**Thematic area:** Epidemiology.

**Title:** The association between pesticide use and cutaneous melanoma: a systematic review and meta-analysis.

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**Background:** Pesticides directly endanger agricultural workers, neighbouring populations, wildlife, and consumers with a short and long term impact on health biological systems. Ecological wisdom demands to monitor methods of pesticide exposure and to improve the current knowledge based on
epidemiological and biological data such as risk assessment indicators. The United States Environmental Protection Agency (USEPA) and the European Environment Agency (EEA) should investigate violations in biocide use, with appropriate public oversight provisions to diminish bias from government and industry. Moreover, USEPA, EEA and all scientific community should improve standards used to determine the safety and relative risk of chemicals allowed on the market.

Epidemiological studies suggested that agricultural workers are at an increased risk of CM because they were exposed to pesticides. However, little is known about the relationship between pesticides and cutaneous melanoma. We performed a systematic review and meta-analysis to investigate the possible association between pesticide exposure and CM. Moreover, we tried to determine the categories of pesticides mainly involved in CM development.

**Methods:** Our analysis was performed up to September 2018 using Medline, Embase and Web of Science. Studies assessing CM risk in licensed pesticide applicators were considered. Strict criteria were established to select independent studies and risk estimates; random effect models, taking into account heterogeneity, were applied. A pooled risk estimate for CM was calculated for the use of each type of pesticide and type of exposure. Between-study and estimates heterogeneity was assessed and publication bias investigated.

**Results:** A total of 9 studies comprising 184389 unique subjects were included (1-9). The summary relative risks for the categories “herbicides - ever exposure”, “insecticides - ever exposure”, “any pesticide - ever exposure” and “any pesticide - high exposure” resulted 1.85 (95% CI: 1.01, 3.36), 1.57 (95% CI: 0.58, 4.25), 1.31 (95% CI: 0.85, 2.04) and 2.17 (95% CI: 0.45, 10.36), respectively. Herbicides and insecticides had no between-study heterogeneity ($I^2=0\%$), while a significant heterogeneity ($I^2>50\%$) was detected for the high exposure to any pesticide. No indication for publication bias was found.

**Conclusions:** Individuals exposed to herbicides are at an increased risk of CM. Future properly designed observational studies are required to confirm this finding.
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