Cancer Mortality at the Older Ages: An Expert Panel Discussion

NOVEMBER | 2024

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An Expert Panel Discussion

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The Mortality and Longevity Strategic Research Program Steering Committee of the Society of Actuaries Research Institute decided to form a group to study older age mortality. A Project Oversight Group (POG) was formed for this purpose and the POG decided to first study cancer.

Cancer is regarded as a significant disease (or group of diseases) and continues to be one of the top causes of death globally. In most cases, cancer is of concern to both public health and private insurance industries. The POG developed a series of questions to explore cancer trends in mortality, incidence rates, demographic trends, detection and treatment technologies, lifestyle factors, and future advances. The questions were asked in an interview style and the expert panel responded with a lively discussion on the topics covered.

The expert panel included:

- Tom Ashley. M.D. FACP, DBIM (Chief Medical Director at Gen Re)
- Brad Heltemes M.D. DBIM, FAAIM (VP Medical Director at Munich Re)
- Gao Xiao (Epidemiologist at SCOR)

This report provides a high-level summary of the expert panel views and opinions from the Zoom discussion that took place on June 24, 2024. Questions covered are found in Appendix A.

Section 1: Understanding Cancer Risk

The panel began the discussion by providing insights into cancer risk at the older ages.

1.1 WHAT IS CANCER?

Classically, cancer has been thought of as uncontrolled tissue growth that evades recognition by our immune system therefore making it very hard for the body to control or eradicate the cells. While there is often a perception that cancer is a single disease, it is in fact a group of diseases with the common characteristic of uncontrollable cell growth. Different types of cancer can have a wide range of clinical course and outcome, with the cancer's impact being quite variable depending on the subtype of cancer and the treatment used.

Cancer is fundamentally a genetic disease. Mutations in the cell genome confer uncontrolled growth, invasion of surrounding tissues, and the development of new blood supply to the cancer. It is the pattern of the mutations that have taken place which distinguishes one cancer from another. The medical community is moving away from defining cancer by the organ it affects because multiple genetic signatures occur in each organ and each genetic signature appears in multiple organs. Statistics often give data by organ. But, with the increasing understanding of the genetic basis of cancer, we are moving beyond the traditional definition by organ.

1.2 FACTORS INFLUENCING CANCER RISK

Some lifestyle factors contribute significantly to cancer risk. About 40% of cancer cases can be attributed to lifestyle risk factors, e.g., smoking, alcohol consumption, obesity, physical inactivity, and poor diet.

There is always some time lag involved at the individual level between lifestyle risk factors and cancer incidence. A delay of 20-30 years could exist between the risk factor exposure and the time of developing cancer, e.g., typically a person needs to smoke for over 20 or 30 years before lung cancer eventually develops. This delay applies equally in the case of populations. For instance, prevalence of smoking started to decrease in the 1960s, and only about 30 years down the line did the mortality rate due to lung cancer start to drop. Indeed, this delay applies to many other risk factors as well, but the duration of the delay varies from one factor to another.

The case of smoking cessation shows that within a year the risk for a heart attack drops dramatically. However, for cancer risk to drop takes longer with gradual reduction. Thus, 10 years of good habits are preferable to five years; this relation between lifestyle and incidence is not linear.

While adopting a healthy lifestyle can reduce cancer risk, we cannot entirely prevent it because it is also influenced by genetic and environmental factors beyond one's control.

Other risk mitigants include screening and immunization. Screening can mitigate morbidity and mortality by detecting cancer early when it is more treatable, but it does not generally reduce cancer incidence. However, in a few situations, screening can identify precursors of cancer that may be treated before progressing, such as colon cancer polyp eradication before the polyps evolve to cancer and Pap screening for treatment of precancerous cervical dysplasia.

There are two currently approved preventative cancer immunizations. HPV vaccines decrease the risks for cervical, anal, and oropharyngeal cancers, and hepatitis B vaccination lessens the likelihood of liver cancer. Similarly, applying sunscreen reduces the risk for skin cancer.

1.3 CANCER AND LIFE EXPECTANCY

Although most cancers impact life expectancy, there are a few specific instances when cancer may not. When cancer of an organ can be removed and the cancer was confined to that organ, and the individual is considered disease-free, it should not further affect life expectancy. An example is endometrial cancer of the uterus. But there are very few such examples, which means that for common cancers, such as those of the breast or lung, all susceptible tissue cannot be removed, and life expectancy could still be affected.

Another mitigating factor would be the age at which one acquires cancer. If one acquires cancer at 80 years of age, life expectancy may be less affected due to other competing mortality risks and the effect of treatment received. In fact, it was indicated that for subjects above 80 years, the gain in life expectancy after being treated for cancer is appreciably lower as compared to younger ages.

Overall mortality rates from cancer have declined over the past two decades. Patients diagnosed with many specific types of cancer today face a considerably better chance of survival compared with patients diagnosed 20 years ago. However, they still had higher mortality risks compared with people without cancer.

Section 2: Cancer Mortality Trends

Differences occur between cancer deaths at the older ages compared to the younger ages. A summary of the five most common causes of cancer death in the UK from 2016-2018 is provided in Figure 1. Results are split for males and females and shown by age. The results show a marked shift in the pattern of cancer deaths by age for both males and females. This data reflects the UK general population, which is perhaps slightly different from an insured population, but the pattern shown in Figure 1 is still very relevant to the U.S. As shown, lung cancer is the leading cause of death for ages 75 and over regardless of sex. Prostate cancer and breast cancer are the second most frequent cancers for men and women, respectively. The third leading cause of death in both sexes is bowel cancer.

In the UK, lung cancer mortality peaks at ages 80-85 then declines. Breast and prostate cancer overtake lung cancer as the leading cause of death at age 90+. In the U.S., where data is available for 85+, lung cancer is the greatest cause of death followed by prostate cancer as second most common.

The high number of lung cancer deaths in the older age groups is primarily due to smoking. Smoking cessation did not begin until the 1960s. People who are now at very high ages were often heavy smokers when they were young. This cohort effect results in high lung cancer mortality rates among the elderly. However, as younger generations age, lung cancer mortality rates are expected to be much lower.

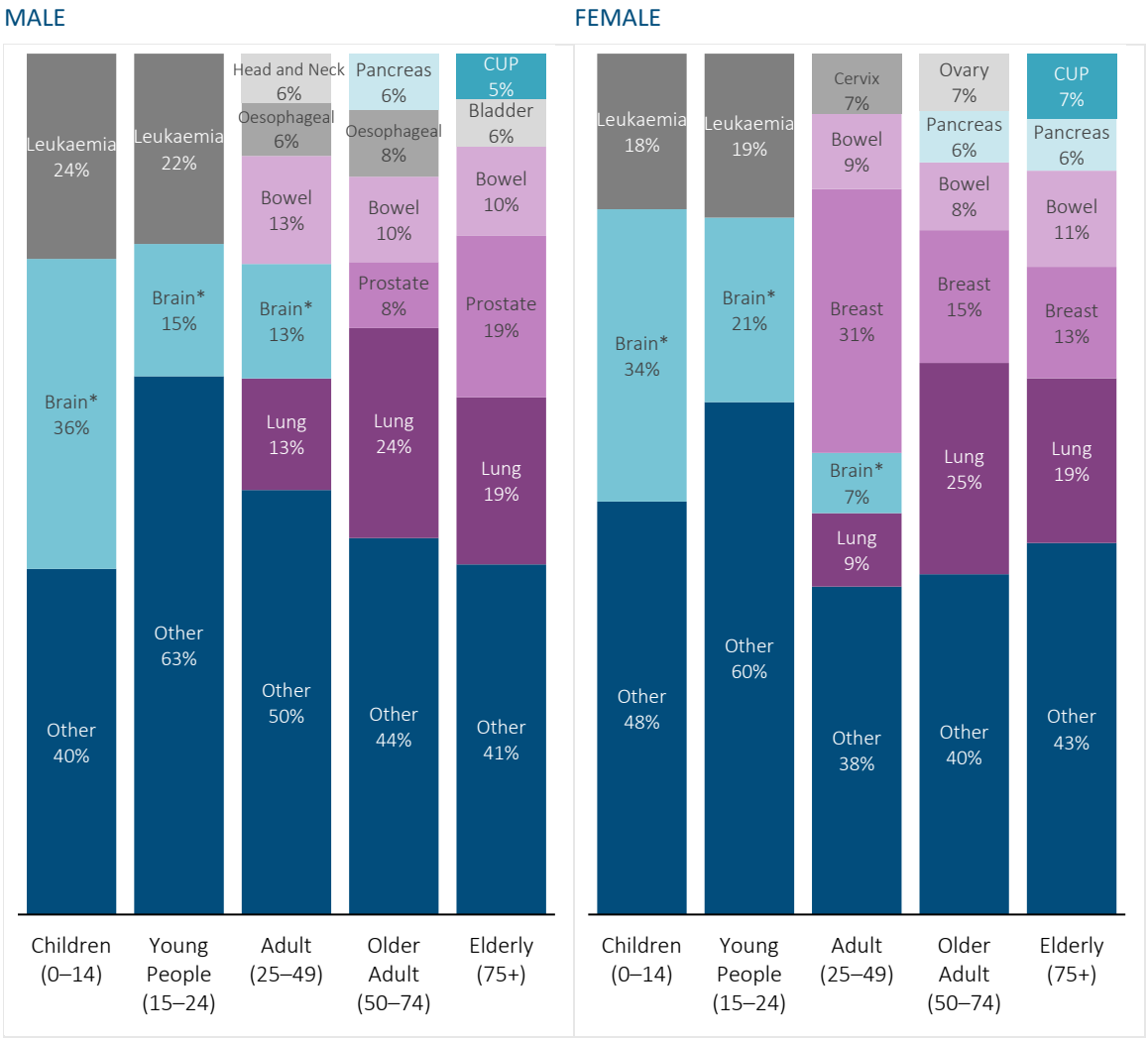
The panel also discussed obesity's role in future cancer trends and noted that obesity is clearly associated with an increased risk of many different types of cancer, but it is difficult to measure its impact. If it is a significant factor, given current treatment for obesity like GLP-1 drugs and expected future obesity treatments, then a reduction in future cancer mortality would likely be expected. However, at the older ages, the impact is likely muted.

Conversely, one panelist did not expect a reduction in obesity would have a major impact on cancer risk. Obesity is linked to lifestyle factors such as diet and physical activity, which are the primary causes of cancer risk. Simply reducing body weight without changing lifestyle would have minimal impact on cancer risk, except possibly for breast cancer after menopause. For other cancers, the impact of reducing obesity on mortality would be minimal.

In thinking about the insured population versus the general population cancer mortality trends, the difference may lie mainly in factors of lifestyle between the two populations. For instance, smoking-related cancers, such as lung cancer and esophageal cancer, are less prevalent in insured populations. However, hematologic malignancies, such as leukemia, non-Hodgkin lymphoma, and myeloma, become more significant in older ages. Overall, regardless of population, cancer risk increases with age, but the impact of most cancers starts to decline in the 80s due to competing causes of death.

Figure 1

THE FIVE MOST COMMON CAUSES OF CANCER DEATH BY SEX, NUMBER OF DEATHS, BY AGE, UK, 2016-2018



Brain* = Brain, other central nervous system (CNS) and intracranial tumors
CUP = Cancer of unknown primary
Source: Cancer Research UK https://www.cancerresearchuk.org/health-professional/cancer-statistics/mortality/age#heading-One and https://www.cancerresearchuk.org/health-professional/cancer-statistics/mortality/age#heading-Two (Accessed October 24, 2024)

2.1 IMPACT OF COVID-19 ON TRENDS?

Cancer mortality improvement has been quite significant over the past two decades with the rate of improvement even accelerating before the pandemic. We are still trying to understand cancer trends during the pandemic as detailed data is only up to 2022. But up until this point, there has been observed declines in age-adjusted cancer mortality for almost every cancer, except a few such as pancreatic and endometrial cancers.

During the pandemic, the healthcare system was overstretched, and this affected much of the population. Delayed treatment and diagnosis would affect the general population as well as the insured population. This may vary in magnitude, but it probably resulted in a temporary slowdown or flattening of the curve in cancer mortality improvements during the pandemic years. However, it is expected that the trends will return to pre-pandemic levels over time.

Recent data from the UK shows an increase in cancer mortality during the pandemic, especially for breast and lung cancers. However, these rates are returning to normal levels as of 2023.

Section 3: Cancer Treatment

In determining the best cancer treatment option, the medical provider must think about an individual's current physical and mental condition. Sometimes, an older person is not a candidate for some kinds of treatment simply because there are other comorbidities present.

Although treatment is moving in the direction of individualized therapies, this type of treatment protocol is still not prevalent. For each type of cancer, there is a standard protocol that might get modified according to the presence of any comorbidities or any need specific to a patient. But we are still far from the place where the basic working protocols of cancer treatment differ substantially from one person to another.

3.1 CANCER STAGES AND GRADES

Identification of cancer stages help medical providers determine the best treatment options. While the significance of the cancer stages depends on the type of cancer, generally stage 1 indicates that the disease is locally confined, while stage 4 indicates metastatic disease. However, for some cancers, stage 4 might be more manageable than a stage 1 for another cancer**.** For example, stage 1 pancreatic cancer still carries a relatively high mortality risk.

In addition to the cancer stage, the grade of the tumor is often an important factor in determining the prognosis and optimal treatment plan. While the stage focuses on the size of the tumor and how far it has spread, tumor grade defines the appearance of the cancer cells. The higher the grade, the more abnormal are the cells. Certain highly differentiated tumors that resemble normal tissue in appearance may not be significantly threatening long-term even when the burden of cancer is large. For example, low-grade prostate cancer carries only a very small risk of mortality, while higher-grade prostate cancers can be highly aggressive even when appearing confined at diagnosis.

While the meaning of the stages and grades are the same for all ages, cancer is more likely to be found in advanced stages in the elderly population. Occult metastases from low-stage and low-grade cancers take a longer time to clinically show any sign and cause mortality. Therefore, such metastases are less likely to occur before other age-related issues in an older person. Human immune systems affect cancer incidence and progression. Typically, at younger ages, our immune systems keep cancer under control. But, as we age, our immune system weakens, and the risk of cancer increases.

3.2 REMISSION VS. CURE

Nowadays, oncologists have nearly ceased using the term "cure." That is because it implies there is no chance of the cancer ever recurring, and yet in most cases there remains at least some chance of recurrence even if very remote. The focus of treatment is on complete remission, which refers to a state when all signs and symptoms of cancer have disappeared. It, however, does not mean a cure. It simply means that there is no evidence to show that it exists.

Although the official definition of partial remission refers to a reduction in tumor burden by at least 50%, it may often be thought of as any reduction in tumor burden. In general terms, partial remission is not as good as complete remission since signs of cancer still exist.

Another helpful definition of complete remission is "no evidence of disease." This implies that with the tools available, no evidence of cancer can be detected. With advances in molecular medicine and the ability to detect cancers with extremely sensitive probes, “no evidence of disease” today is significantly more meaningful, i.e., that no signatures of the cancer's genetics are still present, with much greater precision.

From an underwriting and actuarial perspective, it is important to consider this. With molecular studies looking for minimal residual disease, such as circulating tumor DNA, we might detect evidence of cancer even when there is otherwise no visible evidence of disease. In addition, the advancements in imaging technologies, such as CT, MRI, and PET scans, enhanced by AI, allow the detection of residual disease more effectively than in the past. Similarly, if someone tests negative, it doesn’t necessarily mean they are definitively cured, but it does increase the confidence that they will remain in long-term remission.

3.3 RECURRENT CANCER

The likelihood of remaining in complete remission is not clear-cut. It depends greatly on the individual case, such as the type of cancer, the stage at diagnosis, the grade, the degree of differentiation, and other prognostic factors, including molecular signatures of the cancer.

Generally, cancer recurrence is most likely to occur within the first few years after initial treatment. If a person remains in complete remission for ten years, the risk of recurrence is considered very low in most cases, though it is never zero.

Along with the risk of relapse of the original cancer that had completely gone into remission, there is also the risk of developing a second primary cancer, which is an entirely different entity. In many cancers, the second primary cancer is more important, and it has different implications. Since much of cancer risk has a genetic basis, individuals remain at risk for developing additional cancers. The genetic risk cannot be changed, so the likelihood of a second primary cancer persists.

Section 4: Advances

This section summarizes the panelists discussion on current advances and future prospects in cancer treatment and prevention.

4.1 LIQUID BIOPSIES

Liquid biopsies are already on the market, but population screening has not yet begun. These biopsies are based on fluid collection—mostly blood, but sometimes other fluids—for the identification of cancer. Circulating tumor DNA is often analyzed, but other markers, such as protein signatures, extracellular

vesicles, and tumor-educated platelets, are also being investigated. This is already in use in specific malignancies—especially to identify residual minimal disease and guiding treatment strategies, mainly for lung cancers.

A multicancer early detection test (MCED), can potentially screen for several kinds of cancers simultaneously. The sensitivity of the current tests is quite reasonable but does not encompass all cancers. They are also very specific, which limits the number of false positive results, however, when screening is done among populations with a low prevalence of cancer, false positives still become a problem relative to the rate of true positive results. Though these tests are felt to have significant future potential, their use in current markets is controversial. Continued technological improvements, large scale clinical trials and approval by regulatory agencies, along with acceptance by health care systems and payors will likely lead to broader application. Although a few tests are already on the market and more are being developed, the timing of when these tests will be ready for more widespread application is still unknown.

4.2 IMMUNOTHERAPY

The panelists shared their thoughts about immunotherapy and promising other treatments and the potential impact on mortality. Immunotherapy is a generic term. The effect of immunotherapy differs by type of cancer.

There are many molecular biologic treatments, some of which are very promising but not in use—for example, small interfering RNAs or antisense RNAs—that could really make a change toward individualized therapies based on the specific biology of a tumor and potentially lead to more successful outcomes.

Even mRNA cancer vaccines are a possibility. These vaccines basically use the same technology behind COVID vaccines but are developed to work against an individual's specific cancer. Adoptive T-cell therapies, of which the most prominent currently is CAR T, have been shown to work in some hematologic malignancies. There are approximately 1,600 immunotherapies under study, although most remain in a fairly early stage of development. They will also likely be less toxic and even more valuable for the elderly.

Although many new treatments are in the process of development, their availability for use by the public will take several and possibly many years. The clinical trials are far from the stage of actual application. New treatments are often very expensive, which may restrict accessibility and limit the overall impact of these treatments on near future mortality rates.

In terms of pure innovation, the U.S. is at the top in comparison to other countries. On the other hand, other countries with an integrated health care system generally do a better job of delivering the new treatments to the public than the United States. Given cancer care requires coordination and the U.S. population is aging, this is an important U.S. issue.

Although the U.S. is a leader in cancer treatment innovation and advanced cancer treatments, it falls behind many countries in prevention.

Conclusion

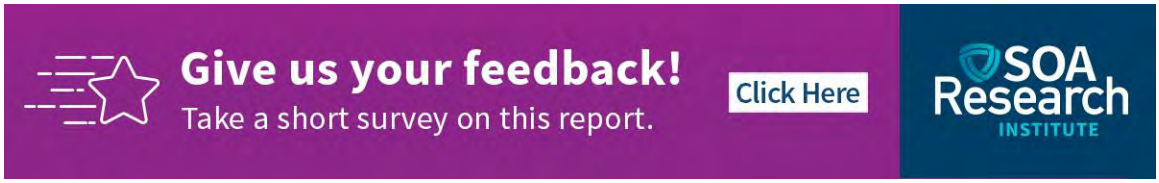
The panelists concluding remarks about cancer mortality offer insights into current and future trends for both the insured and general populations.

"*Both the general and insured populations are showing positive trends in cancer mortality. The trends are almost parallel, but the mortality rate in the general population is much higher compared to the insured*

population. This observation holds true even when looking at major cancer types. So, while the general population has a higher mortality rate, the improvement trends in cancer mortality are similar for both groups."

"*We expect continued improvements in cancer mortality. This has implications for life and longevity insurance, as well as other lines of business. If we turn some terminal cancers into chronic diseases due to improved treatments, it could affect disability and long-term care products. Additionally, as our understanding of cancer classification evolves, it's important to stay updated for critical illness products and risk assessment. We should also focus on individual risk identification for better screening and prevention measures.*"

"*We're on the cusp of a profound improvement in cancer mortality, both for insurance and the general population. We're seeing meaningful progress, but we're still on the flat part of the exponential curve. I can't predict exactly when the curve will steepen, but it's getting closer.*"



Appendix A: Expert Panel Discussion Questions

1. What cancers kill the most people at ages 70+?
    a. How do these cancers vary among this age group, e.g., some are more prevalent in the 70s and others in the 90s?
    b. How do these cancers vary by gender?
    c. Have there been any trends in recent years?
    d. Did COVID-19 and Long COVID affect this, and if so, how?
    e. Are there differences between the life insurance and general populations?

2. Can cancer be prevented or delayed?
    a. If so, how?
    b. If someone has cancer, what specific actions and/or treatments can extend life expectancy?
        i. Are these general actions/treatments or can/should they be personalized?
        ii. Are there alternatives, e.g., natural approaches, if the specific action/treatment doesn't work?
        iii. Is there an expected increase in life expectancy, i.e., would it be similar to someone without cancer, or still somewhat less than this?

3. How is remission defined?
    a. Is it possible to know if someone is just in remission or cured?
    b. How often does someone in remission get cancer again?
    c. Is there some type of pattern as to the specific type of cancer, the stage at which the cancer is first identified, the type of treatment of the cancer, and/or anything else that determines if it comes back?

4. What are the current and future advances for cancer avoidance, diagnosis, and treatment?
    a. Examples include liquid biopsies and immunotherapy.
    b. What are other advances that may be coming and when can we expect them to be available?
    c. Are there any non-drug treatments that work or may work?
    d. Is there a country that you would consider to be the best in terms of least cases, best treatment, etc.?
        i. What is it that this country does differently or is it because of the health of the population?

5. Concluding questions
    a. Is there anything else that we didn't discuss, that is important to know about?
    b. How will everything we discussed specifically affect the life insurance industry?

Acknowledgments

The SOA Research Institute's deepest gratitude goes to the panelists who shared their time and expertise in providing insights on this topic and to the Project Oversight Group for their diligent work in designing and executing the study, drafting the report, and peer reviewing the report for relevance.

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