Practice of Epidemiology

Toward Risk Reduction: Predicting the Future Burden of Occupational Cancer

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Interventions to reduce cancers related to certain occupations should be evidence-based. The authors have developed a method for forecasting the future burden of occupational cancer to inform strategies for risk reduction. They project risk exposure periods, accounting for cancer latencies of up to 50 years, forward in time to estimate attributable fractions for a series of forecast target years given past and projected exposure trends and under targeted reduction scenarios. Adjustment factors for changes in exposed numbers and levels are applied in estimation intervals within the risk-exposure periods. The authors illustrate the methods by using a range of scenarios for reducing lung cancer due to occupational exposure to respirable crystalline silica. Attributable fractions for lung cancer due to respirable crystalline silica could be potentially reduced from 2.07% in 2010 to nearly 0% by 2060, depending on the timing and success of interventions. Focusing on achieving compliance with current exposure standards in small industries can be more effective than setting standards at a lower level. The method can be used to highlight high-risk carcinogens, industries, and occupations. It is adaptable for other countries and other exposure situations in the general environment and can be extended to include socioeconomic impact assessment.

cost of illness; forecasting; neoplasms; occupational exposure

Abbreviations: AF, attributable fraction; REP, risk exposure period.
are proportions of those exposed at different levels of exposure over time for working populations. However, separate risk estimates are generally available for broad categories of exposure levels. For estimation of future burden, risk estimates have been extracted where possible for 4 categories of exposure: high, medium, low, and background.

Exposed population estimation

A risk exposure period (REP), which takes into account cancer latency (time from first exposure to death or to cancer registration), is defined as the exposure period relevant to a cancer appearing in a specific target year. For solid tumors, a latency period of between 10 and 50 years is assumed, and for hematopoietic neoplasms, a 0–20-year latency period is assumed. To predict future burden, the risk exposure windows are projected forward in time, and the estimation is carried out for a series of forecast target years that stretch far enough into the future to account for the latency of cancers currently being initiated (Figure 1). The forecast REPs are divided into estimation intervals so that appropriate adjustment factors for estimation of the proportion exposed, as well as separate relative risk estimates if appropriate, can be applied to each interval. Ten-year intervals are chosen to allow for trends across time and to give reasonable flexibility to the timing of interventions; in practice, any interval could be used up to the data-handling capacity of the software used.

National data sources, such as the Carcinogen Exposure database (data from 1990 to 1993) (7) or employment or industry surveys can be used to estimate proportions of a population exposed to a carcinogen by industry sector. Numbers of workers ever employed in an exposed industry during each REP are estimated using a single-point estimate of exposed workers that is taken from one of these sources and appropriate for a REP for cancers currently appearing. The numbers of people who were ever employed in a particular job/industry during the REP, \( N_{e(REP)} \), can be estimated by using the equation:

\[
N_{e(REP)} = n_0 + \left\{ n_0 \times TO \times t \right\},
\]

where \( n_0 \) is this point estimate, \( TO \) is an employment turnover rate per year estimated to exclude staff turnover within 1 year (Web Table 1, in the Web Appendix, available at http://aje.oxfordjournals.org/), and \( t \) is the length of the REP in years. This is adapted to account for survival of workers to the target year, estimated from national life expectancy data (8) (see equation A1 in the Web Appendix).

Adjustment for changing patterns of employment

The point estimate is adjusted for changing overall employment levels for each estimation interval. Up until 2005 (for the 2001–2010 estimation interval), this was based on estimates of numbers of employees that were obtained from the United Kingdom Labour Force Survey for Great Britain (9) in grouped main industry sectors. A linear trend has been assumed to obtain adjustment factors up to 2025 for exposure trend scenarios (Web Figure 1). The factors (equation A2 in the Web Appendix) are applied by estimation interval.

Adjustment for changing exposure levels

An adjustment factor for changing exposure levels is also estimated based on the shift in the proportion of workers exposed in the different exposure level categories across time. Industry sectors and occupations in which exposure occurs are allocated to general “high,” “medium,” “low,” and “background” exposure categories, assuming distributions of exposure and risk that correspond broadly to those of the studies from which the risk estimates were selected.
The change in the proportion of subjects exposed at each exposure level for each REP estimation interval is estimated assuming a lognormal distribution of exposure levels with a geometric mean estimated from exposure level data across all industries that reduces across time in proportion to an estimated annual percentage fall in exposure levels (equation A3 in the Web Appendix) and a geometric standard deviation that is assumed to remain constant across time. If there are insufficient data to estimate the geometric standard deviation, an approximate value is estimated from the ratio of the maximum and mean exposure levels or by assuming a ratio based on similar exposure experience (equation A4 in the Web Appendix). The proportions of the distributions that move across a series of boundaries represent the numbers of exposed workers moving from the higher exposure levels to the lower exposure levels in the future. These boundaries are the estimated exposure levels separating a “higher” from a “lower” exposure group as the distributions shift with time along an exposure-level axis (equation A5 in the Web Appendix), as illustrated in Figure 2.

The proportions \( p_{hj} \) of workers exposed at each level \( h \) for each forecast year \( j \) are estimated from the area of the exposure level distribution below the boundaries \( T_h \) by using the following equation (equation A6 in the Web Appendix):

\[
p_{hj} = 1 - \text{LOGNORM}(T_h, \ln(GM_j), \ln(GSD_j)).
\]

These proportions are the exposure-level factors for a forecast scenario. For separate industries/occupations, the factor used is the ratio of the proportions of the exposed in the exposure category in the forecast year to the proportion in the origin year (equation A7 in the Web Appendix). For details of how to estimate the proportions when testing the introduction of a new workplace exposure standard, see the Web Appendix.

### Estimating the proportion of the population exposed

After adjustment, the numbers of people ever employed in an exposed industry during the forecast REPs are divided by an estimate of numbers, \( N_{p(REP)} \), of those of working age during the REP who are expected to still be alive according to normal life expectancy (10) in each of the forecast target years (see equation A12 in the Web Appendix), to obtain the proportion of the population exposed (Pr(\( E \))). In estimating \( N_{p(REP)} \) and \( N_{p(REP)} \), retirement ages have been maintained at 65 and 60 years for men and women, respectively, although the method allows for alternative retirement ages.

### Estimating the attributable fraction

Levin’s equation for the AF (11) is used to estimate AFs from the relative risks and the proportions newly exposed in each estimation interval, by industry/occupation and exposure level:

\[
AF_{hi} = \left\{ \frac{\sum_i Pr(E_{hij})(RR_{hij} - 1)}{1 + \left\{ \sum_h \sum_i Pr(E_{hij})(RR_{hij} - 1) \right\}} \right\},
\]

where \( h \) is the exposure level, \( i \) is the industry/occupation, and \( j \) is the estimation interval. A total AF due to the
occupational exposure in each forecast target year is obtained by summing across industries and exposure levels.

Applying a latency distribution

The distribution of cancer latencies between the estimated minima and maxima will affect the estimates of attributable cancers in the forecast target years, as these estimates depend on the timing of an intervention during the REP. Several latency distributions were explored, including a power distribution in which latencies are concentrated towards the 50-year limit of the distribution, which may be more appropriate for some cancers such as mesothelioma (12) (Web Figure 2). However, the best, albeit limited, evidence is for a lognormal distribution (13). An indication of the effect of using alternative distributions is shown in Web Figure 3. For solid tumors, it has been assumed that latency follows this distribution around an average of 35 years and with a standard deviation estimated as one-sixth of the latency range (equation A13 in the Web Appendix). To obtain a corrected distribution of the proportions of attributable cancers expected to appear in the forecast years, latency weights for the assumed distribution are estimated as the probability mass function values for the distribution at each year, averaged across estimation intervals to represent latencies of 50 to 10 years for solid tumors (Web Figure 4). These latency weights are applied to the AF numerator in the third equation by estimation interval.

Estimating attributable numbers

To estimate attributable numbers, the AF is applied to a prediction of total cancer-specific numbers for each forecast target year based on current (2005) cancer rates applied to a population estimate taking into account projected demographic change only (11) (Web Figure 5). Changes in cancer trends due to nonoccupational risk factors are not taken into account. For solid tumors, only cancers in people aged ≥25 years are counted, as these could have been initiated during the REPs being considered. For patients with hemopoietic neoplasms, only those aged 15 years to 84 years (15 years to 79 years for women) are included.

Change scenarios

Alternative scenarios of change can be based on 1) historic and forecasted employment and exposure-level trends, 2) introduction of a range of possible exposure standards or reduction of a current exposure limit, 3) improved compliance to an existing exposure standard, or 4) a planned intervention, such as engineering controls or introduction of personal protective equipment, or industry closure. A fall in relative risk where only a single exposure-level risk estimate is available can also be used. To assess their relative impact on the intervention scenario, results are compared with a baseline scenario of historic trends only or incorporating projected exposure trends such as scenario 1 above.

Adjustment factors for changes in employment levels ($f_{1i}$, equation A2 in the Web Appendix) and exposure levels ($f_{2s}$, equation A7 in the Web Appendix) are used to create the alternative scenarios and are applied to the estimates of numbers ever exposed in the REP ($N_{e,REP}$; equation A1 in the Web Appendix) or to the exposed point estimate $n_0$ before calculating $N_{e,REP}$ to represent change over the forecast exposure periods. The factors are applied by estimation interval ($j$), and factor $f_1$ can also be applied by exposure level ($h$) and by industry/occupation ($i$) to obtain an adjusted estimate of numbers ever exposed ($N_{e,adj(REP)hij}$) as

$$N_{e,adj(REP)hij} = N_{e(REP)hij} \times f_{1hij} \times f_{2ij}.$$

Different adjustment factors are used for different scenarios. For 2011–2020 onward, the factors may be held constant for a baseline scenario, based on underlying trends projected forward in time to represent trend scenario 1, or set arbitrarily to represent intervention scenarios 2–4 described above. An intervention to reduce exposure levels, such as one that lowers an exposure standard, is translated into a shift to a new distribution mean estimated from the proportion of worker exposures now below the exposure standard boundary. This proportion may be the same as the proportion estimated to be below the existing exposure standard (compliance) or may be set to represent compliance of, for example, 90% where no previous standard existed or where compliance is expected to improve. Interventions can be introduced into any estimation interval and can be varied according to workplace size. Four categories are used here: 0 (self-employed), 1–49, 50–249, or ≥250 employees, based on national estimates of the percentages of employees in each size class (14), by grouped main industry sector (agriculture and fishing, utilities mining and manufacturing, construction, and services; Web Figure 6).

Results: example of lung cancer and silica exposure

For illustrative purposes, we forecasted the future burden of lung cancer in Great Britain (attributable cancer registrations) caused by occupational exposure to respirable crystalline silica under different scenarios. Data from the Carcinogen Exposure database were used for initial point estimates of the numbers of workers exposed (554,000 men, including 450,000 in construction and 22,000 in pottery manufacture judged to be exposed at a high level, and 36,000 women, including 16,500 in pottery manufacture; Web Table 2). Relative risk estimates were obtained from studies by Kurihara and Wada (15) (relative risk = 1.32, 95% confidence interval: 1.24, 1.41), Pelucchi et al. (16) (relative risk = 1.17, 95% confidence interval: 1.12, 1.22), and Steenland et al. (17) (relative risk = 1.00, 95% confidence interval: 0.85, 1.30) for the high, low, and background exposure levels, respectively. Employment trends as in Web Figure 1 and an estimated 8% annual fall in exposure levels across all silica-exposed industries (18) were assumed for years up to 2010, with the fall leveling off thereafter, for the baseline scenario and before interventions in the intervention scenarios. Average exposure levels (geometric mean) were estimated to be 0.226 g/m³ in 2003 (geometric standard deviation = 6.4) based on exposures in construction in the Netherlands (19, 20) and were used for all industries. Using these data, we estimated that 67% of workers...
<table>
<thead>
<tr>
<th>Intervention Scenario</th>
<th>Attributable Fraction, %</th>
<th>Attributable Cancer Registrations</th>
<th>Cancer Registrations Avoided</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2010</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current burden</td>
<td>2.07</td>
<td>837</td>
<td></td>
</tr>
<tr>
<td><strong>2060</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scenario 1: baseline scenario (current (2005) employment and exposure levels are maintained)</td>
<td>1.08</td>
<td>794</td>
<td></td>
</tr>
<tr>
<td>Scenarios to test the timing of introduction of a reduced exposure standard</td>
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<td></td>
<td></td>
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<tr>
<td>Scenario 2: introduce an exposure standard of 0.05 mg/m$^3$ in 2010, assuming the same compliance rate (33%) to this standard as was estimated for the 0.1 mg/m$^3$ exposure standard in all workplaces.</td>
<td>0.80</td>
<td>592</td>
<td>202</td>
</tr>
<tr>
<td>Scenario 3: introduce an exposure standard of 0.05 mg/m$^3$ in 2020 with the same compliance rate (33%) in all workplaces.</td>
<td>0.90</td>
<td>666</td>
<td>128</td>
</tr>
<tr>
<td>Scenario 4: introduce an exposure standard of 0.05 mg/m$^3$ in 2030 with the same compliance rate (33%) in all workplaces.</td>
<td>1.02</td>
<td>753</td>
<td>42</td>
</tr>
<tr>
<td>Scenario to test the dynamic exposure standard that reduces as the previous intervention standards based on realized exposure levels take effect</td>
<td></td>
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<tr>
<td>Scenario 5: introduce exposure standard as a) a quarter of the 2001–2010 forecast scenario mean in 2010 with the same compliance rate (33%) as for the existing standard in 2001–2010, then b) quarter the 2011–2020 scenario mean as forecasted under a) in 2020 with the same compliance rate as that for a) in 2011–2020, then c) quarter the 2021–2030 scenario mean as forecasted under b) in 2030 with the same compliance rate as that for b) in 2021–2030. No continuing 8 downward trend.</td>
<td>0.68</td>
<td>499</td>
<td>295</td>
</tr>
<tr>
<td>Scenarios to test effect of compliance by workplace size</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Scenario 6: introduce an exposure standard of 0.05 mg/m$^3$ in 2010 with a 33 compliance rate in workplaces with 0–249 employees and a 90 compliance rate in workplaces with $\geq$250 employees.</td>
<td>0.68</td>
<td>499</td>
<td>295</td>
</tr>
<tr>
<td>Scenario 7: introduce an exposure standard of 0.05 mg/m$^3$ in 2010 with a 33 compliance rate in workplaces with 0–49 employees and a 90 compliance rate in workplaces with $\geq$50 employees.</td>
<td>0.61</td>
<td>451</td>
<td>344</td>
</tr>
<tr>
<td>Scenario 8: introduce an exposure standard of 0.05 mg/m$^3$ in 2010 with a 33 compliance rate in those who were self-employed and a 90 compliance rate in all other workplaces.</td>
<td>0.35</td>
<td>261</td>
<td>533</td>
</tr>
<tr>
<td>Scenario 9: introduce an exposure standard of 0.05 mg/m$^3$ in 2010 with a 90 compliance rate in all workplaces.</td>
<td>0.07</td>
<td>49</td>
<td>745</td>
</tr>
<tr>
<td>Scenarios to test the effect of introducing lower exposure standards versus compliance rate</td>
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<tr>
<td>Scenario 10: introduce an exposure standard of 0.025 mg/m$^3$ in 2010 with the same compliance rate (33) as that for existing standard in 2001–2010 in all workplaces.</td>
<td>0.56</td>
<td>409</td>
<td>385</td>
</tr>
<tr>
<td>Scenario 11: maintain an exposure standard of 0.1 mg/m$^3$ in 2010 with a compliance rate of 90 in all workplaces.</td>
<td>0.14</td>
<td>102</td>
<td>693</td>
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<tr>
<td>Scenario 12: introduce an exposure standard of 0.05 mg/m$^3$ in 2010 with a compliance rate of 90 in all workplaces.</td>
<td>0.07</td>
<td>49</td>
<td>745</td>
</tr>
<tr>
<td>Scenario 13: introduce an exposure standard of 0.025 mg/m$^3$ in 2010 with a compliance rate of 90 in all workplaces.</td>
<td>0.03</td>
<td>21</td>
<td>773</td>
</tr>
<tr>
<td>Scenarios to test the effect of closing industries, transferring workers at high-exposure sites to low-exposure sites, and lowering the relative risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scenario 14: close all mining and manufacturing industries in 2010.</td>
<td>1.10</td>
<td>808</td>
<td>4</td>
</tr>
<tr>
<td>Scenario 15: transfer all those working in high-exposure sites (construction and pottery manufacture) to low-exposure sites in 2010.</td>
<td>0.35</td>
<td>255</td>
<td>556</td>
</tr>
<tr>
<td>Scenario 16: halve the excess risk in 2010 at high and low exposure levels.</td>
<td>0.56</td>
<td>409</td>
<td>402</td>
</tr>
</tbody>
</table>

$^a$Scenario 9 and scenario 12 are the same.
were exposed at levels above the workplace exposure limit of 0.1 mg/m³ in 2001–2010, that is, a compliance rate of 33%, confirmed by evidence that levels of respirable crystalline silica in the United Kingdom construction industry greatly exceed the current workplace exposure limit (21). The boundaries between the high, low, and background exposure levels, which were estimated from the allocation of exposed numbers to these categories, are illustrated in Figure 2.

The intervention scenarios tested are described in Table 1 together with the AFs, numbers of attributable cancer registrations for forecast year 2060 when historic exposures no longer have an effect, and the reduction in that year compared with the baseline scenario of no change. If the 8% annual fall in exposure levels does not continue beyond 2001–2010 (baseline scenario 1), nearly 800 attributable cancers are forecast in 2060. Numbers of cancers tend to rise for the baseline scenario because of rising numbers of total projected lung cancers caused by an aging population. All the figures highlight the lack of any reduction in cancers until after 2030 because of the long latency of the cancer. Introducing a reduced exposure standard (half the current one of 0.1 mg/m³; scenario 2) gives a reduction in both the AF and cancer numbers compared with the baseline; Figure 3 illustrates the effect of delaying the introduction by 10 and 20 years (scenarios 3 and 4, respectively). Scenario 5, in which the exposure standard is reduced as the expected exposure levels fall until 2030, is more effective than just halving the current standard (Table 1).

Scenarios 6–9 represent the introduction of a halved exposure standard (0.05 mg/m³) in 2010 plus the effect of improving compliance to 90% in an increasing range of workplaces from only the largest (≥250 employees; scenario 6) to all workplaces, including the self-employed (scenario 9). Results for these compared with the baseline scenario 1 are shown in Figure 4. Attributable cancers do not disappear totally, as low-level exposure still occurs even with this level of compliance, but the improvement on scenario 2, where noncompliance rates are assumed to be the same as were occurring with respect to the existing exposure standard (0.1 mg/m³), is considerable. The great improvement in cancers avoided when workplaces with <50 workers have an improved compliance rate (scenario 8) compared with reduction in larger workplaces only (scenario 7) highlights the comparative predominance of small enterprises, particularly in the construction industry, which is the most important industry sector for potential silica exposure.

Scenarios 10–13 introduce more options for lowering the exposure standard and simultaneously improving compliance. By comparing scenarios 1, 2, and 10 (33% compliance) with scenarios 11–13 (90% compliance) for standards of 0.1, 0.05, and 0.025 mg/m³, respectively (Table 1 and Figure 5), the effectiveness of enforcement compared with lowering the standard is clearly demonstrated. The effectiveness of scenarios 14–16 (Table 1), which include closing all mining and manufacturing industries (scenario 14), transferring those working at a high-exposure site to a

Figure 3. Results for intervention scenarios that compare the effect of delaying introduction of a reduced exposure standard in terms of A) lung cancer registrations and B) fraction attributable to occupational exposure to respirable crystalline silica in men and women in Great Britain. Black bars and symbols, baseline (2005 employment and exposure levels and exposure standard of 0.1 mg/m³ maintained); dark gray bars and symbols, scenario 2 (exposure standard of 0.05 mg/m³ introduced in 2010, same compliance (33%) with new limit as old (0.1 mg/m³) in all workplaces); light gray bars and symbols, scenario 3 (exposure standard of 0.05 mg/m³ introduced in 2020 with the same compliance in all workplaces); and white bars and symbols, scenario 4 (exposure standard of 0.05 mg/m³ introduced in 2030 with the same compliance for all workplaces).
DISCUSSION

The method and illustrative example described here demonstrate how the nature and timing of measures to reduce exposure can affect the predicted burden of occupational cancer. These methods have the potential for adaptation for use in other countries and can be extended to include socioeconomic impact evaluation. For example, the methods are being utilized for a European Union project assessing the socioeconomic impact of new Occupational Exposure Limits for the European Union for 25 recognized carcinogens. An important finding is that no matter what action is taken now, it is the next generation of workers who stand to benefit because of the long latency of many solid tumor cancers. Absence of occupational exposure data is a major limitation; we have therefore used a pragmatic approach and developed our method using the AF for separate risk estimates applied only to categories of exposures (e.g., high, medium, low, and background). Where no exposure estimates exist, for example, for an occupation for which no single carcinogen or specific high-risk task has been identified, appropriate scenarios of reduced relative risk or numbers exposed can instead be chosen to predict burden. However, it would be possible to extend the methods to incorporate continuous exposure-response distributions if these are available or can be estimated. Methods are transparent to the sources used, so alternative risk estimates and exposure-level or employment-structure trends could be used, for example, to allow for forecast changes in technology or employed numbers specific to the agent or industry.

The choice of risk estimates and Carcinogen Exposure database exposure categories by industry sector were judged to be appropriate for the situation in Great Britain but could, of course, be adapted for other countries and situations. Similarly, the assumptions made for the interventions in Table 1 could be adapted as appropriate. For example, a potential alternative to the baseline scenario used in the silica example could be to extend exposure trends based on historic and forecasted employment and exposure levels in the future. The current rate of compliance to the existing standard of 0.1 mg/m³ for silica was estimated to be about 33% using recent measurement data. We assumed an improvement to 90% in some of our scenarios; this might be difficult to achieve in practice, but the method readily allows comparison of other rates. The comparisons clearly demonstrated that focusing efforts on improving compliance was beneficial compared with reducing the standard.

The occupational AFs have been applied to cancer numbers on the basis of projected population estimates, therefore taking into account demographic change only. This will result in increases in occupational and nonoccupational cancers equally with an aging population, so that...
although the fraction attributable to occupation may fall, the numbers of occupation-attributable cancers may rise. However, the estimates are not affected by the changing contribution of other nonoccupational risk factors. The estimates of prevented cancers can therefore be used to judge the relative effectiveness of intervention scenarios as all other lifestyle or environmental causal factors are held constant.

If there are several risk factors contributing to the burden of a disease, a change in attribution for one factor will result in a change in the attribution of the others. Therefore, attributable numbers rather than AFs represent a more useful estimate of the future cancer burden due to occupation. However, the success of a given occupational-based intervention should be assessed by monitoring exposure levels in the future and using the numbers now exposed at these levels to obtain a reestimated AF that is then applied to registration forecasts from the same baseline (in our case 2005) to obtain achieved attributable numbers that can then be compared with the target forecasts estimated for the intervention.

Information on the process and time issues for cancer causality is generally lacking in occupational settings. Here, a single initiation and latency model is assumed and issues of multicausality are set aside, although we have used risk estimates adjusted for known nonoccupational confounding factors wherever these are available. Assumptions have had to be made about the length and timing of cancer latency for the AF approach, and data indicating the shape of the distribution of cancer latencies are also limited. An alternative approach, the lifetime risk approach, does not require these assumptions but does not lend itself to estimation of trends over time and illustration of the ongoing effects of past exposures as we have presented here.

In summary, we have presented here a method to estimate the future burden of occupational cancer that facilitates testing of the effect of a range of potential interventions. The method is adaptable to situations where data, in particular exposure-level data, are sparse; it is most robust in allowing comparison between different intervention effects and where a broad estimate of future burden across exposures is required. However, it can also be adapted to assess impacts of policy in specific industries and can be adapted to use higher quality exposure data if available. Extension to evaluate burden in the environmental area would be a valuable development.

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REFERENCES


