SCOR
The Art & Science of Risk

A NEW UNDERWRITING SOLUTION

developed to provide insurance coverage
for people with a history of lymphoma

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Introduction and Context

Lymphomas are malignant tumors of the lymphatic system that are present throughout the body. They represent almost half of all blood cancers. Mortality and relapse rates associated with lymphomas depend on several characteristics. One of the most important criteria for prognosis is the type of lymphoma cells that are involved. The aggressiveness of lymphoma cells, along with the spread of the disease as defined by the tumor stage, the age of the patients and the disease-free duration as diagnosis strongly impact mortality.

Advances in cancer screening make it possible to diagnose more patients at an early stage of disease. Improvement of medical treatments also participates in prolonging survival and decreasing cancer-related mortality in lymphoma. As such, patients diagnosed with early-stage lymphoma usually have a more favorable outcome and are more likely to respond to therapy. Recent progress in chemotherapy, immunotherapy, and radiotherapy have created considerable benefits in terms of long-term survival in patients with lymphoma and resulted in an increasing prevalence of long-term survivors with individuals having a background history of lymphoma applying for insurance.

Interestingly, the Kaplan Meier mortality curves analysis shows that the prognosis of lymphomas may eventually vary over time. Indolent lymphomas are slow-growing malignancies that may remain stable for years with minimal treatments. Indolent lymphomas have a minimal risk of lymphoma-related mortality but still have a small risk of transforming into aggressive lymphoma. Conversely, aggressive lymphomas may have a high mortality rate during the first four to five years from diagnosis. Thereby, the mortality rate of aggressive lymphoma significantly decreases with a survival curve plateauing with a low risk of relapse and death over a prolonged period of time.

Another concern related to aggressive lymphoma and the long-term risk is associated with its treatment-related toxicity. As eluded above, aggressive lymphoma with a high risk of death will be treated with aggressive therapies that consist of high doses of chemotherapy with or without bone marrow rescue (autograft), extended radiotherapy, CAR-T cell therapy, and so on. In principle, higher-risk lymphoma, based on pathological subtype and staging, will receive the most aggressive therapies. The intensity of therapy is said to be correlated with long-term effects that started occurring ten years after therapy and consisted of a higher risk of death due to cardiovascular diseases and a second primary cancer. In other words, patients with aggressive lymphoma and/or with extended staging will eventually receive the most aggressive therapies and those who survive will be more likely to develop long-term second cancer and cardiovascular diseases.

INTRODUCING VITAE LYMPHOMA

The complexity of addressing individual risks of survivors in complete remission following a past medical history of lymphoma led us to develop Vitae Lymphoma, a new addition to SCOR's biometric risk calculator. By combining state-of-the-art technologies, actuarial techniques, and medical knowledge, this underwriting solution aims to assess the risk of relapse and death for individuals previously diagnosed with lymphoma based on parameters that are good predictors of recurrence and death. This allows improved accuracy in estimating individualized risk assessment and underwriting.

Lymphomas – tumors affecting the lymphatic system

LYMPHATIC SYSTEM

The body hosts a complex lymphatic network that contains small vessels connected through lymph nodes, which is called the lymphatic system. Vessels and lymph nodes contain cells called lymphocytes that aim to prevent, detect, and defend the body from various bacteria and viruses. B and T cell lymphocytes can develop a memory of past infections that allows them to recognize and clear rapidly microorganisms that previously infected the body. B cells may differentiate into plasma cells that are generating specific antibodies that recognize various antigens. The antibodies block further development of the infection for several years with rapid reactivation of antibody production if novel contact with the same infectious agent is encountered. This latter mechanism called 'humoral reaction' is at the basis of vaccination. Other components such as T cells are cells that come in contact with bacteria or infected cells into express contact cytokines that in turn will kill microorganisms or infected cells. This mechanism is called 'cellular reaction'.

LYMPHOMAS

As with any cellular type in the body, lymphocytes (for example, B, T, and natural killer) may undergo carcinogenic transformation into malignant tumors called lymphomas. The type of lymphoma often refers to B, T or natural killer cells, in reference to the type of cells that become malignant. Thereby, lymphoma is a cancer of the lymphatic system, with an incidence estimated at 14,000 new cases per year. Lymphoma is identified as a proliferation of lymphocytes that can be detected where lymphocytes are usually found, such as, for example, in the blood, in the lymph nodes, in the bone marrow, and in the spleen. However, other organs such as the skin, the brain and any other parts of the body can develop lymphoma. In 85% of cases, lymphoma involves the B cells and in 15% of cases, it concerns the T cells.

Historically, two types of lymphoma have been described - Hodgkin's and non-Hodgkin's lymphoma. This differentiation is made according to the histology of the lymphoma. The difference between Hodgkin's lymphoma and non-Hodgkin's lymphoma is the presence of Reed-Sternberg cells, which are cells derived from a B-cell and only present in Hodgkin's lymphoma. Non-Hodgkin lymphomas have been described as a large set of diseases that contain various histological subtypes. Each of the subtypes may have individual outcomes, as illustrated by the survival curves in Figure 1.

DIFFERENT MORTALITY RISKS ACCORDING TO LYMPHOMA

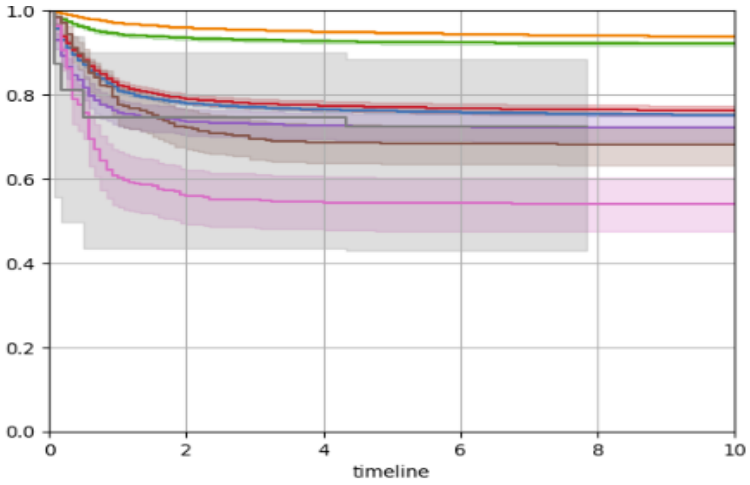

Figure 1: Specific survival curves by lymphoma

The historical description of Hodgkin versus non-Hodgkin lymphoma was related to evidence showing that Hodgkin lymphoma had a better prognosis when treated, while non-Hodgkin's lymphomas were more aggressive cancers. The Kaplan Meier curves (Figure 1) confirm this, and three different groups can be distinguished:

1) The least risky group – 10-year survival probability around 90% - indolent B lymphomas and Hodgkin's lymphomas.
2) Average group - 10-year survival probability between 60% and 80% - peripheral T lymphomas, aggressive B lymphomas, large-cell anaplastic lymphomas and lymphoblastic T lymphomas.
3) High-risk group – 10-year survival probability between 40% and 60% - Natural Killer lymphomas

Vitae Lymphoma – New underwriting solution for people with a history of lymphoma

PHILOSOPHY BASED ON THE SEER DATABASE

The Vitae Lymphoma algorithm was built using the SEER (Surveillance, Epidemiology and End Result) database. This American database has been collecting data since 1973. Today, SEER is the world's largest database specialized in cancer and is recognized by the global medical and scientific community. More than 400,000 observations are added every year. Biometric variables (age at diagnosis, etc.), medical variables (tumor size, tumor stage, etc.), or therapeutic variables (surgery, chemotherapy, etc.) are provided and this database makes it possible to monitor the vital state of the patient. (NIH, s.d.)

The following reasons have led us to select this database:

- **Reliability:** SEER data is built through partnerships with several laboratories and government agencies,ensuring the reliability and accuracy of the information gathered.
- **Scientific validation:** This database is used worldwide by researchers and statisticians to conduct their work and publish figures on cancer incidence, prevalence, and mortality.
- **Size:** It is the largest cancer database in the world, ensuring statistical power of results.
- **Representativity:** This database is representative of the American population in terms of socio-professional criteria. Some ponderations can be applied to adapt to another specific population around the world.

VITAE LYMPHOMA – RISKS ASSESSED ACCORDING TO FOUR CHARACTERISTICS

As mentioned above, the risks associated with lymphomas differ from one type of lymphoma to another. The histology (type of lymphoma) is, therefore, the most important factor in the risks associated with this disease. The stage of the disease also plays an important role. As shown below (Figures 2 and Figure 3), the lower the stage, the higher the survival rates.

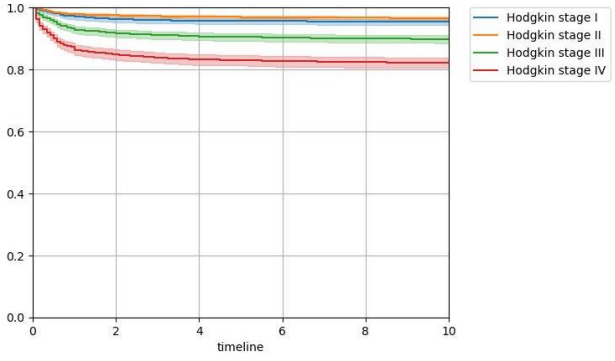

Figure 2: Specific survival curves for Hodgkin lymphoma by stage

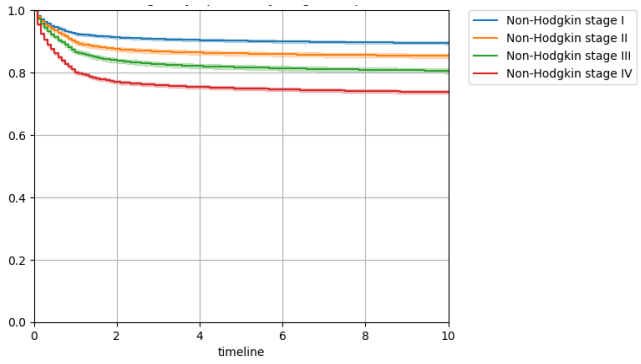

Figure 3: Specific survival curves for non-Hodgkin lymphoma by stage

Concerning patient age, between two individuals with the same risk factors, a younger individual will tend to have lower overall risks than an older individual, even if this is not the most significant factor in the death risk. Finally, based on the conditional survival assessment, the duration since diagnosis will be an important parameter when assessing risk. The longer the time since diagnosis, the greater the chance of survival.

The association of these four characteristics enables a fair assessment of the risks associated with lymphoma.

Lymphomas - short-term and long-term effects on the risks of relapse and death

SHORT-TERM EFFECTS

People affected by lymphoma may have lower life expectancies than those who have not been touched by the disease. The risks of relapse and mortality are different according to the type of lymphoma, but there is an overall trend. At the duration of diagnosis and treatment, the mortality risks are high. However, the risks decrease dramatically with duration, as illustrated in Figure 4.

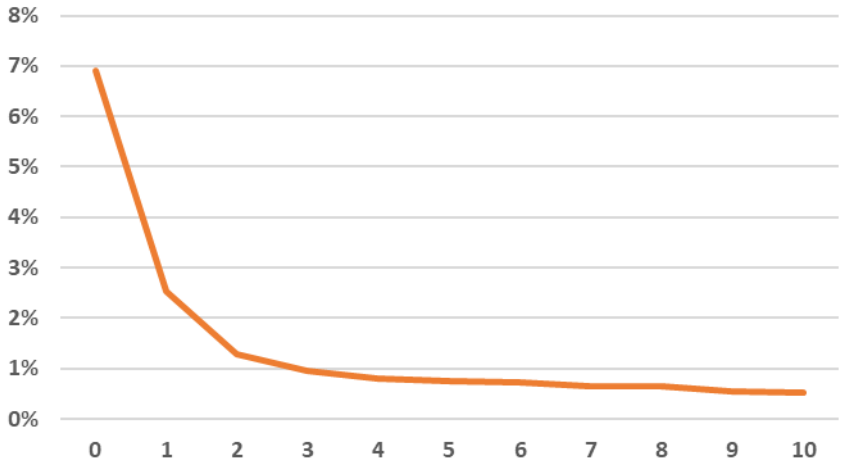

Figure 4: Specific mortality rate according to time since diagnosis
Profile: Age between 18 and 24 years, B aggressive lymphoma, Stage I

LONG-TERM EFFECTS

Lymphomas are tumors that stand out from other cancers because of their long-term effects. Studies have shown that the risk of relapse or of a new lymphoma persists even several years after diagnosis due to the treatment necessary for recovery:

1. The risk of secondary diseases, mainly of the circulatory system, is very high because of treatment.
    - for example, with an SMR of 4.4 - 10 years after diagnosis - to 8.8 - 20 years after diagnosis - for non-Hodgkin's lymphoma (Bluhm EC, 2008)
    - for example, with an SMR of 5.7 for Hodgkin lymphoma, regardless of duration (de Vries S, 2021)
2. Although less risky, indolent B lymphomas have a higher relapse rate over the long term. (Cabanillas, 2013)

Conclusion

The new underwriting solution Vitae Lymphomas provides underwriters with a useful tool to assess the mortality risks for individuals with a history of lymphoma based on associated risk factors (histology, stage, age, and duration since diagnosis). Combining actuarial methods,medical knowledge, and underwriting expertise, Vitae Lymphomas is leveraging medical breakthroughs to support underwriters' day-to-day work.

Please contact us for further information and/or to test the tool.

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