Expert Views

Linking Life Insurance and Multi-Cancer Early Detection Testing:

MODELING AN EFFECTIVE PROGRAM

SCOR
The Art & Science of Risk

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Editor's Note: The objective of this article is to provide information for the industry to use or build upon with the hope that we can extend multi-cancer early detection technology to more policyholders and make a positive impact on their lives. The methods and practices used are a work in progress and represent a framework for understanding how the lives saved with a multi-cancer early detection screening program can be viewed in the context of a life insurance offering. We have made several assumptions based upon potential variables including price, program acceptance, product clinical effectiveness, age, smoking status and others. These variables and assumptions can be modified and customized based upon the specific situation of a company launching a program.

Multi-cancer early detection testing technology is an exciting new frontier, and we are just beginning to realize the possibilities. A simple blood draw that can detect a cancer signal at an early stage, find cancers that are not screened for today, facilitate customized treatment programs or assess the risk of cancer relapses is a reality right now!

Today GRAIL is a leading company in this field, offering Galleri®, a multi-cancer detection test that can reveal a cancer signal for 50 different cancers of which most are not commonly screened for today. The Galleri test uses a simple blood draw and detects if a cancer signal is present and, if so, usually indicates where the cancer is coming from.

One way that GRAIL and others in this field can detect cancer is to analyze changes in cell-free DNA known as methylation and apply advanced AI modeling to discover signatures of cancer in the patterns of methylation. These signatures can be used to test blood to see if it contains evidence for cancer, and if so, what type of cancer. We believe that over time, the DNA methylation signatures will improve and other sources (e.g., DNA, RNA, mRNA, protein and biome can be potentially good candidates as well) will be included, thus allowing for enhanced cancer detection and expanded usage.

This sounds amazing (and it is), but there are limits with today's technology, and we have much more to learn – there may be false positives, early-stage signals are not as predictable as later stage signals, and less severe cancers may not be detected at all. However, even with the limitations of today – lives can be saved!

Galleri is currently being used by forward-thinking individuals, companies offering it as a benefit to their employees and some concierge medical services. A few life insurance programs are also in the process of being launched. Over time this type of test is likely to become part of our annual physical and blood testing. Until then, the life insurance industry is well positioned to help bring this multi-cancer early detection test to a broader market and help policyholders improve their lives through early detection of cancer.

The life insurance and reinsurance industry is unique in that we all share in covering the same lives. In addition, cancer is a leading cause of death and an area where joining together can make a significant difference.

Multi-cancer early detection testing complements Standard of Care (SOC) screening to discover cancer earlier, potentially prior to symptoms presenting. They use an analysis from a blood sample to note the presence of biomarkers associated with cancer and can often identify the cancer's organ of origin.

Determining the Key Characteristics of the Target Population

The key characteristics of the target test population for Galleri testing were chosen to maximize the greatest number of lives saved per tests taken and the availability of the participants. The key characteristics are:

- Participant age greater than 39
- Participant smoking status or equivalent high risk
- Insured population

Participant age

Age impacts the incidence and mortality associated with cancer. In general, aging increases a person's risk of being diagnosed with and dying from cancer.

Figure 1 details the estimated average lives saved per 100,000 in-force for each age group. For example, of 100,000 test participants aged 80-84, 116 lives would be saved in the first year while 465 total would be saved during the first five years.

Figure 1: Lives saved per 100,000 tested per age group over varying periods of time

Age	Year 1	Year 1-2	Year 1-3	Year 1-5
30-39 years	2	4	6	8
40-44 years	4	9	13	18
45-49 years	8	16	24	32
50-54 years	14	29	43	58
55-59 years	25	49	74	99
60-64 years	38	75	113	150
65-69 years	52	104	156	208
70-74 years	71	142	213	284
75-79 years	93	186	279	372
80-84 years	116	233	349	465

This table was based on the 2021 research article on Modeled Reductions in Late-Stage Cancer with Multi-Cancer Early Detection (MCED) tests. That article stated that MCED tests could result in a reduction of 104 deaths per 100,000. Exhibit 1 is an estimated allocation of these 104 lives saved per 100,000 within each adult category across five years based on 2020 cancer mortality data from the CDC and other mortality data from National Vital Statistic Reports.

Figure 1 could be refined if additional information about Lives Saved by age category was available, including the absolute number of expected Lives Saved and the expected incidence rates by cancer type and age category. We understand that the Lives Saved is also impacted by assumptions regarding the growth rate of tumors progressing beyond early cancer stages and by the uptake of viable treatment methods.

We concluded after a review of this chart that testing younger ages had less impact for saving total lives on a per test basis. We chose to include participants aged 40 and older.

Reference: Hubbell, E. et al. Modeled Reductions in Late-stage Cancer with a Multi-Cancer Early Detection Test. Cancer Epidemiol Biomarkers Prev 2021;30:460-468 including supplemental data.

Smoking status of participants

Smoking is associated with a significant increase in the incidence of cancer, but the impact of smoking on the increased risk of developing and dying from cancer depends on the cancer type. Lung cancer and smoking are most closely related, but smoking also has significant impact on many other types of cancer.

We reviewed an August 3, 2022, article from the American Cancer Society (ACS) Journal entitled "Key Risk Factors for the Relative and Absolute 5-year Risks of Cancer to Enhance Cancer Screening and Prevention." In Figure 2 we show the factors from that article for smoking.
This table shows for current smokers a hazard ratio adjusted multivariately of 1.63 for males and 1.54 for females, for an average of 1.59.

Figure 2: Smoking risk factors - Full multivariable models: risk factors for developing any invasive cancer in 5 years among men and women, American Cancer Society Cancer Prevention study cohorts, 1992-2013

VARIABLE	Men				Women			
Smoking history	**Person-years**	**n cancers**	**HR Adjusted minimally**	**HR Adjusted multivariately**	**Person-years**	**n cancers**	**HR Adjusted minimally**	**HR Adjusted multivariately**
Never smoker	259,880	2,456	1.00 (ref)	1.00 (ref)	71,502	4,189	1.00 (ref)	1.00 (ref)
30+ years since quitting	65,902	1,189	1.06 (0.98-1.13)	1.05 (0.98-1.13)	62,025	542	1.03 (0.94-1.13)	1.04 (0.95-1.14)
20<30 years since quitting	70,374	1,150	**1.10 (1.03-1.18)**	**1.09 (1.02-1.17)**	83,954	661	**1.11 (1.02-1.20)**	**1.11 (1.02-1.20)**
10<20 years since quitting	61,055	1,006	**1.24 (1.15-1.34)**	**1.22 (1.14-1.32)**	81,877	580	**1.15 (1.05-1.25)**	**1.14 (1.04-1.24)**
10 years since quitting	58,766	981	**1.41 (1.31-1.52)**	**1.38 (1.28-1.49)**	90,557	706	**1.39 (1.28-1.51)**	**1.37 (1.27-1.49)**
Current smoker	46,205	871	**1.69 (1.56-1.83)**	**1.63 (1.51-1.77)**	77,303	698	**1.55 (1.43-1.68)**	**1.54 (1.42-1.68)**

Insured population

The Lives Saved per test presented in Figure 1 were based on a general population. A pilot program would target individuals with life insurance. In aggregate, life insurance policyholders experience a lower rate of death than the general population for several reasons. For example, the percentage of life insured policyholders who smoke is frequently significantly less than that of the general population.

Because the impact of the Galleri test was measured in the general population but not a life insurance policyholder population, the analysis must be adjusted to a typical life insurance policyholder population.

The following figures illustrate this point. Figure 3.1 illustrates the mortality from cancer in those aged 25-59 in the U.S. population compared to the SCOR Life & Health U.S. mortality rate for insured population, based upon recent analysis. Likewise Figure 3.2 illustrates the results for those aged 60-79.

The key takeaway from these charts is that mortality rates for the general population are 1.4 times as high for ages 25-59 and 1.7 times as high for ages 60-79.

Figure 3.1: Comparison of mortality rates per 100,000 by cause of death (Neoplasms), ages 25-59

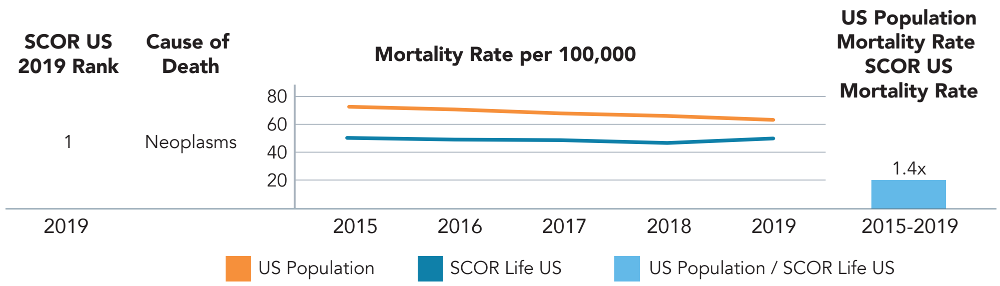
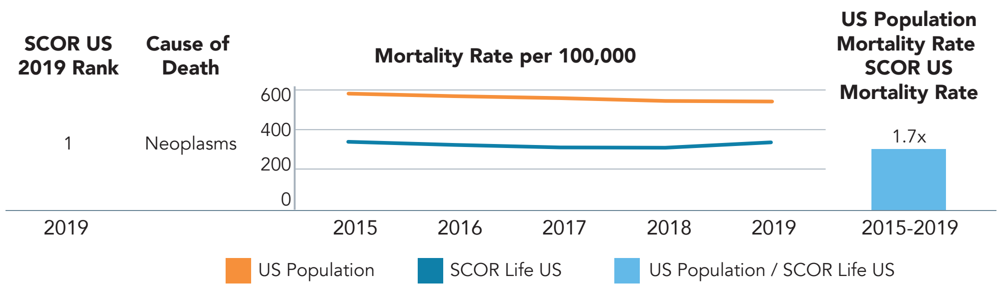


Figure 3.2: Comparison of mortality rates per 100,000 by cause of death (Neoplasms), ages 60-79



Number Needed to Screen

The number needed to screen (NNS) to avoid one death is an important data point used in the financial analyses. The NNS varies by age and risk characteristics. Older aged individuals, those with a previous smoking history, obese individuals, those with a genetic predisposition to cancer and/or a strong family history of cancer are some of the variables associated with a lower NNS. In general, programs with a lower NNS (to avoid one death) are associated with better financial results.

To adjust the Lives Saved data (Figure 1) to an insured population for ages <60, we used 1/1.4 (0.71) and for ages 60+, 1/1.7 (0.59). We combined this insured factor adjustment with the smoking adjustment factor of 1.59 averaged in Figure 2 and applied these to Lives Saved from Figure 1. The total adjustment factors and the target test population are shown below in Figure 4.1.

Figure 4.1: Total adjustment factor, target test population and distribution

Adjustment for Insured Population	Ages 50 to 59	0.71
	Ages 60 +	0.59
Smokers		3.50
Number of In-Force Tested		1,000

Target test population and distribution

Age	Insured Population	Insured Factor	Smokers / High Risk Only	Risk Factor	Total Adjustment	Testing Distribution
40-44 years	Yes	0.71	Yes	1.59	1.14	2%
45-49 years	Yes	0.71	Yes	1.59	1.14	3%
50-54 years	Yes	0.71	Yes	1.59	1.14	4%
55-59 years	Yes	0.71	Yes	1.59	1.14	3%
60-64 years	Yes	0.59	No	1.00	0.59	39%
65-69 years	Yes	0.59	No	1.00	0.59	17%
70-74 years	Yes	0.59	No	1.00	0.59	18%
75-79 years	Yes	0.59	No	1.00	0.59	7%
80-84 years	Yes	0.59	No	1.00	0.59	7%
						100%

Figure 4.2: Projected lives saved per 1,000

Age	No. Tested	Year 1	Year 1-2	Year 1-3	Year 1-5
40-44 years	20	0.001	0.002	0.003	0.004
45-49 years	30	0.003	0.006	0.008	0.011
50-54 years	40	0.007	0.013	0.020	0.026
55-59 years	30	0.008	0.017	0.025	0.034
60-64 years	390	0.086	0.172	0.258	0.344
65-69 years	170	0.052	0.104	0.156	0.208
70-74 years	180	0.075	0.150	0.225	0.300
75-79 years	70	0.038	0.077	0.115	0.153
80-84 years	70	0.048	0.096	0.144	0.192
	1,000	0.318	0.636	0.955	1.273

The testing distribution is based on the expected percentage of policyholders in each age group and by smoking status of the available data of an insured population.
Figure 4.2 shows the projected lives saved per 1,000 tested after adjusting Figure 1 by Figure 4.1 factors.
The highlighted box shows that about one life would be saved for the 1,000 tested within the first three years after the target population is tested.

Projected Financial Results

A simple ROI metric calculates the breakeven point that directly compared test costs to the policy face amounts of saved lives. While a more sophisticated metric might be used, the breakeven was straightforward as it identified most directly the areas where we should test and the amount of savings needed to make a program financially viable.

Life insurance face amount

Avoidance of claims associated with higher face amounts would favorably impact the ROI.

Cost per Galleri test

The cost of the test does not vary by age or any other risk factors and was assumed to be $1,000 per test. A high price can significantly, adversely impact the financial ROI, and cost sharing could mitigate this concern. Partial or complete subsidization of the test cost by the (re)insurance company may make the test more financially affordable for all stakeholders.

Other ROI metrics would consider the ability of a well-launched program to increase the partnership between the involved participants of policyholders, insurance and reinsurance companies. Other metrics for this evaluation could be enrollment, engagement, retention and participant satisfaction.

In our analysis we assumed that the life insurance policyholder would pay one-third of the test costs so the net rounded cost to the (re)insurers was $670.

Figure 5.1 below shows the breakeven face amounts required to recover the total costs of the test by age group and in aggregate for the target population of 1,000 tested.

Figure 5.1: Average face amounts for breakeven with (re)insurer test costs of $670

Age	Number Tested	Testing Costs	Breakeven Average Face Amount			
			Year 1	Year 1-2	Year 1-3	Year 1-5
40-44 years	20	$13,400	$13,186,550	$6,593,275	$4,395,517	$3,296,638
45-49 years	30	$20,100	7,264,911	3,632,455	2,421,637	1,816,228
50-54 years	40	$26,800	4,076,402	2,038,201	1,358,801	1,019,100
55-59 years	30	20,100	2,393,319	1,196,659	797,773	598,330
60-64 years	390	261,300	3,036,727	1,518,364	1,012,242	759,182
65-69 years	170	113,900	2,185,882	1,092,941	728,627	546,470
70-74 years	180	120,600	1,605,712	802,856	535,237	401,428
75-79 years	70	46,900	1,224,790	612,395	408,263	306,197
80-84 years	70	46,900	978,864	489,432	326,288	244,716
	1,000	$670,000	$2,105,453	$1,052,727	$701,818	$526,363

The highlighted areas in Figure 5.1 show that to recoup a testing cost of $670 through savings from claims, the average face amount for the target population should be between $700,000 and $1,050,000.

The highlighted areas in Figure 5.2 show that to recoup a testing cost of $1,000 through savings from claims, the average face amount for the target population should be between $1,047,000 and $1,570,000.

Alternatively, if the target population has an average face amount of $500,000 then to break even in two or three years, the cost of the test to (re)insurers is calculated as between $318 to $477 as show in Figure 6.

The results in Figures 5.1, 5.2 and 6 show an approach for understanding the value of the test and the range of reasonable face amounts for testing. Changing values for cost per test, proportion of test cost paid by the insurers and the potential distribution numbers based upon age meaningfully change the required breakeven face amounts.

Figure 5.2: Average face amounts for breakeven with full $1,000 test cost

Age	Number Tested	Testing Costs	Breakeven Average Face Amount			
			Year 1	Year 1-2	Year 1-3	Year 1-5
40-44 years	20	$20,000	$19,681,418	$9,840,709	$6,560,473	$4,920,355
45-49 years	30	$30,000	10,843,150	5,421,575	3,614,383	2,710,788
50-54 years	40	$40,000	6,084,182	3,042,091	2,028,061	1,521,045
55-59 years	30	30,000	3,572,117	1,786,059	1,190,706	893,029
60-64 years	390	390,000	4,532,429	2,266,214	1,510,810	1,133,107
65-69 years	170	170,000	3,262,510	1,631,255	1,087,503	815,628
70-74 years	180	180,000	2,396,585	1,198,292	798,862	599,146
75-79 years	70	70,000	1,828,044	914,022	609,348	457,011
80-84 years	70	70,000	1,460,991	730,495	486,997	365,248
	1,000	$1,000,000	$3,142,467	$1,571,234	$1,047,489	$785,617

Figure 6: Average test cost for breakeven at $500,000 average face amount

Age	Number Tested	Testing Costs	Breakeven Average Face Amount			
			Year 1	Year 1-2	Year 1-3	Year 1-5
40-44 years	20	$500,000	$25	$51	$76	$102
45-49 years	30	500,000	46	92	138	184
50-54 years	40	500,000	82	164	247	329
55-59 years	30	500,000	140	280	420	560
60-64 years	390	500,000	110	221	331	441
65-69 years	170	500,000	153	307	460	613
70-74 years	180	500,000	209	417	626	835
75-79 years	70	500,000	274	547	821	1,094
80-84 years	70	500,000	342	684	1,027	1,369
	1,000		$159	$318	$477	$636

Summary

The key findings of our financial analysis (assuming a single test) based on improved mortality for the target populations are:

- We determined that younger ages (<50) had lower ROI potential.
- The target test population was primarily older ages (88% were 60+) though we included those aged 40-59 with increased cancer risk (e.g., smoking or equivalent increased risk).
- We determined the need to save approximately one life per 1,000 tested to breakeven on a cost benefit analysis across a target population.
- A time horizon of two to three years for breakeven seemed reasonable for a pilot program, though mortality benefits continued across a longer time horizon.
- The cost per Galleri test (about $1,000) is a limiting factor of who should be tested, how often and at what face amounts.
- SCOR actively supports cost sharing and participates in such programs to bring down testing costs and reach more policyholders with this life-saving technology.
- We recommend considering a target population with life insurance face amounts greater than $750,000 if the total acquisition cost of the test to the insurance company is $670.
- Participation levels of an insured population interested in taking an early cancer screening test was unclear.

As illustrated above, a simple financial projection can be used prior to launching a Galleri pilot program to help identify those who would potentially benefit from an interventional health and wellness program. The analysis anticipates the financial ROI expected from such a program. Additionally, the analysis could be used to understand and justify costs associated with the program and in vendor negotiations to make sure expenses will be reasonable for sustaining it.

The financial projection may be used after program launch as well to analyze the impact of the intervention as program-associated metrics emerge so that the key characteristics can be tweaked for maximal benefit for all stakeholders. The goal is to have an impactful and sustainable program beneficial for all stakeholders.

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