ReFlections

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IN THIS ISSUE

FROM THE EDITORS

We are pleased to welcome you to our newly redesigned ReFlections – RGA's Global Medical Newsletter!

First and foremost, we want to send out a special note of gratitude to Dr. J. Carl Holowaty for his excellent stewardship of this newsletter over the years. With his retirement earlier this year, the editorship of ReFlections has passed to a new team:

- Dr. Phil Smalley, Senior Vice President, Global Chief Medical Officer
- Dr. Dan Zimmerman, Vice President and Medical Director
- Neil Wilkinson, Vice President, Medical Services

ReFlections will continue to be published three times a year and will continue to feature two to three articles of interest per issue. These articles will be researched and written by RGA medical doctors as well as other members of our global complement of experts. Our intent is to continue to provide articles that are interesting, practical, and relevant to your work.

With this issue, some new elements are being introduced. On p. 11, you will find a new column, ReCite, which provides summaries of and links to medical articles that are potential "food for thought" for insurance professionals. Also, while ReFlections continues to be available in printed form, we are also establishing a new digital platform.

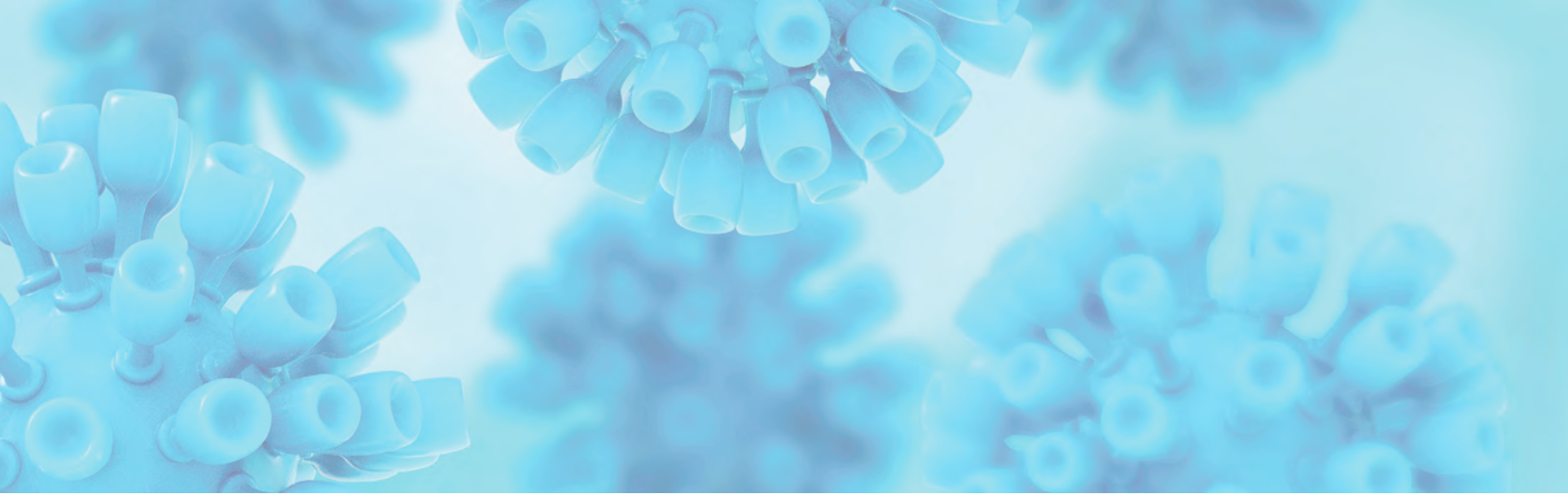
You will see a stronger global emphasis, as appropriate, in the discussions of medical advances, underwriting, claims and insurance products.

Lastly, we will continue to report on the cutting-edge mortality and longevity research at Washington University School of Medicine in St. Louis. This research is funded by The Longer Life Foundation, which is supported by RGA and Washington University in St. Louis.

As always, we welcome and would appreciate any feedback or suggestions for future topics to help us make this newsletter easy to read, enlightening, and valuable to you, our readers.

Thank you,

Phil, Dan and Neil



HEPATITIS C – THE NEW FRONTIER

More than 20 years have passed since the hepatitis C virus (HCV) was identified as the pathogen formerly known as non-A, non-B hepatitis. During that time, the pathophysiology and sequelae of chronic HCV infection, including extra-hepatic manifestations, cirrhosis, end-stage liver disease and hepatocellular carcinoma, were described. In general, treatments have improved incrementally over those years.

Since 2011, great strides have been made therapeutically and most individuals with HCV may now be considered curable. This article will update the reader on these treatments and the implications for both life and living benefits insurance products and claims.

Global Epidemiology

Hepatitis C is a major global health issue. The main burdens of morbidity and mortality come from the sequelae of chronic infection.

It is estimated that approximately 170 million people are infected worldwide, and that 350,000 deaths occur annually due to all HCV-related causes. Current high prevalence areas (> 3.5%) include Central and East Asia, and North Africa/Middle East. Moderate prevalence areas (1.5-3.5%) include: South and Southeast Asia; Andean, Central, and Southern Latin America; Australasia (including Australia and New Zealand), the Caribbean, Oceania (the Pacific islands); Central, Eastern, and Western Europe; and sub-Saharan Africa. The lowest prevalence areas (< 1.5%) are Asia Pacific (encompassing Brunei, Japan, South Korea and Singapore), tropical Latin America and North America.[1]

The causes of high prevalence are several. Egypt for example, has the highest prevalence rate (~10%) in the world due to inadequate infection control during medical and dental procedures. The mass campaigns to control schistosomiasis, which generally spreads through contaminated water, may have also exposed many to the HCV via improperly sterilized glass syringes.[2]

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Daniel D. Zimmerman, M.D., is Vice President and Medical Director of RGA Reinsurance Company and a member of RGA's Global Support Team. He is responsible for case consultation, product development, internal and external education, client support, and representing RGA to key industry professional organizations. He has held leadership positions with the American Council of Life Insurers (ACLI) and participated in program committees of the American Academy of Insurance Medicine (AAIM).

Risk factors for hepatitis C transmission vary among the world's developed and developing regions. Prior to 1992, most hepatitis C infections in developed countries were acquired through blood transfusions and blood products. In developing countries, blood products and unsafe medical practices continue to play a major role in transmission. HCV is also transmitted via injecting drug use, body piercing, tattooing, religious scarification, and sharing of personal care items such as razors, toothbrushes and manicure tools. Worldwide, there is also little doubt that sexual transmission can occur, and the risk increases for individuals who have had multiple partners, in the presence of sexually transmitted infections, and for men who have sex with men.

After epidemiologic investigation, no risk factors can be identified in up to 20% of those infected with hepatitis C.[4, 5]

Extra-Hepatic Manifestations

While hepatitis C primarily affects the liver, it is well recognized that the infection can also cause up to 40% of infected individuals to also develop at least one extra-hepatic condition, such as:

- Cryoglobulinemia
- Membranoproliferative glomerulonephritis
- Hypertension (related to renal disease)
- Leukocytoclastic vasculitis
- Neuropathy
- Porphyria cutanea tarda
- Lichen planus
- Increased risk of DM-2
- Increased risk of lymphoma

These conditions – or the risk of developing these conditions – may or may not be completely mitigated by successful eradication of hepatitis C. The astute underwriter should also consider the possible presence of hepatitis C when any of these conditions are encountered during underwriting and no hepatitis C test results are in the file.

Sustained Viral Response (SVR)

SVR is a desired endpoint of HCV therapy. According to the European Association for the Study of the Liver (EASL), SVR is defined as HCV RNA being undetectable in a sensitive assay (<15 IU/ml) 12 weeks (SVR12) and 24 weeks (SVR24) after completion of treatment.[7] SVR is associated with a 97-100% chance of being HCV RNA-negative during long-term follow-up and can therefore be considered a sign that an HCV infection has been cured.

Until the recent introduction of direct-acting antivirals (DAA), SVR was defined as an undetectable viral level at 24 weeks post-treatment. However, as undetectable levels at 12 weeks post-treatment are currently usually maintained through week 24, many clinical studies now report and define SVR at 12 weeks (SVR12).

Treatment Advances

Significant advances occurred in 2011 with regard to the treatment of HCV when two DAAs were licensed for use in combination with pegylated interferon-alpha and ribavirin. Both boceprevir and telaprevir were approved by the Food and Drug Administration (FDA) in May 2011 and resulted in significantly improved SVR in HCV genotype 1 individuals over pegylated interferon and ribavirin therapy alone.[6]

However, both therapies quickly became obsolete due to the release of newer, more effective agents. Telaprevir was removed from the market in October 2014 and boceprevir will no longer be available after December 2015.

Current Treatment Recommendations

The EASL and the American Association for the Study of Liver Diseases (AASLD), in conjunction with the Infectious Diseases Society of America (IDSA), recently published detailed treatment guidelines for HCV disease.[7, 8] Up-to-date treatment recommendations should be sought from these organizations' websites, as changes may occur frequently due to the rapid evolution of treatment modalities.

Currently, recommendations are provided for all six HCV sub-types, including for those who are treatment-naïve (have never undergone any form of therapy for the disease) or treatment-experienced. There are many new treatment options which now include sofosbuvir, simeprevir and dasabuvir, and combinations of ledipasivir/sofosbuvir and paritaprevir/ritonavir/ombitasvir. Other agents will likely be released in the near future.[8] Additional recommendations are provided for those with other co-morbid conditions, such as co-infection with HIV.

There are multiple advantages of the newer treatment protocols of direct-acting antivirals:

- They may not require co-administration of pegylated interferon-alpha and/or ribavirin, depending on the indication. Thus, they may be deemed "all oral" regimens.
- Most treatment-naïve and treatment-experienced individuals require only 12 weeks of therapy, although some may need up to 24. (Older protocols commonly required 48 weeks.)

- Tolerance of treatment is much improved over interferon-based protocols.
- Although long-term experience is still limited, it is anticipated that the new treatment protocols will also lead to as permanent a state of SVR did the older treatment protocols.

However, the cost of the new treatments can range upward from approximately USD85,000 annually, and may therefore not be accessible to many individuals. Various countries and jurisdictions as well as private health insurers will need to assess the cost and the likelihood of curing an HCV infection versus cost of care for end-stage liver disease, liver transplants, and/or treatment of hepatocellular carcinoma or other extra-hepatic condition(s).

Recent Treatment Studies

In addition to the established, approved treatment regimens currently published by EASL and AASLD/IDSA, research and development continues on alternative and novel treatments.

In a JAMA publication from May 2015, Poordad and others[9] reported on the outcome of administering a 12-week, all-oral combination of daclatasvir, asunaprevir and beclabuvir to 415 patients with HCV genotype 1 (312 treatment-naïve and 103 treatment-experienced) without cirrhosis. SVR at 12 weeks was 92% for those in the treatment-naïve group and 89.3% of the treatment-experienced group. There was a less than 1% discontinuation rate due to adverse side effects.

In the same issue of JAMA, Muir and colleagues[10] presented data from a 12-week all-oral protocol of daclatasvir, asunaprevir and beclabuvir, this time either with or without ribavirin, in patients with compensated cirrhosis and HCV genotype 1 infection. Among this group, 98% of treatment-naïve patients achieved SVR at 12 weeks with ribavirin and 93% without ribavirin. The treatment-experienced group had a 93% SVR at 12 weeks with ribavirin and 87% without ribavirin. The addition of ribavirin was only of benefit to those in the treatment-experienced group. Even prior null responders (i.e., patients who did not obtain viral suppression with previous treatment) responded very well both with and without ribavirin. An accompanying editorial to this article noted that the high response rates, especially among patients with cirrhosis, is substantial and important clinically, given that viral eradication has been shown to delay or decrease chances of decompensation of liver disease and also hepatocellular carcinoma.[11]

Treatment of Hepatitis C and HIV Co-Infection

HCV is also present as a co-infection in 25-30% of persons infected with the human immunodeficiency virus (HIV). For HIV-positive individuals, HCV co-infection rates of 72-95% are seen among injection drug users, among 1-12% of men who have sex with men, and among 9-27% of heterosexuals.[12]

HCV infection causes substantial morbidity and mortality, but those co-infected with HIV are three times more likely to develop cirrhosis or liver decompensation than those only infected with HCV.

Successful achievement of SVR among persons co-infected with HCV and HIV has been demonstrated to lead to a significant decrease in subsequent liver decompensation, liver cancer, and all-cause mortality. Graham[13] pointed out that despite this knowledge, HIV specialists have historically been hesitant to prescribe interferon-alpha and hepatologists have been hesitant to treat HCV in individuals with HIV.

Two very recent studies demonstrated that a very high percentage of those with HIV and HCV can achieve SVR with interferon-free regimens. The first, by Sulkowski[14] and colleagues, used an all-oral protocol of three DAAs – ombitasvir, paritaprevir (plus a ritonavir booster) and dasabuvir – with ribavirin, for 12 or 24 weeks, in those with HCV genotype 1 and those on HIV treatment and full HIV suppression. All of the patients in this group were HCV treatment-naïve or may have failed prior interferon-based treatment. SVR post-treatment was 29 of 31 (94%) for 12 weeks of treatment and 29 of 32 (91%) for 24 weeks. The second study, by Osinusi[15] and colleagues, studied the effects of a 12-week all-oral fixed-dose combination of ledipasvir and sofosbuvir in HCV treatment-naïve HIV co-infected individuals. At 12 weeks post-treatment, the SVR was 49 of 50 (98%). Neither study reported discontinuation of study medication due to adverse side effects.

Essentially, HCV treatment outcomes now for those co-infected with HCV and HIV are equivalent to those mono-infected with HCV. Professional organizations focused on infectious diseases and liver disorders now provide detailed treatment guidelines for co-infected individuals as well. These are not markedly different for those infected only with HCV, except that they give more attention to drug interactions for the co-infected.

An Insurance Medicine Analysis

A 2012 JAMA article[16] presented a study of all-cause mortality among individuals with histologically proven advanced hepatic fibrosis who were treated with interferon-based therapy between 1990 and 2003. The study focused on 530 individuals and compared outcomes of those who achieved SVR with those who did not, and followed the participants for a median of 8.4 years. Compared to those who did not achieve SVR, those who achieved SVR demonstrated significantly reduced all-cause mortality, liver failure, liver-related mortality, need for liver transplantation, and hepatocellular carcinoma.

A 2014 Journal of Insurance Medicine article[17] noted that the data from the above article was not especially useful to assess the mortality risk of insurance applicants with a history of hepatitis C that included advanced hepatic fibrosis and successful treatment. The successfully treated group was the comparison population, not the general population. The researcher created a model to translate the documented improvements into relative terms compared with a suitable general population. He concluded that the mortality of those achieving SVR was only slightly worse than the general population but urged caution in reaching definitive conclusions, given limitations in the data and assumptions that were made to develop the model.

Implications for Insurance Products

Successful treatment of individuals with HCV who have access to novel therapies will likely have the following insurance implications:

Life Insurance

- More applicants will be insurable based on history of cure.
- If a biopsy is performed and the degree of hepatic fibrosis is known, the likelihood of progression after successful treatment is low. Risk assessments can be based upon last known stage of hepatic fibrosis as well as available information regarding liver function and/or imaging.
- There will be a longer life expectancy of those with in-force policies due to reduced likelihood of death from end-stage liver disease (or associated complications) and hepatocellular cancer.

Living Benefits

- Higher upfront costs might be experienced by health insurers to cover new therapies, but they are potentially subject to lower long-term liabilities due to avoidance of health care expenses for liver decompensation and associated complications as well as avoidance of need for liver transplantation.
- Reduced claims may be experienced by critical illness (fewer liver transplant, cancer, and terminal illness claims), total and permanent disability (TPD), income replacement, and hospital cash products.

Summary

Recent advances in the treatment of hepatitis C have led to extremely high rates of sustained viral response and cure. In the short to medium term, accessibility to and affordability of these medications will determine how many of those infected will actually benefit from the advances. For those with access, there will be a much improved risk assessment profile for both life and living benefits products. RF

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RGA MEDICAL TEAM UPDATE

RGA welcomes the following individuals to our global network of medical officers:

- Dr. Lisa Duckett, Vice President and Medical Director
  Chesterfield, Missouri, USA
- Dr. Manisha Kalaver, Associate Director – Medical Services
  Mumbai, India
- Dr. Heather Lund, Chief Medical Officer – Asia
  Hong Kong
- Dr. Catherine Tchoreloff, Consulting Medical Officer
  Paris, France

UNDERWRITING THE QUANTIFIED SELF

During the past 50 years, technology has transformed and personalized many ways to quantify aspects of human life. Nowhere today is this more evident than in the field of medicine.

For years, devices have been available that let individuals engage in basic medical self-quantification, from taking temperatures and blood pressures to evaluating blood sugar levels and testing for pregnancy. Today, medical devices are evolving into configurations that will meet the globe's fast-rising data-driven medical needs. Indeed, smartphone apps and add-ons are available that can perform basic ear, nose and throat exams, wearable patches exist for ongoing electrocardiograms (ECGs),[1] and clothes made of smart fabrics can log vital signs and send them to the cloud.

Medical histories as well have become data points to be logged and maintained. Medical providers now type details about patient visits, exams, discussions, prescriptions and test results – all information points that once took up handwritten sheets of paper in bulky file folders – into record-keeping software which automatically appends the data to the patient's file.

In the future, Watson-style cognitive computing capabilities with natural language interfaces and deep analytics[2] might emerge as well that will guide physicians through patient assessments, diagnoses and treatments.

All of this is important food for thought for insurers.

Individualization of Medicine

Genetics, smart phone technology and computing power are already rapidly transforming the practice of medicine.[3] Many substantial changes to medicine are currently being driven by the expanded understanding of the human genetic code. Although errors in the human genetic code have long been known to cause certain impairments (e.g. Down syndrome, phenylketonuria), the successful sequencing of the human genome has greatly increased knowledge about physiological control mechanisms, enhanced the potential for reducing diagnostic time and expense and might usher in even more dramatic changes.

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Mark Dion is Vice President, Global Underwriting Strategic Innovation for the Global Underwriting Services Team at RGA Reinsurance Company. He is a subject matter expert regarding RGA's underwriting innovations, facultative risk management in the U.S. division, predictive modeling, and development of underwriting manuals and e-underwriting rules.

The past few year have seen a rapid drop in the cost and speed of sequencing. In the U.S., a full sequence now costs close to $1,000 and very basic sequencing for consumers from companies such as 23andMe is about 1/10th of that. (23andMe currently only offers ancestral origins analysis in the U.S., but in Canada, the U.K. and other countries, it offers genetically-determined health risk testing as well.)

The enhanced knowledge of the human genome is now also changing certain fundamental elements of the medical model. Rather than recommending a course of action proven most efficacious for the largest cohort, physicians can now, in certain circumstances, use a patient's individual genome to individualize diagnosis, treatment, and monitoring. Knowing, for example, that a specific gene predicts a possible adverse reaction to certain treatments is highly relevant, as such reactions are a leading cause of death in hospitalized patients and are annually responsible for hundreds of billions of dollars in added healthcare costs.[4] As a practical example, by testing for liver enzymes CYP2D6, CYP2C9, and CYP2C1, physicians can identify patients who might have difficulties with certain common drugs that treat a variety of impairments, enabling adjustments to dosages or the selection of different alternatives.[5]

The enhanced knowledge of the human genome is now also changing certain fundamental elements of the medical model.

Wearable Devices and Ingestible Sensors[6]

For tracking biometrics, portable technology has evolved into wearable technology. Examples include more than just today's near-ubiquitous fitness trackers. "Smart textiles" with embedded sensors now exist in a range of apparel choices. A t-shirt, for example, can be embedded with sensors that track a wearer's vital signs, and a wireless insole has been developed that can measure distribution and motion parameters.[7] Real-time location systems (RTLS) are increasingly being used around the world to tag and track individuals as well as equipment in hospitals and other healthcare settings.

More sophisticated biometric sensors, smaller cameras, and improvements to the interface technology required for humans and larger computing systems are already in development. Sensors utilizing electro-active polymer technology exist that permit the measurement of muscle contractions and there are even biomedical "tattoos" – epidermal electronic patches which can be temporarily affixed onto a patient's body – that can monitor vital signs without the need for invasive procedures.[8]

Wearable items have become sufficiently commonplace to warrant attention from life and health insurers. If such devices are used for medical screening and possibly diagnostic purposes, they must be held to the highest standards regarding sensitivity, specificity, calibration, maintenance, data privacy, and encryption.

New technologies, however, are not limited to external wearables: ingestible sensors, also called "smart pills" (or smart pill systems), have also emerged. These systems, which have already been approved by the U.S. Food and Drug Administration, consist of a pill with an embedded sensor which, once swallowed, integrates with a dermal patch that receives the sensor's signals and then connects to software that captures specific information. The current focus in this area is on wireless patient monitoring to track biosigns and monitor prescription drug adherence, and diagnostic imaging.

The Coming of the Tricorder

The Qualcomm Tricorder XPRIZE, a competition recently launched to develop a medical device along the lines of the tricorder originally posited by the 1966 television series Star Trek, is of particular interest to life and health insurers. Star Trek tricorders came in two forms: a scientific tricorder, which analyzed planetary conditions and composition, and a medical tricorder, which assessed vital signs and made medical diagnoses.

The fundamental goal of the prize, which will award a total of $10 million to three winners, is the development of an all-in-one device that is smaller, faster, more connected and more effective than what currently exists. In the words of the entry materials, the device, which must weigh less than five pounds, should enable "reliable self-diagnosis or assessment" of 16 distinct conditions (13 "core" and a choice of three elective conditions) and five vital signs in a group of 15-30 people over the course of three days,[9] and successfully upload the information to the cloud.

Winning devices must also be able to perform these assessments independently of a health care worker or facility,

and in ways that provides "a compelling consumer experience."

Such a device, if successfully developed and marketed, could fundamentally change how underwriting is done, especially if the range of impairments for which it can screen and diagnose expands. The average consumer could have a wealth of preliminary diagnostic information available before a physician visit. Insurers, also, would ideally have access to the data or be able to use similar devices in underwriting in order to maintain information symmetry and avoid anti-selective activity.

Underwriting Analysis

Along with all the challenges presented, the opportunities inherent in the increased quantification of the self should not be ignored. Consider, perhaps, a world in which every person's genome has been fully mapped and where every home has medical devices to monitor and even diagnose minor as well as major illnesses. It is possible that in such a world, overall morbidity and mortality might improve.

- To share or not to share. As self-quantification becomes more common and less a fad, underwriters will focus more on how the information should be shared. Privacy regulations will address who has access to the information and for what purposes. Insurers and underwriters may need to adjust application questions and underwriting requirements.
- Personal medical device adoption is early in its evolution. It should not be assumed that all consumers will adopt such devices as soon as they are available. With smartphones, for example, the progression of adoption varied until a "tipping point" occurred.
- Personal medical devices are not currently considered diagnostic and have insurance risk. In the case of personal medical devices, most physicians today still require clinical verification of a result obtained from such as device. In addition, such information could allow for anti-selective activity.
- Sensitivity and specificity of the newest wearable/medical devices is lacking. The reliability of these medical devices is still in question, as research about levels of false positive and negative results has not yet been conducted. In medicine and in underwriting, the preferred approach to making changes in practice is based upon scientific studies followed by validation. Both of those steps take time. Until better data emerges about the accuracy and validity of test results from personal medical devices, a cautious view of these results need to be taken.
- Avoid media hyperbole and hype. The actual usefulness or risk threat of any new medical device should be analyzed critically. Focusing on published research, peer-reviewed articles, and patent applications will provide better guidance than secondary news sources that may simply be repeating assertions rather than data.

Into The Future

Underwriting and medical departments throughout the industry are faced with many challenges going forward – not the least of which is information overload. An insurer's primary responsibility is fair assessment of risk with the goal of identifying higher-level risks without misidentifying the lower-level risks.

Insurance companies should remain vigilant and informed about innovations in the medical arena that may significantly impact how risk is assessed. It takes innovations time to mature and gain acceptance. As clients become quantified and quantifiable through new data sources and technologies, it falls to the insurance industry to understand what role that data will play in underwriting risk. RGF

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LONGER LIFE FOUNDATION: INVESTIGATORS IN THE NEWS

The groundbreaking research projects supported by the Longer Life Foundation, the not-for-profit partnership between RGA and Washington University in St. Louis, as well as the investigators conducting the research are increasingly in the news.

The outcomes of many of these research projects have become an integral part of the medical literature. To date, 99 peer-reviewed articles have been published in leading medical journals and several LLF-supported investigators have also won additional grants from the National Institutes of Health (NIH) and other prominent research institutions. Investigators have been invited to speak at major professional gatherings and have achieved leadership positions in their specialties.

Shin-Ichiro Imai, M.D., Ph.D., professor of developmental biology and medicine at Washington University School of Medicine in St. Louis, was interviewed recently in Record, the University's flagship magazine, about his lifelong work in mammalian aging and longevity and the underlying cellular and genetic mechanisms. In 2008 and 2009, LLF supported Dr. Imai's early research into systemic nicotinamide adenine dinucleotide (NAD) biosynthesis as a key to controlling aging and even longevity in mammals, specifically looking at whether nicotinamide mononucleotide (NMN), a key component of this system, could serve as a biomarker of aging. This investigation and the subsequent grants connected to it have since resulted in Dr. Imai's patenting of the use of NMN for the prevention and treatment of metabolic complications of aging such as Type 2 diabetes. Dr. Imai's team, IMAI LAB, has been accepted as a competitor for the Palo Alto Longevity Prize, a life science competition dedicated to research that could result in discoveries of keys to ending aging.

Antimicrobial resistance is garnering more attention in the news today, because antibiotics, long the main line of defense against infection, are continuing to lose their effectiveness. In 2013 and 2014, LLF supported an investigation by Dr. Jeffrey Henderson, an assistant professor of medicine at Washington University School of Medicine in St. Louis and a physician who specializes in infectious diseases, into susceptibility among the elderly to urinary tract infections (UTIs) and whether there might be genetic and biochemical markers that could indicate such susceptibility. This research had built on his past work into UTI susceptibility among younger women. Results of his LLF-supported work were published in the Journal of Biological Chemistry in April 2015. Dr. Henderson has since received additional grant support from the NIH to further investigate the physiological mechanisms governing urine acidity in order to improve the possibility of uncovering effective and natural ways to fight UTIs.

The Longer Life Foundation is honored to support medical and public health research at Washington University in St. Louis. This support enables the launching of new investigations and as well as the building upon current work in ways that strengthen longevity and quality of life. We congratulate these LLF investigators on their successes.

The Foundation will be selecting its 2015 recipients in the fourth quarter and winners and their projects will be featured in the January issue of ReFlections.

The Longer Life Foundation is a not-for-profit partnership between RGA and Washington University's School of Medicine. 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...

Survival and Outcomes Following Bioprosthetic vs Mechanical Mitral Valve Replacement in Patients Aged 50 – 69 Years

Chikwe J, et al. JAMA 2015; 313(14): 1435-42.
http://jama.jamanetwork.com/article.aspx?articleid=2247145

Study compared long-term survival, stroke, reoperation, and bleeding events after bioprosthetic vs. mechanical prosthetic mitral valve replacement among patients aged 50 to 69 years. No significant survival difference was noted between the groups at 15 years. Mechanical valves were associated with lower risk of reoperation, but higher risk of bleeding and stroke. The authors note that these results suggest bioprosthetic mitral valve replacement may be a reasonable alternative to mechanical prosthetic valve replacement in patients aged 50 to 69 years. They also stated the 15-year follow-up was too short to assess lifetime risk, especially risk of reoperation.

Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study

Dalsgaard S, et al. Lancet 2015 Feb 26. DOI:
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)61684-6/fulltext

This study reported on a very large Danish cohort with 1.92 million individuals including 32,061 with ADHD with over 24 million person-years of follow-up. It demonstrated that children, adolescents and adults with ADHD experience decreased life expectancy. Age at initial diagnosis of >17 years predicted higher mortality risk. The presence of co-morbid oppositional defiant disorder and conduct disorder had a significant deleterious effect on mortality.

The Next Epidemic – Lessons from Ebola

Gates, B. N Engl J Med 2015; 372: 1381-4
http://www.nejm.org/doi/full/10.1056/NEJMp1502918

In this Perspective article, Bill Gates provides detailed insight to the recent Ebola epidemic and lays out the challenge for the future, making very specific, goal-directed recommendations for preparing for future epidemics.

Smoking and Mortality – Beyond Established Causes

Carter BD, et al. N Engl J Med 2015; 372: 631-40
http://www.nejm.org/doi/full/10.1056/NEJMsa1407211

Excess mortality related to smoking has been attributed to 21 common smoking-related diseases which account for 83% of the excess mortality experienced by smokers. This study pooled data from five very large U.S. observational studies of individuals aged 55 and older, from both sexes, and followed mortality from 2000 to 2011. Results indicated that 17% of the additional excess mortality in current smokers was attributable to conditions that had not been previously recognized as smoking-related. These included renal failure, intestinal ischemia, hypertensive heart disease, infections, various respiratory conditions, breast cancer, and prostate cancer.

Dose of jogging and long-term mortality: the Copenhagen City Heart Study
Schnohr P, O'Keefe JH, et al. J Am Coll Cardiol 2015;65(5):411–9
http://www.ncbi.nlm.nih.gov/pubmed/25660917
With the expanding adoption of "wearables" that track physical activity and biometrics, there is interest in incorporating this technology into health promotion type insurance products. Insurance medical directors may be asked about pricing credits for documented healthy lifestyle behaviors. The Copenhagen City Heart Study adds to this literature and provides a summary of past studies that report lower all-cause mortality in people who exercise. The findings suggest a U-shaped association between all-cause mortality and dose of jogging; however, the confidence intervals are quite wide due to few deaths in the strenuous jogging group.

Association of Cardiometabolic Multimorbidity With Mortality
The Emerging Risk Factors Collaboration
Di Angelantonio E, et al. JAMA. 2015 Jul 7;314(1):52-60.
http://www.ncbi.nlm.nih.gov/pubmed/26151266
Insurance medical directors are commonly asked how to underwrite the presence of multiple impairments. The Emerging Risk Factors Collaboration group looked at all-cause mortality in 689,300 participants who had a history of diabetes, myocardial infarction, or stroke, alone or in combination. The authors concluded that mortality is multiplicative with these combinations of impairments and associated with significantly shortened life expectancies.

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, Chief Medical Director
RGA Reinsurance Compan

RGA discusses our 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.

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