

Highlights

- Review of Cost Effectiveness of Domestic Radon Remediation
- Review of developments and future trends in Lung Cancer Diagnosis, Treatment and Survival
- Domestic Radon Remediation Programmes remain cost effective, despite improvements in Lung cancer diagnosis, treatment and survival
- Public Participation in Radon Remediation Programmes remains key.

Radon, a gaseous radioactive decay product of naturally-occurring uranium is widely distributed in the environment in rocks and soils and, in certain circumstances, can accumulate in the built environment. Initial studies confirmed a direct link between exposure to both radon gas and its short-lived radioactive progeny, and increased lung-cancer incidence, and demonstrated that radon levels in domestic housing can be sufficiently high to expose occupants to increased risk of lung-cancer. Subsequent studies worldwide have shown that it is cost-effective to detect and reduce domestic radon levels in order to reduce this risk.

Recent advances in the early detection of lung-cancer, coupled with the development of improved treatment procedures, have progressively improved survival from the disease, with the numbers surviving at 5 years doubling over recent years, during which period the real costs of lung cancer treatment have risen by around 30 %. In the meantime, however, in addition to radon and tobacco-smoke, other airborne pollutants have been identified as risk-factors for lung-cancer. This paper reviews both these actual developments and anticipated future trends, and concludes that since these advances in diagnosis and treatment of lung-cancer have had only a modest effect on cost-effectiveness, it is still important to conduct radon monitoring and remediation programmes. While the general increase in life-expectancy improves the cost-effectiveness of radon remediation programmes significantly, reducing tobacco-smoking incidence reduces that cost-effectiveness but with the overall benefit of reducing radon-related lung-cancers. The challenge remains of encouraging affected householders to remediate their homes to reduce radon levels.

Cost-Effectiveness of Radon Remediation Programmes in the UK in the 2020s

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1 Introduction

Lung-cancer accounted for around 35,600 deaths in the United Kingdom (UK) in 2016, representing 21% of all cancer deaths (CRUK, 2018). Although tobacco-smoking has long been identified as the major risk-factor, responsible for around 70% of lung-cancers, radon, by virtue of its radioactive heavy-metal progeny, is now known to be a significant additional risk factor, with the effects of radon and tobacco-smoking together, initially considered to be multiplicative, now regarded as sub-multiplicative. (BEIR VI, 1999).

Radon, a naturally-occurring gaseous radioactive decay product of uranium, is present with varying geographical concentrations in rocks and soils throughout the earth's crust, and in building materials incorporating or manufactured from these. Although radon dissipates rapidly in outdoor air, it concentrates in the built environment, typical ingress routes being cracks in walls and floors, drains and loose-fitting pipes, the mean UK domestic radon concentration being around 20 Bq.m⁻³ (Wrixon et al., 1998).

The most significant radon isotope, ²²²Rn, decays by α -emission (half-life 3.8 days) via a decay-chain ending in the stable lead isotope ²⁰⁶Pb. That decay-chain includes three α -emitting progeny, i.e. ²¹⁸Po, ²¹⁴Po and ²¹⁰Po, which are readily adsorbed onto atmospheric particles. Inhalation of ²²²Rn and these progeny provides the majority of the radiation dose received by the respiratory system (Darby et al., 2001). A direct consequence of this is the well-established association between enhanced levels of environmental radon and increased risk of lung-cancer (BEIR VI, 1999) and the recognition of radon as a significant factor in the incidence of lung-cancer among smokers, these observations being reinforced by case-control studies of residential radon exposure (e.g. Darby et al., 2004).

Public-health initiatives to measure and reduce radon levels have consequently been widely established, and many countries, including members of the European Union and the USA, have now implemented National Radon Action Plans. The cost-effectiveness of such programmes in the UK was first reviewed by Kennedy et al. (1999), who assessed the costs of lung-cancer treatment and the costs and benefits of radon remediation. The survival gain from remediation procedures was estimated using life-expectancy data from cancer registries and the UK National Life Tables. Published costings for lung-cancer treatment at that time were rare: at the time of the Kennedy study, only one analysis relating to the UK had been published (Sanderson et al., 1994), with another (Wolstenholme and Whynes, 1999) then still in press. Sanderson et al. reported unit costs for each element of lung-cancer treatment and the average cost per case, using a sample of 196 patients treated at Southampton General Hospital, UK, around 1990. Kennedy et al. (1999) used lung-cancer data for Northamptonshire from 1996.

A subsequent major study (Gray et al., 2009) included lung-cancer treatment costs taken from Wolstenholme and Whynes (1999), updated to account for inflation. This incorporated an estimate of the costs of improved palliative care, together with revised costs for NHS annual per capita expenditure on all other health-care during added life-expectancy, based on costs for 2007 (DoH, 2007).

In all of these studies, and in our analysis here, the start-up costs, initial publicity and administration running costs of implementing a radon remediation programme are not included.

Subsequent reviews of cost-effectiveness of radon remediation in the UK have addressed the labour and materials costs of radon remediation (Denman et al., 2005), the public response to calls for

43 remediation (Denman et al., 2009), the impact of tobacco-smoking cessation programmes (Denman
44 et al., 2004; Denman et al., 2014), the geographical distribution of radon-bearing rocks (Denman et
45 al., 2013) and the impact of changing the Radon Action Level (Denman et al., 2002). However, there
46 has been no review of the impact of changes in lung-cancer survival since the studies of Kennedy et
47 al. (1999) and Gray et al. (2009). Clinical developments during this period now permit earlier
48 diagnosis and significantly more sophisticated treatment of lung-cancer, both developments
49 contributing towards enhanced survival rates. In addition, general population life-expectancy has
50 risen significantly over the past two decades.

51 This paper reviews the cost-effectiveness of radon remediation programmes in the light of these
52 developments, using official UK Government published datasets, and considers recent concerns that
53 airborne pollution is also a risk-factor for lung-cancer.

54 **2 Materials and Methods**

55 Current and recent (1999 onwards) literature on improvements to lung-cancer diagnosis and
56 treatment has been reviewed. In particular, cost-analyses presented in the report prepared by
57 Incisive Health Ltd¹. for Cancer Research UK² (Birtwistle and Earnshaw, 2014) have been used
58 extensively to develop a new assessment of the impact of advances in diagnosis and treatment of
59 lung-cancer. This report considered colonic, rectal, ovarian and non-small-cell lung-cancers in the
60 UK, and provided separate cost-effectiveness analyses for each of these cancers under three
61 scenarios: the then-current general situation; the outcome of raising standards universally to then-
62 current best practice; anticipated improvements in diagnosis and treatment.

63 **2.1 Lung-Cancer Diagnosis**

64 Lung-cancer is a disease predominantly affecting the elderly, with age-dependent incidence in the
65 UK over the period 2014-16 peaking at age 70-74 for females and 70-79 for males (CRUK, 2018), with
66 average age at diagnosis of 72.1 for females and 72.2 for males (ONS, 2019a). Allowing for age-
67 group demographics, the incidence rate peaks at age 80-84 for females and 85-89 for males
68 (Birtwistle and Earnshaw, 2014), with 67% of new cases being found to be advanced, i.e. Stages III or
69 IV, (NCIN, 2019).

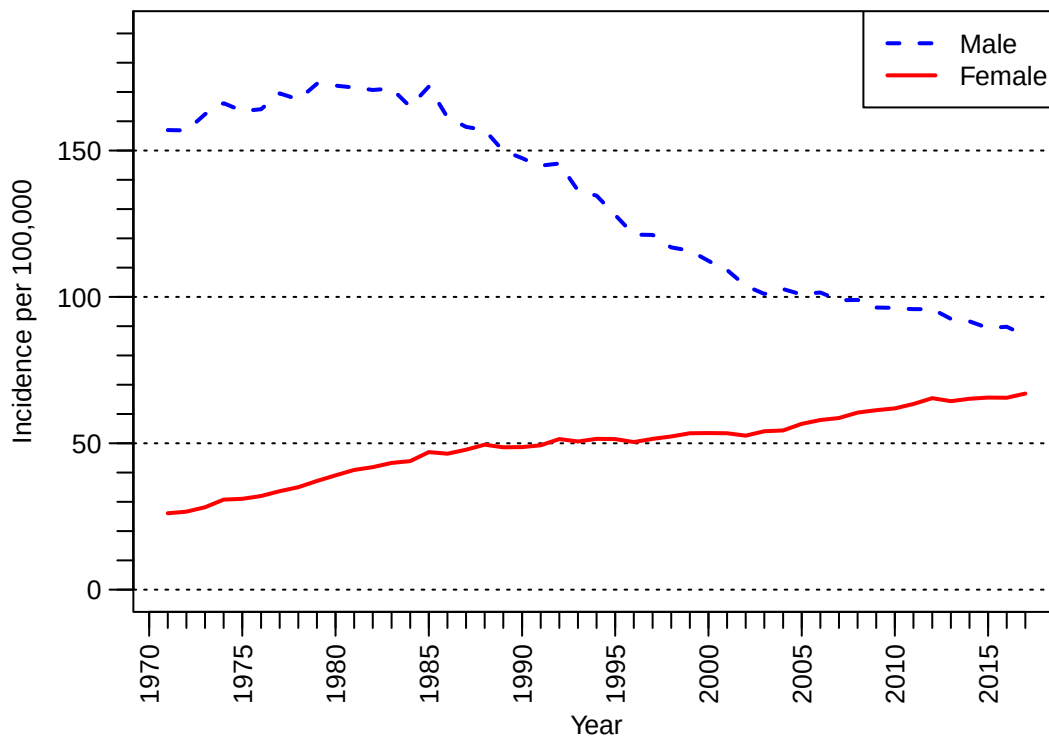
70 Figure 1 demonstrates the variation over time of lung-cancer incidence in males and females from
71 the 1970s to the present. Although lung-cancer incidence in males has remained persistently higher
72 than in females over this period, with incidence declining steadily following a peak around 1980,
73 incidence in females continues to increase with little sign of peaking (ONS, 2019a,b). However, the
74 gap is narrowing steadily, with the male:female incidence ratio decreasing from 3:1 in 1990 to 1.5:1
75 in 2011, and to 1.28:1 in 2017.

76 The decrease in male lung-cancer incidence over recent decades reflects the decline in tobacco-
77 smoking prevalence among men, from 80% in 1950 (Peto et al., 2000) to 16.5% in 2018 (ONS, 2018).
78 In contrast, smoking increased in popularity among women during the second half of the 20th
79 century, rising from 40% in 1950 to a peak of around 50% around 1970 (Peto et al., 2000) before
80 falling, in line with male smoking prevalence, to 13% in 2018 (ONS, 2018). The UK Government White
81 Paper on Smoking (HMSO, 1998) notes a rise in smoking prevalence in young girls from 1988 to 1996.

¹ Incisive Health, 51 Welbeck Street, London, W1G 9HL, England. www.incisivehealth.com

² Cancer Research UK, 2 Redman Place, London, E20 1JQ, England. www.cancerresearchuk.org

82 Due to the often-significant time-lag between the smoking experience and the onset of lung-cancer,
83 the effects of historical changes in smoking habits are still visible in current and recent lung-cancer
84 incidence data.



85
86 Figure 1: Age-standardised annual incidence (per 100,000) of lung-cancer in males and females in
87 England. (ONS, 2019a,b)

88 More than a third of new lung-cancer cases in England are diagnosed when presenting as
89 emergencies (NCIN, 2019); 70% of emergency presentations occur via Accident and Emergency
90 departments, the remainder via emergency GP or inpatient/outpatient referral (NCIN, 2019). There
91 is also evidence that many patients with suspicious symptoms do not seek medical advice promptly
92 (Bjerager et al., 2006; Neal and Allgar, 2005). Poor prognosis, particularly in advanced stages,
93 suggests that easier patient access and screening programmes would facilitate detection at an earlier
94 stage, a supposition confirmed by Campbell et al. (2014), who showed that increased uptake of Chest
95 X-Ray (CXR) assessment for persistent cough in a pilot walk-in scheme in Corby, UK, identified
96 unsuspected lung-cancers at an earlier stage.

97 Low-dose computed tomography (LDCT) has higher tumour detection sensitivity than CXR, and is now
98 emerging as the preferred screening technique, despite delivering a higher radiation dose. However,
99 the rapid spread of lung-cancer dictates frequent screening which, if done by CXR or LDCT, involves
100 significant radiation dose, which could itself induce cancer. At present there is some research
101 support for the value of targeted screening programmes using LDCT (Cressman et al., 2018) for those
102 most at risk, such as tobacco-smokers in deprived areas or people with persistent coughs, and a
103 workshop in the UK noted that this approach was being actively pursued by research and local pilot
104 studies (Moffat et al., 2018).

105 Final results of the Netherlands-Belgian randomised lung-cancer screening (NELSON) trial³ reported
 106 a 26% reduction in lung-cancer mortality in a 10-year follow-up of asymptomatic males, and an
 107 increase to 67% of cancers at diagnosis being early stage and operable (De Koning et al., 2018). In
 108 January 2019, NHS England announced a 10-year plan (NHS, 2019), which included the intention to
 109 extend lung health checks, based on the methodology of a trial in Manchester, UK, targeting high-
 110 risk tobacco-smokers in deprived areas. In the first (baseline, T0) screening round of the Manchester
 111 trial (Crosbie et al., 2019a), 63% of lung-cancers were diagnosed at Stage I and 10.9% at Stage IV.
 112 This represented a significant improvement compared with the distribution of lung-cancers
 113 diagnosed across the same geographical area the year before the trial started (31% Stage I+II and
 114 48% Stage IV). In the second annual screening round (T1) a year later, the trial reported an incidence
 115 of lung-cancer in their target population of 1.6%, with 79% at Stage I (Crosbie et al., 2019b).

116 Birtwistle and Earnshaw (2014) reported the average percentage of initial diagnoses made at each
 117 stage during 2014 in the UK as a whole, together with corresponding figures for the best-performing
 118 Clinical Commissioning Group (CCG). These are shown in Table 1, together with the results from the
 119 Manchester trial.

120 Table 1 – Recently reported UK detection rates for Stages of lung-cancer

Stage	Percentage Diagnosed at each Stage			
	UK Average 2014 (Birtwistle and Earnshaw, 2014)	Best CCG 2014 (Birtwistle and Earnshaw, 2014)	Manchester trial 1st Round T0 (Crosbie et al., 2019a)	Manchester trial 2nd Round T1 (Crosbie et al., 2019b)
1	15%	22.2%	63.0%	79.0%
2	8%	11.8%	17.4%	0.0%
3	22%	18.9%	8.7%	10.5%
4	55%	47.1%	10.9%	10.5%

121
 122 Finally, there is the future prospect of improved early detection using lung-cancer biomarkers, but
 123 this technology is still in the development phase (Roointan et al., 2019).

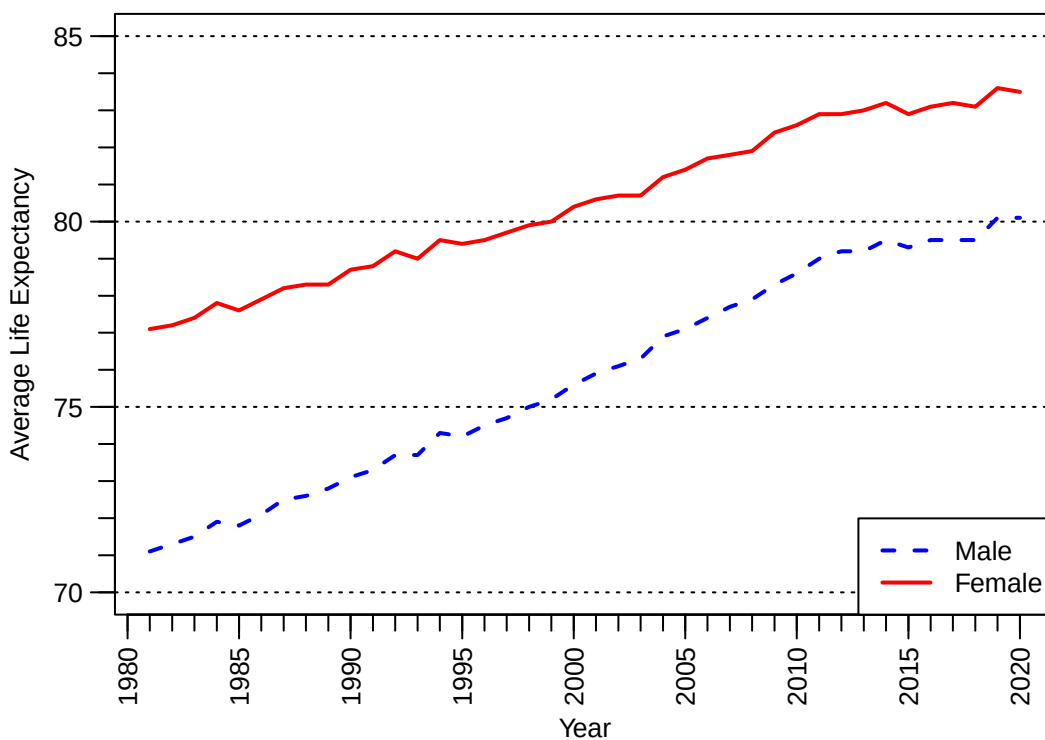
124 2.2 Lung-Cancer Survival

125 Lung-cancer survival has improved over the years. In the USA, 5-year survival was 16% in the period
 126 1986-1991, rising to 24% in 1998-2003 and to 31% in 2004-2009 (Dillman et al., 2014). In the UK, 1-
 127 year survival was 20% in 1999, and had risen to 32% by 2011 (CRUK, 2018), while 5-year survival was
 128 4.6% in 1971-1972, 6.0% in 1990-1991, rising to 9.6% in 2010-2011 (ONS, 2015). Similar trends have
 129 been reported elsewhere. In Norway, although there was only limited improvement in survival of
 130 patients with metastatic disease at diagnosis, 5-year survival in males with localised disease improved
 131 from 26% to 64% (Brustugun et al., 2018). In the UK, a recent report from the Health Foundation
 132 (Richards et al., 2018) has noted that while considerable progress has been made in cancer care in
 133 the last 30 years, considerable work remains to be done to improve diagnosis and treatment to the
 134 optimum.

³ <http://www.nelsonproject.nl>

135 **2.3 Life-Expectancy**

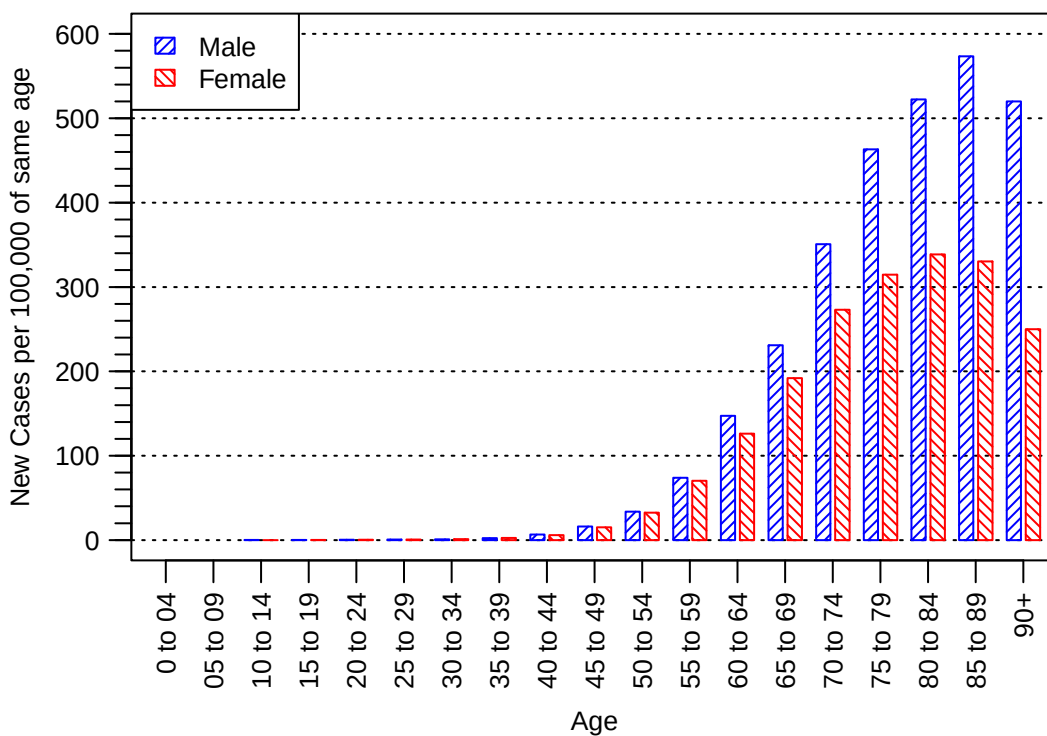
136 Average life-expectancy at birth has continued to increase in England in recent decades, with ONS
137 estimating that the average period life expectancy at birth at 2018 is 79.5 years for males and 83.1
138 years for females (ONS, 2019d). However, the rate of increase is falling (PHE, 2018). The current
139 figures are around 5 years greater than when the data for the Kennedy et al. (1999) study was
140 collected in 1990, at which point the period life-expectancy at birth was 73.1 years for males and 78.7
141 years for females (ONS, 2019d). The trend continues, as shown in Figure (ONS, 2019d), but recent
142 analysis suggests this is now plateauing (Raleigh, 2018). The Public Health Profile of England 2018
143 (PHE, 2018) notes that “less than a century ago, deaths from infectious diseases were common and
144 often death would follow a relatively short period of illness (Griffiths and Brock 2003)”. However,
145 chronic non-communicable diseases are now the leading causes of death and long periods of
146 moderate or severe ill health often precede death (PHE, 2018).



147
148 Figure 2: UK Period life-expectancy at birth. (ONS, 2019d)

149 The population of the UK is ageing. In England in 2017, 1.35 million people were aged 85 and over,
150 almost half a million of whom were aged 90 and over. Population distribution among the elderly is
151 important, as the older a person is, the more likely they are to live with chronic conditions such as
152 dementia, diabetes and musculo-skeletal conditions (PHE, 2018).

153 However, this extension of life-expectancy would not necessarily lead to an increase in the average
154 life-years gained by not contracting lung-cancer, as lung-cancer incidence rate increases with age,
155 reaching a current maximum at around 85 years, as shown in Figure 3 (CRUK, 2018).



156
 157 Figure 3: UK Lung-cancer incidence by age group, 2014-2016 (CRUK, 2018).

158 It is important to recognise that advances in treatment and earlier detection mean that lung-cancer
 159 incidence and life-expectancy data cannot be directly combined. Birtwistle and Earnshaw (2014)
 160 note that increasing life-expectancy and the increasing UK population will result in 1.7% increase in
 161 the number of lung-cancer cases annually.

162 **2.4 Lung-Cancer Treatment**

163 Treatment of lung-cancer can involve surgery, radiotherapy and chemotherapy, depending on the
 164 stage of disease. Surgery is used with curative intent in 49% of cases of localised disease in Stages I
 165 and II, while radiotherapy is used in 16% of cases in these stages (Birtwistle and Earnshaw, 2014).

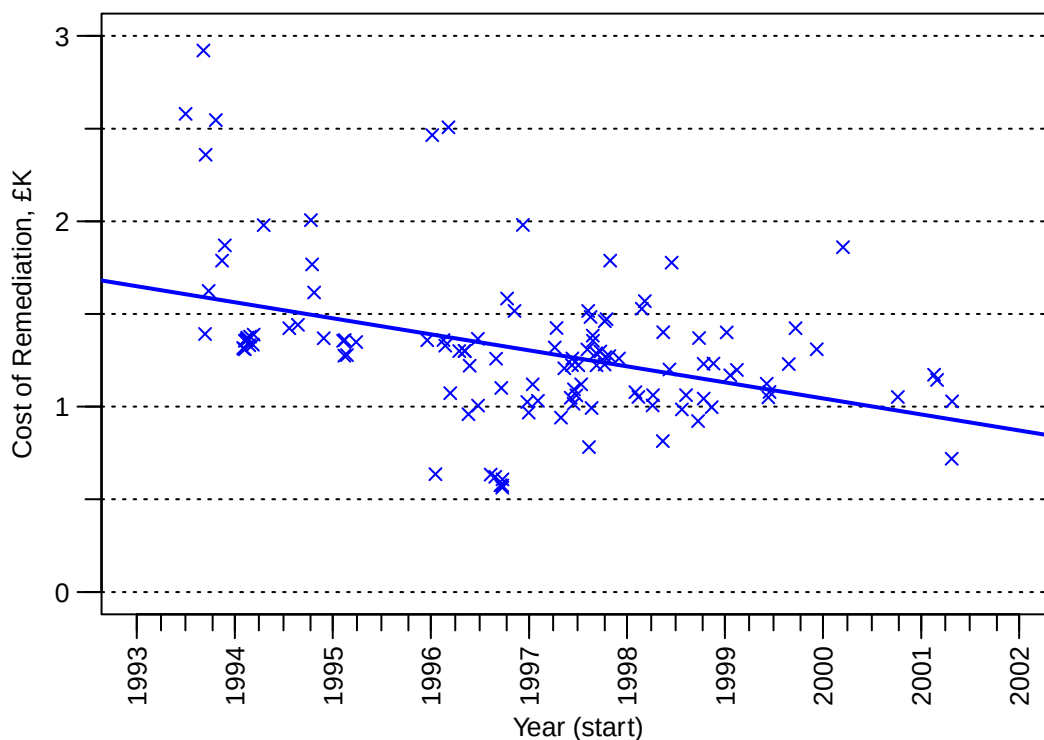
166 Radiotherapy methods have become increasingly complex since the 1990s, with the introduction of
 167 more accurate computer-controlled equipment, able to establish the precise location of the cancer
 168 and to deliver the radiation dose accurately to the tumour without damaging nearby structures.
 169 Magnetic resonance-guided radiotherapy (Chin et al., 2019), gated to patient breathing, has the
 170 ability to target the tumour even more closely. Proton beam therapy is also likely to achieve similar
 171 improvements but at greater cost. Baker et al. (2016), in their review of radiotherapy advances in
 172 the treatment of lung-cancer, note some evidence of improved outcomes, with the caveat that
 173 “clinical benefit of such technology still needs to be demonstrated”. They particularly highlight
 174 whether modern radiotherapy techniques are superior to surgery in patients where surgery is an
 175 option, and note the current lack of evidence for enhanced benefits of proton beam therapy. Mesko
 176 and Gomez (2018), however, suggest that proton therapy will prove to be beneficial for some
 177 subsets, such as centrally-located early disease and previously irradiated tumours. There is also a
 178 role for simple palliative radiotherapy in advanced disease (Birtwistle and Earnshaw, 2014), with 10%
 179 of patients in Stage III and 71% of patients in Stage IV being treated in this way.

180 Surgery has also developed during this time period, from radical lobectomy, which was first reported
181 in 1960, to the introduction of limited resection for Stage I lung-cancers in 1995 (Aokage et al., 2017).
182 The introduction of diagnostic methods to improve the localisation of the disease has led to further
183 clinical trials to establish improved patient outcomes (Aokage et al., 2017). Finally, Birtwistle and
184 Earnshaw (2014) note that chemotherapy is used to palliate advanced disease, with 8% of patients
185 in Stage III and 81% of patients in Stage IV receiving this treatment.

186 **2.5 Radon Remediation**

187 There have been no significant changes in methodologies for radon testing and remediation since
188 the 1990s. The 'gold-standard' radon measurement in the UK remains the three-month etched-track
189 method using two detectors, one placed in the main living-room and one in the main bedroom
190 (Wrixon et al., 1988). If raised levels are found in existing houses, the usual method of remediation
191 is the provision of a sump under the building, together with an extraction pump if necessary. In 1999,
192 Kennedy et al. (1999) quoted the cost of an individual commercial radon measurement as £35; by
193 March 2019, this had risen to around £50. However when corrected for inflation between 1999 and
194 2019 by applying the UK Retail Price Index (RPI), this represents a reduction in the real-terms cost of
195 testing of 20.5% (£27.80 in 1999 terms). It should be noted that UK Value Added Tax (VAT) is levied
196 on both radon testing and remediation works and is included in all of the costs quoted here. The VAT
197 rate increased from 17.5% to 20% in 2011, and this change is reflected within the RPI.

198 Changes in remediation costs are more difficult to quantify, as these vary with the size and
199 characteristics of each house. Figure 4 shows the time evolution of inflation-corrected remediation
200 costs in a series of 123 houses in the counties of Northamptonshire, Oxfordshire and Somerset, UK,
201 remediated by a single contractor between 1993 and 2001. The linear regression line indicates an
202 inflation-corrected average decrease in remediation cost of £86.5 per annum, explains 17% of the
203 variance and is statistically significant with $p \ll 0.001$. The average remediation cost for these houses,
204 again inflation-corrected to January 2019, is £1,311. Similarly, the average remediation cost in 62
205 homes reported by Kennedy et al. (1999), corrected to January 2019, was £1,147, while Gray et al.
206 (2009), using data derived from Naismith et al. (1998) for a sample of 943 houses of varying sizes and
207 characteristics, reported an inflation-corrected average remediation cost of £1,070. All three data-
208 series are contemporaneous. There are no comparable available data from recent years, but the UK
209 Radon Association's most recent advice (2019) states that "Costs are likely to run from around £800
210 for a simple measure, and a single retrofit sump system may cost between £1,000 and £2,000".



211
 212 Figure 4: Cost of remediation of 123 houses in period January 1993 to Apr 2001, corrected by RPI
 213 to January 2019.

214 **2.6 Smoking Incidence**

215 As tobacco-smoking and exposure to radon are sub-multiplicative risk factors for lung-cancer,
 216 smoking prevalence and smoking-cessation programmes will impact on the number of radon-induced
 217 lung-cancers. Modelling, assuming a multiplicative interaction, by Denman et al. (2014) showed a
 218 4% decrease in the cost-effectiveness of radon remediation for every 1% reduction in incidence of
 219 tobacco-smoking. In 2018, 14.7% of UK adults aged 18 and above smoked tobacco, down from 19.9%
 220 in 2010 (ONS, 2018).

221 **2.7 Social Factors**

222 Twigg et al., (2004) analysed the geographical distribution of smoking-attributable mortality in
 223 England, based on published risk factors for mortality of current and ex-smokers from various
 224 diseases, small-area counts of death by cause, and small-area estimates of current and ex-smoking
 225 behaviours. Highest prevalence of tobacco-smoking clustered around the urban areas of inner
 226 London, the Midlands and the North of England, essentially the most deprived areas in the country.
 227 Lung-cancer has the strongest correlation with social deprivation of the four most common cancers
 228 in Scotland (Tweed et al., 2018), and the largest number of excess cases for 37 cancer sites across
 229 socially deprived areas studied in England (NCIN, 2014).

230 In addition to tobacco-smoking, air pollution is estimated as being responsible for 2,328 lung-cancer
 231 deaths in the UK in 2010 (RCP, 2016), somewhat higher than the estimate by Public Health England
 232 (PHE) of around 1,100 deaths from radon-induced lung-cancer (HPA, 2009). Among the potentially
 233 injurious components, there is strong evidence implicating PM2.5 particulates with the incidence of
 234 lung-cancer (Hamra et al., 2014; Huang et al., 2017) but less evidence implicating NO₂ (Hamra et al.,
 235 2015). Air pollution is generally higher in urban than in rural areas, demonstrating significant positive

236 correlation with social deprivation (Briggs et al., 2008). This evidence, together with increased risks
237 of cardiovascular and respiratory diseases, has resulted in national and international campaigns to
238 reduce urban air pollution, especially diesel exhaust emissions.

239 By contrast, three studies reviewing the relation between domestic radon levels and social
240 deprivation in the UK revealed only weak inverse correlation (Briggs et al., 2008; Kendall et al., 2016;
241 Denman et al., 2019). The latter showed that radon is primarily a problem in rural areas in the UK,
242 suggesting that public health campaigns on radon and air pollution can be complementary, and that
243 the growing evidence of air pollution as a significant risk factor for lung-cancer should not affect risk
244 estimates for radon.

245 However, a number of other social factors impact on the estimates of cost-effectiveness of radon
246 remediation. The average household size in England and Wales has been slowly declining from 2.41
247 in 1997 to 2.37 in 2019 (ONS, 2019c) and is predicted to reach 2.16 in 2033 (CLG, 2010); this reduces
248 the net total health benefit from remediating each home. There has also been an increase in the
249 number and density of high-rise apartment blocks in urban areas. This is significant as radon levels
250 are generally lower in higher floors of high-rise buildings.

251 **3 Results**

252 The move to earlier diagnosis, and the improved survival of those with earlier-stage cancers, suggests
253 that meaningful assessment of cost-effectiveness, and particularly its time-dependence, necessitates
254 separate review of each stage and then combination of the results of those separate reviews.

255 **3.1 Life-Years Lost**

256 The Office of National Statistics (ONS) provides estimates of average life-expectancy for people of
257 specific ages, with two principal methods: period life-expectancy, where current mortality rates are
258 used for projections, and cohort life-expectancy, where a trend in mortality rates is estimated from
259 the trend of increasing life-expectancy. At age 72 years, the mean age of lung-cancer diagnosis, the
260 estimated average cohort life-expectancy in England in 2018 is a further 14.3 years for males and
261 16.1 years for females, while the period life-expectancies are 13.6 and 15.5 respectively (ONS,
262 2019d). The following analysis assumes cohort life-expectancy, to reflect continuing improvements
263 in healthcare. Estimates of the average life-years lost for people diagnosed at each stage can be
264 calculated from Birtwistle and Earnshaw (2014), who report values for median survival in the UK at
265 each stage, as shown in Table 2.

266 Table 2: Mean survival and life-years Lost for UK lung-cancer cases, using cohort life expectancy
267 for 2018

Stage	Median Survival (months)	Life-years lost per cancer - Males	Life-years lost per cancer - Females
1	22.5	12.4	14.2
2	10.9	13.4	15.2
3	6.5	13.8	15.6
4	2.6	14.1	15.9

268
269 For the year 2018, and allowing for the higher incidence in males, these figures indicate a UK-wide
270 mean of 14.5 life-years lost per lung-cancer. This analysis assumes that both males and females
271 present with the same staging profile and have similar survival rates. Comparison with the figure of

272 13.5 life-years lost used by Kennedy et al. (1999), indicates that increased general population life-
273 expectancy is more significant than improved early diagnosis and improved treatment for lung-
274 cancer itself. It should be noted that if the male:female ratio remained the same as in 1996, when
275 males constituted 72.3 % of the incidence, mean life-years lost would be lower at 14.2.

276 Countrywide improvement of the standards of diagnosis and treatment to those of the best-
277 performing Clinical Commissioning Group (CCG) in the UK would reduce the total life-years lost in
278 England by 4,275 relative to the level obtaining in 2014 (Birtwistle and Earnshaw, 2014), and would
279 result in little change in the mean life-years lost per lung-cancer, estimated to be 14.4. Although the
280 Manchester trial was targeted at high-risk tobacco-smokers in deprived areas, and therefore did not
281 affect the detection and diagnosis of lung-cancers in the general population including non-smokers
282 (Bhopal et al., 2019), the high detection rates of Stage I cancer in the trial indicate scope for
283 improvement beyond the results for the best-performing CCG.

284 All other considerations remaining unchanged, improved life-expectancy adds directly to the total of
285 life-years lost when an individual contracts, and dies from, lung-cancer. Using the data of Birtwistle
286 and Earnshaw (2014), if all lung-cancers are detected at Stage I, but survival rates do not improve,
287 then the average life-years lost drops to 13.2. With 79% detection of Stage I, the Manchester trial
288 second round nominally achieved an average life-years lost of 13.5.

289 All of the improvements in treatment improve survival, but do not cure lung-cancer. If the best
290 survival rate of 64% (Brustugun et al., 2018) is combined with the best CCG detection rate, the life-
291 years lost will be 12.0. If, in future, a curative treatment is developed for Stage I cancer, but detection
292 rates remain the same, then the average life-years lost drop to 12.5, but if the detection rates of the
293 Manchester trial are combined with the treatment for Stage 1 disease becoming curative, then this
294 drops to 3.0 life-years lost.

295 **3.2 Costs per Stage**

296 Birtwistle and Earnshaw (2014) estimate the current costs of diagnosis and treatment of lung-cancer
297 for each stage of the disease, including the costs of further treatment if the patient relapses. This
298 permits modelling of anticipated costs consequent on the whole UK moving to the best practice of
299 the highest performing CCG. It is estimated that an additional £6.5M would be required to achieve
300 the saving of 4,275 life-years lost, giving an incremental cost-effectiveness of a move to best practice
301 of £1,515 per life-year gained. These values can be combined with diagnosis rates, such as those in
302 Table 3, to provide estimates of costs associated with future improvements in diagnosis and
303 treatment.

304 **4 Discussion**

305 A number of factors have changed since publication in 1999 of the first estimates of the cost-
306 effectiveness of radon remediation in England and Wales. Of these, increased life-expectancy, which
307 impacts on the estimate of life-years lost by lung-cancer mortality, is the most significant and
308 improves the overall cost-effectiveness by approximately 20%. This is balanced to some degree by
309 the reduced prevalence of tobacco-smoking, which has reduced cost-effectiveness by 17% in the
310 same period, and by the contemporaneous reduction in household size.

311 A number of studies investigating differences between males and females with lung-cancer, including
312 an extensive literature review by Frega et al. (2019), have revealed differences in response and
313 survival times to certain chemotherapy treatments. In a sub-group treated by surgery, females in

314 Japan (Nakamura et al., 2017) and Australia and USA (Wainer et al., 2018) had a higher prevalence of
 315 lung-cancer being an adenoma (benign tumour) than males, and consequent improved survival.
 316 However, for the present high-level analysis, such differences can be disregarded, as Ringer et al.
 317 (2005), in their study of the Mid-West US Cancer Registry, report no significant differences between
 318 males and females in staging at presentation, median age of presentation, and overall survival.
 319 Therefore, in this analysis, the median survival was taken as the same for both males and females.

320 However, as Frega et al., (2019) and others note, when treating an individual patient, their sex should
 321 be taken into consideration. Indeed, Frega et al., (2019) suggest that, in the future, developments in
 322 treatments such as immunotherapy may well be more beneficial to female patients than to males.
 323 Moreover, UK 5-year net age-adjusted survival is beginning to show a higher survival for females at
 324 2010-11, with females at 11.6 % (95% CI, 10.6 – 12.7%), males at 8.4% (95% CI, 7.5 – 9.4%), and
 325 overall 9.6% (95% CI, 8.9 – 10.3%) (ONS, 2019b)

326 The increase in costs for diagnosis and treatment are summarised in Table 3. As expected, these
 327 have risen since the initial study of Kennedy et al. (1999), and the values quoted by Birtwistle and
 328 Earnshaw (2014) represent an increase in real terms of 30% when price inflation is taken into account.
 329 The discrepancy of the estimate of Gray et al. (2009), which is 96% higher in real terms is attributed
 330 to their inclusion of hospice and continuing care in their analysis, whereas the other analyses solely
 331 estimate the costs of a specific treatment episode.

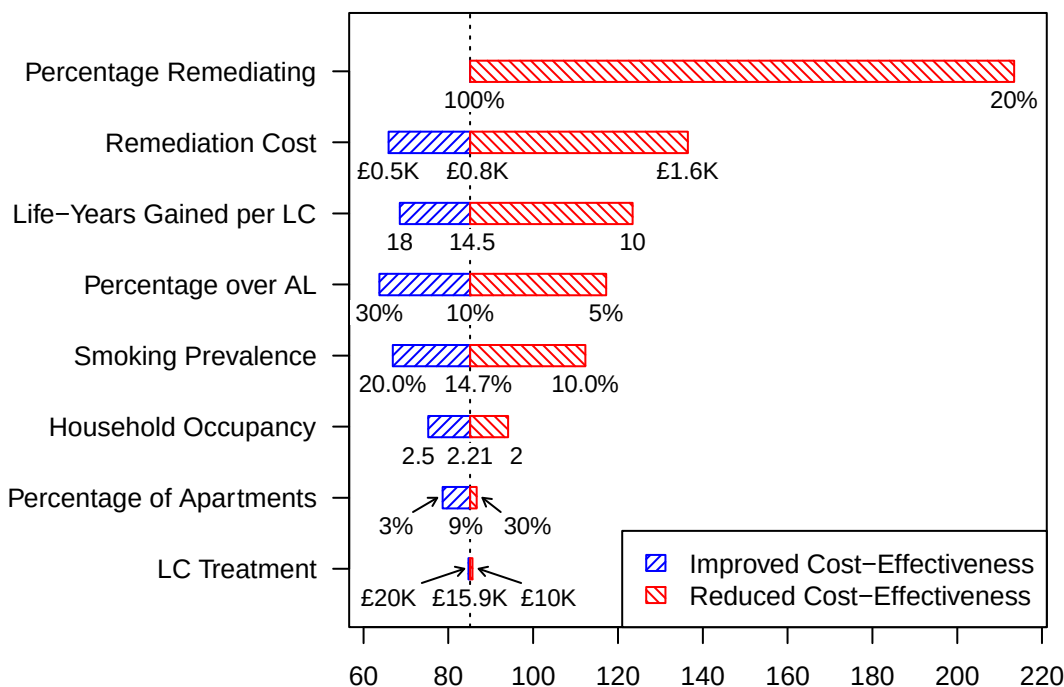
332 Table 3: Health costs per lung-cancer

Study	Kennedy et al. (1999)	Gray et al. (2009)	This Study (2018)	
	1997	2007	UK Average 2014	CCG Best Practice 2014
Mean NHS/hospice cost per lung-cancer case	£6,873	£16,840	£14,238	£14,353
Cost revised by RPI to January 2019 prices	£12,350	£24,250	£15,950	£16,080
Cost relative to Kennedy et al (1999)	1	1.96	1.29	1.30

333 Kennedy et al. (1999) conducted a one-way sensitivity analysis, demonstrating that an increase in
 334 health costs has only a slight reduction in cost-effectiveness. An updated analysis, including the
 335 additional variables discussed here, is presented in Figure 5, where the upper limit for showing the
 336 impact of changes in life-years lost has been taken to be 10, to fit with medium term trends in
 337 diagnosis and treatment. The modelling assumes that all houses with radon concentrations
 338 exceeding the Action Level are remediated. However, in the UK, householder response to finding
 339 elevated radon levels in their homes is modest, with only around 15% remediating and those with
 340 lower incomes being less able or less willing to pay the associated costs (Zhang et al., 2011); similar
 341 response rates have been found elsewhere (Hahn et al., 2019).

343 Figure 5 shows that the degree of householder response has the most significant effect on cost
 344 effectiveness, reducing it by a factor of around 4 if response drops to 20%. It also shows that other
 345 significant factors affecting cost-effectiveness of lung-cancer mitigation measures include the
 346 percentage of houses with radon concentrations found to be over the Action Level – the higher the

347 percentage expected then the better the cost-effectiveness – supporting the concept of locally
 348 targeted remediation programmes for areas with high radon concentrations. Note that radon
 349 concentration in apartment blocks decreases with increasing elevation and reduces the average cost-
 350 effectiveness compared to houses. Increased life expectancy, due to improved healthcare for other
 351 diseases, and other social factors, is a major factor which also improves cost-effectiveness. As noted
 352 in section 3.1, earlier lung-cancer diagnosis will have a modest impact, reducing cost-effectiveness,
 353 while improvements in treatment, and in particular, the future possibility of early-stage disease
 354 becoming curable, will become increasingly significant, possibly making all radon remediation
 355 programmes ultimately redundant. Although the individual cost of treating lung-cancers is high and
 356 increasing, this has little effect on the cost-effectiveness of a radon remediation programme.
 357 Similarly a low-cost breakthrough treatment will reduce cost-effectiveness, but only marginally,
 358 unless it makes a major impact on survival. Therefore the challenge for remediation of radon risks
 359 remains the challenge of establishing public health programmes that ensure public participation.



360
 361 Figure 5: One-way sensitivity analysis for cost-effectiveness (£K per life-year gained annually) of
 362 radon remediation programmes

363 5 Conclusions

364 This paper has considered the developments in lung-cancer diagnosis and treatment, along with
 365 other factors, that have taken place since the first reports that remediation of domestic housing to
 366 reduce radon-induced lung-cancer risk was cost-effective. Lung-cancer treatment costs have risen by
 367 30%, while the numbers surviving 5 years after lung-cancer diagnosis have doubled. It is clear that
 368 radon remediation programmes remain cost-effective and, if anything, are now more cost-effective
 369 than hitherto because of the overall increase in life-expectancy consequent on general
 370 improvements in healthcare, despite current improvements in lung-cancer treatment. The increase
 371 in general life-expectancy is more significant for the cost-effectiveness of radon-remediation
 372 programmes than the impact of reduction in prevalence of tobacco-smoking. While smoking

373 cessation programmes remain more cost-effective than radon remediation programmes, and present
374 an additional opportunity to reduce the risk from radon, the most important factor is achieving full
375 participation of the target group of householders. Therefore, public awareness, targeted public
376 health campaigns and health incentives remain crucial to reducing radon risk in the general
377 population.

378 The growing evidence that urban air pollution, such as PM2.5, is a cause of lung-cancers does not
379 detract from the significance of radon-remediation campaigns. However, it does show that, for the
380 UK at least, radon remediation campaigns should be targeted at rural areas, while air pollution
381 reduction initiatives are appropriate for urban areas.

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