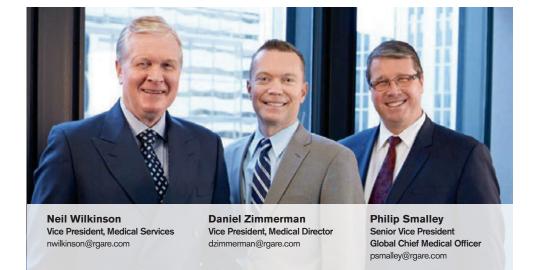
Rections Rega's Global Medical Newsletter

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FROM THE EDITORS

We are delighted to bring to you the latest edition of ReFlections. Over the past few months, we and other RGA associates have had the pleasure of seeing many of you at various industry meetings and seminars, and are gratified to know this newsletter continues to be a must-read for you.

This issue features essential reading on two very timely topics. When HIV and AIDS first emerged into the public consciousness in the 1980s, it was well-known as a death sentence. Until recently, even though therapies had been enabling infected individuals to lead nearly normal lives, HIV was still considered uninsurable for life coverage. Today, the status of HIV/AIDS has clearly changed to that of a chronic illness. The life insurance industry is recognizing this change and is shifting toward a greater openness to covering individuals with HIV. Hilary Henly, Head of Underwriting (Ireland) and Director of Divisional Underwriting Research, RGA Reinsurance Company, together with ReFlections editor Dr. Dan Zimmerman, have penned an article that covers the fundamental issues and concepts today for successful underwriting of persons with HIV/AIDS.

The second article, by Susan L. Wehrman, Vice President, Electronic Health Record Initiatives, discusses the use of patient-generated health data – an issue gathering an increasing amount of attention, due not just to privacy issues, but also to the current ability of insurers to store, use and deploy the data. We trust both articles will become useful items for your research libraries.

A few weeks ago, the Longer Life Foundation, RGA's joint foundation with Washington University School of Medicine in St. Louis, awarded its 2016-2017 research grants. We are pleased to present to you the excellent and diverse group of new investigations that have been named for LLF support, which you can read about on page 12.

We are honored to continue to bring you the latest thinking in the realm of insurance medicine. Please do not hesitate to provide us with feedback or suggestions – this is your newsletter and we are committed to keeping it a useful and valuable resource for you.

Thank you,

Phil, Dan and Neil



HIV: DESIGNING UNDERWRITING GUIDELINES

Abstract

The Human Immunodeficiency Virus (HIV), and its subsequent disease progression Acquired Immune Deficiency Syndrome (AIDS), have presented significant and unprecedented challenges to the insurance industry. These conditions led to concerns of mounting and unfunded liabilities and essentially changed the way that insurance was underwritten. Fortunately, with the development of new therapies, individuals with HIV are living much longer lives and the dire predictions for excess mortality losses for insurers did not materialize. For decades, individuals with HIV were considered uninsurable; however, a paradigm shift has recently occurred in the way insurers view HIV, based upon a growing body of evidence demonstrating improving mortality outcomes for infected individuals.

HIV is now transitioning to an insurable condition, but despite treatment success, it remains a complex disease, and designing insurance products with the right inclusion and exclusion criteria is a challenging task. Insurance medical directors and underwriting manual developers will need to follow medical literature closely and amend their guidelines as needed. This article discusses the main risk factors requiring assessment when coverage for individuals with HIV is being considered.

Introduction

HIV has resulted in millions of deaths globally since first reported in 1981. Today, according to the World Health Organization (WHO), 37 million people around the world were living with a diagnosis of HIV at the end of 2014, 25.8 million of whom were located in sub-Saharan Africa (which is also where 70% of all new infections occur)¹.

With the advent of anti-retroviral therapy (ART) in the mid-1990s, HIV has become a controllable (albeit still chronic) disease. Life expectancies for the HIV-infected, once measured in months or even weeks, are now in the decades for those receiving ART. Indeed, annual death rates for newly-infected HIV patients on ART currently approach those of the general population in short-term follow up. In the longer term, epidemiological studies have reported mortality ratios for those with HIV approaching those observed in individuals with other insurable chronic diseases. Morbidity risk for these individuals, however, continues and is yet to be quantified².

As ART is increasingly allowing those living with HIV to remain active members of society – that is, to continue to work, run businesses, have families and purchase homes – they are needing life insurance cover to protect themselves, their families, and their businesses.

More than 10 years ago, insurers in South Africa and Europe began offering life cover to treated HIV-infected individuals on a limited-term basis. More recently, life insurers in the U.S. and Canada have also begun to develop and offer products to cover HIV-positive individuals.

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Hilary Henly is Head of Underwriting (Ireland) and Director of Divisional Underwriting Research, RGA International Reinsurance Company dac, based in Dublin. She is a Fellow of the Chartered Insurance Institute, and has more than 20 years of experience in both underwriting and claims.



Daniel D. Zimmerman M.D. dzimmerman@rgare.com

Daniel D. Zimmerman, M.D., is Vice President and Medical Director of RGA Reinsurance Company, responsible for case consultation, product development, internal and external education, client support, and representing RGA to key industry professional organizations. He maintains board certifications from the American Board of Internal Medicine (ABIM), the American Board of Pediatrics, and the Board of Insurance Medicine. Depending on inclusion and exclusion criteria selected as defining the better risk, offers can be made on a reasonable percentage of HIV positive applicants. Underwriting ratings can be determined by extrapolating data from various medical studies to ensure the additional premium assessed is fair. Due to the relatively high ratings for many of these applicants and the typical limited-term duration of these products, the placement ratio has been low, but is increasing.

Of note, in some countries durations of policies available to HIV-positive individuals have been extended to renewable term and whole of life products. Still, with low numbers of inforce policies covering HIV-positive insured people, credible claims experience is yet to be determined. This data will need to be followed carefully.

Life Expectancy/Mortality

Deaths from HIV have decreased dramatically over the past two-plus decades. Recent articles reviewing research on HIV mortality outcomes show that people are living longer and the majority of deaths occurring among those on treatment are now no longer due to AIDSdefining illnesses^{3, 4}. These articles, along with the following three studies, can serve as excellent reviews for anyone researching HIV mortality outcomes in the course of developing underwriting guidelines.

The Antiretroviral Therapy Cohort Collaboration (ART-CC) found that between 1996 and 2005, estimated life expectancy at age 20 had increased from 36.1 years to 49.4 years, and the number of those who survived from age 20 to age 44 increased to 85.7% by 20055.

The UK Collaborative HIV Cohort (UK CHIC) study of patients (excluding injection drug users) infected with HIV-1 (the most prevalent form of the virus) who started ART in 2000-08 found that on commencement of treatment, estimated life expectancies for these individuals at age 35 were6:

TABLE 1: ADDITIONAL LIFE EXPECTANCY ((VEADO) EDOBA AOE OF MUTH TREATMENT.
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Cohort	CD4 <200 cells/μL	CD4 200-349 cells/μL	CD4 >350 cells/μL
At start of ART (males)	35	44	46
After 5 years on ART (males)	22	42	46
At start of ART (females)	38	46	44
After 5 years on ART (females)	27	46	51

A study which looked at U.S. and Canadian participants in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) on ART between January 2000 and December 2007 found that overall life expectancy estimates increased from 36.1 to 51.4 years from 2000-2002 to 2006-2007. Table 2 (below) provides a breakdown:

TABLE 2: HIV LIFE EXPECTANCY ESTIMATES			
Criteria	Life expectancy estimates at age 20 (2000-2002)	Life expectancy estimates at age 20 (2006-2007)	
Female	36.6	47.3	
Male	35.9	53.4	
CD4 < 350 cells/μL	31.4	46.9	
CD4 ≥ 350 cells/μL	48.8	68.6	
Overall	36.1	51.4	

Despite improved life expectancies, HIV-infected individuals still experience a higher rate of non-AIDS-related deaths than the general population. This discrepancy in life expectancies could be attributed either to the active HIV infection or to other underlying factors such as higher rates of alcohol use and smoking, co-infection of hepatitis C, or as a result of cardiovascular, cancer or liver disease. The presence of these comorbidities also needs to be assessed by insurers, regardless of undetectable viral load or high CD4 cell counts.

Comorbidities

Increased T-cell turnover in HIV infection causes increased generalized inflammation and endothelial damage. As a result, HIV-infected individuals are at greater risk of developing age-related diseases earlier than the general population.

The most frequently reported cardiac disease manifestations in HIV patients are cardiomyopathy, pulmonary hypertension and pericardial disease. Increased cardiovascular risk may be due to inflammatory lipid alteration, indicated by a higher carotid intimal-media thickness (IMT) in HIV patients8. Older retroviral medications such as zidovudine (Retrovir) and stavudine (Zerit) are also more likely to cause dyslipidemia.

The Veterans Aging Cohort Study (VACS), conducted in the U.S. from 2003-2009, found that male HIV patients were at a 50% increased risk of myocardial infarction (MI) versus non-infected individuals9. More than half of all HIV patients may have ECG abnormalities such as a prolonged QT interval, which can be associated with sudden death¹⁰.

Older HIV patients needing concomitant drugs for age-related conditions may have a higher risk of drug interactions with outcomes such as gastrointestinal intolerance, central nervous system disorders, liver toxicity, dyslipidemia, and loss of bone mass¹¹.

Liver disease is also a major cause of death, and tuberculosis (TB) remains a leading cause of death among HIV-infected individuals in developing nations^{11, 12}. HIV infection has additionally been linked to a risk of insulin resistance with nucleoside reverse transcriptase inhibitors (NRTIs) further increasing insulin resistance and the risk of diabetes¹⁰.

Finally, there has been a documented increase in cancers of the anus, liver, and lung, and in Hodgkin's lymphoma since ART's introduction in 1995. Zidovudine (azidothymidine) and the now discontinued zalcitabine (Hivid) have both been cited as contributing to the carcinogenic effects of ART. Other links have also been made between HIV and non-AIDS-defining cancers specifically caused by infections such as *Heliobacter pylori* in gastric cancer, *Chlamydia pneumoniae* in lung cancer, and human papilloma virus (HPV) in cervical cancer¹³.

Key Prognosticators of Mortality in Applicants with HIV and Risk Selection

Most insurance underwriting guidelines require that an HIV-infected applicant be currently under treatment with ART and can demonstrate adherence to treatment and follow-up for at least six months. Some insurers require a longer period of time to ensure appropriate compliance and medication effectiveness.

Key prognosticators to keep in mind are:

Current Viral Load

Undetectable viral load is an absolute requirement, although consideration could be given if there is a history of viral "blips" – e.g., a transient viral load of up to 400 copies per milliliter which then normalizes quickly.

Nadir CD4 Count

Most underwriting guidelines take a less than favorable view of covering HIV-positive individuals if a history exists of a CD4 + T-cell count of less than 200 cells/ μ L (AIDS, by definition) or of AIDS-defining clinical conditions (per the CDC), as this commonly means there has been significant damage to the immune system and irreversible damage to body systems. An exception to this might be an applicant with comorbid pulmonary TB that has been treated without sequelae.

It should be noted that CD4 counts continue to rise with ongoing ART therapy, thus the nadir CD4 count may be of less importance over time if CD4 recovery has been demonstrably stable. A recent paper demonstrated that after five years of ART, mortality outcomes of patients with low baseline CD4 counts converged with mortality of patients with intermediate and high baseline CD4 counts¹⁴.

Current CD4 Count

A current (within six months of application) CD4 count of at least 350 cells/μL is a minimum requirement for consideration of coverage. However, with new clinical treatment guidelines promoting the commencement of treatment to everyone worldwide with HIV regardless of CD4 count, best-case thresholds for those with CD4 counts greater than 500 cells/μL are now being seen.

While CD4 cell count at diagnosis can be highly predictive of mortality in the first year, this predictive value becomes no longer statistically significant three to four years after ART is initiated. An analysis of patient data from 15 of the 19 cohorts in the ART Cohort Collaboration study found that among 14,208 patients, CD4 cell counts and viral loads at the drug's initiation were no longer prognostic of full-blown AIDS or of death after 36 months¹⁵. Another study, of 14,932 HIV patients in South Africa, found the effect of time on mortality was constant after 36 months on ART for all CD4 counts¹⁶.

Comorbid Risk Factors and Disease

Significant comorbidities generally preclude coverage of HIV-infected individuals.

Companies vary as to what qualifies as a "significant" comorbidity. For example, people

co-infected with HIV and hepatitis viruses tend not to do well clinically. The medical literature also shows that HIV patients are developing and dying prematurely from vascular disease, so a more cautious view should be taken if the applicant also smokes, has diabetes, or has already developed cardiovascular disease.

There is a significant body of literature demonstrating very high mortality in HIV-infected individuals who are also intravenous drug abusers. Comorbid alcohol or drug abuse is a concern, although some underwriting latitude may be permissible for those using medically prescribed marijuana (depending on the indication). As there is also an increased suicide risk in HIV-infected individuals, insurers should also be concerned about any significant psychiatric history.

HIV-infected individuals still experience a higher rate of non-AIDSrelated deaths than the general population.

Determining Underwriting Ratings and Premiums

As with any impairment, there must be evidence to support any proposed extra premium being charged when an applicant has HIV.

Care should be taken to be sure products for this block are fairly underwritten, priced and marketable, and will not damage company solvency.

Rating guidelines developed for covering HIV-positive individuals will depend on the following:

- Type of insurance product
- Term of coverage
- Selection criteria
- Insurable age: Few deaths are expected among very young people, thus it does not take many extra deaths in this cohort to make that group potentially uninsurable
- Smoking status: Even though an applicant with HIV might be assessed for smoker rates, additional loading may also need to be considered

These criteria and ratings will most likely vary by country, depending on availability of testing and access to affordable antiviral therapy and treating specialists.

Conclusion

The recent paradigm shift in the insurability of HIV has been a long-awaited event. Nevertheless, HIV remains a complex and potentially serious disease. Medical insurance directors will need to work closely with their companies' actuarial, business development and marketing departments to ensure that insurance coverage is accurately assessed and priced and that consumer needs and expectations are addressed appropriately.

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RAMIFICATIONS OF UTILITY, IMPORTANCE GAINS FOR PATIENT-GENERATED HEALTH DATA (PGHD)

Abstract

There was a time that medical information flowed in only one direction from doctor to patient. That time has passed. With the advent of several factors - in the U.S., the Meaningful Use standard that governs the use of Electronic Health Records (EHR) and the exchange of patient clinical data among healthcare providers as well as between healthcare providers and insurers or patients¹, the Affordable Care Act and incentive-based reimbursement, and global population health trends - a push has emerged that is shifting the patient's role from passive recipient of care to active member of the care team². Consequently, regulators and providers are searching for solutions to increase patient engagement. This is causing patient-generated health data (PGHD) to emerge as a hot topic.

What is Patient-Generated Health Data?

PGHD, at its most basic level, is any information a patient shares with a provider. Traditionally, this would encompass symptoms as well as family history. However, patients today are increasingly collecting their own biometric data, using an ever-expanding array of personal monitors that can record everything from heart rates and rhythms to steps and glucose levels in real time3.

PGHD is also generating new challenges for healthcare providers due to the fact that participating providers must integrate PGHD into electronic health records as part of Meaningful Use Stage 3 rules by 2018. Even in countries where this requirement is not an issue, healthcare providers will still have to meet the challenge of integrating PGHD into their patient health records.

Indeed, Dr. Gregory Abowd, Distinguished Professor of the School of Interactive Computing at Georgia Tech, predicted in 2011 at an industry forum that "Within five years, the majority of clinically relevant data will be collected outside of clinical settings4." In the five years since that statement, the volume of such data has increased substantially - perhaps not the majority at this point, but still, enough to warrant attention.

PGHD is distinct from data generated within clinical settings in two important ways⁵:

- Patients, not providers, are primarily responsible for capturing and recording the data
- Patients decide how to share or distribute these data to healthcare providers and others

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Susan L. Wehrman, Vice President, Electronic Health Record Initiatives, founded and heads RGA's now four-year-old electronic health record (EHR) initiatives unit, one of the first such units in the insurance industry. EHRI conducts in-depth research and analyses of this fast-evolving segment, monitors all pertinent activity in the U.S. and around the world, and assists clients with EHR-related issues. Sue has an Master of Science (M.S.) degree in Health Information Management, and has published frequently on EHR-related topics.

In Europe, collection of patient reported outcome measures, or PROMs (the continent's PGHD equivalent) has been under way for some time. In the Netherlands, for example, collection of PROMs is mandated for certain types of patients and conditions – mandated, that is, for the providers, who in turn are required to ensure that their patients participate and respond to questionnaires. To meet this need, tools are used that electronically and automatically select validated survey instruments from an integrated library and administer them to patients at appropriate intervals (before, during, and after treatment as indicated), based on the diagnoses. These tools are

generally integrated via standards-based methods with each provider's electronic medical record (EMR).

According to the European Patients' Academy, patient-reported outcomes are important because they provide a patient perspective on a disease or treatment that might not be captured by a clinical measurement, but may be as important to the patient (and their adherence to the treatment) as a clinical measurement⁶.

Insurers today are continually seeking surrogate data as an alternative to more traditional sources

of underwriting data (e.g., paramedical exams and attending physician statements). For example, some insurers are incorporating data elements generated by wearable devices into their pricing and underwriting considerations.

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Usability and Reliability of PGHD

Clinicians continue to be divided as to the utility of patient-generated health data. The latest studies have found that only 15% of physicians recommend patient use of wearables or other health apps to improve health. Some physicians have even stated they will only take a patient's health data seriously if it has been generated from an FDA-approved device⁷.

Primary clinical objections were8:

- Information overload: Clinicians may be overwhelmed with primarily normal readings
- Workload: The cost of and complexity for a practitioner of collecting the data
- Unintended consequences: Clinician liabilities stemming from lack of timely, appropriate review of and action on the data
- Other: Health care providers simply don't know what to do with the results

Conversely, patients in a study conducted by the Society for Participatory Medicine were significantly more enthusiastic about PGHD7:

- 76% would use a clinically-accurate and easy-to-use personal monitoring device
- 57% would share the data generated with a health professional
- 81% would be more likely to use a device if it was recommended by their provider

According to a study by the Pew Research Center that looked at the tracking of health indicators, more than 40% of patients who use tracking devices claim this activity has changed their overall approach to maintaining their health or the health of someone for whom they care. It has also led them to ask their doctors new questions or to seek second opinions. Additionally, one-third states that data from these devices has affected a decision about how to treat an illness or condition9.

Challenges

Some notable challenges related to PGHD use include the following:

- Privacy and security: Devices and applications that collect PGHD can interface into other applications and interact with covered entities; the data then becomes protected health information (PHI).
- Information integrity: Multiple sources can generate the data. The majority of electronic health records systems are only beginning to incorporate patient-collected data - and when they do, providers want them to distinguish which data came from a patient's devices from data obtained by health professionals3.
- Data longevity: PGHD often lack the historical sweep of longitudinal data (e.g., the same input collected at points in time, over years or decades). Because selftracking is still relatively new, PGHD are relatively shortterm data sets and have no baseline for comparison. The data may not be useful for years 10.

Insurance Implications of PGHD

New technologies are simply increasing the volume of raw patient data available, but the data itself does not necessarily convey the context. For example, a patient's weight tracked month after month might not convey anything about his or her health without additional indicators such as diet, lifestyle, age, family history, etc. 11 This is one of the challenges the insurance industry is increasingly facing when trying to make good decisions based on PGHD.

Insurers also have to consider the potential for anti-selection as the asymmetry of knowledge between applicant and underwriter increases (e.g., direct-to-consumer tests for genetic profiles and HIV). Patients currently can decide whether, and with whom, to share their self-generated data. Indeed, 90% of respondents to a recent global survey conducted by Accenture Consulting on patient engagement said they would share data from their apps or wearable devices with medical providers, while 63% said they would share the data with their health plans, and 31% would share it with their employers¹².

Conclusion

Medical directors, pricing actuaries, underwriters, and claims examiners are likely to find themselves breaking new ground when trying to correlate clinical data with PGHD in order to derive the complete story of an insured's health or risk status. The American Health Information Management Association (AHIMA) recommends that with the anticipated growth in use and availability of mobile apps and data collection devices, strategic planning for incorporating this type of data should begin now¹³.

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RGA MEDICAL TEAM UPDATE

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

- Dr. Russel Hide, Medical Officer (General Practice), Johannesburg, South Africa
- Dr. Reema Nathwani, Senior Manager Medical Services (General Practice), Mumbai, India
- Dr. Radhika Counsell, Consulting Medical Officer (Oncology), London, United Kingdom

LONGER LIFE FOUNDATION ANNOUNCES 2016-2017 RESEARCH GRANT RECIPIENTS

The Longer Life Foundation (LLF), the not-for-profit foundation launched in 1998 by Reinsurance Group of America, Incorporated in partnership with Washington University School of Medicine in St. Louis, just announced its research awards for the 2016-2017 year.

In awarding these grants, LLF continues its nearly two decades of supporting groundbreaking investigatory medical research that helps people live longer, better lives and benefits both public health and the insurance industry.

For more information about these grants, we invite you to visit LLF's new website: www.longerlife.org. There, you can find more information about the foundation, the research it has funded, and peer-reviewed articles generated from the research. **E**

FIRST YEAR GRANTS

Thomas J. Baranski, M.D., Ph.D.

Citrulline as Potential Insulin Sensitizer and Longevity Factor

Luis Batista, Ph.D.

The Impact of Progressive Telomere Shortening on Mitochondria Function and **Energy Metabolism**

Kory Lavine, M.D., Ph.D.

Age-Specific Mechanisms Drive the Pathogenesis of Human Heart Failure

SECOND YEAR GRANTS

Adrianus Boon, Ph.D.

Identification of Human Genetic Variants for High Risk of Severe Influenza

Yiing Lin, M.D., Ph.D.

Remote Detection of TP53 and β-catenin Mutations in Liver Cancer

Jason Weber, Ph.D.

Using Anti-Viral Biomarkers to Predict Breast Cancer Aggressiveness

Jun Yoshino, M.D., Ph.D.

Identification of Novel Blood Biomarkers and Mediators of Obesity-Induced Insulin Resistance

LONGEVITY RESEARCH PROGRAM

Luigi Fontana, M.D., Ph.D.

Metabolic and Molecular Effects of Intermittent Fasting and Mediterranean Diet

ReCite

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

The Impact of Communicating Genetic Risks of Disease on Risk-Reducing Health Behaviour: Systematic Review with Meta-Analysis

Hollands GJ et al. BMJ 2016;352:i1102

http://dx.doi.org/10.1136/bmj.i1102

The authors conducted a meta-analysis of studies in which one group received individualized DNA-based estimates of the risk of developing conditions where the risk might be reduced by behavioral change. They found no evidence that communicating risk resulted in any change in behaviors such as smoking cessation, diet, or physical activity. They concluded that communicating DNA-based risk estimates does not change behavior based on current evidence and that performing genetic testing or searching for risk-conferring gene variants for common complex diseases is not supported. This study provides insight during this age of direct-to-consumer genetic testing and insurance industry discussion regarding use of genetic testing for wellness and health-promotion programs.

Randomized Trial of Longer-Term Therapy for Symptoms Attributed to Lyme Disease Berende A et al. N Engl J Med 2016 Mar 31;374(13):1209-20

http://www.ncbi.nlm.nih.gov/pubmed/27028911

This study compared individuals with persistent symptoms attributed to Lyme disease who had either temporally proven Lyme disease or a positive IgG or IgM immunoblot assay to Borrelia burgdorferi. All received two weeks of intravenous ceftriaxone, and thereafter, three different cohorts received placebo, doxycycline, or clarithromycin-hydroxychloroquine for an additional 12 weeks. Overall, those treated with longer-term antibiotics had no additional beneficial quality-of-life effects compared with those receiving shorter treatment. The sequelae of acute Lyme disease remain controversial in the medical literature and can have significant impact on living benefits insurance products. This article adds additional evidence to the body of medical literature assessing the impact of longer-term use of therapeutic antibiotics in these individuals.

Nomenclature Revision for Encapsulated Follicular Variant of Papillary Thyroid Carcinoma: A Paradigm Shift to Reduce Overtreatment of Indolent Tumors

Nikiforov YE et al. JAMA Oncol. 2016 Apr 14

http://www.ncbi.nlm.nih.gov/pubmed/27078145

Twenty-four thyroid pathologists developed consensus diagnostic criteria for encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC). They compared individuals with invasive and non-invasive disease. Of those individuals with non-invasive disease treated only with lobectomy and followed for 10 to 26 years, all were alive with no evidence of disease. Based on these results, the pathologists recommend renaming non-invasive EFVPTC to noninvasive follicular thyroid neoplasm with papillary-like nuclear features or NIFTP. They noted that this reclassification would result in a significant reduction in psychological and clinical consequences associated with the diagnosis of cancer. From an insurance medicine perspective, this change should also allow a more favorable mortality underwriting assessment and may impact the qualification of individuals with these specific non-malignant tumors for certain living benefits.

Migraine and Risk of Cardiovascular Disease in Women: Prospective Cohort Study

Kurth T et al. BMJ 2016;353:i2610

http://www.bmj.com/content/353/bmj.i2610

Consistent associations between migraine history and increased cardiovascular disease (CVD) and outcomes were demonstrated in the Nurses' Health Study II participant cohort. After adjustment for potential confounding factors, migraine was associated with an increased risk of CVD, as measured by hazard ratios (HR) (CVD, 1.50; myocardial infarction, 1.39; stroke 1.62; and anginal coronary revascularization procedures, 1.73). The HR for cardiovascular death associated with migraine was 1.37. The authors concluded that women with migraine should be evaluated for cardiovascular risk. Insurers have long considered the morbidity risk of migraines and the associated impact on occupational and impairment-based products. This study should alert medical directors, underwriters, and product development specialists to the potential additional risks posed by migraines on a broader range of living benefit and mortality products.

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Assistant Professor, Medicine, Division of Hematology, Washington University School of Medicine in St. Louis

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