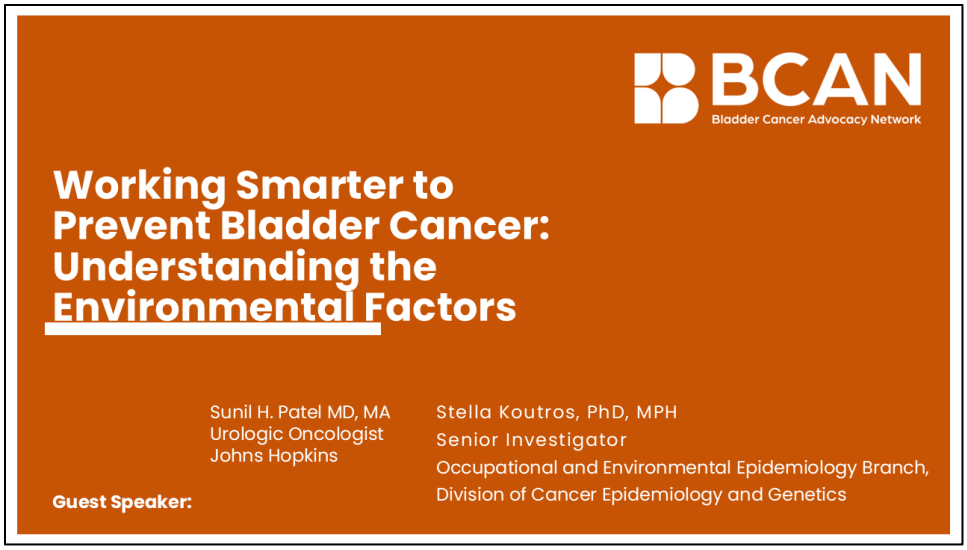
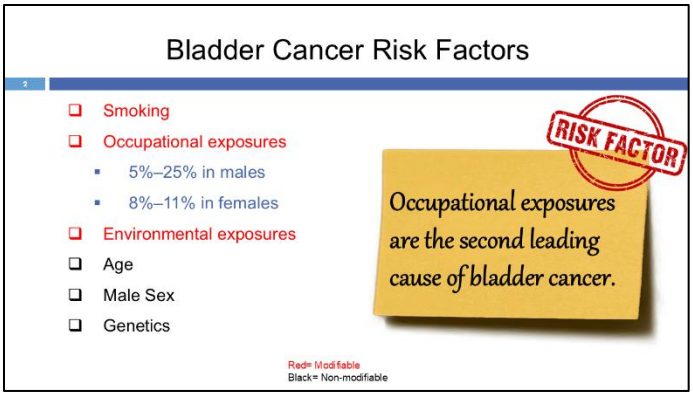
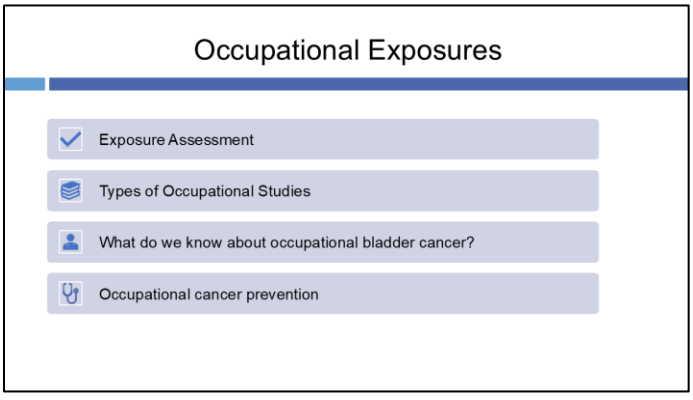


Dr. Stella Koutros:



So today, as the others said, I'm going to be talking about occupational exposures in bladder cancer. Like Dr. Patel, I should say, and I think we always say that the number one risk factor and the number one way you can prevent bladder cancer is to quit smoking. Smoking is really the most important risk factor for bladder cancer, but we've also recognized that occupational exposures are really important as well and can account for up to a quarter of bladder cancer cases. So I'll be focusing in on those in my next few slides.

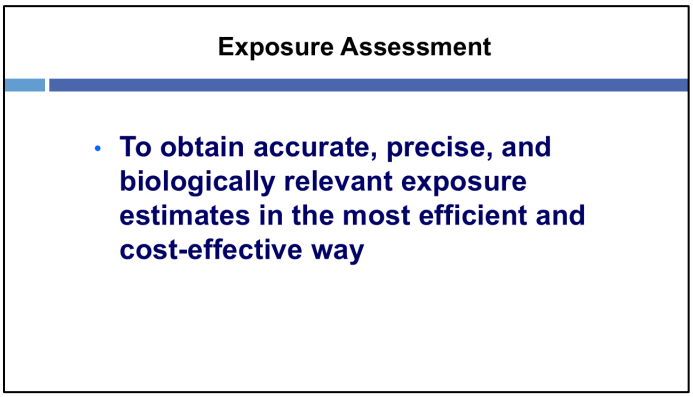
Dr. Stella Koutros:



I'll talk a little bit quickly and briefly about some of the terms we use when we think about occupational studies and the different types of studies. And then I'll dive into what key things we know already about occupational risk factors in bladder cancer, and then just a few words at the end about prevention.

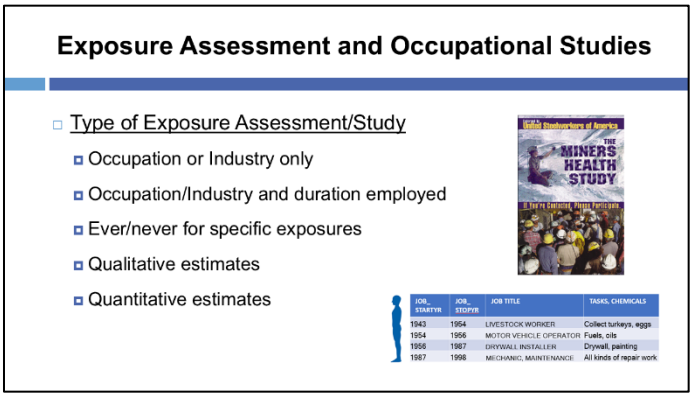
Dr. Stella Koutros:

So, one of the primary considerations when reading an occupational study or a study about an exposure is the assessment of that exposure. So we call that exposure assessment, and that is really just a fancy word for how you obtain accurate and precise estimates in the most efficient and cost-effective way. So if a study's trying to look at a relationship between an exposure in bladder cancer, we really want to understand what they're doing to kind of characterize that for a person and how they characterize it over that person's life.



Dr. Stella Koutros:

This has really important implications for the quality of the study. So today I'll talk about some of the exposures that have some of the most evidence for bladder cancer, but also if there's one thing I can leave you with is thinking about if you end up reading a study on your own, what you might consider about the exposure assessment will really help you understand what is really key about understanding the quality of that study.

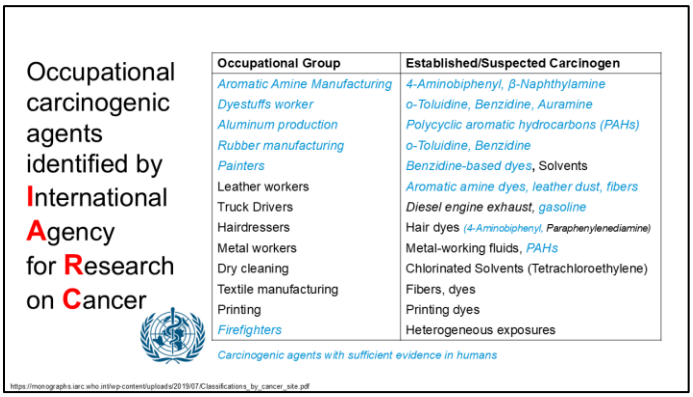


So sometimes in occupational studies, we study sort of occupational groups like truck drivers, and that's what we sort of call occupation or industry only. We sort of look at just a group of people who are working in a certain type of job. It's even better if we have some more information, like how long a person did that, like how many years they did that, but it's even better when we have really more detailed information about specific exposures.

Like if you're a truck driver, were you exposed to engine exhaust, and if you were exposed to engine exhaust, even better if we can sort of quantify that in a more quantitative way. So the more we can do that, the sort of better the quality of the study tends to be and sort of the better the inferences we can make about the risks for bladder cancer.

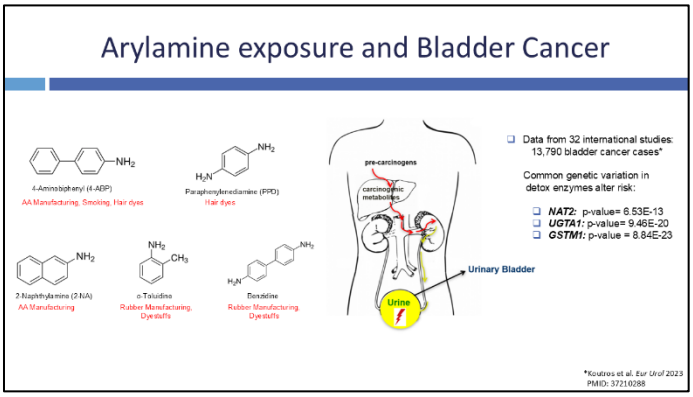
Dr. Stella Koutros:

So, one source of compiled information about cancer comes from the International Agency for Research on Cancer. This table's a lot, but it's a little bit of a summary about many of the occupations and workplace exposures that have been classified as bladder carcinogens because there's been decades of research in showing certain positive links and the things that are in the light blue are those with, which they have considered have sufficient evidence in humans. And the little PDF link at the bottom is a link to a table where you can look at sort of what's known about bladder cancer. I've just put some of the occupational things here, but they include other things as well.



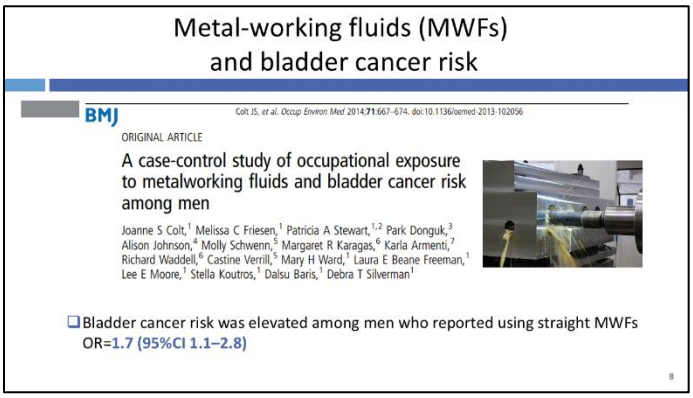
Dr. Stella Koutros:

One kind of key or commonality between a lot of the chemicals that were in that table are these group of chemicals that have a similar chemical structure. They're called aromatic amines. And we know that these particular chemicals are specifically damaging to the bladder and have largely been identified in studies of workers who ended up developing very high rates of bladder cancer in sort of different occupational settings.



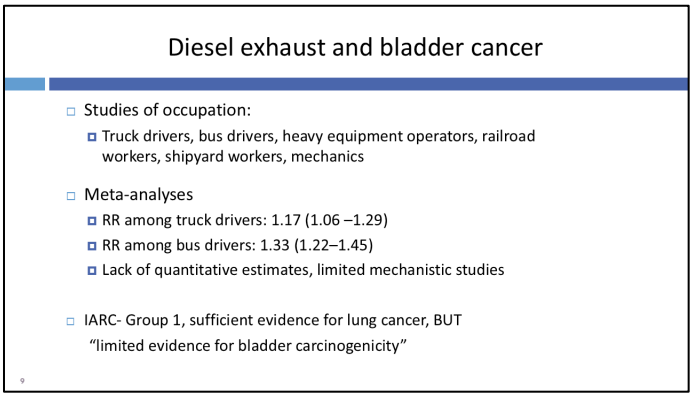
My group also has conducted some really large scale genetic studies where we've also shown that important sort of inherited genetic variation and certain key genes that are responsible for sort of metabolizing these chemicals and getting rid of them from the body are important modifiers of risk. And many of the people affected by these exposures are typically in industrial and manufacturing settings, which have become a little bit less common over the last several decades. So next, I'll just talk about a few other exposures that are more commonly reported among contemporary occupations.

Dr. Stella Koutros:



So metal-working occupations have been associated with increased bladder cancer in over 20 studies. So some specific jobs that have these exposures are precision metal workers or metal-working or plastic-working machine operators. And people who do these jobs are using what are called metal-working fluids. So they're used in metal machining to lubricate cool and remove debris from metal parts that are being drilled, ground or milled or some kind of type of machining work. So these metal-working fluids contain some certain chemicals that are suspected, some known and some suspected to be carcinogenic.

Dr. Stella Koutros:

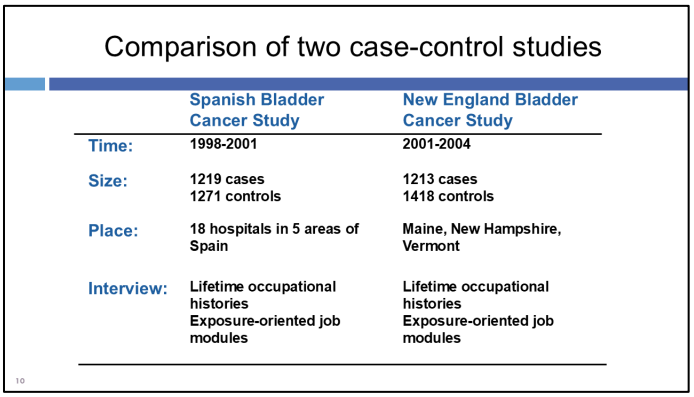


Another sort of exposure that's been linked to bladder cancer is exposure to diesel exhaust because of several studies of specific occupational groups who have high levels of exposure that have had increased bladder cancer risk, in particular truck drivers and bus drivers, but not a lot of studies really could go beyond that and get to those more quantitative estimates of exposure.

And initially, when IARC reviewed some of the literature, they said, "Well, we're not really sure there's not really enough good data about this for bladder cancer yet."

Dr. Stella Koutros:

One thing that I have been involved in is a combination of two case control studies that were conducted around the same time period, and they were similar in size.

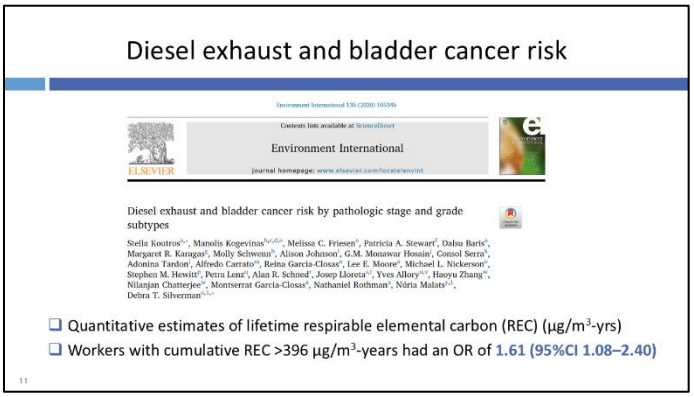


One was in Spain, and another one is here in New England, which is the study that Dr. Patel had mentioned. Both of these studies had identical questionnaires. We collected really detailed information about a person's lifetime occupational history, as well as these job modules to get really detailed information on different exposures.

And we pulled the data from these two studies.

Dr. Stella Koutros:

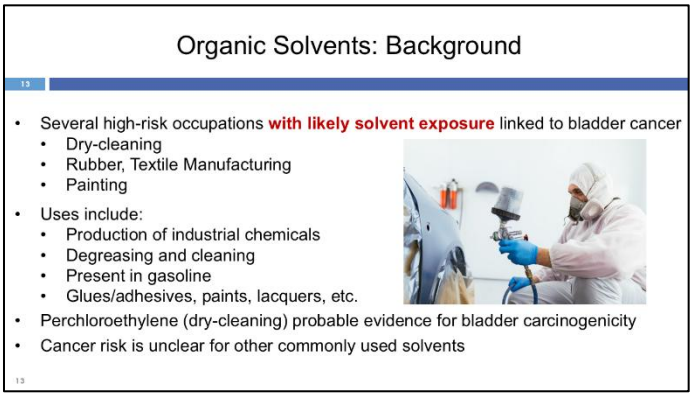
And in 2020, we published results that found that workers had elevated levels of diesel exhaust exposure had a higher risk for bladder cancer compared to people who were not exposed.



And so this was, I think, a study where we were able to provide some of that quantitative exposure data, which was sort of an element that had been missing on this topic before.

Dr. Stella Koutros:

Another set of exposures of interest that we've been sort of studying lately are organic solvents. So many of the occupational groups that have been noted to have higher bladder cancer rates happen to also have exposure to solvents, including people in dry cleaning and rubber textile manufacturing, painting.

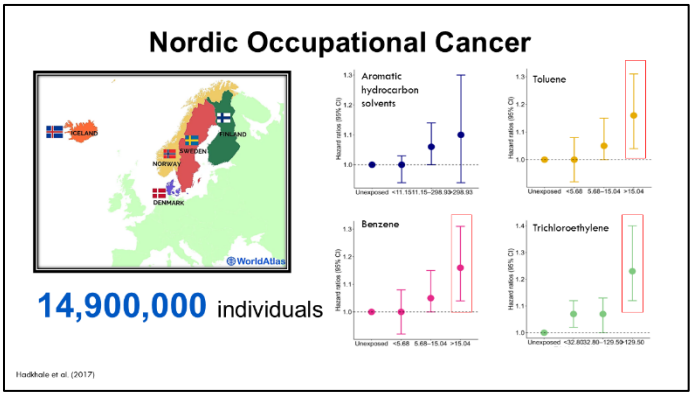


And there's sort of a diverse sort of set of tasks and chemicals that would sort of include the use of solvents, including degreasing

and cleaning. It's also present in gasoline and a lot of paints and glues. So there are a lot of different sort of sources for potential exposure to solvents.

Dr. Stella Koutros:

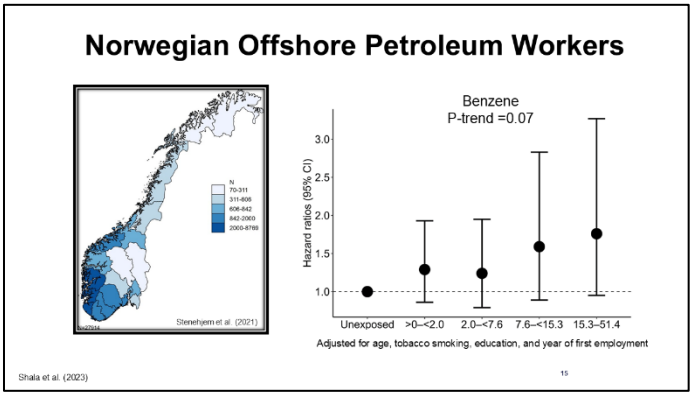
So a few years ago, there was this really large study from the Nordic countries that showed that there was some suggestion of an association between certain organic solvents and bladder cancer risk. And two of the solvents in this group seemed to be associated with a risk at the highest levels of exposure.



And another one of these chemicals, one at the bottom there, trichlorethylene is something that's used very similar to a chemical that's used in, it's a dry cleaning solvent, which has been also linked to bladder cancer before. So there was some initial sort of signal here there might be something going on for bladder cancer.

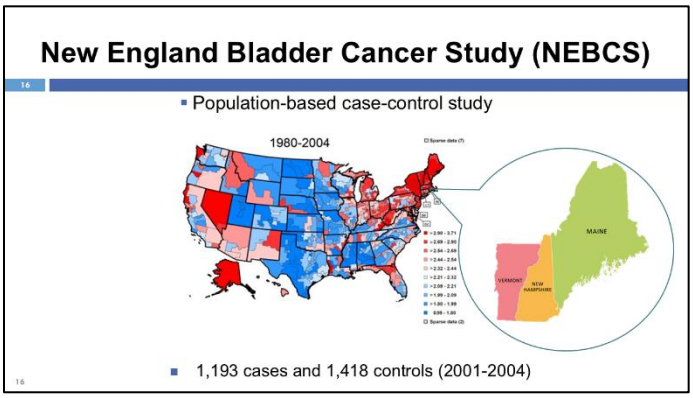
Dr. Stella Koutros:

And a little after this study, there was a large prospective case cohort study of Norwegian offshore petroleum workers, which showed an increasing exposure to benzene after adjusting for smoking and other factors and an increased risk of bladder cancer, sort of building on this literature for linking solvents in bladder cancer.



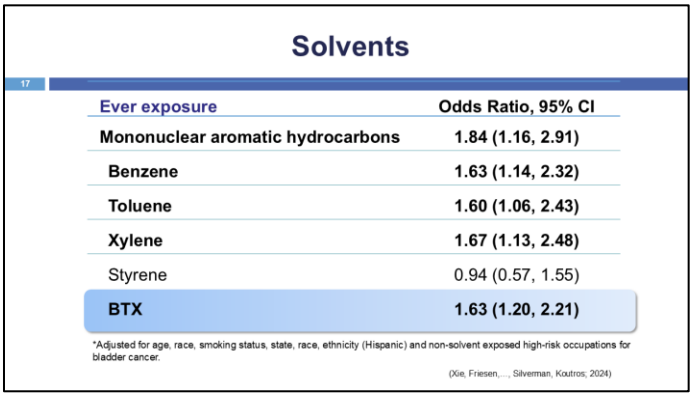
Dr. Stella Koutros:

So to follow up on these findings, my colleagues and I at the NCI looked at the relationship between solvents and in the general population of people who developed bladder cancer in the New England region where our study was conducted.



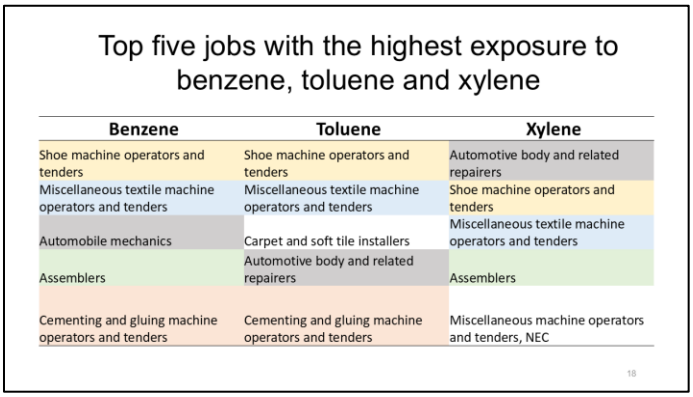
Dr. Stella Koutros:

And we were able to use these lifetime job histories and specific details again about the tasks and chemicals that people used on the job and found that there was also, we did find these increasing risks with exposure to sort of benzene, toluene and xylene. And then the three is a group, which is called BTX because they kind of often co-occur. And an important additional element of this is that we've also been able to really carefully adjust for smoking and also other types of occupational exposures because there are many that have been linked to bladder cancer as well.



Dr. Stella Koutros:

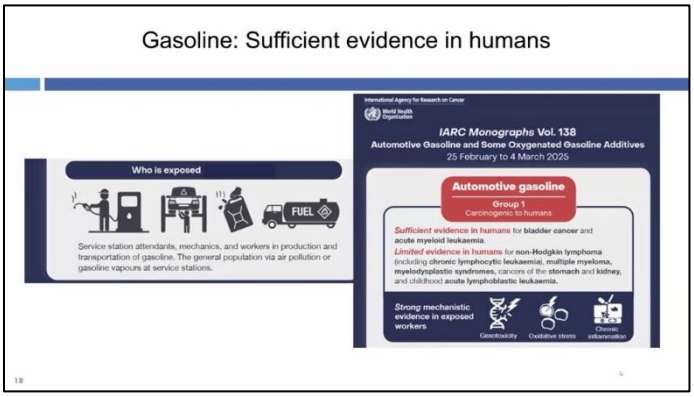
This chart just shows some of the jobs that were reported to have the highest levels of exposure to BTX. And you can sort of see here, they're color coded. Several types of machine operators in different industries can be exposed in shoes and textiles, but also auto mechanics and workers involved in autobody repair.



This group was particularly interesting because they ended up reporting a lot of gasoline use as a solvent. It turns out it's fairly common for people to use gasoline as sort of a cheap solvent for degreasing and cleaning parts.

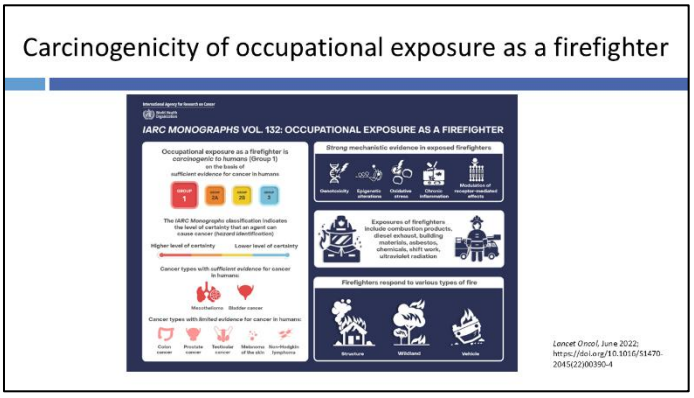
Dr. Stella Koutros:

And shortly after our study, IARC summarized sort of the overall cancer literature on gasoline and found that there was enough sufficient evidence in the literature in human studies that exposure to gasoline was shown to increased the risk for bladder cancer. And this is the summary of those findings which are online.



And it includes several... This would impact and sort of cover several working populations, including service station attendance, mechanics and workers in sort of production and transportation of gasoline. So potentially a lot of occupational groups exposed.

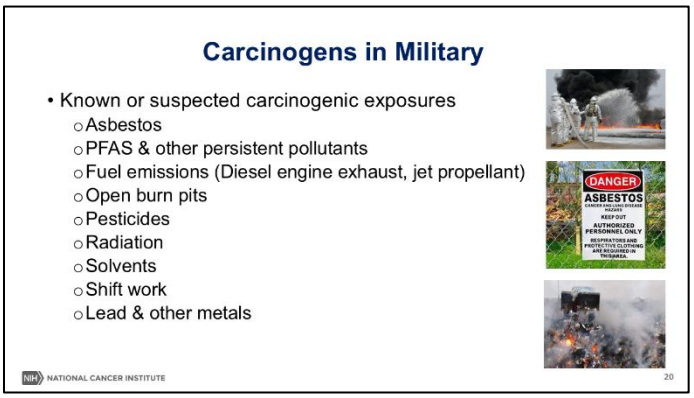
Dr. Stella Koutros:



So as I mentioned earlier, there's evidence that some occupational groups have these higher rates of bladder cancer and recently evidence had also been synthesized about firefighters and the increased risk for bladder cancer observed in this population.

And sometimes we can observe these higher rates in working populations, but we sort of have to do more work to understand what are the underlying specific exposures causing these elevations and risk. And so firefighters are exposed to a really wide range of things, including combustion products, diesel exhaust, asbestos, other building materials, and several other really heterogeneous exposures.

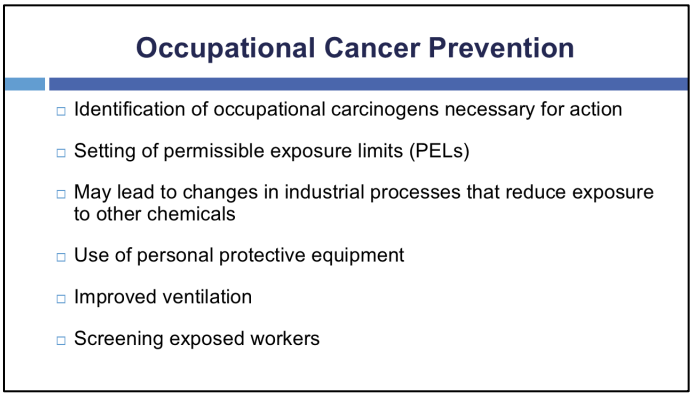
Dr. Stella Koutros:



Another group of interest are those who serve in the military. Like firefighters, this group is exposed to a really wide range of suspected carcinogens depending on the timing and location of military service and occupation. So there's still a lot more work needing to sort of help us understand what the direct connections are between exposures and military service and potential risks for bladder cancer.

Dr. Stella Koutros:

Ultimately, the studies we sort of really quickly covered today are important for identifying sort of occupational carcinogens in the workplace so that we can take some action to minimize these exposures and decrease any exposures when we can. For example, over time, diesel technology has changed really significantly to drastically reduce emissions compared to engines decades ago.



And our education about the risks from workplace exposures and how we can protect ourselves is also really an important strategy for reducing the burden of these exposures. In the future, we may even be able to develop some strategies for screening high risk populations for early detection as those kind of methods improve in the clinic and to try to prevent the development of bladder cancer altogether.