ReFlections

RGA's Global Medical Newsletter

Volume 60, September 2023

Dr. Adela Osman
Vice President
Head of Global Medical
adela.osman@rgare.com

Dr. Daniel D. Zimmerman, DBIM
Senior Vice President
Chief Science Advisor
dzimmerman@rgare.com

IN THIS ISSUE

FROM THE EDITORS

Welcome to the September 2023 issue! We have several interesting and timely articles. First is the second part of Dr. SiNing Zhao's comprehensive article about autism. **Dr. Zhao**, Regional Medical Director – Asia, reviews the many issues impacting insurers as the number of children and adults diagnosed with autism continues to increase rapidly.

A first-time *ReFlections* author, **Dr. Megan Leivant**, Vice President and Medical Director, U.S. Mortality Markets, contributes an article on the latest developments in bladder cancer, one of the most prevalent cancers worldwide. This issue also features a preview of research being undertaken jointly by RGA with the University of Leicester in the U.K., exploring the impact of lifestyle factors on mortality and morbidity. Authors **Kishan Bakrania**, Senior Health Data Scientist, Global Data and Analytics, **Richard Russell**, Vice President, Head of Health Data Analytics, Global Data and Analytics, and **Dr. Kevin Somerville**, Medical Director, Underwriting Research and Manual Development, discuss the anticipated insights which may impact future approaches to underwriting and pricing.

The **Longer Life Foundation** (LLF) also announces its annual list of grant recipients for 2023-2024. This year marks the 25th anniversary that the Foundation has been supporting groundbreaking research into factors impacting health and longevity. We are also proud to present a short video commemorating LLF's anniversary. A link to the video is available on page 19.

Please enjoy this issue of *ReFlections*! And do not hesitate to let us know how we can continue to improve it for you.

AN UPDATE ON AUTISM SPECTRUM DISORDER PART 2: THROUGH AN INSURANCE LENS

Abstract

During the past 30 years, autism spectrum disorder (ASD) has emerged as one of the faster-growing diagnosed disorders of childhood. Its growth in prevalence among children has led to the need for a much greater focus on this area from not only a clinical lens, but also an insurance one.

Autism is also not just a disorder of children. According to the CDC, more than 5.4 million adults (>2% of the population) in the U.S. alone have ASD. In addition, a 2022 study found that adults with autism comprise 0.6% of the world's adult population.

An additional concern with ASD is the many comorbidities linked to it that are known to impact the health and wellbeing of those with the disorder.

Assessing risk for ASD, however, is still inherently difficult due to the heterogeneity of its manifestations, as well as gaps in the clinical understanding of its pathogenicity, its potential comorbidities, and its variable long-term prognosis. This usually means that in addition to clinical information, social, educational, and behavioral information is routinely required in order to develop a comprehensive assessment when reviewing applications indicating ASD in the medical history.

This article, the second of two parts, provides a comprehensive review of the insurance medicine view of ASD and issues around its assessment when underwriting. To read Part I, please click here.

Applications to Insurance

As Autism Spectrum Disorder (ASD) prevalence, awareness, and research have grown over the past 15 years, so have the juvenile insurance market. In the last five years, this segment has been a leading growth sector, with annual global growth forecasted at approximately 10% to 15%.[1] This growth partly reflects increasing awareness of and knowledge about juvenile diseases in general (and ASD in particular) among insurers and the buying public, greater growth in disposable income, more options available for healthcare and therapies for younger ASD individuals, and rising healthcare costs.

Coverage needs for juveniles overall are growing quickly. Awareness and understanding are increasing of ASD as well as other chronic neurodevelopmental disorders, and of the fact that ASD's physical and economic outcomes are similar to those of adults with critical illnesses.

ABOUT THE AUTHOR

Dr. SiNing Zhao, MBBS, FANZCA, FHKCA, FHKAM
SiNing.Zhao@rgare.com

Dr. SiNing Zhao, MBBS, FANZCA, FHKCA, FHKAM, Regional Medical Director, Asia, is responsible for product development, thought leadership, internal and external education, client support, industry representation and case consultation in Asia. Based in Hong Kong, her particular focus is on the Hong Kong, Korea, and Japan markets. Prior to joining RGA, Dr. Zhao was a Medical Director with a direct insurer.

Dr. Zhao earned her Bachelor of Medicine, Bachelor of Surgery (MBBS) degree from the University of Western Australia. She has a specialist qualification in Anaesthesiology and is a fellow with the Australian and New Zealand College of Anaesthetists, Hong Kong College of Anaesthesiologists and Hong Kong Academy of Medicine. She also has extensive clinical experience in tertiary teaching hospitals in Australia and Hong Kong, as well as specialty training in intensive care medicine.

This is generating rising demand for products for this age group – particularly for juveniles with special needs. Families of children with such needs are seeking insurance products that will provide appropriate and supportive treatment and management benefits. A large number of products now specifically target this demographic, and more are on the way, as families with a child who has had an ASD diagnosis may be motivated early to purchase insurance coverage for their child to guard against long-term health implications.

Understanding ASD Applicant Risk

With ASD prevalence on the rise and greater diversification of juvenile insurance products, more families are seeking long-term life and living benefits insurance options for their affected children.

Insurance companies will need to know how to stratify the risk properly for life, total and permanent disability (TPD), and critical illness coverage options.

- **Mortality Risk.** Overall, mortality risk for children and young adults in the general population is very low, and for children and young adults with ASD, also very low in absolute numbers. However, when compared with the non-affected segment of this demographic, the overall risk is higher.[2] A long-term longitudinal study following an ASD cohort found the absolute risk was about double that of the general population in the younger age group.[3] Causes are often linked to injuries and accidents sustained through misadventure, or due to comorbid psychiatric, neurological, or developmental disorders.[4]

  With associated comorbidities, the mortality risk rises even further. Psychiatric disorders affecting mood or anxiety, for example, increases ASD mortality risk slightly,[5, 7] but epilepsy approximately triples the risk[6]. Evidence also shows that younger adults with ASD have higher rates of suicide attempts later in life, independent of any associated psychiatric illness.[8]

- **Morbidity Risk.** Many comorbid conditions occur with ASD, or ASD is a part of the wider spectrum of symptoms found in developmental situations. For example, about 40% to 50% of individuals with Tuberous Sclerosis Complex, a genetic condition where benign tumors develop in major organs such as the brain, heart, lung, and kidney, leading to potential serious effects on organ function, also have ASD.

  Commonly occurring comorbid conditions of ASD include:[9]

  - Neurodevelopmental disorders
    - ADHD
    - Intellectual disability
  - Psychiatric disorders
    - Anxiety and mood disorders (often worsen in adolescence and adulthood)
    - Severe aggression
    - Self-harm behaviors
  - Medical conditions
    - Epilepsy
    - Tuberous Sclerosis Complex
    - Feeding and gastrointestinal difficulties
    - Weight extremes
    - Sleep difficulties
    - Self-care challenges (e.g., dental or skin care), which can lead to hygiene-related problems

Prognosis

The natural progression of ASD generally leads to poorer outcomes for social, psychological and physical wellbeing. In some cases, through early intervention and ongoing care strategies, some with mild ASD are able to live and function a close to normal life. In others, however, the individual with ASD is unable to function independently, requires higher levels of general and mental care, and finds it difficult to obtain and maintain employment.[10]

Severity of outcomes can be difficult to predict accurately, especially for children under three years of age. As firm evidence suggesting clear predictive signs and symptoms is lacking, future long-term mortality, morbidity, and functional capabilities need to be extrapolated from current states of function and interventions being undertaken. Even though great improvements are possible in cases where symptoms are or become mild or may be non-impactful, a person with ASD is still likely to retain some features of the disorder as they grow into adulthood.[11]

Prognostic Factors[12, 13, 14]

Prognostic factors for children with ASD indicating more favorable outcomes include:

- Early intervention
- Active participation in therapies
- Higher cognitive abilities
- Ability to play
- Better verbal communication abilities
- Attempts to socialize, share, show interest in others
- Fewer or less severe comorbid conditions (e.g., less severe ADHD)
- Lack of hospitalizations related to ASD and its associated comorbidities
- Able to participate in certain mainstream activities (e.g., school)

Conversely, prognostic factors that may indicate less favorable outcomes include:

- Lack of socialization, sharing, or interest in others by age 4
- Limited verbal vocabulary by age 5
- Severe ASD symptoms
- Lower cognitive abilities (such as IQ <70)
- Comorbid conditions, genetic conditions
- More frequent hospitalizations related to ASD and associate comorbidities
- Less access to therapies / lack of therapeutic interventions
- Older age at diagnosis
- High level of care requirements

As children grow older, the focus of the above factors will evolve into areas such as schooling, independent living and function, employment, and serious co-morbid complications.

Assessment of ASD underwriting cases, both for juveniles and adults, will likely need closer and more careful review. When assessing the risk, it may be prudent to account for both baseline risk and age-appropriate prognostic markers. This more individualized approach may be more nuanced and balanced, and could increase risk assessment accuracy, especially for very young patients.

In understanding the disease, it also indicates that how a child with ASD is assessed for cover is likely to differ depending on the product. Risk appetite for traditional life and critical illness (CI) products, for example, might be different from that for TPD and CI products that include specific neurodevelopmental and juvenile benefits.

Case Studies: Case 1

Applicant information

- Application for a 3-year-old male for a traditional life/CI/TPD bundled product
- Diagnosed with ASD at age 2½ (six months prior)
- Therapy begun upon diagnosis and monitored by developmental pediatrician
- No other medical history items noted on application form
- No current medications

In many instances, limited information may be presented upon first application and will require additional information to assess correctly, such as:

- Developmental history – cognitive function, milestones
- Verbal communication capabilities
- Social function capabilities
- Severity level
- Any schooling, whether mainstream or not
- What therapies have been undertaken and their results
- Comorbidities, any underlying related disorders

Discussion

The additional information can help stratify the likely risk into mild, moderate, and severe cases. Depending on the type of coverage, risk appetite of the product, and also underwriting guidelines in place, there may be different outcomes for this case.

In the case of a toddler-age child only recently diagnosed, it may be prudent to postpone writing cover until the child is older in order to enable a more comprehensive assessment. Many insurers may choose to postpone consideration until the child is in school and has had longer duration of therapy and/or treatments to see if functional capabilities and symptoms have stabilized in order to assess and stratify risk with more accuracy.

In cases involving very young applicants with ASD, underwriting frameworks may be in place to utilize available information and extrapolate into the different categories. In such cases, where a decision on long-term outcomes is made within the limits to be placed on very young applicants, it is important to weigh any factors that may predict a better outcome (such as early diagnosis or early intervention) versus less favorable factors (such as low cognitive functioning and associated comorbidities).

In general, for living benefits cover such as CI and TPD for very young ASD-diagnosed applicants, appropriate exclusions for ASD disease management and complications will often be warranted.

Case Studies: Case 2

- Application for a 16-year-old male traditional life/TPD/CI bundled product
- Diagnosed with ASD at age 5
- Initial symptoms: speech delay, reduced social interaction, repetitive behaviors
- ASD managed by pediatrician and psychiatrist
- Underwent behavioral therapy regularly
- No medications for ASD prescribed to date
- Currently in mainstream school with additional support
- Able to function well and independently both in and outside of school
- Still has some trouble socializing and making friends, but does attempt
- No comorbid disorders
- Only biannual follow-ups

Discussion

This case is that of an older adolescent with a longer history of ASD.

The history provided has more detail, enabling a clearer and more precise overall picture of the applicant's ASD history, treatments over time, disease progression, and current severity level.

Although more information was provided for this individual than for the individual in Case 1, it still may be prudent to request additional complementary material, such as school reports, recent psychiatrist/treating physician reports, and cognitive or behavioral testing outcomes, so as to corroborate the available history.

This case has several indicators of potentially positive outcomes, as his symptoms have been shown to have diminished over time due to long-term interventions and therapy. Based on this history, he may have a milder form of ASD and so is likely to have a more favorable prognosis in terms of mortality and morbidity. He therefore may be a candidate for the insurance.

Still, as per the previous case, appropriate exclusions for living benefits coverage for ASD and its complications may be warranted.

Product Development

Development of products that cover ASD, especially as part of CI plans, has been rising. It is mainly being driven by customer demand and awareness of this population's healthcare issues and needs.

Like mental health, neurodevelopmental disorders were traditionally on the exclusions list. Newer product designs, however, are recognizing that the burden of disorders such as ASD may be similarly impactful to traditional CI diagnoses.

When formulating benefits for ASD cover, it is essential that critical disease factors be incorporated to ensure benefit appropriateness as well as cost and utilization risk containment.

Considerations around factors such as anti-selection, appropriate levels of monetary coverage that reflect the longer term, chronic, and costly nature of ASD, and the likelihood of high utilization of additional benefits, should be taken into account. The difficulty in long-term prognostication for very young ages as well as certain aspects of disease pathophysiology, progression, and impact on mortality and morbidity, can impact decisions on cost, pricing, and segmentation. Despite these challenges, it is worthwhile to consider expanding coverages to include ASD and provide benefits to a vulnerable population in need.

Conclusion

ASD is a chronic condition with increasing prevalence, mainly due to better screening and caregiver awareness. Over the past decade, improvements in understanding and treating the disease have seen better outcomes in prognosis. However, the potential comorbid disease associations and other genetic factors still predispose a child with ASD to higher mortality risk, morbidity complications, and in most cases a lower quality of life compared to the general population.

As prevalence of ASD is expected to continue rising among juveniles, people with this disorder are likely to be encountered more frequently by insurers. While the disorder itself is multifaceted and individual cases can vary substantially, some general principles can guide risk assessments.

- Understand the disease afresh: spend time learning about its issues, including pathogenesis, symptoms, diagnosis, treatment and prognosis; and ask for information from a broad range of diagnostic, therapeutic, and functional information sources, such as:
  - Doctors (pediatricians, psychiatrists)
  - Clinical psychologists
  - Therapists
  - School reports
    - Educational
    - Counselors
  - Therapists
  - Social workers
  - Assess each case on its own merit
    - Every case will involve a complex assessment of potential current and future risk.
    - Not all cases will fit neatly into existing underwriting guidelines.
    - Multiple subject matter experts may be needed to analyze the information and determine possible outcomes.
    - When in doubt, ask for help (e.g., medical officers) and get to a solution together.

References

1. https://www.businessresearchinsights.com/market-reports/juvenile-life-insurance market-100276
2. https://pubmed.ncbi.nlm.nih.gov/18579647/
3. https://pubmed.ncbi.nlm.nih.gov/26752506/
4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4814267/
5. https://pubmed.ncbi.nlm.nih.gov/26752506/
6. https://pubmed.ncbi.nlm.nih.gov/22348343/
7. https://pubmed.ncbi.nlm.nih.gov/28872268/
8. https://pubmed.ncbi.nlm.nih.gov/33972922/
9. https://psycnet.apa.orgrecord/2020-87393-001
10. https://pubmed.ncbi.nlm.nih.gov/30860939/
11. https://pubmed.ncbi.nlm.nih.gov/22473372/
12. https://pubmed.ncbi.nlm.nih.gov/3610999/
13. https://pubmed.ncbi.nlm.nih.gov/15796118/
14. https://www.who.int/news-room/fact-sheets/detail/autism-spectrum-disorders

BLADDER CANCER: OVERVIEW, TREATMENT CHALLENGES, AND TRENDS

Abstract

Bladder cancer is the most common malignancy of the genitourinary system and one of the ten most prevalent cancers worldwide. Its high propensity for recurrence often requires lengthy and costly treatment regimens to reduce both recurrence and progression. Non-muscle-invasive urothelial carcinoma accounts for more than 80% of cases, including the high-risk carcinoma in situ*. Intravesical chemotherapy and immunotherapy using bacille Calmette-Guerin (BCG) have been treatment mainstays for two decades, but in recent years newer therapies have been in development to help address both the global shortage of BCG and the issue of BCG-unresponsive disease.*

This article will provide background on bladder cancer, with a particular focus on current and in-development treatments for non-muscle-invasive disease.

Background

Bladder cancer, the most prevalent malignancy of the genitourinary system, is the sixth most common type of cancer in the U.S. and the tenth most common worldwide. Globally, an estimated 600,000 people are diagnosed with it each year, and more than 82,000 of these cases occur in the U.S. Additionally, approximately 200,000 bladder cancer-related deaths (17,000 in the U.S.) occur per year worldwide. Geographically, North America and Western Europe have the highest incidence rates of bladder cancer, while Central America and Middle and West Africa have the lowest.[1,2]

Categories and Types

Bladder cancer can be characterized as either epithelial or nonepithelial (mesenchymal) based on where the tumor originated. Epithelial neoplasms account for 99% of all bladder cancers (Figure 1). Urothelial carcinoma, a specific type of epithelial neoplasm, is the most common histologic type, present in up to 90% of cases in North America and Western Europe combined.

ABOUT THE AUTHOR

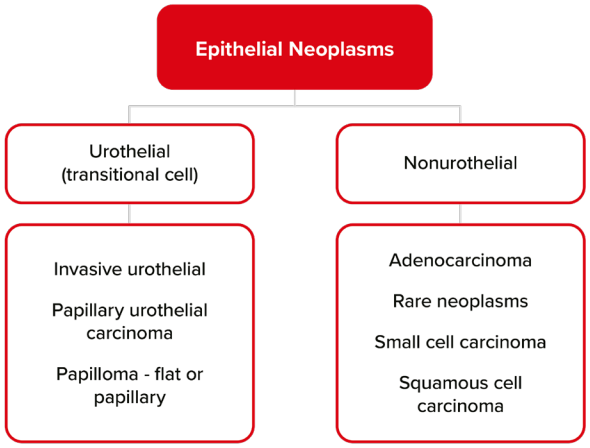
Megan Leivant, M.D.
Megan.Leivant@rgare.com

Dr. Megan Leivant, Vice President and Medical Director for RGA Reinsurance Company, assesses mortality risk for facultative life referrals, provides medical education and training for underwriters, and contributes to RGA underwriting manual development.

Prior to joining RGA in 2021, Megan was a medical director with General Re Life Corporation and OneAmerica. She also has a decade of experience in outpatient medical practice and has served as a physician reviewer for the Medical Review Institute of America.

Megan's Bachelor of Arts (B.A.) in biological sciences is from DePauw University, and her Doctor of Medicine (M.D.) is from Indiana University School of Medicine. She is a diplomate of the American Board of Internal Medicine, an Education Committee member of the American Academy of Insurance Medicine, and a member of the American College of Physicians.

Figure 1: Types of Epithelial Bladder Tumors

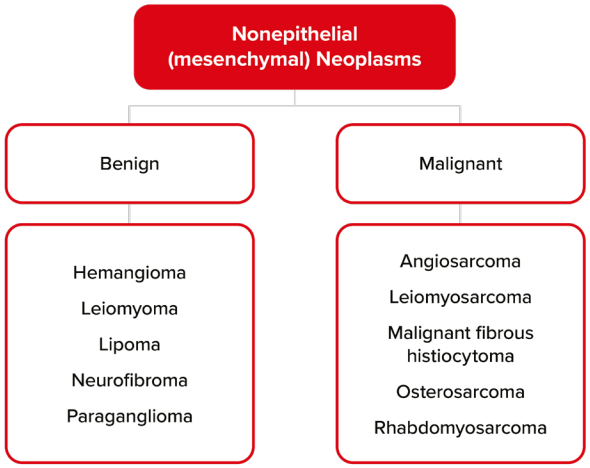


The urinary bladder and genitourinary tract are lined with urothelial cells, which are specialized transitional epithelial cells. These cells are constantly exposed to environmental toxins as the kidney filters them through the urine, making them prone to malignant transformation.[3]

Nonurothelial bladder tumors, which arise from cells other than the urothelium, make up the remaining proportion of epithelial neoplasms, including subtypes such as adenocarcinoma, small cell carcinoma, and squamous cell carcinoma. Squamous cell carcinoma is the most prevalent type in the Middle East and Africa due to its association with the parasitic disease schistosomiasis.

Nonepithelial or mesenchymal neoplasms, which account for only 1% of all bladder tumors, arise within the bladder's connective tissue layers (Figure 2).

Figure 2: Types of Nonepithelial Bladder Tumors



Risk Factors

Approximately 80% of bladder cancer cases are attributable to identifiable and avoidable risk factors. The majority of these are environmental exposures such as cigarette smoking, the number one risk factor, which accounts for 50% to 65% of cases due to the presence of carcinogens such as polycyclic aromatic hydrocarbons and beta-naphthylamine[4] in cigarette smoke. Occupational exposure to aromatic amines, which are found in paints, metals, petroleum goods, rubber, and manufacturing dyes, account for another 10% to 20% of cases.

Additional risk factors include chronic bladder inflammation due to recurrent cystitis, hereditary factors, past pelvic radiation treatment, presence of arsenic in drinking water, certain medications, increased BMI, male gender, and advancing age. In the U.S. alone, more than 90% of bladder cancers occur in individuals ages 55 or older, with a median age of 73 at time of diagnosis.[5]

Symptoms and Diagnosis

Painless hematuria is the characteristic presenting sign or symptom associated with bladder cancer. It can be microscopic or grossly visible. Dysuria, urinary frequency, and urinary urgency are other common presentations. Diagnostic evaluation follows a risk-stratified approach that typically includes urinalysis demonstrating >3 RBC/HPF, renal ultrasound, and cystoscopy, the last of which is considered the gold standard test.

Urine cytology can be used as an adjunct to cystoscopy, but it has low sensitivity for diagnosing low-grade tumors. This low sensitivity has resulted in the development of tests that can detect multiple urine-based tumor biomarkers, which have numerous potential applications in the detection of urothelial bladder cancer. These tests target markers such as the differential expression of DNA, RNA, cellular markers, and tumor-related proteins.

Urine-based tumor markers have been found to have greater sensitivity than urine cytology for detection of low-grade tumors, but to be inferior to urine cytology with regard to specificity. False positive tests can also occur, especially in situations such as concomitant UTI,

renal calculi, or prior intravesical treatment. One study found that urinary biomarker tests miss 18% to 43% of patients with bladder cancer and yield false-positive results in 12% to 26% of individuals who do not have bladder cancer.[6]

Although this lack of specificity has limited the definitive clinical application of these biomarker tests, numerous potential applications still do exist.[7] For example, urine biomarkers could assist in the initial diagnosis of bladder cancer by risk-stratifying which individuals should undergo subsequent cystoscopy and imaging evaluation of the genitourinary tract. Similarly, biomarkers could aid in the surveillance of non-muscle-invasive bladder cancer (NMIBC) by serving as an adjunct to urine cytology to help detect the presence of low-grade tumors that might otherwise be missed, or cystoscopy to potentially serve in lieu of the procedure altogether.

Bladder cancer recurrence rate far surpasses that of all other cancers.

Staging

Bladder cancers can be divided into non-muscle-invasive and muscle-invasive disease. Pathologic staging of bladder cancer is contingent on the magnitude of tumor invasion into deep layers of the bladder. NMIBC accounts for 80% of newly diagnosed bladder cancers, including tumors in stage 0 subgroups Ta (70%-75%) and Tis (5%-10%), and the stage I subgroup T1 (20%-25%).[8]

NMIBC can be further stratified into low- and high-risk categories, with varying degrees of risk for progression and recurrence. According to the 2021 European Association of Urologists (EAU) guidelines, low-risk tumors are solitary, low-grade (Ta), less than three centimeters in diameter, and not carcinoma *in situ*. High-risk tumors include carcinoma *in situ* (Tis), high-grade disease, stage T1 lesions, and low-grade (Ta) tumors that are either multiple, recurrent, and/or large (more than 3 cm in diameter). Low-risk tumors have a 0%-4% risk of progression that increases to 30%-40% for high-risk lesions. It is estimated that 31%-78% of NMIBC cases recur within five years of diagnosis, a rate far surpassing that of all other cancers.[9]

Muscle-invasive disease, characterized by malignant extension into the detrusor muscle, includes tumors determined to be stages II through IV.

Table 1: Bladder Cancer TNM Staging	
Primary tumor (T)	
T category	**T criteria**
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Noninvasive papillary carcinoma
Tis	Urothelial carcinoma *in situ*: "Flat tumor"
T1	Tumor invades lamina propria (subepithelian connective tissue)
T2	Tumor invades muscularis propria
pT2a	Tumor invades superficial muscularis propria (inner half)
pT2b	Tumor invades deep muscularis propria (outer half)
T3	Tumor invades perivesical soft tissue
pT3a	Microscopically
pT3b	Macroscopically (extravesical mass)
T4	Extravesical tumor directly invades any of the following: Prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
T4a	Extravesical tumor invades directly into prostatic stroma, seminal vesicles, uterus, vagina
T4b	Extravesical tumor invades pelvic wall, abdominal wall
Regional Lymph Nodes (N)	
N category	**N criteria**
NX	Lymph nodes cannot be assessed
N0	No lymph node metastasis
N1	Single region lymph node metastasis in the true pelvis (perivesical, obdurator, internal and external iliac, or sacral lymph node)
N2	Multiple region lymph node metastasis in the true pelvis (perivesical, obdurator, internal and external iliac, or sacral lymph node metastasis)
N3	Lymph node metastasis to the common iliac lymph nodes
Distant Metastasis (M)	
M category	**M criteria**
M0	No distant metastasis
M1	Distant metastasis
M1a	Distant metastasis limited to lymph nodes beyond the common iliacs
M1b	Non-lymph-node distant metastases

Source: UpToDate[20]

Treatment

Management of each type of bladder cancer differs significantly and poses unique challenges. Radical cystectomy, with or without platinum-based neoadjuvant chemotherapy, is the treatment of choice for surgically amenable muscle-invasive disease but carries a high morbidity risk (60%) and a near 3% risk of mortality.[10] Conversely, transurethral resection of a bladder tumor (TURBT), with or without intravesical chemotherapy or immunotherapy, is preferred for non-muscle-invasive disease.

Tumors with low risk for recurrence benefit from a single immediate instillation of one of the two intravesical chemotherapeutics, gemcitabine or mitomycin C, following TURBT to help eradicate residual disease. High-risk NMIBC requires a restaging TURBT six weeks following the initial procedure (given the up to 50% risk of understaging), followed by adjuvant immunotherapy with intravesical bacille-Calmette Guerin (BCG). BCG, the live attenuated form of mycobacterium bovis, is the most widely used intravesical therapy for bladder cancer. Treatment courses often span one to three years for intermediate to high-risk tumors and involve a robust induction and maintenance schedule.[11]

For more than two decades, BCG immunotherapy has been the treatment of choice for individuals with high-risk NMIBC, especially carcinoma *in situ*, because it delays tumor progression, reduces the need for cystectomy, and improves survival. BCG does have limitations, however, as recurrence rates for cases where it is used approach 40% at two years, treatment failure occurs in 30% to 50% of cases, it can be poorly tolerated due to adverse side effects, and there may be diminished immunologic response over time.[12]

Management of each type of bladder cancer differs significantly.

Challenges and Advances

Since 2019, BCG has been in short supply worldwide due to an unforeseen reduction in the number of pharmaceutical manufacturers in the market, leaving affected individuals with suboptimal treatment options depending on the severity of disease.[13] Since then, the investigative focus has shifted to biomarkers to target responsiveness to therapy. In the past few years, such alternative regimens have been developed and successfully implemented, including the use of intravesical chemotherapies mitomycin C and gemcitabine, sequential gemcitabine/docetaxel, and even initial radical cystectomy in certain high-risk situations.

Therapeutic options for individuals with NMIBC are evolving to include gene therapy, immune checkpoint inhibitors, targeted therapy, and antibody-drug conjugates (ADCs), which are a monoclonal antibody chemically linked to a drug. Adstiladrin (nadofaragene firadenovec), one such ADC, is a recombinant nonreplicating adenovirus vector with complete response rates of up to 53%, and was approved by the U.S. Food and Drug Administration in early 2023 for BCG-unresponsive NMIBC.[14, 15]

Three immune checkpoint inhibitors have also been approved for individuals with locally or advanced metastatic bladder cancer. One of these treatments, Keytruda (pembrolizumab), approved in 2020, is a programmed cell-death protein 1 (PD-1) inhibitor that demonstrated a 41% response rate for BCG-unresponsive carcinoma *in situ* in the KEYNOTE-057 trial.[16, 17] There is a pending phase III evaluation of pembrolizumab plus CG0070, an oncolytic virus therapy, following phase II trial results showing complete response in 85% of individuals with BCG-unresponsive NMIBC.[18]

Molecular profiling is being performed to predict which subtypes of NMIBC respond to BCG, and multiple trials are also underway to investigate alternative therapies for BCG-unresponsive bladder cancer. A recent study uncovered three distinct BCG response subtypes, one of which had a lower recurrence-free and progression-free survival, thus allowing for more targeted treatment for people unlikely to respond to BCG.[19]

Conclusion

Bladder cancer is a disease recognized for its high propensity for recurrence. NMIBCs, the majority of cases, often require prolonged and costly treatment. Cystoscopy remains the gold standard for diagnosis, but the expanding availability of urine tumor biomarkers offers a potential adjunct in both the identification of bladder cancers as well as ongoing surveillance. The evolution of novel therapeutics, such as gene therapy or immune checkpoint inhibitors to address BCG-unresponsive disease and the ongoing BCG shortage, is also providing greater opportunities for individuals to achieve lasting treatment response while postponing or even avoiding radical cystectomy. Such responses could pose a more favorable underwriting outlook. RF

References

1. https://www.cancer.org/cancer/types/bladder-cancer/about/key-statistics.html
2. https://www.iarc.who.int/cancer-type/bladder-cancer/
3. https://pubmed.ncbi.nlm.nih.gov/36042998/
4. https://pubmed.ncbi.nlm.nih.gov/32183076/
5. https://acsjournals.onlinelibrary.wiley.comdoi10.3322/caac.21763
6. https://pubmed.ncbi.nlm.nih.gov/26501851/
7. https://pubmed.ncbi.nlm.nih.gov/33858747/
8. https://jnccn.org/view/journals/jnccn/18/3 article-p329.xml
9. https://pubmed.ncbi.nlm.nih.gov/34511303/
10. https://bjui-journals.onlinelibrary.wiley.com/doi/0.11 11/bju.14718
11. https://jnccn.org/view/journals/jnccn/18/3/article-p329.xml
12. https://pubmed.ncbi.nlm.nih.gov/36853609/
13. www.enddrugshortages.com
14. https://pubmed.ncbi.nlm.nih.gov/33253641/
15. https://jamanetwork.com/journals/jama/fullarticle/2800443
16. https://www.cancer.gov/types/bladder/research
17. https://pubmed.ncbi.nlm.nih.gov/34051177/
18. https://www.urologytimes.com/view/oncolytic-immunotherapy-cg0070-plus-pembrolizumab-shows-promise-in-bcg-unresponsive-nmibc
19. https://pubmed.ncbi.nlm.nih.gov/37224225/
20. https://www.uptodate.com/contents/clinical-presentation-diagnosis-and-staging-ofbladdercancer?search=bladder%20cancer&source=searchresult&selectedTitle=1~150&usage_type=default&displayrank=1#references

EXPLORING THE IMPACT OF LIFESTYLE FACTORS ON MORTALITY AND MORBIDITY USING UK BIOBANK DATA

Abstract

When underwriting life and health insurance, determining how multiple rating factors, such as lifestyle, comorbidities, and mortality, can interact with and impact one another remains challenging. To unravel this, RGA is collaborating with world-renowned researchers from the University of Leicester (U.K.) to enable scientists as well as insurers to realize the potential and limits of lifestyle information for disease and death prognostication. The research aims to bring direct and significant value to insurance medical directors and underwriters by generating critical and novel insights that will enhance medical knowledge and support the development of underwriting philosophies and strategies.

Introduction

Insurers have long understood that lifestyle factors thought of as "unhealthy," such as smoking, sedentary behaviors, poor eating habits, and excessive (or inadequate) sleep, can contribute to chronic health conditions and adverse outcomes. What insurers have largely lacked, however, is the ability to quantify the influences and interactions of these activities on the health and longevity of life and living benefits insurance applicants.

Improved risk assessment, for example, could enable premium pricing that reflects individual applicant risks more precisely and ultimately strengthens insurer underwriting practices. For customers, a better understanding of how lifestyle factors can affect health, life expectancy, and quality of life (possibly coupled with financial or other incentives) could lead to behavior changes and, through insurance-linked wellness programs, greater engagement with their insurance providers as partners in health.

This research study, sponsored by RGA and conducted by the University of Leicester, a leading university in the U.K., has as its objective making enhanced risk knowledge a risk assessment reality. Using some of the best data available, from the UK Biobank, this research will help quantify how everyday life factors such as physical activity, diet, and hours of sleep, can impact chronic health conditions such as cancer, diabetes, and cardiovascular disease, and refine industry data on related mortality outcomes.

ABOUT THE AUTHORS



Kishan Bakrania, Ph.D.
Kishan.Bakrania@rgare.com

Kishan Bakrania, Ph.D., is a Senior Health Data Scientist in RGA's Global Data and Analytics (GDA) department. His doctorate in epidemiology, Master of Science (M.Sc.) in medical statistics, and Bachelor of Science (B.Sc.) in mathematics, are from the University of Leicester.

Richard Russell, Ph.D.
rrussell@rgare.com

Richard Russell, Ph.D., is Vice President, Head of Health Data Analytics in RGA's Global Data and Analytics department. Previously, he was a Postdoctoral Research Fellow at City, University of London for two years, and at Moorfields Eye Hospital, London. His Bachelor of Science (B.Sc.) in biotechnology, Master of Science (M.Sc.) in bioinformatics (with distinction), and Ph.D. in statistics are from Imperial College London. He has authored more than 30 peer-reviewed articles for journals such as The Lancet, BMJ Open, PLoS One, and Annals of Actuarial Science.

Dr. Kevin Somerville, D.M.
kevin.somerville@rgare.com

Kevin Somerville MbCHb, DM, FRCP, FRACP is Medical Consultant to RGA's Global Underwriting Manuals, Research and Development team. He graduated in Medicine from Auckland University, New Zealand and his Doctorate in Medicine is from Nottingham University. Since 1997 he has worked in Insurance Medicine with a particular and evolving interest in evidence-based risk assessment.

The database used for this research is the UK Biobank, a large prospective study that provides accredited researchers direct access to a comprehensive database of health metrics from half a million middle-aged participants. These data have been and are being used by researchers to conduct a variety of studies about topics related to health and longevity.[1]

Findings from this research, which are expected by 2023's fourth quarter, are anticipated to enhance underwriting considerations, pricing, and recommendations for insurer life and living benefits wellness programs.

This article provides a brief background to the concept of wellness as it is conceived of and utilized in the life insurance industry, introduces and highlights RGA's goals for our collaborative UK Biobank database research, and demonstrates how the findings might be utilized to enhance underwriting philosophies and pricing estimates. Lastly, it will showcase the wider industry value from this project.

Wellness' Unexplored Potential

The incorporation of wellness, as an initiative and a goal, into life and living benefits insurance first emerged more than 20 years ago. Although it has been an accelerating trend ever since, our industry has yet to either realize the full potential of or understand the limits of wellness initiatives.

Strategically implementing wellness programs and initiatives in our products requires a deep understanding of the associations between lifestyle behaviors and health outcomes. New and more inclusive data sources, ongoing developments in technology, and advanced approaches to integrating biometric information into insurance products are all moving such initiatives beyond mere engagement and marketing schemes. Insurers now see them not only as tools for gathering additional underwriting evidence but also, importantly, as tools that can improve customer health and wellbeing.

In 2021, RGA and RGAX surveyed more than 100 life and health insurers from around the world about current and

future wellness-related products, initiatives, and strategies as well as challenges and potential opportunities.[2] The survey found that insurers see great potential for wellness initiatives to support their policyholders' overall physical, mental, and financial health:

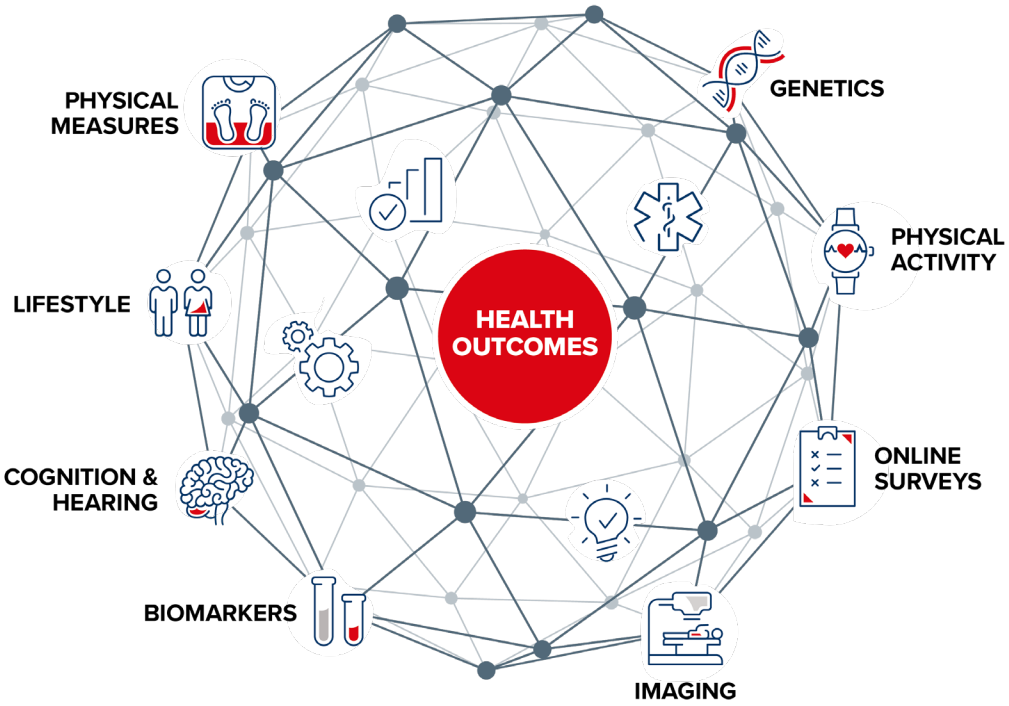
- 85% of insurers globally indicated wellness is a top priority, particularly after the onset of COVID-19.
- Wellness program implementations among insurers are increasing globally, with 57% of respondents offering wellness-related products, digital tools and services, mental health support, and/or financial planning tools.
- Top areas for growth in wellness-related products, strategies, and initiatives are in chronic disease management, mental health, and financial welfare.

Data-driven evidence will be needed to help insurers achieve the full potential of their wellness initiatives.

Why UK Biobank Data?

The UK Biobank is a large biomedical database containing both broad and in-depth information about the health of its participants, which comprise more than half a million U.K. adults between ages 37 and 73 at baseline (2006 to 2010). The database includes not only participant routinely linked mortality and morbidity outcome data, but also comprehensive lifestyle and wellness metrics. Participants provided a broad range of biological, cognitive, demographic, health, lifestyle, mental, social, and wellbeing data, and continue to do so today (Figure 1).

Figure 1: Breadth and Depth of UK Biobank



Adapted from UK Biobank

When compiling the database, several steps were taken to ensure ethnic, geographical, and socioeconomic heterogeneity, as well as broad distribution across as many exposures as possible. This was done to allow reliable detection of generalizable relationships between demographic characteristics and health outcomes. Participant recruitment was via invitations mailed to people in the targeted age cohort – those registered with the U.K.'s National Health Service (NHS) who lived within 25 miles of one of the 22 study assessment centers located throughout England, Scotland, and Wales.

Although the UK Biobank is not necessarily representative of the general population, as it has already been shown to have "healthy volunteer" selection bias – that is, participants, who are self-selected from the overall database, are healthier than the general U.K. population.[3] Still, it is sufficiently illustrative of standard insured lives, making studies of this population of particular interest and relevance to insurers.

Research Goals

Life and health underwriting philosophies typically contain criteria relating to several different aspects of health, including biological, physical, mental, and lifestyle. As the UK Biobank is a sizable data resource that permits research into many of these aspects of human health, this has given RGA's underwriters, with input from our chief medical officers, the opportunity to formulate a broad range of research questions they considered to be of highest importance for the UK Biobank to be used to investigate.

Tackling these questions will help strengthen and expand RGA's underwriting philosophies and wellness strategies. A baseline normative wellness dataset, as well as other easily measured attributes within the conventional standard risk pool, is a prerequisite for assessing substandard risks. Table 1 shows some examples of how the deliverables from this study may impact the different functions of RGA's underwriting methodology.

Table 1: Translating Potential Findings

	Example	Potential action
Guidelines	In comparison to BMI, waist circumference is observed to be a better predictor of inferior health outcomes in overweight males	Revise the guidelines accordingly
Rating tables	After controlling for traditional rating factors, resting heart rate shows novel relationships with the outcomes of interest in certain subpopulations	Understand the evidence and update the appropriate rating table
Calculators	Simple, easy-to-collect metrics such as self-reported walking pace is observed to be a strong differentiator of mortality risk in older adults	Fittingly incorporate walking pace into the relevant calculator

Wider Value

This collaborative research will enable insurers to focus on the utility of current and future underwriting factors such as lifestyle (including physical activity) and easily measured variables such as heart rate. The hope and expectations are that these items can complement more traditional rating factors such as age and sex, and comorbidities such as high blood pressure, to predict mortality and morbidity outcomes. There is even the potential for incorporating lifestyle factors in underwriting in ways that can supplement traditional approaches to risk. Data-driven research can help insurers identify and segment risk more effectively, calculate the impact wellness factors can have on life and health experience, and potentially optimize underwriting decisions. It will also enable us to justify, through trusted data, our approaches to risk assessment.

Summary

Can new evidence from the UK Biobank make an impact on insurance underwriting? The answer, we trust, will be yes. The goals of this research are:

- Improve the underwriting philosophy and best-estimates for pricing
- Enhance wellness product development
- Generate additional critical insights into health and wellness, further supporting the results of the recent RGA & RGAX Global Wellness Survey Report
- Publish peer-reviewed articles on this research in medical, actuarial, and insurance journals for public interest and benefit
- Create a pool of knowledge that has sizable benefit to clinical researchers that could lead to better interventions in primary care (e.g., support healthcare providers in encouraging people to engage in healthier lifestyle choices) and significant public health implications
- Make a positive impact on society

Conclusion

As people are living longer, more will assuredly live with multiple diseases and conditions that impair health, making a deeper understanding of how combinations of risk factors affect mortality and morbidity extremely valuable. With interest in wellness rising rapidly across the insurance industry, the output from this project has the potential to create and provide critical insights to enhance underwriting and pricing for wellness products, as well as to inform consumers on ways to improve their health and longevity.

References

1. https://www.ukbiobank.ac.uk/
2. https://www.rgare.com/knowledge-center/article/redefining-wellness-global-survey-sheds-new-light-on-opportunities-for-insurers
3. https://pubmed.ncbi.nlm.nih.gov/28641372/

Longer Life Foundation

An RGA/Washington University Collaboration

The Longer Life Foundation (LLF), a collaboration of RGA and Washington University School of Medicine in St. Louis, is proud to announce its newest research grant recipients. These individuals are investigating some of the most important health and wellness issues of the day.

To find out more about the LLF and the research it has funded to date, please visit www.longerlife.org or reach out to Dr. Daniel D. Zimmerman at dzimmerman@rgare.com or Dr. Preeti Dalawari at preeti.dalawari@rgare.com.

We are pleased to announce the release of a promotional video commemorating the Longer Life Foundation's 25 years of providing proof-of-concept grants to medical and public health researchers at Washington University in St. Louis. Please click here to watch!

Longer Life Foundation 2023-2024 Grants	
Investigator, Project Title	**Project Description**
Milan Chheda, M.D. (Year 2) Glioblastoma and the Senescent Brain Microenvironment	Brain tumors increase in frequency with age. To date, all approved therapies target tumor cells. This study takes a different approach, by treating the aging brain. It is hypothesized the aging brain environment helps cause these tumors to grow and senescent cells play a causative role in the development of brain tumors. Therapies will be tested that target senescent cells in the brain which may prolong survival in animal models of disease. If successful, this work can be rapidly brought to the clinic, and will have application to treatment in people.
Hrishikesh Kulkarni, M.D. M.S.C.I. (Year 2) Amplification Loop Between Mitochondria and Complement in ARDS	The overarching goal of this proposal is to enhance both the survival and quality of life after acute respiratory distress syndrome (ARDS), a major cause of mortality. Pathways by which mitochondria released from the lung during injury activate complement will be dissected to assess how complement modulates mitochondrial respiration and homeostasis during lung epithelial injury.

Investigator, Project Title	Project Description
Laura Marks, M.D., Ph.D. (Year 2) Pathogenesis and Outcomes of Invasive S. aureus Infections	The epidemic of invasive Staphylococcus aureus infections among people who inject drugs (PWID) poses a significant public health and economic burden. By determining etiology of injection drug use-associated infections and identifying risks associated with transmission of invasive staphylococcal infections among PWID, this study will make a critical contribution to the improved care of PWID as well as to the healthcare of patients at risk for invasive S. aureus infections due to other causes.
Jessica Silva-Fisher, Ph.D. (Year 2) Long Non-Coding RNAs as Biomarkers for Multiple Myeloma Progression	The overall research goal of this proposal is to understand why and how multiple myeloma progresses and to address the critical need for better prognostic biomarkers, improved diagnoses, and the creation of targeted therapies. Many studies focus on the 2% of genes in the genome that are protein-coding, but this proposal will analyze long non-protein coding RNAs which are often overlooked.
Ali Javaheri, B.S., M.D., Ph.D., Longevity Research Program (Year 2 of 3) Dietary Protein and Cardiovascular Health	Research will continue to evaluate the effect of high protein intake and amino acids on factors involved in atherogenesis. In addition, a new research direction will be pursued which focuses on cancer therapy-induced damage to heart and skeletal muscle cells, which is a major cause of morbidity and mortality in cancer survivors.
Gautam Dantas, Ph.D. (Year 1) Exfoliome Characterization of Alzheimer's Disease Patients	There is a growing body of evidence highlighting the role of the gut microbiome (GM) and inflammation in neurogenerative conditions such as Alzheimer's Disease (AD). The research proposes a novel and non-invasive approach to studying the effects of the GM on the host by sequencing host mRNA in stool, the exfoliome, representing the host gut response to the GM. This will be done in healthy, preclinical, and symptomatic AD patients' stool, and integrating it with already existing GM composition data.
Leslie Gewin, M.D. (Year 1) Peroxisomal Fatty Acid Metabolism and the Kidney Aging	With aging, kidney function declines, making the senior population vulnerable to chronic kidney disease, which affects almost 15% of the U.S. population. The peroxisome is an overlooked part of cells that is very important for the metabolism of fats, the preferred energy source for an important part of the kidney. This proposal tests the hypothesis that enhancing peroxisomal metabolism may protect kidney tubules against aging.
Natalie Niemi, B.S., Ph.D. (Year 1) Targeting Excessive Mitophagy to Mitigate Age-related Muscle Dysfunction	Sarcopenia, the age-linked involuntary decline of skeletal muscle mass and function, substantially contributes to frailty and diminished quality of life in the elderly. The long-term goal of this study is to test the therapeutic potential of targeting regulators of mitochondrial protein phosphorylation in correcting age-induced skeletal muscle pathology.
Elizabeth Pollina, B.A., Ph.D. (Year 1) Neuronal Activity-dependent DNA Repair in Healthy Aging	The aging population is expected to develop increased incidences of neurodegenerative disease and dementia, but the molecular mechanisms that underlie these complex processes remain poorly understood. This proposal aims to understand how neuronal activity-dependent gene expression and DNA damage repair can regulate brain aging by leveraging a newly identified, activity-inducible protein complex, NPAS4:NuA4.

RGA THOUGHT LEADERSHIP PUBLICATIONS

RGA's thought leaders publish content on many topics of interest to insurers. Here are links to some articles and white papers published recently on the RGA Knowledge Center.

Avian Influenza Virus – What Insurers Need to Know

Hilary Henly, FCII
Global Medical Researcher – Strategic Research
Global Actuarial Pricing and Research
RGA

Coffee Consumption – How Much is Too Much? And How Little is Not Enough?

Hilary Henly, FCII
Global Medical Researcher – Strategic Research
Global Actuarial Pricing and Research
RGA

Life and Health Insurers' Future? Promoting Wellbeing

Julianne Callaway, FSA, ACAS, MAAA
Vice President, Senior Actuary – Strategic Research
Global Actuarial Pricing and Research
RGA

Global Health Brief: Understanding Medically Necessary (Medical Necessity)

Colin Weston
Vice President, Head of Global Claims
International Health
RGA

Feel the Burn(out)

Hilary Henly, FCII
Global Medical Researcher – Strategic Research
Global Actuarial Pricing and Research
RGA

Quantifying Quantified Health

Raajeev Bhayana
Chief Underwriter
RGA Global Health

Peter Ying
Senior Actuary, Global Products
RGA Global Health

Simon Dreyer
Senior Vice President and Chief Actuary
RGA Global Health

John Rutherford
Senior Vice President and
Head of Global Health
RGA Global Health

ReCite

Publications relevant to insurance medicine appearing recently in research literature

A Common Allele of HLA is Associated With Asymptomatic SARS-CoV-2 Infection

Augusto DG, et al. Nature.2023 Jul 19; 620: 128-36.
https://doi.org/10.1038/s41586-023-06331-x

During the first year of the SARS-CoV-2 (COVID-19) pandemic, researchers at the University of California, San Francisco (UCFS) used a smartphone-based app to track symptoms and outcomes among infected individuals. For this research, 29,947 individuals were recruited from its bone marrow registry for tracking. They identified 1,428 unvaccinated registry members who had tested positive between February 2020 and the end of April 2021. Of these, 20% remained asymptomatic for at least two weeks before and after testing positive. These individuals carried at least one copy of HLA-B 15:01, a variant of the gene HLA, compared to 9% of those who reported symptoms. Those who carried two copies of the variant were more than eight times more likely to not feel sick.

The researchers also found that T cells in these individuals responded to the coronavirus's NQK-Q8 peptide despite never having been exposed to SARS-CoV-2. They concluded that exposure to some seasonal coronaviruses containing a similar peptide, NQK-A8, enabled T cells in these individuals to quickly recognize SARS-CoV-2 and mount a faster and more effective immune response. Risk factors for severe COVID-19, such as being older, overweight, and having chronic diseases (e.g., diabetes), did not appear to have a role in remaining asymptomatic.

Editor's Note: *Further research into this association might enable identification of new ways of promoting immune protection against coronaviruses that could be used in future development of vaccines or drugs. This will be critical for insurers as we prepare for the next pandemic.*

Personality and Risk of Incident Stroke in Six Prospective Studies

Stephen Y, et al. Stroke. 2013 Jun 16; 54(8): 2069-76.
https://doi.org/10.1161/STROKEAHA.123.042617

This study adopted a systematic approach, using a multi-cohort design, to examine associations between the Five Factor Model of Personality traits (neuroticism, extraversion, openness, agreeableness, and conscientiousness) and incident stroke. Data used was from six large longitudinal samples of adults ranging in age from 16 to 104 years old. The personality traits, demographic factors, and clinical and behavioral risk factors were assessed at baseline, and stroke incidence was tracked over seven to 20 years of follow-up.

Meta-analyses indicated that higher levels of neuroticism correlated to higher incident stroke risk whereas higher conscientiousness was protective, and extraversion, openness, and agreeableness were unrelated to stroke incidence. The study also found that BMI, diabetes, blood pressure, physical inactivity, and smoking as additional covariates partially accounted for these associations.

Editor's Note: *Increasing evidence is supporting the role of certain personality traits as determinants for the development of cardiovascular disease. Insurers might need to consider including these factors into the regular cardiovascular risk assessment profiles in the future, as more data becomes available.*

Gut Microbiome Composition May Be an Indicator of Preclinical Alzheimer's Disease

Ferreiro AL, et al. Science Translational Medicine. 2023 Jun 14; 15(700).
https://doi.org/10.1126/scitranslmed.abo2984

In this cross-sectional study, researchers compared the taxonomic composition and gut microbial function in a cohort of 164 cognitively normal individuals, 49 of whom showed biomarker evidence of early preclinical Alzheimer's disease (AD). Accounting for clinical covariates and dietary intake, it was found that gut microbial taxonomic profiles of individuals with evidence of preclinical AD were distinct from those of individuals without such evidence. The change in gut microbiome composition correlated with β-amyloid (Aβ) and tau pathological biomarkers, as measured by PET imaging, but not with biomarkers of neurodegeneration. Neurodegeneration is considered to be a later event than the appearance of Aβ and tau biomarkers, suggesting that the gut microbiome may change much earlier in the disease process. The study also identified specific gut bacteria associated with preclinical AD. Inclusion of these microbiome features improved the accuracy, sensitivity, and specificity of machine learning classifiers for predicting preclinical AD status when tested on a subset of the cohort.

Editor's Note: *With aging populations increasing around the world, it is advisable for insurers to monitor developments in this area of research. Early signatures of gut dysbiosis in conjunction with preclinical AD markers may become a screening tool for AD and inform future gut microbiome-directed therapies that could potentially slow AD progression. Please see p. 20 of this issue for information about related Longer Life Foundation-supported research on this topic by Dr. Gautam Dantas, Washington University School of Medicine in St. Louis.*

MEDICAL TEAM UPDATE

Dr. Rachael James, MBBS, M.D., B.Sc., FRCP, has joined RGA as a Consulting Medical Officer in RGA's London (U.K.) office. Previously, she held a similar position with Legal and General. A cardiac disease specialist, she is also a U.K. Consultant Cardiologist at the Sussex Cardiac Centre, University Hospitals Sussex NHS Foundation Trust, in Brighton, U.K., where she is the lead clinician for echocardiography, cardiac disease in pregnancy and infective endocarditis. She is a Fellow of the Royal College of Physicians and a recent council member of the British Cardiovascular Society, the British Society of Echocardiography, and the U.K. Maternal Cardiology Society.

Dr. Pramodh Nathaniel, B.Sc., MBBS, MPH, TM, recently joined RGA as Chief Medical Officer, RGA Australia and New Zealand. He is an experienced medical director having worked in a broad range of specialities, including insurance medicine, occupational medicine, travel and tropical medicine, public health, emergency medicine, and aviation and retrieval medicine. During the COVID-19 pandemic, he served as a Chief Medical Advisor to banks, investment firms, and security companies. Previous roles included Chief Medical Officer for AIA Australia, TAL, and Medical Adviser to Tokio Marine Management Australasia – Sydney. He is a Fellow of the Australasian College of Tropical Medicine and the Faculty of Travel Medicine and is an active participant in insurance CMO forums.

Peter Farvolden, Ph.D., has joined RGA as a Mental Health Consultant. Based in Toronto, he is a clinical psychologist whose focus has been on psychological safety and health in the workplace as well as using technology to make treatment more accessible. His research and clinical experience includes work as a psychologist with the Anxiety Disorders Clinic at McMaster University Medical Centre. He was also a Research Scientist in the Mood and Anxiety Program at the Centre for Addiction and Mental Health (CAMH) and Clinical Director of its Psychological Trauma Program and the Work Stress and Health Program. He has held academic appointments at the University of Waterloo and the University of Toronto, and is currently an Associate Member in the Department of Psychology at Toronto Metropolitan University.

Dr. Paul Davis, MBBS, FRACP, recently retired from his post as Chief Medical Officer, RGA Australia. For his more than 20 years with RGA, the global medical function benefited from his many decades of experience as a cardiologist and in internal medicine. A valued contributor to many issues of *ReFlections*, his knowledge and experience benefited RGA's underwriting, product development, claims management, education, and medical research. He will be missed by all who had the privilege of working with him, and we wish him a joyful retirement.

RECENT WEBCASTS

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

Critical Illness Protection – New Frontiers, New Customers

Umair Ali
Vice President, Business Initiatives
Critical Illness and Supplemental Insurance
RGA

Take a Breather: Common Lung Diseases

Kim Vu, M.D.
Vice President, Medical Director
U.S. Mortality Markets
RGA

The ABCs of PFTs

Kim Vu, M.D.
Vice President, Medical Director
U.S. Mortality Markets
RGA

No Guts, No Glory: Inflammatory Bowel Diseases, Part I

Maryam B. Shapland, M.D., DBIM
Vice President, Medical Director
U.S. Mortality Markets
RGA

No Guts No Glory: Inflammatory Bowel Diseases, Part II

Maryam B. Shapland, M.D., DBIM
Vice President, Medical Director
U.S. Mortality Markets
RGA

The security of experience. The power of innovation.