 2001, the rates used by ICRP (2007) for a composite European–American population and for a composite Asian population were employed to provide alternative LAR estimates.

### 3. Results

#### 3.1. Uncertainties on thyroid cancer risk and comparison with ICRP nominal values

Summary statistics for LAR (% per Bq) following an acute ingestion or inhalation of <sup>131</sup>I and <sup>129</sup>I are given in tables 3 and 4, respectively, where they are compared with the nominal ICRP based values.

**Table 3.** Uncertainty analysis of lifetime attributable risk (%LAR  $\times 10^{-6}$ , per Bq intake) of thyroid cancer incidence resulting from ingestion of  $^{129}\text{I}$  or  $^{131}\text{I}$ .

	1 year old female		10-year old female		20-year old female	
	$^{129}\text{I}$	$^{131}\text{I}$	$^{129}\text{I}$	$^{131}\text{I}$	$^{129}\text{I}$	$^{131}\text{I}$
<i>LAR using ICRP nominal risk coefficients, R60, R103</i>						
ICRP 60 (R60)	8.3	6.9	7.3	2.1	4.0	0.85
ICRP 103 (R103)	2.5	2.1	2.2	0.64	1.22	0.26
<i>LAR using BEIR VII ERR model for thyroid cancer</i>						
Mean	22.9	15.7	9.2	2.1	2.54	0.43
Median	15.9	11.5	6.4	1.55	1.79	0.31
GSD	2.3	2.2	2.3	2.1	2.2	2.1
$Q_L$	3.0	2.5	1.3	0.33	0.37	0.07
$Q_U$	84.7	54.2	34.2	7.0	9.2	1.43
<i>Ratio of LARs from BEIR VII model and ICRP nominal risk coefficients</i>						
Mean/R103	9.2	7.5	4.2	3.3	2.1	1.7
$Q_U$ /R103	34.0	25.9	15.5	10.9	7.6	5.6
R103/ $Q_L$	0.8	0.8	1.7	1.9	3.3	3.6
Mean/R60	2.8	2.3	1.3	1.0	0.6	0.5
$Q_U$ /R60	10.3	7.8	4.7	3.3	2.3	1.7
R60/ $Q_L$	2.7	2.8	5.6	6.3	10.9	11.9

GSD—geometric standard deviation.

 $Q_U$ —the upper 97.5 percentile. $Q_L$ —the lower 2.5 percentile.Statistics represent the combined results from three separate runs ( $n = 500$  iterations each).

The mean and median values are given, together with the geometric standard deviation, and the 95 percentiles: the 2.5% ( $Q_L$ ) and 97.5% ( $Q_U$ ) values. It can be seen that the distributions are broadly similar for both routes of intake; the geometric differences between mean or lower/upper quantile values and the nominal ICRP values are essentially the same for both routes, and very similar for both radioisotopes. The geometric ranges are similar for each age at intake—a GSD of 2.1–2.3 reflects a 95% range of a factor of 20–30. However, as expected, the risk per unit intake is substantially greater for the younger ages at exposure, showing large differences between the age- and sex-dependent value and the age-, sex- and population-averaged nominal ICRP values; for example, the ratio of the mean value to the ICRP Publication 103 (ICRP 2007) based value is 7.5 for ingestion by the 1 year-old female compared with 1.7 for the adult female. In addition to the age- and sex-specific effects, scoping calculations indicate that the differences between the mean value and nominal value also result to a lesser extent from the lognormal uncertainty on the slope parameter,  $\beta_F$ , which positively skews the distribution, and also on the uncertainty distribution assumed for DDREF which is centred on the BEIR VII value of 1.5 rather than the ICRP value of 2. These calculations also show that the uncertainty on  $\beta_F$  dominates the uncertainty on the distribution of risk.

The ratios of the ICRP nominal risks to  $Q_L$  or  $Q_U$ , whichever is the greater, are 28, 12 and 6 for inhalation of  $^{131}\text{I}$  by 1, 10- and 20-year olds, respectively, using the ICRP Publication 103 values, and 9, 7 and 14, respectively, using the ICRP Publication 60 values.

**Table 4.** Uncertainty analysis of lifetime attributable risk (%LAR  $\times 10^{-6}$ , per Bq intake) of thyroid cancer incidence resulting from inhalation of  $^{129}\text{I}$  or  $^{131}\text{I}$  as methyl iodide vapour.

	1 year old female		10 year old female		20 year old female	
	$^{129}\text{I}$	$^{131}\text{I}$	$^{129}\text{I}$	$^{131}\text{I}$	$^{129}\text{I}$	$^{131}\text{I}$
<i>LAR using ICRP nominal risk coefficients, R60, R103</i>						
ICRP 60 (R60)	5.8	4.8	5.2	1.42	2.9	0.60
ICRP 103 (R103)	1.74	1.45	1.57	0.43	0.87	0.18
<i>LAR using BEIR VII ERR model for thyroid cancer</i>						
Mean	16.1	11.4	6.6	1.5	1.8	0.31
Median	11.2	7.9	4.5	1.1	1.3	0.22
GSD	2.3	2.3	2.3	2.2	2.3	2.3
$Q_L$	2.1	1.5	0.89	0.22	0.23	0.04
$Q_U$	63.5	40.9	24.0	5.2	6.3	1.2
<i>Ratio of LARs from BEIR VII model and ICRP nominal risk coefficients</i>						
Mean/R103	9.3	7.8	4.2	3.5	2.1	1.7
$Q_U$ /R103	36.5	28.2	15.3	12.2	7.2	6.4
R103/ $Q_L$	0.82	1.0	1.8	2.0	3.8	4.1
Mean/R60	2.8	2.4	1.3	1.1	0.63	0.52
$Q_U$ /R60	11.0	8.5	4.6	3.7	2.2	1.9
R60/ $Q_L$	2.7	3.2	5.8	6.5	12.7	13.7

GSD—geometric standard deviation.

 $Q_U$ —the upper 97.5 percentile. $Q_L$ —the lower 2.5 percentile.Statistics represent the combined results from three separate runs ( $n = 500$  iterations each).

These are the UFs, for inhalation of  $^{131}\text{I}$ , and broadly similar UFs are derived for ingestion of  $^{131}\text{I}$ , and for inhalation and ingestion of  $^{129}\text{I}$  (tables 3 and 4).

### 3.2. Risk model structure uncertainty

Comparisons of the best point estimates of risk obtained using the ERR models of BEIR VII, UNSCEAR, ICRP, RERF and EPA are provided in table 5; for completeness the risks for males are given as well as the risks for females. It can be seen that amongst the ERR models, the BEIR VII estimate is comparable with the UNSCEAR and ICRP estimates, but higher than the RERF and EPA estimates by a factor of 2–3. Although EAR risk models are not generally used for the assessment of thyroid cancer risk, for comparison purposes we calculated the thyroid cancer LAR using ERR and EAR model combinations using the risk models of UNSCEAR, ICRP and RERF, with each model contributing 50%; BEIR VII and EPA only present ERR thyroid cancer risk models, so it is not possible to use model combinations. It can be seen that the LAR estimate based upon the BEIR VII ERR model is within a factor of 2 of the LAR estimates obtained using the ERR/EAR model combinations, suggesting that the choice of model has a relatively small effect on the estimate of risk.

**Table 5.** Comparison of best point estimates<sup>a</sup> of cancer risk (%LAR  $\times 10^{-6}$ ) calculated using ERR models and 50/50 ERR/EAR model combinations, considering ingestion of 1 Bq of <sup>131</sup>I by members of the population of the England and Wales.

Risk models	Age at exposure					
	1 year old		10-year old		20-year old	
	Female	Male	Female	Male	Female	Male
BEIR VII ERR	9.00	1.80	1.20	0.24	0.21	0.05
UNSCEAR ERR	10.00	3.30	0.85	0.27	0.21	0.07
EPA ERR	5.00	1.90	0.35	0.12	0.11	0.04
RERF ERR	3.24	0.84	0.60	0.15	0.15	0.04
ICRP ERR	8.70	1.75	1.20	0.24	0.21	0.05
RERF (0.5ERR + 0.5EAR)	10.47	2.57	1.70	0.43	0.36	0.09
ICRP (0.5ERR + 0.5EAR)	9.85	3.10	2.43	0.42	0.40	0.11
UNSCEAR (0.5ERR + 0.5EAR)	16.20	4.40	1.60	0.38	0.42	0.11

<sup>a</sup> All estimates adjusted assuming a DDREF of 2.  
 ERR—excess relative risk; EAR—excess absolute risk.  
 EAR models are not presented by BEIR VII or EPA.

### 3.3. Dependence of risk on population assumptions

The LAR estimates derived here are based upon the background thyroid cancer incidence rates for the population of England in 2001. As the excess radiation-induced risk of thyroid cancer is based upon the application of an ERR model, this excess risk will depend upon the background thyroid cancer incidence rate. Consequently, we have performed LAR computations based upon alternative background thyroid cancer incidence rates. Tables 6 and 7 show the results of applying the ERR models and the 50/50 ERR/EAR model combinations to the thyroid cancer incidence rates assumed by ICRP (2007) for their composite European–American population and composite Asian population (ICRP 2007); for completeness risks for both females and males are shown. The LARs using these alternative background thyroid cancer incidence rates are within a factor of 2–3 of the values obtained using the rates for the population of England in 2001.

## 4. Discussion

This paper quantifies uncertainties in best estimates of the radiation-induced excess risk of thyroid cancer incidence for variously aged female members of the general public of England and Wales resulting from ingestion and inhalation of <sup>129</sup>I or <sup>131</sup>I. The BEIR VII thyroid cancer risk model, the primary risk model used in this study, gives lower ERRs for males than females, so excess risks will be higher in females, who also have higher background rates of thyroid cancer incidence. The analysis accounts for uncertainties in the biokinetic model for iodine and in empirical thyroid cancer risk models. It is important to emphasise that the calculated distributions reflect uncertainty on the population-averaged value of cancer risk for each age group in the specified population, rather than inter-subject variation in cancer risk within the population. The uncertainty on the best estimate of the population mean can be compared with the nominal ICRP values derived for the same exposure pathway as a tool to assess the reliability of the protection quantity (Puncher 2014). It should be noted that in the

**Table 6.** Comparison of point estimates<sup>a</sup> of cancer risk (%LAR  $\times 10^{-6}$ ) calculated using ERR models and 50/50 ERR/EAR model combinations, considering ingestion of 1 Bq of <sup>131</sup>I by members of the ICRP (2007) composite European–American population.

Risk models	Age at exposure					
	1 year old		10-year old		20-year old	
	Female	Male	Female	Male	Female	Male
BEIR VII ERR	14.9	2.97	2.00	0.40	0.35	0.07
UNSCEAR ERR	15.8	4.81	1.49	0.44	0.34	0.11
EPA ERR	8.50	3.04	0.57	0.19	0.17	0.06
RERF ERR	5.30	1.31	1.04	0.25	0.25	0.06
ICRP ERR	14.5	2.88	1.96	0.39	0.35	0.07
RERF (0.5ERR + 0.5EAR)	11.4	2.76	1.89	0.45	0.41	0.09
ICRP (0.5ERR + 0.5EAR)	12.7	2.97	2.07	0.49	0.47	0.11
UNSCEAR (0.5ERR + 0.5EAR)	19.1	5.08	1.89	0.49	0.48	0.13

<sup>a</sup> All estimates adjusted assuming a DDREF of 2.  
ERR—excess relative risk; EAR—excess absolute risk.  
EAR models are not presented by BEIR VII or EPA.

**Table 7.** Comparison of point estimates<sup>a</sup> of cancer risk (%LAR  $\times 10^{-6}$ ) calculated using ERR models and 50/50 ERR/EAR model combinations, considering ingestion of 1 Bq of <sup>131</sup>I by members of the ICRP (2007) composite Asian population.

Risk models	Age at exposure					
	1 year old		10-year old		20-year old	
	Female	Male	Female	Male	Female	Male
BEIR VII ERR	19.60	2.60	2.60	0.35	0.47	0.06
UNSCEAR ERR	17.60	4.50	1.60	0.41	0.39	0.09
EPA ERR	10.10	2.70	0.70	0.17	0.22	0.05
RERF ERR	6.20	1.20	1.20	0.23	0.31	0.06
ICRP ERR	19.10	2.50	2.60	0.34	0.47	0.06
RERF (0.5ERR + 0.5EAR)	11.90	2.70	2.00	0.45	0.44	0.10
ICRP (0.5ERR + 0.5EAR)	15.10	2.80	2.40	0.47	0.53	0.11
UNSCEAR (0.5ERR + 0.5EAR)	20.0	4.90	1.90	0.48	0.51	0.12

<sup>a</sup> All estimates adjusted assuming a DDREF of 2.  
ERR—excess relative risk; EAR—excess absolute risk.  
EAR models are not presented by BEIR VII or EPA.

current ICRP system, the nominal cancer incidence coefficient for each tissue is further adjusted for detriment, which accounts for differences in cancer lethality, quality of life reduction and relative cancer-free life lost as a result of exposure (ICRP 2007). These quantities are also dependent on age at exposure and sex, and on population variation in cancer survivability, so reliability should formally be assessed by comparing best estimates of detriment-adjusted values with the nominal detriment-adjusted values (Puncher and Harrison 2012). The present paper does not apply an age-, sex- and population-specific detriment

adjustment to the calculated best estimates of risk; but it is judged that the effect of not including this is small when compared with the effect of the uncertainties in the biokinetic and thyroid cancer risk models considered here, and therefore the application of detriment adjustment is unlikely to have any important effect on the difference between the best estimates of cancer risk and the nominal values reported here.

In this analysis the calculated distributions reflect uncertainty on the values of the population means; this is because the distributions assumed for the cancer risk and biokinetic model parameters represent epistemic uncertainties that affect risk estimates for all members of the population, and hence also the population mean value of risk per unit intake. Strictly speaking, the analysis should also account for the additional indirect effect of biokinetic parameter variability on the population mean risk per unit intake using a two stage Monte Carlo process; parameter variability can affect the value of the population mean if the model is very nonlinear (Puncher and Harrison 2012). However, the influence of the latter is likely to be very small in the present analysis because the distribution of risk coefficients is clearly dominated by uncertainties in the risk model parameter values rather than biokinetic model parameter values; as noted above, the most significant contributor to this is uncertainty in the dose response parameter,  $\beta_F$ . This result is consistent with an analysis by Pawel *et al* (2007) who also found that uncertainties in the risk model generally made the greatest contribution to overall uncertainties in cancer risk estimates for internal emitters.

The current ICRP (2007) nominal incidence risks are derived for an age- and sex-averaged mixed population representing a combination of a composite European–American population based on three population groups, and a composite Asian population based on four population groups. The risk estimates obtained from specific risk models that take account of the variation of the excess risk in relation to age at exposure and sex would be expected to be higher than the ICRP nominal risks for intakes by 1 year old and 10-year old females because of the established higher risk of radiation-induced thyroid cancer in females and those exposed at a young age. It is noteworthy that this difference is greater in the case of nominal values based on ICRP Publication 103 (ICRP 2007) risk analyses than for the corresponding ICRP Publication 60 (ICRP 1991) values. This difference between ICRP nominal risk coefficients of about a factor of three arises from the use of different risk models for thyroid cancer: the Publication 60 coefficient (ICRP 1991) was derived from an older EAR model for thyroid cancer published by NCRP (1985), based primarily on a follow-up of North American subjects exposed to external x-radiation for the treatment of benign disease in childhood, whereas the Publication 103 model (ICRP 2007) was based on the later study of Ron *et al* (1995), combining two case-control studies and five cohort studies of exposure to external sources of radiation (one of these being the Japanese atomic-bomb survivor cohort), and including a much larger number of individuals (120 000) than considered by NCRP (1985).

Comparisons of modelled risk estimates calculated using available ERR models for thyroid cancer showed differences in LAR estimates of a factor of 2–3. These differences reflect the underlying assumptions in each model; for example, the BEIR VII ERR model assumes that, after an initial latent period of five years, the ERR remains constant throughout the remainder of life, whereas the EPA ERR model assumes some attenuation of risk with time since exposure. Examination of the effect of assuming that risks might be better represented by a combination of ERR and EAR models, assuming 50/50 ERR/EAR model combinations, showed differences of factors of up to 2–3 from the equivalent 100% ERR models. The factors influencing the excess thyroid cancer risks predicted by models are likely to be better determined by further epidemiological evidence obtained from studies of those exposed for medical reasons and those exposed to radioiodine from the Chernobyl accident.

Any cancer risk model that assumes that the radiation-induced excess risk is dependent to a large extent upon the background rate of incidence (i.e. that the ERR plays a major role in determining the excess risk when the background rate of cancer varies between populations) implies that the magnitude of the excess risk will be sensitive to the background rate pertaining in the population of interest. We have examined the influence of the background rate of thyroid cancer incidence by using the rates assumed by ICRP (2007) for composite European–American and Asian populations in addition to the rates for the 2001 population of England. This shows that the derived LAR varies by a factor of 2–3 depending on the assumed background thyroid cancer incidence rate. The importance of this aspect of the analysis is that thyroid cancer incidence rates in the UK are not static but are increasing with time. This may be due to the increasing ability to detect small tumours, more complete registration of cases, or an increase in the presence of major thyroid cancer risk factors in the UK, or some combination of these. Whatever the explanation, if the radiation-induced excess thyroid cancer risk is dependent to some extent on the background risk of thyroid cancer, then an increase in the background risk will lead to an increase in the excess risk produced by exposure to radiation. Further, increasing longevity will also lead to an increase in LAR since there is a greater lifespan in which a radiation-induced thyroid cancer may become evident.

The scope of the present study is confined to the estimation of differences between the best estimate of age-, sex- and population-specific thyroid cancer risk and the nominal risk associated with dose coefficients for iodine, accounting for uncertainties in the models used to derive them. The objective was not to determine best estimates of radiogenic thyroid cancer risk arising from the environmental exposure pathways to which they may be applied, although account is taken of the likely chemical form and route of exposure. Nevertheless, to fully assess the reliability of a dose coefficient, it is also important to consider the exposure pathway in which it is applied. For example, the risk estimates calculated here assume an acute intake of 1 Bq at 1, 10 and 20 years of age, which cover the range of ages at exposure considered by ICRP for members of the public (ICRP 1996). In reality, such an acute exposure pattern is more relevant to accident scenarios rather than those incurred from routine environmental releases. With regard to routine releases, individuals will incur very low exposures from intakes throughout life. Therefore, for a given intake starting at 1 year of age, a chronic, rather than acute, exposure pattern will result in a substantially lower overall lifetime risk than that incurred from the same level of (acute) intake at the same age.

The data presented in this paper illustrate the need for care in interpreting dose coefficients and assessed doses for members of the public of different ages and sexes. Epidemiological studies have provided good evidence that risks of radiation-induced thyroid cancer show a strong dependence on sex and age-at-exposure, with substantially greater risks for exposures of females in early childhood falling to notably lower values in adulthood (UNSCEAR 2013, ICRP 2007). Most other cancers show less pronounced age-at-exposure effects, but also display a generally greater sensitivity at younger ages (UNSCEAR 2013). For radiological protection purposes, ICRP uses the available data to calculate nominal detriment values applying to a composite world population and considering all adults (for workers) or all ages (for the general public) (ICRP 2007). That is, the values are age-, sex- and population-averaged to apply to all adults, for the control of exposures of workers, or the whole population, for the control of exposures of the public. ICRP considers the control of public exposures in planned, existing and emergency situations using effective dose, calculated using tissue weighting factors that relate to overall detriment. In each case, control will involve optimisation of protection below constraints or reference levels of effective dose that apply to members of the public of all ages. The use of effective dose in this way allows all radiation exposures to be considered and controlled together. ICRP additionally uses the concept of the Representative Person to replace the previous

designation of a critical group—the Representative Person is taken to be representative of the most exposed individuals for a particular circumstance of exposure, for example, for discharges of radionuclides from a nuclear installation (ICRP 2007). In some circumstances, the Representative Person might be a young child because estimated doses are greater than for other age groups. In setting constraints and reference levels, and implementing procedures to ensure optimisation of protection, consideration may be given to the possibility that the excess risks associated with exposure of the specified age-group might be substantially greater than indicated by nominal detriment values. For example, it is clear from the results presented in this study that it would be inappropriate to interpret effective dose resulting from an acute intake of  $^{131}\text{I}$  or  $^{129}\text{I}$  by a one-year-old child using the ICRP population-averaged value of nominal detriment. For such an exposure, it may be appropriate to consider the use of a lower constraint or reference level and/or more rigorous consideration of optimisation than if the exposure was exclusively to an adult population.

In nuclear accident situations, doses from iodine radioisotopes may be substantial, notably the high thyroid doses ( $>1\text{ Gy}$ ) received by many children living in heavily contaminated areas of the former USSR following the Chernobyl accident in 1986, which has led to several thousand additional cases of thyroid cancer among those exposed as children in these areas (UNSCEAR 2011). However, doses to the UK public resulting from planned activities are generally of the order of microsieverts of effective dose. At such very low doses and dose rates, uncertainties in any inferred risk will be greater than those presented in this study; the assumption of direct proportionality of excess risk and dose regardless of the magnitude of the dose becomes much more uncertain at very low doses. Recent studies (Veiga *et al* 2016, Lubin *et al* 2017) have provided evidence of a linear dose response for thyroid cancer at doses  $<100\text{ mGy}$ , and although the data are consistent with no threshold dose, a threshold below  $\sim 40\text{ mGy}$  could not be excluded (Lubin *et al* 2017). Therefore, for very low thyroid doses of a few microgray the resulting risk, if any, cannot be quantified using epidemiological data, although the assumption of direct proportionality of risk and dose down to very low doses is reasonable for the purposes of this study (ICRP 2007). Further, doses may be delivered over many years, as are those resulting from releases of  $^{129}\text{I}$  from radioactive waste repositories, for example, and differences in risk as a function of age at exposure will then not be important.

In order to detect the level of excess risk of thyroid cancer predicted by current models when low doses are received, very large numbers of exposed children would be necessary. For example, to achieve reasonable statistical power to detect the predicted excess risk of thyroid cancer in a study of infants each receiving a  $50\text{ mGy}$  acute thyroid dose, the lifetime follow-up of a cohort of about 30 000 infants (and a comparison group of around 60 000 unexposed infants) would be required. An illustration of the difficulties of detecting the predicted excess risks of thyroid cancer comes from the study of thyroid cancer among those exposed at a young age to substantial discharges of  $^{131}\text{I}$  from the Hanford nuclear installation in the USA during the early years of operations (Davis *et al* 2004): even a study of these exposures involving nearly 3500 people exposed at a young age (mean thyroid dose,  $174\text{ mGy}$ ) did not have sufficient power to permit the detection of any excess thyroid cancers among those most at risk from the discharges (UNSCEAR (2013)).

## 5. Conclusions

This uncertainty analysis of best estimates of excess risk of thyroid cancer incidence for female members of the population of England and Wales gave values for the inhalation of  $^{131}\text{I}$  (with 95% confidence) within a factor of 28, 12 and 6, for 1 year, 10-year and 20-year olds, respectively, of ICRP Publication 103 nominal risk values (ICRP 2007), and 9, 7 and 14,

**Table 8.** Uncertainty factors<sup>a</sup> for ICRP dose coefficients used to protect female members of the public of England and Wales from exposure via ingestion or inhalation of <sup>131</sup>I and <sup>129</sup>I.

Radioisotope	Age group (Females)	Uncertainty factors (UFs)	
		ICRP Publication 60	ICRP Publication 103
<sup>131</sup> I	1 year old	9	28
	10-year old	7	12
	Adult (20-year old)	14	6
<sup>129</sup> I	1 year old	11	37
	10-year old	6	16
	Adult (20-year old)	13	8

<sup>a</sup> The UF is an estimate of the 95% probable geometric difference between the best estimate of risk and the nominal risk.

respectively, of ICRP Publication 60 values (ICRP 1991). For <sup>129</sup>I, the corresponding values were 37, 15 and 7, respectively, and 11, 6 and 13, respectively. These values are obtained from the ratios of upper 97.5 percentile ( $Q_U$ ) to ICRP value, or ICRP value to lower 2.5 percentile ( $Q_L$ ), whichever ratio is the greater, and they define the UFs for the ICRP dose coefficients for inhalation of these iodine radioisotopes. Broadly similar values were derived for ingestion of the radioisotopes, and the UFs are summarised in table 8, where the larger of the inhalation UF or ingestion UF for each age group and ICRP nominal risk is presented for each radioisotope.

Examination of the influence of the choice of risk models, and the combination of risk models (i.e. the combination of ERR and EAR models), together with assumptions about the background rates of thyroid cancer incidence, shows that the point estimates of thyroid cancer risk are likely to be within a factor of 2–3 of the principal point estimates adopted for this study. Thyroid cancer risk models will improve in accuracy as more data become available from medical and Chernobyl studies, but excess risks are also likely to be influenced by factors such as increasing background thyroid cancer incidence rates in the UK. Even though recent studies indicate an excess thyroid cancer risk that is directly proportional to dose down to low doses of ~40 mGy, for very low doses of a few microgray from routine releases of radioiodine the actual risk, if any, will not be discernible epidemiologically, but is assumed to exist at the levels predicted by standard risk models.

These findings illustrate the need for care in using ICRP dose coefficients and interpreting dose assessments for members of the public of different ages and sexes. In general, doses will be very small fractions of constraints or reference levels and age- and sex-related differences in inferred risks will not be important, and neither will ethnicity. However, it is clear that estimates of lifetime attributable risk per mGy are substantially greater for 1 year old infants than for adults. Depending on the circumstances of the exposures, therefore, it may be appropriate to take account of such differences in considerations of the optimisation of protection, particularly in assessing higher doses resulting from short-term accidental releases.

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