

5 July 2019

IARC Monographs Meeting 124: Night Shift Work (4–11 June 2019)

Questions and Answers

For <u>Volume 124</u> of the *IARC Monographs on the Identification of Carcinogenic Hazards to Humans*, the Working Group was tasked with evaluating shift work that involves circadian disruption, which includes both working at night and working in a job that involves rapidly crossing many time zones (e.g. as part of an airplane cockpit or cabin crew).

The Working Group defined night shift work as work, including transmeridian air travel, during the regular sleeping hours of the general population. A brief summary of the results of the *IARC Monographs* evaluation has been published in <u>The Lancet Oncology</u>.

What is the result of the evaluation?

The Volume 124 meeting has ended, and the final conclusion is that night shift work is *probably carcinogenic to humans* (Group 2A).

There is *limited* evidence in humans for the carcinogenicity of night shift work. Positive associations have been observed between night shift work and cancers of the breast, prostate, colon, and rectum. There is *sufficient* evidence in experimental animals for the carcinogenicity of alteration in the light–dark schedule. There is also *strong* mechanistic evidence in experimental systems, based on evidence of effects consistent with immunosuppression, chronic inflammation, and cell proliferation.

What does this evaluation mean?

The classification indicates the strength of the evidence that a substance or agent causes cancer. The *IARC Monographs* programme seeks to identify cancer hazards, meaning the potential for the exposure to cause cancer. However, it does not indicate the level of cancer risk associated with exposure at different levels. The cancer risk associated with substances or agents that are assigned the same classification may be very different, depending on factors such as the type and extent of exposure and the size of the effect of the agent at a given exposure level.

A classification in Group 2A means that the agent is *probably carcinogenic to humans*. This category is used when there is *limited* evidence of carcinogenicity in humans and *sufficient* evidence of carcinogenicity in experimental animals. *Limited* evidence means that a positive association has been observed between exposure to the agent and cancer but that other explanations for the observations (technically termed chance, bias, or confounding) could not be ruled out.

What type of exposure is involved?

Exposure to night shift work (including transmeridian air travel) is widespread. It has been estimated that about 20% of workers in North America, Europe, and elsewhere are employed outside the standard

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daytime work shift. Higher percentages of night shift workers are seen in the manufacturing, medical, retail, service (including information technology), and transportation sectors. Whereas some occupational settings that have night shift work occur in a stationary location (e.g. a factory, restaurant, or hospital), others involve transmeridian air travel (e.g. an aircraft).

How was the evaluation conducted?

The evaluation was carried out by a Working Group of 27 independent international experts from 16 countries, who gathered in Lyon, France, for the *Monographs* meeting. The experts reviewed all relevant studies in the publicly available scientific literature on night shift work. They critically reviewed the scientific evidence according to strict scientific criteria (see the <u>Preamble to the IARC Monographs</u>) to determine the strength of the available evidence that night shift work causes cancer.

They critically reviewed four types of data:

- the situations in which people are exposed to night shift work;
- epidemiological studies of cancer in humans exposed to night shift work (scientific evidence of carcinogenicity in humans);
- experimental studies of cancer in laboratory animals exposed to alteration in the light–dark schedule (scientific evidence of carcinogenicity in animals); and
- studies of key carcinogenic characteristics of the agent (scientific evidence on carcinogen mechanisms), that is, studies in night shift workers and in laboratory animals exposed to alteration in the light–dark schedule.

During the second part of the meeting, the entire Working Group combined these into overall evaluations of carcinogenicity to humans.

What studies were evaluated?

A large number of studies have been published on cancer among workers in different settings who worked the night shift or who worked in airplane crews. These include studies of specific types of workers (e.g. nurses, factory workers, and airplane cabin and cockpit crew members), as well as people in the general population who may have worked in any job that involved night work.

How does night shift work affect the circadian system?

Night shift work alters exposure to the natural light–dark schedule and disrupts circadian (that is, daily) rhythms. The most pronounced effect of night shift work is the disruption of these circadian rhythms of normal body function. It is unknown to what extent these disruptions may lead to cancer.

What is the risk of developing cancer from night shift work?

The *IARC Monographs* classification does not indicate the level of risk associated with exposure. That would require a risk assessment. The classification indicates the strength of the evidence that a substance or agent causes cancer, or it identifies hazard.

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The distinction between *hazard* and *risk* is important. An agent is considered a cancer hazard if it is capable of causing cancer under some circumstances. Risk measures the probability that cancer will occur, taking into account the level of exposure to the agent. The *IARC Monographs* programme may identify cancer hazards even when risks are very low with known patterns of use or exposure. Recognition of such carcinogenic hazards is important, because new uses or unforeseen exposures could lead to risks that are much higher than those currently seen.

The Working Group determined that there was *limited* evidence for night shift work causing several types of cancer in humans but did not try to estimate what the level of cancer risk might be for different levels of exposure to night shift work.

How can people who are exposed to night shift work reduce their risk of developing cancer?

IARC does not make recommendations about individual actions that may be taken after exposure to a potential carcinogen. If you have been exposed to night shift work and are concerned about your health, you may consult your physician for advice.

What is IARC's recommendation as a result of this evaluation? Should governments take measures to protect workers?

IARC does not recommend regulations, legislation, or public health interventions, which remain the responsibility of individual governments and other international organizations.

However, health and regulatory agencies include *IARC Monographs* evaluations in their consideration of actions to prevent exposure to potential carcinogens.

Why is the evidence still considered to be limited for cancer in humans? Aren't there more studies now?

The Volume 124 Working Group reviewed all published studies of cancer in humans and night shift work, using standard methods to search and screen the literature. The Working Group thoroughly assessed the quality of each study to identify studies that could provide the most information about different types of cancer that may be related to night shift work. The cancer sites with the most information were the breast, prostate, colon, and rectum.

Although a large number of new studies have been published since the previous *IARC Monographs* evaluation of shift work, in 2007, they have used many different methods (some of better quality than others) to measure exposure to night shift work. Some large and informative studies did not find an association of night shift work with breast cancer or other cancer types. Other large and informative studies did find a positive association between night shift work and these cancer types. There are several possible explanations for these different findings. The conclusion of the Working Group was that, although a positive association has been found overall between night shift work and cancers of the breast, prostate, colon, and rectum, other explanations for the observations, such as bias, could not be ruled out with reasonable confidence.

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What are the limitations of the IARC Monographs evaluation?

The *IARC Monographs* evaluation is based on publicly available, published studies. There is always the possibility that new evidence may arise after a *Monographs* meeting that could shed new light on whether night shift work causes cancer.

This evaluation puts night shift work in the same category as working as a hairdresser or barber. Does this mean that these exposures are equally dangerous?

The cancer risk associated with substances or exposure circumstances that are assigned the same classification may be very different, depending on factors such as the type and extent of exposure and the size of the effect of the agent at a given exposure level.

Why did the IARC Monographs programme evaluate night shift work?

Shift work involving circadian disruption was previously evaluated by an <u>IARC Working Group in 2007</u> and was determined to be *probably carcinogenic to humans* (Group 2A). Since then, shift work was accorded high priority for re-evaluation during 2015–2019 by the Advisory Group convened in 2014 to recommend future topics for the *IARC Monographs*. The Advisory Group's recommendation for re-evaluation was based on the large number of studies that have been published since the previous *IARC Monographs* evaluation.

The agent was initially named "shift work that involves circadian disruption", but during the *Monographs* meeting, the Working Group chose to rename the agent as "night shift work", which better reflects both the exposure conditions and the existing studies of cancer and mechanisms in humans.

For more information about the meeting and its participants, please follow the links below:

More information on *IARC Monographs* Volume 124
Preliminary List of Agents
Preliminary List of Participants
Call for Data (closing date 6 May 2019)
Call for Experts (closing date 16 October 2018)
Request for Observer Status (closing date 15 January 2019)
WHO Declaration of Interests for this volume
Code of Conduct
Confidentiality Undertaking
Instructions for Authors

More information on the *IARC Monographs* evaluations can be found through the links below: *IARC Monographs* Q&A Preamble to the *IARC Monographs* Previous evaluation of shift work: <u>Volume 98</u> (published in 2010)