SCOR UNDERWRITING CANCER PROJECT

OPTIMIZING INDIVIDUAL CANCER-RATING ASSESSMENTS BASED ON UPDATED ALGORITHMS

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SCOR
The Art & Science of Risk

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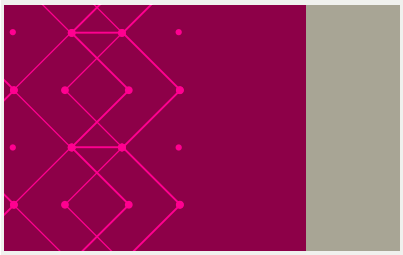


Cancer represents a major cause of death worldwide and is associated with a high level of morbidity. Three risk factors for cancer are predominant in terms of prevalence: smoking, ageing and the obesity prevalent in Western countries, but other factors can be frequently associated with cancer. The incidence of most cancers has been increasing over the last 50 years, while progresses in the detection and management of cancers have led to significant increases in both prevalence and survival.

As a result, the number of patients newly diagnosed and those deemed long term cancer 'survivors' - patients fit and alive at more than five years after diagnosis - has been increasing worldwide, yielding new challenges for insurance companies. Risk factor evaluations are becoming more important to try to predict the evolution of critical illness prevalence at various ages. Furthermore, long-term survivors have been constantly challenging insurance companies for better coverage, who have adapted in return by offering innovative products and underwriting approaches for these new classes of customers.

Over the last 30 years, underwriting cancer has been based on the site of origin, pathological subtype, staging - TNM (Tumour size, lymph Nodes affected, Metastases scoring system) or AJCC stage (classification system developed by the American Joint Committee on Cancer) - immediate sequels or comorbidities related to cancer (and/or associated treatments), potential long-term complications from cancer therapy and any recurrence. While more epidemiological data are becoming available, the estimation of an individual risk from peer-reviewed trials or studies often remains a challenge.

Herein, we have developed a mathematical model based on easily obtainable variables, which can allow an accurate estimate of the excess mortality rate of these individuals. To study this approach, tumours with various biological and clinical features were selected. Highly heterogeneous tumours, such as breast cancer, and tumours with lower heterogeneity, such as colon cancer, were chosen to test how the proposed algorithm operates in tumour types from various backgrounds. Comparison of solid tumours that always display higher heterogeneity compared to haematologic malignancies led to also trying to develop a specific tool for haematological malignancies. However, the discussion of this is outside the scope of this paper.

Introduction

The increasing cancer incidence, the high prevalence of patients cured from cancer or living long-term – with or without recurrences – and the progress made in diagnosis and therapy have led to an increasing number of patients diagnosed with 'early' or low-stage cancers, often having better prognosis, more likely to have curative treatment, and giving rise to more so-called 'long term survivors'.

Because of an increasing incidence and prolonged overall survival at all stages of cancer, the number of cancer survivors has increased notably over the last 20 years. Recent data obtained in early 2014 yielded an overall estimate of about 14.5 million cancer survivors in the United States, which accounts for more than 4% of the entire US population. Based on current epidemiology trends, the number of cancer survivors in the US is projected to increase by 31% by 2024, to reach nearly 19 million patients. This represents an increase of more than four million survivors over a period of 10 years. As a result of these recent epidemiological patterns, a fair number of long-term cancer survivors will be actively engaged in professional, financial, social and familial activities and therefore seeking various risk coverages by insurance companies. Underwriters will then increasingly be facing patients with prior history of cancer. To properly balance the task of developing novel insurance products with the changes in cancer-related prognosis, algorithms and related simplified prognostic factor calculators have been developed, allowing accurate identification of categories of patients at risk for earlier relapses. This approach has also shown that a prior history of cancer does not preclude curability and does not always justify simply declining coverage based on this history. For instance, the five-year overall survival probability was 41% in the 1950s, and is now around 66.5%, so the majority of patients with cancer are surviving the initial five-year period. The question now is: how do we as insurers adjust the estimations of death and relapse over relatively long periods, while also balancing the overall cancer risk and the needs of the patient/insured?

Epidemiology and underwriting of cancers

Breast cancer stands (TEXT BOX 1) as the most common cancer in women, with approximately 182 000 women diagnosed with breast cancer annually in the United States, accounting for approximately 26% of all cancers among women.

Colorectal cancer (TEXT BOX 2) is the third most common cancer in men worldwide (746 000 new cases in 2012, 10% of the total number of cancer cases) and the second in women (614 000 new cases in 2012, 9.2% of the total number of cancer cases).

Underwriting cancer has typically been based on primary tumour type, staging (TNM or AJCC stage), immediate sequels or comorbidities related to cancer (and/or to treatments), potential long-term complications from cancer therapy and any recurrence. The estimation of an individual risk from peer-reviewed trials or studies remains a challenge; therefore, tools that allow adjusting a rating to an individual cancer risk are urgently needed (TEXT BOX 3). Additionally, long-term survivors have been challenging insurance companies to adapt offers and ratings to these new classes of customers. In the meantime, previous occurrence or history of cancer may be regarded as a high-risk event that requires careful evaluation when trying to evaluate individual risk of relapse, death from cancer and life threatening toxicities.

Overall, TNM classification or stage grouping is useful to establish the prognosis of a given population at diagnosis (TEXT BOX 4). Ratings using the early versions of SOLEM (SCOR Underwriting Manual) were adjusted to fit the average estimate of survival at diagnosis of a given population. In this publication, we introduce a new methodology based on algorithms that consider individual prognostic data. Interestingly, this methodology is flexible, allowing the implementation of current data and additional parameters as new scientific and medical data becomes available. Thus, the current model functions for the entire patient population and aims to individualise the ratings in the context of all available patient characteristics. To illustrate the benefit of underwriting using the new methodology, we selected breast and colon cancers, which are among the most frequent tumour types with both good potential long-term survival and highly variable individual outcomes.

TEXT BOX 1

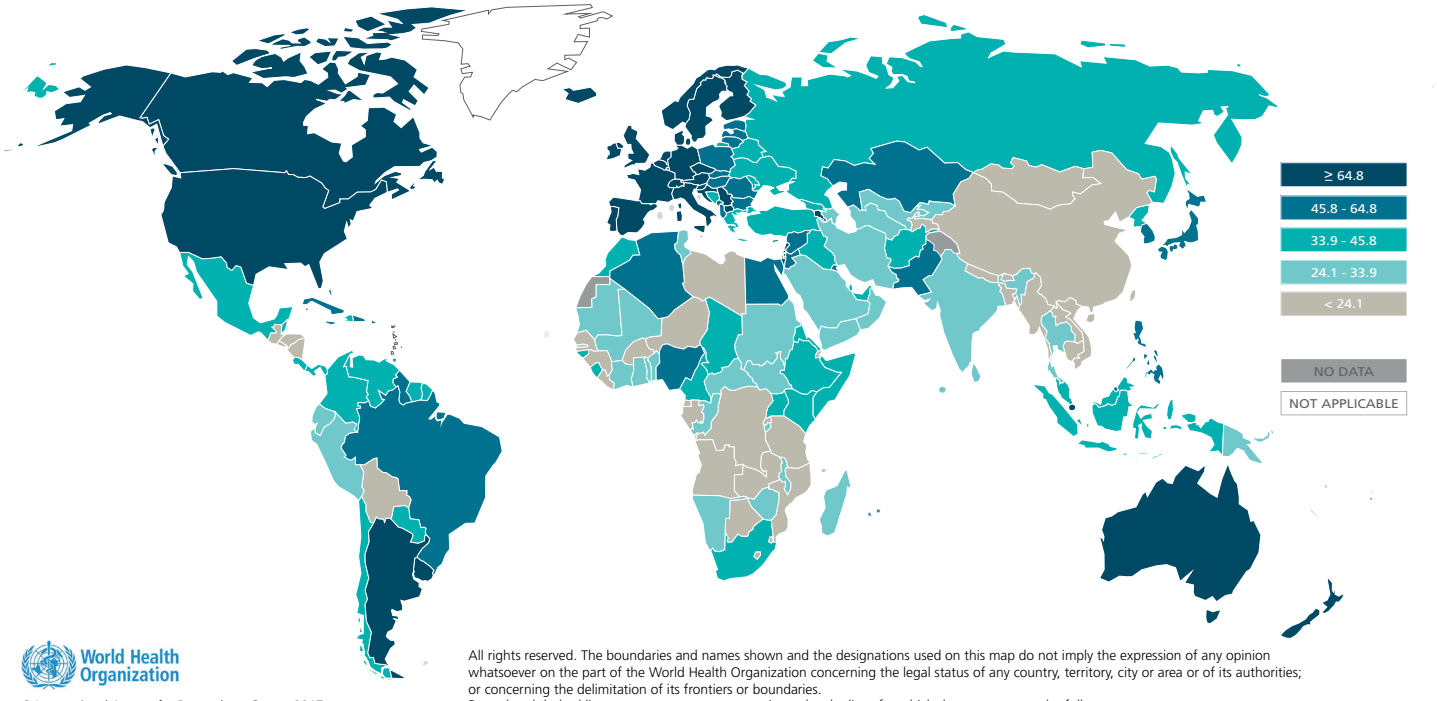
EPIDEMIOLOGY OF BREAST CANCER

Each year, 40 000 women die of breast cancer in the United States, making it the second-leading cause of cancer deaths among American women after lung cancer. The lifetime risk of dying of breast cancer is approximately 3.4%. The worldwide incidence of female breast cancer varies markedly, being highest in the United-States and Northern Europe, intermediate in Southern and Eastern Europe and South America, and lowest in Asia. From 1983 to 1987, the age-adjusted incidence rate of breast cancer varied by factor of approximately five between countries (see **FIGURE 1** below). However, incidence rates have been rising in traditionally low-incidence Asian countries, particularly in Japan, Singapore and urban areas of China, as these regions make the transition toward a Western-style economy and pattern of reproductive behaviour. Breast cancer incidence increases sharply with age, becoming considerable before age 50. In premenopausal women, the incidence rate is similar in most countries, ranging from 8%-9% per year. The incidence rate of breast cancer increases throughout life until menopause and then slows down substantially thereafter, ranging 2%-3% per year in post-menopausal women. Improvements in early diagnosis and health care have led to an increased incidence of breast cancer in Western countries, resulting in 3.2 million women who have survived breast cancer for at least five years.

ESTIMATED AGE-STANDARDIZED RATES (WORLD) OF INCIDENCE CASES, FEMALES, BREAST CANCER, WORLDWIDE IN 2012

Data source: GLOBOCAN 2012 - Map production: IARC (http://gco.iarc.fr/today) - World Health Organization

FIGURE 1



World Health Organization

TEXT BOX 2

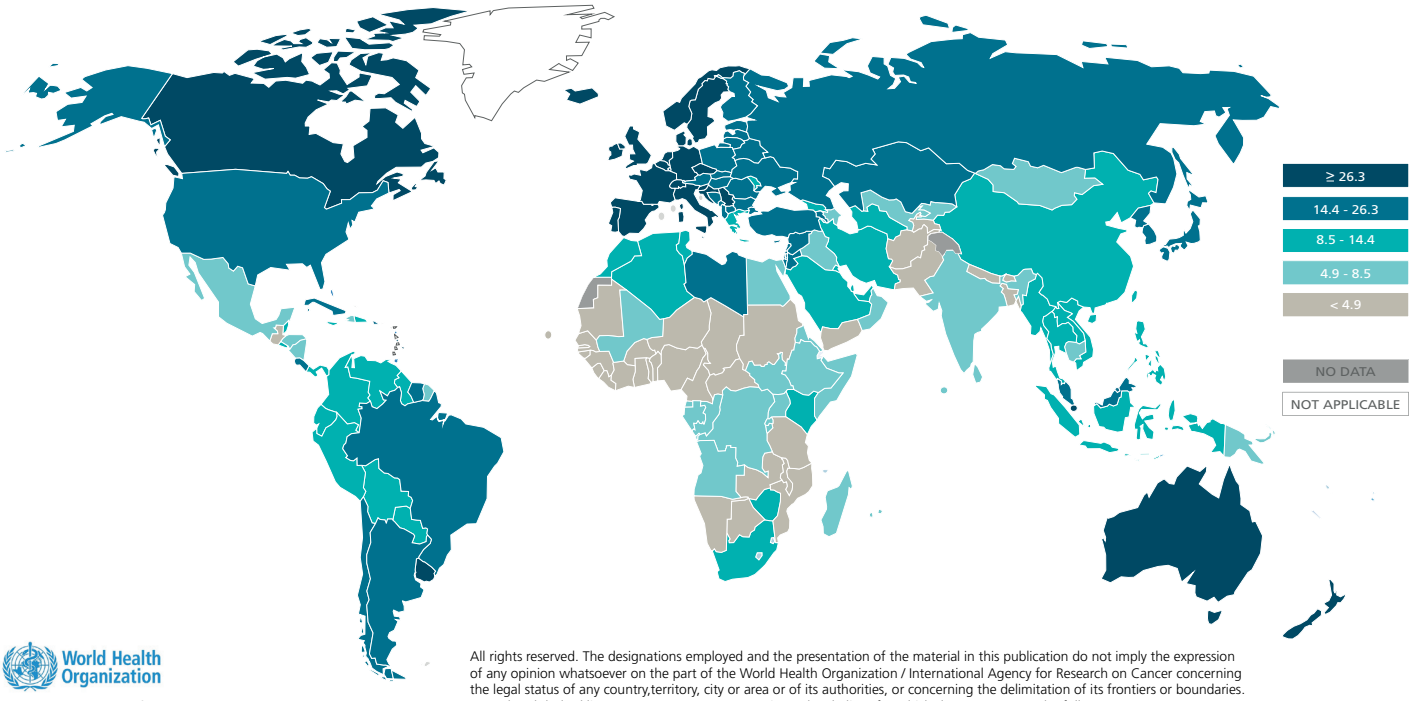
EPIDEMIOLOGY OF COLON CANCER

For colon cancer, one can anticipate roughly 1.2 million new cases and 600 000 deaths per year. There is wide geographical variation in incidence globally, ranging from an Age Standardised Rate (ASR) of 3.8 cases per 100 000 persons in western Africa to 44.8 per 100 000 in Australia/ New Zealand (see FIGURE 2 below). Moreover, rapid increases have been noted in previously low-risk countries such as Spain, several countries in Eastern Europe and Asia, which have been ascribed to changes in dietary patterns and risk factors towards a so-called Western-lifestyle. Unlike other cancers, such as lung cancer, no single risk factor accounts for most cases of colon cancer. Well-established risk factors include older age and male gender, along with many other factors which often coincide and interact, such as: family history of colorectal cancer, inflammatory bowel disease, smoking, excessive alcohol consumption, high consumption of red or processed meat, obesity and diabetes. Established preventive factors include regular physical activity, use of hormone replacement therapy, daily aspirin intake (with risk reduction in the order of 20-30%) and colonoscopy with removal of precancerous lesions such as polyps. Data showing a potential protective effect from dietary habits are less consistent. The hereditary forms of colorectal cancers determined by well-known genetic aberrations (familial adenomatous polyposis, Lynch syndrome…) account for fewer than 5% of all cases.

ESTIMATED AGE-STANDARDIZED RATES (WORLD) OF INCIDENCE CASES, BOTH SEXES, COLORECTAL CANCER, WORLDWIDE IN 2012

Data source: GLOBOCAN 2012 - Map production: IARC (http://gco.iarc.fr/today) - World Health Organization

FIGURE 2



World Health Organization

TEXT BOX 3

WHY LOOK AT NOVEL PROGNOSTIC PARAMETERS FOR UNDERWRITING?

Why are the ratings for cancer still not adjusted for individual risk? To illustrate this issue, we will discuss an example later in this study where both a 12% and a 48% risk of death previously yielded the same underwriting ratings (see the section Rating colon cancer). In order to understand current pitfalls, it is important to remember that while most statistics define prognostic parameters for a population at initial diagnosis, some evidence allows better personalisation of individual prognostic factors. As a result, the patients who will eventually have the best outcome (the patients hypothetically cured who will make up the bulk of long-term survivors) but who show one or more poor prognostic factors at diagnosis, are likely to be heavily penalized in terms of rating by having this poor prognostic factor. As knowledge in oncology grows, prognostic factors will continue to be fine-tuned (for example by tumour biology characteristics), helping to better adjust the rating to the individual patient risk and predicted outcome. In clinical practice, the NHS and several medical universities have already developed calculators aimed at looking at probable individual outcomes in order to help patients and doctors make better decisions about treatment options.

Why do standard rating models only consider prognosis and risk at the time of the initial cancer diagnosis (based usually on surgery or pathology results)? Historically, prognostic parameters have always been defined at the time of initial diagnosis and few studies have been provided with the aim of defining prognostic factors at later stages of survival. Another peculiar feature associated with the analyses of survival results in oncology and other areas of medicine is that the longer an individual survives, the higher her/his likelihood of expected survival is at any point in time. Because poor prognosis patients will have already died, the expected survival for long-term survivors is continuously increasing over time. As a result, the five-year overall survival for survivors three years after diagnosis is expected to be much better than the five-year expected survival at time of diagnosis. This fact is important to consider for insurance as we are constantly weighing various prognostic parameters over time. Later in this review, we will discuss the differences between overall, relative and conditional survival.

How do we incorporate progresses in cancer therapy to optimize ratings? The last five decades have been associated with tremendous medical progress that has influenced overall curability and survival of patients with cancer. However, innovative therapies that rapidly affect the possibility of survival for patients in clinical practice will only be seen in studies, statistics and epidemiology figures after a considerable delay (usually not before 10 years), after which they can be translated for insurance purposes. Ratings are therefore often lagging behind breakthrough therapies in oncology. Incorporating updated medical knowledge in underwriting thus requires the ability to input new parameters and criteria easily into the formula, something this methodology is able to do.

Why is there so much debate about cancer ratings in insurance? Whenever you attend an industry meeting or discuss with colleagues from other companies, it is remarkable to see how people can disagree with each other on the rating to apply for the same cancer. This only highlights the assortment of ratings that have been based on established market habits and variability in algorithms that address patient prognosis. Cancer survivors are claiming their rights to resume a normal life, including the opportunity to obtain insurance coverage. Given the growing number of cancer survivors, governments and insurers are increasingly sensitive to this particular situation and will continue to broaden the options and products available for these individuals. In order to accommodate this, there is a need for more reliable parameters that provide individually adapted ratings.

Material and methods

OBJECTIVES

The objective of the 'SCOR underwriting cancer project' was to develop new tools or models with a rigorous scientific method in order to propose evidence-based ratings adapted for the needs of cancer survivors and insurers.

REQUIREMENTS

- To establish up-to-date evidence-based ratings, understanding that ratings may adapt, evolve and need to be revisable over time according to market needs and new medical data.
- To accurately identify potential risks for insurers.
- To gather teams from diverse parts of the world to work together to try to unify widely different underwriting practices and to incorporate specific parameters that allow for country specific factors.

DIFFICULTIES AND PITFALLS

- Various pre-existing Life Manuals.
- Established rating habits (marketing, extra mortality, surmortality…) and the poor 'reputation' of cancer in terms of relapse and survival.
- The international dimension of the project including country-related specificities arising from geographical, cultural, legal and sociological variation.

The project also needed to combine strong medical and mathematical backgrounds with reliable epidemiological and statistical data to allow the computing of a large and robust cancer database. Based on the above factors, we decided to focus on colon and breast cancer.

DATA

Data were obtained from the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute (NCI). The SEER Program is the only comprehensive source of population-based information in the United States that includes information for last known vital status, dates of birth, diagnosis, sex and various characteristics of the cancer.

We studied non-metastatic patients diagnosed in the period 2001-2011 with breast cancer only (ICD-O-3 topography C50) and colon cancer only (ICD-O-3 topography C18; morphology 8140, 8480, 8481 and 8490). We excluded patients if the reporting source of the diagnosis was either 'Death certificate only' or 'Autopsy only'. Patients with missing information were also excluded from the study.
The study focused only on non in situ tumours, malignant tumours and primary site tumours. For breast cancer, the final database consisted of 489 317 entries and 32 493 deaths due to breast cancer only, covering 86.8% of the initial database.
For colorectal cancer, the final database consisted of 160 300 entries and 23 756 deaths due to colon cancer only.
It covered 81.2% of the initial database.
To ensure that no bias was introduced during the data cleaning process, the model was also calibrated on the whole dataset. This control step did not reveal any major concerns.

STATISTICAL METHODS

It is standard in population-based studies to use relative survival to measure the excess mortality of breast cancer in the population. In this study, we opted to focus directly on the net cancer-specific survival as the SEER database records causes of death. This choice was made for, and supported by the following two reasons: first, we avoid any basis risk, as we do not have direct access to the underlying general population mortality. Secondly, for both breast and colon cancer mortality – there are no short-term side effects due to treatment and thus we do not have to measure any indirect mortality.

The SEER database contains over a hundred variables. A first step allowed us to target the most relevant variables to predict breast and colon cancer mortality.

After a stepwise selection and a quality control with the ROC (Receiver Operating Characteristic), the following criteria were targeted:

12 variables for breast cancer	9 variables for colon cancer
01. **Sex**	01. **Sex**
02. **Age**	02. **Age**
03. **Stage T** (T of the TNM classification)	03. **Stage T** (T of the TNM classification)
04. **Grade**	04. **Grade**
05. **Size**	05. **Size**
06. **Number of positive nodes** (N of the TNM classification)	06. **Number of positive nodes** (N of the TNM classification)
07. **Number of tested nodes**	07. **Number of tested nodes**
08. **Race**	08. **Race**
09. **Marital status**	09. **Marital status**
10. **Oestrogen hormonal receptor**	
11. **Progesterone hormonal receptor**	
12. **Histology of the cancer**	

Due to regulatory policies and practices, the variables of sex and race were removed from the study. We also did not consider any cross effects, as the model needs to be both comprehensive and efficient.

Our statistical model used for predicting patient cancer mortality is similar to the scoring models that are widely used in the banking industry. We based our approach on a logistic regression that estimates the mortality of patients as a function of their characteristics at diagnosis and the number of years since diagnosis.

Algebraically, the probability $\Pi(x) = P_T(Y = 1|X = x)$ is the death (mortality) of the patient T years after diagnosis (surgery of the primary site). The patient's characteristics are represented by the variable X. Finally, the full model is expressed as follows:

$$\Pi(x) = P_T(Y = 1|X = x) = \frac{e^{\beta_0+\beta_1 x_1+..+\beta_n x_n}}{1 + e^{\beta_0+\beta_1 x_1+..+\beta_n x_n}}$$

The estimation of the model parameters ß was obtained using maximum likelihood methods. The model was developed on the statistical software SAS®.

Results

CROSS VALIDATION

To ensure the robustness of our scoring model, numerous controls were performed with the Kaplan-Meier estimator. In FIGURES 3 & 4 the Kaplan-Meier and scoring survival curves for different stages - the dotted lines plot the lower and upper confidence intervals at 95% of the Kaplan-Meier estimator.

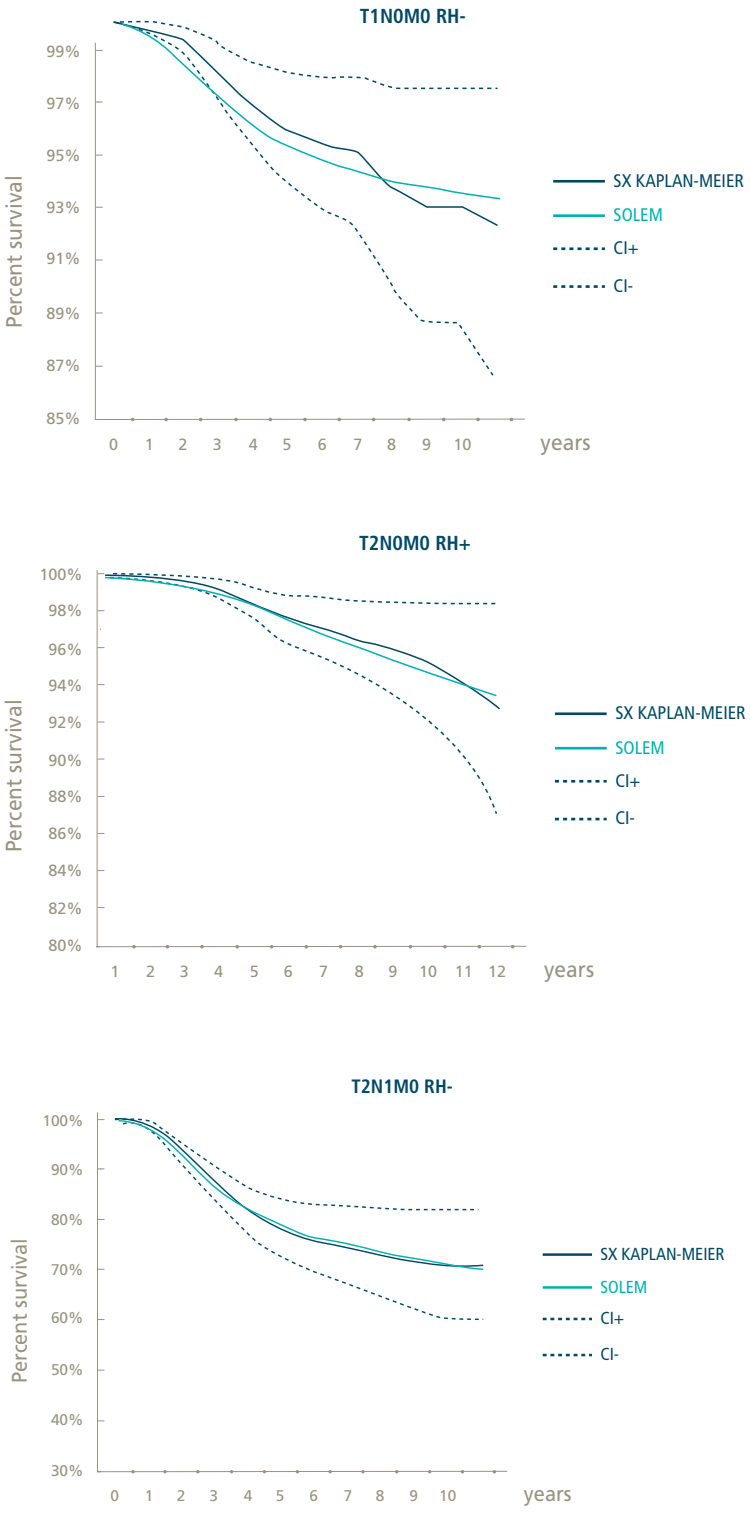
We selected combinations of variables that are associated with clinically relevant cases in order to have a sufficient number of patients to compute the Kaplan-Meier estimator: in breast cancer, this included 1 989 cases for the pT1N0M0 HR-, 3 951 cases for the pT2N0M0 RH+ and 1 121 cases for the pT2N1M0 RH-. In colon cancer, 670 cases for the pT1N0M0, 197 cases for the pT2N1M0 and 3 607 cases for the pT3N0M0 were analysed.

SURVIVAL CURVES

For breast and colon cancer, we showed that the output of the scoring model was close to that of the Kaplan-Meier survival curves and within the 95% confidence intervals. This observation demonstrates that the scoring model accurately predicts the mortality of patients in those two tumour types. We further tested multiple variables and as shown in FIGURES 3 & 4, the model also predicted with accuracy the overall survival estimate of patients with breast and colon cancers.

BREAST CANCER SURVIVAL CURVES

FIGURE 3



COLON CANCER SURVIVAL CURVES

FIGURE 4

Corrected conditional survival

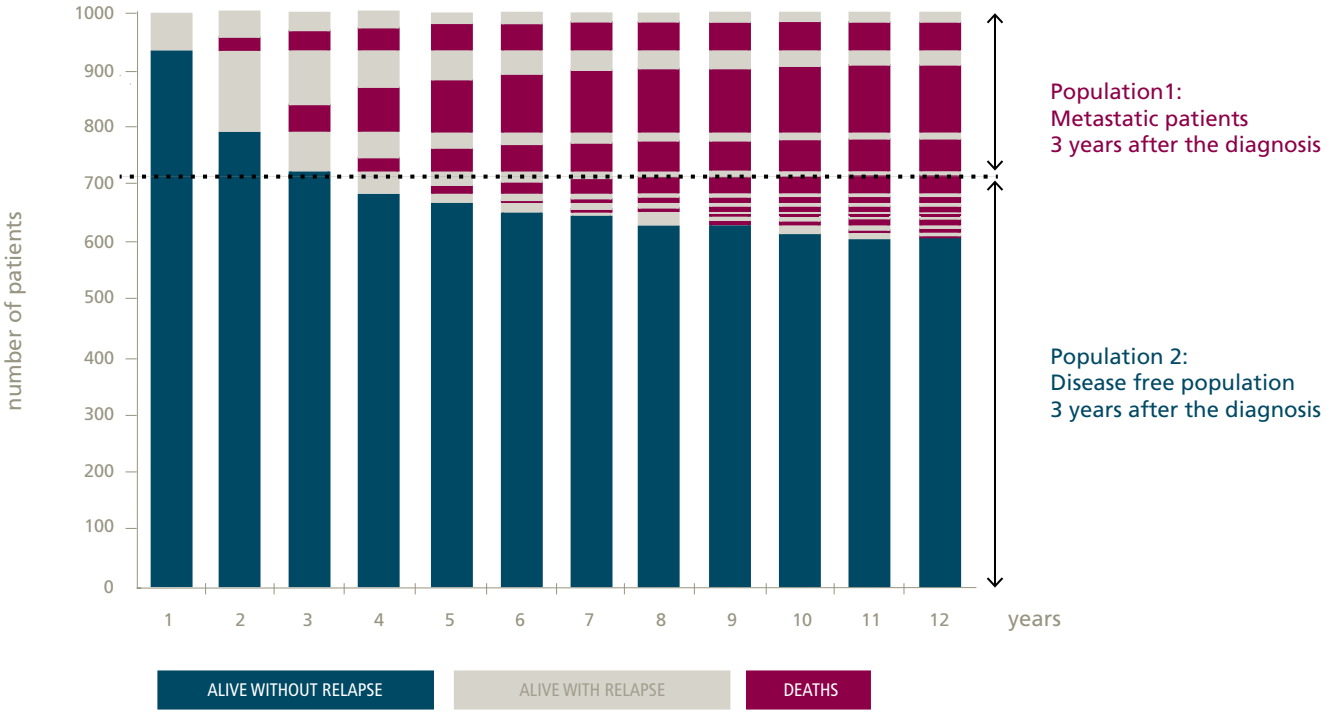
BREAST CANCER

For each possible combination of patient characteristics, our model predicts the underlying breast cancer survival curves and the patterns of cancer relapses. FIGURE 5 below presents the evolution of survival/deaths/relapses for a pT2N1M0 Grade 3 HR- breast cancer on a standardized population of 1 000 people.

Each year after treatment, a portion of the population relapses – grey areas representing the relapses appear each year – and some of these develop metastases that eventually lead to death – red areas representing deaths, which colour over the grey areas over time. Let us consider the deaths that will take place either in the population that is disease-free (population 2 in FIGURE 5), or in the population that relapsed within the first 3 years (population 1 in the figure).

SURVIVAL, DEATH AND RELAPSES FOR BREAST CANCER

FIGURE 5



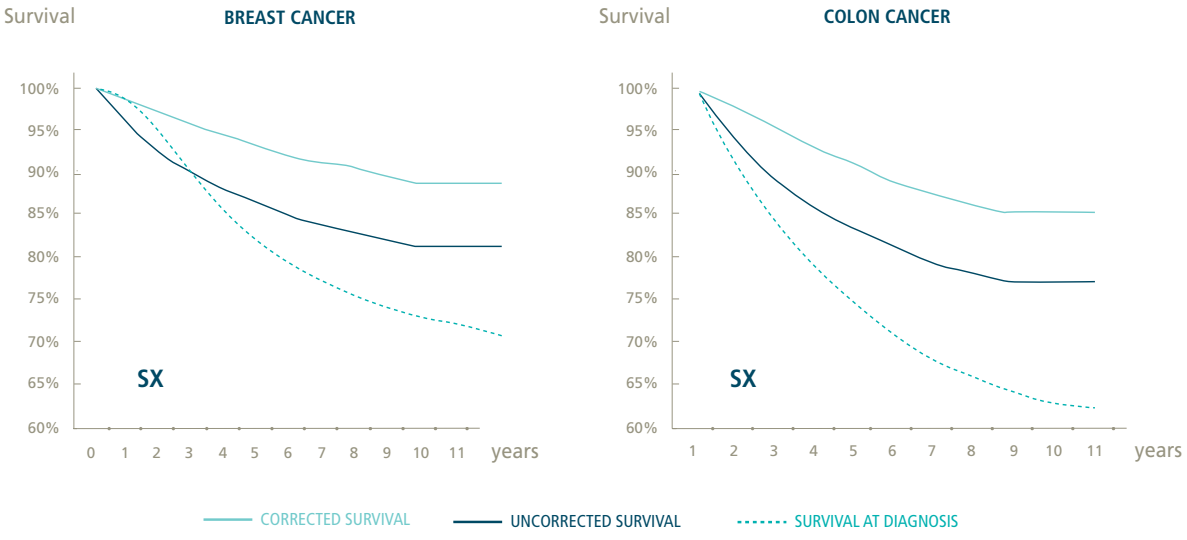
With our modeling, we are able to split these two populations and compute the corrected conditional survival by removing from the calculation the population that became metastatic in the first 3 years.

Classical approaches in reference manuals take into account prognosis and risk. Rating is often based on Kaplan-Meier estimates (dotted blue curve in FIGURE 6 below) that presents an estimated survival at diagnosis for a T2N1M0 grade 3 breast cancer and a pT3N1 Grade 3 colon cancer.

A first improvement is to use the conditional survival curve, the dark blue curve that takes into account the fact that patients who are still alive 3 years after initial diagnosis have a better survival rate. Our approach goes further and considers the underwriting selection that is performed when a patient seeks insurance, which normally removes patients who have had relapses. Thus, we can adjust the conditional survival curve to derive the 'corrected' conditional survival curve plotted in light blue. As shown, this translates in a huge change in the estimation of prognosis, making it possible to offer lower premiums for disease-free insureds.

CORRECTED CONDITIONAL SURVIVAL

FIGURE 6



TEXT BOX 4

PATTERNS OF EVOLUTION IN HR POSITIVE AND NEGATIVE BREAST CANCERS

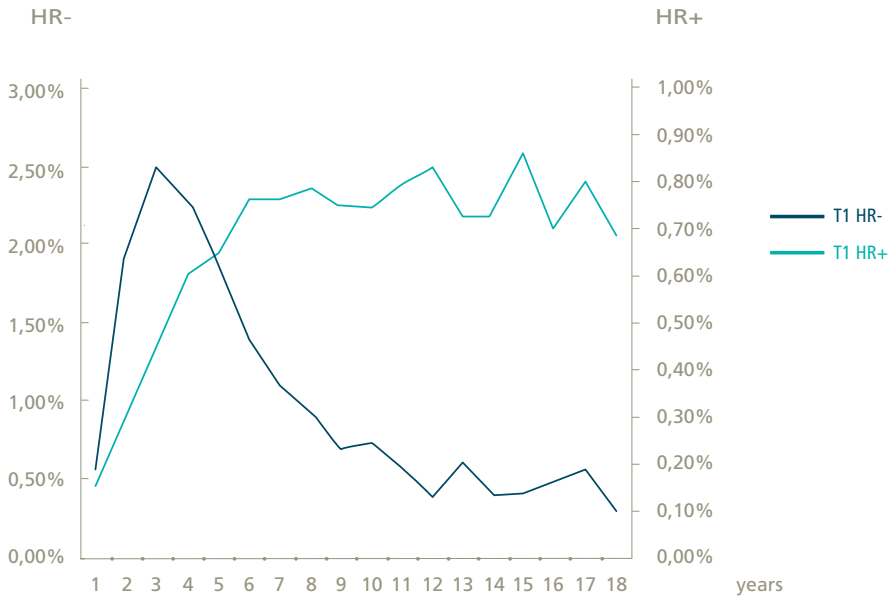
Breast cancer stands as a heterogeneous disease with a variety of different histological subtypes that may or may not express hormone receptors (oestrogen and progesterone receptors). Breast cancer is known to produce micro-metastases that spread from the primary site and then stay dormant for various durations before becoming relapses. Hormonal receptors are known to have significant impact on prognosis. Variability in hormonal receptor (HR+ and HR-) expression may lead to different natural history that can influence time to tumour progression, relapse and overall survival. Therefore, two different models were developed to take into account these specificities. At diagnosis, a substantial amount of data has shown that patients with HR- carry a worse prognosis than HR+ patients. However, the natural history also shows that HR- patients either may relapse early (high tumour growth kinetics) or not, in which case they can be considered as cured. The low incidence of relapse occurring 10 years after therapy suggests that patients with HR- tumours who are free of relapse at 10 years have low risk of subsequent recurrences and may be considered as cured.

Conversely, HR+ patients may present lower tumour kinetics compared to HR-, which induces sparse early recurrences or deaths, but rather much later onset of relapse and recurrence with tumour-related death that can continue to occur more than 10 years after the initial diagnosis. Therefore, although HR+ is usually associated with longer survival than HR- breast cancer, the late onset of recurrences also suggests that this later form of breast cancer may never really be considered as cured.

Mortality patterns are shown in FIGURE 7 comparing Kaplan-Meier mortality estimates between T1 HR+ and T1 HR-. This figure displays the increasing mortality rates of T1 HR+ that rise for six to seven years before plateauing with an almost constant risk of relapse ranging 0.7-0.85% thereafter. Interestingly, the mortality rate spikes at 2.5% at three years for HR- patients but constantly declines thereafter, approaching zero after 10 years.

KAPLAN-MEIER MORTALITY ESTIMATES BETWEEN T1 HR+ AND T1 HR-

FIGURE 7



CONDITIONAL AND CORRECTED CONDITIONAL SURVIVAL IN BREAST CANCER

Using previous models, we have shown that breast cancer specific survival curves can be estimated from the time of initial diagnosis and are closely linked over a 10-year period for HR- and over the lifetime for HR+ breast cancers. However, the probability of survival for individuals may also increase over time as poor prognostic patients dying early from cancer are censored from Kaplan-Meier estimates (being progressively removed from statistics) which increases over time the cohort of patients with a better prognosis. This in turn makes the likelihood of survival increase the longer one survives after the initial cancer.

In pT2N1M0 HR- breast cancer patients, the risk of death by cancer at the time of surgery is almost 21%. Three years later, the patient being alive ensures that he/she did not yet fall into the higher-risk category, which provides an increased probability of survival and reduces the risk of death at 5 years to 19%. Similarly, if the patient remains alive for five more years – obviously identifying the individual retrospectively as a good prognosis patient – the subsequent 5-year risk of death, taking into account the survival already incurred, falls down to 15%.

The concept that the probability of surviving an additional number of years increases after a patient has already survived a number of years following the diagnosis of a disease is known as conditional survival.

Conditional survival means in essence that a patient who already survived for x-years has an increased survival probability compared to that probability at the time of diagnosis. Unfortunately, conditional survival is not enough for medical underwriting purposes. Among patients alive x-years following the diagnosis there is a mix of patients alive either with no evidence of disease or with cancer that has already relapsed. Obviously, an underwriter may accept an applicant with a past medical history of cancer only if they have remained disease-free for a sufficient period of time. This has led the world of insurance to develop the concept of 'disease-free conditional survival' or 'corrected conditional survival'. Taking this lack of relapse at a certain time point into account, the corrected risk of death at 5 years for this pT2N1M0 patient is now reduced from 15% to 8%. Therefore, conditional overall and disease-free survival at a certain time point are important to revisit for the prognosis of patients, and to propose adjusted underwriting evaluations, understanding for instance that for pT2N1M0 patients with a 21% risk of death at diagnosis, this may reduce to only 8% a few years later, if the patient remains disease-free.

RATING COLON CANCER

In colon cancer, durations of postponement at the time of primary diagnosis range ≥1-5 years, subsequently followed by a specific rating that depends on the initial T staging and grading for patients with no lymph nodes (N0). Usually, whenever lymph nodes are involved (N1 or N2), more severe restrictions are applied, regardless of the T staging or tumour grading, lymph node involvements being thought to supersede other prognostic parameters such as T stage. Indeed local disease (either N0, stage I-II or Dukes A-B) always has a better prognosis than tumours with lymph-node involvements (N1-2 or stage III or Dukes C).

Interestingly, simple estimations of prognosis may sometimes lead to a blurred understanding of rating evaluations. When considering the risk of death at 5 years, it is roughly 10% in localized tumours versus 50% in more advanced stages. While pT1N1 Grade 1 colon cancer has a risk of death at 5 years of 12%, the risk of death at 5 years for a pT4N1 Grade 3 colon cancer is 48% (calculation made using colon cancer adjuvant online calculator). Based on the above prognostic factor, (i.e. considering N1 as the most important prognostic factor surpassing the prognostic value of T staging and grading) and using the current way of rating colon cancer, the same ratings will apply despite very different individual cases and prognostic risks. The same rating will apply for both a T1 Grade 1 tumour and a T4 Grade 3 tumour, due to the lymph node involvement, despite very different prognostic risks and expectations of survival.

Looking at additional cases, we can see other types of discrepancies between the medical prognosis and the current underwriting approach for colon cancer. For instance, considering locally involved N0 patients with advanced T stages such as pT4N0 Grade 3 colon cancer, the risk of death at 5 years reaches 23%. However, because this category falls into the N0 group of diseases, and the current rating system takes N positivity as an overpassing parameter, a pT4N0 Grade 3 patient will have a more favorable rating than a pT1N1 Grade 1 patient, despite an obviously worse expected survival rate. As shown in FIGURE 4, lymph node involvement seen in the T2N1M0 cases, result in further discrepancies that do not allow for adjusting a rating to an appropriate prognostic evaluation.

CONDITIONAL AND CORRECTED CONDITIONAL SURVIVAL IN COLON CANCER

With the previous model, we are able to compute colon cancer specific survival curves over a 10-year period. If we take the example of a pT3N1M0 colon cancer, the risk of death by cancer at five years is around 40%, which is five years after the initial diagnosis (usually the time of surgery). If the patient is still alive three years after the initial diagnosis, the risk of death at five years is now reduced to 19% and if they are alive five years after this (eight years after diagnosis) the 5-year risk of death is reduced to 11%. This again is what we call the conditional survival: if a patient has already survived a number of years, his prognosis improves. If we use the approach that we previously explained for breast cancer and remove the patients that are not disease-free at x-years after diagnosis, we can calculate the 'disease-free conditional survival' or 'corrected conditional survival'.

By considering this effect for underwriting purposes, the corrected risk of death at five years for this pT3N1M0 applicant is now reduced to 8%, allowing for improved ratings and earlier offers on these patients who remain disease-free.

CONCLUSION

The modeling of breast cancer mortality has been a major step forward in a global project that aims to refresh the SOLEM cancer methodology. In colon cancer, we have been able to remodel the short-term cancer mortality. We have great confidence that we will eventually be able to apply this methodology to other cancers.

Our mathematical model, based on easily obtained variables by the underwriter, can accurately estimate the risk of death of an individual based on her/his excess mortality rate according to colon and breast cancer history. The model does take into account the corrected conditional survival (disease-free conditional survival), permitting a tailored and evidence-based approach for the underwriter.

This model can incorporate any number of variables according to new prognostic parameters that could emerge over time. Implementation of any new variable such as a new molecular prognosis marker (KRAS, MSI status…) already known or to come, can be easily added into the algorithm as new information is released in the SEER database.

Interestingly, pricing can be theoretically adjusted each year, as the SEER database is updated annually, permitting advances and progresses in oncology to be incorporated into the pricing. Therefore, from the insurer's point of view, this new method gives us confidence in our evaluation and risk control of these cancer risks, as every part of the methodology is fully documented, tested, evidence based and adjustable for new factors.

The application of this model permits to better fulfil the various insurance needs of cancer patients by providing earlier access to insurance, more equitable pricing, individual risk adjusted ratings and by facilitating access to insurance for otherwise declined applicants.

ACKNOWLEDGEMENTS

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Glossary

CONDITIONAL SURVIVAL

The conditional survival is the probability of surviving cancer having already survived a number of years.

INCIDENCE

An incidence rate is the number of new cases of a disease divided by the number of persons at risk for the disease.

NET CANCER-SPECIFIC SURVIVAL

The net cancer-specific survival is the probability of surviving cancer in the absence of other causes of death. This measure is not influenced by changes in mortality from other causes, and so, can prove useful for comparing survival over time or between groups of patients. (Ref: Boer et al. 2003)

RELATIVE SURVIVAL

The relative survival is defined as the ratio of the 'proportion of observed survivors' (all causes of death) in a 'cohort of cancer patients' to the 'proportion of expected survivors' in a 'comparable cohort of cancer-free individuals'. The formula is based on the assumption of independent competing causes of death. Because a cohort of cancer-free individuals is difficult to obtain, expected life tables are being used instead, assuming that the cancer deaths are a negligible proportion of all deaths.

SDR

A Standardized Death Rate is a crude death rate that has been adjusted for differences in age composition between the region under study and a standard population.

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