ReFlections

RGA's Global Medical Newsletter

Volume 37, January 2016

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IN THIS ISSUE

FROM THE EDITORS

Welcome to the January 2016 edition of ReFlections! This issue, the first of the new year, continues our mission to educate, inform and enlighten.

It was a pleasure to see so many of our friends and colleagues at the recent American Academy of Insurance Medicine (AAIM) Triennial meeting in Colorado Springs. Hopefully, everyone found it as educational and inspirational as we did.

This edition features an article by Dr. Philip Smalley, Senior Vice President and Global Chief Medical Officer for RGA International Corporation, which discusses the history and intricacies of developing Critical Illness (CI) products. It also features an article by Hilary Henly, Head of Underwriting (Ireland) and Director of Divisional Underwriting Research, RGA Reinsurance Company, and one of ReFlections' frequent contributors. Her article provides a comprehensive review and update on the medical status of cervical cancer. We trust both articles will provide the reader with practical and usable information.

We are also continuing our new and popular section, ReCite, in which we provide links to recent and relevant journal articles we believe will be of interest to medical directors and underwriters.

Lastly, we include an update of recent developments at the Longer Life Foundation. Eight research grants were made for 2015 – 2016, funding innovative projects on topics of interest to all in the insurance industry.

Please feel free to provide any feedback and suggestions to us! We want to make this as useful and practical as possible to you – our readers.

Thank you,

Phil, Dan and Neil

CRITICAL ILLNESS INSURANCE: A MEDICAL PERSPECTIVE

Critical Illness, as a product, is currently more than 30 years old and has proven vitally important to many markets around the world. Given the speed at which medical science is evolving, can the product continue to retain its fundamental spirit and still remain sustainable? Over the past decade, it has experienced extensive evolution: new standalone and rider structures as well as new product features have emerged, and the number of covered conditions has grown considerably. The impairment definitions themselves have also undergone substantial refinement, enabling them to provide far greater precision while keeping current with medical advances. All of these changes are driving increasing complexity in CI, emphasizing the pivotal role insurance medical directors must play in CI product design and pricing in order to ensure the product's profitability and marketability. This article reviews the important considerations and challenges of which insurance company medical departments must be aware to ensure this product continues to be successful.

Critical Illness insurance is, in its essence, a simple product: it provides a lump sum payment to an insured upon diagnosis of a covered impairment as defined within the contract. The product, however, is not simple at all, and its complexities are growing fast. Currently, CI is available in several design configurations: policies specifically for juveniles and females; policies featuring scaling and partial payments; and multi-pay policies, with buckets enabling full payouts should the policyholder need to claim more than once. Policy options such as buy-back and recurrence benefits can also be purchased.

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Philip Smalley, M.D., is Senior Vice President and Global Chief Medical Officer for RGA International Corporation. An internal medicine specialist, Dr. Smalley engages in case consultation, client support and education, and product development, and frequently represents RGA at key industry and professional meetings. He is a Past President of the Canadian Life Insurance Medical Officers association and a Fellow of the Royal College of Physicians and Surgeons of Canada.

TABLE 1: TODAY'S CI PRODUCTS, COVERAGES

Female Critical Illness	Covers female-specific impairments as well as general impairments that are more commonly seen in women, such as gynecologic cancers, bone fractures due to osteoporosis, rheumatoid arthritis, lupus nephritis, pregnancy complications, etc.
Juvenile Critical Illness	Covers impairments more common to children, including Down's syndrome, cerebral palsy, muscular dystrophy, congenital heart disease, cystic fibrosis, etc.
Scaled Critical Illness	Payouts are graded based on disease severity or clinical stage.
Early-pay Critical Illness	Provides partial payment for covered conditions at early stages, such as carcinoma in situ, diabetes complications, removal of an organ, etc.
Multi-pay Critical Illness	Allows multiple claims for impairments that are unrelated or in different disease or organ system buckets.
Buy-back Option	A policy option that allows a policyholder to "buy back" an amount of CI cover after a first claim to cover a second, unrelated claim.
Recurrence Benefit	After a CI claim, this benefit allows for a second claim for the same CI impairment (usually for a lower coverage amount).

Impairments to Cover

In CI's early days, only the so-called Big Four illnesses – heart attack, cancer, stroke, and coronary artery bypass surgery – were covered. Since then, the product and its features have evolved substantially. As Table 1 shows, CI products today come in a range of structures that can cover single and multiple impairment incidences.

The roster of impairments a CI product can cover has grown as well. Insurance companies today compete to provide the widest selection of illnesses, with some products now covering more than 175 diseases and conditions. Several products also incorporate "catch-all" impairments, such as total and permanent disability (TPD), terminal illness, and loss of independent existence, which is adding further complexity.

When developing CI products, insurers need to determine which impairments are the most appropriate to cover, depending on the market to be served and its financial needs. The optimal number of covered impairments varies by market, but usually ranges from 13 to 23 conditions. Insurers also need to be able to underwrite the selected impairments effectively. It is best not to cover impairments that are difficult to clearly define with objective criteria or diseases open to potential negative impacts of medical advances.

Definitions in CI policies need clear, well-crafted, and unambiguous language

The spirit of the product also needs to be maintained. CI definitions need exclusions and severity clauses in order not to cover non-critical conditions where financial loss to the insured upon diagnosis is minimal. For example, policies should not cover every type of burn, otherwise a sunburn would qualify. Also, not every abnormality incidentally found on a cranial CT scan should be covered, and CI carriers should not have to pay out for easily treatable minor cancers such as non-melanoma skin cancers that have good prognoses and do not generally result in significant financial loss to the insured.

As a general rule, for large-payout CI impairments, it is best to cover only serious, life-changing impairments that will shorten life expectancy, are expensive to treat, and commonly leave the insured with significant sequelae.

Drafting CI Definitions

Definitions in CI policies need clear, well-crafted, and unambiguous language to describe benefit triggers for each covered impairment in every country and market where it is offered. Language must also be legally defensible: a stray "and" or "or" could leave insurers vulnerable to litigation. Definitions also might be different for a Group CI product versus an Individual CI product. An example of this is in the definition of a progressive degenerative impairment such as Alzheimer's disease. In an individual product, Alzheimer's can be defined so that it pays out at a very advanced stage of the disease, whereas in a group product, it might be defined so that it pays out at a lower severity – a level when an insured's capacity to work might first be impacted.

Also, if long-term guarantees on premium rates are used, wordings that offer more "future-proofing" would need to be incorporated into each CI definition.

It is also essential to not try to plug every hole in a CI definition. Doing so could make the product too complex for agents and the buying public to understand.

CI definitions should have the following characteristics:

- Clarity in describing what is and what is not covered
- A match with the issuing insurance company's pricing and marketing goals
- Close agreement, within reason, with existing clinical disease definitions
- Clearly written and objective claims triggers
- Resilience to and/or ability to accommodate to ongoing medical advances in order to maintain the spirit of the product

In certain markets, model language for use by insurers in impairment definitions already exists. In the U.K., for example, CI impairment definitions are maintained and supported by the Association of British Insurers for utilization by all insurance companies. In other markets, insurers have developed their own definitional language, usually in tandem with a reinsurer or other product architect.

There are pros and cons to adopting industry-wide CI definitions but again, medical directors play important roles in designing and updating these industry CI definitions.

Finding the right balance for these definitions, so language is clear, medically correct and understandable to claims adjudicators as well as to agents and policyholders, is best accomplished using a team approach, with representatives from the insurer's medical, legal, claims, pricing and marketing divisions weighing in.

Impact of Medical Advances

The speed at which advances are taking place in medicine, from increased screenings, new biomarkers and diagnostics to new therapies and cures, is having a dramatic impact upon CI in terms of product design, pricing, and most of all, its definitions.

Certain CI definitions that demanded more invasive or antiquated diagnostic technologies have needed to be updated to meet current clinical practices, which use newer, less invasive diagnostic technologies such as genetic tests and recently discovered biomarkers. Also, changes in recent years to the clinical definitions of heart attack, cancer, stroke and Alzheimer's due to new research developments have led to unexpected increases in claims experience in certain markets. For example, the incorporation of troponin test results into the clinical definition of heart attack has led to increased incidence of myocardial infarction diagnoses. In addition, new and less invasive surgical techniques such as cardiac keyhole surgeries and transvascular aortic and heart valve surgeries have led to necessary changes in CI definitions.

As new imaging and screening tests are discovered and developed, the potential to detect incidental impairments is increasing – impairments that may have no impact on the insured's life and therefore might not warrant an approved claim. In addition, the rising worldwide trend of screening for various cancers – especially those affecting the breast, prostate and thyroid – are resulting in dramatic increases in incidence rates for these cancers, especially at the early stages. In Korea, for example, national thyroid cancer screenings resulted in a 15-fold increase in diagnosis from 1993 to 2011, without any change in thyroid cancer mortality.

Finally, new cures might mean that a once-critical condition might not be life-challenging in the future. For example, some types of cancers which once needed expensive bone marrow transplants can now be treated with less expensive oral medications.

The Medical Director's Growing Role

Medical directors at insurance companies are playing increasingly important roles in the development of CI products. They assist actuaries to ensure the products are priced adequately and affordably. They work with product development teams to ensure the right impairments are covered and defined clearly in ways that will help mitigate the potential impact of future medical advances. They also contribute expertise in underwriting cases and claims adjudication.

With the newer scaled CI products, actuaries are needing medical director input regarding distribution of disease by stage or severity. Medical teams are being called upon to provide information for multi-pay products about the mortality associated with each covered illness and the interdependencies of various illnesses in combination. In addition, medical directors provide important input regarding incidence rate trends, the likely impact of medical advances, and the potential impact on a product's design of removing or altering a particular definition or exclusion, or reducing the waiting or survival period.

Currently, claims adjudicators at insurers that sell CI are seeing several areas of debate as well as claim challenges, where medical directors are providing important input. Some of these include the following:

- Malignant versus borderline or pre-malignant conditions surrounding carcinoids, gastrointestinal stromal tumors, and bone marrow pathologies
- The non-melanoma skin cancer CI exclusion and its impact on claims for cutaneous lymphoma and dermatofibroma sarcoma
- Claims for stroke, multiple sclerosis, head trauma and benign brain tumor where there are questions about permanent neurological deficits
- Whether incidental imaging findings coupled with certain symptoms constitute a valid CI claim for particular covered conditions
- Whether or not an acute Takotsubo cardiomyopathy diagnosis is claimable under the heart attack CI definition
- The validity of a CI claim for heart attack when certain diagnostic test results are missing

How these controversies are handled at claim time depends on the market, local legal precedent, and the definition used in the CI contract. The best team approach to these problematic claims involves the insurer, the reinsurer, and legal counsel (as appropriate).

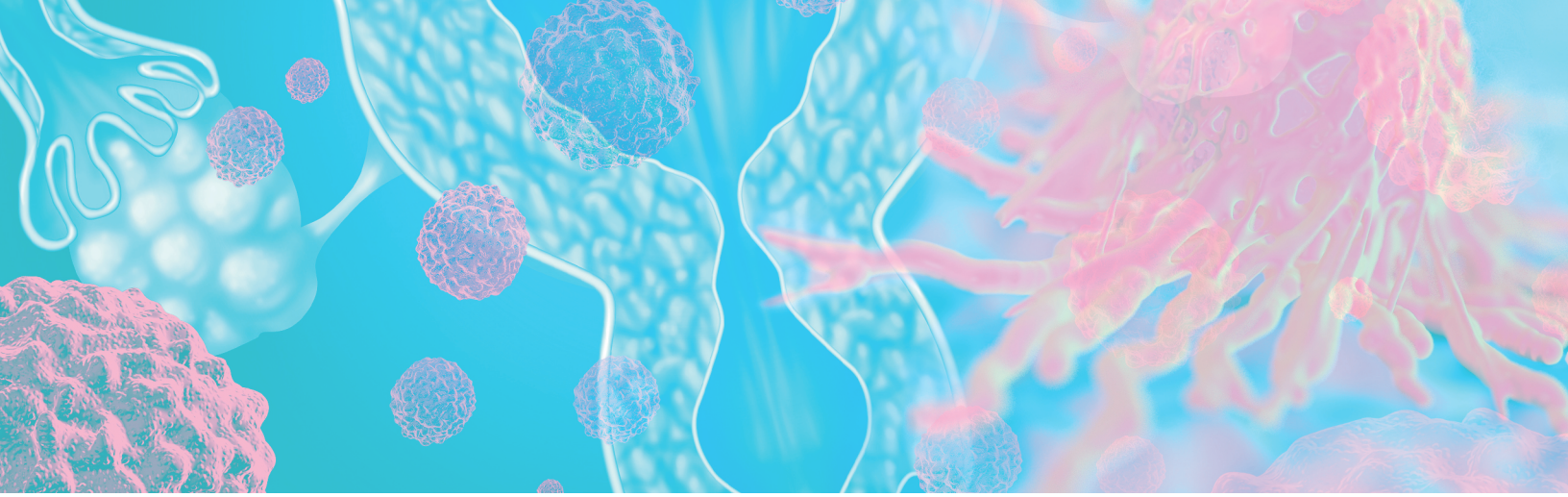
Summary

Keeping CI products as simple and as marketable as possible is becoming increasingly essential. CI definitions must be well-worded with clear claims triggers and kept current with medical science.

Insurance medical directors play pivotal roles in CI product design and pricing to ensure the product's sustainability and affordability. As long as all parties are aware of the impact of medical advances, CI can continue to develop profitably and serve an important public need. RF

RGA MEDICAL TEAM UPDATE

RGA welcomes Dr. Valerie Kaufman, M.D., DBIM, FACC, Vice President and Medical Director, to our global network of medical officers. Dr. Kaufman, who will be based in RGA's Chesterfield, Missouri (U.S.) office, has more than 25 years of insurance industry experience and three board certifications (cardiology, insurance medicine, and internal medicine). She is a past President of the American Academy of Insurance Medicine, and has spoken frequently on cardiologic topics at local, regional and national industry meetings.



CERVICAL CANCER UPDATE – 2016

Over the past few decades, there has been a significant reduction in the incidence of cervical squamous cell carcinoma (SCC) in the U.S., Canada, Australia (New South Wales) and in nearly all European countries, due primarily to the development of the Papanicolaou (Pap) test and its widespread use. There are two main types of cervical cancers: squamous cell cancer (SCC) and adenocarcinoma (ADC). More than two-thirds are SCCs while 15% are ADC. One uncommon type, small cell neuroendocrine carcinoma (SNEC), has a much poorer survival rate than either SCC or ADC[9]. Three-quarters of all cervical cancers are known to be caused by two types of human papillomavirus – HPV 16 and 18[3]. The two vaccines that provide the most effective protection against the most common types of HPV are Gardasil and Cervarix, approved by the U.S. Food and Drug Administration (FDA) in 2006 and 2009, respectively.

Histological staging is the most important predictor of cervical cancer survival. Recurrence rates vary from 8% to 26% of all patients, with a median time to recurrence of between seven months and three years following initial treatment[5]. This article will look at assessment factors that need to be considered in product development, underwriting and claims adjudication.

About Cervical Cancer and its Risk

The main causative agent for cervical cancers is human papillomavirus (HPV) infection. Such infections rarely have physically obvious symptoms. They can usually only be diagnosed via direct visual examination of the cervix itself and administration of a Pap test, during which surface cells are removed and then assessed under a microscope for abnormalities.

The World Cancer Research Fund and American Institute for Cancer Research have found 12 high-risk varieties of HPV (specifically HPV 16 and 18, which are responsible for three-quarters of all cervical cancers, as well as HPV 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59) that increase the risk of an infection progressing to cervical cancer. Other factors that increase cervical cancer risk include estrogen-progesterone oral contraceptive pill (OCP), presence of the human immunodeficiency virus (HIV), and smoking[3].

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HPV infection frequently resolves without treatment, but women experiencing persistent HPV infections are at risk of developing precancerous cervical conditions. Abnormal Pap test results are termed either low-grade squamous intraepithelial lesions (LSIL) or high-grade squamous intraepithelial lesions (HSIL)[12], terms that describe the type of cells viewed. Cervical intraepithelial neoplasia (CIN) 2 and 3 biopsy results denote a precancerous condition with potential to develop into cancer: 1/3 to 1/2 of HSIL and CIN 2 or 3 lesions might develop into invasive cervical cancer, 10% to 15% of CIN 1 and LSIL lesions progress further[14].

Incidence Trends

As of 2012, cervical cancer was the fourth most common cancer among women and the seventh most common overall worldwide[3]. More than half a million new cases were diagnosed globally that year, with 80% occurring in developing countries. Squamous cell carcinoma (SCC) is responsible for 75% to 90% of all cervical cancer malignancies.

Poverty has long been a driver of high cervical cancer incidence rates. A U.S. study in the 1990s found that women in high-poverty counties had at least a 1/3 higher incidence rate than those in low-poverty counties[10]. It is the most common cancer among black women in the Southern African countries of Swaziland, South Africa, Botswana, Lesotho, and Namibia. In Australia, although general incidence rates are low, the incidence rate for Aboriginal women is six to eight times higher than for non-Aboriginal women. Lack of screening and subsequent delays in diagnosis are considered to be the primary contributing factors to this higher rate[13].

Poverty is, however, not the only driver: health factors also play a role. Cervical cancer risk is higher for women who have experienced one full-term pregnancy versus those who have never been pregnant. In addition, it is 77% higher for girls aged 17 or under who have experienced a full-term pregnancy, compared to women older than age 25[3].

A sizable health factor in cervical cancer is smoking. An estimated 7% of cases are linked to the habit. Cervical SCC risk is found to be 1.5 times higher for current smokers than for current non-smokers, and is 73% higher for those exposed to tobacco smoke than for those who have never been exposed.

The risk of cervical SCC risk in those with one first-degree relative (parent or sibling) diagnosed with cervical cancer can be as much as 80% higher than for the general population[3].

Pap smear tests, which sample cells from the ectocervix and not from the glandular epithelium (where ADC arises), has substantially reduced cervical SCC incidence. A study in Sweden of 12,527 women between the ages of 32 and 38 found that those screened for HPV and by Pap tests had a 40% reduction in their risk of CIN 2 or 3 or full-blown cervical cancer, compared to those who only had Pap tests[12]. Additionally, a study in India of 131,746 women age 30 to 57 found that having had a single HPV test and subsequent treatment significantly reduced the numbers of advanced cervical cancer cases as well as mortality from the disease[15].

Mortality/Survival Trends

In 2012, 265,000 deaths were reported from cervical cancer globally[11]. Socioeconomic factors and ethnicity also play a large part in cervical cancer mortality. In the U.S., high-poverty counties have a 70% higher mortality than low-poverty counties[10]. Globally, a wide variance in survival rates has been found: the five-year age-standardized relative survival rate in Uganda is 19%, but 76% in South Korea and 77% in Hong Kong. Additionally, in Singapore, 81% of cases are diagnosed at localized stage but only 7% of those diagnosed in Chennai, India occur at the same stage[17].

Combined results of studies show, in Table 1 (below) five-year survival in the different stages of cervical cancer[14].

TABLE 1: FIVE YEAR RATES

	Stage 1A	Stage 1B	Stage IIA	Stage IIB	Stage III	Stage IV
5-year survival, %	90-95%	80-85%	50-65%	40-50%	25-30%	<5%

- In the EUROCARE 4 study (those diagnosed between 2000 and 2002), one-, five- and ten-year relative survival rates for cervical cancer were 84.3%, 65.2% and 59%, respectively[6].
- Farley et al. investigated 273 women in the U.S. between 1988 and 1999 and found no difference in survival between Stage I ADC and Stage I adenosquamous carcinoma (ASC), but there was a significant decrease in survival at FIGO Stage II to IV for ASC[2]. (FIGO = International Federation of Gynecology and Obstetrics)
- Intaraphet et al.'s study of over 2,000 Thai patients during the period 1995 to 2011 showed the following survival by histological type[9]:

TABLE 2: SURVIVAL RATES FOR CERVICAL CANCER TYPES

Stage I or IIA	Squamous cell carcinoma	Adenocarcinoma	Small cell neuroendocrine carcinoma
5-year survival	88.1%	90.3%	64%
10-year survival (surgery)	95.3%	96.2%	55.6%
10-year survival (surgery plus chemotherapy)	87.5%	100%	70.3%
10-year survival (radiotherapy)	82%	90.3%	64%
10-year survival (chemotherapy alone)	88.1%	90.3%	64%
Stage IIB and above	**SCC**	**ADC**	**SNEC**
5-year survival	49.7%	39.1%	18%

Data published in the *International Journal of Gynecology and Obstetrics* and illustrated in Table 3 on the next page show the following survival rates for patients treated between 1999 and 2001[2].

TABLE 3: SURVIVAL RATES 1999 – 2001					
Stage	1 year (%)	2 year (%)	3 year (%)	4 year (%)	5 year (%)
IA1	99.8	99.5	98.3	97.5	97.5
IA2	98.5	96.9	95.2	94.8	94.8
IB1	98.2	95.0	92.6	90.7	89.1
IB2	95.8	88.3	81.7	78.8	75.7
IIA	96.1	88.3	81.5	77.0	73.4
IIB	91.7	79.8	73.0	69.3	65.8
IIIA	76.7	59.8	54.0	45.1	39.7
IIIB	77.9	59.5	51.0	46.0	41.5
IVA	51.9	35.1	28.3	22.7	22.0
IVB	42.2	22.7	16.4	12.6	9.3

Diagnosis and Treatment

The most common sign of cervical cancer is abnormal bleeding between menstrual periods or following intercourse, douching or after a pelvic exam, or heavier or longer bleeding than usual. Increased vaginal discharge may also be a sign[1]. If cervical cancer is present, tumor stage is determined at the time of primary diagnosis and is not altered, even upon recurrence.

Cervical intraepithelial neoplasias and carcinoma *in situ*

Cryotherapy can cure between 91% and 100% of CIN 1, 75% to 96% of CIN 2 and 70% to 92% of CIN 3 lesions. Large loop excision of the transformation zone (called LLETZ in the U.K. and LEEP in the U.S.) can also be used; however, up to 20% of post-LLETZ biopsies have shown disease at the margins, and these women are at high risk of recurrence and of developing invasive cervical cancer[14].

Invasive cervical cancer

Stage IA1 cervical cancers are usually treated with a simple hysterectomy, which generally clears affected women of the disease. Those with Stage IA2 and IB cervical cancers are generally treated with radical hysterectomy and bilateral pelvic lymphadenectomy.

For women being treated by conization (cone biopsy) and/or radiotherapy, no significant difference in outcome has been found between treating Stage IB1 and IIA cervical cancers by radiotherapy only or by radical hysterectomy. Post-operative radiotherapy is used in patients with lymph node involvement.

Stage IB2 patients are not suitable candidates for surgery as there is usually pelvic and para-aortic lymph node metastasis. These patients are treated with chemoradiotherapy (cisplatin or cisplatin/5-fluorouracil [5FU]). Stage IIB and Stage III cervical cancers are treated concurrently with chemoradiotherapy (cisplatin plus 5FU).

Patients with Stage III or IVA cervical cancers who are treated with radiation, 5FU and cisplatin show a five-year survival rate of 63% compared to 57% for those treated only by radiotherapy, and a recurrence rate of 42% for those with combined therapy compared to 62% in those treated by radiotherapy alone[8].

Advanced cervical cancer is frequently treated with palliative chemotherapy, but some patients with metastatic disease can be treated with extended-field irradiation, which has been shown to have a 27% five-year survival rate. Use of the chemotherapy drug Epirubicin has also been found to be effective in the treatment of Stage III cervical cancer as well as in adjuvant therapy in preventing distant relapse (recurrence of cancer elsewhere in the body). Serum tumor marker CA-125 may be elevated in those with advanced or recurrent disease but should not be used as a marker for cervical cancer[8, 14].

Recurrence Rates

Recurrence rates vary from 8% to 26%, with a median time to recurrence of between seven months and three years[5]. Patients with Stage IB or IIA cancers have a 10% to 20% relapse rate while up to 75% of patients who have nodal metastasis or locally advanced disease will relapse. Even with combined chemoradiation therapy, 20% to 40% of all Stage II patients will relapse. Prognosis is better where the tumor recurrence is less than 3 cm, with no side wall attachment and where recurrence is more than six months following treatment[7, 8].

- A study by Perez et al. found the ten-year actuarial incidence of distant metastasis was 3% in Stage IA, 16% in Stage IB, 31% in Stage IIA, 26% in Stage IIB, 39% in Stage III and 75% in Stage IVA[7].
- A study of 106 patients in Beijing, China between 1999 and 2013 with Stage IA-IIB cervical cancers recorded a median period to recurrence of 13 months[16].
- A study of 120 patients in Bangladesh with Stage IB-IIA cervical cancer found that at year four 42% had relapsed. The median time to recurrence was 19 months for local recurrence and 33 months for distant recurrence. Eighty percent of patients who relapsed did so within three years of diagnosis[18]. Table 4 (below) shows the association of recurrence with prognostic factors.

TABLE 4: RECURRENCE AND PROGNOSTIC FACTORS

Prognostic factors	% with recurrence	Local recurrence (%)	Distant recurrence (%)
Node positive	57	23	7
Node negative	29	12	6
SCC	39	29	12
Adenocarcinoma	63	6	1
Stage IB	38	6	3
Stage IIA	42	29	11

HPV Prevention

Vaccinations against the two most common types of HPV, which can cause between 40% and 60% of LSIL and HSIL cancers, are recommended for both males and females of ages 11 and 12, although it can be given to children as young as age nine. Gardasil may also be given to males and females between ages 13 and 26, which can protect against HPV 6, 11, 16 and 18, while Cervarix can protect against HPV 16 and 18[1].

It will take many years for the full benefit of vaccination to be achieved and before a potential discount can be offered to those vaccinated. The earliest effects will be seen in women ages 20 to 29. With 80% vaccination coverage in women aged 12 and 13, a study in the U.K. projects an eventual 63% reduction in invasive cancer, a 51% reduction in CIN 3 and a 27% reduction in cytological abnormalities before age 30[4].

Summary

HPV 16 and 18 are responsible for up to three-quarters of cervical cancers globally, with squamous cell carcinoma responsible for 75% to 90% of all cases. It will be several years before the full benefit of vaccination is first seen in women between the ages of 20 to 29 and before a potential discount could be offered to those who received the vaccine.

HPV 16 and 18 are responsible for up to three-quarters of cervical cancers globally

Nearly all patients with Stage IA1 cervical cancers and patients with Stage IB1 or IIA cervical cancer can be cleared of the disease with a simple hysterectomy. No significant difference in outcome has been found between treating the disease by radiotherapy only or by radical hysterectomy.

Patients with Stage III or IVA cervical cancer who are treated by radiation plus 5FU and cisplatin have a recurrence rate of 42%, compared to 62% of those treated by radiotherapy alone. Up to 75% of patients who have nodal metastasis or locally advanced disease will relapse, and even among those treated with combined chemoradiation therapy, 20% to 40% of Stage II patients will also relapse.

The American Joint Committee on Cancer (AJCC) advises that the results of the pathologic evaluation should not be allowed to change the clinical stage but be recorded separately; hence, it is the clinical stage upon which the risk evaluation should be made as well as pricing assumptions for product development.

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LONGER LIFE FOUNDATION: LATEST NEWS

The Longer Life Foundation (LLF) recently announced its selection of research grant recipients for the 2015-2016 year.

The eight investigations being funded, three of which are in their second year, are:

John Holloszy, M.D., Director, and Luigi Fontana, M.D. Ph.D., Associate Director, Longevity Research Program
Long-Term Health Benefits of Caloric Restriction: Does Intermittent Fasting Mimic the Anti-Aging and Health Benefits of Calorie Restriction in Humans? (second year)

Stephen Oh, M.D. Ph.D.
Functional Dissection of Age-Related Differences in Disease Phenotype in Polycythemia Vera

Jason D. Weber, Ph.D.
Using Anti-Viral Biomarkers to Predict Breast Cancer Aggressiveness

Jun Yoshino, M.D. Ph.D.
Identification of Novel Blood Biomarkers and Mediators of Obesity-Induced Insulin Resistance

Zachary Pincus, Ph.D.
Early-Adulthood Predictors of Mortality and Morbidity

Jean E. Schaffer, M.D.
snoRNAs and Long-Term Risk of Diabetic Complications (second year)

Matt Ciorba, M.D.
A Randomized Control Trial of the Probiotic LGG for Prevention of Side Effects in Patients Undergoing Chemoradiation for Gastrointestinal Cancer (second year – first year 2012)

Adrianus Boon, Ph.D.
Identification of Human Genetic Variants for High Risk of Severe Influenza Disease

In January 2016, LLF will be rolling out its new website. This site, www.longerlife.org, will have a new look as well as a robust content management system that will provide greater ease of access to information about all of LLF's investigations to date.

The Longer Life Foundation is a not-for-profit partnership between RGA and the Washington University School of Medicine, an internationally recognized academic medical institution located in St. Louis, Missouri (U.S.). Founded in 1998, LLF supports and funds independent research into longevity and enhancing quality of life and wellness.

ReCite

Interesting and relevant articles to the field of insurance medicine recently appearing in the literature...

Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy
Templin C, et al. The New England Journal of Medicine 2015 Sep;373:929-38.
http://www.nejm.org/doi/full/10.1056/NEJMoa1406761
Takotsubo cardiomyopathy is a difficult history to underwrite and can be a very complicated critical illness claim to adjudicate. This article sheds some light on this clinical entity and also discusses some of the concerning long-term morbidity and mortality related to this diagnosis.

Cardiometabolic Risks and Severity of Obesity in Children and Young Adults
Skinner AC, et al. New England Journal of Medicine 2015 Oct 1;373:1307-17.
http://www.nejm.org/doi/full/10.1056/NEJMoa1502821
National Health and Nutrition Examination Survey (NHANES) data was analyzed for children and young adults with BMI > 85th percentile. Results demonstrated that the greater the severity of obesity, the higher the risks for low HDL, elevated triglycerides and glycated hemoglobin, and high systolic and diastolic blood pressure. Insurers should keep this information (and risk) in mind as most policies issued to juveniles do not require medical or paramedical exams and blood testing.

Left Atrial Appendage Closure as an Alternative to Warfarin for Stroke Prevention in Atrial Fibrillation: A Patient-Level Meta-Analysis
Holmes DR Jr, et al. Journal of the American College of Cardiology 2015 Jun 23;65(24):2614-23.
http://www.ncbi.nlm.nih.gov/pubmed/26088300
This meta-analysis of two recent trials compared warfarin treatment to the Watchman LAA Closure device. Rates of overall stroke were similar, but significantly fewer hemorrhagic strokes (HR 0.22) and cardiovascular/unexplained death (HR 0.48) were seen in patients treated with LAAC. While long-term data is lacking, insurers can be cautiously optimistic that left atrial appendage closure may provide similar if not better results.

Efficacy of fewer than three doses of an HPV-16/18 AS04-adjuvanted vaccine: combined analysis of data from the Costa Rica Vaccine and PATRICIA trials
Kreimer AR, Struyf F, et al. The Lancet Oncology 2015 July; 16(7):775-86.
http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(15)00047-9/fulltext

Cervical cancer is a leading cause of female cancer death worldwide. The HPV vaccine against the serotypes responsible for cervical cancer has been an exciting development. The Costa Rica Vaccine Trial suggested that the HPV-16/18 AS04-adjuvanted vaccine Cervarix provided equivalent efficacy regardless of the number of doses received. New data show similar protection for four years in both full and naïve cohorts of women aged 15 to 25 years, irrespective of the number of doses received in the PATRICIA trial. From the combined data, two doses given six months apart also provided similar cross-protection to three additional strains: HPV-31/33/45. This should help reduce the incidence of HPV-associated cervical cancers and have a positive impact on several types of insurance products.

RECENT WEBCASTS

Anticipating Infectious Disease Impacts in an Increasingly Globalized World

Presenter: **Dr. Kamran Khan, MPH, FRCPC**
Clinician-Scientist, Division of Infectious Diseases, St. Michael's Hospital Associate Professor, Division of Infectious Diseases, University of Toronto, Founder of BlueDot

Presenter: **Dr. J. Carl Holowaty, DBIM**
Senior Vice President, Chief Medical Director (Retired)
RGA Reinsurance Company

New infectious diseases are emerging faster today than ever before, just as many known diseases are reemerging. In an increasingly globalized world, tomorrow's epidemics could infect millions and have vast health and economic consequences. This webcast will cover what we currently know about emerging global infectious diseases, and what tools are available to help the insurance industry better plan for and respond to tomorrow's inevitable epidemics.

Electronic Health Records Data: Are You Ready?

Presenter: **Sue Wehrman**
Vice President, Electronic Health Records Initiatives
RGA Reinsurance Company

Moderated by: **Kathryn Cox**
Senior Vice President, Business Development, U.S. Markets
RGA Reinsurance Company

We discuss RGA's vision for EHRs with respect to life insurance, current initiatives related to these records, and strategies for utilization of structured and unstructured data from electronic medical data sources.

The security of experience. The power of innovation.

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