What is common between sweets, buildings and sunscreens?

*On the risk assessment and regulation of chemicals in Europe*

Prof. Guseva Canu

Unisanté, Department of Occupational and Environmental Health
TiO$_2$ - Titania
Physical properties of TiO$_2$

- White inorganic compound
- Occurs naturally as a solid
- Insoluble in water, even in its particle form
- Extremely high melting point of 1,843ºC and boiling point of 2,972ºC
- Refractive index (ability to scatter UV light) very high >>> diamond
- **Photocatalytic activity** under UV light

=> Resistant, extra-white, bright, protective, aesthetic, very promising

https://tdma.info/uses-of-titanium-dioxide/
https://www.youtube.com/watch?v=7ObnoGtDi0Q&t=93s/
What is titanium dioxide?

• White inorganic compound

• As a white pigment, TiO₂ is one of the most important raw materials for paints and coatings

• As a photocatalyst, titanium dioxide can be added to paints, cements, windows and tiles in order to decompose environmental pollutants.

• Beyond paints, catalytic coatings, plastics, paper, pharmaceuticals and sunscreen, some lesser-known applications include packaging, commercial printing inks, cosmetics, toothpastes, and food (E171)
What do we know regarding TiO$_2$ safety?

Titanium dioxide (TiO$_2$) is considered as an inert and safe material and has been used in many applications for decades. Although TiO$_2$ is permitted as an additive (E171) in food and pharmaceutical products we do not have reliable data on its absorption, distribution, excretion and toxicity on oral exposure.

https://www.ncbi.nlm.nih.gov › articles › PMC3423755

Titanium dioxide in our everyday life; is it safe? - NCBI - NIH

Conclusions

Until relevant toxicological and human exposure data that would enable reliable risk assessment are obtained, TiO$_2$ nanoparticles should be used with great care.
What do we know regarding TiO$_2$ safety?

- Currently available Occupational Exposure Limits (OEL) in μg/m$^3$
NIOSH framework of Risk Assessment & Risk Management

- **Research and Tools**
  - Toxicology & epidemiology
  - Exposure analysis
  - Risk analysis

- **Evaluation**

- **Risk Characterization**
  - Weight of evidence
  - Severity & likelihood
  - Variability & uncertainty

- **Workplace Actions**
  - Engineering controls & PPE
  - Exposure monitoring
  - Worker training
  - Medical monitoring

- **Implementation**

- **Risk Management**
  - Occupational safety & health guidance
  - Exposure limits
  - Communication

- **Decision-making**
WHO risk analysis framework

Risk Assessment
- Science based

Risk Management
- Policy based

Risk Communication
- Interactive exchange of information and opinions concerning risks
US NRC Risk Assessment/Risk Management framework

RESEARCH
- Laboratory and field observations of adverse health effects and exposures to particular agents
- Information on extrapolation methods for high to low dose and animal to human
- Field measurements, estimated exposures, characterization of populations

RISK ASSESSMENT
- Hazard identification (Does the agent cause the adverse effect?)
- Dose-Response Assessment (What is the relationship between dose and incidence in humans?)
- Exposure Assessment (What exposures are currently experienced or anticipated under different conditions?)

RISK MANAGEMENT
- Consider prevention approaches, including engineering controls and use of personal protective equipment.
- Evaluate efficacy and efficiency of approaches and utility of other protective measures.
- Implement appropriate risk reduction and prevention options.
Hazard identification

• Slowly soluble particles not otherwise regulated or classified (TWA of total suspended particles or dusts)

• Case report Yamadori et al. (1986) reported a papillary adenocarcinoma of the lung and titanium dioxide-associated pneumoconiosis in a male titanium dioxide packer with 13 years of potential dust exposure and a 40-year history of tobacco smoking.

• 1st assessment IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 47 (IARC, 1989) => Not classifiable as to its carcinogenicity to humans (group 3)
IARC Classification framework

- **ESLC**: Evidence suggesting lack of carcinogenicity

### Evidence in Experimental Animals
- **Sufficient**
  - Group 1 (carcinogenic to humans)
- **Limited**
  - Group 2A (probably carcinogenic)
  - Group 2B (possibility carcinogenic) (exceptionally, Group 2A)
- **Inadequate**
  - Group 2B (possibly carcinogenic)
  - Group 3 (not classifiable)

### Evidence in Humans
- **Sufficient**
- **Limited**
- **Inadequate**
- **ESLC**

ESLC: Evidence suggesting lack of carcinogenicity
IARC evaluation Framework for human data

- Cancer in humans
  - Preamble Part B, Section 6(a)
- Cancer in experimental animals
- Mechanistic and other relevant data

**Sufficient evidence**
- Causal relationship has been **established**
- Chance, bias, and confounding **could be ruled out with reasonable confidence**

**Limited evidence**
- Causal interpretation is **credible**
- Chance, bias, or confounding **could not be ruled out**

**Inadequate evidence**
- Studies permit **no conclusion** about a causal association

**Evidence suggesting lack of carcinogenicity**
- Several adequate studies covering the full range of exposure levels are mutually consistent in not showing a positive association at any observed level of exposure
- Conclusion is limited to cancer sites and conditions studied
Hazard identification

- 2\textsuperscript{nd} assessment in 2006 Volume 93 (IARC, 2010) => Possibly carcinogenic to humans (Group 2B)
  - There is \textit{inadequate evidence} in humans for the carcinogenicity of titanium dioxide.
  - There is \textit{sufficient evidence} in experimental animals for the carcinogenicity of titanium dioxide

\textbf{Human carcinogenicity data}
- Chen & Fayerweather (1988); Fayerweather \textit{et al.} (1992), USA
- Fryzek \textit{et al.} (2003), USA
- Boffetta \textit{et al.} (2004), 6 EU countries

\textit{All the studies had methodological limitations.} ...None of the studies was designed to assess the impact of particle size (fine or ultrafine) or the potential effect of the coating compounds on the risk for lung cancer.”
And what happened since?

In the USA, *NIOSH Current Intelligence Bulletin (April 2011)*

- Quantitative risk assessments for fine and ultrafine TiO$_2$
  - Hazard identification in humans

### Lung cancer mortality

<table>
<thead>
<tr>
<th>Europe</th>
<th>SMR (95% CI)</th>
<th><em>Boffetta et al (2001)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Males 1.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finland 0.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female 0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>France 1.42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany 1.51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy 0.97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norway 0.79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK 1.09</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Amérique du nord</th>
<th>US SMR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fryzek et al</td>
<td>1.00 (0.80-1.30)</td>
</tr>
<tr>
<td>Chen &amp; Frayerweather (2003)</td>
<td>0.52 (??-??)</td>
</tr>
<tr>
<td>Ellis et al (2010)</td>
<td>0.90 (0.75-1.05)</td>
</tr>
<tr>
<td>Ellis et al (2013)</td>
<td>1.02 (0.84-1.22)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Canada</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study I</td>
<td>1.1 (0.7-2.0)</td>
</tr>
<tr>
<td>Study II</td>
<td>1.2 (0.8-1.9)</td>
</tr>
<tr>
<td>Pooled</td>
<td>1.0 (0.8-1.5)</td>
</tr>
</tbody>
</table>

And what happened since?

In the USA, *NIOSH Current Intelligence Bulletin (April 2011)*

- Quantitative risk assessments
  - Dose-response data in rats:
    - lung cancer and pulmonary inflammation
  
  ![Diagram](image)

NIOSH recommends exposure limits of 2.4 mg/m³ for fine TiO₂ and 0.3 mg/m³ for ultrafine (including engineered nanoscale) TiO₂, as time-weighted average (TWA) concentrations for up to 10 hours per day during a 40-hour work week. NIOSH has determined that ultrafine TiO₂ is a potential occupational carcinogen, but that there are insufficient data at this time to classify fine TiO₂ as a potential occupational carcinogen. However, as a precautionary step, NIOSH used all of the animal tumor response data when conducting dose-response modeling and determining separate RELs for ultrafine and fine TiO₂. These recommendations represent levels that over a working lifetime are estimated to reduce risks of lung cancer to below 1 in 1,000. NIOSH realizes that knowledge about the health effects of nanomaterials is an evolving area of science. Therefore, NIOSH intends to continue dialogue with the scientific community and will consider any comments about nano-size titanium dioxide for future updates of this document. (Send comments to nioshdocket@cdc.gov.)

NIOSH urges employers to disseminate this information to workers and customers and requests that professional and trade associations and labor organizations inform their members about the hazards of occupational exposure to respirable TiO₂.
And what happened since?

In the EU

TiO₂ = poorly soluble, low-toxicity particles
EU CLP Regulation (Classification, Labelling and Packaging of chemicals)

- The identified hazards must be communicated to other actors in the supply chain, including consumers (via a label and a safety data sheet)
- The objective is to alert stakeholders to the presence of a danger and the need to manage the associated risks
- The CLP classification affects other EU laws such as the Workers Directive (CMD 2004/37 / EC), which sets binding OELs and BLVs
- Revision in the frame of the CLH procedure
CLH procedure for CLP regulation revision

- **Steps of the CLH process**
  - CLH intention
  - Dossier submission
  - Accordance check
  - Public consultation
  - RAC opinion development
  - Adopted RAC opinion
  - Inclusion in Annex VI

- **Timeline**
  - November 2014
  - November 2015
  - February 2016
  - May 31 – July 15 2016
  - March-Sept. 2017
  - September 14 2017
  - December 2020

- **Actors**
  - Dossier submitter (France)
  - ECHA / RAC
  - Parties concerned, including Member States
  - European commission
Approach followed by France (ANSES) for TiO2

- Systematic review of TiO2 production worker cohorts
- Critical assessment of bias using the OHAT method and gradation of the level of evidence

**USA:** Chen & Fayerweather, 1988; Ellis et al., 2010 & 2013; Fryzek et al., 2003

**Europe:** Boffetta et al., 2004

**Restrospective industry-based cohort mortality studies**

<table>
<thead>
<tr>
<th>Country</th>
<th>Workers</th>
<th>Gender</th>
<th>Plants</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.I. du Pont de Nemours and Company plants</td>
<td>1576 males 1935-1983</td>
<td>2</td>
<td>2 plants</td>
</tr>
<tr>
<td></td>
<td>5054 &amp; 3807 males 1935-2006</td>
<td>3</td>
<td>3 plants</td>
</tr>
<tr>
<td></td>
<td>4241 workers 1960-2000</td>
<td>4</td>
<td>4 plants</td>
</tr>
</tbody>
</table>

**ANSES** = The French Agency for Food, Environmental and Occupational Health & Safety
Mortality among workers employed in the titanium dioxide production industry in Europe

Paolo Boffetta1,2,3, Anne Soutar4, John W. Cherrie4,5, Fredrik Granath2, Aage Andersen6, Ahti Anttila7, Maria Blettner8, Valerie Gaborieau1, Stefanie J. Klug9, Sverre Langard9, Daniele Luce10, Franco Merletti11, Brian Miller4, Dario Mirabelli11, Eero Pukkala7, Hans-Olov Adami1 & Elisabete Weiderpass1,2,*

Abstract

Objectives: To assess the risk of lung cancer mortality related to occupational exposure to titanium dioxide (TiO2). Methods: A mortality follow-up study of 15,017 workers (14,331 men) employed in 11 factories producing TiO2 in Europe. Exposure to TiO2 dust was reconstructed for each occupational title; exposure estimates were linked with the occupational history. Observed mortality was compared with national rates, and internal comparisons were based on multivariate Cox regression analysis.

Results: The cohort contributed 371,067 person-years of observation (3.3% were lost to follow-up and 0.7% emigrated). 2652 cohort members died during the follow-up, yielding standardized mortality ratios (SMRs) of 0.87 (95% confidence interval [CI] 0.83–0.90) among men and 0.58 (95% CI 0.40–0.82) among women. Among men, the SMR of lung cancer was significantly increased (1.23, 95% CI 1.10–1.38) however, mortality from lung cancer did not increase with duration of employment or estimated cumulative exposure to TiO2 dust. Data on smoking were available for over one third of cohort members. In three countries, the prevalence of smokers was higher among cohort members compared to the national populations.

Conclusions: The results of the study do not suggest a carcinogenic effect of TiO2 dust on the human lung.

Key words: titanium dioxide, mortality, lung cancer, occupation.
Mortality among workers employed in the titanium dioxide production industry in Europe

Paolo Boffetta¹,²,³, Anne Soutar⁴, John W. Cherrie⁴,⁵, Fredrik Granath², Aage Andersen⁶, Ahti Anttila⁷, Maria Blettner⁸, Valerie Gabotieau¹, Stefanie J. Klug⁸, Sverre Langard⁹, Daniele Luce¹⁰, Franco Merletti¹¹, Brian Miller⁴, Dario Mirabelli¹¹, Eero Pukkala⁷, Hans-Olov Adami¹ & Elisabet Weidemann¹²,∗

Table 4. Standardized mortality ratios of selected causes by country

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Country</th>
<th>Finland</th>
<th>France</th>
<th>Germany*</th>
<th>Italy</th>
<th>Norway</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>Obs/Exp</td>
<td>224/276.1</td>
<td>305/313.8</td>
<td>1015/1131.7</td>
<td>89/99.8</td>
<td>84/96.0</td>
<td>902/1102.4</td>
</tr>
<tr>
<td></td>
<td>SMR</td>
<td>0.81</td>
<td>0.97</td>
<td>0.90</td>
<td>0.89</td>
<td>0.87</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>0.71-0.92</td>
<td>0.87-1.09</td>
<td>0.84-0.95</td>
<td>0.72-1.10</td>
<td>0.70-1.08</td>
<td>0.77-0.87</td>
</tr>
<tr>
<td>All malignant neoplasms</td>
<td>Obs/Exp</td>
<td>34/51.2</td>
<td>125/103.3</td>
<td>319.5/298.3</td>
<td>28/37.1</td>
<td>21/23.6</td>
<td>279/312.9</td>
</tr>
<tr>
<td></td>
<td>SMR</td>
<td>0.66</td>
<td>1.21</td>
<td>1.07</td>
<td>0.75</td>
<td>0.89</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>0.46-0.93</td>
<td>1.01-1.44</td>
<td>0.96-1.20</td>
<td>0.50-1.09</td>
<td>0.55-1.36</td>
<td>0.79-1.00</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>Obs/Exp</td>
<td>12/15.8</td>
<td>36/25.4</td>
<td>128.5/84.8</td>
<td>12/12.4</td>
<td>4/5.0</td>
<td>114/104.7</td>
</tr>
<tr>
<td></td>
<td>SMR</td>
<td>0.76</td>
<td>1.42</td>
<td>1.51</td>
<td>0.97</td>
<td>0.79</td>
<td>1.09</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>0.39-1.32</td>
<td>0.99-1.96</td>
<td>1.26-1.79</td>
<td>0.50-1.69</td>
<td>0.21-2.02</td>
<td>0.90-1.31</td>
</tr>
</tbody>
</table>

SMR, standardized mortality ratio; CI, confidence interval.

* Observed deaths are not integer values (except for all causes of death) because of correction factors for missing causes of deaths.
### Healthy worker survivor effect (HWSE)

#### Table 5. Standardized mortality ratios of lung cancer by duration of employment and time since first employment

<table>
<thead>
<tr>
<th>Years of employment</th>
<th>1–10</th>
<th>10.01–20</th>
<th>20.01–30</th>
<th>30.01+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obs/Exp</td>
<td>7.0/7.1</td>
<td>12.1/9.7</td>
<td>40.9/16.6</td>
<td>17.8/15</td>
<td>77.7/48.4</td>
</tr>
<tr>
<td>SMR</td>
<td>0.99</td>
<td>1.24</td>
<td>2.47</td>
<td>1.19</td>
<td>1.61</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.4–2.03</td>
<td>0.64–2.15</td>
<td>1.78–3.36</td>
<td>0.71–1.90</td>
<td>1.27–2.01</td>
</tr>
<tr>
<td>Obs/Exp</td>
<td>9.0/9.2</td>
<td>10.1/7.7</td>
<td>11.2/9.7</td>
<td>3.2/7.2</td>
<td>33.5/33.7</td>
</tr>
<tr>
<td>SMR</td>
<td>0.98</td>
<td>1.31</td>
<td>1.15</td>
<td>0.44</td>
<td>0.99</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.45–1.86</td>
<td>0.62–2.4</td>
<td>0.57–2.03</td>
<td>0.09–1.22</td>
<td>0.67–1.37</td>
</tr>
<tr>
<td>Obs/Exp</td>
<td>–</td>
<td>–</td>
<td>38.8/34.7</td>
<td>–</td>
<td>115.5/92.5</td>
</tr>
<tr>
<td>SMR</td>
<td>–</td>
<td>–</td>
<td>1.12</td>
<td>–</td>
<td>1.25</td>
</tr>
<tr>
<td>95% CI</td>
<td>–</td>
<td>–</td>
<td>0.80–1.54</td>
<td>–</td>
<td>1.03–1.49</td>
</tr>
<tr>
<td>Obs/Exp</td>
<td>16.0/16.3</td>
<td>53.2/50.9</td>
<td>120.6/88.0</td>
<td>116.6/93.9</td>
<td>306.5/248.3</td>
</tr>
<tr>
<td>SMR</td>
<td>0.98</td>
<td>1.03</td>
<td>1.37</td>
<td>1.25</td>
<td>1.23</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.56–1.59</td>
<td>0.78–1.37</td>
<td>1.14–1.64</td>
<td>1.04–1.50</td>
<td>1.10–1.38</td>
</tr>
</tbody>
</table>

SMR, standardized mortality ratio; CI, confidence interval.

*a* Observed deaths are not integer values because of correction factors for missing causes of deaths.
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Table 6. Relative risk of mortality from lung cancer and non-malignant respiratory diseases for estimated cumulative exposure to respirable TiO₂ dust

<table>
<thead>
<tr>
<th>Cumulative exposure (mg)</th>
<th>Lung cancer</th>
<th>Non-malignant respiratory diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–0.73</td>
<td>0.73–3.43</td>
</tr>
<tr>
<td></td>
<td>3.44–13.19</td>
<td>13.20 +</td>
</tr>
<tr>
<td>Linear trend, p-value</td>
<td>0.5</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Results of Cox regression analysis.
CLP Expertise conclusion

• Given the methodological bias in dose-response assessment and a statistically significant increase in lung cancer mortality reported in two publications, France has established that human data are not sufficient to conclude that there is no carcinogenic effect in humans and cannot contradict the carcinogenic effects observed in rats

• Need to re-analyze existing data and / or a meta-analysis

ECHA RAC decision

• Classification as a category 2 carcinogen (suspected human carcinogen) by inhalation for TiO2 in all its forms

• Inclusion in Annex VI of the CLP Regulation
And then...

- Industrial repost

---

**ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON TITANIUM DIOXIDE**

<table>
<thead>
<tr>
<th>Date</th>
<th>Country</th>
<th>Organisation</th>
<th>Type of Organisation</th>
<th>Comment number</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.07.2016</td>
<td>Belgium</td>
<td>EuPC (European Plastics Converters)</td>
<td>BehalfOfAnOrganisation</td>
<td>5</td>
</tr>
</tbody>
</table>

**Comment received**

Cerame-Unie, the Europe including bricks & roof tile material & decorative ware, I accounts for more than 21%

No cases of pulmonary fibrosis of Dupont "Epidemiologic Dec;30(12):937-42 gave TiO2 as a carcinogen category 3 classification, which was made by France.

---

**Comment received**

This business employs 187 people in Europe. We manufacture wallcoverings. Titanium Dioxide is an important component of our products and it is great concern to us if this material were to be classed as a carcinogen. We have used TiO2 within our products for over fifty years and during this time we have followed all statutory requirements for dust control and we are unaware of any health issues experienced by our employees through exposure to TiO2 in the workplace. The prospect that we may have to label our rolls of wallpaper as containing a carcinogen will potentially cause customers to stop buying our products due to misplaced concerns about a hazard when the potential for exposure to that hazard is very low.

Substitution of TiO2 for other materials would not be economic and will raise the cost of products at a time when the whole of Europe does not need any further inflationary pressures. This proposed re-classification if adopted will decimate the DIY industry in Europe.

As its already written, there is no evidence, that any product containing TiO2 has caused cancer. Not a single case is known.

And the customers using products containing TiO2 will not come in a situation like mice in a TiO2 dust filled air. TiO2 is bound in liquids and pastes, there is simply no TiO2 dust. Because of this and the fact that there is no sufficient replacement for TiO2 at the time we support any position which does not have to label products containing TiO2 in liquid or pasty form.

RAC response to comments on carcinogenicity (human data)

RAC independently assessed all the epidemiological studies available up to now, including four studies initially not assessed by DS, but mentioned during PC (Ellis et al., 2010, Ellis et al., 2013, Hext et al., 2005 and Thompson et al., 2016) RAC agreed with the general assessment made by Thompson et al. that epidemiological data support a moderate level of confidence for the human evidence and therefore can be used for carcinogenicity risk evaluation. RAC considers that human data do not consistently suggest an association between occupational exposure to TiO2 and risk for lung cancer as far as no specific TiO2 micro and nano particle sizes and/or specific physical forms are regarded. However, one cohort study by Boffetta et al. (2004) deals specifically with the respirable fraction of TiO2 dust (calculated from total dust) and suggests that there is no clear dose–response relationship expressed as RR for lung cancer; generally we do not have sufficient amount of relevant studies. In addition, Boffetta et al. (2004) indicated in their paper and Hext et al. (2005) repeated in their summary paper that the investigated TiO2 concentrations in the occupational environment generally could be too low to cause lung cancer. Therefore RAC concludes that the animal carcinogenicity studies cannot be overruled.
And finally...

https://echa.europa.eu/fr/substance-information/-/substanceinfo/100.033.327

<table>
<thead>
<tr>
<th>Type of TiO2 exposure variable</th>
<th>Observed lung cancer</th>
<th>Model 1*</th>
<th>Model 2*</th>
<th>Model 3*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Binary exposed Vs non-exposed</strong></td>
<td>14 3.75 [0.79-17.9]</td>
<td>4.34 [0.85-22.15]</td>
<td>3.77 [0.79-17.95]</td>
<td></td>
</tr>
<tr>
<td><strong>Categorical annual average exposure Vs non-exposed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[0-0.3] mg/m³</td>
<td>7 4.04 [0.79-20.63]</td>
<td>5.94 [1.07-32.99]</td>
<td>4.15 [0.81-21.21]</td>
<td></td>
</tr>
<tr>
<td>[0.3-2.4] mg/m³</td>
<td>3 1.68 [0.26-10.93]</td>
<td>1.64 [0.24-11.11]</td>
<td>1.64 [0.25-10.67]</td>
<td></td>
</tr>
<tr>
<td>&gt;2.4 mg/m³</td>
<td>4 28.28 [4.57-175.15]</td>
<td>12.97 [1.86-90.74]</td>
<td>27.33 [4.35-171.84]</td>
<td></td>
</tr>
<tr>
<td><strong>Continuous annual average exposure (mg/m3)</strong></td>
<td>16 2.10 [1.37-3.22]</td>
<td>1.70 [1.03-2.79]</td>
<td>2.07 [1.34-3.20]</td>
<td></td>
</tr>
<tr>
<td><strong>Continuous cumulative exposure (mg/m3-year), 0 lag</strong></td>
<td>16 1.02 [0.97-1.06]</td>
<td>-</td>
<td>-</td>
<td>1.02 [0.97-1.06]**</td>
</tr>
<tr>
<td>5-year lag</td>
<td>9 1.02 [0.98-1.07]</td>
<td>-</td>
<td>-</td>
<td>1.02 [0.98-1.07]**</td>
</tr>
<tr>
<td>10-year lag</td>
<td>5 1.03 [0.99-1.08]</td>
<td>-</td>
<td>-</td>
<td>1.03 [0.98-1.08]**</td>
</tr>
<tr>
<td>15-year lag</td>
<td>1 1.04 [0.98-1.11]</td>
<td>-</td>
<td>-</td>
<td>1.04 [0.98-1.11]**</td>
</tr>
</tbody>
</table>

Hazard ratios and associated 95%-confidence intervals are adjusted for calendar period in Model 1; for calendar period and exposure duration in Model 2; for calendar period, exposure duration and smoking status in Model 3, except for cumulative exposure variable ** adjusted only for calendar period and smoking status in Model 3.

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Re-analysis of the EU data

Main conclusions

• Association between cumulative exposure and lung cancer mortality, after correction of the HWSE
• Exposure reduction corresponds to a significant reduction in the number of lung cancer deaths
• The safety of NIOSH REL (2.4 mg / m³) seems questionable
Essential Public Health Operations

- EPHO3: Health protection (environmental, occupational, food safety etc.)
- EPHO10: Advancing public health research to inform policy & practice

Statistiques

La population active suisse est championne en Europe

A fin 2018, la population active (15-64 ans) participant au marché du travail en Suisse a augmenté à 84,2%, contre 81,3% en 2010, juste derrière l'Islande avec 88,7%.

https://www.24heures.ch/economie/population-active-suisse-championne-europe/story/10701185
Essential Public Health Operations

- **EPHO3**: Health protection (environmental, occupational, food safety etc.)
- **EPHO10**: Advancing public health research to inform policy & practice

**Healthy worker, healthy citizen: the place of occupational health within public health research in Switzerland**

I. Guseva Canu¹ · M. François² · H. Graczyk³ ⁴ · D. Vemez¹

**Fig. 1** Evolution of the number of yearly publications in public health, occupational health and its related disciplines, and environmental epidemiology in the six selected Swiss public health institutions in Switzerland, 2008–2017
Thank you for your attention!

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