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LETTER FROM THE EDITOR

Dear readers:

Our final 2014 issue of *ReFlections* features an article on the topic of bladder cancer by Dr. Nontuthuzelo Thomas, RGA's Chief Medical Research Officer in South Africa, discussing the underwriting of this condition as it relates to both life and non-life related insurance products. The second article was written by Hilary Henly, RGA's head of underwriting in Ireland, examining the impact of NT-proBNP biomarkers from an underwriter's perspective. The third article has been written by Jeff Heaton, who helps all of us better understand the coding standards of Electronic Medical Records. The issue also provides information about the newest research grants from the Longer Life Foundation and news about RGA's On Demand webcasts.

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BLADDER CANCER

By Nontuthuzelo Thomas M.B.CH.B.

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Overview of epidemiology

Bladder cancer is a common disease worldwide. Incidence varies across the globe, with the highest burden of disease in developed countries. The less-developed countries are following closely, with increasing incidence as bladder cancer emerges as an important cause of morbidity and mortality all around the world. These observed disease trends are driven by both the ageing populations in developed nations as well as increasing exposure to environmental carcinogens in less-developed countries.

In published data, bladder cancer is consistently one of the top 20 cancers in both males and females. Age-standardized global incidence rates have been quoted as 2.5 per 100,000 in females and as high as 10.1 per 100,000 in males.

According to the World Health Organization, the single most important environmental risk factor for bladder cancer is tobacco use. Smoking is associated with a two- to three-fold increase in bladder cancer incidence compared with non-smokers. While the bladder itself is not directly exposed to tobacco smoke, it is well-established

that polyaromatic hydrocarbons that circulate in the blood stream of smokers are largely responsible for the carcinogenic effects on the urothelium. Another risk factor that is worth mentioning as it contributes to bladder cancer incidence is occupational carcinogens. This is why underwriters must always be on high alert when dealing with certain occupations particularly if there is a classic history of hematuria. Examples of such occupations are:

- Dry cleaners
- Painters
- Paper production workers
- Rope-and-twine industry workers
- Dental workers
- Physicians
- Barbers
- Beauticians

In developing countries, chronic bladder infection with *Schistosoma haematobium* or so-called bilharzia is an important risk factor for squamous cell carcinoma (SCC) of the bladder, especially in regions like Egypt where this parasitic infection is endemic. The risk factors that lead to cancer are:

- Worm burden
- Chronicity of infection
- Host inflammatory response
- Concentration of N-nitrosamines in urine

Bladder cancer can also be directly correlated with other medical treatments, for example, previous pelvic radiation, and chemotherapy with cyclophosphamide, which increases the risk of bladder cancer via exposure to acrolein, a urinary metabolite of cyclophosphamide. Other cases that are at risk of bladder cancer are spinal cord injury patients that require long-term indwelling catheters, which have shown a multi-fold increase in the risk of developing SCC of the bladder. The mechanical/irritant effect of the in-situ catheter is deemed a likely pathophysiological mechanism.

In Western countries and the U.S., the life time probability of a white male developing bladder cancer is estimated at one in 25. The overall survival over eight years is 75% according to SEER data published in the *Oncologist* 2003, but males have a higher five-year survival rate by all stages compared with females.

It is worth mentioning that, in the developed world, the overall mortality associated with bladder cancer has been reduced significantly over the past two decades. This is attributable to several factors of which the most important are:

- Tobacco control measures resulting in reduced smoker prevalence
- Reduced occupational exposure to aromatic amines
- Early bladder cancer detection and intervention

There is no strong association between genetic risk factors and bladder cancer. Smoking emerges as the single most important risk factor for this disease.

Symptomatology

Up to 90% of cases present with painless sporadic gross hematuria. This blood in the urine is unpredictable and may disappear for weeks before reappearing. Other common bladder irritation symptoms are reports of frequency, urgency and dysuria.

In more advanced cases of bladder cancer there may be complete anuria, chronic lower back pain, bone pain and cancer cachexia. In rare cases there might be a palpable fixed mass upon physical examination of the lower abdomen, and this is considered a sinister sign as it implies quite advanced bladder cancer.

Investigations

The work-up of a bladder cancer patient involves urinalysis with resultant cytology and culture of the urine sample. Cystoscopy is considered the gold standard in bladder cancer diagnosis. The combined use of cystoscopy and endoscopic biopsy allows for direct visualization of the internal bladder wall with accurate sampling of abnormal looking lesions. This is important, as bladder cancer can be multi-focal. Typically the lesions that are visualized at cystoscopy are papillary formations or flat tumors along the transitional epithelium.

Imaging studies of the upper urinary tract are an integral part of the hematuria workup. Computed tomography (CT) scans of the abdomen and pelvis with contrast are also recommended. Two commonly used alternative techniques are magnetic resonance imaging (MRI) and renal ultrasonography. A few centers still perform intravenous pyelography (IVP) for upper tract imaging. The IVP was once considered as the gold standard for diagnosis of bladder lesions but is being slowly replaced by more modern means of investigation.

There are no specific blood tests or tumor markers for the diagnosis of bladder cancer. Several urinary tumor markers are commercially available; however, they are not diagnostic but rather an adjunct to imaging and direct visualization.

Bladder cancer staging

From pathohistological specimens we know that bladder cancer is commonly found in the transitional epithelium, also known as urothelium, which forms the inner lining of the bladder. The commonest type of cancer in the bladder

is transitional cell carcinoma, accounting for more than 90% of all bladder cancers. Other less-common types of cancer in the bladder are squamous cell carcinoma and adenocarcinoma.

Over the years various bladder cancer staging/classification systems have been adopted and published in medical literature. The most-widely utilized is the American Joint Committee on Cancer staging with the corresponding TNM staging.



The most-commonly diagnosed stage of cancer is early bladder cancer, i.e., non-muscle invasive disease. These early cancers can be readily identified after cystoscopy and biopsy of suspicious lesions in the bladder wall. Detection is through direct visualization of abnormal lesions in the urothelium.

Treatment

Smoking cessation is an important part of the management of bladder cancer. Continued use of tobacco is undesirable.

Superficial bladder cancers or early-stage (non-muscle invasive) cancers are managed surgically with transurethral resection. A transurethral resection (TUR), also known as a transurethral resection of the bladder tumor (TURBT), is the most common surgical treatment. TURBT is minimally invasive and does not leave a clearly visible scar on the abdomen. This means that TURBT cases will retain their bladders with respective preservation of bladder functions.

After eradication of cancer, the biggest challenge with bladder cancer management is recurrence. This is one of the most persistent cancers and, despite optimal surgical resection, has a high risk of recurrence of up to 80% of all cases having at least one recurrence. Factors associated with recurrence can be outlined as:

- Tumor size >15mm
- High-grade cytology wash out
- Positive resection margins
- Short interval between surgery and first recurrence

The treatment approach in response to recurrent bladder cancer includes intravesical therapy with various chemotherapeutic agents and immunotherapy. A commonly used duo of chemotherapy agents for this purpose is mitomycin and thiotepa. The immunotherapy that is the most utilized is Bacillus Calmette-Guerin (BCG). While BCG is effective, it has a side effect profile that is poor, which has encouraged the exploration of newer agents that will hopefully have much better tolerability.

More-aggressive disease can be treated with a partial cystectomy or a radical cystectomy. A radical cystectomy is major abdominal surgery that entails the surgical excision of the complete bladder, adjacent pelvic lymph nodes and part of the urethra. In males this may also include the prostate, vas deferens and seminal vesicles. In females this procedure may include removal of the cervix, uterus, ovaries, fallopian tubes and the upper part of the vagina.

Guidelines for follow-up

The high rate of disease recurrence and disease progression in early bladder cancer underscores the need for careful follow-up studies. As outlined above, most cases may still have an intact bladder so the number of patients under surveillance is quite high.

The 2011 EAU guidelines include schedules for follow-up cystoscopy, urinary cytology and imaging in patients with Ta and T1 tumors. This schedule depends on the risk of recurrence and possible progression. For follow-up in patients with no visible tumor in the bladder but positive cytology, the guidelines recommend biopsies and investigation of extravesical locations.

The NCCN 2012 guidelines further specify that cystoscopy and urinary cytology should be performed every 3-6 months for two years and then at increasing intervals as deemed appropriate by the attending practitioner.

Prognosis

The most significant prognostic factors for bladder cancer are grade, depth of invasion, and the presence of CIS. In patients undergoing radical cystectomy for Stage III-IV bladder cancer, the presence of nodal involvement is the most important prognostic factor. Early bladder cancer without evidence of muscle invasion has a good prognosis, with five-year survival rates of 82-100%.

As mentioned earlier, bladder cancer has the highest recurrence rate of any malignancy, so even though most patients with bladder cancer can be treated initially with organ-sparing therapy, most experience either recurrence or progression. Risk factors for recurrence and progression include the following:

- Female gender
- Larger tumor size >15 mm
- Multifocality of lesions
- High tumor grade
- Advanced stage of bladder cancer
- Presence of carcinoma-in-situ

Advanced bladder cancer with metastasis has a poor prognosis. Published data shows a relative five-year survival of less than 15% for all Stage IV cancers.

Golden nuggets for underwriters

1. High index of suspicion if there is a combination of occupations that work with solvents and a classic history of hematuria
2. Previous bladder cancer carries a high risk of recurrence so treatment dates are important
3. Unsuccessful smoking cessation carries a poorer prognosis

Golden nuggets for claims assessment

1. For critical illness claims, a cytology report is not enough to stage bladder cancer
2. Terminal illness benefits are payable for cases that cannot be treated with radical cystectomy
3. Early bladder cancer is not usually disabling but can result in a poor work attendance record

What's new in bladder cancer?

Telomerase levels can be measured in the urine samples of individuals with bladder cancer. This could become a modern form of non-invasive and cost-effective means of bladder cancer screening. There is currently ongoing research into refining the specificity and sensitivity of available urine assays for telomerase levels to detect the presence of bladder cancer particularly in asymptomatic patients. The new generation telomerase assays utilize variations like TeloTAGGG or with gold nanoparticles. The most likely probability is that these assays are unlikely to replace cystoscopy but may have a role in screening programs for sub-sets of high risk patients. To date no consensus guidelines have been published for clinical practice but this is one to watch in cancer underwriting! ■



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DO BIOMARKERS MEAN BUSINESS?

By Hilary Henly ACII (DLDU/DLDC)

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The purpose of this two-part article is to look at biomarkers (with a focus on NT-proBNP) in use or under investigation in the medical world that are not currently widely used in the insurance market. We look at how we might use them in risk assessment methods, with an aim to improve experience, pricing and profitability. Consideration is given to how biomarkers can be used in the insurance environment, the problems in using these biomarkers, NT-proBNP versus the stress ECG and mortality and morbidity statistics.

Introduction

According to the American Cancer Society, the five-year relative cancer survival rates have risen from 55% in 1987-89 to 68% in the period 2003-09. Specifically, leukemia, myeloma, prostate cancer and NHL overall survival have improved by more than 15%¹; however, ischemic heart disease, stroke and COPD remain the leading causes of death worldwide. The average life expectancy in 2012 of the global population was 70 years of age, up six years from 1990; the U.S. has added four years to its average age at death from 75 to 79, China is up from 69 to 75, the U.K. 76 to 81 and India 58 to 66 years of age¹².

Discoveries in gene sequencing and enhanced diagnostic tools have pushed us into a new world of biomarkers and screening tests for a myriad of commonplace diseases. Biomarkers are indicators for processes that are involved in disease development and can be used for diagnosis, as an indicator of disease progression or to influence methods of treatment and management of disease. The insurance industry has already been using PSA as a screening tool for some time but there are still inherent problems in its application, since values can be raised for reasons other than prostate cancer. Any new test must be used in the appropriate context and the quality of the research data considered before implementing its use. As NT-proBNP is not used in clinical practice for screening purposes, the insurance industry is presented with a dilemma in how the biomarker should be used at the underwriting stage. For insurance purposes, we also need to consider the introduction of any new tests and the impact on the client, with the overall cost to the business.

Over-screening can lead to unnecessary worry, investigations and cost at the expense of business. The tests performed on clients should actually add value to the underwriting process and contribute to the overall profitability of the business. Our job is not to diagnose disease but to measure risk exposure of death or disease and to protect the book of underwriting business from undue losses. How we do this is defined by each company's underwriting philosophy and stance in relation to screening tools. 45% of U.S. insurers were believed to be using NT-proBNP as a screening test in 2011⁶, rising to 60% in 2013⁷ and it is increasingly being used around the world in place of the stress ECG.

What is NT-proBNP?

Two forms of BNP circulate in the plasma, BNP-32 and the inactive pro-hormone N-terminal fragment BNP (NT-proBNP). NT-proBNP is a peptide hormone discovered more than 20 years ago, which is produced in the ventricles in response to an increase in heart wall stress due to ventricular pressure and volume overload, hypertrophy and ischemia. While NT-proBNP is not associated with high blood pressure, it has been shown to be associated with arterial stiffness and is a predictor of an increased risk of atrial fibrillation as well as a marker for the presence of hypertrophic cardiomyopathy. It may also add value in the progression in renal disease, systemic lupus and ankylosing spondylitis. This biomarker separates all CHF and non-CHF patients with 90% sensitivity⁸. NT-proBNP is now used in the diagnosis and treatment of heart failure and is an accepted clinical practice. It may also be a valid marker for asymptomatic late cardiac damage and left ventricular dysfunction in persons treated with cardio-toxic (anthracycline therapy) chemotherapy and chest-area radiotherapy for cancer⁶. The test is not used in clinical practice as a routine cardiovascular screening test but we are seeing it being used by some insurance companies to help fine-tune their risk stratification.

NT-proBNP is now used in diagnosis and the treatment of heart failure and is an accepted clinical practice. Its primary use is in follow up of people with a diagnosis of heart failure and not for screening purposes, which is where the dilemma arises in its use for insurance purposes. A further difficulty in using NT-proBNP arises in the quantification of reference ranges.

Mortality and Morbidity associated with elevated NT-proBNP*

Various studies have been carried out over the years, examining risk of death and probability of heart failure. Of these, the most prominent ones are examined below. It is clear that NT-proBNP adds value when looking at it from an underwriting perspective, but the problem lies in how to interpret the result and use the value in deciding on the application of any extra morbidity and mortality rate.

- The Framingham offspring showed increasing levels of BNP and NT-proBNP above the 80th percentile were associated with increased risk of death of 62% and 76% respectively and a three and five times risk of heart failure⁸.
- A nine-year follow-up study by the Mayo clinic of 2042 persons showed that NT-proBNP was independently predictive of mortality and heart failure in the general population free of CHF⁹.
- In a study by Clark, Kaufman and the Clinical Reference Laboratory, male mortality doubled where NT-proBNP range was 101-300 and up to 2.5 times in the >300 band in all sexes⁶.
- The Heart and Soul study Kaplan-Meier estimates of survival showed a progressive decrease in survival from the first (<64) to the fourth (>455) quartile⁸.
- The PREVENT study found that each doubling of NT-proBNP is associated with an increased risk of cardiovascular and all-cause mortality by 1.46¹³.
- The ADHERE study of 48,000 patients indicated that NT-proBNP had prognostic mortality values of 430 and above¹¹.
- The Northwick Park Hospital study showed that a normal NT-proBNP virtually excluded several major cardiovascular diseases. The negative predictive value was 99% in ruling out AF, VHD or significant LVSD, and 96% in ruling out DHF (diastolic heart failure) although it was less effective in ruling out Left Ventricular Hypertrophy⁴.

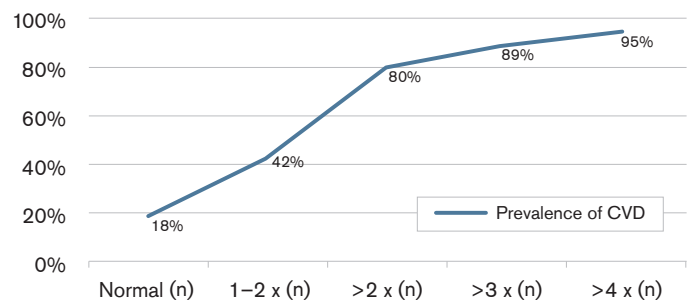
Reference ranges and the problems with applying them at underwriting

It has been indicated that risk increases significantly above 300pg/mL in men and 200pg/mL in women, taking into account age, smoker status and other CAD factors³. While there is an increase in morbidity and mortality as NT-proBNP rises, there is no clear cut-off point in rising levels. There are several factors that lead to variances in recorded values:

- NT-proBNP may be higher in females due to the lower hemoglobin concentration or due to age-related fibrosis and subtle diastolic dysfunction⁴.

- At age 50 and above there is value in using it as a screening tool, but gender must be taken into consideration when looking at cut-off values³.
- It is important to consider BMI, as NT-proBNP levels are lower in obese individuals.
- Smokers were found to have a mean NT-proBNP twice as high as non-smokers in one study but this has not been found to be true across all studies⁵.
- NT-proBNP readings are significantly higher in those with severe fibrosis and cirrhosis in liver disease as well as chronic Hepatitis A, B and liver cancer^{5 6}.
- NT-proBNP has been found to be raised in marathon runners, long-distance cycling and maximal exercise but always normalizes within 72 hours of rest⁶.
- It is increased in women, African Americans and Hispanic subjects, in menopause and often raised in anemia¹¹.
- A study by the Department of Cardiovascular medicine in Northwick Park Hospital, U.K. of 2320 subjects > 45 years old found the following cut-off values:
 - 100pg/mL for men aged 45-59 and 172pg/mL for men aged 60+
 - 164pg/mL for women aged 45-59 and 225pg/mL for women aged 60+
- Subjects with raised NT-proBNP had significant cardiovascular disease⁶

Prevalence of CVD with NT-proBNP values



NT-proBNP versus the stress ECG

The stress ECG evaluates exercise capacity and any subsequent exertion symptoms such as dyspnea and fatigue. A normal stress ECG excludes a diagnosis of symptomatic heart failure¹⁰; however, it is a poor tool in the assessment of LV dysfunction, whereas NT-proBNP is a well-established base for this and is a valuable marker in decreased LV ². As with any underwriting test or procedure, we need to consider both the hard and soft cost associated with the addition of any new underwriting requirement. NT-proBNP

*unless otherwise stated, NT-proBNP is noted in pg/mL

test is relatively inexpensive, costing about \$40 per test, a much less costly option than a stress ECG test. The soft cost is associated with postponing cases that are otherwise healthy, with a risk of upsetting the client and/or agent and potential loss of good business. Problems arise in underwriting if a test or biomarker has low sensitivity/specificity and is not very predictive of all-cause mortality.

- NT-proBNP may be advantageous over stress ECG where the stress test only reflects total plaque burden and is not influenced by unstable atheromatous lesions⁵.
- NT-proBNP test is simple to carry out as a routine blood test and is inexpensive.
- NT-proBNP may also be helpful in assessing cases of aortic stenosis and mitral regurgitation when results of recent echocardiograms are unavailable¹³.
- Oudejans et al. showed that NT-proBNP >440 had the same sensitivity as a resting ECG but twice the specificity in subjects with heart failure⁶.
- NT-proBNP may also be helpful in assessing cases of aortic stenosis and mitral regurgitation when results of recent echocardiograms are unavailable¹³.
- The City General Hospital, Copenhagen study showed levels of NT-proBNP increase with rising age and NT-proBNP increases with decreasing LVEF ($p < 0.050$). NT-proBNP > 357 pmol/l (97pg/mL) identified those with an LVEF of < 40% (sensitivity 73%, specificity 82%) and the NPV below this value was 98%².

Conclusions

While there is an associated increase in morbidity and mortality as NT-proBNP rises, there is no clear cut-off point in rising levels and here lies a dilemma in how to apply extra rates in underwriting. While NT-proBNP is already being used as a useful screening tool in place of the stress ECG in some markets, consideration should also be given to

While it is possible to use NT-proBNP as an alternative screening tool for the stress ECG, consideration should also be given to its use as an enhancement tool to better define morbidity or mortality risk.

the benefits of using it as an enhancement tool to better define morbidity or mortality risk in different age categories or product ranges. Further thought could be given in using new biomarkers from an underwriting, or even in claims perspective, and more questions need to be asked as to what we are actually losing or gaining over existing screening methods

and the impact on overall business. Using new biomarkers in the correct context could offer greater flexibility, faster turnaround times and speedier decisions, improved underwriting terms, reduce costs of screening and improve experience by more accurately defining risk, providing an opportunity for increased business volume.

Many of the current screening tests used in insurance focus on cardiovascular disease; the reality is that a higher proportion of claims in some product lines come from cancer related disease and as an industry we need to think about any imbalance in screening methods. The use of evolving biomarkers may have a place in the future of applicants applying for cover, particularly for cancer survivors and those with a history of chemo-radiotherapy. This is an area still under development and research continues into defining the protective value of these biomarkers. ■

The second part of this article will appear in the next issue of ReFlections, and will discuss Cystatin C, RDW and ProPSA.

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UPDATE ON EBOLA OUTBREAK

In the Summer 2014 issue of *ReFlections*, we included an article on infectious diseases in an increasingly globalized world, by Dr. Kamran Khan, a leading expert on epidemic and pandemic disease spread, including Ebola.

RGA is continuing to monitor the spread of Ebola and the protocols being applied to treat patients and control further spread of the disease.

RGA recently shared our findings with our clients on the current status and how we view the risk from an underwriting point. We will continue to share updates via client communications as the situation warrants.



EMR CODING STANDARDS: UNDERSTANDING ENCYCLOPEDIAS, DICTIONARIES, AND BICYCLE LOCKS

By Jeff Heaton

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There are many different EMR coding systems. Standards such as ICD-10, ICD-9, SNOMED, LOINC, RxNorm, UNII, CPT, and others are frequently seen. These standards are used to encode such concepts as drugs, medical procedures, diagnoses, and lab results. There is much overlap. ICD-10-CM and SNOMED-CT both are capable of encoding medical procedures. Someone who has only ICD10-CM codes might assume that transition into SNOMED is a simple translation. This was my assumption when I initially started to learn EMR coding standards.

In this article I present the big picture of how these coding standards fit together. I group these standards into families that have similar concepts. Most importantly, I will highlight difficulties that arise when one creates a system that must unify two underlying coding standards. I classify the EMR coding standards into the following three groups.

- Code Sets
- Vocabularies
- Combinational Codes

This is not a formal classification of EMR coding standards. These three groups are simply how I think of the coding standards.

Code Sets

An EMR code set is somewhat like an encyclopedia – it contains complete concepts. It is obvious to see how many articles are covered by an encyclopedia; likewise, it is easy to see how many concepts are covered by a code set. Like an encyclopedia, every code in a code set is of some degree of importance. Encyclopedias do not contain nonsense articles – neither do code sets.



Most EMR coding standards are code sets. Specific examples include ICD10-CM, ICD9, GPI, NDC, UNII, and Read codes. It is relatively easy to transform a concept from one code set to another. To perform this transformation a crosswalk is typically used. Often the crosswalk maps a code directly from the source code set to a single code in the target code set. Nevertheless, one will often have to deal with one of the following situations:

- The concept for the code to be translated simply does not exist in the target code set.
- The target code set is more-detailed than the code set it is being translated from. This leads to several potential code matches.
- The target code set is less-detailed than the code set being translated from. This leads to a single code match that is less-descriptive than the original code.

The first case really does not happen very often. Most crosswalks will usually map a code to some equivalent, but the crosswalk is not always one-to-one. ICD10 includes laterality details; however, ICD9 does not. Laterality allows a code to track which side of the body it is referring to. For example, an ICD-10 code that specifies a burn to the left hand can only be crosswalked to an ICD9 code that specifies a burn to the hand. In this case, the code translation was successful, but detail was lost. A similar problem occurs when the ICD9 code for a burn to the hand is crosswalked to ICD10. When such a crosswalk is attempted, there will be several potential ICD10 codes, as ICD10 specifies which hand, as well as if this were an initial or subsequent visit to the doctor for this condition.

Vocabularies

An EMR code vocabulary is somewhat like a dictionary, in that it contains a listing of small units that can be combined into larger concepts. However, unlike the encyclopedia, the words in a dictionary are building-blocks to create more-complex concepts. An encyclopedia might contain an article on “Coronary Artery Bypass Graft”, whereas a dictionary would not. The dictionary might contain the individual words “coronary”, “artery”, “bypass”, and “graft.” However, the entire concept is not represented as a single entry in the dictionary.

It is easy to count the number of entries in the dictionary; however, it is impossible to determine how many concepts can be represented using these words. Some EMR coding standards are vocabularies. SNOMED and RxNorm are examples of vocabularies. An individual SNOMED or RxNorm component might not tell you a great deal. For example, the SNOMED code 7771000 means “left.” Alone, this does not tell one a great deal. Is the code referring to the left hand, the left eye, or the left ventricle of the heart? An EMR vocabulary provides the words to construct concepts. Most EMR vocabularies have rules that

specify how these codes can be strung together. This is very similar to English grammar. These rules help software to determine if a SNOMED or RxNorm statement is valid. However, just because a statement is valid, it does not mean it has meaning. This is true of English as well. Consider the following sentence.

Colorless green ideas sleep furiously.

This sentence was proposed by Noam Chomsky in 1957 as an example of a grammatically correct, yet completely meaningless sentence. Software can easily determine if a concept, encoded in an EMR vocabulary, is invalid. However, it is much more difficult for software to determine if the concept is meaningless. Such a determination requires a deeper understanding of medicine than computers currently have.

Combination Codes

EMR combinational coding standards are like a bicycle lock – many concepts can be created by adjusting combinations of fixed code positions. A bicycle lock usually has three or more dials used to specify digits in the combination. Once the lock's dials are aligned to the correct digits, the lock opens. It is easy to calculate how many different combinations are possible. If there are three dials, each with digits 0-9, then there are 10^3 , or 1000, different combinations.

Examples of combinational EMR coding standards include LOINC and ICD10-PCS. These combinational EMR codes work similar to the lock. LOINC codes are always six characters in length; similarly, ICD10-PCS codes are always seven characters in length. Each position has a separate meaning and can be set to a variety of values. For ICD10-PCS, the seven positions have the following meaning:

1. Section
2. Body System
3. Root Operation
4. Body Part
5. Approach
6. Device
7. Qualifier

ICD10-PCS is used to encode procedures that are performed on patients. There are a variety of different values that can be selected for each of these positions. Using these codes, a variety of procedures can be encoded, but not all of these codes have useful meaning.

Making Sense of the Standards

There are a variety of different EMR coding standards. These coding standards are not always interchangeable, even when two standards represent the same information. When translating between two different coding standards it is always important to consider if one is translating between code sets, vocabularies or combinational codes.

It is particularly difficult to translate between a code set and a vocabulary. Additionally, the direction of the transfer determines the difficulty. It is much more difficult to translate from a vocabulary to a code set than it is to crosswalk from a code set to a vocabulary. Consequently, it is easier to crosswalk from ICD10 to SNOMED than it is to crosswalk from SNOMED to ICD10. This is because it is possible to create a translation for every ICD10 code. However, because SNOMED is a vocabulary, there is no way to determine every possible SNOMED encoding in advance. This means that every possible SNOMED encoding cannot be accounted for in the crosswalk.

While crosswalking between coding standards is possible, it is rarely automatic. Companies and groups such as International Health Terminology Standards Development Organization (IHTSDO), Medispan, and Safe Script provide such crosswalks. These groups are only able to create such utilities with the combined efforts of doctors, EHR experts and information technology experts.

In the U.S., government requirements for EMR handling currently allow for multiple coding standards. It is important to design systems to handle these varying standards. After October 1st, 2014, stage 1 Meaningful Use allows Providers to use either ICD-9 or SNOMED as the code for clinical patient problems/diagnosis and ICD-10 as the code for billing. Ultimately, stage 2 Meaningful Use requires Providers to use SNOMED as the code for clinical patient problems/diagnosis and ICD-10 as the code for billing. The providers will not have to pick the diagnosis codes for billing as the SNOMED will be mapped to ICD -10. ■

References

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2. ICD10 - <http://cms.gov/Medicare/Coding/ICD10/index.html>
3. LOINC - <http://loinc.org/>
4. RxNorm - <http://www.nlm.nih.gov/research/umls/rxnorm/>
5. Safe Script - <http://www.safescript.com/>
6. Medispan - <http://www.medispan.com/>
7. IHTSDO - <http://www.ihtsdo.org/>



By Jeff Heaton
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Jeff Heaton recently joined the Electronic Health Records (EHR) Initiatives team at RGA as an EHR Informatics Scientist. In one of his first tasks, he was asked to create a utility to allow an underwriter to enter information on a code-by-code basis. This required mapping the CDC-provided XML files to an Oracle database, while preserving the hierarchical nature of the codes.

LONGER LIFE FOUNDATION ANNOUNCES NEWEST GRANTS

Over the 16 years since the creation of the Longer Life Foundation (LLF), 86 funded groundbreaking research projects have led to advances in the fields of longevity, genomics, critical illnesses such as diabetes, cancers and cardiac diseases, obesity research, and public health and wellness issues. RGA's financial support for this research to date totals more than \$4.4 million, and has aided remarkable growth in the number of Washington University in St. Louis academicians and scientists now engaged in this important research.

The seven projects being funded for 2014-2015 are:

1. **Long-Term Health Benefits of Caloric Restriction: Does Intermittent Fasting Mimic the Anti-Aging and Health Benefits of Calorie Restriction in Humans?** (seventh year), John Holloszy, M.D., Director, and Luigi Fontana, M.D. Ph.D., Associate Director, Longevity Research Program
2. **A Prospective, Randomized Trial of Sentinel Lymph Node Biopsy Versus No Additional Staging in Patients with Clinical T1-2 N0M0 Invasive Breast Cancer and Negative Axillary Ultrasound** (second year), Amy E. Cyr, M.D.
3. **Discovery of Urinary Tract Infection Biomarkers to Predict Longevity in the Elderly** (second year), Jeffrey Henderson, M.D. Ph.D.
4. **Effect of Dietary Macronutrient Composition on Glycemic Control and Cardiovascular Risk Factors** (second year), Dominic N. Reeds, M.D.
5. **Plasma DNA Mutations as Biomarkers of Hepatocellular Carcinoma**, Yiing Lin, M.D., Ph.D.
6. **snoRNAs and Long-Term Risk of Diabetic Complications**, Jean E. Schaffer, M.D. Jean E. Schaffer, M.D.
7. **Prognostic and Therapeutic Value of Nuclear pSer137-Pfn1 for Breast Cancer**, Jieya Shao, Ph.D.

Of the above research grants, three will fund an additional year of research, and one reflects the LLF's ongoing support of the Longevity Research Program, now in its seventh year, which continues to investigate aspects of the Caloric Restriction with Optimum Nutrition (CRON) eating plan on the lifespans and biometrics of its adherents.

At this point, more than 65 articles about LLF-funded research projects and their results have been published in peer-reviewed scientific journals. LLF researchers have also been cited in the consumer press.

The research funded by the Foundation is a substantial contribution to the body of research on mortality, public health and quality of life, and it is research RGA is committed to continuing to advocate and support. ■



The Longer Life Foundation is a not-for-profit partnership between RGA and Washington University's School of Medicine, created in 1998. The LLF supports and funds independent research into longevity and enhancing quality of life and wellness.

The LLF recently announced its selection of research grant recipients for the 2014-2015 year.

ON DEMAND WEBCASTS

RGA and industry experts discuss the topics below in our 2014 webcasts.

Managing Post-Level Term Experience

Learn more about the results of two recently published reports, “Report on the Lapse and Mortality Experience of Post-Level Premium Period Term Plans (2014)”, sponsored by the Society of Actuaries, and “Report on the Survey of Post-Level Premium Period Lapse and Mortality Assumptions for Level Premium Term Plans (2013)”. These reports show the impact of policyholder behavior on post-level term experience and provide information about product designs, pricing assumptions and strategies for managing this experience.

Presenter: Tim Rozar
Senior Vice President,
Global Research and Development
RGA Reinsurance Company

Presenter: Derek Kueker
Actuary, Global Research and Development
RGA Reinsurance Company



The Predictive Nature of Credit Data for Mortality

RGA recently partnered with TransUnion in a groundbreaking joint research study to better understand the predictive nature of credit data for life insurance. Tune in to this webcast to learn about the results of the study as well as the potential applications of this data in lead generation, risk selection and in-force management.

Presented by: RGA and TransUnion



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