

ReFlections

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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

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FROM THE EDITORS

Welcome to our May 2023 issue. Here in St. Louis, spring has definitely sprung! Wherever you are, we hope you are keeping well.

Dr. SiNing Zhao, Regional Medical Director – Asia, in her first appearance in *ReFlections*, contributes the first of a well-researched two-part article on autism. Part I, which you will find beginning on Page 2, focuses on an update of autism from a clinical point of view – an understanding of which is increasingly important for insurance medical and risk assessment professionals.

Peter Hovard, Ph.D., Lead Behavioral Scientist, also new to *ReFlections*, has contributed an article detailing RGA's research into how questionnaires in insurance applications can improve disclosure of smoking and alcohol consumption behaviors using the theories and tools of behavioral science.

The issue is rounded out with an article by *ReFlections* editor **Dr. Daniel Zimmerman**, DBIM, Chief Science Advisor, who reviews the current status of research into the underlying mechanisms of aging and the potential implications for future morbidity and mortality trends.

We are saddened to report that Dr. William A. Peck, a cofounder of the **Longer Life Foundation**, RGA's research collaboration with Washington University School of Medicine in St. Louis, recently passed away. The LLF page in this issue honors his long and productive life.

We trust you will find this issue both interesting and informative. Please do not hesitate to let us know how we can continue to improve *ReFlections* for you.

Daniel Zimmerman *Adela Osman*

AN UPDATE ON AUTISM SPECTRUM DISORDER PART 1: THROUGH A CLINICAL 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 first of two parts, provides a clinical review of ASD, and the second part, in the September issue, will focus on insurance medicine's view and assessment of ASD.

Introduction

Autism spectrum disorder (ASD) is commonly described as a neurodevelopmental disorder characterized by persistent deficits in social communication and social interaction together with restricted and repetitive patterns of behavior, interests, and activities.¹

It is estimated that since the 1990s, prevalence of ASD has steadily increased due to a multitude of factors. According to the U.S. Centers for Disease Control and Prevention (CDC), in 2000, U.S. prevalence in children was approximately 1 in 150. By 2018, that number rose to approximately 1 in 44.² Worldwide prevalence has also seen a substantial uptick. Estimated global prevalence as of 2022, according to the World Health Organization (WHO), was 1 in 100 children,³ a number nearly double that of 10 years ago, when worldwide prevalence was 62 in 10,000.^{4,3}

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 anesthesiology 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.

With the combination of ASD's increased prevalence, medicine's greater understanding of it as well as of its growing health and social impact, it is not surprising to see that insurance customers, who are the main care providers for these individuals, are seeking broader and more targeted coverage for ASD healthcare needs. The market's greater focus on providing more tailored juvenile products is contributing to improving coverage options for persons with ASD as well.

Understanding the Disorder

The most recent update of the International Classification of Diseases (ICD), version 11, describes ASD as "Characterized by persistent deficits in the ability to initiate and to sustain reciprocal social interaction and social communication, and by a range of restricted, repetitive, and inflexible patterns of behavior, interests, or activities that are clearly atypical or excessive for the individual's age and sociocultural context."⁴

Certain behavioral actions can be indicative of ASD. Commonly expressed social deficits include lack of social-emotional reciprocity, difficulty in interpreting nonverbal communication, and challenges in initiating and maintaining human relationships.

Those with ASD also prefer repetitive, stereotyped movements or experiences. Introducing anything new into customary routines can be challenging both for the patient and the caregiver. ASD individuals can also be very sensitive to certain neurosensory inputs, such as particular sounds.

These signs and symptoms typically first emerge in early childhood, but some manifestations may not be overt in situations where the social interactions are not new and therefore not challenging to the child.

ASD can also occur alone or with other neurodevelopmental, mental, or behavioral conditions. Language or learning impairments may also be associated but do not necessarily occur in all cases.⁵

Table 1: Medical Syndromes With Symptoms Similar to ASD	
Williams Syndrome	Fragile X Syndrome
Tardive Dyskinesia	Angelman Syndrome
Prader-Willi Syndrome	Rett Syndrome
Landau-Kleffner Syndrome	

Source: <https://www.autism.org/related-disorders/>⁶

Pathogenesis

The underlying etiologies of ASD have not yet been fully elucidated. The current accepted understanding is that many cases may have a genetic component. This is supported by evidence that shows differences in sex distribution (far more prevalence among males than females) and increased prevalence among siblings and family members.





Many genes known to be associated with ASD are also associated with neurological development or function in some way (e.g., neurogenesis or synaptic functioning) and are expressed in the central nervous system. Despite these associations, no genetic linkage has yet been identified that is specific to ASD. Most likely, its genetic component involves interplay among certain genes, their variants, how they are expressed, and other external influencing factors.^{7,8}

Environmental and perinatal factors have also been determined to increase the risk of developing ASD. Many of these factors center around the conception or perinatal period, which indicates how impacts on neurogenesis can increase the likelihood of development of ASD. Older parental age, for example, has been shown to be a factor in increased ASD risk, likely due to the greater potential for spontaneous mutations or alterations in genetic expression due to age.⁹ Perinatal risks have also been studied, but to date no single specific risk has been identified.

What the evidence has shown so far is that conditions that adversely affect neonatal or maternal health can lead to an increased risk profile for ASD. Neonatal conditions such as low birth weight and prematurity,¹⁰ and maternal conditions such as diabetes, preeclampsia,¹¹ and obesity, can all potentially contribute to ASD development.^{12,13} Exposure to certain medications taken by the mother during pregnancy, such as valproic acid¹⁴ and selective serotonin reuptake inhibitors (SSRIs), have been shown to increase ASD risk as well. Whether it is the exposure to medications, or the combination of such exposure with the possible genetic linkage to the underlying neurological or psychiatric

indication for use, there seems to be an increase in ASD risk in children of mothers who continued these medications during pregnancy.¹⁵ However, in many cases, the risk to the mother and child of stopping certain medications might outweigh the potential ASD risk, and so would not preclude use of these medications.¹⁶

A note about vaccines: Although vaccines had been controversially linked to ASD by some reports in the past, a large body of epidemiological research and evidence has since conclusively shown there is no link at all between vaccines and development of ASD.^{17,18}

Prevalence

Prevalence of ASD varies from country to country and region to region, depending on the methodology used and the area studied. However, one well-recognized worldwide trend in ASD is fast-rising prevalence. Current approximate overall prevalence (children and adults) ranges from 1 in 40 to 1 in 500 across the U.S., Europe, and Asia.¹⁹

This increased prevalence is due to many factors. Most ascribe it mainly to the better understanding and awareness of this disorder by the public and medical communities. With this has come better and earlier detection of cases through screening and referrals for clinical assessment, as well as the development of more dedicated services for individuals with ASD and their caregivers and families. However, the lack of access to testing and care services in some regions may mean a number of children are undetected until later in life; sometimes not until adulthood.^{20,21} This situation was made even more difficult during the past few years, as some

studies suggest the COVID-19 pandemic may have contributed directly to delayed screenings for younger children with ASD.⁴⁴

There is also the likelihood that the increased prevalence may be due to a truer representation and clearer understanding of the condition. In the past, many ASD cases may have been misdiagnosed as either a learning disorder or an intellectual disability but can now be more accurately recognized. There may also be a true increased prevalence of ASD, as multiple social, economic, and environmental factors have been linked to a rise in prevalence for childhood developmental disorders overall.²²

Prevalence among children and adults is similar, and the higher concordance among siblings points to a genetic pathophysiology in many cases.²⁴ Males are also known to be more likely to be diagnosed with ASD than females, with some studies show prevalence among males to be as much as four times that of females. However, other comprehensive studies indicate that this number may be overestimated, and that females may be underdiagnosed.²³

Clinical Assessment

Early diagnosis and intervention are critical to enabling those with ASD to receive appropriate treatment and improve prognoses. For proper evaluation and diagnosis, however, there needs to be an awareness of the condition by the primary caregivers as well as opportunities to screen for the disorder.

It is of vital importance as well that primary caregivers are educated about early signs and symptoms that may suggest the presence of ASD. Most commonly, a primary caregiver will be aware something is “off” due to the differences in the progression of a child’s social skills compared to their cognitive skills. For very young children, normal social milestones such as eye contact, smiling, and showing affection can be impacted, and early pathological repetitive behaviors (such as hand flapping) and fixations (certain obsessive behaviors) can also be present.

Screening through various community health services, routine check-ups, and reports from teachers are other vital ways of picking up cases among younger individuals.²⁵

Table 2: Early ASD Indicators in Children	
Age	Signs/symptoms
<6 months	<ul style="list-style-type: none"> • Decreased visual fixation
6-12 months	<ul style="list-style-type: none"> • Reduced response to name • Reduced gaze to faces • Lack of shared smiles • Limited to no vocalizations • Fixations on certain things or actions
12-24 months	<ul style="list-style-type: none"> • Limited sharing, interests, or attention • Problems with eye contact • Initiative and receptive language delay • Lack of response to name • Lack of imaginative and imitative play • Verbal and non-verbal communication deficits

Source: <https://pubmed.ncbi.nlm.nih.gov/31843864/>²⁶



Table 3: Early Manifestations Reported by Caregivers	
Social, language, behavior delays or deficits	Lack of pretend play or gesturing
Frequent tantrums or intolerance to change	Repeating words, phrases, actions over and over
Does not respond to name, prefers being alone	Obsessive over certain things, dislikes change
Avoids eye contact	Unusual sensitivities to sounds, smells, tastes

Clinical Intervention

After initial determination of the possibility of ASD, referral for a comprehensive evaluation is the next critical step. This is usually done by a specialist clinician with expertise in ASD evaluation and treatment. The evaluation should incorporate a thorough medical history, physical examination, and investigational bloodwork, to determine the following: if the child meets the diagnostic criteria for ASD (usually according to DSM 5-TR criteria); the child’s neurodevelopmental status as well as strengths and weaknesses; whether there may be an underlying organic cause of the ASD symptoms; and if any other associated conditions or comorbidities are present. The severity of each of the symptoms is also assessed, and graded, using the three levels of severity described in the DSM 5 criteria.

Table 4: ASD Severity Levels		
Level 1	Requiring support	<ul style="list-style-type: none"> • Difficulty initiating social interactions • Organization and planning problems can hamper independence
Level 2	Requiring substantial support	<ul style="list-style-type: none"> • Social interactions limited to narrow special interests • Frequent restricted/negative behaviors
Level 3	Requiring very substantial support	<ul style="list-style-type: none"> • Severe deficits in verbal and nonverbal social and communication skills • Great distress/difficulty changing actions or focus

Source: <https://www.verywellhealth.com/what-are-the-three-levels-of-autism-260233>²²

Assessment of severity is crucial to determining what type of care support may be required going forward and may also be an important indicator of future prognosis.²⁷ The assessment process may require multiple consultations and, in many cases, the assistance of a multidisciplinary team. Through this, a proper diagnosis can be arrived at and a thorough and individualized treatment and management plan can be formulated for a child’s specific needs and severity level.²⁸

Associated Comorbidities

An important part of the comprehensive assessment is screening for associated conditions such as genetic disorders, neurological or psychiatric pathologies, and other medical issues.

Developmental conditions commonly found include global or specific learning and language delays. ADHD as well as anxiety, depression, or other mood disorders may also be present in young to





adolescent children. Older children or young adults may exhibit aggression or self-harming behaviors. In terms of medical conditions, ASD is linked with epilepsy, fine and gross motor incoordination, feeding problems, gastrointestinal issues, and sleep disorders.²⁹

Apart from the medical history and physical examination, additional investigations are often required to complete the full diagnostic picture. This includes referrals for formal genetic testing as well as metabolic and biochemical screening to rule in or out any organic causes. Focused neurological diagnostic tests such as MRI or EEG may also be useful in cases with certain associated conditions such as epilepsy.³⁰

Treatments/Therapies

ASD is a chronic condition. Once a diagnosis is confirmed, a multidisciplinary holistic management plan needs to be developed for the patient according to their age and specific needs.

Chronicity also means management plans and therapies will need to evolve over time as the individual ages.

The current goal of ASD management is not curative. Rather, it is to optimize quality of life by facilitating improvements, if possible, in independence and social functioning. Often, an individual's entire family, including siblings, will be involved in the caregiving and therapies. Support should be provided to the main caregivers so that specific interventions can be implemented where necessary. This also extends to other settings such as

schools, as the child is likely to need specialized care and attention for their educational needs.³¹

Overall goals of ASD therapy may include^{32, 33} promoting and developing positive behaviors, such as social and communication skills, independent and adaptive skills, and education and cognitive skills. Goals may also include helping to manage negative behaviors such as non-functional or maladaptive behaviors and rigidity in thinking and behaviors.


To best achieve the goals of therapy, some key factors that may maximize outcomes are:^{34, 35}

- **Timing.** Research has shown that early diagnosis and early intervention can positively impact ASD children and be crucial for their longer-term prognosis. Intensive therapy and treatments may foster improvements that over time can minimize the impacts to the child's quality of life. Together with improving existing symptoms, there is also evidence to show early diagnosis and intervention may prevent other problematic behaviors from developing.
- **Multidisciplinary team approach.** Individualized and targeted therapy for the child needs to be addressed in a holistic manner, as multiple aspects may require intervention through various specialists, including:
 - Developmental pediatrician
 - Child psychiatrist and psychologist
 - Speech pathologist
 - Occupational therapist
 - Social worker
 - School teachers

Behavioral Interventions

Behavioral interventions have been extensively studied in the two-year-old to adolescent age range and have been found to be some of the most effective treatments for ASD.³⁶ Within this age range, the most efficacious treatments, according to evidence, have been:

- Behavioral approaches
- Developmental approaches
- Naturalistic Behavioral Developmental Interventions (NBDI)
 - NBDI integrates therapy into the child's everyday life through a developmental systems approach, to ensure development of skills in one domain (e.g., learning a symbol, such as a new word or gesture, in one activity) are integrated with development of skills in other domains (e.g., using the word or gesture to sustain engagement with another person and in other activities). Skills are taught in the course of a child's typical daily interactions, experiences, and routines, with multiple materials and by multiple people.⁴¹
- Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH)³⁸
 - The TEACCH program is used to promote learning and development – in particular, communication and social skills, independence, coping skills and skills for daily life, such as dressing, washing, cleaning teeth, and so on. Tailored to each child's individual needs, it centers around structured teaching in a classroom setting through using schedules and physically organized spaces to make daily life predictable for children and help them understand their daily activities.
- Psychotherapy (e.g., cognitive behavioral therapy [CBT])
- Group-based Social Skills Interventions (GSSIs) (effective for adolescents)



**The current goal of
ASD management
is not curative.**

For children under age two, an integrative developmental behavioral model focusing on social, speech, and communication skills through exploratory play and sensory stimulation has proven beneficial.

Among older adolescents, the treatment/therapy focus should shift to helping them learn skills to maintain desirable behaviors and reduce maladaptive behaviors. Training in developing the ability to perform adult activities should also start at this age range to prepare them for adulthood.

Pharmacological Treatment

ASD has no known cure, and no currently known efficacious pharmacological treatment.

That being said, certain pharmacological options for psychiatric or neurodevelopmental conditions that co-occur with ASD should be considered, especially when these conditions and other behaviors lead to a severely impacted quality of life and interference with other therapies and treatments. They should only be started when other treatment modalities are in place and maximized.³⁷

A careful analysis of the risk and benefit of each pharmaceutical treatment option should be undertaken, then closely monitored and consistently followed. The potential for polypharmacy reactions is also present and the attempt to minimize interactions should be reviewed.

Table 5: Current Pharmacological Interventions and Indications of Usage

Indications	Medications	Actions	Adverse Effects
Irritability, aggression, emotional instability	aripiprazole, risperidone	Atypical antipsychotic, acts mainly at dopamine and serotonin receptors	Drowsiness, gastrointestinal (vomiting, appetite changes, constipation), extrapyramidal effects
ADHD	methylphenidate (MPH), atomoxetine, extended release guanfacine	Noradrenaline and dopamine effects	Appetite changes, irritability, headaches, sleep problems, emotional disturbance
Restricted, repetitive behaviors	SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, sertraline)	Affects serotonin reuptake	Mood and energy changes, insomnia, gastrointestinal upset
Sleep	melatonin	Impacts sleep/wake cycle	Drowsiness, headache
Hyperactivity, irritability	N-Acetylcysteine	Acts as an antioxidant and contributes to production of glutathione, one of the main central nervous system antioxidants	Gastrointestinal upset, drowsiness
Social, communication challenges	oxytocin	Acts as a neuropeptide, potentially affecting neural pathways that play roles in social/communication	Increased appetite, energy, restlessness

Source: <https://pubmed.ncbi.nlm.nih.gov/36625807/>³⁸

Complementary Therapies

Not surprisingly, a large number of caregivers (and patients) pursue alternative or complementary therapies to treat, cure, or alleviate the symptoms of ASD. While many therapies are available (treatments, medications, and supplements), unequivocal evidence showing efficacy over existing treatments and/or placebo is still lacking. It is important that before a complementary approach is considered, the primary clinician treating the child is consulted.³⁹

A healthy lifestyle should still be encouraged for ASD children. This includes a well-balanced and nutritious diet, avoidance of neurotoxins, a good amount of physical and social activity, and adequate sleep. All of these support the goal of having an overall better functioning child or adult who can live with and function better with their ASD.⁴⁰

Conclusion

As ASD continues to rise in prevalence, it will require a persistent effort to continue vital research into its pathogenesis and pathophysiology in order to further break down the mysteries of this difficult and disabling disorder. In parallel, greater screening and awareness means that the potential to implement early intervention treatment in young children is increased, and with that hopefully an improvement in

the quality of life through the utilization of multiple modes of therapy. However, despite the advances in knowledge and treatment of ASD during the last 20 years, it remains a chronic lifelong condition that is associated with increased morbidity. Therefore, the need for better access to care and having the resources to initiate and maintain care is vital, and it is within this space that insurers can find themselves playing an invaluable role in helping a person with ASD journey towards a better and longer life. ^{REF}

Part 2, which will cover the insurance implications in depth, will be in the September 2023 edition of ReFlections.

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IMPROVING SMOKING AND ALCOHOL DISCLOSURES USING BEHAVIORAL SCIENCE

Abstract

Applicant disclosure is a basic need for accurate and fair life insurance underwriting. In recent years, companies have increased their use of behavioral science research and are incorporating its techniques into many parts of the application process to improve disclosure rates. However, it is similarly vital that applicants have a smooth and pleasant experience when completing these forms. Behavioral techniques to improve questions often include breaking the “ask” into smaller and more digestible items. This might appear to make the question longer, although it may also make each item simpler to respond to, making the process simpler and more effective at capturing disclosures overall. In this article, we discuss RGA’s latest behavioral science research, which assessed the trade-offs between optimizing questions for alcohol and smoking disclosure, applicants’ experience of answering the questions, and what the results might teach about designing simple and effective applications.

Introduction

Research has shown that even small adjustments to certain questions on life insurance applications, informed by behavioral science techniques, can lead to better disclosure rates¹ by mitigating certain psychological sources of misdisclosure.²

The techniques can include:

- Reframing binary “yes or no” questions to conceal the underlying underwriting rule, making purposeful misdisclosure more difficult
- Cueing applicants’ memory of their behaviors by providing greater specificity in questions, for example, by asking separate questions about the various alcoholic drink types
- Reducing cognitive load (i.e., the mental effort required to answer a question) by breaking down general questions requiring complex thought into smaller pieces
- Reducing the possibility of an applicant experiencing stigma, (i.e., feelings of shame or embarrassment) around sensitive questions by providing response scales and wordings that subtly normalize the target behaviors

At first glance, these techniques might appear to make the specific questions longer, with more elements for an applicant to consider. Questions revised with these techniques might also take up more

ABOUT THE AUTHOR



Peter Hovard, Ph.D.
Peter.Hovard@rgare.com

As the Lead Behavioural Scientist for RGA Global Data Analytics, U.K.-based Peter Hovard and his team develop research and practical methods for observing the actual ways people absorb, process, and react to information. The focus is on understanding how people actually think and behave, rather than how it is assumed they do, and using this knowledge to help RGA’s clients design products, communications, and processes across the insurance journey. This may include applications that encourage honesty, motivate lifestyle behavior change, and improve return-to-work outcomes.

Prior to joining RGA in 2020, Peter was the behavioural science lead for Royal Sun Alliance (RSA) in the U.K. where he established the use of behavioral research and intervention design to improve outcomes for insurance customers.

Peter received both a Bachelor of Science (B.Sc.), with honours, in psychology with American studies, and a Ph.D. in the psychology of appetite and eating behavior, from the University of Sussex (U.K.). Peter’s research is featured in articles in academic journals such as *Flavour*, *Nutrition Bulletin*, and *Frontiers in Psychology*.

visual space. This raises concerns for some insurers about applicant experience: does it make an application more time consuming and/or challenging to complete?

Recent RGA behavioral science research into certain aspects of application question design is determining that these concerns may be unwarranted. Despite the questions appearing to be longer, they are turning out to be cognitively and emotionally easier for applicants to provide responses to them.

Designing Simple Underwriting Questions

When it comes to question design, simplicity is generally the goal. Often, insurers assume that simplicity comes from removing information or items in a question so that it appears shorter on a page. However, a psychological view suggests that achieving optimal simplicity comes from understanding how applicants process the information needed to produce a cogent and informative answer. Hence, there may be little trade-off overall between improved disclosures and applicant experience when using questions that allow people to process smaller amounts of information in one go but appear longer. Indeed, there may even be positive impacts.

We tested this hypothesis in a study using a randomized control trial format. The study utilized a pool of 8,000 participants from the U.S., Canada, South Africa, and Australia in nationally representative samples (proportionally represented the demographic distributions of each country). Different versions of application questions were presented to the participants as part of a survey that simulated an insurance application. Subjective user experience, amount of time spent on questions, and amount of information disclosed per question format was measured. We then used regression models to explore what impact the different question types had on the amount of information provided in responses while keeping other variables, such as the devices participants used and their demographics, constant.

Here is what we found for questions on smoking and alcohol use.

Smoking

We tested enhanced versions of an insurance application smoking question alongside the typical binary style question (“Have you smoked or used nicotine products in the last two years? Yes/No”).

The enhanced versions asked: “When was the last time you smoked or used nicotine products?” and provided four, six, or eight response options. Each option related to a different usage time period. For example, the question with four response options let the respondent choose among “in the last 12 months,” “between 12 months and 2 years ago,” “2 or more years ago”, and “never.” Those with six or eight response options let the applicant provide even greater specificity.

Providing these options both hides the underwriting rule and subtly destigmatizes smoking, making it more difficult for applicants to purposefully misdisclose and psychologically easier for them to be honest.

Findings

The enhanced versions of the questions with six or eight response options, but not the four-option version, led to significantly increased disclosure rates. Each of the two enhanced versions with more response options yielded an additional three percentage points of respondents disclosing they had smoked within the past two years compared to the typical binary question. (The four-option version also did not show an increase in disclosure.)

The key concern for insurers is whether adding more options might make for a lengthier responding process. We found, however, that the difference was very small. The typical binary question took an average of one and a half seconds less to answer than the four-option version, two seconds less than the six-option enhanced version, and two and a half seconds less than the eight-option version (Figure 1).

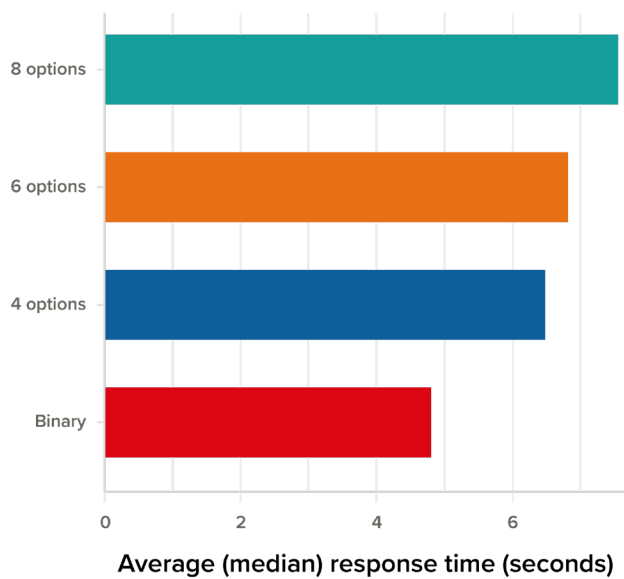
Interestingly, those who disclosed smoking activities took slightly longer to respond to questions around smoking than those who did not, but only when answering the enhanced questions. This, perhaps, suggests that the



question stimulated additional thought before producing a response.³ The multiple option response technique is purposefully used in question design to help users engage mindfully.⁴ Interestingly, non-disclosers did not seem to have this issue.

This is a benefit for the applicant and the insurer, as the small increase in response time when using the enhanced questions yielded increased smoking disclosures, while response time for non-smokers was not affected.

Figure 1: Response Time for Smoking Questions by Response Options (outliers removed)



We then explored how study participants experienced the actual process of answering the smoking question. We found no meaningful differences among the question types in terms of how easy or quick the question was to answer or how confident the participants felt about the accuracy of their responses. In fact, the enhanced questions were found to improve participants' recall of the last time they smoked.

Overall, the tradeoffs between increased disclosure rates and applicant experience favor using behavioral science-enhanced questions: the increased response time is negligible and only present for those disclosing smoking, while the only noticeable difference in respondent

perceptions of answering the enhanced questions are positive.

Alcohol

Alcohol consumption is usually assessed in life insurance applications using an open format question, such as "In a typical week, how many alcoholic drinks do you consume?"

There are two concerns with this approach:

- It is complicated for applicants to work out and then provide an accurate answer. They must think through and remember their alcohol consumption, decide what a typical week's consumption consists of, and then create a reasonable estimate.
- High levels of alcohol consumption carry a stigma, therefore applicants might be embarrassed to admit how much they actually consume.

The open-format question generally results in applicants estimating a number of drinks in a given time period that "feels" right and seems socially acceptable, rather than making the effort to provide a more accurate accounting. This reflects a behavioral science concept known as "satisficing," in which people make "good enough" choices and decisions rather than taking the time to make optimal or well-thought-out decisions and judgements.⁵

We previously found that grouping types of alcoholic drinks and frequency of their consumption into categories, such as, "How many pints of beer/glasses of wine/shots of hard liquor do you drink in a typical week?" and then asking applicants to provide their response using a numerical scale, could improve disclosure rates.¹ The questions, it was thought, would more effectively elicit an applicant's recall, reduce mental effort required to do so, and anchor their perspective of what is socially acceptable. If a respondent's level of alcohol consumption is, for example, towards the middle of the scale provided, it may feel less embarrassing to them to indicate as much on the application.

As with the smoking question, providing more choices for the applicant to select among may make the actual question appear longer, but may also improve applicants' experience and disclosures.



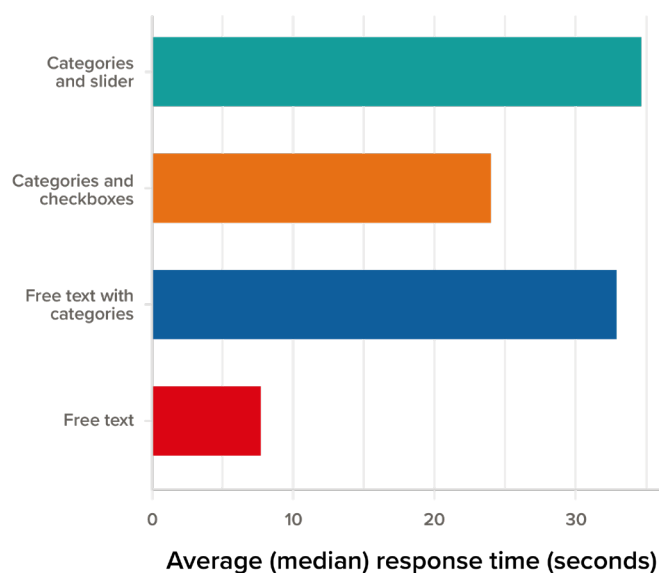
We tested this hypothesis by structuring questions that split alcohol consumption experience into categories that used either free text input, checkboxes, or a sliding scale as the response mechanisms. We also, for some respondents, used a typical free text question, which asked about total alcohol consumption generically in order to have a control group for comparison.

Findings

We first replicated previous findings by splitting types of alcoholic beverages (wine, beer, hard liquor) into categories and then provided either free text input boxes, a sliding scale, or a series of checkboxes for applicant responses. As with prior research, we again found that the individual drink checkbox and sliding scale versions increased disclosure rates. In fact, in this study, we found participants disclosed more than three times the level of alcoholic beverage consumption than they did when responding to a typical free text question.

Our focus, as previously mentioned, was on whether the enhanced questions might affect applicants' experience in responding to them. We found that using beverage categories also increased average response time to the question, although as with the smoking question, the differences were small (Figure 2). The checkbox version was quicker for respondents to answer than the other enhanced versions and took around 15 seconds longer to answer than a free text question.

Figure 2: Response Time to Answer Either Typical or Enhanced Alcohol Questions (outliers removed)



We also found no differences in terms of perceived ease, speed, confidence in accuracy, or effortful mental processing between the free text and the checkbox versions. Indeed, the checkboxes were seen as significantly more useful to respondents in helping them remember their alcohol consumption than the other question types.

Overall, the disclosures and mental processing improvements were a significant win for an average response time increase of 15 seconds.


Enhanced Questions Bring Order to Underlying Complexities

We had set out to test whether tradeoffs might exist between increased disclosure rates and applicant experience when using behaviorally enhanced questions. In the case of both smoking and alcohol, the enhanced questions clearly produced better disclosure rates with minimal impacts on applicants' experience.

In both categories, response times were only slightly higher when using the enhanced versions. For example, an additional 3% of participants disclosing smoking activity were obtained in exchange for an additional two seconds of average response time. This would seem a strong reason for using enhanced questions.

Participants' subjective experience of answering the questions was not negatively impacted by the behavioral enhancements. In fact, they described an improved ability to remember their behavior for both smoking and alcohol-related activities. This supports our hypothesis that categories stimulate participants' memories, making disclosures easier to elicit.

To think through one's behavior and categorize it appropriately can be deceptively challenging. Typically, when a question requires a binary or free text response, the easiest route for respondents is to automatically respond with "no" or to estimate small, socially acceptable numbers. By presenting categories within enhanced question structures, a portion of the mental processing is already done for the applicant. The enhancements create, in fact, the structure that applicants would have to otherwise mentally create for themselves. Providing the enhancements disrupts the automatic "no" or "small amount" responses that are otherwise mentally easiest for respondents.

And here we come back to simplicity. As Apple's former chief designer Jony Ive has stated, simplicity is "much more than the absence of clutter. It's about bringing order to complexity."⁶ When designing application forms, insurers would benefit from taking this stance. Visually longer questions may seem counterintuitive, but because these formats do the mental categorizing and organizing work that applicants would otherwise have to do themselves, the end result is not only better disclosure rates, but also noticeable improvements in applicants' ability to remember answers without negative impacts on their experience. 

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WHAT'S NEW WITH OLD? RECENT ADVANCES IN THE SCIENCE OF AGING

Abstract

The last decade has seen rising interest in and research efforts into the underlying drivers and mechanisms of aging. The incentive for this enthusiasm is much more than an academic exercise. If these drivers and mechanisms can be elucidated, then perhaps they can also be leveraged to prevent, slow, or even reverse aging processes. While no appreciable therapeutic interventions for aging are currently available (at least for humans), there is great hope that eventually human healthspans and possibly lifespans can be extended by population-wide implementation of material advances in anti-aging therapies. While certainly of great interest to society, these advances, if realized, could impact insurers' fundamental morbidity and mortality actuarial assumptions and overall business models.

This article will review recent controversies and developments in aging research and update what to anticipate in the coming years.

Introduction

Globally, people are living longer. According to the World Health Organization (WHO), every country in the world has experienced growth in both the number and size of the elder cohort in their populations. By 2030, the WHO estimates that one in every six people in the world will be age 60 or older, and the population age 60 and older will increase from one billion (as of 2020) to 1.4 billion. By 2050, the world's population of people age 60 and older will nearly double to 2.1 billion.¹

Despite recent reductions in life expectancy due to COVID-19, much of the observed increase in life expectancy during the 20th century was attributable to improvements in public health, sanitation, and nutrition, as well as reduced deaths due to more effective preventative measures and treatments for communicable diseases. Additionally, medical advances and primary and secondary prevention for non-communicable diseases (such as coronary artery disease) have contributed significantly to mortality improvement trends.^{2,3}

What will be needed to ensure long-term mortality rates continue to improve? Is "what got us here, will get us there" a viable strategy? While it will remain important to continue to study the social, economic, and medical factors impacting life expectancy, it is now also imperative to dive deeper into the fundamental biological mechanisms and drivers of aging. Through further understanding and research in this area of

ABOUT THE AUTHOR



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

Daniel D. Zimmerman, M.D., DBIM, is Senior Vice President and Chief Science Advisor for RGA Reinsurance Company. In this role, he is responsible for scientific thought leadership, executive and C-suite advisement, and mentorship. Additionally, he serves as editor of *ReFlections*, RGA's global medical newsletter, and is the Executive Sponsor of the RGA U.S./Latin America LGBTQ+ employee resource group. He is a director of the RGA Foundation.

Dan is also Managing Director of the Longer Life Foundation, www.longerlife.org. This not-for-profit collaboration between RGA and Washington University School of Medicine in St. Louis funds the study of factors that either predict the mortality and morbidity of select populations or influence improvements in longevity, health, and wellness.

Dan received his medical degree from the University of Wisconsin School of Medicine and Public Health and his undergraduate degree in Medical Microbiology and Molecular Biology from the University of Wisconsin – Madison, Wisconsin (U.S.). He has held leadership positions with the American Council of Life Insurers (ACLI), participated in program committees of the American Academy of Insurance Medicine (AAIM), and frequently represents RGA to key industry professional organizations. He has also contributed several articles to the *Journal of Insurance Medicine, On The Risk, ThinkAdvisor, and Best's Review*.



science, material increases in healthspans – the length of life lived without significant disease or impairment – and lifespans – the total time between birth and death – may be achieved.

Aging Defined

Many have attempted to define aging, and most definitions have similar and common verbiage. The WHO, for example, defines aging as follows:

“At the biological level, aging results from the impact of the accumulation of a wide variety of molecular and cellular damage over time. This leads to a gradual decrease in physical and mental capacity, a growing risk of disease and ultimately death. These changes are neither linear nor consistent, and they are only loosely associated with a person’s age in years. The diversity seen in older age is not random.”¹

World-renowned nutrition and aging researcher Dr. Luigi Fontana has defined aging similarly:

“Aging is a fascinating but complex and dynamic biological process. It is characterized by progressive functional and structural deterioration of multiple cells, tissues, and organ systems.”⁴

Both of these definitions are descriptive in nature, but do not provide specifics about the underlying mechanisms *per se* or explain why aging processes occur (or must occur). The WHO’s definition is particularly interesting, as it

states that aging is not a linear process and is only loosely associated with chronological age. The non-randomness of aging’s diversity of expression seen at older ages indicates that multiple factors, both potentially modifiable and non-modifiable, are driving variations in aging. Nonetheless, aging ultimately and unequivocally results in death.

Is Aging a Disease?

Historically, aging has been considered a “natural” process – one that is immutable and inevitable and thus does not technically meet the criteria of a disease. On the other hand, aging has been and is a well-recognized risk factor and contributor to particular age-related diseases. Even the very definition of disease has been debated in the philosophical context. In these terms, “disease” has been defined as a state that has been medically described and evaluated as a “bad thing to have.” One recent paper examining whether aging is a disease noted, “from the pragmatist perspective, it can be seen that the notion of aging is going through a conceptual change, and aging can today be understood as a not radically different process from any other condition that is usually considered a disease.”⁵

There is strong evidence that by focusing research on aging pathways (and considering those pathways pathological processes), multiple seemingly unrelated diseases could be addressed simultaneously. According to a recent Lancet editorial, “if aging can be viewed as a pathological process, then it allows researchers to look at



the pathophysiological mechanisms of aging itself with a view to finding targetable mechanisms of action that slow the rate of aging.” This approach could also result in improving healthspans as well as overall lifespans.⁶

Nonetheless, categorizing aging as a disease *per se* remains controversial. As noted above, some argue that aging is a normal, natural process experienced by everyone, whereas diseases only affect some of the population. Additionally, the processes of aging are also not always directly related to chronological age and are heterogeneous. Characterizing aging as a disease *per se* risks worsening age-related discrimination which already exists.⁶

The most recent WHO International Classification of Diseases (ICD-11), published January 2022, had proposed adding the term “old age” under the MG2A diagnostic category (that of symptoms, signs, or clinical findings not elsewhere classified). Additionally, an extension code was initially included in the category’s causality section, which defined “aging-related” as “caused by pathological processes which persistently lead to the loss of [an] organism’s adaptation and progress in older ages.” This action was, however, met with much opposition by clinicians who stated that “referring to people by an undefined chronological age led to very serious real-world challenges for being used inappropriately and erroneously.” After formal consultation with and feedback to the WHO, the term “old age” was retracted and replaced by “aging associated decline in intrinsic capacity” and in the extension code, “pathological” was changed to “biological.”

Thus, although the ICD-11 issue is settled for the time being, debate persists.⁷

From an economic standpoint, there may be value in targeting aging as a disease. One analysis demonstrated that targeting aging may offer greater economic gains in the U.S. than eradicating specific diseases and showed that slowing down aging enough to achieve one year of increased life expectancy could have a general economic value of \$38 trillion. The authors noted the costs of any treatments which target aging must be low and have widespread population access to realize the full value of social gains.⁸

Aging is a complex process and must be considered as a whole.

Major Hallmarks of Aging

Significant effort and research have gone into elucidating the mechanisms and drivers (often termed “hallmarks”), whether considered normal or pathological, which cause aging. Since 2013, nearly 300,000 articles addressing the subject have been published, which is as many as published on the topic during the preceding century.

Hallmarks of aging have been described as needing to fulfill three criteria:

- Age-associated manifestation(s)
- Acceleration of aging by experimentally accentuating them
- Opportunity to decelerate, stop, or reverse aging by therapeutic interventions

Carlos Lopez-Otin *et al.* recently published an extensive literature review on the hallmarks of aging, which updates a similar review performed a decade earlier.⁹ The authors have identified 12 specific

hallmarks of aging, some of which are interconnected, and have focused on the molecular, cellular, and systemic processes that mechanistically account for their manifestations. This supports the hypothesis that aging is a complex process and must be considered as a whole. They also noted that the 12 hallmarks of aging can be sorted into three categories: primary, antagonistic, and integrative. While prior research validated evidence for anti-aging intervention effectiveness in non-mammalian model organisms, more recent findings are beginning to corroborate their effectiveness for mammals, increasing their relevance for humans.

Table 1: Hallmarks of Aging	
Primary – reflect damage affecting the genome, telomeres, epigenome, proteome, and organelles	
Hallmark	Description
Genomic instability	Genome integrity constantly threatened and damaged by endogenous and exogenous stressors
Telomere attrition	DNA damage occurring at the ends of chromosomes (telomeres) after multiple cell divisions
Epigenetic alterations	Epigenetic changes include DNA methylation patterns, abnormal modification of histones, chromatin remodeling, and deregulated function of non-coding RNAs
Loss of proteostasis	Impaired protein homeostasis leading to accumulation of misfolded, oxidized, or glycated protein, often forming aggregates
Disabled macroautophagy	Impaired sequestration and digestion of cytoplasmic material
Antagonistic – reflect responses to primary factors	
Hallmark	Description
Deregulated nutrient-sensing	Dysfunction of mechanisms in innate evolutionary nutrient-sensing capabilities
Mitochondrial dysfunction	Mitochondria are the energy “powerhouses” of the cell and can trigger inflammation Functional deterioration due to mitochondrial DNA mutations, deficient proteostasis, reduced turnover of the organelle
Cellular senescence	Characterized by stable proliferative arrest in the cell cycle resulting from multiple mechanisms
Integrative – reflect failure of compensation for primary and antagonistic processes	
Hallmark	Description
Stem cell exhaustion	Causes reduction of tissue renewal at steady state and with injury
Altered intercellular communication	Causes increased “noise” in the system and compromises homeostatic and hormetic (phased response to stress) regulation
Chronic inflammation	Aging-associated inflammation – “inflammaging”
Dysbiosis	Dysfunctional gut microbiome negatively impacts overall maintenance of health


Source: <https://pubmed.ncbi.nlm.nih.gov/36599349/>



The identification of the hallmarks of aging is enabling a basic understanding of their drivers and mechanisms and is forming a basis for research into anti-aging therapies. While each hallmark can be targeted, yielding potential tangible benefits for both healthspans and lifespans, it will be important to develop rational strategies for intervening in human aging.⁹

Notably, aging as a therapeutic target is not recognized by the U.S. Food and Drug Administration, thus drugs intended to treat aging must target a specific disease that often results from the aging process in order to demonstrate efficacy and gain approval.¹⁰

Conclusion

The understanding of the (patho)physiological processes that comprise aging in humans has experienced many significant advances in the last decade. Not only are the fundamental hallmarks of aging being elucidated, great effort is also being undertaken to develop therapies which might decelerate, stop, or reverse the aging process. Insurers would benefit from following these developments closely and considering their potential impact on morbidity and mortality actuarial assumptions and projections for both in force and new business modeling. 

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Longer Life Foundation


An RGA/Washington University Collaboration

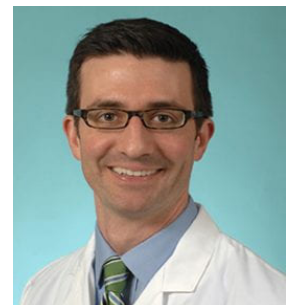
The Longer Life Foundation (LLF), a collaboration between RGA and Washington University School of Medicine in St. Louis, is celebrating its 25th year of enhancing longevity and health through research. Please read on for the Foundation's latest news, and to learn more about LLF's activities and events, 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.

It is with great sadness we report the passing of **Dr. William A. Peck**, retired Dean of Washington University School of Medicine in St. Louis and Vice Chancellor of the University, in February 2023 at the age of 89. Dr. Peck, together with Greig Woodring, retired President and Chief Executive Officer of RGA, cofounded the Longer Life Foundation 25 years ago – an act of vision reflecting his career-long dedication to supporting medical research and mentoring researchers. Dr. Peck, a physician-scientist, had a 14-year tenure as both Dean and Vice Chancellor (1989-2003), during which he successfully strengthened Washington University in St. Louis into a center for research and clinical excellence. After his retirement, he established the Center for Economics and Health Policy within Washington University's Institute for Public Health, which has grown to become a nationally recognized leader in health policy. To read Dr. Peck's full obituary, please click [here](#).

LLF VIDEOS

The fourth video of our investigator series, an interview with current grant recipient **Dr. Nathan O. Stitzel**, is now available on LLF's dedicated YouTube channel. Dr. Stitzel, whose research focus is on the role of genetics in cardiovascular disease, discusses his current investigation into the SVEP1 protein and the increasing understanding of its role as a causal element for multiple chronic diseases of aging. To view the interview, please click [here](#).

A commemorative 25th anniversary video, highlighting LLF's past, present, and future, is due for release in the coming months. Watch this space! 



RGAs THOUGHT LEADERSHIP PUBLICATIONS

RGAs 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.

Synthetic Biology Shows Future Promise for Diagnostics, Therapeutics, and Vaccines



Hilary Henly, FCII
Global Medical Researcher
GAPR Global Research
RGA

Psychedelics and Mental Health – a Review of the Current Research



Lauren Garfield, Ph.D., MPH
Senior Underwriting Research Consultant
U.S. Mortality Markets
RGA

Gene Therapy: The Next Big Thing



Mary T. Paquette, RN, BSN, CCM
Executive Director
ROSE© Program
U.S. Group Re
RGA



Melinda Baxter, RN, BSN, CCM
Senior Medical Risk Consultant
ROSE© Program
U.S. Group Re
RGA

The Emerging Use of Psychedelic Substances



Hilary Henly, FCII
Global Medical Researcher
GAPR Global Research
RGA

A Call to Action: The Insurance Industry and Mental Health (Geneva Assoc. report)



Dr. Steve Woh
Chief Medical Officer, Claims Manager
Global Health
RGA



Erin Crump
Vice President
Business Initiatives
RGA International

New Therapies Take Giant Steps Toward Treating Sickle Cell Disease



Hilary Henly, FCII
Global Medical Researcher
GAPR Global Research
RGA



Medical Director Role in Life and Health Insurance



Dr. Adela Osman, MBBCh
Vice President, Head of Global Medical
Global Health
RGA

Experimental Treatments – Current Considerations (GHB)




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

Digital Health and its Impact on the Growth and Profitability of the Health Insurance Sector



Dr. Dennis Sebastian
Vice President, Head of Health
RGA Middle East

MEDICAL TEAM UPDATE

Dr. Sajel Kana has joined RGA as Consultant Geneticist. Based in Miami, Florida (U.S.), she is a clinical geneticist in the Division of Clinical Genetics at Nicklaus Children’s Hospital. She is board-certified by the American Board of Medical Genetics, a diplomate of the American College of Medical Genetics and Genomics, and a member of the American Society of Human Genetics. 

Lifelong Endurance Exercise and its Relation With Coronary Atherosclerosis

De Bosscher R, et al. European Heart Journal. 2023. ehad152.

<https://doi.org/10.1093/eurheartj/ehad152>

A recent study raises the question of whether long-term endurance exercise may, paradoxically, lead to coronary atherosclerosis. Results from the Master@Heart study demonstrated lifelong endurance athletes had more coronary plaques than otherwise healthy and fit people with an equally low cardiovascular risk profile. The lead author was quoted in Medscape: “The worst thing you can do is nothing at all. As soon as you do a little bit of exercise – just brisk walking or jogging up to three hours a week – it seems that’s where you get the most benefit. And after that, we tend to see an increase in coronary plaque burden.” The study also concluded that lifelong endurance sport participation is not associated with a more favorable coronary plaque composition and that longitudinal research is needed to reconcile these findings with the risk of cardiovascular events in endurance athletes.

Editor’s Note: *Insurers frequently underwrite endurance athletes who generally have favorable mortality and morbidity risk profiles. While the results of this study are not likely immediately actionable from an insurance point of view, it is worthwhile for insurers to monitor further developments and research in this niche area.*

Comparison of Mental Health Symptoms Before and During the COVID-19 Pandemic: Evidence From a Systematic Review and Meta-Analysis of 134 Cohorts

Sun Y, et al. BMJ. 2023 Mar 8; 380: e074224

<https://www.bmj.com/content/380/bmj-2022-074224>

Sun and colleagues present an exhaustive systematic review of the medical literature on the mental health impact of COVID-19. They focused on general mental health, anxiety symptoms, and symptoms of depression in multiple segments of the population. Many studies and media reports have suggested COVID-19 has had a significant negative impact on mental health. However, the authors indicate many of these reports used methodologies which were not designed to estimate prevalence and can be misleading.

Their review of 137 studies (134 cohorts), which compared symptoms during the pandemic with pre-COVID-19 outcomes in the same cohorts, showed no negative changes in the general population for general mental health or anxiety symptoms, and a minimal worsening of depression symptoms. Notable among subgroups, women experienced disproportionate worsening of general mental health, anxiety symptoms, and depression symptoms.

Editor’s Note: *While not minimizing the serious stress and anxiety the pandemic has caused for many, this study concludes the overall impact on the general population’s mental health may have been less than some studies or the media have reported. The longer-term impact on mental health, especially for women, continues to bear watching closely. Insurers should continue to monitor product lines such as disability insurance for tangible impact.*

Hallmarks of Aging: An Expanding Universe

Lopez-Otin C, et al. Cell. 2023 Jan 19; 186(2): 243-78.

<https://doi.org/10.1016/j.cell.2022.11.001>

In this comprehensive review, the authors present, in great detail, science's current understanding of the underlying mechanisms and drivers of aging. They have identified 12 hallmarks of aging characterized by their age-associated manifestations, the acceleration of aging by experimentally accentuating them, and the opportunity to decelerate, stop, or reverse aging by therapeutic interventions. The 12 hallmarks are: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, disabled macroautophagy, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, altered intercellular communication, chronic inflammation, and dysbiosis.

Editor's Note: *The elucidation of the fundamental drivers of aging and the growing importance of "geroscience" are critical areas of research which are of great interest to insurers. This research has the potential to alter morbidity and mortality trends as well as increase healthspan and possibly lifespan.*

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.

Myocardial Infarction Claims: The Ups and Downs of Troponin Testing



Dr. Nick Boon (Retired)
Consulting Medical Officer
RGA

Troponins have been the gold standard for detection of severity of myocardial injury for more than a decade. In this webcast, Dr. Boon discusses how myocardial infarction is currently defined, how troponin testing fits into the definitions, and current best practices to adjudicate myocardial infarction critical illness claims.

<https://www.rgare.com/knowledge-center/media/videos/myocardial-infarction-claims-the-ups-and-downs-of-troponin-testing>



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