ReFlections

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IN THIS ISSUE

FROM THE EDITORS

Happy New Year, and welcome to the January 2022 issue of *ReFlections*! As always, we hope you, your families, and your loved ones continue to be safe and well.

We are about to enter our third year of the pandemic. So many of us had hoped that by now, the worst of COVID-19 would be behind us, but the virus is continuing to mutate and remains a daily factor in our lives. Fortunately, our industry has demonstrated remarkable resilience in the face of this disease, and we are sure it will continue to do so.

This issue's three articles explore an intriguing selection of topics. Frequent *ReFlections* contributor **Dr. Sheetal Salgaonkar, MBBS, MD, DBIM**, Vice President and Global Medical Director, RGA India, returns to our pages with a detailed case study on serum protein tests and how they should be considered in risk assessment.

Climate change's impact on the world and on insurance continues to grow, and **Dr. Georgiana Willwerth-Pascutiu, DBIM**, Vice President and Medical Director, RGA Toronto, also a frequent contributor, explores climate change's current challenges and opportunities for our industry.

The third article, an eye-opening examination of sleep and medicine, is the first *ReFlections* article by co-editor **Dr. Adela Osman**, Chief Medical Research Officer, RGA South Africa.

The Longer Life Foundation, RGA's research collaboration with Washington University School of Medicine in St. Louis, continues to yield substantial results. You can read about the latest research from two of its investigators on page 20.

We hope you find this issue interesting and informative. Please don't hesitate to let us know how we can continue to improve *ReFlections* for you.

Dan and Adela

HYPERGLOBULINEMIA AND RISK ASSESSMENT: A CASE STUDY

Abstract

Total serum protein, along with its components serum albumin and globulin, are frequently encountered in insurance applications. The globulins, though the smaller fraction, can be a red flag for underwriters; when elevated they can indicate impairments such as infections, chronic inflammation, or neoplasia. An elevated globulin level is generally a clinical indication to order a serum protein electrophoresis (SPEP). The main clinical value of an SPEP is to determine which of the four globulin proteins is elevated, and to differentiate between monoclonal and polyclonal gammopathies. The differentiation is vitally important, as monoclonal gammopathies, which are indicated by evidence of a monoclonal (M) band on the SPEP, may indicate malignant or premalignant conditions.

This article presents an interesting case study of an elevated serum globulin level incidentally detected in the course of an insurance application process. The cause turned out to be monoclonal gammopathy of undetermined significance (MGUS), which is the most common monoclonal gammopathy.

Serum Proteins

Total serum protein is a test commonly administered as part of the individual insurance application process. It measures the total amount of protein in the blood, as well as providing amounts of serum albumin and globulin, the two major types of blood proteins. The typical reference range for this test is 6 to 8 g/dl.

Albumin, which is made in the liver, is the most abundant protein in serum, with a reference range of 3.5 to 5 g/dl. Globulin generally comprises a much smaller fraction, with a reference range of 1.5 to 3.0 g/dl, and as total globulin values are generally arrived at by subtracting the albumin number from the total protein value, the certainty of globulin measurement is limited by the accuracy of the method used to calculate total protein and albumin.

Globulin contains many important proteins such as carrier proteins, enzymes, complement, and immunoglobulins. Most of these are synthesized in the liver, while immunoglobulins are synthesized by the plasma cells.

Most instances of elevated serum protein stem either from dehydration, in which blood volume decreases, thereby concentrating proteins, and increased production of specific proteins, which is more common. Immunoglobulins are the most commonly overproduced proteins and are generally elevated in the presence of infection and hematological neoplasm.[1]

Elevated globulin levels require underwriter awareness, as they may indicate disease states, and thus higher mortality risk. A 2014 study by Fulks et al., for example, found that persons with globulin values greater than 3.2 g/dl experience excess mortality, and those with values of greater than 4.0 g/dl have approximately double the excess mortality risk across all ages and sexes.[2] Protein levels both higher or lower than the reference range can also indicate other causes, including pregnancy, diabetes, anemia, and more.

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Dr. Salgaonkar has been a part of the Federation of Indian Chambers of Commerce & Industry's Task Force for Critical Illness and was a member of the subcommittee for Policy Formulation on Financial Inclusion of Persons with Disabilities for India's insurance industry. She is also Treasurer of the Indian Insurance Medical Officer's Association (IMOK) and was the scientific chair of the International Committee for Insurance Medicine's 2019 meeting, which was held in Mumbai. She has made significant contributions to the course curriculum of the Underwriting Diploma and the Advanced Underwriting Diploma, a joint initiative of the Association of Insurance Underwriters and the Insurance Institute of India.

The albumin/globulin (A/G) ratio is an additional metric that can be used to indicate disease states. It is not a specific marker, however, as it can change if albumin or globulin levels increase or decrease. It is important to be aware that an A/G ratio of less than 1 is clinically significant, as it can indicate either that globulin production has increased to a level exceeding that of albumin or that albumin production has reduced or ceased.

Table 1 (below) lists the many impairments related to blood protein level abnormalities.[3]

Table 1: Blood Protein Levels and Impacts

Type of protein	Normal % in blood	Causes if higher	Causes if lower
Albumin	56%	Dehydration	• Chronic cachectic (wasting) diseases • Chronic infections • Hemorrhage • Burns • Protein-losing enteropathies • Impaired liver function (resulting in decreased albumin synthesis) • Malnutrition • Nephrotic syndrome • Pregnancy
Alpha 1 globulins	3%	Pregnancy	• Alpha1-antitrypsin deficiency
Alpha 2 globulins	~13%	• Adrenal insufficiency • Adrenocortico-steroid therapy • Advanced diabetes mellitus • Nephrotic syndrome	• Malnutrition • Megaloblastic anemia • Protein-losing enteropathies • Severe liver disease • Wilson's disease
Beta globulins	~16%	• Biliary cirrhosis • Carcinoma (sometimes) • Cushing's disease • Diabetes mellitus (some cases) • Hypothyroidism • Iron deficiency anemia • Malignant hypertension • Nephrosis • Polyarteritis nodosa • Obstructive jaundice • Third-trimester pregnancy	• Protein malnutrition
Gamma globulins	12%	• Amyloidosis • Chronic infections (granulomatous diseases) • Chronic lymphocytic leukemia • Cirrhosis • Hodgkin lymphoma • Malignant lymphoma • Multiple myeloma • Waldenstrom's macroglobulinemia • Rheumatoid arthritis and other connective tissue disorders	• Agammaglobulinemia • Hypogammaglobulinemia

At this point, let us consider the applicant:

55-year-old male, nonsmoker
Applying for US$5 million of term life insurance
No significant personal or family medical history

He underwent a series of blood tests as part of his life insurance application process, which yielded the following results:

Hemoglobin	13.7 g/dl
Platelets	269 x 10^9/L
Total WBC count	7.7 x 10^9/L
Fasting blood sugar	5.5 mmol/L or 99 mg/dl
ALT (alanine aminotransferase)*	35 IU/L
AST (aspartate aminotransferase)**	22 IU/L
Total protein	8 g/dl
Albumin	3.5 g/dl
Globulin	4.5 g/dl
Serum creatinine	76 umol/L or 0.86 mg/dl
ESR (erythrocyte sedimentation rate)	22 mm/hr

**can also appear as SGPT (serum glutamic pyruvic transaminase)*
***can also appear as SGOT (serum glutamic oxaloacetic transaminase)*

Primary abnormality: Although the total serum protein result of 8 g/dl is still within normal range, the globulin result of 4.5 g/dl, which is higher than the reference range, is concerning.

Differential diagnosis: Elevated globulins can indicate infections, chronic inflammation, or neoplasia.

Which further investigation(s) would be helpful? In general, an elevated total serum protein level – something usually found incidentally – is a clinical indication to order serum protein electrophoresis (SPEP). In this particular case, even though total serum protein was within the normal range, the elevated globulin would prompt a request for further testing.

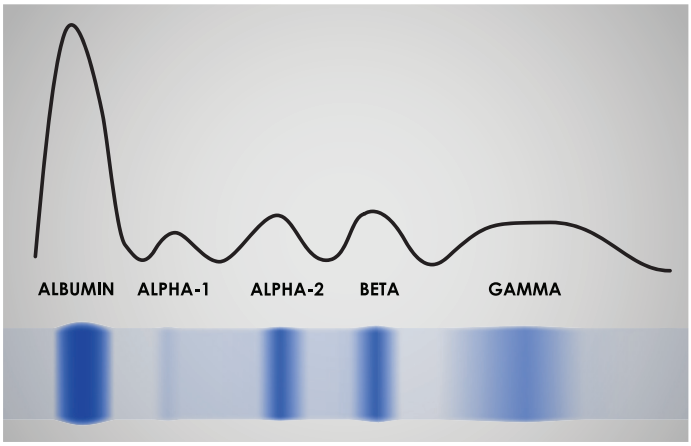
About Serum Protein Electrophoresis

SPEP is specifically used to separate and analyze amounts of the five main blood serum proteins: albumin and the four types of globulins – alpha 1 globulin, alpha 2 globulin, beta globulin, and gamma globulin. The test separates the proteins based on physical properties such as molecule size and strength of electrical charge.

To conduct the test, serum is placed upon a specific medium and an electrical charge is then applied. Albumin molecules, which are larger and have a strong net negative charge, will migrate along the x axis toward the positive electrode. Globulins, being smaller molecules with weak negative charges, will move toward the negative electrode with the gamma peak closest to the negative electrode. The amounts of each protein are then measured.

The bands and graph seen in the SPEP in Figure 1 (below) depicts the amounts of albumin and the four main globulins found in a healthy individual.

Figure 1. Sample Serum Protein Electrophoresis



As for the applicant, his elevated serum globulin level caused his case to be postponed for further evaluation. He consulted a hematologist, who advised him to undergo additional blood tests, including an SPEP, which together determined a diagnosis of monoclonal gammopathy of undetermined significance (MGUS). The applicant then submitted this additional information to the insurance company for further review.

The results of the applicant's follow-up blood tests are in Table 2, on the next page.

Table 2: Results of Post-Referral Blood Tests and SPEP	
Component	**Result**
Monoclonal (M) band	8.3 g/L
Paraproteins: • IgG • IgA • IgM	 • 13.5 g/L • 0.53 g/L • 0.54 g/L
Serum-free kappa	4.7 g/L
Serum-free lambda	6.6 g/L
Kappa-lambda ratio	0.7
Hemoglobin	12.8 g/dl
White blood cells	7.4 x 10^9/L
Neutrophils	5.8 x 10^9/L
Platelets	220 x 10^9/L

Key questions to be addressed during underwriting:

- What does this diagnosis mean?
- What is the applicant's risk of progression to multiple myeloma?
- Can life insurance be offered?

Gammopathy Types

A gammopathy is defined as a higher than normal level of gamma globulin in the blood. Gammopathies can be either polyclonal or monoclonal. Distinguishing between the two types is of paramount importance when assessing both health and insurability.

Polyclonal gammopathies: These are characterized by increased levels of more than one type of immunoglobulin, and usually signify nonmalignant conditions such as inflammatory or reactive disorders.[3] This diagnosis is associated with a broad or diffuse peak in the gamma globulin band of the SPEP (as seen in Figure 1, p. 4).

The most common causes of polyclonal gammopathies are infections. These can include: parasitic infections such as malaria, schistosomiasis, strongyloidiasis, and leishmaniasis; fungal infections such as paracoccidiodomycosis and histoplasmosis; bacterial infections such as brucellosis and rickettsial conditions; and spirochete infections such as borrelia (Lyme disease).

They can also be present in certain viral infections such as hepatitis, varicella zoster (chicken pox), and Epstein-Barr, as well as in chronic liver disease, autoimmune diseases such as rheumatoid arthritis and Sjogren's syndrome, acquired immune deficiency syndrome (AIDS), nonhematologic cancers, and certain malignant lymphomas and lymphoproliferative disorders.[4]

Monoclonal gammopathies: The critical hallmark of a monoclonal gammopathy is the presence on an SPEP of a sizable and narrow spike in the gamma globulin band. That spike, known as an M (for monoclonal) band (or spike) or M protein or paraprotein, is caused by the clonal proliferation of plasma cells. It is associated with malignant or premalignant conditions, as shown in Table 3.[5]

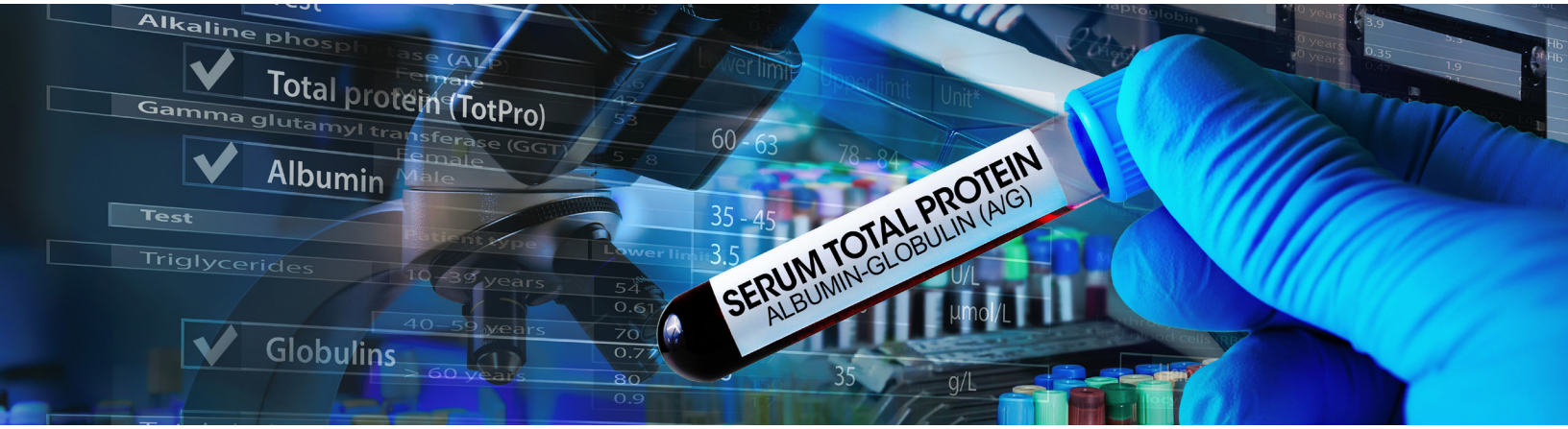
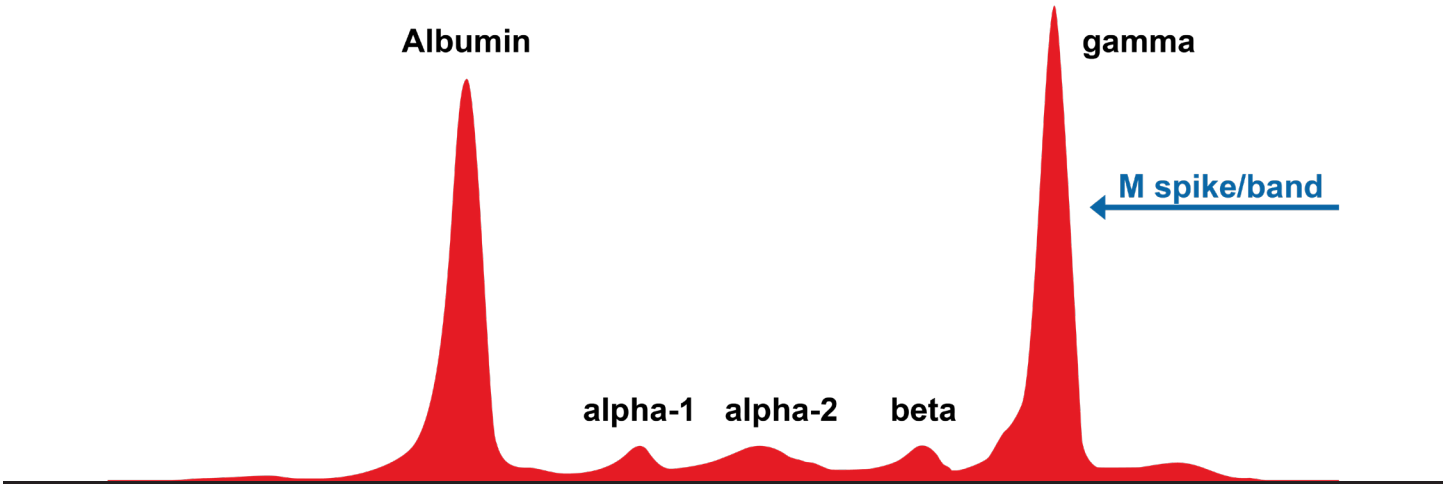


Figure 2: Monoclonal Gammopathy (M Protein) Band on SPEP in Patient with Multiple Myeloma[9]



If a monoclonal spike is present in an SPEP's gamma region, laboratories will usually perform immunofixation, a method to determine the spike's specific immunoglobulin class (most often IgG or IgA; rarely IgM, D, or E). It is also important to then determine the types and amounts of free light-chains and the serum free light-chain (FLC) assay ratio, in order to diagnose the possible impairment.

Human immunoglobulin has two identical light chains – kappa and lambda – each of which is encoded on a different chromosome. In healthy individuals, the majority of serum light chains bind to heavy chains to form antibodies, so normal serum will have low free light-chain and heavy-chain amounts.

The ratio (or proportion) of kappa to lambda light-chains in serum indicates whether there is an excess amount of one type of light-chain versus the other, and so can be used as an indicator of diseases specific to each as well as disease progression or remission.

A kappa-lambda ratio of between 0.26 and 1.65 is considered normal. A ratio of less than 0.26 indicates overproduction of lambda light-chains, whereas one higher than 1.65 indicates overproduction of kappa light-chains.

Table 3: Diseases Associated With M Protein Spikes
Multiple myeloma
Smoldering myeloma
Monoclonal gammopathy of undetermined significance (MGUS)
Waldenstrom's macroglobulinemia
POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes)
Solitary plasmacytoma
AL (amyloid light chain) amyloidosis
Light chain deposition disease
Monoclonal gammopathy of renal significance (MGRS)

About MGUS

MGUS is the most common monoclonal gammopathy. It is a clinically asymptomatic premalignant clonal plasma cell or lymphoplasmacytic proliferative disorder. MGUS is often discovered incidentally for patients while undergoing

routine blood tests or evaluation for other conditions. Its prevalence increases with age, affecting up to 2% of persons age 50 or older and about 3% of those older than age 70.[6]

The International Myeloma Working Group's criteria for diagnosing MGUS are as follows:[7]

- <30 g/L serum paraprotein (monoclonal M protein)
- <10% clonal bone marrow plasma cells
- No myeloma-defining events (e.g., hypercalcemia, renal insufficiency, anemia, or bone lesions)

A diagnosis of MGUS is important, as patients can be at risk of progressing to multiple myeloma. The average risk of progression is 1% per year.[6, 7] The following three factors can be considered adverse risks in MGUS. In the criteria, each factor is given a score of 1 for calculating the risk group.

- Type of paraprotein: IgA and IgM (both are associated with a higher risk of progression)
- M protein concentration: >1.5 g/dl
- Abnormal serum FLC (kappa-lambda) ratio: <0.26 or >1.65

Individuals diagnosed with MGUS therefore need to be followed up regularly. Current guidelines recommend follow-up blood tests every three to four months in the first year, followed by monitoring every 6 to 12 months thereafter.[8]

Table 4: Risk of Progression to Multiple Myeloma at 20 Years[6, 7]

Risk Group/Score	% Risk of Progression
Low/0	5
Low-intermediate/1	21
High-intermediate/2	37
High/3	58

Case Assessment

In the case presentation, given that the diagnosis was of an IgG MGUS, the paraprotein level was 0.83 g/dl, and serum FLC ratio was 0.7, he is in the low-risk group with a score of 0, indicating a 5% risk of progression at 20 years. Therefore, life insurance can be offered with a moderate rating.

Conclusions/Key Takeaways

- Elevated globulin levels can indicate infections, chronic inflammation, or hematological neoplasm.
- Polyclonal gammopathies usually indicate nonmalignant conditions, whereas monoclonal gammopathies indicate premalignant or malignant conditions. Hence, distinguishing them is of paramount importance.
- The critical hallmark of a monoclonal gammopathy is evidence of a monoclonal (M protein or paraprotein) spike in the gamma globulin band of an SPEP.
- MGUS is the most common monoclonal gammopathy and is often discovered as an incidental finding on routine screening tests.
- Risk stratification of MGUS (i.e., whether it will progress to multiple myeloma and if so, how quickly) can be based on the type and concentration of monoclonal paraprotein detected as well as the serum FLC (kappa-lambda) ratio.

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PRIORITIZING LIFE AND HEALTH IN A CHANGING CLIMATE THROUGH INNOVATIVE INSURANCE SOLUTIONS

Abstract

Climate change is one of the largest and most important health hazards humanity has ever faced. The World Economic Forum's Global Risks Report 2021 has placed environmental degradation as one of the five most damaging global risks every year for the past decade.[1]

During the past several years, the earth's changing climate, the pace of which has been accelerating, is becoming more broadly acknowledged as both an environmental and a public health crisis. Its natural as well as man-made drivers, and the exposures and vulnerabilities they create, are becoming more widely understood and recognized as risk factors needing both attention and mitigation.

Countries and companies around the world are accelerating their exploration of how best to take the necessary steps to successfully transition their economies into greater environmental sustainability. The insurance industry is also adapting, developing environmentally sustainable business models and using robust, forward-looking methodologies to analyze climate change's impacts.

Could the life insurance industry play a more significant and active role in mitigating climate change? Moreover, could the industry create the much-needed culture and awareness that might guide current customers and applicants toward steps they can take to reduce their carbon footprints?

The answer, clearly, is yes. To Matt Blakely, RGA's Vice President, Corporate Responsibility and Sustainability, the current historic moment is pushing companies, communities, and indeed countries, to act. Insurers, he says, need to adapt to the changing climate, but also to recognize the opportunities being presented to take big steps that can stop, and perhaps even reverse, climate change's acceleration.

This article explores the evolving nature of climate change analytics, and outlines and cites the opportunities to design innovative life and health insurance solutions for environmentally aware and carbon-conscious applicants that can benefit both humans and nature.

Introduction

Climate – that is, average long-term trends in weather – is remarkable. It impacts air, water, food, and shelter – the fundamentals of human existence – and the effects of its changes over the past several decades are clear and observable on every continent (including Antarctica) and in every human cell.

Health impairments connected with climate change include heat- and pollution-related respiratory and cardiovascular diseases, injuries, infectious diseases, and the physical and mental health of populations experiencing displacement and forced migration due to floods or drought.

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These impacts have shown remarkable variability, not just between the general population and vulnerable groups, but also among different geographies, ethnicities, and socioeconomic groups. Everyone on the planet will likely face increasing and more widespread climate change-driven impacts on mortality and morbidity in the future.

Since the year 1900 – considered the end of the pre-industrial period – the earth's average temperature has risen by slightly more than 1°C. The Paris Agreement, ratified in 2016 (coincidentally one of the warmest years on record), set a goal of restricting the average global temperature rise from 1900 to 2100 to well below 2°C and pursuing efforts to limit the actual increase to no more than 1.5°C. This goal was reaffirmed at the recent COP26 global climate summit in Glasgow, with a statement that read "Secure global net-zero by mid-century and keep 1.5 degrees (Celsius) within reach." (Reaching net-zero means that the amount of greenhouse gases produced are counterbalanced by the amount removed from the atmosphere.)

Over the past few decades, climate change's warming trend has accelerated substantially. Because of this, the insurance industry now needs to navigate a complex and evolving business environment. Not just countries, but companies as well, are working actively to transition into reducing net carbon emissions safely and sustainably. This transition has risks, including legal and public policy changes, reputation and market risk, and possible disruptions in existing business, governmental, and economic systems, as new frameworks and supporting technologies are developed, tested, and adopted.

Insurers have responded by moving to actively monitor and assess local and global climate risks on an ongoing basis. In 2016, not surprisingly, this work accelerated, with insurers increasingly focusing on developing sophisticated stress models to estimate climate change's many impacts and assess how actively governments around the world are responding.

Insurers are also engaging with regulators by sharing knowledge and expertise to answer important questions regarding available best practices, tools, and methodologies. This enables a better general understanding of the complex and synergistic nature of climate change risks and of their potential consequences for humanity.

While the current state of climate change could bring about important challenges to the insurance industry, it is also creating opportunities for insurers to play an instrumental role in helping societies adapt to and mitigate the potential short- and long-term health risks and impacts.

Short- and Long-Term Health Risks

Climate and human health are profoundly intertwined. The negative health effects of increasingly volatile weather patterns and events, such as higher frequency and severity of heat waves and more extreme global surface temperatures, can be both direct and indirect. They can range from greater potential for food and water shortages and contamination to increased capacity for the spread of vector-borne (particularly water-borne) diseases and more air pollution.

These effects are deeply synergistic, in that they cascade into a feedback loop that has strengthened over the years and continues to worsen conditions. Indeed, the 2020 report of The Lancet Countdown, an international collaboration that tracks the climate's emerging health profile, emphasized that climate change's impacts, and its developing exposures and vulnerabilities, are worsening.[1]

Heat and Health

Non-optimal atmospheric temperatures – that is, extreme highs and lows – are known to be associated with a substantial morbidity and mortality burden. And the changes in non-optimal temperature trends due to climate change are creating definite shifts in the burden.

A large mortality study published in July 2021 in *The Lancet* used ambient temperature data from 750 locations in 43 countries to assess the mortality and morbidity burden over a 20-year period (2000 to 2019). The researchers determined that more than five million extra deaths per year (i.e., 9.43% of global mortality) could be attributed to abnormally cold and hot temperatures.[7]

Interestingly, the increase in heat-related mortality and the decrease in cold-related mortality yielded a net reduction in mortality for the period.[7]

Global warming may slightly reduce the number of temperature-related deaths, largely because of the lessening in cold-related mortality, albeit with significant geographical variations. Long-term, the mortality burden is expected to increase because hot-weather-related mortality will continue to increase.

Globally, the past seven years have been the hottest since such recordkeeping began in the 1800s, with 2021 tied with 2016 as the hottest years on record.[6]

The consequences of human exposure to extreme heat are well-documented and understood. It can cause heat exhaustion and heatstroke, acute and chronic kidney disease, and exacerbate lung conditions such as asthma and cardiovascular conditions such as heart failure. Extreme heat exposure also has known mental health impacts, ranging from depression and anxiety to increased risk of interpersonal and collective violence.

People older than age 65 (especially those with comorbidities), the socioeconomically challenged, and communities lacking access to fresh water and a basic electricity infrastructure, are especially vulnerable to the effects of climate change.

Two of the more worrying statistics in the 2020 Lancet Countdown report were that vulnerable populations globally experienced an additional 475 million heatwave events in 2019, and that since 2010, there had been a 53.7% increase in heat-related mortality among those older than age 65. Indeed, 296,000 estimated heat-related deaths were registered in 2018, the majority of which were in Japan, eastern China, northern India, and central Europe.[1]

These trends continued in 2020, with the 2021 Lancet Countdown reporting a new high of 3.1 billion more person-days of heatwave exposure among people older than age 65 and a record high of an estimated 345,000 deaths in 2019. People facing social disadvantages, older than 65, or under one year of age, were the most impacted by the record-breaking temperatures, which topped 40°C in North America's Pacific Northwest region in June 2021.[6]

The impact of high atmospheric temperatures on mortality vary by region, both within and between countries, but can be modified by local physical infrastructure factors such as availability of urban green space, increased access to cooling measures such as air conditioning, and social policies that include outreach programs to protect the vulnerable.[2] A recent meta-analysis by a group of U.S. researchers highlighted that human vulnerability to extreme heat events can vary, depending on time of year, geographic location, and available physical infrastructure. The analysis, which used historical mortality and temperature data from 208 U.S. cities to quantify observed changes in heat vulnerability from 1973 to 2013, found that many communities had adapted to climate change, which yielded substantial drops in estimated heat-related mortality. The researchers assumed a 2°C increase in mean temperature since 1900, and found that modifying measures caused projected U.S. mortality to fall by more than 97% for 2003-2013 data compared with 1973-1982 data. Importantly, the researchers also concluded that if the pace of climate change continues to accelerate, the capacity of communities

to adapt to it could reach a limit, which would mean that needed infrastructure changes may not be able to be implemented quickly enough to reduce vulnerability.

Another important consideration is that certain adaptive cooling measures – specifically, use of air conditioning – could substantially increase emission levels of carbon dioxide (CO_2) and fine particulate matter. As these are considered the two main culprits of global warming, increased use of adaptive cooling measures could further accelerate global warming and health impairment trends.

Emissions and Health

Multiple studies cite air pollution as the world's fifth leading mortality risk factor, after poor diet, high blood pressure, tobacco use, and high blood sugar.

The third principal component of air pollution, in addition to fine particulate matter and CO_2, is methane. The 2021 Lancet Countdown Report states that atmospheric CO_2 concentrations have reached a concerning milestone, as they are now 50% higher than in the pre-industrial era.[5]

More than one million deaths occur every year due to particulate matter from coal-fired power plants. $PM_{2.5}$, considered the most dangerous type of fine particle, is composed of sulfates, nitrates, and black carbon (i.e., soot). These particles can penetrate deep into lungs and affect the cardiovascular system. Prolonged exposure can lead to increased incidence of and mortality from ischemic heart disease and stroke, dementia, chronic obstructive pulmonary disease (30% of worldwide COPD mortality is air pollution-related), end-stage kidney disease, and cancers of the lung, larynx, pancreas, and breast.

CO_2, which comes primarily from burning fossil fuels, is a major component of greenhouse gases (GHGs). Fossil fuel use, whether coal, oil, or natural gas, contributes 73% to all GHGs,[3] and the Intergovernmental Panel on Climate Change (IPCC) has determined that fossil fuels are today the major cause of rising average global temperatures.

The third type of emission, methane, stems from current animal agriculture practices, and are responsible for 20% to 30% of all GHG emissions. GHGs are made up of water vapor, CO_2, methane, nitrous oxide, and ozone. Methane emissions from meat and dairy livestock, the principal sources, grew by 16% from 2000 to 2017, with 93% coming from ruminants (cud-chewing animals such as cattle, buffalo, sheep, and goats).

Wildfires, another contributor to atmospheric emissions, and droughts, which create the conditions for wildfire susceptibility, have also been increasing dramatically. Nearly 60% of countries around the world had an increase in the number of days people were exposed to very high or extremely high fire danger in 2017-2020, compared with the years 2001-2004. In addition, 72% of countries had increased human exposure to wildfires across the same period.[6]

Wildfires are a crucial element in the climate change feedback loop: rising atmospheric temperatures lead to drier vegetation, which leads to more fires ignited by lightning storms, which increases particulate matter emissions, including CO_2, which plays a role in the rising global temperature. This feedback loop is generating poorer air quality and is having significant human health consequences, including increased incidence of injury and of non-infectious diseases such as cardiorespiratory conditions and cancers.

Shifting Perspectives

Exposure to climate change's impacts is already yielding numerous negative health consequences. A key to managing and hopefully reducing climate-related mortality and morbidity may be to prevent further degradation of the environment.

To avoid climate change's worst health consequences, researchers agree that global average temperature must not rise more than 1.5°C between 1900 and 2100. To achieve this, researchers have stated that GHG emissions must halve by 2030 and reach net zero by 2050. This means emissions must be reduced by 7.6% annually. This may seem almost impossible, but COVID-19 showed it could be done: GHG emissions fell by 5.8% in 2020, according to the Lancet Countdown 2021 report,[6] producing the lowest annual amount of such emissions in at least three decades.

Although this dramatic decline was almost entirely attributable to the pandemic-driven economic contraction and not to any specific climate-associated proactive measures, it demonstrated that under extreme circumstances, countries can substantially and successfully modify emissions generation. The decline was, unfortunately, short-lived: emissions rose in 2021.[6]

By placing health and wellness at the center of climate change mitigation and adaptation policies, remarkable benefits may be achieved. A February 2021 study by Hamilton et al., offered a glimpse into the future by modeling how certain wellness-related actions aimed at mitigating GHG emissions in nine selected countries (Brazil, China, Germany, India, Indonesia, Nigeria, South Africa, U.K., and U.S.), such as eating less agriculturally-produced meat, increasing consumption of fruit, vegetables, and plant-based protein sources, and engaging in more individual physical activity, could substantially improve human health while also improving the environment.[3]

The Hamilton study compared the potential health effects of maintaining the Current Pathway Scenario (CPS) (i.e., no change in the nationally determined commitments toward mitigating climate change) with a Sustainable Pathways Scenario (SPS), in which countries adhere more closely to achieving the goals of the Paris Agreement and prioritize human well-being. The researchers determined that such a shift could generate, by 2040, an annual reduction in the nine countries of 1.18 million air pollution-related deaths, 5.86 million diet-related deaths, and 1.15 million deaths due to physical inactivity.[3]

Diet is one of the leading risk factors for premature death globally. Diets high in red meat have been shown to be a factor in mortality from neoplasms and diabetes mellitus. In addition, the 2021 Lancet Countdown reported that excess red meat consumption contributed to an estimated 842,000 deaths in 2018, a 1.8% rise from 2017.[6] Consuming more plant-based foods and reducing consumption of red meat and processed foods can improve the environment (by reducing agricultural emissions) as well as human health. As for physical activity, the projected reduction of mortality from more walking and cycling was remarkable: 1.15 million deaths in all nine countries could be avoided in 2040 by following the SPS.

What Can Life Insurers Do?

For life insurers, ongoing monitoring and analyses of climate data and trends will enable companies to assess climate change's current and potential impacts on mortality and morbidity. This data will impact everything from product design, pricing, in-force management, and underwriting new business, to operating models, risk management practices, and investment assets. Climate-focused transitions can create stranded assets, and can also create new opportunities for investment that will ensure insurance companies have the capital to pay future claims.

The next 10 years are seen by climate researchers as critical in determining how climate change-focused adaptation and mitigation efforts can be increased by finding robust and reliable solutions to enable successful transitions by both countries and companies to a lower carbon emissions future.

The current pandemic is a reminder that health depends on climate, and a healthy and biodiverse ecosystem is an essential component of wellness. The planet is currently undergoing a biodiversity crisis, with approximately one in every eight species under threat of extinction. Fortunately, the future of human and environmental health can be shaped by actions taken now.

Finding Solutions

As the life insurance industry carefully navigates its transition toward a more sustainable ecological posture, it is becoming apparent that the industry's understanding of climate-driven risks must continue to improve. Fortunately, the evolving framework for these transitions is helping to clarify and possibly strengthen the industry's role, as it is generating

opportunities to develop new types of insurance products and to promote the transformations needed to mitigate climate change.

Some opportunities could include:

- Linking the consumer and the climate as "co-beneficiaries" by addressing climate change and human well-being simultaneously
- Developing green insurance products that benefit the applicant and the environment
- Engaging with applicants to drive and incentivize positive behaviors for a more sustainable future
- Committing to net-zero asset portfolios backing life insurance liabilities

How can life insurers play a role in influencing societal behavior and thereby improve the state of the natural world?

Life insurers currently have an unprecedented opportunity to take certain steps that could make a real difference in the planet's environmental future. Creating innovative products that can educate, encourage, empower, and incentivize environmentally conscious applicants could be key to cultivating a healthier ecosystem and a more sustainable future. Combining the passion for environmental sustainability on the part of many current and potential customers with the industry's extensive expertise in underwriting and actuarial science can result in products designed to benefit both applicants and the environment, and ultimately play a strategic role in improving the health of Planet Earth and all living organisms upon it.

Taking steps such as developing and implementing business and investment models that incorporate environmental sustainability and creating insurance solutions that focus on improving personal and environmental health can also yield a brighter and more sustainable future.

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WHY SLEEP MATTERS

Abstract

For centuries, sleep was considered a passive state of absolute repose of the brain. In 1953, however, the discovery of rapid eye movement (REM) sleep and non-REM (NREM) sleep made it clear that sleep is an active process that is fundamental for healthy brain function.

Even though the relationship between sleep and health is now well-documented and sleep is known to be key to human physical and mental well-being, many people still have the incorrect notion that sleep is a luxury that can be minimized or even skipped in order to accommodate busy lives and endless to-do lists.

Phrases such as "I'll sleep when I die" or "You snooze, you lose" represent the modern "always on" ethos. This, combined with the push by many cultures toward success at any cost, has led societies around the world to glamorize and celebrate sleep deprivation. Indeed, sleep has come to be treated as a dull chore performed reluctantly and out of obligation, and one that needs to be dispatched with as quickly as possible. This attitude has led to a global sleep deprivation crisis: insufficient sleep is currently acknowledged as a public health epidemic that is often unrecognized, underreported, and has sizable economic costs.

Sleep Deprivation, Sleep Deficiency, Insomnia: Are They All the Same?

Sleep disorders are a group of ailments affecting a sizable segment of the world's population (approximately 35% to 50% of U.S. adults alone). They compromise sleep and result in fewer objective hours of sleep, lower quality sleep, and potential impacts on both physical and cognitive health.

A formal diagnosis of a sleep disorder is initially based on sleep duration, defined as the total amount of time a person needs to spend asleep in a night to be well-rested. For adults, that amount is between seven and nine hours, and for children and teens, between eight and ten hours.

Being well-rested, however, is more than just how many hours are spent asleep; it also refers to the quality of sleep experienced.

The phrase "sleep deprivation" is generally used to describe voluntarily reduced sleep time. Causes can include work obligations, lifestyle choices (e.g., staying up late to binge-watch a TV series), and poor or inadequate sleep hygiene (e.g., maintaining uncomfortable bedroom temperatures, ingesting caffeine or alcohol close to bedtime, having irregular bedtimes).

The terms "sleep deficiency" and "sleep insufficiency" are used more frequently to refer to medical conditions that can reduce quantity and/or quality of sleep, and keep a person from waking up refreshed.[1] Sleep apnea, for example, is a condition where dozens of nightly awakenings occur due to stoppage of breathing, which compromises both sleep duration and quality. Insomnia disorder, which is defined in the Diagnostic

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Dr. Adela Osman is the Chief Medical Research Officer for RGA South Africa, responsible for all medical aspects of the claims, underwriting, product development, and pricing functions. She also leads RGA South Africa's research and development efforts and is a frequent presenter, sharing her expertise through webinars, articles, and other media. As part of the executive team, Dr. Osman regularly engages with clients to support their business objectives.

Dr. Osman graduated from University of the Witwatersrand in 2005 with a Bachelor of Medicine and Surgery (MBBCh). After completing her internship and community service, she worked as a Medical Officer in state hospitals before joining a private practice and focusing on family health.

Dr. Osman has completed specialized training in disability medicine and impairment with the American Board of Independent Medical Examiners (ABIME). She further expanded her studies with the ABIME by successfully completing medico-legal report writing and court testimony training, which equips her to act as an independent medical examiner and scientific expert witness. She is currently chairperson of the Medical and Underwriting Standing Committee of the Association for Savings and Investments South Africa (ASISA), which protects the right of the risk industry to underwrite, manage quality assurance of risk information, and draft best practice underwriting guidelines for the South African market.

and Statistical Manual-5 (DSM-5) as difficulty falling asleep, staying asleep, or early morning awakenings despite the opportunity to get adequate sleep, is another cause of sleep deficiency. Insomnia can result in feeling unrefreshed upon awakening, low energy levels, mood swings, poor quality of life, and impaired work performance, and can ultimately lead to significant psychological distress.[2]

A third medical condition is narcolepsy, a chronic neurological disorder that affects the brain's ability to control sleep-wake cycles. It is far rarer than insomnia or sleep apnea, affecting approximately one of every 2,000 people, and is characterized by persistent drowsiness and overwhelming urges to sleep (sleep attacks), sometimes called excessive daytime sleepiness (EDS), regardless of how much objective sleep the person may have had. People with narcolepsy can also experience episodes of microsleep, cataplexy, and vivid hallucinations and/or sleep paralysis just before falling asleep or upon awakening. These episodes can occur at any time, which can leave the individual at great risk. If left untreated, narcolepsy can have a substantial effect on daily work and leisure activities and can interfere with cognitive function as well.[22]

How Poor Sleep Affects the Body

Sleep plays a fundamental role in the effective functioning of most body systems.[3] Both sleep deprivation and insufficient sleep lead to the derailment of bodily systems, which can have serious and far-reaching health effects.

Acute sleep deprivation increases the risk of unintentional errors and accidents as a result of slowed reaction time and risk of microsleeps (sleeps that last from a few to several seconds, during which the individual is unaware of having slept). Individuals who are sleep-deprived are also more likely to struggle in school and work settings or to experience mood changes that may affect personal relationships.

Chronic insufficient sleep can create significant risks to physical and mental health and is known to contribute to a wide range of health problems, such as:

Cardiovascular diseases

Studies have found strong associations between sleep deficiency and cardiovascular diseases (CVDs),[4] including high blood pressure, coronary heart disease, heart attack, and stroke. Inflammation is a well-established key mechanism in CVD risk and as sleep deprivation is associated with increased inflammation and negative cardiovascular outcomes,[5] there could be a possible mechanism linking sleep deficiency with CVD.

Hoevenaar-Blom, et al., in a 12-year prospective study of 20,432 healthy men and women in the Netherlands, found that individuals who slept six or fewer hours a night had a 15% higher risk of CVD incidence and a 23% higher risk of coronary heart disease (CHD) incidence compared to people who regularly slept seven to eight hours a night. When sleep quality of the two groups was compared, individuals with shorter sleep durations and poorer subjective sleep had a 63% higher risk of CVD and

79% higher risk of CHD than those who had normal sleep durations and good sleep quality.[6]

Diabetes

The importance of sleep to hormone and glucose metabolism was first documented more than four decades ago. Sleep deprivation alters glucose homeostasis, leading to insulin resistance and increased risk of diabetes. One postulation is that initiation of slow-wave sleep is associated with a decrease in the brain's use of glucose, stimulation of growth hormone release, inhibition of cortisol secretion, decreased sympathetic nervous system activity, and increased vagal tone (which is associated with lower heart rate and increased heart rate variability). All of these correlates of slow-wave sleep affect total body glucose homeostasis; therefore low amounts of slow-wave sleep, which normally occur in aging individuals and in those experiencing sleep disorders, is associated with decreased glucose tolerance.[7]

One study directly tested this hypothesis by selectively suppressing slow-wave sleep in healthy young adults and examining its effects on their glucose tolerance. The amount of slow-wave sleep was reduced by nearly 90% without reducing total sleep duration. Intravenous glucose tolerance tests (GTTs) were performed after two nights of undisturbed sleep and again after three nights of slow-wave sleep suppression. After suppression of slow-wave sleep, GTTs showed insulin sensitivity had decreased by around 25%, dropping to levels reported in aging individuals and in populations at high risk for diabetes.[7] Additional research continues to support the hypothesis.

It is thus evident that the body's ability to regulate blood sugar is impacted by insufficient sleep, increasing the risk of metabolic conditions.[8]

Obesity

Sufficient epidemiological evidence exists to support a link between sleep loss and obesity. A 2009 study found that people tend to consume more calories and carbohydrates when they do not get enough sleep, due to diminished activity in the brain's appetitive evaluation regions.[9] This, combined with excess subcortical responsivity in the amygdala, has been shown to result in the selection of foods most capable of triggering weight gain,[10] and appears to be one of several ways sleep difficulties may be tied to obesity and problems maintaining a healthy weight.

Immunodeficiency

Sleep is a portion of the 24-hour circadian cycle, which affects most living things on Earth and governs biological processes. Many immune functions display prominent cycles that are in synchrony with the light-dark cycle, reflecting the synergistic actions of sleep and circadian rhythms on these functions.[11] Prolonged sleep curtailment and its accompanying stress response invoke a persistent production of pro-inflammatory cytokines, best described as chronic low-grade inflammation. This chronic inflammation induces immunodeficiency, as evidenced by studies that show diminished immune response to vaccination against influenza after six days of restricted sleep[12] and enhanced susceptibility to the common cold with poor sleep efficiency.[13]

Pain

Sleep loss has been shown to amplify the brain's pain-sensing regions and to block its natural analgesia centers. Sleep-deprived individuals are therefore at higher risk of developing pain or of feeling as if their pain is worsening.[14] Pain may also cause sleep interruption and curtailment, resulting in a negative cycle of worsening pain and sleep.

Mental health disorders

Sleep and mental health are known to be closely intertwined. Decades of research have shown that sleep disturbances are highly prevalent in mental health disorders and are associated with adverse effects upon cognitive, emotional, and interpersonal functioning. Impaired sleep has strong associations with many, if not all, mental health conditions (MHC), and sleep problems have traditionally been viewed as a consequence of MHC.[15] While this is not contested, evidence also suggests that problems sleeping can contribute to the formation of new MHCs[16] and to the maintenance of existing ones.

Growing evidence also suggests an association between both short and long duration of habitual sleep with adverse health consequences. A recent dose-response meta-analysis of prospective studies provided further evidence that sleep duration that is either too short or too long is associated with higher risk of all-

cause mortality and cardiovascular events, with the lowest risk at approximately seven hours per day of sleep duration. Short and long sleep duration may also share some relevant mechanisms in relation to all-cause mortality and cardiovascular events in that extreme sleep duration on both sides was associated with elevated C-reactive protein. Distinctive mechanisms with their own characteristics, however, may operate at either end of the spectrum, and longer term randomized controlled trials will be needed to determine causality and to elucidate the underlying mechanisms.[23]

Impact on Insurance

Sleep deficiency is associated with higher mortality risk and productivity losses at work. Financial and nonfinancial costs associated with inadequate sleep are substantial: the U.S. Centers for Disease Control and Prevention (CDC) estimates that as many as 6,000 deaths in the U.S. each year are caused by drowsy driving alone.[17] Sleep deficiency has also been calculated to incur hundreds of billions in added U.S. healthcare costs[18] as well as more than $400 billion in productivity losses per year.[19]

Growing evidence suggests an association between sleep duration and adverse health consequences.

Currently, sleep insufficiency is being exacerbated by the COVID-19 pandemic. "Coronasomnia," the term used, is characterized by symptoms that include an increase in sleep problems since the pandemic's start as well as anxiety, depression, and stress.

Impaired sleep quality is also associated with the massive increase in screen time throughout the world's populations. A 2020 study concluded that sleep quality can be negatively impacted by using mobile phones or tablets for more than eight of every 24 hours, using them for at least 30 minutes after the lights have been turned off for sleep, and keeping the devices within easy reach after bedtime.[20]

Because of the adverse effects of insufficient or impaired sleep on health, well-being, and productivity, sleep quality may play an important and potentially modifiable role in multiple health conditions as well as risk stratification in the insurance sector.

Currently, many wellness programs take sleep quantity and quality into account, but insurers do not routinely use sleep monitoring results as a risk rating factor during underwriting. With the advent of wearables and advances in app technology, however, consumers are increasingly self-monitoring sleep, which could indicate an opportunity for insurers to start using metrics related to sleep more routinely to stratify risk.

Conclusion

Humans sleep approximately one-third of their lifetimes. The value of sleep, even as a risk stratification factor, is often underrated. Sleep plays a vital role in good health and well-being throughout life and promoting sufficient good quality sleep should become a key focus of the insurance industry.

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Longer Life Foundation

An RGA/Washington University Collaboration

The Longer Life Foundation (LLF) is a collaboration of RGA and Washington University School of Medicine in St. Louis. Founded in 1998, LLF funds carefully curated investigations of scientific and public health factors predicting and impacting health and wellness.

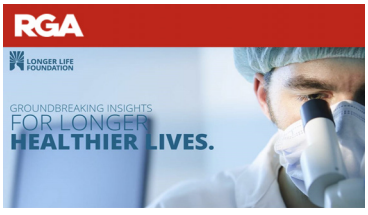
To learn more, please visit www.longerlife.org or reach out to Dr. Daniel D. Zimmerman at dzimmerman@rgare.com, Dr. Dave Rengachary at drengachary@rgare.com, or Dr. Preeti Dalawari at preeti.dalawari@rgare.com.

Robert M. Musen retired from LLF's Board of Governors at the end of 2021. For more than 20 years, the Foundation has benefited from Bob's knowledge and wisdom. We are grateful for his many years of leadership and service and wish him well.

The Fall 2021 Advisory Group meeting featured presentations from two second-year LLF grant recipients about their cutting-edge research. **Devesha Kulkarni, Ph.D.**, discussed her investigation into the role of gut microbiota in obesity, and **Alex Holehouse, Ph.D.**, spoke about his work into predicting the impact of genetic variations within intrinsically disordered protein regions.

LLF's Grand Rounds sponsorships continue: On September 23, 2021, **Dr. Jacquelyn Y. Taylor, Ph.D.**, **PNP-BC, RN, FAHA, FAAN,** presented a virtual talk titled, "A Research Trajectory in Hypertension Genomics." She focused on her career as a researcher into worldwide health disparities for common chronic conditions among vulnerable populations. She also covered the importance of mentorship, pilot funding, and interdisciplinary contributions to scientific endeavors.

On January 6, 2022, LLF sponsored a Grand Rounds by **Jeffrey P. Henderson, M.D., Ph.D.** LLF is a long-time supporter of Dr. Henderson's research. Our most recent grant to him, in 2021, supported his investigation into prognostic biomarkers of severe disease in COVID-19 patients.



LLF NEWSLETTER

The December 2021 issue of the LLF Newsletter is available here.

RECENT WEBCASTS

RGA's most recent webcasts, available for viewing at your convenience, focus on topics of interest to underwriters, claims managers, and insurance medical directors.


Blood Cancer: The Causes, The Research, The Future
(running time 17:00)
Dr. Daniel D. Zimmerman, DBIM, Senior Vice President, Head of Global Medical, RGA; and Grant Challen, Ph.D., Associate Professor, Department of Medicine, Division of Oncology, Stem Cell Biology, Washington University School of Medicine in St. Louis
https://www.rgare.com/docs/default-source/marketing/global-claims-podcast/blood-cancer-podcast.html

This webcast, part of RGA's Take 10 podcast series, examines the fascinating field of blood cancer, delving into Professor Challen's cutting-edge research into specific gene mutations and their role in blood cancers and exploring what the future may hold in terms of clinical advancements and prevention.

Type 2 Diabetes: Remission?
Dr. Daniel D. Zimmerman, DBIM, Senior Vice President, Head of Global Medical, RGA Reinsurance Company

Part I: Possibilities and Implications (running time 10:05)
https://www.rgare.com/knowledge-center/media/videos/type-2-diabetes-remission-part-1-possibilities-and-implications
Part II: Interventions and Guidance (running time 10:34)
https://www.rgare.com/knowledge-center/media/videos/type-2-diabetes-remission-part-2-interventions-and-guidance

Diabetes mellitus has long been considered a chronic illness which, once diagnosed, would be an intractable and permanent part of that person's life. Currently emerging research, however, is cause for optimism, as several studies indicate reversal to the point remission is possible.


Opioid Addiction and its Impact on Actuarial Science
(running time 7:36)
Gayle Kanchanapume, Executive Director, Global Claims Value Added Specialist, RGA Australia; and Dr. James Kim, Medical Director, Centers for Pain Management, Brampton, Ontario, Canada
https://www.rgare.com/knowledge-center/media/videos/opioid-addiction-and-its-impact-on-actuarial-science

Addiction to opioids, whether legal or illicit, and its consequences, continues to be an issue for clinicians and insurers. Presenters Dr. Kim, who is also a medical consultant to RGA, and Ms. Kanchanapume engage in a lively discussion about this important topic.

ReCite

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

Association of Bariatric Surgery with Major Adverse Liver and Cardiovascular Outcomes in Patients with Biopsy-Proven Nonalcoholic Steatohepatitis

Aminian A, et al.
JAMA. 2021 Nov 11; 326(20): 2031-42.
https://jamanetwork.com/journals/jama/fullarticle/2786270

The obesity epidemic continues to present ongoing challenges to clinical and insurance medicine. This study sought to assess the impact of bariatric surgery on serious adverse outcomes in patients with nonalcoholic steatohepatitis (NASH), a type of fatty liver disease. The authors indicated that no prior therapy had been shown effective.

In this study of 1,158 participants with confirmed NASH, more than half of whom were women, 650 underwent bariatric surgery (Roux-en-y or sleeve gastrectomy) and 508 served as a control group with nonsurgical management. The surgical intervention group experienced significantly lower risk of incident major adverse liver outcomes and major adverse cardiovascular events. (Four of the patients in the surgical group, however, did die within the first year of the procedure due to surgical complications.)

Editor's Note: *Non-alcoholic fatty liver disease is commonly encountered during underwriting. Biopsy-proven NASH is seen less often, but its importance remains significant. Results of this study are fundamentally reassuring and add to the growing body of evidence demonstrating beneficial metabolic effects of bariatric surgery.*

Genome-Wide Association Analyses Highlight Etiological Differences Underlying Newly Defined Subtypes of Diabetes

Mansour Aly D, et al.
Nature Genetics. 2021 Nov 4; 53(11):1534-42.
https://www.nature.com/articles/s41588-021-00948-2

In recent years, a growing body of evidence has emerged indicating significant variability and heterogeneity within type 2 diabetes mellitus. Namely, it is being reproducibly divided into five subtypes, each of which has different disease progressions and associated risks of complications. The authors used genome-wide association and genetic risk score analysis to study genetic drivers of the different subtypes. Overall, results support the presence of at least partially distinct genetic backgrounds reflecting possible different etiologies.

Editor's Note: *Insurers should be aware of the accumulating evidence that type 2 diabetes is a heterogenous disease with several subtypes, each of which is associated with different outcomes. This may impact future underwriting approaches and pricing exercises.*

Effect of Intra-Articular Platelet-Rich Plasma vs. Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients with Knee Osteoarthritis: The RESTORE Randomized Clinical Trial

Bennell KL, et al.
JAMA. 2021; 326(20): 2021-30.
https://jamanetwork.com/journals/jama/fullarticle/2786501

Despite a lack of high-quality evidence of the efficacy of platelet-rich plasma (PRP) injections for knee osteoarthritis (OA), the use of PRP as a therapeutic agent is increasing. The authors conducted a randomized, placebo-controlled study with 288 participants with mild to moderate medial knee OA, comparing leukocyte-poor PRP with saline placebo. At 12 months, results indicated a non-significant difference in symptoms or joint structure. The authors concluded the findings do not support the use of PRP in the treatment of knee OA.

Editor's Note: *Insurers engaged in disability or health cover should familiarize themselves with the current indications and clinical uses of PRP therapy. As this study demonstrates, clinical practice may not necessarily be consistent with evidence-based findings.*

Long-Term Cognitive Decline After Stroke: An Individual Participant Data Meta-Analysis

Lo JW, et al.
Stroke. 2021 Nov 15.
https://doi.org/10.1161/STROKEAHA.121.035796

After stroke, it is common for patients to develop cognitive impairment. The authors studied factors to determine the trajectory and magnitude of cognitive change after stroke. Almost 1,500 patients with a mean age of 66.3 years were followed for a median of 2.68 years. One-step individual participant data meta-analysis was used to examine the rate of change in cognitive function and risk factors for cognitive decline. Recurrent stroke and older age were associated with a more rapid decline in global cognition and overall decline was also significantly faster compared with stroke-free controls.

Editor's Note: *Stroke in insured lives can have significant impact on quantity and quality of life as well as many product lines. While cognitive decline is a known complication of stroke, this study adds further understanding to the differences in trajectory, specifically as related to global cognition post-stroke.*

RGA THOUGHT LEADERSHIP PUBLICATIONS

RGA publishes content on many topics of interest to insurers. Here are links to some recent publications:

Global Health Brief: Update – Robotic Surgery
By Dr. Fathul Rahman, Associate Director, Health Claims Management, Labuan Health, RGA
https://www.rgare.com/knowledge-center/media/articles/global-health-brief-update-robotic-surgery

Healthcare Ripple Effects of the COVID-19 Pandemic
By Anna Currie, Underwriting Research and Development Manager, RGA UK
https://www.rgare.com/knowledge-center/media/covid-19/healthcare-ripple-effects-of-the-covid-19-pandemic

Predicting Cognitive Decline: Advances in Pre-Clinical Diagnosis of Alzheimer's Disease
By Hilary Henly, FCII, Global Medical Researcher, RGA
https://www.rgare.com/knowledge-center/media/research/predicting-cognitive-decline-advances-in-pre-clinical-diagnosis-of-alzheimer-s-disease

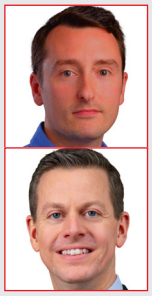
Vaccination Status: Insurance Pricing Considerations
By Neil Parkin, Head of Business Development, South Africa, RGA
https://www.rgare.com/knowledge-center/media/research/vaccination-status-insurance-pricing-considerations

What Will It Take to Wipe Out SARS-COV-2 … Or Is The Coronavirus Here to Stay?
By Hilary Henly, FCII, Global Medical Researcher, RGA
https://www.rgare.com/knowledge-center/media/research/what-will-it-take-to-wipe-out-sars-cov-2

Capturing Climate Change: The Challenge of Modeling Long-Term Life and Health Risks in a Warming World
By Dr. Georgiana Willwerth-Pascutiu, DBIM, Vice President and Medical Director, Global Medical, and Chris Falkous, FIA, Vice President, Senior Biometric Insights Actuary, Global Data and Analytics, RGA
https://www.rgare.com/knowledge-center/media/articles/capturing-climate-change-the-challenge-of-modeling-long-term-life-and-health-risks-in-a-warming-world

COVID-19 Brief: Global Vaccine Equity – Are We In This Pandemic Together?
By Gayathri Ravi Shankar, Knowledge Management and Information Specialist, Strategic Research, RGA
https://www.rgare.com/knowledge-center/media/covid-19/covid-19-brief-global-vaccine-equity-are-we-in-this-pandemic-together

Cardiovascular Aging: Causes and Intervention
By Hilary Henly, FCII, Global Medical Researcher, RGA
https://www.rgare.com/knowledge-center/media/research/cardiovascular-aging-causes-and-intervention



The Predictive Utility of Polygenic Risk Scores (abstract only)
By Richard Russell, Lead Health Data Scientist, Global Data and Analytics, RGA; Peter Banthorpe, Managing Director, RGA; Cathryn Lewis, Professor of Genetic Epidemiology and Statistics, Statistical General Unit, King's College London; et al.
https://www.rgare.com/knowledge-center/media/research/the-predictive-utility-of-polygenic-risk-scores

Genetics and Insurance: Challenges and Opportunities III
By Dr. John Lefebre, FRCPC, Vice President and Senior Global Medical Director, Global Medical; Dr. Sheetal Salgaonkarm, MBBS, MD, DBIM, Vice President and Medical Director, Global Medical; Dr. Georgiana Willwerth-Pascutiu, DBIM, Vice President and Medical Director, Global Medical; Hilary Henly, FCII, Global Medical Researcher; and Dr. Daniel D. Zimmerman, DBIM, Senior Vice President, Head of Global Medical, RGA.
https://www.rgare.com/knowledge-center/media/research/genetics-and-insurance-challenges-and-opportunities-iii

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