



you are here: [science media centre](#) > [roundups for journalists](#) > expert reaction to iarc monographs evaluating the carcinogenicity of talc

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Post

expert reaction to IARC monographs evaluating the carcinogenicity of talc

Scientists react to an IARC evaluation of carcinogenicity of talc.

Prof Paul Pharoah, Professor of Cancer Epidemiology, Cedars-Sinai Medical Center, said:

“IARC have changed the classification of talc from class 2B (possible carcinogen) in previous reports to 2A (probable carcinogen) in this report. This change appears to primarily rest on mechanistic evidence from experimental laboratory systems. There was also evidence from some animal models (rats). Extrapolating from model systems and animal models to humans is problematic and the evidence for carcinogenicity in humans is extremely weak. Many observational studies have shown an association between talcum powder use in the genital area and ovarian cancer risk. However, such a correlation may easily be explained by other factors that are associated with both talc and with ovarian cancer (so-called confounders). Moreover, the reported associations with different types of ovarian cancer – which are known to be very different in their risk factors and underlying biology – are not consistent with the observed association being causal.

“In addition, even if the observed association were causal, the associated risk would be very small.

“My interpretation of all the evidence is that women who have used genital talc in the past should not worry about their future risk of ovarian or other cancers.”

Prof Kevin McConway, Emeritus Professor of Applied Statistics, Open University, said:

“This isn’t the first time that IARC, the WHO’s International Agency for Research on Cancer, has made an assessment of the carcinogenicity of talc. Their last publication on it was in 2010, and concluded that the use of talc in the genital area was, to use their terminology,

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“It’s really important to understand what these classifications by IARC actually mean, because the most obvious interpretation is actually misleading. When IARC classifies a substance in this series of publications, it is not saying anything specifically about whether exposure to the substance *does* increase the risk of cancer, in humans, at any particular amount of exposure or in any particular circumstances. Instead they aim to answer the question of whether the substance has the *potential* to cause cancer, under some conditions that IARC do not specify.

“At first sight this may seem an odd way to go about things – surely what we want to know is whether the substance actually increases cancer risk, and if so, in what quantities and under what circumstances. But it’s not uncommon, when considering potentially harmful substances or activities, to start by looking at the *hazard*, that is the potential that the substance *could* increase risk of something bad happening, and not the actual *risk* to people exposed in certain ways.

“A recent example that might make the distinction clearer, though it caused a lot of confusion at the time, was the IARC assessment of the artificial sweetener aspartame, originally published last year (2023). IARC concluded that aspartame was “possibly carcinogenic to humans”. So they were saying that aspartame maybe presents a hazard, that is, a potential risk, under some unspecified circumstances. But, unusually, at the same time a different WHO agency, that is responsible for assessing risk of food additives, published a report that concluded that in fact aspartame did not present an actual risk of cancer in humans, when it is consumed in the amounts that are actually added to foods and drinks. These two publications were deliberately co-ordinated to come out at the same time, but that does not usually happen. On the face of it, the two agencies seemed to be contradicting one another – but in fact they weren’t, they were providing answers to two different questions, one about the potential for risk (that is, the hazard) and the other about actual risk in practice.

“As far as I know, there isn’t a coordinated publication on actual risk of talc. So all the IARC classification tells us is that there is probably a potential for an increased risk of ovarian cancer in humans, but under circumstances that IARC do not define.

“The evidence that IARC use to come to this conclusion on hazard is of several kinds. Some comes from animal studies, in which laboratory rats breathed in talc, and were found to have increased numbers of tumours of various kinds (not ovarian). Some comes from studies in animals and in cell cultures and provides evidence on how exposure to talc can change what happens to in cells.

“But none of that investigates whether those processes operate in human beings, in the ways that were studied. There have been studies in humans, which found increased risks of ovarian cancers in people who used talc compared to people who did not use it. But these are observational studies – the talc users and the non-users differed in many other ways apart



This possibility of bias in the findings led the experts consulted by IARC to consider the evidence that talc causes ovarian cancer to be limited. Rightly, they aren't saying that talc *cannot* cause ovarian cancer in humans. But they can't at all be sure that in fact it *does* cause an increase in risk, at the levels of exposure that might happen in normal use of talc or indeed in any other circumstances of use.

“So really we're in the rather unsatisfactory position that IARC say that using talc can probably cause cancer in humans under certain circumstances that they don't define. This is a somewhat more definite conclusion than their 2010 version that didn't go farther than saying talc could possibly cause cancer. The change from 'possibly' to 'probably' seems mainly to be because more evidence from observational studies has been obtained since the previous IARC publication. But that extra evidence wasn't considered enough to move talc to the IARC's highest classification of cancer hazard, which would drop the 'probably' and simply say that that the substance can cause cancer.

“In summary, IARC's experts still leave some room for doubt that using talc can ever cause human cancers at all, though they believe it probably can, and they haven't pronounced on the circumstances under which it might actually increase ovarian cancer risk in real life. There's still a lot of uncertainty here.”

Further information.

“There is rather more detail in a brief journal article in *Lancet Oncology* at [https://doi.org/10.1016/S1470-2045\(24\)00384-X](https://doi.org/10.1016/S1470-2045(24)00384-X), though the full details won't appear until the full IARC monograph eventually appears, quite possibly a year or more from now.

IARC have also published a Q&A document at <https://www.iarc.who.int/wp-content/uploads/2024/07/QA-Mono-Vol136.pdf>. They also publish a Q&A document on the whole process of producing these evaluations, at <https://monographs.iarc.who.int/wp-content/uploads/2018/07/IARCMonographs-QA.pdf>. Page 4 of that document gives a brief explanation of the difference between hazard and risk.”

<https://www.iarc.who.int/news-events/iarc-monographs-evaluate-the-carcinogenicity-of-talc-and-acrylonitrile-iarc-monographs-volume-136/>

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Prof Kevin McConway: “I am a Trustee of the SMC and a member of its Advisory Committee. My quote above is in my capacity as an independent professional statistician.”



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