TOP TAKEAWAYS

Systematic review finds limited evidence of a relationship between talc and pulmonary cancers.

CENTER FOR TRUTH IN SCIENCE

In an independent systematic review of studies on the potential health hazards of talc, published in *Frontiers in Public Health*, on October 11, 2022, Stantec, a Boston-based research firm, has determined that it is likely that there is no association between inhaled talc and respiratory cancers.

The objective of this work was to apply rigorous systematic review methods to critically evaluate and synthesize the scientific evidence addressing any possible relationship(s) between talc exposure and pulmonary cancers, specifically lung cancer and pleural mesothelioma. The review included studies on occupational exposure, as well as the personal use of talc-containing products (primarily talcum powders and cosmetics), integrating three types of studies: epidemiological, toxicological, and mechanistic studies that identify potential underlying modes of action (MOA). This has not been done since the International Agency for Research on Cancer (IARC) published its monograph in 2010.

The team of scientists found suggestive evidence of no association between inhaled talc and lung cancer at human relevant exposure levels. The researchers used a hybrid methodology based on the United States Environmental Protection Agency's Integrated Risk Information System (IRIS) Program and the National Academies of Science criteria.

WHY IT MATTERS

This is one of the most comprehensive systematic reviews to date of existing research on talc—a compound used in cosmetic powders, ceramics, paints, rubber, and many other products. The results raise questions on the validity of pending lawsuits claiming that talc exposure causes cancer.

Key findings include:

- Suggestive evidence of no association [1] between inhaled talc and lung cancer.

"Systematic review methods are evolving, but their core principles provide transparent and reproducible guidance for assessing and synthesizing scientific evidence on whether chemical substances can cause health effects, including cancer, in humans. This is critical to ensuring that policy and regulations are based on robust science and not unduly influenced by sporadic observed associations or untested hypotheses."

- Heather Lynch, M.P.H., Stantec

BACKGROUND

Talc is a naturally occurring mineral composed of magnesium, silicon, oxygen, and hydrogen. It can also be referenced as hydrated magnesium silicate. Talc has been safely used for centuries (dating back to ancient Egypt) worldwide in products such as face, body and baby powders, cosmetics, deodorant, toothpaste, chewing gum, and much more.

1. Limited/suggestive evidence: Evidence is suggestive of no association between exposure of a specific agent and a health outcome in humans, but is limited because chance, bias, and confounding could not be ruled out. (Institute of Medicine, 2009)

REVIEW METHODS

The review integrated three types of studies: human epidemiological, animal, and mechanism of action (MOA) or mechanistic studies. It incorporated the strongest aspects from the U.S. Institute of Medicine (IOM) and several U.S. EPA frameworks for systematic reviews.

The authors also followed the highly respected guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) to increase the strength and transparency of the work, as well as to improve the literature searches, which are the foundations of systematic reviews. Study quality was determined by adapting the U.S. Toxic Substance Control Act (TSCA) framework.

Methods used in the systematic review of the potential carcinogenicity of inhaled talc in humans:

- Strictly followed PRISMA guidelines and incorporated aspects from Institute of Medicine (as of 2015 the National Academy of Medicine) and several EPA frameworks for systematic reviews.
- Evaluated and integrated the epidemiological, animal, and mechanistic literature on talc and pulmonary cancers.
- Detailed data abstraction and study quality evaluation, adapting the Toxic Substances Control Act (TSCA) framework.
- The literature search and selection process identified 22 primary studies, with the most information available for pulmonary cancers.
- Results of the analysis emphasize the importance of consideration of biological plausibility and study quality in systematic review.

KEY FINDINGS

Animal studies - Overall, in available animal studies, there is indeterminate evidence that talc is associated with lung tumors in rodents based on negative findings in several high-quality studies and species.

Mechanistic studies - Overall, the mechanistic evidence is insufficient to support an MOA whereby talc induces lung cancer.

- Talc was negative for mutagenicity (ability to cause genetic mutations in cells) and other forms of genotoxicity (ability to damage a cell's genetic information, causing cancer) in all available bioassays.
- Data from studies of how talc acts in the body over time indicate there is a rapid clearance from the lung and body after it is inhaled in single doses, and there is no translocation of talc to other organs after either single or repeated exposures.
- While the evidence for possible carcinogenic mechanisms of talc is limited, a genotoxicity MOA can be ruled out with confidence.
- A few studies provide evidence of some possible inflammatory MOA; however, these are limited to animal studies and mechanistic investigations.

MORE KEY FINDINGS

Human epidemiological studies - Lung cancer mortality was not elevated among most of the cohorts of talc miners and millers exposed to high levels of respirable talc and accessory minerals.

- No excess of malignant mesothelioma has been reported in any of the available epidemiological studies of talc miners and millers heavily exposed to talc.
- When considered together, the moderate confidence in study findings, large study populations, long duration of follow up, and consistency of null findings indicate that talc exposure is not associated with mesothelioma.
- Given the moderate confidence in study quality ratings and a lack of a consistent association between occupational talc exposure and lung cancer mortality, the available epidemiological evidence does not demonstrate a causal association between talc exposure and lung cancer deaths.

CONCLUSIONS

This systematic review generated suggestive evidence of no association (Institute of Medicine) between inhaled talc and pulmonary cancers, including lung cancer and mesothelioma.

This conclusion is based on the integration of evidence from animal experiments, mechanistic evaluations, and epidemiological studies all of reasonable methodological quality.

The body of epidemiological evidence is reasonably large and robust for lung cancer and mesothelioma and provides the most weight in the integration. It is complemented by the number of high-quality animal studies, as well as the lack of convincing mechanistic evidence.

The conclusions reached in this systematic review are similar to those of IARC. Findings for pulmonary cancers are consistent with IARC's classification of inhaled talc not containing asbestos or asbestiform fibers as "not classifiable" as to its carcinogenicity, as it identified no clear increase in cancer risk in animals and humans, and no clear MOA for carcinogenesis was identified (IARC, 2010).

"This research brings clarity to the ongoing courtroom debates about the effects of talc exposure. The findings of this comprehensive review should ensure that future discussions on talc will be based on validated science, and produce regulatory and judicial decisions that foster innovation, benefit consumers and protect public health."

- Jacob Traverse, President of Center for Truth in Science

This systematic review was funded by the Center for Truth in Science, an independent non-profit organization dedicated to exploring the intersection of science, justice and the economy.

The research plan and summary were described by Margaret Murray, Ph.D., research director of Center for Truth in Science, and performed by a highly qualified group of toxicologists and epidemiologists from April to September, 2021.

To view the full independent systematic review, visit https://doi.org/10.3389/fpubh.2022.989111